

Health systems constraints and facilitators of national immunization programs in low- and middle- income countries



DR EDINA AMPONSAH-DACOSTA

AMPEDI001

Submitted in partial fulfilment of the requirements for the degree

MASTER OF PUBLIC HEALTH

(Health Systems Specialization)

At

UNIVERSITY OF CAPE TOWN

March 2019

Supervised By:

A/Prof Jill Olivier

Dr Benjamin Kagina

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

Plagiarism Declaration

I, Dr Edina Amponsah-Dacosta, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 15 March 2019

Abstract

Like most health interventions, National Immunization Programs (NIPs) are embedded within health systems. This means that NIPs and health systems exist in a constant interaction. Vaccine preventable diseases are widely recognized as the chief cause of morbidity, disability and mortality worldwide and NIPs are understood to be one of the most cost-effective interventions against this burden. In low- and middle- income countries (LMICs), where the burden of disease is high, NIPs have been reported to perform at suboptimal levels. It has been suggested that this suboptimal performance of NIPs can be associated with the poor state of health systems in LMIC. Despite this, the interaction between NIPs and health systems is poorly understood. In addition to this, systematic evidence on how health systems constraints and facilitators impact on the performance of NIPs in LMICs is scarce. To address this evidence gap, a systematic review study was conducted, that involved an initial scoping review of the evidence-base on NIPs and health systems in LMICs from which a logic model was developed. This logic model was then applied as a guide for a qualitative systematic review aimed at assessing the health systems constraints and facilitators of NIP performance in sub-Saharan Africa. The findings of this review suggest that well-performing NIPs are those that operate within enabling health systems, characterized by the availability of strong political endorsement for vaccines, clear governance structures and effective collaboration with global partners. Despite this, significant health systems constraints persist and include the limited capacity of health workers in sub-Saharan Africa, weak country infrastructure, poor service delivery, inadequate vaccine communication and ineffective community engagement in immunization programs. This systematic review study contributes to our limited understanding of the interaction between NIPs and health systems. In addition, the findings show how system-wide constraints and facilitators impact on the performance of NIPs. These findings have relevance for ongoing health systems strengthening initiatives, especially where NIPs are concerned.

Acknowledgements

I would like to extend my profound gratitude to my supervisor and co-supervisor, A/Prof Jill Olivier and Dr Benjamin Kagina, who dedicated their invaluable time and expertise in ensuring the successful completion of this work. I am most grateful for your expert input, mentorship and patient supervision throughout this process.

My appreciation also goes to staff and colleagues at the Vaccines for Africa Initiative (VACFA) for their immense support and for allowing me to take the time to complete this thesis.

Finally, I would not have made it this far without my strong support system. I am very grateful to friends and family who tirelessly spurred me on. The journey towards attaining my Master of Public Health degree has been many years in the making and this has required much support and sacrifice from the people I love dearly. To my parents, Dr Francis Amponsah-Dacosta and Mrs Cynthia Amponsah-Dacosta, thank you for believing in my dreams, however outlandish they may seem at times. To my brothers Maxwell and David Amponsah-Dacosta who are convinced I *walk on water* and have tricked me into thinking it too, I am greatly indebted to you!

Acronyms

AIDS	Acquired Immune Deficiency Syndrome
EPI	Expanded Program on Immunization
GAVI	Global Alliance for Vaccines and Immunizations
GVAP	Global Vaccine Action Plan
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
LMICs	Low- and Middle- Income Countries
MPH	Master of Public Health
NIP	National Immunization Program
NITAG	National Immunization Technical Advisory Group
PAHO	Pan American Health Organization's
SAGE	Strategic Advisory Group of Experts
WHO	World Health Organization

Glossary

Global Development Partners	External or third-party agencies who support developing countries to achieve global targets by contributing technical, financial and human resources
Expanded Program on Immunization	A global health program developed by the WHO with the intent of making essential vaccines available to all children
Health Systems	A collective of organizations, people and actions, whose primary intent is to promote, restore or maintain health
Health Systems Constraints	Barriers to effective health systems functioning which negatively affect the availability, acceptability, affordability and quality of health services
Health Systems Facilitators	Determinants that positively impact the performance of health systems and improve the availability, acceptability, affordability and quality of health services
Health Program	A health intervention or strategy intended to promote the health of populations, and reduce the incidence of morbidity, disability and mortality
Immunization	Administration of a biological preparation, either a vaccine or immunoglobulin, to confer immune protection against disease
Mass Immunization Campaign	Administration of vaccines to large populations in one or more locations over short periods of time
National Immunization Program	A national health program designed for the timely delivery of vaccines to all age groups as deemed appropriate for a given country
Systematic review	Use of systematic methods to identify, collect, critically appraise and synthesize secondary data to provide new and meaningful explanations
Thematic analysis	A descriptive approach to analysing a qualitative data set
Vaccine	A biological preparation designed to confer immune protection by mimicking natural infection without causing disease

Source; Author, (drawing on and adapting commonly held definitions)

Table of Contents

Plagiarism Declaration	i
Abstract	ii
Acknowledgements	iii
Acronyms	iv
Glossary	v
Part A: Review Protocol	1
Introduction	1
Problem statement and purpose	2
Review question	2
Review objectives	2
Methods	3
<i>Review approach</i>	3
<i>Phase 1: Scoping review</i>	4
<i>Phase 2: Systematic review</i>	5
<i>Phase 3: Policy considerations</i>	9
Ethical considerations	10
Timeline	10
Estimated budget for the review	10
References	11
Part B: Scoping Review	1
Background	1
Methods	2
National Immunization Programs in LMICs	3
<i>The public health impact of NIPs in LMICs</i>	4
<i>The vaccine policy landscape in LMICs</i>	6
<i>Governance, organization, and management of NIPs in LMICs</i>	7
<i>The human resource capacity of NIPs in LMICs</i>	8
<i>The impact of new vaccine introduction on cold chain and logistics management</i>	9
<i>Vaccine service delivery in LMICs</i>	9
<i>The state of vaccine communication and community partnerships in LMICs</i>	10
<i>Immunization data generation and use in LMICs</i>	11
<i>Financing NIPs in LMICs</i>	12
Health systems in LMICs	13
<i>The interface between NIPs and health systems in LMICs</i>	16

Conclusion	20
References.....	20
Part C: Systematic Review	1
Abstract	1
Keywords.....	1
Key messages	2
Introduction	2
Methods	5
Results	7
<i>Characteristics of studies included in this review</i>	<i>7</i>
<i>Health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa</i>	<i>12</i>
Discussion.....	21
Conclusion	25
References.....	26
Appendix 1: Human Papillomavirus Vaccine Introduction Worldwide	1
Appendix 2: Literature Search Strategy	8
Appendix 3: Critical Appraisal Skills Programme (CASP) Appraisal Tool	9
Appendix 4: Data Extraction Table.....	14
Appendix 5: Health Policy and Planning Journal Guidelines.....	28

Tables and Figures

Part A

Table 1: Template of data extract sheet.....	7
Table 2: Timeline of research activities.....	10
Table 3: Estimated research budget.....	10
Figure 1: Schematic representation of the phased approach to the systematic review study.....	4

Part B

Table 1: Examples of key terms used in the search strategy.....	2
Table 2: The expanded program on immunization over the past four decades.....	4
Figure 1: The critical components of national immunization programs.....	6
Figure 2: The WHO health systems framework.....	14
Figure 3: A logic model for in-depth assessment of the interface between NIPs and health systems.....	19

Part C

Table 1: Characteristics of studies included in the systematic review.....	9
--	---

Table 2: Summary of health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa.....	13
Figure 1: Global progress in the implementation of nationwide HPV immunization programs.....	4
Figure 2: Flowchart of the literature search and selection process for the systematic review.....	8
Figure 3: Summary of health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa.....	19

Part A: Review Protocol

Health systems constraints and facilitators of national immunization programs in low- and middle- income countries

“The ultimate goal is to manage quality. But you cannot manage it until you have a way to measure it, and you cannot measure it until you can monitor it”- Florence Nightingale¹

Introduction

Immunization is one of the most cost-effective interventions for reducing the burden of morbidity, disability and mortality worldwide (Rémy et al. 2015; Greenwood 2014; WHO et al. 2009; Andre et al. 2008). In support of the value of immunization, Plotkin et al. (2013) declare that, “the impact of vaccination on the health of the world's people is hard to exaggerate. With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction and population growth.”² For these reasons, national immunization programs (NIPs), which serve as platforms for the delivery of routine immunization services, are widely recognised as one of the most significant investments in countries’ health systems (Rémy et al. 2015; Shen et al. 2014).

Over the past four decades, global efforts have been focused on realizing universal access to essential vaccines (WHO 2015; Chan 2014; WHO 2013; WHO et al. 2009). These efforts to expand the reach of vaccines have been intensified in low- and middle- income countries (LMICs), particularly within the sub-Saharan African region, where the burden of vaccine preventable diseases and need for intervention are the greatest (WHO 2018; SAGE 2016; WHO 2013).

Global immunization coverage rates have been consistently reported to be lower in LMICs compared to most high-income countries (WHO 2018; SAGE 2016; WHO et al. 2009). One of the determinants of this disparity has been the state of the health system in LMICs. Compared to high-income countries, health systems in some LMICs have been characterized by fragile health infrastructure and poor service delivery (Mills 2014; Shen et al. 2014; Kruk and Freedman 2008). Given the importance of health systems functioning to the success and sustainability of NIPs, it follows that critical steps need to be taken to ensure optimal health systems performance in LMICs (Shen et al. 2014; Balabanova et al. 2010). Such health systems strengthening initiatives could be supported by systematic evidence on the state of health systems and NIPs in LMICs.

¹ Quoted in: Kilshaw ME. 1992. Implementing an effective quality assurance program. In: Gelman D (ed). *Medical Administration in Canadian Hospitals*. Ottawa: Canadian Medical Association, Chapter FI.

² Originally quoted in Plotkin SA, Mortimer EA. 1988. *Vaccines*. Philadelphia: Saunders.

Problem statement and purpose

The past decade (between 2008–2018) can be considered a watershed period for NIPs worldwide. This period has seen the introduction of new vaccines and improved vaccine technologies intended to reinforce global efforts towards countering the devastating effects of emerging and re-emerging vaccine preventable diseases (WHO 2015). Within this same period, the World Health Assembly implemented the Global Vaccine Action Plan (GVAP) which was endorsed by 194 member states to initiate the ‘Decade of Vaccines’. One of the visions of the GVAP is to advance the cause of universal access to lifesaving vaccines between 2011 and 2020 (WHO 2015; WHO 2013). These intensified efforts have also been accompanied by health systems strengthening initiatives in LMICs (Adam et al. 2012; Balabanova et al. 2010; Galichet et al. 2010). This is because it has increasingly become apparent that the success of NIPs in LMICs is dependent on the performance of the health systems which deliver them (SAGE 2016; Shen et al. 2014; Samb et al. 2009).

There is much in the published literature about the public health impact of NIPs in LMICs (Feikin et al. 2016; Greenwood 2014; Samb et al. 2009; Andre et al. 2008). In comparison, there is insufficient systematic evidence about the interaction of NIPs with the broader health systems within which they are embedded (Hyde et al. 2012; Bosch-Capblanch et al. 2011). As a result, there is insufficient evidence to assess the capacity of health systems to sustain this critical public health intervention in some LMICs. For this reason, a systematic review study is proposed for the identification, synthesis and analysis of the existing evidence-base on the interaction between NIPs and health systems in LMICs. This much needed systematic evidence could foster proactive approaches to maximizing and strengthening the interaction between the programmatic (or NIPs) and the systematic (the broader health system) in yielding the greatest possible public health outcomes within LMICs.

Review question

The proposed systematic review study seeks to address the following research question; *How do health systems constraints and facilitators impact on the performance of national immunization programs in sub-Saharan Africa?*

Review objectives

1. To describe the scope of published literature available on NIPs and health systems in LMICs.
2. To systematically review the existing evidence-base on how health systems constraints and facilitators impact on the performance of NIPs in sub-Saharan Africa.
3. To describe the potential research, policy and practice implications of this systematic review.

Methods

Review approach

A descriptive study design will be adopted, using a qualitative systematic review approach. Qualitative systematic reviews synthesize research evidence from the best available empirical qualitative studies in developing evidence-based recommendations on a topic of interest (Butler et al. 2016). Compared to quantitative systematic reviews, qualitative approaches are a less commonly used method of enquiry in public health research, but are rapidly becoming critical components of the research toolkit (Butler et al. 2016; Evans and Pearson 2001). This is because qualitative systematic reviews are invaluable to the comprehensive assessment of complex real-world phenomena rooted in experiences and perceptions which cannot be measured through standard quantitative approaches. For this reason, qualitative systematic reviews are useful for generating rich sources of high-quality evidence necessary to inform policy and practice (Butler et al. 2016; Seers 2015; Evans and Pearson 2001).

While there are various formats available for conducting qualitative systematic reviews, the Campbell systematic review is the best fit for addressing the proposed review question on account of the research focus and the intended outcomes of the review (Campbell Corporation 2017; Campbell et al. 2003; Britten et al. 2002; Hawker et al. 2002; Dixon-Woods and Fitzpatrick 2001). Campbell systematic reviews are typically concerned with factors affecting the successful implementation of interventions as well as the effects of interventions, with the intent of informing research, policy and practice (Campbell Corporation 2017).

The review process will span across three phases as shown in Figure 1. Phase 1 will comprise of an initial scoping review which will critically appraise the existing evidence-base to provide an in-depth understanding of what is already known about NIPs and health systems in LMICs. Themes emanating from Phase 1 will then be applied in a systematic review of how health systems constraints and facilitators impact on the performance of NIPs in Phase 2. Based on the outcomes of Phase 1 and 2, it will then be possible to make relevant research, policy and practice considerations for NIPs and health systems in LMICs (Phase 3).

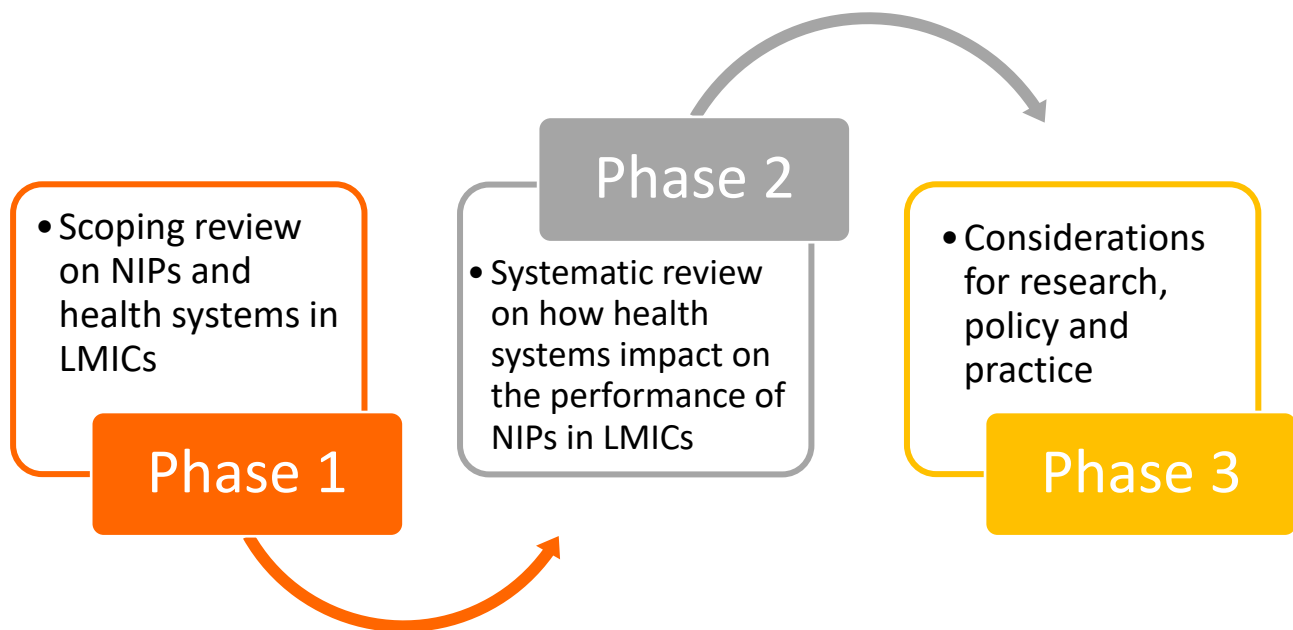


Figure 1: Schematic representation of the phased approach to the systematic review study

Phase 1: Scoping review

According to Grant and Booth (2009), a scoping review “provides a preliminary assessment of the potential size and scope of available research literature”. This initial review process is useful for accommodating the large bodies of literature available on broad fields of interest like NIPs and health systems (Peterson et al. 2017; Davis et al. 2009). In this way, a scoping review can be used to identify gaps for future research (Peterson et al. 2017; Davis et al. 2009; Grant and Booth 2009). This method of review often involves a process of mapping the existing evidence-base to understand what is already known about the broad review question. By contextualizing the knowledge-base it will then be possible to frame a well-defined review question for the systematic review to be conducted in Phase 2 (Peterson et al. 2017; Davis et al. 2009).

An electronic literature search for relevant peer-reviewed and grey literature on NIPs and health systems in LMICs will be conducted. Search terms and search term synonyms for both NIPs and health systems will be used to retrieve literature sources. For NIPs, terms to be used in the search strategy will include, immuni*³; vaccination; vaccine, ‘vaccine technology’; ‘vaccination program’; ‘expanded program on immunization’; and ‘vaccine preventable diseases’. Those for health systems will include ‘global health’; ‘health service’; ‘health information’; ‘health financing’; ‘health workforce’; governance; and ‘health systems performance’. The geographic focus for the search strategy will be restricted to LMICs as defined by the World Bank

³ The * denotes truncation and prompts the search engine to retrieve all possible variants of the word including immunization and immunisation.

(<http://data.worldbank.org/about/country-and-lending-groups>). The expected outcome of the scoping review is a descriptive, narrative summary of the evidence-base on NIPs and health systems in LMICs.

Phase 2: Systematic review

For the systematic review, an electronic search for peer-reviewed and grey literature documenting relevant research on health systems constraints and facilitators in sub-Saharan Africa⁴ will be performed. The systematic review will further explore how these health systems constraints and facilitators impact on the performance of NIPs, using human papillomavirus (HPV) immunization programs in sub-Saharan Africa as a proxy.⁵ The HPV immunization programs present a unique challenge to health systems in sub-Saharan Africa with coverage rates in the region reported to be among the lowest (1.2%) in the world (Bruni et al. 2016). It will be worth exploring how health systems constraints and facilitators impact on the introduction and performance of HPV immunization programs in sub-Saharan Africa. For this purpose, literature sources will be sought through electronic databases such as PubMed (core clinical journals, MEDLINE, and nursing journals), Web of Science (MEDLINE, Web of Science core collection, biological abstracts, SciELO citation index), Scopus (includes EMBASE-indexed journals), and EBSCOhost (academic search premier, Africa-wide information, eBook collections, health sources – consumer edition, nursing and academic edition, MEDLINE).

To conduct the literature search through these databases, multiple search terms will be generated from the review question. Combinations of these search terms and search term synonyms will be created using Boolean operators like 'AND' and 'OR', and then inputted into the search engines of the various databases as appropriate.

Inclusion criteria

The search strategy will include;

1. Peer-reviewed primary research articles, reviews, electronic books and book chapters, editorials, comments and – among other relevant sources of grey literature – dissertations or theses, conference proceedings, and reports.
2. Literature sources published between 2008 and 2018. This will ensure that the most recent evidence is systematically reviewed to generate relevant recommendations.

⁴ Sub-Saharan Africa was selected as a geographical focus for the systematic review after Phase 1 (scoping review) was completed. During the scoping review, it was identified that health systems constraints on NIP performance appear to be more prevalent within sub-Saharan Africa compared to other low- and middle- income regions of the world. The review protocol was therefore adapted to reflect this in Phase 2.

⁵ An adaptation was made to this protocol after Phase 1 was complete, during which the HPV immunization focus for Phase 2 was decided.

Exclusion criteria

The exclusion criteria for the search strategy is as follows:

1. Literature sources published in languages other than English will be excluded.
2. Published literature without abstracts or summaries will be excluded as these will be required during the initial screening process. Where abstracts or summaries are available but full texts are not accessible for review, these will also be excluded.
3. The search strategy will exclude all literature sources concerned with veterinary immunization programs unless they are directly impacting on human health and the health system (for example, human rabies vaccination).
4. Finally, research conducted in LMICs outside of the WHO sub-Saharan African region, or in high-income countries (as defined by the World Bank) will be excluded.

All full text literature sources will be imported into Rayyan, a web-based application for systematic reviews (Ouzzani et al. 2016). Based on the eligibility criteria, full texts will be screened in Rayyan. The full texts selected for inclusion will then be critical appraised.

Critical appraisal

Full texts selected for inclusion in the systematic review will be critically appraised for quality by assessing the appropriateness of the research questions or objectives, the methods used, and the findings reported. Concepts of ethics, rigour and reflexivity will also be carefully considered. This appraisal process will be conducted with the assistance of published appraisal tools⁶ developed by the Critical Appraisal Skills Programme (<http://www.casp-uk.net/>) for health research. These appraisal tools have been used in previous qualitative systematic reviews (Chan 2013; Kane et al. 2007; Walter et al. 2004).

A summary of the quality assessment will be captured onto a database and made available to two independent reviewers (MPH supervisors). The independent reviewers will conduct further appraisals of the literature sources using the quality assessment summary. Quality assessments made by the primary reviewer and the two independent reviewers will then be triangulated and a final decision made about the eligibility of full texts for inclusion in the review process.

⁶ This includes a set of eight critical appraisal tools designed for the assessment of the quality of cohort studies, case control studies, diagnostic studies, clinical prediction rule, randomised controlled trials, systematic reviews, qualitative studies, and economic evaluations.

Data extraction

Data will be extracted from eligible full texts, identifying health systems constraints and facilitators, and noting their relevance to the performance of NIPs in sub-Saharan Africa. A data extraction form will be used to keep a systematic record of summaries of the data extracted from each literature source. By generating a historical trail, it will be possible to ensure traceability and validity of the data extraction process, as well as reduce the risk of human errors during the review process (Tranfield et al. 2003). To ensure reliability of the data extracted, the extraction process will be conducted by the primary reviewer and supervised at all stages by the two independent reviewers (MPH supervisors). Summaries of the data extracted will also be comprehensively audited by all three reviewers and final decisions reconciled. This will be an opportunity to resolve any potential discrepancies that may emerge from the data set prior to the analysis stage. Table 1 shows a template of the data extraction sheet to be used.

Table 1: Template of data extraction sheet

Study Details				Context		Data Extraction			
No.	Author, Year	Title	Country	Underlying Context	Availability / Type of HPV Immunization Program	Main Theme	Health Systems Constraint	Health Systems Facilitator	Comments

Source; Author

Data analysis

The final audited data summaries will serve as the basis on which the data synthesis and analysis will be performed. Typically, thematic analysis is the go-to approach in qualitative systematic review studies (Thomas and Harden 2008). This is because the thematic analysis approach is highly flexible and can be used across a wide range of epistemologies and research questions to produce rich, detailed, yet complex, nuanced accounts from a qualitative data set (Vaismoradi et al. 2013; Thomas and Harden 2008; Braun and Clarke 2006). A rigorous thematic analysis will be a suitable approach for searching and identifying prominent threads and themes on the interaction between NIPs and health systems in sub-Sharan Africa. Thomas and Harden (2008) propose three broad stages for thematic synthesis and analysis of qualitative research for systematic

reviews, and these will be adopted and performed iteratively. In the first stage, the primary reviewer will fully engage with the extracted data in generating initial codes from the text, using inductive and deductive approaches. These coded extracts will then be subjected to descriptive treatment to develop themes and potential sub-themes which capture the main conceptions about the review focus. It is with these thematic extracts that analytic themes will be generated in the final stage to provide meaningful and integrated accounts and new explanations of the data set (Nowell et al. 2017; Vaismoradi et al. 2013; Thomas and Harden 2008; Braun and Clarke 2006). Additionally, themes emanating from the scoping review will be used to enhance the data analysis process. Finally, given that health systems are highly context specific, careful consideration will be given to the prevailing contexts (geographic, political, sociocultural, socioeconomic and disease epidemiology) within sub-Saharan Africa (WHO 2007).

Rigor

To minimize the risk of information bias and enhance the transparency, trustworthiness and reproducibility of the proposed systematic review, this review protocol has been developed to explicitly detail the study design and methods to be used (Drucker et al. 2016). Since Campbell systematic reviews encourage the use of a diverse source of literature, including both published and grey literature, the risk of selection and publication bias will be minimized. In addition to this, published appraisal tools (<http://www.casp-uk.net/>) will be used to assess the risk of selection bias and to evaluate the efforts taken to minimize bias in the research studies selected for review. Finally, approaches suggested by Nowell et al. (2017) on how to ensure trustworthiness during the thematic analysis process will be adhered to. This will include regular reviewer triangulation and peer debriefing, keeping an audit trail throughout the review process, and providing thick descriptions of context when analysing and interpreting the data set (Nowell et al. 2017).

Risks and benefits

As a systematic review, this is a no risk study. However, the findings of the proposed systematic review could potentially expose poorly performing health systems within sub-Saharan Africa. Given that any data presented will be directly extracted from literature sources already available in the public domain, there will be minimal to no risk to these health systems as a consequence of conducting the review. Instead it is anticipated that findings from the review could enrich policy debates and guide key decision-makers to ensure the optimal performance of their health systems. Essentially, a systematic review of this kind may provide a set of 'lessons learned' with regards to how critical public health interventions like NIPs could be capitalized on, in scaling-up national health systems strengthening efforts within LMICs.

Study limitations

The geographical focus of the proposed systematic review is restricted to the sub-Saharan African region. This is a limitation because the outcomes of the review cannot be generalized to countries outside of this classification. However, our interest in this geographical region stems from the fact that sub-Saharan Africa continues to underperform in comparison to other regions of the world, where global immunization targets are concerned (Mihigo et al. 2017; SAGE 2016). In addition to this, there is insufficient systematic evidence on the subject matter from the sub-Saharan Africa region. The proposed systematic review is therefore intended to contribute to bridging the evidence gap in sub-Saharan Africa. Excluding studies published in languages other than English could be a missed opportunity as they may contain empirical evidence on the interaction between NIPs and health systems that are relevant to this systematic review. Given the time and resource constraints for this MPH thesis, it will not be possible to retrieve and translate literature sources which have been published in languages other than English. Finally, the use of one immunization program (the HPV immunization program) as a single tracer-indicator may not give a comprehensive assessment of the performance of NIPs and health systems in all sub-Saharan African countries. In reality, a plurality of NIP activities, as well as other health and non-health programs interact within a health system (Samb et al. 2009). Ultimately, any analytically generalizable claims drawn from the findings of the proposed systematic review will have to be carefully considered in the context of these caveats.

Phase 3: Policy considerations

Based on the findings of this systematic review study, policy-relevant recommendations will be made for NIPs and health systems in sub-Saharan Africa. It is also anticipated that the findings of the review will have implications for current practice and future research in the fields of NIPs and health systems in LMICs. Appropriate dissemination of the findings will be crucial to informing evidence-based reform in public health policy and practice in the real-world setting. Accordingly, this systematic review will be disseminated through publications in internationally accredited, peer-reviewed journals and presented at local, national and international congresses. The primary author works for the Vaccines for Africa Initiative which hosts annual African vaccinology courses. These courses are targeted at key stakeholders working within the field of vaccinology throughout the African continent. The Annual African Vaccinology course will therefore serve as an effective platform for the dissemination of the findings of the review. Electronic and hard copies of the thesis emanating from this systematic review will also be made available for public access through the library services at the University of Cape Town. The systematic review is also targeted at key policy makers in both health and non-health sectors. For this reason, the findings of the systematic review will also be repackaged into policy briefs and presented at relevant workshops that are accessible to these stakeholders.

Ethical considerations

No human subjects will be directly involved in this study. All literature sources that will be used during the systematic review are readily available in the public domain. For these reasons, formal ethical clearance to conduct this study is not required. All works of other investigators that will be used in the systematic review will be duly acknowledged as appropriate.

Timeline

It is expected that this systematic review study will be conducted over the course of an 11-month period, from the initial development of the review protocol to the final thesis submission for examination purposes. The various research activities to be performed are as depicted in the proposed timeline provided in Table 2.

Table 2: Timeline of research activities

Activity	Proposed Timeline										
	March 2018	Apr 2018	May 2018	Jun 2018	Jul 2018	Aug 2018	Sep 2018	Oct 2018	Nov 2018	Dec 2018	Jan 2019
Review protocol development											
Scoping review											
Data collection											
Data extraction and analysis											
Write-up of manuscript											
Finalization of thesis											

Source; Author

Estimated budget for the review

All research activities for this systematic review study will be self-funded and undertaken in the primary author's country of residence in partial fulfilment of the requirements for an MPH degree. As this is a systematic review study, there are no direct costs arising as a result of conducting the research. The primary author declares to have no conflict of interest. Table 3 provides an estimation of the minimum expected costs.

Table 3: Estimated research budget

Item Description	Units	Unit Cost (ZAR)	Total Cost (ZAR)
Pens	5	4.00	20.00
Pencils	5	3.00	15.00
Note pads	5	10.00	50.00
Printing (two copies of review protocol and the final thesis)	350	3.50	1225.00
Incidentals		1000.00	1000.00
Total		1020.50	2310.00

Source; Author

References

- Adam T, Hsu J, de Savigny D et al. 2012. Evaluating health systems strengthening interventions in low-income and middle-income countries: Are we asking the right questions? *Health Policy and Planning* **27**:i19.
- Andre FE, Booy R, Bock HL et al. 2008. Vaccination greatly reduces disease, disability, death and inequity worldwide. *Bulletin of the World Health Organization* **86**:140-146.
- Balabanova D, McKee M, Mills A et al. 2010. What can global health institutions do to help strengthen health systems in low income countries? *Health Research Policy and Systems* **8**:22.
- Bosch-Capblanch X, Kelly M, Garner P. 2011. Do existing research summaries on health systems match immunisation managers' needs in middle- and low-income countries? Analysis of GAVI health systems strengthening support. *BMC Public Health* **11**:449.
- Braun V, Clarke V. 2006. Using thematic analysis in psychology. *Qualitative Research in Psychology* **3**:77-101.
- Britten N, Campbell R, Pope C et al. 2002. Using meta ethnography to synthesise qualitative research: A worked example. *Journal of Health Services Research and Policy* **7**:209-215.
- Bruni L, Diaz M, Barrionuevo-Rosas L et al. 2016. Global estimates of human papillomavirus vaccination coverage by region and income level: A pooled analysis. *Lancet Global Health* **4**:e463.
- Butler A, Hall H, Copnell B. 2016. A guide to writing a qualitative systematic review protocol to enhance evidence-based practice in nursing and health care. *Worldviews on Evidence-Based Nursing* **13**:241-249.
- Campbell Corporation. 2017. Campbell Policies and Guidelines Series No. 1. <https://www.campbellcollaboration.org/library/campbell-collaboration-systematic-reviews-policies-and-guidelines.html>.
- Campbell R, Pound P, Pope C et al. 2003. Evaluating meta-ethnography: A synthesis of qualitative research on lay experiences of diabetes and diabetes care. *Social Science and Medicine* **56**:671-684.
- Chan M. 2014. Beyond expectations: 40 years of EPI. *Lancet, The* **383**:1697-1698.
- Chan ZCY. 2013. A systematic review of critical thinking in nursing education. *Nurse Education Today* **33**:236-240.
- Davis K, Drey N, Gould D. 2009. What are scoping studies? A review of the nursing literature. *International Journal of Nursing Studies* **46**:1386-1400.
- Dixon-Woods M, Fitzpatrick R. 2001. Qualitative research in systematic reviews. *BMJ* **323**:765-766.
- Drucker AM, Fleming P, Chan A. 2016. Research techniques made simple: Assessing risk of bias in systematic reviews. *Journal of Investigative Dermatology* **136**:e114.
- Evans D, Pearson A. 2001. Systematic reviews of qualitative research. *Clinical Effectiveness in Nursing* **5**:111-119.
- Feikin DR, Flannery B, Hamel MJ et al. 2016. Vaccines for children in low- and middle-income countries. In: Black RE, Laxminarayan R, Temmerman M, Walker N (ed). *Reproductive, Maternal, Newborn and Child Health*. 3rd edn. Washington, DC: World Bank Group, 187-204.
- Galichet B, Goeman L, Hill PS et al. 2010. Linking programmes and systems: Lessons from the GAVI health systems strengthening window. *Tropical Medicine and International Health* **15**:208-215.
- Grant MJ, Booth A. 2009. A typology of reviews: An analysis of 14 review types and associated methodologies. *Health Information and Libraries Journal* **26**:91-108.

- Greenwood B. 2014. The contribution of vaccination to global health: Past, present and future. *Philosophical Transactions of the Royal Society of London* **369**:20130433.
- Hawker S, Payne S, Kerr C et al. 2002. Appraising the evidence: Reviewing disparate data systematically. *Qualitative Health Research* **12**:1284-1299.
- Hyde TB, Dentz H, Wang SA et al. 2012. The impact of new vaccine introduction on immunization and health systems: A review of the published literature. *Vaccine* **30**:6347-6358.
- Kane GA, Wood VA, Barlow J. 2007. Parenting programmes: A systematic review and synthesis of qualitative research. *Child: Care, Health and Development* **33**:784-793.
- Kruk ME, Freedman LP. 2008. Assessing health system performance in developing countries: A review of the literature. *Health Policy* **85**:263-276.
- Mihigo R, Okeibunor J, Anya B et al. 2017. Challenges of immunization in the African region. *The Pan African Medical Journal* **27**:12.
- Mills A. 2014. Health care systems in low- and middle-income countries. *The New England Journal of Medicine* **370**:552-527.
- Nowell LS, Norris JM, White DE et al. 2017. Thematic analysis: Striving to meet the trustworthiness criteria. *International Journal of Qualitative Methods* **16**:1-13.
- Ouzzani M, Hammady H, Fedorowicz Z et al. 2016. Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews* **5**:210.
- Peterson J, Pearce PF, Ferguson LA et al. 2017. Understanding scoping reviews: Definition, purpose, and process. *Journal of the American Association of Nurse Practitioners* **29**:12-16.
- Plotkin S, Orenstein W and Offit P. 2013. Vaccines. 6th edn. Edinburgh, UK: Saunders.
- Rémy V, Zöllner Y, Heckmann U. 2015. Vaccination: The cornerstone of an efficient healthcare system. *Journal of Market Access & Health Policy* **3**:27041.
- SAGE. 2016. 2016 midterm review of the global vaccine action plan. Available at: http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2016_EN.pdf.
- Samb B, Evans T, Dybul M et al. 2009. An assessment of interactions between global health initiatives and country health systems. *Lancet, The* **373**:2137-2169.
- Seers K. 2015. Qualitative systematic reviews: Their importance for our understanding of research relevant to pain. *British Journal of Pain* **9**:36-40.
- Shen AK, Fields R, McQuestion M. 2014. The future of routine immunization in the developing world: Challenges and opportunities. *Global Health, Science and Practice* **2**:381-394.
- Thomas J, Harden A. 2008. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology* **8**:45.
- Tranfield D, Denyer D, Smart P. 2003. Towards a methodology for developing evidence-informed management knowledge by means of systematic review. *British Journal of Management* **14**:207-222.
- Vaismoradi M, Turunen H, Bondas T. 2013. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing and Health Sciences* **15**:398-405.
- Walter FM, Emery J, Braithwaite D et al. 2004. Lay understanding of familial risk of common chronic diseases: A systematic review and synthesis of qualitative research. *Annals of Family Medicine* **2**:583-594.
- WHO. 2018. World health statistics 2018: Monitoring health for the SDGs, sustainable development goals. Available at: <http://apps.who.int/iris/bitstream/handle/10665/272596/9789241565585-eng.pdf?ua=1>.
- WHO. 2015. WHO's mission and vision in immunization and vaccines 2015-2030. Available at: http://www.who.int/immunization/documents/general/WHO_Mission_Vision_Immunization_Vaccines_2015_2030.pdf?ua=1.
- WHO. 2013. Global vaccine action plan 2011-2020. *Vaccine*. Available at: <https://www.unicef.org/immunization/files/GVAP.pdf>.
- WHO, UNICEF and World Bank. 2009. State of the world's vaccines and immunization. Geneva, Switzerland: World Health Organization.
- WHO. 2007. Everybody's business - strengthening health systems to improve health outcomes: WHO's framework for action. Geneva, Switzerland: World Health Organization. Available at: <http://www.who.int/iris/handle/10665/43918>.

Part B: Scoping Review

A scoping review of national immunization programs and health systems in low- and middle-income countries

Background

The World Health Organization (WHO), together with key development partners¹, are at the forefront of global initiatives to prevent disease and improve the health of populations worldwide. One of these initiatives is to provide universal access to potent vaccines² against infectious diseases through country-level platforms known as national immunization programs (NIPs) (WHO 2015; Greenwood 2014; Andre et al. 2008). According to the WHO (2018a), NIPs can be defined as the “organizational component of Ministries of Health charged with preventing disease, disability, and death from vaccine-preventable diseases in children and adults”.

National immunization programs do not operate in isolation. They are embedded in countries’ health systems and often form part of an essential package of primary health services provided by national governments (WHO 2015). Well-performing NIPs *should* be guided by informed health policy and operate within enabling health systems (WHO 2018a). National immunization managers and policy-makers thus rely on robust evidence to make informed decisions necessary to safeguard the performance of their NIPs (WHO 2018a; Bosch-Capblanch et al. 2011; Levine et al. 2011). For this reason, expanding the pool of evidence on NIPs and health systems cannot be undervalued. This is particularly relevant for some low- and middle- income countries (LMICs) where evidence-based initiatives to improve NIP performance and strengthen health systems are limited (WHO 2015; WHO 2013a; Adam et al. 2012; WHO 2007). Additionally, the interface between NIPs and their health systems in LMICs is neither sufficiently understood, nor adequately documented in the published literature (Samb et al. 2009). Ultimately, there is insufficient evidence to assess the capacity of health systems to sustain continuously evolving NIPs in LMICs.

This scoping review maps the existing evidence-base on NIPs and health systems in LMICs. The organizational components of NIPs and their functions are presented. In addition to this, the state of health systems in LMICs is addressed. This will advance the limited understanding of how NIPs in LMICs interact with their health systems. Such evidence could contribute to health systems strengthening initiatives, at least where NIPs are

¹ These development partners include WHO’s financial and technical partners, global agencies and civil society organizations.

² Vaccine potency refers to a quantitative measure of the ability of a vaccine to achieve its intended biological effect, such as eliciting a protective immune response in the recipient.

concerned. Key themes emerging from this scoping review will also form the basis of a detailed systematic review.

Methods

This scoping review was conducted in two parts; the first to understand what is already known about NIPs in LMICs, and the second to collate existing evidence on health systems in LMICs. For this purpose, peer-reviewed and grey literature were sourced from several electronic databases; PubMed, Web of Science, Scopus (includes EMBASE-indexed journals), and EBSCOhost. Additional searches for grey literature were carried out through organizational websites like WHO (<http://www.who.int/en/>), and GAVI, the Vaccine Alliance (GAVI; <https://www.gavi.org/>). Supplementary searches for peer-reviewed and grey literature which may have been missed during the primary searches were also conducted through bibliographic searches, and internet searches in Google Scholar. Key terms used in the search strategy are presented in Table 1. There were no publication date restrictions applied to the search strategy. This was done to increase access to a wide scope of evidence. Only relevant studies conducted in LMICs and published in English were considered for review.

Table 1: Examples of key terms used in the search strategy

	Search terms
NIPs	Immuni*; vaccination; "immunization program"; "expanded program on immunization"; vaccine; "vaccine preventable disease"; "health information systems"; "health policy"; "health governance"; "human resource"; "logistics management"; "cold chain"; "service delivery"; "health communication"; "health financing"
Health systems	"Health system"; "global health"; "health service delivery"; "health information systems"; "health financing"; governance; "health workforce"; "medical technology"; vaccine; "vertical health programs"; "health systems strengthening"; "health systems performance"
LMICs	
Economy terms	"deprived countries"; "developing countries"; "less developed country"; "low gross national; low income countries"; "middle income country"; "middle income economies"; "poor economy"; "third world"; "transitional country"; "under developed economies"
Country terms	LMICs listed as per World Bank classification (http://data.worldbank.org/about/country-and-lending-groups)
Region terms	"East Asia and Pacific"; "Europe and Central Asia"; "Latin America and the Caribbean"; "Middle East and North Africa"; "South Asia"; "Sub-Saharan Africa"

Source; Author

Note: The * denotes truncation and prompts the search engine to retrieve all possible variants of the word; immunize, immunise, immunization, and immunisation.

Database-specific LMICs search terms have been compiled and are accessible from the Health Sciences Faculty Library website (<http://www.medical.lib.uct.ac.za/>), University of Cape Town.

National Immunization Programs in LMICs

The WHO (2018b) defines immunization³ as “the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine.” Vaccines can be defined as biological preparations designed to mimic natural infection without causing disease (Backx and Freedman 2013; Clem 2011). Thus, when administered, vaccines prime the immune system to recognise a specific disease-causing organism and destroy it before it can cause disease (WHO 2018b). This actively induced form of immunity is often long-lasting (Backx and Freedman 2013; Clem 2011).

The usefulness of immunization in preventing potentially life-threatening diseases in individuals and interrupting transmission within populations was recognized very early on as a tool to control and eradicate diseases worldwide (Backx and Freedman 2013). It is on this basis that WHO established the Expanded Program on Immunization (EPI) in 1974 as a platform for the delivery of routine childhood immunization (Chan 2014; WHO 2013b; Okwo-Bele and Cherian 2012). A timeline summarizing key moments in the history of the EPI is provided in Table 2.

Since the 1980s, WHO member states have progressively adopted the EPI into country-specific NIPs. These NIPs serve as a platform for the timely delivery of vaccines considered important for a given country (WHO 2013b). Key services provided through NIPs include: routine universal childhood immunization, supplementary immunization activities including mass immunization campaigns, school-based and adolescent vaccination programs, introduction of new, improved or underused vaccines into existing NIPs, emergency vaccination responses to pandemic threats or disease outbreaks, and immunization services for at-risk populations such as health care workers, veterinarians, international travellers, pregnant women and the elderly (Walldorf et al. 2017; Feikin et al. 2016; WHO et al. 2009).

³ Immunization may be active; involving the administration of a vaccine to confer long term immune protection, or passive; involving the transfer of immunity from an immune to a non-immune host to confer short term immune protection. The term used throughout this thesis refers to active immunization.

Table 2: The expanded program on immunization over the past four decades

Year	Event
Pre-1974	<ul style="list-style-type: none"> ▫ Edward Jenner reports on a process of vaccination that would protect against small pox in 1798 ▫ Development and licensure of vaccines against various diseases including small pox begins in earnest in the late 1800s ▫ WHO launches a global small pox eradication program in 1967
1974	<ul style="list-style-type: none"> ▫ Poor immunization coverage rates recorded; estimated at < 5% in LMICs ▫ Building on the small pox eradication program infrastructure, WHO launches the EPI with the objective of ensuring that children throughout the world have access to much needed vaccines ▫ Four vaccines are included in the EPI to protect against six childhood deadly diseases; diphtheria, tetanus, tuberculosis, measles, polio, and whooping cough ▫ Health systems in LMICs at this time are relatively weak or non-functional
1975 – 1980	<ul style="list-style-type: none"> ▫ Last case of small pox recorded in Merca District, Somalia in 1977 ▫ A goal is set to make immunization against the six childhood deadly diseases available to every child in the world by 1990 ▫ EPI is progressively adopted by all WHO member states
1981 – 1986	<ul style="list-style-type: none"> ▫ WHO establishes a standardized immunization schedule in 1984, to be adopted by member states for their NIPs
1987 – 1992	<ul style="list-style-type: none"> ▫ In 1987, ≥700 000 measles-related deaths averted in LMICs by immunization ▫ World Health Assembly (comprising all Ministers of Health of all member states) passes a resolution in 1988 to eradicate polio by 2000 ▫ Goal of universal access to immunization is not achieved by 1990 ▫ Move by most LMICs to institutionalize country-specific immunization programs (or NIPs) based on the EPI blueprint ▫ In 1991, an amended global target of vaccinating 80% of the world’s children is achieved
1999 – 2004	<ul style="list-style-type: none"> ▫ WHO establishes the Strategic Advisory Group of Experts (SAGE) on Immunization in 1999 tasked with providing WHO with guidance on global policies and strategies ▫ In 2000, GAVI is established to support EPI in some LMICs with the intent of extending the reach of childhood immunization. GAVI’s financial support of key immunization services in LMICs is a game-changer in the history of EPI ▫ Goal to eradicate polio by 2000 is not achieved. Wild type polio infections remain prevalent in some LMICs
2005 – 2010	<ul style="list-style-type: none"> ▫ In 2005, WHO recommends inclusion of vaccines against Haemophilus influenzae type b, and hepatitis B into EPI schedules worldwide
2011 – 2014	<ul style="list-style-type: none"> ▫ Global immunization coverage in <1-year-olds estimated at 85% by 2011 ▫ The Global Vaccine Action Plan (GVAP) is implemented in 2011 with a vision to ensure that all children in the world have access to life saving vaccines by 2020 ▫ By 2014, cases of wild type polio infections are reduced globally by 99%, and 80% of the world is certified polio-free ▫ WHO recommends all NIPs include vaccines against human papillomavirus (HPV), rotavirus, rubella, and <i>Streptococcus pneumoniae</i>
2018	<ul style="list-style-type: none"> ▫ WHO recommends use of new typhoid conjugate vaccine targeted at children ≥6 months of age, making early prevention of typhoid possible

Source; Author (Chan 2014; WHO 2013b; Okwo-Bele and Cherian 2012; Keja et al. 1988)

The public health impact of NIPs in LMICs

Vaccine preventable diseases are widely recognized as the chief cause of childhood morbidity, disability and mortality worldwide (Brenzel 2015; WHO 2013b; Andre et al. 2008). The highest burden of vaccine preventable diseases has historically been recorded in LMICs (WHO 2018b; Dbaibo et al. 2016; Brenzel 2015; Gentile et al. 2010; Miller and Sentz 2006). However, since the advent of universal childhood immunization in 1974, WHO

estimates that globally, 2 – 3 million deaths related to vaccine preventable diseases are averted each year. This positive impact can be largely attributed to the success of NIPs in reducing the high burden of vaccine preventable diseases, particularly in LMICs (Feikin et al. 2016; Chan 2014; WHO 2013b; Okwo-Bele and Cherian 2012). Some of the greatest public health gains recorded in the literature include the near-eradication of wild type polio, the marked progress towards elimination of measles, and a significant decline in under-five mortality due to measles, tetanus, diphtheria, pertussis and rotavirus-related diarrhoea (WHO 2018c; Sindhu et al. 2017; Feikin et al. 2016; Dbaibo et al. 2016; SAGE 2016; Toole 2016).

Despite the significant progress made, LMICs still have some way to go in controlling the existing burden of vaccine preventable diseases (Dbaibo et al. 2016; Toole 2016; SAGE 2016). In the 2016 midterm review of the progress made towards universal access to immunization, the Strategic Advisory Group of Experts on Immunization (SAGE) highlighted countries like South Sudan, Syria and Yemen, as those struggling to meet immunization targets. In these countries, the challenges faced are primarily a result of ongoing political conflict (SAGE 2016). The SAGE report also identified other challenges in countries without ongoing political conflict. For examples, in some LMICs with stable and predictable political environments, failure to provide reliable universal immunization services was associated with weak health systems, suboptimal governance structures, and failure to effectively integrate NIPs into routine primary health care (SAGE 2016).

The successes and challenges of routine immunization in LMICs can be considered as a function of all the organizational and programmatic elements of NIPs (Shen et al. 2014). Shen et al. (2014) identify eight core elements of NIPs, namely; (1) policy, standards, and guidelines; (2) governance, organization, and management; (3) human resources; (4) vaccine, cold chain, and logistics management; (5) service delivery; (6) communication and community partnerships; (7) data generation and use; and (8) sustainable financing (Figure 1). For a well-performing NIP, these eight elements function within an enabling health system. Each of these elements are closely related and any weak link could potentially jeopardize the success of NIPs (Shen et al. 2014).

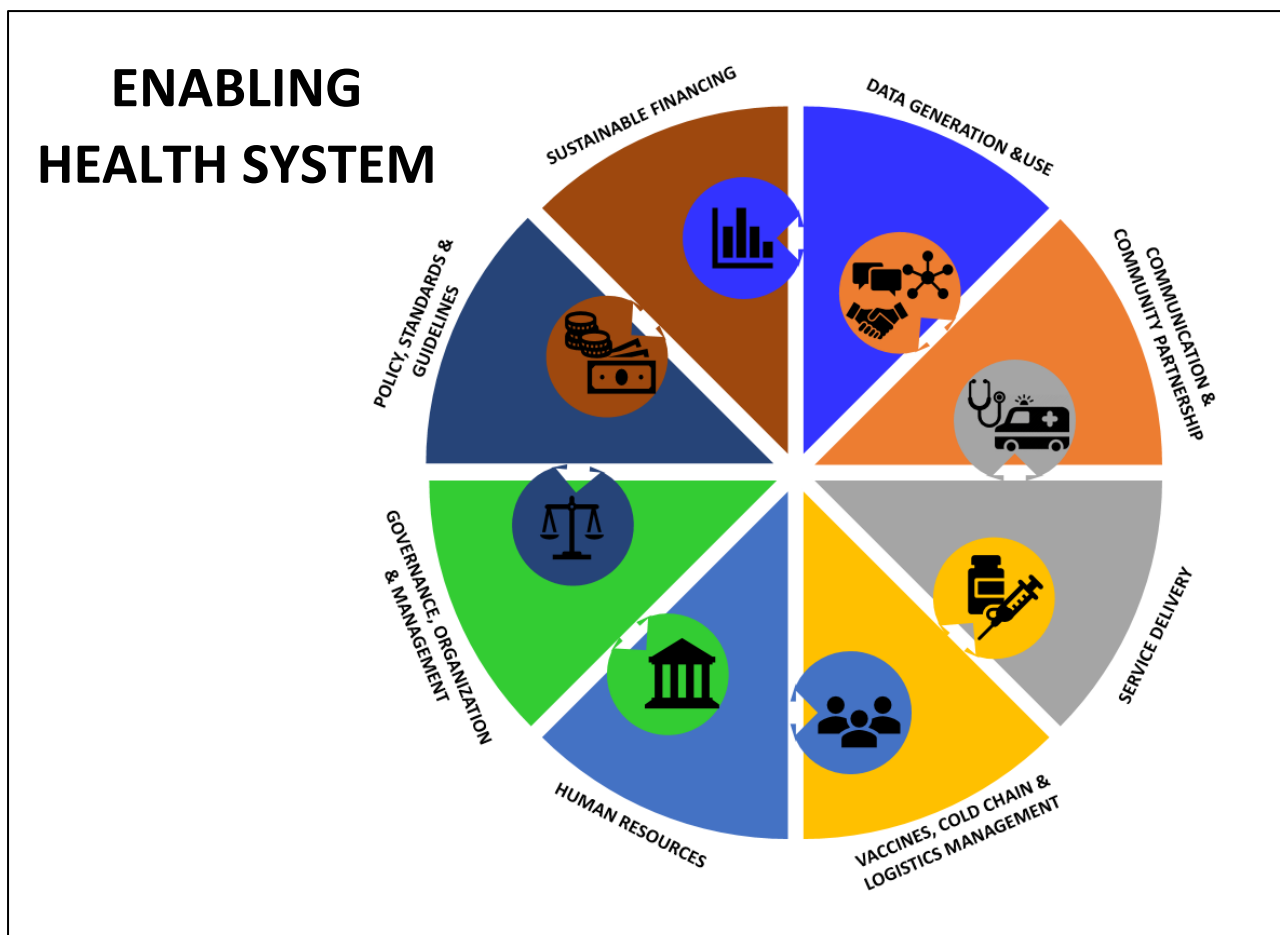


Figure 1: The critical components of national immunization programs [Source; Author, (drawing on Shen et al. 2014)]

The vaccine policy landscape in LMICs

Where NIPs are concerned, the policy landscape often comprises of key decision-making by a network of expert advisory committees who operate at global, regional and country levels (WHO 2017). At the global level, the WHO, with the support of SAGE, develops policies, standards and technical guidelines on immunization priorities and strategies, and assists LMICs in adapting and implementing them (WHO 2017; Levine et al. 2011). National governments have the autonomy to generate country-level vaccine policies, drawing on WHO recommendations and the public health priorities of the country (Howard et al. 2018; WHO 2017; Levine et al. 2011). In this regard, country-level policies address – among other issues – new vaccine introductions, immunization strategies (examples include the target populations and the vaccine supply chain), and NIP financing mechanisms (Poorigussarakul et al. 2016; Li et al. 2016; Levine et al. 2011). To ensure a standardized, transparent and accountable national vaccine policy-making process, the WHO recommends

that all member states commit to Regional Technical Advisory Groups on Immunization and establish National Immunization Technical Advisory Groups (NITAGs)⁴ by 2020 (WHO 2015; Duclos et al. 2013; Levine et al. 2011).

The NITAGs have long been established in most high-income countries with remarkable outcomes for the performance of their NIPs (WHO 2017; Duclos et al. 2013). As at the end of 2016, 79 of 194 WHO member states⁵ reported having functional NITAGs that met all six process indicators⁶. Of this total, 50 were established in LMICs; 45 in middle-income countries and five in low-income countries (Howard et al. 2018; SAGE 2017). Despite the progress made in establishing NITAGs in LMICs, the technical capacity of newly founded groups is still lacking (Howard et al. 2018; SAGE 2017; Duclos et al. 2013). Howard et al. (2018) caution that without adequate financial and technical support, the effectiveness and sustainability of NITAGs in LMICs could be threatened.

Governance, organization, and management of NIPs in LMICs

Over the past four decades, the knowledge-base has evolved from considering governance of NIPs as the exclusive duty of national governments, to a shared responsibility, involving subnational or district governments, the communities they serve and development partners (Shen et al. 2014; WHO 2009a; Gauri and Khaleghian 2002). Governance functions may include, but are not limited to;

...developing standards and guidelines; securing vaccine supply and distribution; preparing training materials and supervisory tools and implementing training; developing and carrying out communication strategies; planning the introduction of new vaccines; organizing immunization campaigns; collecting, analysing, and providing reports on vaccine coverage, disease surveillance, and budget execution; and maintaining relationships with external agency counterparts (Shen et al. 2014).

To ensure a well-functioning NIP, it is proposed that these managerial and technical functions are devolved to the district level and executed through a bottom-up approach (Shen et al. 2014). Accordingly, WHO recommends exhaustive planning at the district level, detailing immunization strategies, resource needs, and monitoring and evaluation (Shen et al. 2014; WHO 2009a). Where district-level microplanning has been

⁴ A NITAG is an independent advisory body appointed to inform national immunization policy by providing expert recommendations to the government.

⁵ Overall, 124 countries reported the existence of a NITAG at various stages of development. Of the 70 countries that did not report the existence of a NITAG, 31 were in the African region.

⁶ The six process indicators pertain to the existence of a NITAG, (i) with formal terms of reference, (ii) with a legislative or administrative basis, (iii) with \geq five areas of expertise represented, (iv) that meets at least once a year, (v) whose agenda and background documents are distributed \geq one week prior to meetings and (vi) whose members are required to disclose conflicts of interest.

implemented, a strengthening effect on routine immunization services and the broader health system has been reported (Ismail et al. 2017; O'Connell and Wonodi 2016; Diamenu and Eshetu 2005). Shen et al. (2014) argue however that the success of district-level governance in the most dependent LMICs is often challenged by weak capacity of district health managers as well as resource constraints. Approaches to mitigate these challenges in resource-limited LMICs have been proposed and include the strengthening of Inter-agency Coordinating Committees to harmonize planning and mobilization of technical, material and financial inputs from all stakeholders (Shen et al. 2014; Grundy 2010). In addition to this, it is recommended that countries maximize their links with technical advisory bodies and development partners (Shen et al. 2014).

The human resource capacity of NIPs in LMICs

As NIPs mature and cater for continuously evolving immunization services, the need for an adequate and well-trained human resource capacity also increases. The capacity of the health workforce has been a major challenge in some LMICs. The shortage of health care workers within the sub-Saharan African region has been a persistent public health concern (WHO 2018c). Sub-Saharan Africa is known to be the region with the lowest number of health care workers (below the WHO target of 2.28 health care workers per 1 000 population) (Crisp and Chen 2014; Kinfu et al. 2009). In South Africa for example, staff shortages have been reported as a barrier to delivering effective immunization services (Tladi and Mothiba 2016). This means that the responsibility of delivering health services including routine immunization is often left to a lean health workforce. It has been suggested that NIPs have contributed to resolving the challenge with staff shortages. Kamso et al. (2016) found that by funding human resources, the Global Polio Eradication Initiative has contributed to narrowing the gap in the capacity of the health workforce within the African region. However, other studies report that immunization services such as mass immunization campaigns rather exacerbate the situation as health care workers are often absorbed during these campaigns (Bonnenberger et al. 2015).

One of the proposed solutions to the human resource problem in LMICs is to strengthen the capacity of the existing health workforce. This can be achieved by effectively integrating NIPs into routine primary health care and investing in innovative and appropriate training (Shen et al. 2014). For example, the use of training DVDs and mobile phones to improve communication and microplanning during immunization programs has been piloted in several LMICs with successful outcomes (Ismail et al. 2017; Stokx et al. 2016; Thapa et al. 2016; Xeuatvongsa et al. 2016). Aside from building technical capacity, it is also recommended that health care workers should be trained to value the importance of generating and using data for NIPs (Shen et al. 2014). In addition to this, it is important that health care workers value caregivers and provide acceptable immunization services to ensure that they return to complete the immunization schedule. Good immunization practice and values can be reinforced through regular and appropriate supervision (Shen et al. 2014).

The impact of new vaccine introduction on cold chain and logistics management

Vaccine cold chain⁷ and logistics management requirements have drastically evolved as new and improved vaccines have been introduced into NIPs (Robertson et al. 2017; Lloyd and Cheyne 2017; Zaffran et al. 2012). Cold chain and logistics systems are necessary for storing, transporting, tracking and delivering potent vaccines. Most vaccines may permanently lose their potency or induce unintended immunological reactions if kept at inappropriate temperatures. Thus, cold chain and logistics systems should consistently meet stringent international requirements (Shen et al. 2014; Zaffran et al. 2012). Poorly managed vaccine cold chain and logistics systems undermine the performance of NIPs by compromising the potency and availability of vaccines. In some low-income countries with already weak vaccine supply chains, introduction of new vaccines often becomes an added burden (Brison and LeTallec 2017; Zaffran et al. 2012).

Financing and managing the vaccine cold chain is usually a country-led initiative (Shen et al. 2014). In LMICs, this is often wrought with challenges as national governments have other health and non-health programs competing for financial resources. Diverting resources to competing priorities compromises the vaccine supply chain (Brison and LeTallec 2017; Shen et al. 2014). A review of the evidence shows that while LMICs have made substantial progress in financing and managing their cold chain systems, key targets are yet to be met (Brison and LeTallec 2017; Ogboghodo et al. 2017; Lee et al. 2016; Torres-Rueda et al. 2015). Studies conducted in LMICs suggest that vaccine systems strengthening will require scaling-up cold chain management training for health care workers, reinforcing appropriate supervision, and investing in state-of-the-art cold chain equipment (Ogboghodo et al. 2017; Brison and LeTallec 2017; Eriksson et al. 2017; Lee et al. 2016; Zaffran et al. 2012). Where these measures have been adopted, reductions in vaccines stock-outs and improved access to, and coverage of vaccines have been reported (Guillermet et al. 2017; Prosser et al. 2017). Other innovative approaches have sought to alleviate the demands on already overburdened health care workers and also circumvent resource limitations in LMICs by developing thermostable vaccines with minimal cold chain requirements (Zipursky et al. 2014; WHO 2012; Braun et al. 2008).

Vaccine service delivery in LMICs

The evidence-base on NIPs in LMICs is heavily focused on vaccine service delivery. This is because the quality of vaccine service delivery is recognized as integral to vaccine accessibility which impacts on the rate of immunization coverage (Shen et al. 2014). Findings from the SAGE 2016 midterm review indicate that global immunization coverage has stalled in recent years, increasing by only 1% between 2010 and 2015 (SAGE 2016). This is substandard when compared to the immunization coverage rates recorded between 2000 and 2008,

⁷ Cold chain equipment include active refrigeration systems like cold and freezer rooms for main storage, as well as passive systems which include refrigerated vehicles, cold boxes and vaccine carriers for the delivery of vaccines.

which consistently increased from 73% to 82% (SAGE 2016). Substantial global disparities in immunization coverage have been identified as contributing to the observed stagnation (SAGE 2016). The impact of political instability and weak health systems on immunization coverage rates in some countries have been addressed previously (see *Public health impact of NIPs in LMICs*). There is further evidence to suggest that significant inequalities in accessing vaccines still exist in some LMICs (Arsenault et al. 2017). These inequalities are perpetuated by underlying socioeconomic dimensions. At the country level, poverty has been cited as the single most important barrier to vaccine access (Arsenault et al. 2017). At the individual level, maternal factors such as old age and low level of education have been identified to influence immunization seeking behaviour (Arsenault et al. 2017; Gibson et al. 2015). As it stands, the goal of reaching universal immunization coverage by 2020 may not be achieved without effective scale-up of vaccine service delivery in LMICs (SAGE 2016).

The suggested strategies to improve equity in vaccine service delivery include intensifying efforts to extend access to hard-to-reach populations like rural communities, the under-immunized⁸ and the unimmunized⁹ (Arsenault et al. 2017; SAGE 2016; Shen et al. 2014). Uddin et al. (2015) evaluated the impact of a mobile phone intervention for improving immunization coverage rates in rural, hard-to-reach communities in Bangladesh. The study found that text message reminders of immunization dates sent to caregivers significantly improved immunization coverage rates within the population (Uddin et al. 2015). A similar positive impact was observed in rural communities in the Lao People's Democratic Republic (Xeuvatvongsa et al. 2016). In Kenya and the Philippines, text reminders did not only improve immunization coverage rates but also increased adherence to national immunization schedules (Garcia-Dia et al. 2017; Gibson et al. 2017).

The state of vaccine communication and community partnerships in LMICs

Vaccine uptake is also greatly influenced by public trust in vaccines as well as how the public values NIPs (Kaufman et al. 2017; Ozawa, Grewal et al. 2016; Shen et al. 2014). Public trust in vaccines can be encouraged through advocacy, education, and social and community mobilization. Vaccine communication and community mobilization have been gaining popularity in the NIP 'blueprint'. This is because they are increasingly being recognised as key strategies for promoting the use of immunization services (Shen et al. 2014; Waisbord and Larson 2005). Kaufman et al. (2017) developed a comprehensive framework integrating communication interventions from both routine immunization and immunization campaign contexts. Based on this framework, the purpose of vaccine communication was to, "inform or educate; remind or recall; enhance community ownership; teach skills; provide support; facilitate decision making and enable

⁸ Under-immunized refers to children whose immunization status is suboptimal for their age according to the recommended immunization schedule.

⁹ Unimmunized refers to children who have never received the recommended vaccines.

communication” (Kaufman et al. 2017). Health care workers serve as one of the most influential sources of information on vaccines and immunization. Essentially, the quality of vaccine communication provided by health care workers is integral to caregivers’ decision-making. However, it is reported that health care workers in some LMICs are ill-equipped to perform this role (Shen et al. 2014; Waisbord and Larson 2005). Accordingly, Chama-Chiliba et al. (2017) found that poor communication between health care workers and caregivers in Zambia contributed to dissatisfaction with immunization services.

The available literature concurs that vaccine communication can be improved through locally adapted and appropriate strategies (Habib et al. 2017; Bedford et al. 2017; Gopichandran 2017; Shen et al. 2014). The importance of providing health care workers with adequate training and supervision cannot be overstated. In addition to this, there is a need to encourage community engagement throughout the design and implementation of immunization services. Community participation has been shown to improve the performance of NIPs, even during major health and political crises as reported by Bedford et al. (2017) and Habib et al. (2017) respectively.

Gopichandran (2017) suggests that it is through continuous community engagement that public trust in vaccines can be encouraged. The level of trust in vaccines is varied worldwide. While vaccine hesitancy is prevalent in some high-income countries where the burden of vaccine preventable diseases is low, the trust in, and demand for, vaccines is relatively high in LMICs (Shen et al. 2014). Thus, interventions targeted at increasing vaccine acceptability in LMICs will generally require renewed investments in vaccine communication in order to counter any misinformation (Gopichandran 2017; Shen et al. 2014).

Immunization data generation and use in LMICs

High quality and reliable immunization data is central to informing policy and programmatic decisions. Two main sources of immunization data are identified in the literature, namely the national Demographic and Health Surveys, and routine administrative reports (Shen et al. 2014). The challenge in some LMICs is the discrepancies in immunization data reported at local, district and national levels, compared to those reported by WHO (Shen et al. 2014). In Brazil, for example, Novaes et al. (2015) identified frequent discrepancies in immunization coverage data recorded at the local facility level, compared to that recorded through an established national system. Errors in reporting immunization data have been attributed to poor supervision and the inaccurate use of denominators. In other instances, countries fabricate reports in order to appear to meet immunization targets (Shen et al. 2014). This significantly impedes the appropriate use of immunization data in improving the performance of NIPs in these countries (Shen et al. 2014).

In an effort to strengthen immunization data generation and use in all member states, WHO and the United Nations Children's Fund encourage reporting national data through a joint reporting process (Shen et al. 2014). Home-based immunization records and immunization registries have proven to be useful in ensuring reliable data collection at the country level (Kriss et al. 2016; Novaes et al. 2015; Shen et al. 2014). In addition, disease surveillance systems such as the Global Measles and Rubella Laboratory Network support active surveillance in several LMICs (Xu et al. 2017; Shen et al. 2014).

Financing NIPs in LMICs

There is much in the published literature about the cost-effectiveness of delivering effective routine immunization services in LMICs (Menzies et al. 2017; Aljunid et al. 2016; Mogasale et al. 2016; Ahanhanzo et al. 2015; Portnoy et al. 2015; Alkoshi et al. 2014; Castañeda-Orjuela et al. 2013; Bakır et al. 2012; Babigumira et al. 2011; Bishai et al. 2011). The available evidence demonstrates rising costs of financing NIPs in LMICs as programs expand to include new vaccines, and reach larger populations and extended age groups (Ozawa, Grewal et al. 2016; Brenzel 2015; Portnoy et al. 2015). It is reported that the bulk of funding for NIPs is often required to finance vaccine service delivery, procurement of vaccines, and maintenance of cold chain and logistics systems (Geng et al. 2017; Ozawa, Grewal et al. 2016). Historically, financing NIPs has been challenging in LMICs on account of budget constraints (Brenzel 2015). National governments face mounting pressure with allocating limited resources to both health and non-health sectors. Without appropriate financing mechanisms dedicated to NIPs, large populations in LMICs may not be able to access lifesaving vaccines (Ozawa, Grewal et al. 2016; Brenzel 2015).

The Pan American Health Organization's (PAHO) revolving fund was established in 1977 to assist the 41 countries and territories in the Americas to finance their NIPs (PAHO 2015). Through the PAHO revolving fund, member states pool their limited resources to procure high quality vaccines at discounted prices (PAHO 2015). More recently in 2000, an innovative financing mechanism known as GAVI¹⁰ was established to assist 73 of the most dependent LMICs worldwide to finance procurement, and introduction of new and underused vaccines into their NIPs (Kallenberg et al. 2016; Brenzel 2015). The establishment of GAVI has been a watershed moment in the history of the EPI. According to Kallenberg et al. (2016) the period since its inception has seen rapid uptake of vaccines in GAVI-funded LMICs, a significant contribution to the control of vaccine preventable diseases worldwide.

¹⁰ The GAVI alliance includes the World Bank, WHO, the United Nations Children's Fund, and the Bill and Melinda Gates Foundation.

To maximize the reach of GAVI funds and ensure that the poorest countries have access to the assistance they need, GAVI has set an eligibility threshold (gross national income of US\$1,000 per capita) beyond which countries will have to transition out of GAVI support. In 2015, the first 20 LMICs¹¹ entered the transition phase of GAVI funding (Kallenberg et al. 2016). By the end of the GAVI funding period, these countries are expected to self-finance all their vaccines and will join some 40 middle-income countries who were never eligible for GAVI support (Kallenberg et al. 2016).

Ghana is a prime example of a GAVI-funded country that experienced a rapid increase in its gross national income (estimated at \$1 480 in 2015) and crossed the GAVI eligibility threshold 15 years earlier than predicted by the International Monetary Fund (Kallenberg et al. 2016). During its time as a GAVI funded country, Ghana has been able to introduce eight new vaccines into its NIP. After 2019, Ghana will have to come to terms with a rapid decline in GAVI support and will have to take necessary steps towards self-financing its NIP (Kallenberg et al. 2016).

Health systems in LMICs

It has been suggested that health programs like NIPs, are only as effective as the health systems in which they are embedded (Atun et al. 2008; Kruk and Freedman 2008; WHO 2007; Mills et al. 2006). According to the WHO (2007) the term health systems refers to a collective of “all organizations, people and actions whose primary intent is to promote, restore or maintain health”. The dimensions and overall goals of health systems are presented in Figure 2.

¹¹ Countries that entered the transition phase of GAVI funding in 2015 are Cameroon, Côte d’Ivoire, Djibouti, Ghana, India, Kyrgyzstan, The Lao People’s Democratic Republic, Lesotho, Mauritania, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Sao Tome and Principe, Senegal, The Solomon Islands, South Sudan, Sudan, Yemen, and Zambia.

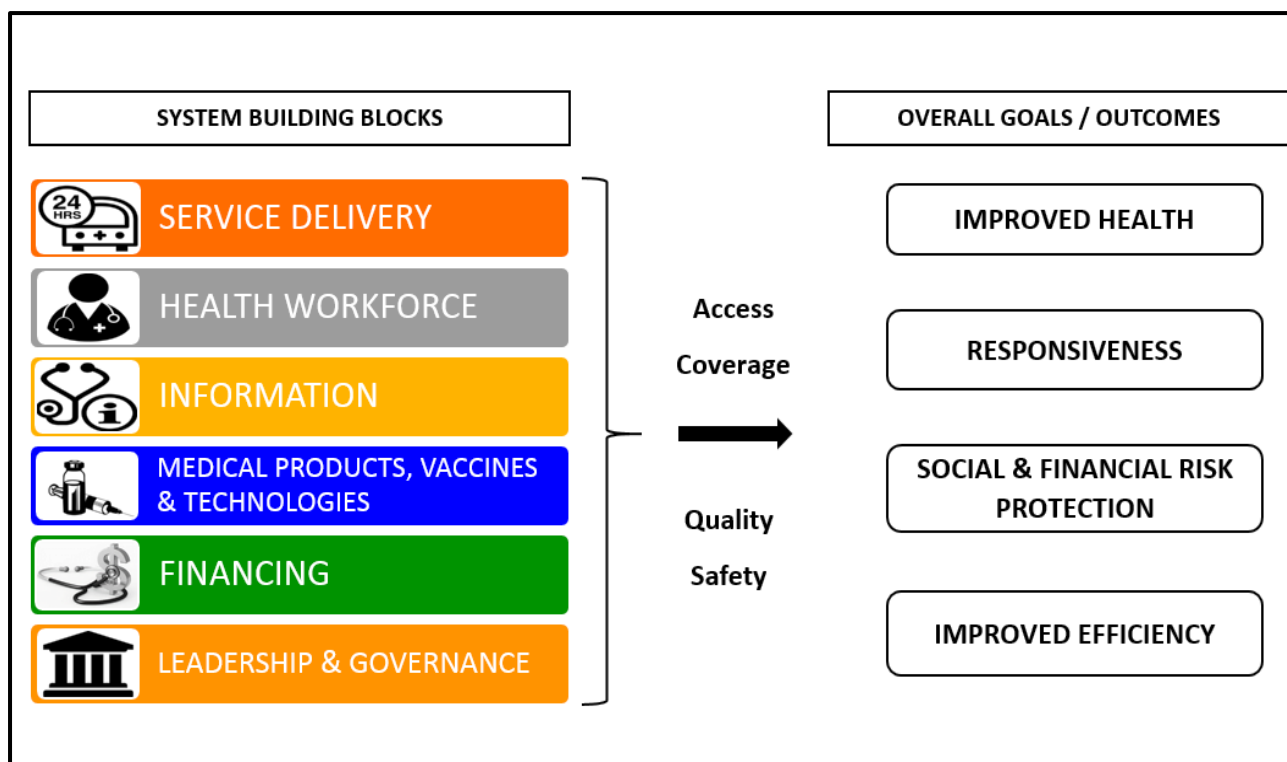


Figure 2: The WHO health systems framework [Source; Author, (drawing on WHO 2007)]

These dimensions are not mutually exclusive, but exist in a constant dynamic interaction to achieve optimal health systems functioning (WHO 2007). De Savigny and Adam (2009) describe this dynamic interaction among the six health systems dimensions as, “how one [dimension] affects and influences the others, and is in turn affected by them”. Essentially, this dynamic interaction is non-linear, but rather a complex relationship among the six dimensions, giving rise to a system (Sheikh et al. 2011; de Savigny and Adam 2009). It is important to note however that the determinants of a well-performing health system go beyond these six dimensions to include the broader context within which they are situated (van Olmen et al. 2012; WHO 2007).

The dynamism of health systems is such that even countries with similar levels of income, education and health expenditure differ in their ability to attain key health goals (Papanicolas and Jha 2017; WHO 2007). As such, health systems contexts matter in how the performance of national and international health sectors are assessed (WHO 2009b; WHO 2007). The evidence-base is in agreement that there is no single blueprint of ideal health systems performance that cuts across all country-contexts (Papanicolas and Jha 2017; Atun 2012; WHO 2009b; WHO 2007). However, well-performing health systems have shared characteristics, and these may include,

Procurement and distribution systems that actually deliver interventions to those in need. They are staffed with sufficient health workers having the right skills and motivation. And they operate with financing systems that are sustainable, inclusive, and fair (WHO 2007).

While these characteristics may be true of most health systems in high-income countries, this is not always the case in LMICs. Historically, the health systems of some LMICs have been characterized by poor governance, weak organizational and institutional capacity, and fragile health infrastructure (including financial, physical and human resources) (WHO 2018c; Swanson et al. 2015; Mills 2014; Olafsdottir et al. 2011; Mills et al. 2006). Health systems in LMICs are further challenged by a disproportionate burden of diseases like malaria, HIV/AIDS, tuberculosis, and other vaccine preventable diseases (WHO 2018c). Altogether, these systems weaknesses mean that the quality of health service delivery has been less than desirable, and key health targets¹² are often difficult to achieve (Phillips et al. 2015; WHO 2009c; Mills et al. 2006; Ranson et al. 2003; Hanson et al. 2003).

Within the past three decades, growing concerns for the state of health systems in LMICs have spurred an expansion in research and interventions aimed at strengthening health systems (Phillips et al. 2015; Mills 2014; Atun 2012; Adam et al. 2012; Mills et al. 2006). Innovative approaches to strengthening health systems in LMICs have become even more imperative considering the substantial technical and financial investments directed at disease-specific health programs¹³ (Mills 2014; Atun 2012; Balabanova et al. 2010). Accordingly, major development partners like GAVI, the Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund), and the United States President's Emergency Plan for AIDS Relief, increasingly encourage the inclusion of health systems strengthening proposals as part of countries' funding applications (Mills 2014; WHO 2009c).

Health systems strengthening is often targeted at sustained improvements to performance drivers such as governance, organizational, and institutional structures in order to achieve and sustain better health services and health outcomes (Swanson et al. 2015; Chee et al. 2013; WHO 2007). Ultimately, comprehensive health systems strengthening initiatives are those that continuously improve on all six dimensions of the health system while managing the dynamic interactions among them (WHO 2011; WHO 2007). While major development partners aim for this level of health systems strengthening within the LMICs they support, there has been some criticism that disease-specific investments only achieve incomplete success because wider

¹² According to the WHO, global health targets may be grouped into seven thematic areas; (i) reproductive, maternal, new born and child health; (ii) infectious diseases; (iii) non-communicable diseases and mental health; (iv) injuries and violence; (v) universal health coverage and health systems; (vi) environmental risks; (vii) health risks and disease outbreaks.

¹³ These are often vertical health programs targeted at priority disease conditions like malaria, HIV/AIDS, tuberculosis, and vaccine preventable diseases.

health services often remain underfunded and weakly supported (Mills 2014; Chee et al. 2013). Additionally, it has been suggested that the plurality of disease-specific health programs places further demands on already fragile health systems in LMICs (Balabanova et al. 2010; WHO 2009c; Marchal et al. 2009; Kallings 2008).

It is undeniable that sustained investments in disease-specific health programs have significantly improved health systems and health outcomes in most LMICs (Balabanova et al. 2010; WHO 2009c; Marchal et al. 2009). However, it has been argued that investments in these disease-specific programs have largely achieved health systems support more than systems-wide strengthening (Chee et al. 2013; Marchal et al. 2009). The long-term goal is to yield maximum health returns on the investments made in disease-specific health programs in LMICs. This is most likely to be achieved by continuously strengthening health systems to be effective, efficient and responsive (Marchal et al. 2009; Mills et al. 2006). Taken together, it is not surprising that there is great interest in the interaction between disease-specific health programs and the health systems that deliver them, and how this interaction impacts on health systems performance (WHO 2009c).

The interface between NIPs and health systems in LMICs

By reviewing the existing evidence-base it is clear that NIPs are not restricted to the Medical Products, Vaccines and Technologies dimension of the health system. Instead, the eight components of NIPs continuously operate and interact across all six dimensions of the health system. Where this interaction between NIPs and health systems is concerned, some studies have shown that NIP services such as new vaccine introductions and supplementary immunization activities like mass immunization campaigns, may have both positive and negative impacts on health systems in LMICs (Postolovska et al. 2018; Andrus et al. 2016; Wang et al. 2013; Hyde et al. 2012).

Over and above the established public health impact of immunization, Lahariya et al. (2016) found that new vaccine introductions into the Indian NIP improved health equity, as well as the efficiency and utilization of wider health services. Hyde et al. (2012) also reports that introducing new vaccines into country NIPs facilitates the widespread use of new technologies like auto-disable syringes and state-of-the-art cold chain systems, within the broader health system. Furthermore, reports of capacity development for health care workers and expansion of health services as a consequence of introducing new vaccines in LMICs have also been sufficiently documented in the literature (Torres-Rueda et al. 2015; Nyirenda et al. 2014; Burchett et al. 2014). In the case of supplementary immunization activities, there have been significant opportunities to strengthen political support for national and international health targets, scale-up disease surveillance systems, and improve health communication and social mobilization (Andrus et al. 2016; Mounier-Jack et al. 2014; Closser et al. 2014).

Where negative influences on the health system have been reported, these have been moderate and often short-lived (Postolovska et al. 2018; Torres-Rueda et al. 2015). For example, it has been reported that intensive immunization campaigns sometimes disrupt routine health services by diverting limited financial, technical and human resources from them. This negatively impacts health access and contributes to reduced volumes of consultations in primary health care facilities for the duration of the campaigns (Bonenberger et al. 2015; Mounier-Jack et al. 2014; Verguet et al. 2013; Loevinsohn et al. 2002). Over the long term however, such moderate negative impacts could have substantial cumulative system-wide effects, some of which may be unintended (Mounier-Jack et al. 2014). In their investigation of the interaction between polio eradication campaigns and the health system, Closser et al. (2015) found increased public distrust in the Pakistani health system. This is because the national government appeared willing to provide door-to-door polio immunization while other basic needs remained unmet (Closser et al. 2015). It has been suggested that distrust in the health system eventually spills over into immunization systems and negatively influence NIP performance (Ozawa, Paina et al. 2016). It is important to caution however, that most negative effects are observed in countries with unstable health systems, while developed health systems are able to withstand disruptions or avoid them altogether (Wang et al. 2013; Hanvoravongchai et al. 2011).

Very limited systematic evidence comprehensively explores the interface between NIPs and health systems from a *health systems perspective*. Where evidence is available, the focus is narrow, and key aspects such as the governance and information systems dimensions are not fully explored (Bosch-Capblanch et al. 2011). Given the interaction between NIPs and their health systems, it can be expected that certain health systems facilitators or barriers could have a knock-on effect on the performance of NIPs. For example, it has been reported that strengthening wider health services increases vaccine uptake in LMICs (Vélez et al. 2014). Additionally, health systems barriers to well-performing NIPs have been identified, and include weak health infrastructure, inequitable financing mechanisms and unresponsive health services (Nishtar et al. 2013; Grundy and Moodie 2009). It may be worth conducting an in-depth exploration of these health systems facilitators and barriers. Such evidence could expand our understanding of the challenges experienced in scaling-up NIPs in some LMICs.

This scoping review does not suggest that empirical research studies exploring the interface between NIPs and their health systems should always examine all six dimensions of the health system. However, by adopting a comprehensive health systems approach that factors in all six dimensions, it is possible to identify potential health systems constraints or facilitators which impact on the performance of NIPs in LMICs (Lahariya 2015; Adam et al. 2012). In relation to this, Bosch-Capblanch et al. (2011) suggest that high quality systematic evidence on health systems in LMICs is generally scarce. Additionally, the limited evidence that is available

does not adequately meet the needs of immunization managers and key decision-makers (Bosch-Capblanch et al. 2011). Generating evidence on the performance of health systems for stakeholders involved in NIPs would require some guidance from an appropriate framework. While there are several analytical and strategic frameworks proposed for assessing the performance of health systems, these frameworks differ in their starting points, operationalization, as well as process and outcome measures (Mounier-Jack et al. 2014; WHO 2011; Kruk and Freedman 2008; Arah et al. 2003; Murray and Evans 2003; Murray and Frenk, 2000). It is also established that no single framework can holistically evaluate the interaction between disease control interventions and the health system (Mounier-Jack et al. 2014). It is for these reasons that we propose the logic model shown in Figure 3 for an in-depth assessment of the interface between NIPs and health systems. This logic model takes into full consideration, the eight components of NIPs as described by Shen et al. (2014) and all six dimensions of the health system (WHO 2007) which gives rise to six cross-cutting themes, namely; (i) the governance and policy landscape, (ii) the capacity of the health workforce, (iii) the availability of potent vaccines, cold chain, and logistics systems, (iv) the quality of health service delivery, (v) the state of health information systems and community partnerships, and (vi) the availability of equitable and sustainable health financing. In addition to this, unique regional and country-level contexts have been factored into the logic model. The reasoning behind this logic model is that the interaction among the six cross-cutting themes – which are influenced by underlying contextual factors – will determine whether key NIP targets (like optimal immunization coverage and improved population health) are attained.

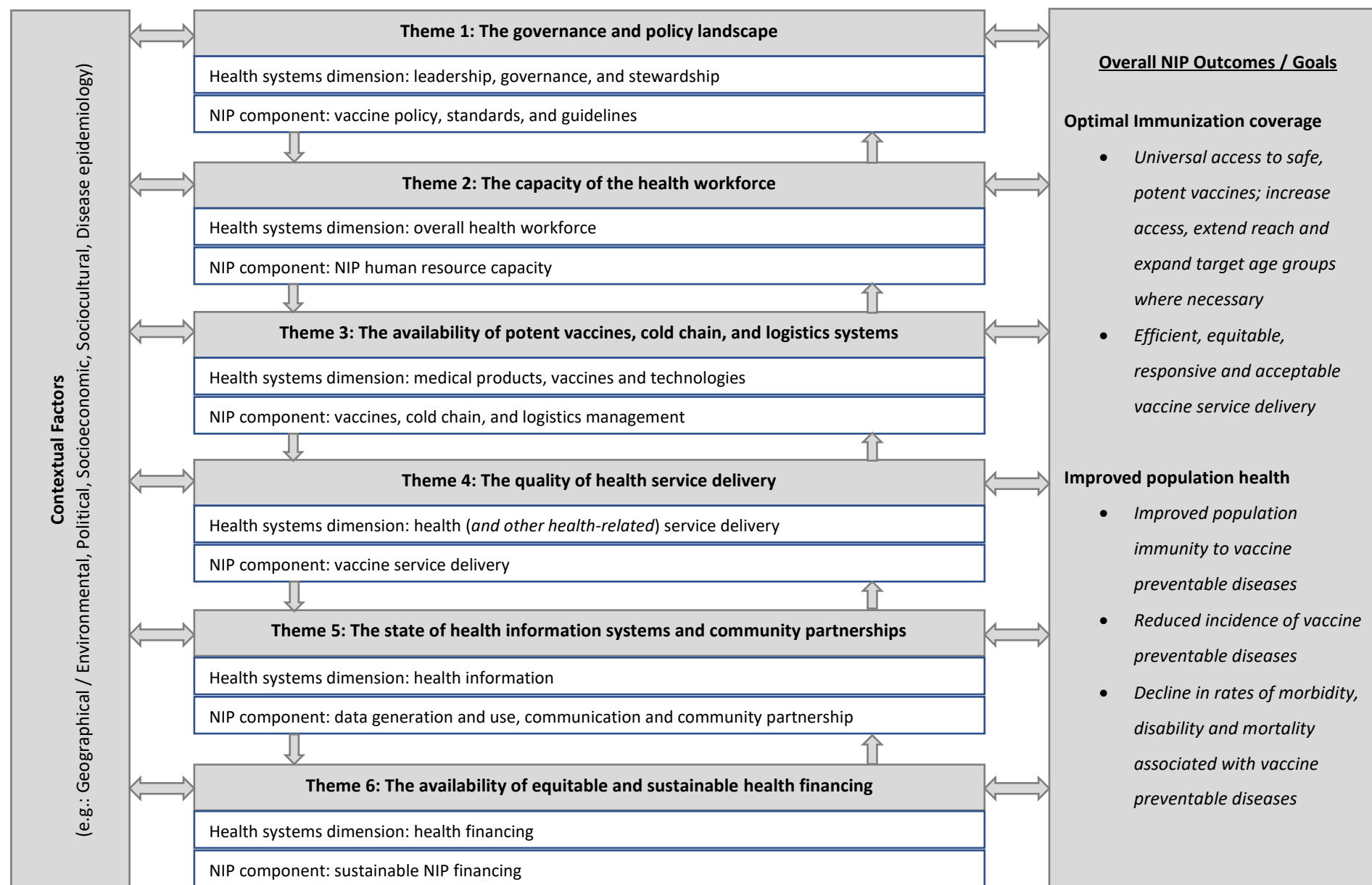


Figure 3: A logic model for in-depth assessment of the interface between NIPs and health systems [Source; Author]

Conclusion

The positive public health impact of NIPs in LMICs, at least over the past four decades (1974 – 2018) of the EPI, is irrefutable. It is evident that in order to sustain and improve on the gains achieved thus far, there is a need for robust evidence to inform ongoing health systems strengthening initiatives in LMICs. This much needed evidence includes information on how health systems constraints and facilitators impact on the performance of NIPs in LMICs. This scoping review therefore argues for a systematic and comprehensive assessment of the interaction between NIPs and health systems in LMICs, with a focus on how health systems functioning impacts on the performance of NIPs.

References

- Adam T, Hsu J, de Savigny D et al. 2012. Evaluating health systems strengthening interventions in low-income and middle-income countries: Are we asking the right questions? *Health Policy and Planning* **27**:i19.
- Ahanhango CD, Huang XX, Le Gargasson J et al. 2015. Determinants of routine immunization costing in Benin and Ghana in 2011. *Vaccine* **33**:A71.
- Aljunid S, Maimaiti N, Nur AM et al. 2016. Cost-effectiveness of HPV vaccination regime: Comparing twice versus thrice vaccinations dose regime among adolescent girls in Malaysia. *BMC public health* **16**:71.
- Alkoshi S, Maimaiti N, Dahlui M. 2014. Cost-effectiveness analysis of rotavirus vaccination among Libyan children using a simple economic model. *The Libyan Journal of Medicine* **9**:26236.
- Andre FE, Booy R, Bock HL et al. 2008. Vaccination greatly reduces disease, disability, death and inequity worldwide. *Bulletin of the World Health Organization* **86**:140-146.
- Andrus JK, Cochi SL, Cooper LZ et al. 2016. Combining global elimination of measles and rubella with strengthening of health systems in developing countries. *Health Affairs* **35**:327.
- Arah OA, Klazinga NS, Delnoij DMJ, Ten Asbroek AHA, Custers T. 2003. Conceptual frameworks for health systems performance: A quest for effectiveness, quality, and improvement. *International Journal for Quality in Health Care* **15**:377-398.
- Arsenault C, Harper S, Nandi A et al. 2017. Monitoring equity in vaccination coverage: A systematic analysis of demographic and health surveys from 45 Gavi-supported countries. *Vaccine* **35**:951-959.
- Atun R. 2012. Health systems, systems thinking and innovation. *Health Policy and Planning* **27**:iv4–iv8.
- Atun R, Bennett S, Duran A. 2008. When do vertical (stand-alone) programmes have a place in health systems? *World Health Organization*, on behalf of the European Observatory on Health Systems and Policies. Available at: <http://www.who.int/iris/handle/10665/107977>.
- Babigumira JB, Levin A, Burgess C et al. 2011. Assessing the cost-effectiveness of measles elimination in Uganda: Local impact of a global eradication program. *The Journal of Infectious Diseases* **204**:S123.
- Backx M, Freedman A. 2013. Immunization. *Medicine* **41**:628-634.
- Bakır M, Türel O, Topachevskiy O. 2012. Cost-effectiveness of new pneumococcal conjugate vaccines in Turkey: A decision analytical model. *BMC Health Services Research* **12**:386.
- Balabanova D, McKee M, Mills A et al. 2010. What can global health institutions do to help strengthen health systems in low income countries? *Health Research Policy and Systems* **8**:22.
- Bedford J, Chitnis K, Webber N et al. 2017. Community engagement in Liberia: Routine immunization post-Ebola. *Journal of Health Communication* **22**:81.
- Bishai D, Johns B, Nair D et al. 2011. The cost-effectiveness of supplementary immunization activities for measles: A stochastic model for Uganda. *The Journal of Infectious Diseases* **204**:S115.
- Bonenberger M, Aikins M, Akweongo P et al. 2015. What do district health managers in Ghana use their working time for? A case study of three districts. *PLoS One* **10**:e0130633.

- Bosch-Capblanch X, Kelly M, Garner P. 2011. Do existing research summaries on health systems match immunisation managers' needs in middle- and low-income countries? Analysis of GAVI health systems strengthening support. *BMC Public Health* **11**:449.
- Braun LJ, Tyagi A, Perkins S et al. 2008. Development of a freeze-stable formulation for vaccines containing aluminium salt adjuvants. *Vaccine* **27**:72-79.
- Brenzel L. 2015. What have we learned on costs and financing of routine immunization from the comprehensive multi-year plans in GAVI eligible countries? *Vaccine* **33**:A98.
- Brison M, LeTallec Y. 2017. Transforming cold chain performance and management in lower-income countries. *Vaccine* **35**:2107-2109.
- Burchett HE, Mounier-Jack S, Torres-Rueda S et al. 2014. The impact of introducing new vaccines on the health system: Case studies from six low- and middle-income countries. *Vaccine* **32**:6505-6512.
- Castañeda-Orjuela C, Romero M, Arce P et al. 2013. Using standardized tools to improve immunization costing data for program planning: The cost of the Colombian Expanded Program on Immunization. *Vaccine* **31**:C79.
- Chama-Chiliba CM, Masiye F, Mphuka C. 2017. Assessing care-givers' satisfaction with child immunisation services in Zambia: Evidence from a national survey. *Vaccine* **35**:5597.
- Chan M. 2014. Beyond expectations: 40 years of EPI. *Lancet, The* **383**:1697-1698.
- Chee G, Pielemeier N, Lion A et al. 2013. Why differentiating between health system support and health system strengthening is needed. *The International Journal of Health Planning and Management* **28**:85-94.
- Clem AS. 2011. Fundamentals of vaccine immunology. *Journal of Global Infectious Diseases* **3**:73-78.
- Closser S, Cox K, Parris TM et al. 2014. The impact of polio eradication on routine immunization and primary health care: A mixed-methods study. *Journal of Infectious Diseases* **210**:S513.
- Closser S, Jooma R, Varley E et al. 2015. Polio eradication and health systems in Karachi: Vaccine refusals in context. *Global Health Communication* **1**:32-40.
- Crisp N, Chen L. 2014. Global supply of health professionals. *The New England Journal of Medicine* **370**:950-957.
- Dbaibo G, Tatochenko V, Wutzler P. 2016. Issues in pediatric vaccine-preventable diseases in low- to middle-income countries. *Human Vaccines and Immunotherapeutics* **12**:2365-2377.
- Diamenu S, Eshetu M. 2005. Bringing immunization services closer to communities: The reaching every district approach in Ghana.
- Duclos P, Dumolard L, Abeyasinghe N et al. 2013. Progress in the establishment and strengthening of national immunization technical advisory groups: Analysis from the 2013 WHO/UNICEF joint reporting form, data for 2012. *Vaccine* **31**:5314-5320.
- Eriksson P, Gessner BD, Jaillard P et al. 2017. Vaccine vial monitor availability and use in low- and middle-income countries: A systematic review. *Vaccine* **35**:2155-2161.
- Feikin DR, Flannery B, Hamel MJ et al. 2016. Vaccines for children in low- and middle-income countries. In: Black RE, Laxminarayan R, Temmerman M, Walker N (ed). *Reproductive, Maternal, Newborn and Child Health*. 3rd edn. Washington, DC: World Bank Group, 187-204.
- Garcia-Dia M, Fitzpatrick J, Madigan E et al. 2017. Using text reminder to improve childhood immunization adherence in the Philippines. *Computers, Informatics, Nursing* **35**:212-218.
- Gauri V, Khaleghian P. 2002. Immunization in developing countries: Its political and organizational determinants. *World Development* **30**:2109-2132.
- Geng F, Suharlim C, Brenzel L et al. 2017. The cost structure of routine infant immunization services: A systematic analysis of six countries. *Health Policy and Planning* **32**:1174-1184.
- Gentile A, Bhutta Z, Bravo L et al. 2010. Pediatric disease burden and vaccination recommendations: Understanding local differences. *International Journal of Infectious Diseases* **14**:e658.
- Gibson DG, Ochieng B, Kagucia EW et al. 2017. Mobile phone-delivered reminders and incentives to improve childhood immunisation coverage and timeliness in Kenya (M-SIMU): A cluster randomised controlled trial. *Lancet Global Health* **5**:e438.

- Gibson DG, Ochieng B, Kagucia EW et al. 2015. Individual level determinants for not receiving immunization, receiving immunization with delay, and being severely underimmunized among rural western Kenyan children. *Vaccine* **33**:6778-6785.
- Gopichandran V. 2017. Public trust in vaccination: An analytical framework. *Indian Journal of Medical Ethics* **2**:98-104.
- Greenwood B. 2014. The contribution of vaccination to global health: Past, present and future. *Philosophical Transactions of the Royal Society of London* **369**:20130433.
- Grundy J. 2010. Country-level governance of global health initiatives: An evaluation of immunization coordination mechanisms in five countries of Asia. *Health Policy and Planning* **25**:186-196.
- Grundy J, Moodie R. 2009. An approach to health system strengthening in the Democratic Peoples Republic of Korea (North Korea). *The International Journal of Health Planning and Management* **24**:113-129.
- Guillermet E, Alfa DA, Gbodja R et al. 2017. Professional changes induced by a redesigned immunization supply chain in the Comé Health Zone, Benin. *Vaccine* **35**:2189-2194.
- Habib MA, Soofi S, Cousens S et al. 2017. Community engagement and integrated health and polio immunisation campaigns in conflict-affected areas of Pakistan: A cluster randomised controlled trial. *Lancet Global Health* **5**:e603.
- Hanson K, Ranson MK, Oliveira-Cruz V et al. 2003. Expanding access to priority health interventions: A framework for understanding the constraints to scaling-up. *Journal of International Development* **15**:1-14.
- Hanvoravongchai P, Mounier-Jack S, Oliveira Cruz V et al. 2011. Impact of measles elimination activities on immunization services and health systems: Findings from six countries. *The Journal of Infectious Diseases* **204**:S89.
- Howard N, Bell S, Walls H et al. 2018. The need for sustainability and alignment of future support for National Immunization Technical Advisory Groups (NITAGs) in low and middle-income countries. **22**:1-3.
- Hyde TB, Dentz H, Wang SA et al. 2012. The impact of new vaccine introduction on immunization and health systems: A review of the published literature. *Vaccine* **30**:6347-6358.
- Ismail A, Tabu C, Onuekwusi I et al. 2017. Micro-planning in a wide age range measles rubella (MR) campaign using mobile phone app, a case of Kenya, 2016. *The Pan African Medical Journal* **27**:16.
- Kallenberg J, Mok W, Newman R et al. 2016. Gavi's transition policy: Moving from development assistance to domestic financing of immunization programs. *Health Affairs* **35**:250.
- Kallings LO. 2008. The first postmodern pandemic: 25 years of HIV/AIDS. *Journal of Internal Medicine* **263**:218-243.
- Kamso J, Mvika ES, Ota MOC et al. 2016. The contribution of the polio eradication initiative to narrowing the gaps in the health workforce in the African Region. *Vaccine* **34**:5150-5154.
- Kaufman J, Ames H, Bosch-Capblanch X et al. 2017. The comprehensive 'Communicate to Vaccinate' taxonomy of communication interventions for childhood vaccination in routine and campaign contexts. *BMC Public Health* **17**:1-11.
- Keja K, Chan C, Hayden G et al. 1988. Expanded programme on immunization. *World Health Statistics Quarterly* **41**:59-63.
- Kinfu Y, Dal Poz MR, Mercer H et al. 2009. The health worker shortage in Africa: Are enough physicians and nurses being trained? *Bulletin of the World Health Organization* **87**:225-230.
- Kriss JL, Goodson J, Machekeyanga Z et al. 2016. Vaccine receipt and vaccine card availability among children of the apostolic faith: Analysis from the 2010-2011 Zimbabwe demographic and health survey. *The Pan African Medical Journal* **24**:47.
- Kruk ME, Freedman LP. 2008. Assessing health system performance in developing countries: A review of the literature. *Health policy* **85**:263-276.
- Lahariya C, Paruthi R, Bhattacharya M. 2016. How a new health intervention affects the health systems? Learnings from pentavalent vaccine introduction in India. *The Indian Journal of Pediatrics* **83**:294-299.
- Lahariya C. 2015. "Health system approach" for improving immunization program performance. *Journal of Family Medicine and Primary Care* **4**:487-494.
- Lee BY, Haidari LA, Prosser W et al. 2016. Re-designing the Mozambique vaccine supply chain to improve access to vaccines. *Vaccine* **34**:4998-5004.
- Levine OS, Bloom DE, Cherian T et al. 2011. The future of immunisation policy, implementation, and financing. *Lancet, The* **378**:439-448.

- Li T, Lv M, Lei T et al. 2016. Who benefits most from influenza vaccination policy: A study among the elderly in Beijing, China. *International Journal for Equity in Health* **15**:45.
- Lloyd J, Cheyne J. 2017. The origins of the vaccine cold chain and a glimpse of the future. *Vaccine* **35**:2115-2120.
- Loevinsohn B, Aylward B, Steinglass R et al. 2002. Impact of targeted programs on health systems: A case study of the polio eradication initiative. *American Journal of Public Health* **92**:19-23.
- Marchal B, Cavalli A, Kegels G. 2009. Global health actors claim to support health system strengthening - is this reality or rhetoric? *PLoS Medicine* **6**:e1000059.
- Menzies NA, Suharlim C, Geng F et al. 2017. The cost determinants of routine infant immunization services: A meta-regression analysis of six country studies. *BMC Medicine* **15**:178.
- Miller MA, Sentz JT. 2006. Vaccine-preventable diseases. In: Bos ER, Jamison T, Baingana F, Feacham RG, Makgoba M, Hofman KJ, Rogo HO (ed). *Disease and mortality in Sub-Saharan Africa*. 2nd edn. Washington, DC: World Bank Publications, 163-178.
- Mills A. 2014. Health care systems in low- and middle-income countries. *The New England Journal of Medicine* **370**:552-527.
- Mills A, Rasheed F and Tollman S. 2006. Strengthening health systems. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, Jha P, Mills A, Musgrove P (ed). *Disease control priorities in developing countries*. 2nd edn. New York, USA: Oxford University Press, 87-102.
- Mogasale V, Ramani E, Wee H et al. 2016. Oral cholera vaccination delivery cost in low- and middle-income countries: An analysis based on systematic review. *PLoS Neglected Tropical Diseases* **10**:e0005124.
- Mounier-Jack S, Burchett HED, Griffiths UK et al. 2014. Meningococcal vaccine introduction in Mali through mass campaigns and its impact on the health system. *Global Health, Science and Practice* **2**:117-129.
- Murray CJL and Evans D. 2003. Health systems performance assessment: Debates, methods and empiricism. Albany: World Health Organization. Available at: <http://apps.who.int/iris/handle/10665/42735>.
- Murray CJL and Frenk J. 2000. A framework for assessing the performance of health systems. *Bulletin of the World Health Organization* **78**:717-731.
- Nishtar S, Boerma T, Amjad S et al. 2013. Pakistan's health system: Performance and prospects after the 18th Constitutional Amendment. *Lancet, The* **381**:2193-2206.
- Novaes ML, de Almeida RM, Bastos RR. 2015. Assessing vaccine data recording in Brazil. *Revista Brasileira de Epidemiologia* **18**:745-756.
- Nyirenda LJ, Ingstad Sandberg K, Justice J. 2014. When are health systems ready for new vaccines? The introduction of pneumococcal vaccine in Malawi. *Forum for Development Studies* **41**:317-336.
- O'Connell M, Wonodi C. 2016. Routine immunization consultant program in Nigeria: A qualitative review of a country-driven management approach for health systems strengthening. *Global Health, Science and Practice* **4**:29.
- Ogboghodo EO, Omuemu VO, Odijie O et al. 2017. Cold chain management practices of health care workers in primary health care facilities in Southern Nigeria. *Pan African Medical Journal* **27**:34.
- Okwo-Bele J, Cherian T. 2012. The expanded programme on immunization: A lasting legacy of smallpox eradication. *Vaccine* **29**:D79.
- Olafsdottir AE, Reidpath DD, Pokhrel S et al. 2011. Health systems performance in sub-Saharan Africa: Governance, outcome and equity. *BMC Public Health* **11**:237.
- Ozawa S, Grewal S, Portnoy A et al. 2016. Funding gap for immunization across 94 low- and middle-income countries. *Vaccine* **34**:6408-6416.
- Ozawa S, Paina L, Qiu M. 2016. Exploring pathways for building trust in vaccination and strengthening health system resilience. *BMC Health Services Research* **16**:131-141.
- PAHO. 2015. Operating procedures of the PAHO revolving fund. Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=18304&Itemid=270.
- Papanicolas I, Jha AK. 2017. Challenges in international comparison of health care systems. *JAMA* **318**:515-516.
- Phillips JF, Sheff M, Boyer CB. 2015. The astronomy of Africa's health systems literature during the MDG era: Where are the systems clusters? *Global Health, Science and Practice* **3**:482-502.

- Pooripussarakul S, Riewpaiboon A, Bishai D et al. 2016. What criteria do decision makers in Thailand use to set priorities for vaccine introduction? *BMC Public Health* **16**:1-7.
- Portnoy A, Ozawa S, Grewal S et al. 2015. Costs of vaccine programs across 94 low- and middle-income countries. *Vaccine* **33**:A108.
- Postolovska I, HELLERINGER S, Kruk ME et al. 2018. Impact of measles supplementary immunisation activities on utilisation of maternal and child health services in low-income and middle-income countries. *BMJ Global Health* **3**:e000466.
- Prosser W, Jaillard P, Assy E et al. 2017. System redesign of the immunization supply chain: Experiences from Benin and Mozambique. *Vaccine* **35**:2162-2166.
- Ranson MK, Hanson K, Oliveira-Cruz V et al. 2003. Constraints to expanding access to health interventions: An empirical analysis and country typology. *Journal of International Development* **15**:15-39.
- Robertson J, Franzel L, Maire D. 2017. Innovations in cold chain equipment for immunization supply chains. *Vaccine* **35**:2252-2259.
- SAGE. 2017. SAGE April 2017 National Immunization Technical Advisory Groups: Background paper. Available at: http://www.who.int/immunization/sage/meetings/2017/april/1_NITAGs_background_document_SAGE_April_2017.pdf.
- SAGE. 2016. 2016 midterm review of the global vaccine action plan. Available at: http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2016_EN.pdf.
- Samb B, Evans T, Dybul M et al. 2009. An assessment of interactions between global health initiatives and country health systems. *Lancet, The* **373**:2137-2169.
- de Savigny D, and Adam T (Eds). 2009. Systems thinking for health systems strengthening. Alliance for Health Policy and Systems Research, World Health Organization. Available at: https://apps.who.int/iris/bitstream/handle/10665/44204/9789241563895_eng.pdf;jsessionid=4BAE493880CAB85A68ABA549EE620127?sequence=1.
- Sheikh K, Gilson L, Agyepong IA, Hanson K, Ssengooba F, Bennett S. 2011. Building the field of health policy and systems research: Framing the questions. *PLoS Medicine* **8**: e1001073.
- Shen AK, Fields R, McQuestion M. 2014. The future of routine immunization in the developing world: Challenges and opportunities. *Global Health, Science and Practice* **2**:381-394.
- Sindhu KN, Babji S, Ganesan S. 2017. Impact of rotavirus vaccines in low and middle-income countries. *Current Opinion in Infectious Diseases* **30**:473-481.
- Stokx J, Dochez C, Ochieng P et al. 2016. Evaluation of a training DVD on pneumococcal conjugate vaccine for Kenyan EPI healthcare workers. *Education for Health* **29**:35-41.
- Swanson RC, Atun R, Best A et al. 2015. Strengthening health systems in low-income countries by enhancing organizational capacities and improving institutions. *Globalization and Health* **11**:5.
- Thapa S, Khanal S, Shakya SR et al. 2016. Real-time monitoring of vaccination campaign performance using mobile phones - Nepal, 2016. *Morbidity and Mortality Weekly Report* **65**:1072-1076.
- Tladi FM, Mothiba TM. 2016. Challenges faced by professional nurses when implementing the Expanded Programme on Immunisation at rural clinics in Capricorn District, Limpopo: Original research. *African Primary Health Care and Family Medicine* **8**:1-5.
- Toole MJ. 2016. So close: Remaining challenges to eradicating polio. *BMC Medicine* **14**:43.
- Torres-Rueda S, Burchett HE, Griffiths UK et al. 2015. New pneumococcal conjugate vaccine introductions in four sub-Saharan African countries: A cross-country analysis of health systems' impacts. *African Health Sciences* **15**:868-877.
- Uddin J, Shamsuzzaman M, Horng L et al. 2015. Use of mobile phones for improving vaccination coverage among children living in rural hard-to-reach areas and urban streets of Bangladesh. *Vaccine* **34**:276-283.
- van Olmen J, Criel B, Bhojani U et al. 2012. The health system dynamics framework: The introduction of an analytical model for health system analysis and its application to two case-studies. *Health, Culture and Society* **2**:1-21.
- Vélez LF, Sanitato M, Barry D et al. 2014. The role of health systems and policy in producing behavior and social change to enhance child survival and development in low- and middle-income countries: An examination of the evidence. *Journal of Health Communication* **19**:89-121.

- Verguet S, Jassat W, Bertram MY et al. 2013. Impact of supplemental immunisation activity (SIA) campaigns on health systems: Findings from South Africa. *Journal of Epidemiology and Community Health* **67**:947-952.
- Waisbord S, Larson H. 2005. Why invest in communication for immunization: Evidence and lessons learned. New York, USA: Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (Baltimore) and UNICEF.
- Walldorf JA, Date KA, Sreenivasan N et al. 2017. Lessons learned from emergency response vaccination efforts for Cholera, Typhoid, Yellow Fever, and Ebola. *Emerging Infectious Diseases* **23**:S216.
- Wang SA, Hyde TB, Mounier-Jack S et al. 2013. New vaccine introductions: Assessing the impact and the opportunities for immunization and health systems strengthening. *Vaccine* **31**:B128.
- WHO. 2018a. National Immunization Programme (NIP). Available at: <http://vaccine-safety-training.org/national-immunization-programmes.html>.
- WHO. 2018b. Immunization. Available at: <http://www.who.int/topics/immunization/en/>.
- WHO. 2018c. World health statistics 2018: Monitoring health for the SDGs, sustainable development goals. World Health Organization. Available at: <http://apps.who.int/iris/bitstream/handle/10665/272596/9789241565585-eng.pdf?ua=1>.
- WHO. 2017. Global, regional, and national advisory committees on immunization. Available at: <http://www.who.int/immunization/policy/committees/en/>.
- WHO. 2015. WHO's mission and vision in immunization and vaccines 2015-2030. Available at: http://www.who.int/immunization/documents/general/WHO_Mission_Vision_Immunization_Vaccines_2015_2030.pdf?ua=1.
- WHO. 2013a. Global Vaccine Action Plan 2011-2020. Vaccine. Available at: <https://www.unicef.org/immunization/files/GVAP.pdf>.
- WHO. 2013b. The expanded programme on immunization. Available at: http://www.who.int/immunization/programmes_systems/supply_chain/benefits_of_immunization/en/.
- WHO. 2012. Revolutionary meningitis vaccine breaks another barrier; first to gain approval to travel outside cold chain. Available at: http://www.who.int/immunization/newsroom/menafrivac_20121114/en/.
- WHO. 2011. Monitoring the building blocks of health systems: A handbook of indicators and their measurement strategies. Geneva, Switzerland: World Health Organization. Available at: http://www.who.int/healthinfo/systems/WHO_MBHSS_2010_full_web.pdf.
- WHO, UNICEF and World Bank. 2009. State of the world's vaccines and immunization. Geneva: World Health Organization. Available at: http://apps.who.int/iris/bitstream/handle/10665/44204/9789241563895_eng.pdf;jsessionid=7AFC6AA00A36DB726100FDD8F5FAA7BF?sequence=1.
- WHO. 2009a. Microplanning for immunization service delivery using the Reaching Every District (RED) strategy. Available at: <http://www.who.int/iris/handle/10665/70450>.
- WHO. 2009b. Systems thinking for health systems strengthening. Geneva, Switzerland: World Health Organization.
- WHO (Maximizing Positive Synergies Collaborative Group). 2009c. An assessment of interactions between global health initiatives and country health systems. *Lancet, The* **373**:2137-2169.
- WHO. 2007. Everybody's business - strengthening health systems to improve health outcomes: WHO's framework for action. Available at: https://www.who.int/healthsystems/strategy/everybodys_business.pdf.
- Xeuvatvongsa A, Datta SS, Moturi E et al. 2016. Improving hepatitis B birth dose in rural Lao People's Democratic Republic through the use of mobile phones to facilitate communication. *Vaccine* **34**:5777-5784.
- Xu W, Zhang Y, Wang H et al. 2017. Global and national laboratory networks support high quality surveillance for measles and rubella. *International Health* **9**:184-189.
- Zaffran M, Vandelaer J, Kristensen D et al. 2012. The imperative for stronger vaccine supply and logistics systems. *Vaccine* **31**:B80.
- Zipursky S, Djingarey MH, Lodjo J et al. 2014. Benefits of using vaccines out of the cold chain: Delivering Meningitis A vaccine in a controlled temperature chain during the mass immunization campaign in Benin. *Vaccine* **32**:1431-1435.

Part C: Systematic Review

Health systems constraints and facilitators of human papillomavirus immunization programs in sub-Saharan Africa: A systematic review

*Targeted Journal: Health Policy and Planning*¹

Edina Amponsah-Dacosta²

Abstract

Given the vast investments made in national immunization programs (NIPs) and the significance of NIPs to public health, it is important to understand what influences the optimal performance of NIPs. It has been established that well-performing NIPs require enabling health systems. However, systematic evidence on how the performance of health systems impacts on NIPs is lacking, especially from sub-Saharan Africa. We conducted a qualitative systematic review to synthesize the available evidence on health systems constraints and facilitators of NIPs in sub-Saharan Africa, using human papillomavirus (HPV) immunization programs as a proxy. Fifty-four articles published between 2008 and 2018 were found to be eligible. Data extraction was guided by a logic model on the interface between NIPs and health systems. A cross-cutting thematic analysis of the extracted data was performed. This systematic review provides evidence necessary for informing ongoing health systems strengthening initiatives in sub-Saharan Africa. There is evidence to suggest that NIPs in sub-Saharan Africa have surmounted significant health systems constraints and have achieved notable public health success. This success can be attributed to strong political endorsement for vaccines, clear governance structures and effective collaboration with global partners. Despite this, significant health systems constraints persist in service delivery, vaccine communication, community engagement, the capacity of the health workforce and sustainable financing. These constraints could derail further progress if not addressed through health systems strengthening efforts. There is a need to expand the research agenda to include comprehensive evaluation of health systems constraints and facilitators of NIPs within sub-Saharan Africa.

Keywords

Africa; Cervical cancer; Health systems; Human papillomavirus; HPV vaccine; Immunization; National Immunization Programs

¹ Instructions for authors in Appendix 5.

² For the purpose of this thesis, the student is the sole and first author of this systematic review.

Key messages

- National immunization programs (NIPs) are embedded within health systems. However, the interactions between NIPs and health systems are poorly understood.
- This systematic review provides evidence of how NIPs and health systems interact by reporting on the health systems constraints and facilitators of NIPs in sub-Saharan Africa.
- Strong political will, clear governance structures and effective collaboration with global partners have been major facilitators of NIPs in sub-Saharan Africa.
- Despite this, significant health systems constraints persist in service delivery, vaccine communication, community engagement, the capacity of the health workforce and sustainable financing.
- The findings of this review have relevance for ongoing health systems strengthening initiatives in sub-Saharan Africa, especially where NIPs are concerned. By providing a better understanding of what works – *and does not work* – for NIPs, health systems strengthening initiatives could be better designed to adequately respond to the burden of vaccine preventable diseases in sub-Saharan Africa.

Introduction

It has become increasingly apparent that some of the major challenges experienced in scaling-up the performance of national immunization programs (NIPs) in low- and middle- income countries (LMICs) are not necessarily program-specific, but rather challenges in wider health systems functioning (SAGE 2016). This is in line with the notion that NIPs exist in a continuous interaction with the health systems that deliver them (SAGE 2016; Shen et al. 2014; Samb et al. 2009). As such, major health systems constraints could have a significant impact on how NIPs perform. For example, financial, technical, logistical, political and socioeconomic constraints have all been cited as negatively impacting on the overall performance of NIPs in LMICs (SAGE 2016). Unfortunately, these health systems constraints on effective NIP performance appear to be even more prevalent within the sub-Saharan Africa region (SAGE 2016).

In sub-Saharan Africa, NIPs have undergone steady advancements since the establishment of the Expanded Program on Immunization in 1974 (WHO 2013a). Tremendous progress has been made in increasing access to lifesaving vaccines and reducing the burden of vaccine preventable diseases in the region (Machingaidze et al. 2013; Arevshatian et al. 2007). Despite this, sub-Saharan Africa continues to lag in meeting global

immunization targets (Mihigo et al. 2017; SAGE 2016). Although substantial investments have been dedicated to NIPs in sub-Saharan Africa, this has not been enough to improve their performance to the levels required to significantly reduce the disproportionate burden of vaccine preventable diseases in the region. In this regard, global actors have recognized the harrowing state of health systems within sub-Saharan Africa as a major barrier to achieving further progress in improving the performance of NIPs (SAGE 2016). This has contributed to making health systems strengthening in sub-Saharan Africa a matter of global public health priority (SAGE 2016). It has been argued however, that while ongoing health systems strengthening efforts are absolutely vital, they have not been able to achieve their intended outcomes (Chee et al. 2013; Marchal et al. 2009). Some of the challenges faced have been attributed to the fact that health systems constraints are not adequately defined and as such interventions are often poorly designed and weakly targeted in the long term (Chee et al. 2013; Goeman et al. 2010; Marchal et al. 2009). Systematic evidence on how health systems constraints (and facilitators) impact on the performance of NIPs in sub-Saharan African could be very useful in better informing health systems strengthening efforts in the region. Unfortunately, such evidence is lacking.

We report on a systematic review study which sought to determine how health systems constraints and facilitators impact on the performance of NIPs in sub-Saharan Africa. Given that NIPs serve as a platform for the delivery of several immunization services (these include routine childhood immunization programs, adolescent immunization programs, mass immunization campaigns, emergency vaccination services and introduction of new, improved or underused vaccines into existing NIPs), an in-depth review incorporating the mass of these services would not be appropriate. As such, a single immunization program – the human papillomavirus (HPV) immunization program – was selected as a proxy or tracer immunization program for the purpose of this systematic review. Our interests in HPV immunization programs stem from the fact they present a unique challenge to health systems in sub-Saharan Africa compared to routine childhood immunization programs. Foremost is the fact that HPV vaccines are not widely accessible through NIPs in most sub-Saharan Africa countries as compared to other regions of the world (*see Figure 1 and Appendix 1 for further details*).

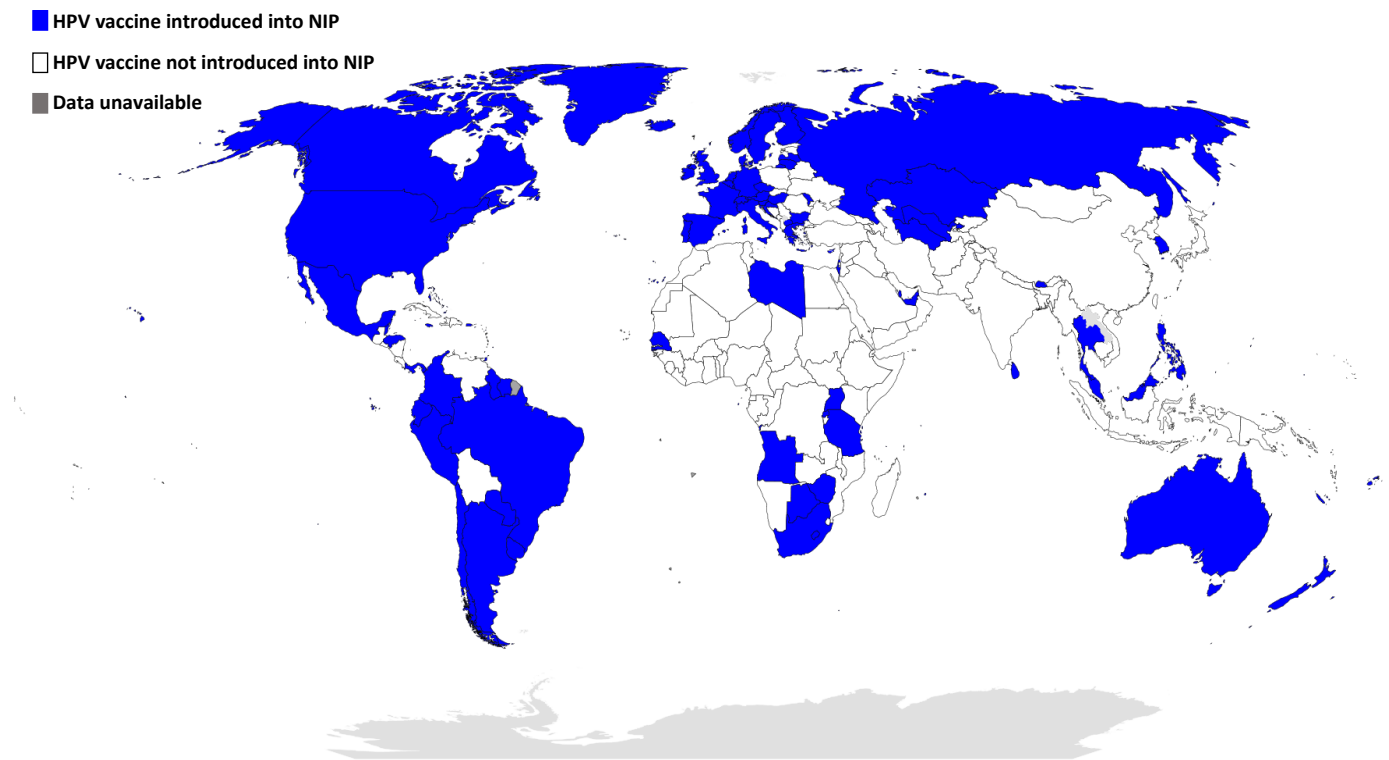


Figure 1: Global progress in the implementation of nationwide HPV immunization programs

Note: Data from countries with planned or partial HPV vaccine introduction, or HPV vaccine demonstration projects are not represented here [Source; Author, (drawing on data from <http://www.hpvcentre.net>, WHO 2018a; Gallagher et al. 2018; LaMontagne et al. 2017; Herrero et al. 2015)]

Three HPV vaccines are currently licensed for use; the four-valent³ vaccine was licensed in 2006, the bivalent vaccine in 2007 and the nine-valent vaccine in 2014 (WHO 2017a; Herrero et al. 2015). All three prophylactic HPV vaccines have been proven to be safe and effective against persistent HPV infections which lead to a broad spectrum of diseases and cancers (Garland et al. 2016; Herrero et al. 2015; Lu et al. 2011). In addition to this, all three vaccines confer immune protection against the HPV oncogenic types 16 and 18 which are implicated in 70% of all cervical cancers. Cervical cancer in turn, accounts for 84% of all HPV-associated cancers (WHO 2017b; WHO 2017a). Given the burden of the disease, the World Health Organization (WHO) recognizes prevention of cervical cancer as priority and recommends that member states introduce the HPV vaccine into their NIPs (WHO 2017b). The schedule recommended by WHO is two doses of the HPV vaccine, administered six months apart and prioritizing adolescent girls between the ages of nine and 14 years, prior to sexual debut (WHO 2017b).

³ This refers to the number of strains (or types) of HPV that are targeted in the vaccine.

As at November 2018, about 102 countries and overseas territories had established nationwide HPV immunization programs (WHO 2018b; WHO 2018a; Gallagher et al. 2018; LaMontagne et al. 2017; Herrero et al. 2015). Of this total, only 12 countries⁴ are in sub-Saharan Africa (Gallagher et al. 2018; LaMontagne et al. 2017). Another major challenge is the fact that HPV immunization coverage rates in sub-Saharan Africa are reported to be among the lowest (1.2% among 10 – 20-year-old females) in the world (Bruni et al. 2016). This implies that a substantial proportion of adolescent girls are excluded from the full benefits of the HPV vaccine. This is most concerning, considering that cervical cancer incidence rates in the region are among the highest (31.0 per 100 000 women) in the world (de Martel et al. 2017; Louie et al. 2009). In addition, cervical cancer is one of the most common causes of cancer-related deaths among women in sub-Saharan Africa (De Vuyst et al. 2013). Evidently, the status of HPV immunization programs in sub-Saharan Africa is a matter of major public health concern. Expanding access to lifesaving HPV vaccines is a significant challenge for NIPs and health systems in the region (Wigle et al. 2013; Denny et al. 2012; Sankaranarayanan et al. 2012). There is an obvious need for intervention informed by evidence on the health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa. Such evidence is currently lacking and is worth exploring through systematic review methods.

Methods

A systematic review study was conducted to assess how health systems constraints and facilitators impact on the performance of NIPs in sub-Saharan Africa. For this purpose, an initial scoping review was performed to gain an in-depth understanding of the interaction between NIPs and health systems (*see Part B*). One of the primary outcomes of the scoping review was a logic model, describing the interface between NIPs and health systems, which addresses six cross-cutting themes, namely; (i) the governance and policy landscape, (ii) the capacity of the health workforce, (iii) the availability of potent vaccines, cold chain and logistics systems, (iv) the quality of health service delivery, (v) the state of health information systems and community partnerships and (vi) the availability of equitable and sustainable health financing. Drawing on the themes emanating from this logic model, a qualitative systematic review was conducted to address the following research question; *How do health systems constraints and facilitators impact on the performance of HPV immunization programs in sub-Saharan Africa?*

A search strategy was developed using key search terms and search term synonyms which focused on three thematic areas; NIPs, health systems and HPV immunization programs. The full search strategy is available in Appendix 2. Using this search strategy, peer-reviewed and grey literature sources were sought through

⁴ Countries that have introduced the HPV vaccine into their NIPs are Angola, Botswana, Lesotho, Mauritius, Rwanda, São Tomé and Príncipe, Senegal, Seychelles, South Africa, Tanzania, Uganda, Zimbabwe.

electronic databases such as PubMed, Web of Science, Scopus and EBSCOhost. In addition, supplementary searches for literature sources which may have been missed during the initial electronic search were conducted through internet searches in Google Scholar as well as organizational websites like WHO (<http://www.who.int/en/>), GAVI, the Vaccine Alliance (<https://www.gavi.org/>) and the HPV Information Centre (<http://www.hpvcentre.net/>). The last date of the literature search was August 2018.

With regards to the eligibility of studies for this review, only the full texts of empirical studies conducted and published between 2008 and 2018 were considered eligible for inclusion. This is because the past 10 years has been characterized by intensified global efforts to implement HPV immunization programs, especially in sub-Saharan Africa (LaMontagne et al. 2017; Sankaranarayanan et al. 2012). Reviewing studies conducted within this period therefore enhanced the relevance of the review findings. Eligible studies also included those which used qualitative, quantitative and mixed method study designs. However, modelling studies, reviews, descriptive reports and commentaries reporting on secondary research findings were excluded from review. In addition, studies published in languages other than English were excluded because of the time and resource constraints on the thesis from which this systematic review emanated. Finally, studies reporting on interventions other than HPV immunization programs were excluded from the review.

After selection, full texts of eligible studies were critically appraised for the appropriateness of the methods used and the findings reported. Ethical considerations and rigour were also assessed. Evidence of reflexivity, where appropriate, was assessed throughout the texts including authors' affiliations, research funding and declaration of potential conflict of interest. The quality appraisal was conducted with the assistance of published appraisal tools (*see Appendix 3 for an example*) developed for multiple study designs by the Critical Appraisal Skills Programme (<http://www.casp-uk.net/>). These appraisal tools have been used previously in other qualitative systematic reviews (Chan 2013; Kane et al. 2007; Walter et al. 2004).

The analytical approach for this systematic review was guided by the logic model developed as part of the preliminary scoping review (*see Part B*). Study findings related to health systems constraints and facilitators of HPV immunization programs were extracted and organized according to the six themes of the model. During the first stage of the analysis process, full texts were imported into Rayyan, a web-based application for systematic reviews, where they were screened for eligibility (Ouzzani et al. 2016). Eligible studies were then coded using inductive and deductive approaches. The codes used were related to the types of health systems constraints and facilitators reported in the study findings. Relevant findings from each study were then extracted and recorded in a database (*see Appendix 4 for a summary of the data extracted for this review*). The extracted data set was then subjected to rigorous thematic analysis with careful consideration for prevailing contextual factors reported for the relevant countries.

Given that majority of sub-Saharan African countries are yet to implement nationwide HPV immunization programs through their NIPs, we explored outcomes on health systems constraints to implementation. Where studies investigated potential or anticipated health systems constraints and facilitators to the performance of nationwide HPV immunization programs should they be implemented, these outcomes were also considered for this review. Where HPV immunization programs have been introduced in sub-Saharan African countries as part of their NIPs or through demonstration projects⁵, it was also worth exploring study findings related to health systems constraints and facilitators to the acceptance and uptake of the HPV vaccine.

Results

Characteristics of studies included in this review

The literature search yielded a total of 356 published records. Overall, 355 of these records were retrieved from electronic databases, while a search in Google Scholar yielded an additional record. No additional unique records were found through organizational websites. Of the total output, 54 full text articles were found to be eligible for inclusion in the systematic review. Figure 1 shows the screening and selection process for this systematic review.

⁵ Vaccine demonstration projects are pilot campaigns conducted in advance of nationwide roll-out of a vaccine. They are targeted at a subset of the population with the aim of building capacity to inform nationwide vaccine introduction.

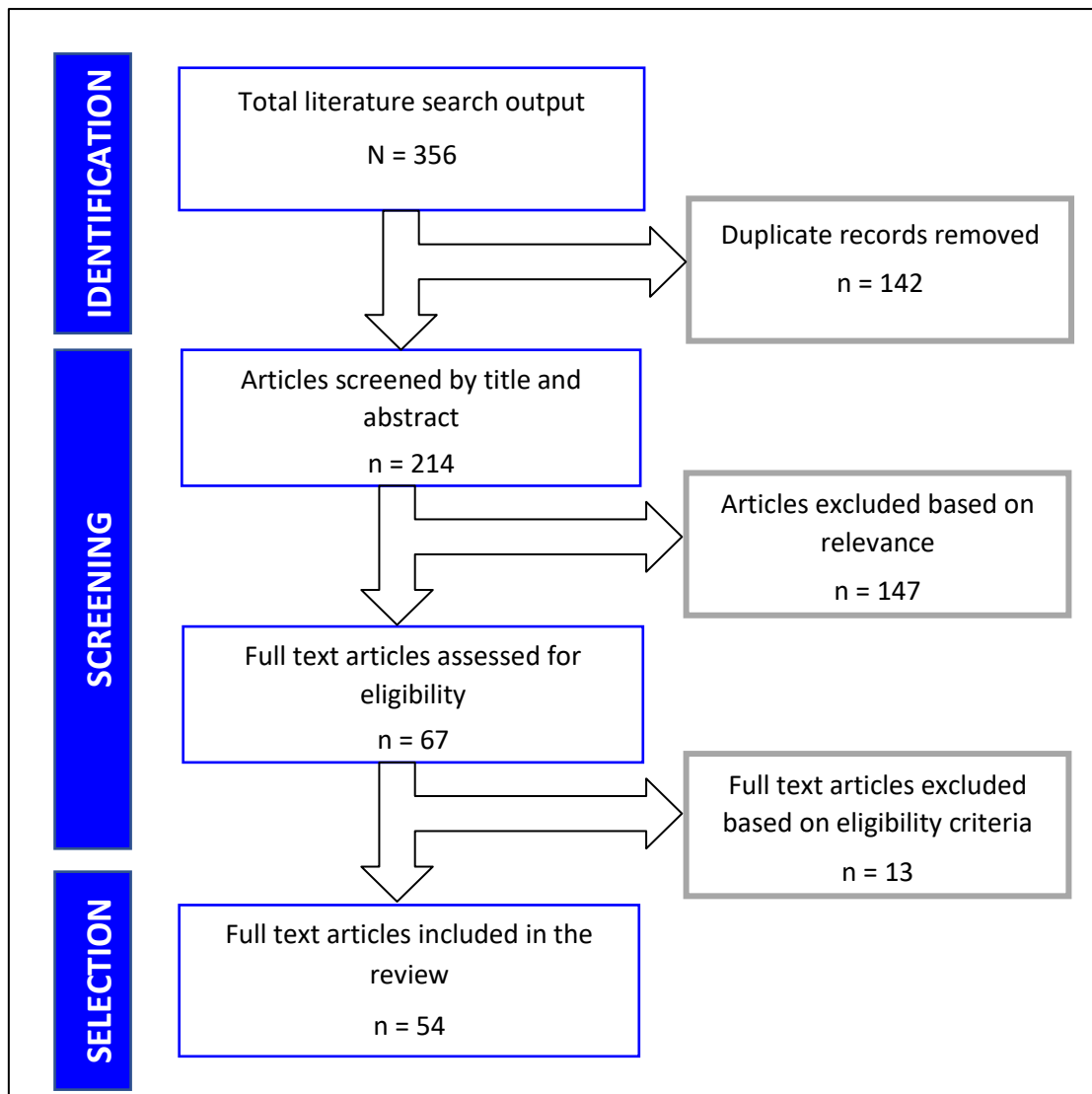


Figure 2: Flowchart of the literature search and selection process for the systematic review

The 54 full text articles included in this review reported on studies conducted in 20 countries in SSA, namely; Botswana, Burundi, Cameroon, Côte d'Ivoire, Gambia, Ghana, Kenya, Lesotho, Madagascar, Malawi, Mali, Mozambique, Niger, Nigeria, Rwanda, Senegal, South Africa, Tanzania, Uganda and Zambia. The majority of articles focused on South Africa (10), Nigeria (8), Kenya (6) and Uganda (6). Where articles reported on findings from multiple countries, only those findings relating to sub-Saharan African countries were extracted. The majority (31) of studies made use of qualitative study designs, while others adopted mixed method (10), or quantitative (10) study designs. A population-based intervention study and a project evaluation were also included in this review (see Table 1).

Table 1: Characteristics of studies included in the systematic review

No.	Author, year	Title	Country	Study design	Availability of HPV vaccine*
1	Audu et al, 2015	Awareness and perception of human papilloma virus vaccine among healthcare professionals in Nigeria	Nigeria	Cross-sectional, questionnaire-based	Not available
2	Ayissi et al, 2012	Awareness, acceptability and uptake of human papilloma virus vaccine among Cameroonian school-attending female adolescents	Cameroon	Cross-sectional, questionnaire-based	Demonstration project
3	Bardaji et al, 2018	Awareness of cervical cancer and willingness to be vaccinated against human papillomavirus in Mozambican adolescent girls	Mozambique	Quantitative, cross-sectional	Demonstration project
4	Botha et al, 2015	The Vaccine and Cervical Cancer Screen (VACCS) project: acceptance of human papillomavirus vaccination in a school-based programme in two provinces of South Africa	South Africa	Quantitative	Demonstration project
5	Botwright et al, 2017	Experiences of operational costs of HPV vaccine delivery strategies in Gavi-supported demonstration projects	African Countries	Quantitative	Demonstration project
6	Chigbu et al, 2017	The impact of community health educators on uptake of cervical and breast cancer prevention services in Nigeria	Nigeria	Prospective population-based intervention	Demonstration project
7	Coleman et al, 2011	HPV vaccine acceptability in Ghana, West Africa	Ghana	Qualitative, questionnaire-based	Available in the private sector only
8	De Groot et al, 2017	Knowledge, attitudes, practices and willingness to vaccinate in preparation for the introduction of HPV vaccines in Bamako, Mali	Mali	Qualitative, household survey	Demonstration project
9	DiAngi et al, 2011	A cross-sectional study of HPV vaccine acceptability in Gaborone, Botswana	Botswana	Cross-sectional, survey	Available in the private sector only
10	Francis et al, 2011	A qualitative analysis of South African women's knowledge, attitudes, and beliefs about HPV and cervical cancer prevention, vaccine awareness and acceptance, and maternal-child communication about sexual health	South Africa	Qualitative	Available in the private sector only
11	Francis et al, 2010	Examining attitudes and knowledge about HPV and cervical cancer risk among female clinic attendees in Johannesburg, South Africa	South Africa	Quantitative	Not available
12	Friedman et al, 2014	Preparing for human papillomavirus vaccine introduction in Kenya: implications from focus-group and interview discussions with caregivers and opinion leaders in Western Kenya	Kenya	Qualitative	Not available
13	Harries et al, 2009	Preparing for HPV vaccination in South Africa: key challenges and opinions	South Africa	Qualitative	Available in the private sector only
14	Hoque, 2015	Acceptability of human papillomavirus vaccination among academics at the University of KwaZulu-Natal, South Africa	South Africa	Qualitative, cross-sectional	Available through NIP
15	Hoque, 2016	Factors influencing the recommendation of the Human Papillomavirus vaccine by South African doctors working in a tertiary hospital	South Africa	Quantitative, cross-sectional	Available through NIP
16	Hoque et al, 2013	Human Papillomavirus vaccination acceptability among female university students in South Africa	South Africa	Qualitative, cross-sectional	Available in the private sector only
17	Hutubessy et al, 2012	A case study using the United Republic of Tanzania: costing nationwide HPV vaccine delivery using the WHO Cervical Cancer Prevention and Control Costing Tool	Tanzania	Quantitative	Not available

18	Kamya et al, 2017	Evaluating global health partnerships: a case study of a Gavi HPV vaccine application process in Uganda	Uganda	Mixed-methods case study	Available through NIP
19	Katz et al, 2013	A qualitative analysis of factors influencing HPV vaccine uptake in Soweto, South Africa among adolescents and their caregivers	South Africa	Qualitative	Available in the private sector only
20	Ladner et al, 2012	Assessment of eight HPV vaccination programs implemented in lowest income countries	Lesotho and Cameroon (non-African countries included)	Mixed-methods	Demonstration project
21	Ladner et al, 2014	Performance of 21 HPV vaccination programs implemented in low and middle-income countries, 2009-2013	African countries (non-African LMICs included)	Quantitative	Demonstration project
22	LaMontagne et al, 2011	Human papillomavirus vaccine delivery strategies that achieved high coverage in low- and middle-income countries	Uganda (non-African LMICs included)	Mixed-methods, cross-sectional	Demonstration project
23	Levin et al, 2013	Delivery cost of human papillomavirus vaccination of young adolescent girls in Peru, Uganda and Viet Nam	Uganda (non-African LMICs included)	Mixed-method	Demonstration project
24	Mabeya et al, 2018	Uptake of three doses of HPV vaccine by primary school girls in Eldoret, Kenya; a prospective cohort study in a malaria endemic setting	Kenya	Cross-sectional, questionnaire-based	Demonstration project
25	MacPhail et al, 2013	Using HPV vaccination for promotion of an adolescent package of care: opportunity and perspectives	South Africa	Qualitative, cross-sectional	Available in the private sector only
26	Makwe and Anorlu, 2011	Knowledge of and attitude toward human papillomavirus infection and vaccines among female nurses at a tertiary hospital in Nigeria	Nigeria	Qualitative, cross-sectional	Not available
27	Masika et al, 2015	Knowledge on HPV vaccine and cervical cancer facilitates vaccine acceptability among school teachers in Kitui County, Kenya	Kenya	Mixed-methods, cross-sectional,	Demonstration project
28	Massey et al, 2017	Human papillomavirus (HPV) awareness and vaccine receptivity among Senegalese adolescents	Senegal	Quantitative, questionnaire-based	Demonstration project
29	Moodley et al, 2013	High uptake of Gardasil vaccine among 9-12-year-old schoolgirls participating in an HPV vaccination demonstration project in KwaZulu-Natal Province, South Africa	South Africa	Mixed-methods	Available in the private sector only
30	Morhason-Bello et al, 2015	Willingness of reproductive-aged women in a Nigerian community to accept human papillomavirus vaccination for their children	Nigeria	Quantitative, multi-stage household survey	Available in the private sector only
31	Msyamboza et al, 2017	Implementation of a human papillomavirus vaccination demonstration project in Malawi: successes and challenges	Malawi	Mixed-method, cross-sectional	Demonstration project
32	Mugisha et al, 2015	Feasibility of delivering HPV vaccine to girls aged 10 to 15 years in Uganda	Uganda	Qualitative	Demonstration project
33	Ndizeye et al, 2018	Knowledge and practices of general practitioners at district hospitals towards cervical cancer prevention in Burundi, 2015: a cross-sectional study	Burundi	Descriptive, cross-sectional	Not available
34	Ngabo et al, 2017	A cost comparison of introducing and delivering pneumococcal, rotavirus and human papillomavirus vaccines in Rwanda	Rwanda	Quantitative	Available through NIP
35	Odunyemi et al, 2018	Effect of nursing intervention on mothers' knowledge of cervical cancer and acceptance of	Nigeria	Quasi-experimental study	Available in the private sector only

		human papillomavirus vaccination for their adolescent daughters in Abuja - Nigeria			
36	Ogembo et al, 2014	Achieving high uptake of human papillomavirus vaccine in Cameroon: lessons learned in overcoming challenges	Cameroon	Project evaluation	Demonstration project
37	Okunade et al, 2017	Knowledge and acceptability of human papillomavirus vaccination among women attending the gynaecological outpatient clinics of a university teaching hospital in Lagos, Nigeria	Nigeria	Descriptive, cross-sectional	Available in the private sector only
38	Poole et al, 2013	A cross-sectional study to assess HPV knowledge and HPV vaccine acceptability in Mali	Mali	Qualitative, cross-sectional	Not available
39	Ports et al, 2013	Barriers and facilitators to HPV vaccination: perspectives from Malawian women	Malawi	Qualitative	Not available
40	Quentin et al, 2012	Costs of delivering human papillomavirus vaccination to schoolgirls in Mwanza Region, Tanzania	Tanzania	Mixed-methods	Demonstration project
41	Remes et al, 2012	A qualitative study of HPV vaccine acceptability among health workers, teachers, parents, female pupils, and religious leaders in northwest Tanzania	Tanzania	Qualitative	Not available
42	Tchounga et al 2012	Cervical cancer prevention in reproductive health services: knowledge, attitudes and practices of midwives in Côte d'Ivoire, West Africa	Cote d'Ivoire	Qualitative, cross-sectional	Available in the private sector only
43	Torres-Rueda et al, 2016	HPV vaccine introduction in Rwanda: impacts on the broader health system	Rwanda	Mixed-methods	Available through NIP
44	Tuhiro et al, 2014	Effect of school-based human papillomavirus (HPV) vaccination on adolescent girls' knowledge and acceptability of the HPV vaccine in Ibanda District in Uganda	Uganda	Cross-sectional, mixed-methods	Demonstration project
45	Tuhiro et al, 2017	Perceptions of human papillomavirus vaccination of adolescent schoolgirls in western Uganda and their implications for acceptability of HPV vaccination: a qualitative study	Uganda	Qualitative	Demonstration project
46	Ugwu et al, 2013	Acceptability of human papilloma virus vaccine and cervical cancer screening among female health-care workers in Enugu, Southeast Nigeria	Nigeria	Cross-sectional, questionnaire-based	Available in the private sector only
47	Umeh et al, 2016	Mothers' willingness to pay for HPV vaccines in Anambra state, Nigeria: a cross sectional contingent valuation study	Nigeria	Cross-sectional, survey	Available in the private sector only
48	Urasa and Darj, 2011	Knowledge of cervical cancer and screening practices of nurses at a regional hospital in Tanzania	Tanzania	Descriptive, cross-sectional	Available in the private sector only
49	Venturas and Umeh, 2017	Health professional feedback on HPV vaccination roll-out in a developing country	Zambia	Qualitative	Demonstration project
50	Vermandere et al, 2015	Implementation of an HPV vaccination program in Eldoret, Kenya: results from a qualitative assessment by key stakeholders	Kenya	Qualitative	Demonstration project
51	Vermandere et al, 2014	Determinants of acceptance and subsequent uptake of the HPV vaccine in a cohort in Eldoret, Kenya	Kenya	Qualitative, longitudinal study	Demonstration project
52	Wamai et al, 2013	Awareness, knowledge and beliefs about HPV, cervical cancer and HPV vaccines among nurses in Cameroon: an exploratory study	Cameroon	Qualitative, questionnaire-based	Demonstration project
53	Watson-Jones et al, 2015	Access and attitudes to HPV vaccination amongst hard-to-reach populations in Kenya	Kenya	Qualitative	Demonstration project
54	Watson-Jones et al, 2012	Reasons for receiving or not receiving HPV vaccination in primary schoolgirls in Tanzania: a case control study	Tanzania	Qualitative	Demonstration project

Source; Author

Note: *Availability of the HPV vaccine at the time the studies were conducted

Most studies (33/54) were primarily concerned with assessing knowledge, awareness, and acceptability of the HPV vaccine among key populations such as adolescents, parents and caregivers, health workers, teachers and religious leaders (*see Table 1*). The articles also reported on the availability of the HPV vaccine in the relevant countries at the time each study was conducted. This information tended to change in some countries overtime and presented a unique opportunity to assess the evolution of health systems constraints and facilitators to HPV immunization programs in these countries. Overall, the HPV vaccine was reported to be available through the NIPs of South Africa, Rwanda and Uganda. In most countries where the studies were conducted, the HPV vaccine was only available through demonstration projects (*see Table 1*). Nine articles reported on studies which were conducted at a time when the HPV vaccine was not available, either through NIPs, demonstration projects or in private health facilities. These studies were mainly focused on determining the feasibility of implementing HPV immunization programs in the relevant countries by assessing potential health systems constraints and facilitators.

Health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa

We synthesized the available evidence on health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa. Findings pertaining to health systems constraints to HPV vaccine introduction into NIPs, as well as health systems constraints and facilitators of HPV vaccine acceptance and uptake, and the overall performance of HPV immunization programs (include existing nationwide programs or demonstration projects, and future HPV immunization programs) in sub-Saharan Africa were all considered during this review. The findings of this review have been organized and reported under the six cross-cutting themes of the logic model on the interface between NIPs and health systems as described previously (*see Part B*).

The governance and policy landscape

This theme explored findings related to leadership, management and stewardship throughout the HPV vaccine policy- and decision-making cascade. The evidence highlights the importance of clear governance⁶ and management structures, the involvement of political champions, the support of policy influencers (including governmental and non-governmental organizations), and the role of strong and inclusive partnerships to the optimal performance of HPV immunization programs in sub-Saharan Africa (*see Table 3*) (Kamya et al. 2017; Torres-Rueda et al. 2015; Mugisha et al. 2015; Ladner et al. 2014; Harries et al. 2008). For example, prior to the implementation of an HPV immunization program in South Africa, Harries et al. (2008) sought to identify potential barriers and facilitators of such a program. It was reported that strong collaboration between the

⁶ Where NIPs are concerned, governance functions include the decision- and policy-making that goes into developing of immunization program-related standards and guidelines, overall program organization, as well as training and supervision. These functions cut across global, national, sub-national and local or facility levels.

national Departments of Health and Education, as well as between the private and public health sectors were necessary to support and sustain an HPV immunization program (Harries et al. 2008). These findings were echoed in studies conducted in Rwanda and Uganda where the HPV vaccine had been introduced as part of NIPs (Kamya et al. 2017; Torres-Rueda et al. 2015). In addition, Kamya et al. (2017) recognized the role of the First Lady of Uganda as a champion of the HPV vaccine. This level of endorsement ensured that the HPV immunization program remained a priority in the national policy agenda. It was also reported that a diverse and inclusive network of stakeholders from governmental and non-governmental agencies, having past immunization partnership experience and assigned clear roles and responsibilities, were invaluable to a GAVI HPV vaccine application process in Uganda (Kamya et al. 2017). Apart from the national level, the role of governance structures and processes at the health facility level were also identified as critical to HPV immunization programs. In a study that assessed how HPV vaccine introduction impacted on the Rwandan health system, it was reported that extensive planning and supervision at the health facility level contributed to the successful integration of the HPV vaccine into the NIP (Torres-Rueda et al. 2015).

Table 2: Summary of health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa

Theme (n*)	Health Systems Constraints	Health Systems Facilitators
The governance and policy landscape (5)	<ul style="list-style-type: none"> • Weak involvement of Ministries of Education and Finance 	<ul style="list-style-type: none"> • Clear governance and management structures • Political champions steering and endorsing the agenda for introduction of HPV immunization nationwide • Partnerships between all stakeholders – Departments of Health, Finance and Education, private and public health sectors • Participation of actors with past immunization partnership experience • Appropriate supervision, training and planning at the facility level • Non-governmental partners playing advocacy and management roles • Support of policy influencers
The capacity of the health workforce (17)	<ul style="list-style-type: none"> • Inadequate training of health workers leading to low level of knowledge about HPV infection, cervical cancer and the HPV vaccine • Fragile health worker capacity 	<ul style="list-style-type: none"> • Adequately trained health workers who can provide sound recommendations to clients about the HPV vaccine • Availability of a well-trained school health team • Community health workers as source of information and serving as community mobilizers
The availability of potent vaccines, cold chain and logistics systems (3)	<ul style="list-style-type: none"> • Limited availability and accessibility of the HPV vaccine 	<ul style="list-style-type: none"> • Conducting national cold chain inventory and ensuring adequate capacity of the cold chain prior to introduction of the HPV vaccine in NIPs
The quality of health service delivery (16)	<ul style="list-style-type: none"> • Adopting age-based, or health facility-based community outreach vaccine delivery strategies • Health resource constraints • Greater resource requirements associated with creating new vaccine delivery infrastructure 	<ul style="list-style-type: none"> • Implementing mixed vaccine delivery models comprising both grade-based and health facility-based outreach strategies • Availability of well-functioning NIPs instilling trust in immunization and improving acceptance and uptake

	<ul style="list-style-type: none"> • Logistical challenges of HPV vaccine delivery given the underdevelopment of adolescent health services • Long distance to health facilities delivering HPV vaccine • Physical barriers to accessing schools, e.g. long distance, unsafe and poor terrain during rainy seasons • Poor accessibility of schools and communities for vaccinators due to poor road networks 	
The state of health information systems and community partnerships (33)	<ul style="list-style-type: none"> • Inadequate sensitization campaigns leading to low level of awareness about the HPV vaccine and the vaccination program • Inadequate engagement with fathers and male teachers • Poor access to information about HPV, cervical cancer and HPV vaccine, for individuals living in hard-to-reach communities, and among populations with low literacy levels • Low level of knowledge about safety and effectiveness of the HPV vaccine • Misinformation about the side-effects, safety and benefits of the HPV vaccine • Misconceptions about other vaccines • Negative media reports and interference • Exclusive reliance on paper-based vaccine records 	<ul style="list-style-type: none"> • Evidence-based health promotion strategies involving intensive community mobilization and sensitization • Effective community engagement involving key stakeholders; adolescents, parents (including fathers), teachers, municipal and religious leaders • Adequate information, education and communication, especially on vaccine safety and efficacy issues. Prioritizing hard-to-reach communities • Consideration for culturally appropriate communication about HPV, cervical cancer and HPV vaccination • Adequate communication about all vaccines • Strengthening surveillance of adverse events following immunization
The availability of equitable and sustainable health financing (8)	<ul style="list-style-type: none"> • Non-integration of HPV vaccination programs within existing NIP • High financial costs of social mobilization and HPV vaccine delivery as adolescents are not “typical” clients of the health system • Adopting an age-based vaccine delivery strategy – less cost effective • High cost of the HPV vaccine • Cost of delivering vaccines to adolescents is higher than that of routine childhood immunization 	<ul style="list-style-type: none"> • Planning appropriate delivery strategies based on local context – country specific strategies • Intensive investments in community mobilization and sensitization increases vaccine acceptance and uptake • Implementing a grade-based delivery strategy – more cost-effective • GAVI funding and support • Adopting free HPV immunization services

Source; Author

Note: *Numbers in parenthesis represent the number of articles which reported findings related to each theme. Some articles reported on findings pertaining to more than one theme. A detailed description of each of the studies used and the themes they relate to is presented in Appendix 4.

The capacity of the health workforce

The size and competency of the health workforce emerged from the evidence-base as priority issues where HPV immunization programs were concerned. Majority of studies relating to health workers were conducted at a time when the HPV vaccine was not widely available to the general population, either because it was yet to be introduced in the country or was only available through the private health sector. In a study conducted by Remes et al. (2012) health workers identified staff shortages as a potential constraint to an HPV immunization program, were it to be introduced in Tanzania. The major health systems constraint identified in other studies however, was the inadequate training of the existing workforce in sub-Saharan Africa. Several studies reported that health workers (including doctors, nurses and midwives) exhibited suboptimal levels of

knowledge on HPV infection, the pathogenesis and prevention of cervical cancer, the availability, safety and effectiveness of the HPV vaccine and the HPV immunization schedule (Ndizeye et al. 2018; Venturas and Umeh 2017; Hoque 2016; Audu et al. 2014; Tchounga et al. 2014; Wamai et al. 2013; Remes et al. 2012; Makwe and Anorlu 2011; Urasa and Darj 2011). When the HPV vaccine was not widely available, the proportion of health workers with optimal knowledge about the safety and effectiveness of the HPV vaccine ranged from 13% among nurses in Nigeria (Makwe and Anorlu 2011) to 55% among general practitioners in Burundi (Ndizeye et al. 2018). However, this increased to 78.9% when the HPV vaccine was available through demonstration projects (Wamai et al. 2013). Health workers' limited knowledge about the safety of the HPV vaccine was reported to negatively impact on their acceptance of the vaccine for their adolescent daughters as well as their ability to recommend the vaccine to their clients (Venturas and Umeh 2017; Hoque 2016; Audu et al. 2014; Wamai et al. 2013; Makwe and Anorlu 2011). In a study conducted in Cameroon where an HPV vaccine demonstration project was ongoing, 69.7% of nurses surveyed, indicated that they often recommended the vaccine to their clients. However, 63.9% of these nurses remained concerned about the potential side effects of the vaccine (Wamai et al. 2013). Poor access to appropriate training was cited as the primary reason for the suboptimal level of knowledge about HPV infection, cervical cancer and HPV immunization, among health workers in sub-Saharan African countries (Venturas and Umeh 2017; Tchounga et al. 2014; Urasa and Darj 2011).

Where health workers received adequate training, it was reported that they were capable of providing sound recommendations about the HPV vaccine to clients, thereby positively influencing acceptance and uptake of the vaccine (Odunyemi et al. 2018; Chigbu et al. 2017; Katz et al. 2013). Additional facilitators of HPV immunization programs included the involvement of well-trained school health teams as well as community health workers who were reported to play a key role in health promotion and social mobilization for HPV immunization (Watson-Jones et al. 2015; Moodley et al. 2013).

The availability of potent vaccines, cold chain and logistics systems

Research evidence on how the availability of the HPV vaccine, and the capacity of cold chain and logistics systems (for vaccine delivery, transport, and storage), impact on the performance of HPV immunization programs in sub-Saharan Africa was rather limited. Studies conducted by Okunade et al. (2017) and Ugwu et al. (2013) addressed the limited availability of the HPV vaccine and how this served as a barrier to acceptance and uptake of the vaccine in Nigeria. At the time both studies were conducted, the HPV vaccine was not widely available to the general population but was provided through the private health sector at a cost (Okunade et al. 2017; Ugwu et al. 2013). With regards to cold chain and logistics systems, Torres-Reuda et al. (2015) reported that the Rwandan NIP conducted a cold chain inventory to assess the capacity of the system prior to

the introduction of the HPV vaccine. This formed part of the planning and training implemented in advance of introducing the HPV vaccine into the NIP.

The quality of health service delivery

There was much in the literature about the health systems constraints and facilitators to accessing quality health services that are safe, people-centred, integrated and efficient, and how this impacts on the performance of HPV immunization programs in sub-Saharan Africa (*see Table 3*). Studies exploring the most efficient and effective HPV vaccine delivery models were well represented in the evidence-base (Msyamboza et al. 2017; Botwright et al. 2017; Watson-Jones et al. 2015; Ladner et al. 2014; Ogembo et al. 2014; Moodley et al. 2013; Levin et al. 2013; Ladner et al. 2012; Hutubessy et al. 2012; Quentin et al. 2012; LaMontagne et al. 2011). Two main HPV vaccine delivery models, namely, the school-based and the health facility-based vaccine delivery strategies were explored. Overall, the findings were consistent, suggesting that adopting a school-based vaccine delivery strategy where eligibility to receive the vaccine was based on school grade or class and not on the age of the recipient, was the most effective model (Msyamboza et al. 2017; Mugisha et al. 2015; Ladner et al. 2014; Moodley et al. 2013; Ladner et al. 2012; LaMontagne et al. 2011). This is because, the school-based strategy was reported to achieve higher HPV immunization coverage rates compared to the health facility-based strategy (Mugisha et al. 2015; Ladner et al. 2014; Ladner et al. 2012; LaMontagne et al. 2011).

Several challenges to delivering the HPV vaccine through the school-based strategy in sub-Saharan Africa have been documented however, and these include, absenteeism, high school dropout rates among girls, and girls transferring out of the district at the time of the immunization programs (Msyamboza et al. 2017). Physical barriers to accessing the HPV vaccine through schools have also been reported in some hard-to-reach communities in Kenya. These barriers have been associated with non-attendance or delayed enrolment in schools because of long distances (up to 10km) and safety concerns with possibly encountering wildlife on the way to school (Watson-Jones et al. 2015). In areas like this, where road networks are poorly developed or unsafe, vaccinators have been reported to experience difficulty in accessing schools in order to provide HPV immunization (Masika et al. 2015). To mitigate these challenges, a mixed vaccine delivery model is highly recommended in the literature and involves coupling the school-based strategy with community outreach immunization campaigns. This mixed vaccine delivery model has been shown to be feasible in sub-Saharan Africa, expanding the reach of HPV immunization programs, improving adherence to the immunization schedule, and scaling-up immunization coverage rates (Msyamboza et al. 2017; Ogembo et al. 2014; Ladner et al. 2012).

It was evident from the studies reviewed that the introduction of the HPV vaccine has exposed gaps in the development of adolescent and school health services in sub-Saharan Africa. This has been considered in the evidence-base as a constraint to HPV immunization programs because of the logistical challenges to providing health services to a previously underserved adolescent population and the greater resource requirements associated with creating new vaccine delivery infrastructure (Ngabo et al. 2015; Remes et al. 2012; Harries et al. 2008). A study conducted in South Africa by McPhail et al. (2013) also identified gaps in the appropriate integration of the HPV immunization program with other adolescent health services such as sex education, screening and preventive services, assistance with substance abuse and provision of other adolescent vaccines.

The state of health information systems and community partnerships

Three main dimensions were explored under this theme; (i) health information, education and communication about HPV infection, cervical cancer and HPV immunization, (ii) community partnerships during HPV immunization programs, and (iii) the generation and use of surveillance and immunization data. After reviewing the evidence-base, the state of health information systems and community partnerships emerged as the most researched theme where HPV immunization programs in sub-Saharan Africa are concerned (see *Table 2*).

Several studies were conducted to assess the level of awareness about HPV infection, cervical cancer and HPV immunization among general populations in sub-Saharan Africa. Study participants included key stakeholders like adolescents, women of reproductive age, parents or caregivers, teachers, opinion leaders, religious leaders, and university students and academics (Bardají et al. 2018; De Groot et al. 2017; Massey et al. 2017; Okunade et al. 2017; Turiho et al. 2017; Botha et al. 2015; Hoque 2015; Masika et al. 2015; Morhason-Bello et al. 2015; Vermandere et al. 2015; Turiho et al. 2014; Vermandere et al. 2014; Hoque et al. 2013; MacPhail et al. 2013; Poole et al. 2013; Ports et al. 2013; Ayissi et al. 2012; Remes et al. 2012; Watson-Jones et al. 2012; Coleman et al. 2011; Francis et al. 2011; DiAngi et al. 2011; Francis et al. 2010). Majority of these studies found that the level of awareness among the general population was rather limited. With the exception of university academics, the proportion of the general population found to be aware of HPV infection, cervical cancer, and the HPV vaccine was generally low, and ranged from 8.6% to 36.5%, 61% to 87%, and 0% to 40%, respectively (Okunade et al. 2017; De Groot et al. 2017; Massey et al. 2017; Friedman et al. 2014; Ports et al. 2013; Remes et al. 2012; Coleman et al. 2011; DiAngi et al. 2011; Francis et al. 2010). In comparison, the highest level of awareness about HPV (100%) and cervical cancer (96%) was recorded among university academics (Hoque 2015).

The low level of awareness demonstrated among the general population was reported to fuel misconceptions about the safety and benefits of the HPV vaccine. Some misconceptions about the potential side effects of the vaccine included infertility and death, while some feared that introduction of the vaccine would promote promiscuity and early sexual debut among adolescent girls (Morhason-Bello et al. 2015; Ogembo et al. 2014; Watson-Jones et al. 2012). Other studies also reported that some participants believed that the HPV vaccine would prevent HIV and pregnancy, or even safeguard the fertility of adolescent girls (Turiho et al. 2017; Vermandere et al. 2015). Ultimately, low level of awareness was a major constraint to the acceptance and uptake of the HPV vaccine in sub-Saharan Africa (Vermandere et al. 2014). When intensive social mobilization and community sensitization interventions were implemented to provide culturally appropriate information about the risks of cervical cancer and the safety and effectiveness of the HPV vaccine (often as part of vaccine demonstration projects; *see Figure 3*), an increase in vaccine acceptance and uptake was reported (Bardaji et al. 2018; De Groot et al. 2017; Botha et al. 2015; Hoque 2015; Masika et al. 2015; Vermandere et al. 2015; Turiho et al. 2014; Ports et al. 2013; Ayissi et al. 2012; Coleman et al. 2011; DiAngi et al. 2011). Participants also identified health workers as their most trusted source of information about the HPV vaccine (Massey et al. 2017; Ports et al. 2013; Ayissi et al. 2012). Engaging key stakeholders like adolescents (both males and females), parents (including fathers) or caregivers, municipal and religious leaders, and school teachers, at the onset of HPV immunization programs was considered as a major facilitator to vaccine acceptance and uptake (Masika et al. 2015; Vermandere et al. 2015; Ogembo et al. 2014; Ports et al. 2013).

Very few studies reported on how the generation and use of surveillance and immunization data (including immunization coverage data) impacted on the performance of HPV immunization programs in sub-Saharan Africa. Where studies explored this dimension, the evidence found was rather limited. For example, a study conducted to assess the capacity of school health teams to carry out future HPV immunization in schools within the KwaZulu Natal province of South Africa, found that the reliance on paper-based vaccine records would be a major constraint to real-time monitoring and evaluation of the immunization program. To mitigate this challenge, the use of electronic data capturing methods was recommended (Moodley et al. 2013). In addition to this, Torres-Rueda et al. (2015) highlighted the importance of strengthening the surveillance of adverse events following immunization in Rwanda where a nationwide HPV immunization program was already in existence (*see Figure 3*).

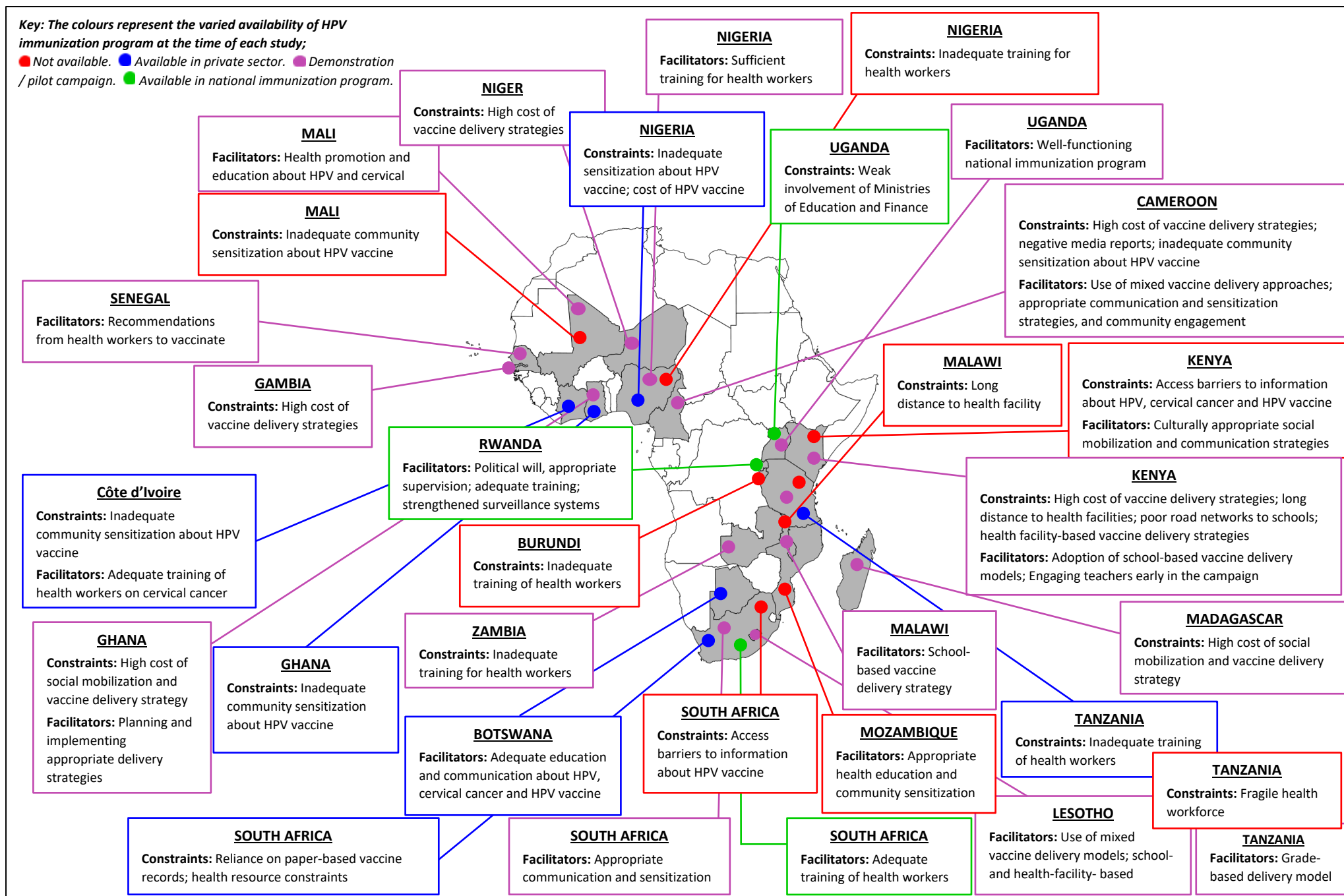


Figure 3: Summary of health systems constraints and facilitators of HPV immunization programs in sub-Saharan Africa [Source; Author, (drawing on studies included in the systematic review)]

The availability of equitable and sustainable health financing

The final theme examined national health financing mechanisms in sub-Saharan Africa, including the availability of equitable and sustainable financing mechanisms for HPV immunization programs. Research evidence on this theme was found to be limited. None of the studies included in the review addressed any dedicated financing mechanisms earmarked for the introduction and sustainable delivery of the HPV vaccine. Instead, the available evidence on financing was mainly focussed on determining the economic and financial costs of social mobilization campaigns and HPV vaccine delivery models (Botwright et al. 2017; Ngabo et al. 2015; Levin et al. 2013; Hutubessy et al. 2012; Quentin et al. 2012).

With the exception of South Africa, HPV vaccine procurement costs were largely covered by external funding sources (from organizations like GAVI, Program for Appropriate Technology in Health, and the Gardasil Access Program), in countries where the HPV immunization program had been implemented as part of demonstration projects or NIPs (Botwright et al. 2017; Ngabo et al. 2015; Mugisha et al. 2015; Ladner et al. 2014). In most cases, national governments are expected to co-finance the cost of delivering the vaccine. However, this was a major constraint to implementing HPV immunization programs, given that the financial cost of introducing and delivering the HPV vaccine was significantly higher than that of routine childhood vaccines (Ngabo et al. 2015; Levin et al. 2013). Reasons given for this included the fact that the infrastructure for delivering vaccines to adolescents was largely underdeveloped prior to the introduction of the HPV vaccine in sub-Saharan Africa. As such financial costs were reported to be higher in countries that could not leverage existing immunization infrastructure and had greater resource requirements (Botwright et al. 2017; Ngabo et al. 2015).

It was reported that a substantial cost component was required to train health workers, cover per diems, organize effective social mobilization and community sensitization campaigns, and deliver the vaccine through the school-based strategy (Botwright et al. 2017; Ngabo et al. 2015; Levin et al. 2013; Hutubessy et al. 2012). With regards to the school-based vaccine delivery strategy, adopting an age-based eligibility approach was found to be a constraint to HPV immunization programs as it was less cost-effective compared to the grade-based approach (Quentin et al. 2012). However, delivering the HPV vaccine through health facilities incurred lower economic costs compared to the school-based strategy, but achieved lower immunization coverage rates (Levin et al. 2013). To offset the cost of delivering the HPV vaccine, some countries charged a fee for immunization, while in other countries, the vaccine was only available through the private health sector at unaffordable costs (Odunyemi et al. 2018; Okunade et al. 2017; Umeh et al. 2016; Ogembo et al. 2014; Ugwu et al. 2013). In these countries, socioeconomic constraints to accessing the HPV vaccine negatively impacted on vaccine acceptance and uptake.

Discussion

There is growing consensus that the success of key health programs in achieving improved population health is highly dependent on the performance of their health systems (Balabanova et al. 2010; Travis et al. 2004). In this regard, previous systematic reviews have assessed the health systems constraints and facilitators to the effective performance of several health programs, such as those targeted at HIV anti-retroviral treatment, prevention of mother-to-child transmission of HIV, and the prevention and control of breast cancer, as well as other chronic diseases (Bowser et al. 2017; Watt et al. 2017; Colvin et al. 2014). The primary intent of these reviews is to build up the evidence-base required to inform health systems strengthening efforts. This has been spurred by the realization that strong health systems are able to withstand acute shocks or avoid them altogether, in order to provide health programs with the support they require to be effective (Wang et al. 2013; Hanvoravongchai et al. 2011; Balabanova et al. 2010; Travis et al. 2004). To date, no rigorous systematic evidence exists on the health systems constraints and facilitators of NIPs, especially from the sub-Saharan African region.

At the World Health Assembly held in May 2012, 194 member states endorsed the Global Vaccine Action Plan. One of the visions of the Global Vaccine Action Plan is to advance universal access to immunization between 2011 and 2020 (WHO 2015; WHO 2013b). To date, regional efforts have been heavily focussed on routine childhood immunization programs which have achieved remarkable public health success within the subcontinent (Machingaidze et al. 2013; Arevshatian et al. 2007). However, if sub-Saharan Africa is to have a chance of achieving the vision of the Global Vaccine Action Plan, countries will have to scale-up the performance of existing immunization programs, introduce and improve the uptake of underused vaccines and extend access to lifesaving vaccines to underserved and hard-to-reach populations (Bonner et al. 2018; Nanni et al. 2017; WHO 2013b). Scaling-up HPV immunization programs, which target the adolescent population, presents a unique opportunity to contribute to attaining the vision of the Global Vaccine Action Plan. In this regard, Nanni et al. (2017) advocate for “global consensus, political will, policies, global and country infrastructure, and financing mechanisms” in order to accelerate universal access to the HPV vaccine for adolescent populations in low- and middle- income regions like sub-Saharan Africa. To facilitate this, it is important to provide decision-makers with robust systematic evidence of what works (*and what does not work*) for HPV immunization programs in sub-Saharan Africa, especially where health systems are concerned.

The findings of this systematic review are in agreement with the recommendations made by Nanni et al. (2017). In sub-Saharan African countries like Uganda where national governments have strongly endorsed the HPV vaccine and have made concerted efforts through national policy to ensure that the vaccine is widely available to the population, HPV immunization programs have been successfully implemented as part of NIPs,

and vaccine acceptance and uptake has significantly improved (Kamya et al. 2017; Mugisha et al. 2015). Global infrastructure for HPV immunization programs have typically come in the form of external funding, and expert and technical support from organizations like GAVI, Program for Appropriate Technology in Health, and the Gardasil Access Program (Botwright et al. 2017; Mugisha et al. 2015; Ngabo et al. 2015; Ladner et al. 2014). The support of these global partners has been instrumental in facilitating the introduction of HPV immunization programs in sub-Saharan Africa, either through demonstration projects or NIPs (Gallagher et al. 2018; Gallagher et al. 2017b; Ladner et al. 2014; Oluwole and Kraemer 2013). While these health systems facilitators have achieved some progress for HPV immunization programs in sub-Saharan Africa, the region continues to fall short in meeting global targets for implementing HPV immunization programs. In addition to this, HPV immunization coverage rates in sub-Saharan Africa are recorded among the lowest in the world (Gallagher et al. 2018; LaMontagne et al. 2017; Gallagher et al. 2017a; Bruni et al. 2016). These persistent challenges may be the result of significant health systems constraints in sub-Saharan Africa, as has been suggested previously (SAGE 2016; Wigle et al. 2013; Bello et al. 2011).

The most recurrent health systems constraint identified by this systematic review was the low level of knowledge and awareness on HPV infection, risk of cervical cancer, and the safety and effectiveness of the HPV vaccine, among general populations in sub-Saharan Africa. This finding is highly relevant given the well-established link between levels of knowledge, awareness and attitudes towards the HPV vaccine, and vaccine acceptance and uptake (Maseko et al. 2015; Hopkins and Wood 2013; Garcini et al. 2012; Kessels et al. 2012). The gap identified in the level of knowledge and awareness among the general population is not unique to the sub-Saharan Africa context and has been reported in other parts of the world where HPV immunization programs have long been in existence (Cartmell et al. 2018; Hendry et al. 2013). Nonetheless, this calls into question the effectiveness of existing HPV vaccine communication strategies in sub-Saharan Africa. Key stakeholders, including adolescents and their caregivers, depend on reliable communication in order to make informed decisions about lifesaving HPV vaccines and take ownership of their health (Bonner et al. 2018). Evidently, there is a need to strengthen health systems in sub-Saharan Africa by reinforcing the role of health promotion activities, especially where HPV immunization programs are concerned. Where intensified social mobilization and community sensitization campaigns have been implemented, this was shown to increase the demand for the HPV vaccine. In addition to this, the importance of designing culturally appropriate communication strategies which are also accessible to populations living in hard-to-reach communities, was emphasized in the literature (Watson-Jones et al. 2015; Friedman et al. 2014).

The limited capacity of health workers was identified as another major health systems constraint to the performance of HPV immunization programs in sub-Saharan Africa. Overall, health workers demonstrated

suboptimal levels of knowledge and awareness about HPV infection, risk of cervical cancer, and the safety and effectiveness of the HPV vaccine. These findings are consistent with those reported in other resource limited settings (Chawla et al. 2016; Ali et al. 2010; Nganwai et al. 2008). In contrast, reports from some high resource settings indicate high levels of knowledge and awareness about HPV infection, cervical cancer and the HPV vaccine, among health workers (Rosen et al. 2018). This is a matter of major public health concern in sub-Saharan Africa, given that cadres like nurses and community health workers are at the frontline of HPV immunization programs and have been identified as the most trusted source of information on HPV immunization (Massey et al. 2017; Watson-Jones et al. 2015; Ports et al. 2013; Ayissi et al. 2012). There is a need, therefore, to reinforce the capacity of health workers in sub-Saharan Africa. This can be achieved through continued training and education to ensure that health workers can provide sound vaccine recommendations to their clients.

Historically, adolescents have not been the 'typical' client-base of most health systems. However, with the introduction of HPV immunization programs, this notion is beginning to change (Nanni et al. 2017; MacPhail et al. 2013; Ladner et al. 2012). This systematic review has found that poorly developed adolescent and school health services present a significant challenge to effectively delivering HPV vaccines in sub-Saharan Africa. This is further compounded by weak country infrastructure, including underdeveloped and unsafe road networks, as well as geographically inaccessible schools and health facilities, which create physical barriers to reaching target populations with the HPV vaccine (Msyamboza et al. 2017; Watson-Jones et al. 2015; Masika et al. 2015). A review by Sankaranarayanan et al. (2012) which sought to address the infrastructure requirements for HPV immunization programs in sub-Saharan Africa found that although leveraging existing NIP resources (for example human resources and cold chain and logistics systems) could improve the performance of HPV immunization programs, greater investments in infrastructure are still needed. This calls for intersectoral collaboration within national governments, involving relevant Ministries like Health, Education and Finance. Improving adolescent and school health services to support HPV immunization programs and administration of other adolescent vaccines also deserves particular attention in the health policy agenda in sub-Saharan Africa (Nanni et al. 2017).

Finally, this review found that significant financial constraints impact on the introduction of HPV immunization programs and the delivery of the vaccine to adolescents in sub-Saharan Africa. The HPV vaccine is more costly than other routine childhood vaccines. In addition, the HPV vaccine delivery models incur higher financial and economic costs when compared to routine childhood immunization programs (Ngabo et al. 2015; Levin et al. 2013). These financial barriers are intensified when considered in light of unique sub-Saharan African contextual issues, such as the limited health budgets of some national governments and the high burden of

diseases which has given rise to multiple health programs (such as those targeting malaria, HIV, and other vaccine preventable diseases) competing for the limited resources (Bello et al. 2011). Altogether, these financial constraints significantly obstruct the widespread implementation of HPV immunization programs in sub-Saharan Africa (Gallagher et al. 2018). While substantial investments have been made by global partners, co-financing commitments make HPV vaccine introduction unaffordable for some national governments in sub-Saharan Africa (Gallagher et al. 2018). Increasing national investments in HPV immunization programs will require reforms in health policy, although this will have to be informed by country-specific evidence on the resources need and the most effective financing mechanisms to be adopted.

In 2019, other sub-Saharan African countries like Ethiopia, Kenya, Malawi and Nigeria will be looking to introduce HPV immunization programs nationwide (*see Appendix 1*). While this will be an impressive move towards expanding access to lifesaving HPV vaccines within the region, it is important that key decision-makers take into consideration the health systems constraints and facilitators presented in this review. Countries could draw on the health systems facilitators to well-performing HPV immunization programs in developing country-specific standards and guidelines for their immunization programs. The findings on health systems constraints also serve as a set of 'lessons learned' for HPV immunization programs in sub-Saharan Africa so far, and could be used to inform interventions to scale-up the performance of existing immunization programs or to guide the implementation of new HPV immunization programs where necessary.

Although this systematic review assessed health systems constraints and facilitators to HPV immunization programs, the findings have significant relevance for scaling-up NIPs in general. The major health systems constraints and facilitators pertaining to service delivery, the health workforce, vaccine communication and community partnerships, as well as governance and policy are applicable to almost all services delivered through NIPs. For example, barriers to accessing vaccines due to ineffective service delivery, staff shortages, lack of awareness about vaccines, weak engagement with key populations, as well as poor governance and policy structures have all been suggested to negatively impact on the performance of NIPs in most LMICs, and the findings of this review are in support of this (Mihigo et al. 2017; SAGE, 2016; Shen et al. 2014). What has not been sufficiently addressed in the existing literature is how to overcome these constraints and strengthen broader health systems to support NIPs in performing their functions. In addition to this, detailed considerations of the cost effectiveness of strengthening the broader health system in anticipation of scaling-up NIP performance is scarce. This systematic review provides evidence on health systems facilitators which can be leveraged in developing interventions to mitigate some of the system-wide barriers to scaling-up NIPs. It is important to caution, however, that HPV immunization programs have some unique characteristics when compared with other NIP activities. First, HPV immunization programs are targeted at the adolescent

population while most NIP services have typically been focused on infants and children. Secondly, the vaccine delivery models for HPV immunization programs are also different from those typically used in other NIP services. As such certain variations exist in terms of some of the health systems functions needed to support HPV immunization programs compared to routine childhood immunization services, as discussed previously. Despite this, NIPs are beginning to evolve towards a 'life-course approach' to immunization by expanding target age groups and extending immunization services to adolescents and adults who have been previously underserved (Langley 2015; Mehta 2014). In this regard, the findings of this systematic review could be useful for informing health systems strengthening initiatives to support the expanding scope of NIPs, especially in sub-Saharan Africa.

This review has some limitations which include the geographical restriction to countries within the sub-Saharan African region. The findings and recommendations of the review may not be generalizable to parts of the world that do not share similar contexts with sub-Saharan Africa. The language restriction applied during the search strategy is another limitation as relevant studies conducted and published from non-Anglophone countries may have been missed. It is also worth noting that most studies on knowledge and awareness were based on self-reporting and might be subject to reporting bias. Finally, the use of HPV immunization programs as a proxy for NIPs may not give a comprehensive assessment given some of the programmatic differences with other routine childhood immunization programs. The generalizability of the findings of this systematic review for other NIP services may therefore require further investigation, adapting and using the logic model on the interface between NIPs and health systems.

Conclusion

This systematic review provides evidence of how NIPs and health systems interact by reporting on the health systems constraints and facilitators of NIPs in sub-Saharan Africa. In addition, the findings show how these system-wide constraints and facilitators impact on the performance of NIPs. There is evidence to suggest that NIPs in sub-Saharan Africa have surmounted significant health systems constraints and have achieved notable public health success. This success can be attributed to strong political endorsement for vaccines, clear governance structures and effective collaboration with global partners. Despite this, important health systems constraints persist and could derail further progress if not addressed through health systems strengthening efforts. Gaps in the evidence-base pertaining to cold chain and logistics systems, data generation and use, as well as national financing mechanisms needed to sustain NIPs in sub-Saharan Africa were also identified. This calls for an expansion of the research agenda, not only to address these gaps, but to also continuously evaluate health systems constraints and facilitators of NIPs in sub-Saharan Africa.

The findings of this review are relevant to ongoing health systems strengthening initiatives in sub-Saharan Africa. By enhancing our understanding of what works – *and does not work* – for NIPs, health systems strengthening initiatives could be better designed to adequately respond to the burden of vaccine preventable diseases in sub-Saharan Africa.

References

- Ali SF, Ayub S, Manzoor NF et al. 2010. Knowledge and awareness about cervical cancer and its prevention amongst interns and nursing staff in tertiary care hospitals in Karachi, Pakistan. *PLoS One* **5**:e11059.
- Arevshatian L, Clements CJ, Lwanga SK et al. 2007. An evaluation of infant immunization in Africa: Is a transformation in progress? *Bulletin of The World Health Organization* **85**:449-457.
- Audu BM, Bukar M, Ibrahim AI et al. 2014. Awareness and perception of human papilloma virus vaccine among healthcare professionals in Nigeria. *Journal of Obstetrics and Gynaecology* **34**:714-717.
- Ayissi C, Wamai R, Oduwo G et al. 2012. Awareness, acceptability and uptake of human papilloma virus vaccine among Cameroonian school-attending female adolescents. *Journal of Community Health* **37**:1127-1135.
- Balabanova D, McKee M, Mills A et al. 2010. What can global health institutions do to help strengthen health systems in low income countries? *Health Research Policy and Systems* **8**:22.
- Bardají A, Mindu C, Augusto OJ et al. 2018. Awareness of cervical cancer and willingness to be vaccinated against human papillomavirus in Mozambican adolescent girls. *Papillomavirus Research* **5**:156-162.
- Bello FA, Enabor OO, Adewole IF. 2011. Human papilloma virus vaccination for control of cervical cancer: A challenge for developing countries. *African Journal of Reproductive Health* **15**:25-30.
- Bonner K, Banura C, Basta NE. 2018. HPV vaccination strategies targeting hard-to-reach populations: Out-of-school girls in LMICs. *Vaccine* **36**:191-193.
- Botha MH, van der Merwe, F H, Snyman LC et al. 2015. The vaccine and cervical cancer screen (VACCS) project: Acceptance of human papillomavirus vaccination in a school-based programme in two provinces of South Africa. *South African Medical Journal* **105**:40-43.
- Botwright S, Holroyd T, Nanda S et al. 2017. Experiences of operational costs of HPV vaccine delivery strategies in Gavi-supported demonstration projects. *PLoS One* **12**:e0182663.
- Bowser D, Marqusee H, El Koussa M, Atun R. 2017. Health system barriers and enablers to early access to breast cancer screening, detection, and diagnosis: A global analysis applied to the MENA region. *Public Health* **152**:58-74.
- Bruni L, Diaz M, Barrionuevo-Rosas L et al. 2016. Global estimates of human papillomavirus vaccination coverage by region and income level: A pooled analysis. *Lancet Global Health* **4**:e463.
- Cartmell KB, Young-Pierce J, McGue S et al. 2018. Barriers, facilitators, and potential strategies for increasing HPV vaccination: A statewide assessment to inform action. *Papillomavirus Research* **5**:21-31.
- Chan ZCY. 2013. A systematic review of critical thinking in nursing education. *Nurse Education Today* **33**:236-240.
- Chawla PC, Chawla A, Chaudhary S. 2016. Knowledge, attitude & practice on human papillomavirus vaccination: A cross-sectional study among healthcare providers. *The Indian Journal of Medical Research* **144**:741-749.
- Chee G, Pielemeier N, Lion A et al. 2013. Why differentiating between health system support and health system strengthening is needed. *The International Journal of Health Planning and Management* **28**:85-94.
- Chigbu CO, Onyebuchi AK, Onyeka TC et al. 2017. The impact of community health educators on uptake of cervical and breast cancer prevention services in Nigeria. *International Journal of Gynecology and Obstetrics* **137**:319-324.
- Coleman MA, Levison J, Sangi-Haghpeykar H. 2011. HPV vaccine acceptability in Ghana, West Africa. *Vaccine* **29**:3945-3950.
- Colvin CJ, Konopka S, Chalker JC et al. 2014. A systematic review of health system barriers and enablers for antiretroviral therapy (ART) for HIV-infected pregnant and postpartum women. *PLoS One* **9**:e108150.
- De Groot AS, Tounkara K, Rochas M et al. 2017. Knowledge, attitudes, practices and willingness to vaccinate in preparation for the introduction of HPV vaccines in Bamako, Mali. *PLoS One* **12**:e0171631.

- de Martel C, Plummer M, Vignat J et al. 2017. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *International Journal of Cancer* **141**:664-670.
- De Vuyst H, Alemany L, Lacey C et al. 2013. The burden of human papillomavirus infections and related diseases in sub-Saharan Africa. *Vaccine* **31**:F46.
- Denny LA, Sankaranarayanan R, De Vuyst H et al. 2012. Recommendations for cervical cancer prevention in sub-Saharan Africa. *Vaccine* **31**:F74.
- DiAngi YT, Panozzo CA, Ramogola-Masire D et al. 2011. A cross-sectional study of HPV vaccine acceptability in Gaborone, Botswana. *PLoS One* **6**:e25481.
- Francis SA, Battle-Fisher M, Liverpool J et al. 2011. A qualitative analysis of South African women's knowledge, attitudes, and beliefs about HPV and cervical cancer prevention, vaccine awareness and acceptance, and maternal-child communication about sexual health. *Vaccine* **29**:8760-8765.
- Francis SA, Nelson J, Liverpool J et al. 2010. Examining attitudes and knowledge about HPV and cervical cancer risk among female clinic attendees in Johannesburg, South Africa. *Vaccine* **28**:8026-8032.
- Friedman AL, Oruko KO, Habel MA et al. 2014. Preparing for human papillomavirus vaccine introduction in Kenya: Implications from focus-group and interview discussions with caregivers and opinion leaders in Western Kenya. *BMC Public Health* **14**:855.
- Gallagher KE, LaMontagne DS, Watson-Jones D. 2018. Status of HPV vaccine introduction and barriers to country uptake. *Vaccine* **36**:4761-4767.
- Gallagher KE, Howard N, Kabakama S et al. 2017a. Human papillomavirus (HPV) vaccine coverage achievements in low and middle-income countries 2007-2016. *Papillomavirus Research* **4**:72-78.
- Gallagher KE, Howard N, Kabakama S et al. 2017b. Lessons learnt from human papillomavirus (HPV) vaccination in 45 low- and middle-income countries. *PLoS One* **12**:e0177773.
- Garcini LM, Galvan T, Barnack-Tavlaris JL. 2012. The study of human papillomavirus (HPV) vaccine uptake from a parental perspective: A systematic review of observational studies in the United States. *Vaccine* **30**:4588-4595.
- Garland SM, Kjaer SK, Muñoz N et al. 2016. Impact and effectiveness of the quadrivalent human papillomavirus vaccine: A systematic review of 10 years of real-world experience. *Clinical Infectious Diseases* **63**:519-527.
- Goeman L, Galichet B, Porignon DG et al. 2010. The response to flexibility: Country intervention choices in the first four rounds of the GAVI Health Systems Strengthening applications. *Health Policy and Planning* **25**:292-299.
- Hanvoravongchai P, Mounier-Jack S, Oliveira Cruz V et al. 2011. Impact of measles elimination activities on immunization services and health systems: Findings from six countries. *The Journal of Infectious Diseases* **204**:S89.
- Harries J, Moodley J, Barone MA et al. 2008. Preparing for HPV vaccination in South Africa: Key challenges and opinions. *Vaccine* **27**:38-44.
- Hendry M, Lewis R, Clements A et al. 2013. "HPV? Never heard of it!": A systematic review of girls' and parents' information needs, views and preferences about human papillomavirus vaccination. *Vaccine* **31**:5152-5167.
- Herrero R, González P, Markowitz LE. 2015. Present status of human papillomavirus vaccine development and implementation. *Lancet, Oncology* **16**:e216.
- Hopkins TG, Wood N. 2013. Female human papillomavirus (HPV) vaccination: Global uptake and the impact of attitudes. *Vaccine* **31**:1673-1679.
- Hoque ME. 2016. Factors influencing the recommendation of the human papillomavirus vaccine by South African doctors working in a tertiary hospital. *African Health Sciences* **16**:567-575.
- Hoque ME. 2015. Acceptability of human papillomavirus vaccination among academics at the University of KwaZulu-Natal, South Africa. *South African Family Practice* **57**:318-321.
- Hoque ME, Ghuman S, Hal GV. 2013. Human papillomavirus vaccination acceptability among female university students in South Africa. *Asian Pacific Journal of Cancer Prevention* **14**:4865-4869.
- Hutubessy R, Levin A, Wang S et al. 2012. A case study using the United Republic of Tanzania: Costing nationwide HPV vaccine delivery using the WHO Cervical Cancer Prevention and Control Costing Tool. *BMC Medicine* **10**:136.
- Kamya C, Shearer J, Asiimwe G et al. 2017. Evaluating global health partnerships: A case study of a Gavi HPV vaccine application process in Uganda. *International Journal of Health Policy and Management* **6**:327-338.

- Kane GA, Wood VA, Barlow J. 2007. Parenting programmes: A systematic review and synthesis of qualitative research. *Child: Care, Health and Development* **33**:784-793.
- Katz IT, Nkala B, Dietrich J et al. 2013. A qualitative analysis of factors influencing HPV vaccine uptake in Soweto, South Africa among adolescents and their caregivers. *PLoS ONE* **8**:e72094.
- Kessels SJM, Marshall HS, Watson M et al. 2012. Factors associated with HPV vaccine uptake in teenage girls: A systematic review. *Vaccine* **30**:3546-3556.
- Ladner J, Besson M, Rodrigues M et al. 2014. Performance of 21 HPV vaccination programs implemented in low and middle-income countries, 2009-2013. *BMC Public Health* **14**:670.
- Ladner J, Besson M, Hampshire R et al. 2012. Assessment of eight HPV vaccination programs implemented in lowest income countries. *BMC Public Health* **12**:370.
- LaMontagne DS, Barge S, Le NT et al. 2011. Human papillomavirus vaccine delivery strategies that achieved high coverage in low- and middle-income countries. *Bulletin of the World Health Organization* **89**:830B.
- LaMontagne DS, Bloem PJN, Brotherton JML et al. 2017. Progress in HPV vaccination in low- and lower-middle-income countries. *International Journal of Gynecology and Obstetrics* **138**:7-14.
- Langley JM. 2015. Adolescent immunization – protecting youth and preparing them for a healthy future. *International Journal of Pediatrics and Adolescent Medicine* **2**:1-6.
- Levin CE, Van Minh H, Odaga J et al. 2013. Delivery cost of human papillomavirus vaccination of young adolescent girls in Peru, Uganda and Viet Nam. *Bulletin of The World Health Organization* **91**:585-592.
- Louie KS, de Sanjose S, Mayaud P. 2009. Epidemiology and prevention of human papillomavirus and cervical cancer in sub-Saharan Africa: A comprehensive review. *Tropical Medicine and International Health* **14**:1287-1302.
- Lu B, Kumar A, Castellsague X et al. 2011. Efficacy and safety of prophylactic vaccines against cervical HPV infection and diseases among women: A systematic review and meta-analysis. *BMC Infectious Diseases* **11**:13.
- Machingaidze S, Wiysonge CS, Hussey GD. 2013. Strengthening the expanded programme on immunization in Africa: Looking beyond 2015. *PLoS Medicine* **10**:e1001405.
- MacPhail C, Venables E, Rees H et al. 2013. Using HPV vaccination for promotion of an adolescent package of care: Opportunity and perspectives. *BMC Public Health* **13**:493.
- Makwe CC, Anorlu RI. 2011. Knowledge of and attitude toward human papillomavirus infection and vaccines among female nurses at a tertiary hospital in Nigeria. *International Journal of Women's Health* **3**:313-317.
- Marchal B, Cavalli A, Kegels G. 2009. Global health actors claim to support health system strengthening - is this reality or rhetoric? *PLoS Medicine* **6**:e1000059.
- Maseko FC, Chirwa ML, Muula AS. 2015. Cervical cancer control and prevention in Malawi: Need for policy improvement. *The Pan African Medical Journal* **22**:247.
- Masika MM, Ogembo JG, Chabeda SV et al. 2015. Knowledge on HPV vaccine and cervical cancer facilitates vaccine acceptability among school teachers in Kitui County, Kenya. *PLoS ONE* **10**:e0135563.
- Massey PM, Boansi RK, Gipson JD et al. 2017. Human papillomavirus (HPV) awareness and vaccine receptivity among Senegalese adolescents. *Tropical Medicine and International Health* **22**:113-121.
- Mehta B, Chawla S, Kumar V, Jindal H, Bhatt B. 2014. Adult immunization: The need to address. *Human Vaccines and Immunotherapeutics* **10**:306–309.
- Mihigo R, Okeibunor J, Anya B et al. 2017. Challenges of immunization in the African Region. *The Pan African Medical Journal* **27**:12.
- Moodley I, Tathiah N, Mubaiwa V et al. 2013. High uptake of Gardasil vaccine among 9 - 12-year-old schoolgirls participating in an HPV vaccination demonstration project in KwaZulu-Natal, South Africa. *South African Medical Journal* **103**:318-321.
- Morhason-Bello IO, Wallis S, Adedokun BO et al. 2015. Willingness of reproductive-aged women in a Nigerian community to accept human papillomavirus vaccination for their children. *Journal of Obstetrics and Gynaecology Research* **41**:1621-1629.
- Msyamboza KP, Mwangomba BM, Valle M et al. 2017. Implementation of a human papillomavirus vaccination demonstration project in Malawi: Successes and challenges. *BMC Public Health* **17**:599.

- Mugisha E, LaMontagne DS, Katahoire AR et al. 2015. Feasibility of delivering HPV vaccine to girls aged 10 to 15 years in Uganda. *African Health Sciences* **15**:33-41.
- Nanni A, Meredith S, Gati S et al. 2017. Strengthening global vaccine access for adolescents and adults. *Vaccine* **35**:6823-6827.
- Ndizeye Z, Vanden Broeck D, Vermandere H et al. 2018. Knowledge and practices of general practitioners at district hospitals towards cervical cancer prevention in Burundi, 2015: A cross-sectional study. *Globalization and Health* **14**:4.
- Ngabo F, Levin A, Wang SA et al. 2015. A cost comparison of introducing and delivering pneumococcal, rotavirus and human papillomavirus vaccines in Rwanda. *Vaccine* **33**:7357-7363.
- Nganwai P, Truadpon P, Inpa C et al. 2008. Knowledge, attitudes and practices vis-a-vis cervical cancer among registered nurses at the Faculty of Medicine, Khon Kaen University, Thailand. *Asian Pacific Journal of Cancer Prevention: APJCP* **9**:15-18.
- Odunyemi FT, Ndikom CM, Oluwatosin OA. 2018. Effect of nursing intervention on mothers' knowledge of cervical cancer and acceptance of human papillomavirus vaccination for their adolescent daughters in Abuja - Nigeria. *Asia-Pacific Journal of Oncology Nursing* **5**:223-230.
- Ogembo JG, Manga S, Nulah K et al. 2014. Achieving high uptake of human papillomavirus vaccine in Cameroon: Lessons learned in overcoming challenges. *Vaccine* **32**:4399-4403.
- Okunade KS, Sunmonu O, Osanyin GE et al. 2017. Knowledge and acceptability of human papillomavirus vaccination among women attending the gynaecological outpatient clinics of a university teaching hospital in Lagos, Nigeria. *Journal of Tropical Medicine* **2017**:1-6.
- Oluwole D, Kraemer J. 2013. Innovative public-private partnership: A diagonal approach to combating women's cancers in Africa. *Bulletin of the World Health Organization* **91**:691-696.
- Ouzzani M, Hammady H, Fedorowicz Z et al. 2016. Rayyan - A web and mobile app for systematic reviews. *Systematic Reviews* **5**:210.
- Poole DN, Tracy JK, Levitz L et al. 2013. A cross-sectional study to assess HPV knowledge and HPV vaccine acceptability in Mali. *PLoS One* **8**:e56402.
- Ports KA, Reddy DM, Rameshbabu A. 2013. Barriers and facilitators to HPV vaccination: Perspectives from Malawian women. *Women and Health* **53**:630-645.
- Quentin W, Terris-Prestholt F, Chagalucha J et al. 2012. Costs of delivering human papillomavirus vaccination to schoolgirls in Mwanza Region, Tanzania. *BMC Medicine* **10**:137.
- Remes P, Selestine V, Chagalucha J et al. 2012. A qualitative study of HPV vaccine acceptability among health workers, teachers, parents, female pupils, and religious leaders in northwest Tanzania. *Vaccine* **30**:5363-5367.
- Rosen BL, Shepard A, Kahn JA. 2018. US health care clinicians' knowledge, attitudes, and practices regarding human papillomavirus vaccination: A qualitative systematic review. *Academic Pediatrics* **18**:S65.
- SAGE. 2016 midterm review of the global vaccine action plan. Available at: http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2016_EN.pdf.
- Samb B, Evans T, Dybul M et al. 2009. An assessment of interactions between global health initiatives and country health systems. *Lancet, The* **373**:2137-2169.
- Sankaranarayanan R, Anorlu R, Sangwa-Lugoma G et al. 2012. Infrastructure requirements for human papillomavirus vaccination and cervical cancer screening in sub-Saharan Africa. *Vaccine* **31**:F52.
- Shen AK, Fields R, McQuestion M. 2014. The future of routine immunization in the developing world: Challenges and opportunities. *Global Health, Science and Practice* **2**:381-394.
- Tchounga BK, Jaquet A, Coffie PA et al. 2014. Cervical cancer prevention in reproductive health services: Knowledge, attitudes and practices of midwives in Côte d'Ivoire, West Africa. *BMC Health Services Research* **14**:165.
- Torres-Rueda S, Rulisa S, Burchett HED et al. 2015. HPV vaccine introduction in Rwanda: Impacts on the broader health system. *Sexual and Reproductive Healthcare* **7**:46-51.
- Travis P, Bennett S, Haines A et al. 2004. Overcoming health-systems constraints to achieve the Millennium Development Goals. *Lancet, The* **364**:900-906.

- Turiho AK, Okello ES, Muhwezi WW et al. 2017. Perceptions of human papillomavirus vaccination of adolescent schoolgirls in western Uganda and their implications for acceptability of HPV vaccination: A qualitative study. *BMC Research Notes* **10**:431.
- Turiho AK, Okello ES, Muhwezi WW et al. 2014. Effect of school-based human papillomavirus (HPV) vaccination on adolescent girls' knowledge and acceptability of the HPV vaccine in Ibanda District in Uganda. *African Journal of Reproductive Health* **18**:45-53.
- Ugwu EO, Obi SN, Ezechukwu PC et al. 2013. Acceptability of human papilloma virus vaccine and cervical cancer screening among female health-care workers in Enugu, Southeast Nigeria. *Nigerian Journal of Clinical Practice* **16**:249-252.
- Umeh IB, Nduka SO, Ekwunife OI. 2016. Mothers' willingness to pay for HPV vaccines in Anambra state, Nigeria: A cross sectional contingent valuation study. *Cost Effectiveness and Resource Allocation: C/E* **14**:8.
- Urasa M, Darj E. 2011. Knowledge of cervical cancer and screening practices of nurses at a regional hospital in Tanzania. *African Health Sciences* **11**:48-57.
- Venturas C, Umeh K. 2017. Health professional feedback on HPV vaccination roll-out in a developing country. *Vaccine* **35**:1886-1891.
- Vermandere H, Naanyu V, Degomme O et al. 2015. Implementation of an HPV vaccination program in Eldoret, Kenya: Results from a qualitative assessment by key stakeholders. *BMC Public Health* **15**:875.
- Vermandere H, Naanyu V, Mabeya H et al. 2014. Determinants of acceptance and subsequent uptake of the HPV vaccine in a cohort in Eldoret, Kenya. *PLoS ONE* **9**:e109353.
- Walter FM, Emery J, Braithwaite D et al. 2004. Lay understanding of familial risk of common chronic diseases: A systematic review and synthesis of qualitative research. *Annals of Family Medicine* **2**:583-594.
- Wamai RG, Ayissi CA, Oduwo GO et al. 2013. Awareness, knowledge and beliefs about HPV, cervical cancer and HPV vaccines among nurses in Cameroon: An exploratory study. *International Journal of Nursing Studies* **50**:1399-1406.
- Wang SA, Hyde TB, Mounier-Jack S et al. 2013. New vaccine introductions: Assessing the impact and the opportunities for immunization and health systems strengthening. *Vaccine* **31**:B128.
- Watson-Jones D, Mugo N, Lees S et al. 2015. Access and attitudes to HPV vaccination amongst hard-to-reach populations in Kenya. *PLoS One* **10**:e0123701.
- Watson-Jones D, Tomlin K, Remes P et al. 2012. Reasons for receiving or not receiving HPV vaccination in primary schoolgirls in Tanzania: A case control study. *PLoS One* **7**:e45231.
- Watt N, Sigfrid L, Legido-Quigley H et al. 2017. Health systems facilitators and barriers to the integration of HIV and chronic disease services: A systematic review. *Health Policy and Planning* **32**:iv13-iv26.
- WHO. 2018a. WHO immunization, vaccines and biologicals database May 2018. Available at: <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM426457.pdf>.
- WHO. 2018b. WHO regional office for Africa. Available at: <https://www.afro.who.int/>.
- WHO. 2018c. National Immunization Programme (NIP). Available at: <http://vaccine-safety-training.org/national-immunization-programmes.html>.
- WHO. 2017a. Human papillomavirus vaccines: WHO position paper, May 2017. *Weekly Epidemiological Record* **92**:241-268.
- WHO. 2017b. Human papillomavirus vaccines: WHO position paper, May 2017 - Recommendations. *Vaccine* **35**:5753-5755.
- WHO. 2015. WHO's mission and vision in immunization and vaccines 2015-2030. Available at: http://www.who.int/immunization/documents/general/WHO_Mission_Vision_Immunization_Vaccines_2015_2030.pdf?ua=1.
- WHO. 2013a. The expanded programme on immunization. Available at: http://www.who.int/immunization/programmes_systems/supply_chain/benefits_of_immunization/en/.
- WHO. 2013b. Global Vaccine Action Plan 2011-2020. Vaccine. Available at: <https://www.unicef.org/immunization/files/GVAP.pdf>.
- WHO. 2007. Everybody's business - strengthening health systems to improve health outcomes: WHO's framework for action. Geneva, Switzerland: World Health Organization. Available at: <http://www.who.int/iris/handle/10665/43918>.

Wigle J, Coast E, Watson-Jones D. 2013. Human papillomavirus (HPV) vaccine implementation in low and middle-income countries (LMICs): Health system experiences and prospects. *Vaccine* **31**:3811-3817.

Appendix 1: Human Papillomavirus Vaccine Introduction Worldwide

Country / Territory	Income	Introduction of HPV vaccine in NIP	Year of Introduction	Comment
East Asia and Pacific				
American Samoa	UMIC	No		Partial introduction in parts of the country in 2013
Australia	HIC	Yes	2007	
Brunei Darussalam	HIC	Yes	2012	
Cambodia	LMIC	No		HPV vaccine demonstration project launched in January 2017 with intent to scale-up to a national program in 2019
China	UMIC	No		Approved for use by the Chinese Food and Drug Administration in 2016
Cook Islands		Yes	2011	
Fiji	UMIC	Yes	2013	
French Polynesia	HIC			No data found on HPV immunization program
Guam	HIC	Yes	2012	
Hong Kong SAR, China	HIC	No		HPV vaccine demonstration project launched in October 2016 for 3 years
Indonesia	LMIC	No		HPV vaccine demonstration project launched in 2016
Japan	HIC	No		HPV vaccine introduced nationwide in 2011, but suspended in 2013
Kiribati	LMIC	Yes	2011	
Korea, Democratic People's Republic	LIC	No		No nationwide HPV immunization program
Korea, Republic	HIC	Yes	2016	
Lao PDR	LMIC	No		HPV demonstration project launched in October 2013
Macao SAR, China	HIC	Yes	2013	
Malaysia	UMIC	Yes	2010	
Marshall Islands	UMIC	Yes	2008	
Micronesia, Federated States	LMIC	Yes	2009	
Mongolia	LMIC	No		HPV vaccine demonstration project rolled out between 2009 to 2013
Myanmar	LMIC	No		No nationwide HPV immunization program
Nauru	UMIC	No		No nationwide HPV immunization program
New Caledonia	HIC	Yes	2011	
New Zealand	HIC	Yes	2008	
Niue		Yes		No data found on year of HPV vaccine introduction
Northern Mariana Islands	HIC	Yes	2008	
Palau	HIC	Yes	2009	
Papua New Guinea	LMIC	No		HPV vaccine demonstration project launched in 2017
Philippines	LMIC	Yes	2016	
Samoa	UMIC	No		No nationwide HPV immunization program

Singapore	HIC	Yes	2010	
Solomon Islands	LMIC	No		HPV vaccine demonstration project launched in 2015
Taiwan, China	HIC	No		HPV vaccine demonstration project launched in 2008. Introduction announced for November 2018
Thailand	UMIC	Yes	2017	Introduced in August 2017
Timor-Leste	LMIC	No		No nationwide HPV immunization program
Tonga	UMIC	No		No nationwide HPV immunization program
Tuvalu	UMIC	No		No nationwide HPV immunization program
Vanuatu	LMIC	Yes	2015	
Vietnam	LMIC	No		HPV vaccine demonstration project rolled-out between in 2008 to 2010
Wallis and Futuna		No		No nationwide HPV immunization program
Europe and Central Asia				
Albania	UMIC	No		No nationwide HPV immunization program
Andorra	HIC	Yes	2014	
Armenia	UMIC	No		HPV vaccine demonstration project launched in 2017 for 2 years
Austria	HIC	Yes	2014	
Azerbaijan	UMIC	No		No nationwide HPV immunization program
Belarus	UMIC	No		No nationwide HPV immunization program
Belgium	HIC	Yes	2007	
Bosnia and Herzegovina	UMIC	No		No nationwide HPV immunization program
Bulgaria	UMIC	Yes	2012	
Croatia	HIC	Yes	2016	
Cyprus	HIC	Yes	2016	
Czech Republic	HIC	Yes	2012	
Denmark	HIC	Yes	2009	
Estonia	HIC	No		No nationwide HPV immunization program
Faroe Islands	HIC			No data found on HPV immunization program
Finland, Republic	HIC	Yes	2013	
France	HIC	Yes	2007	
French Guiana				Commercialized since 2007 following recommendation in France
Georgia	LMIC	No		HPV vaccine demonstration project was launched
Germany	HIC	Yes	2007	
Gibraltar	HIC	Yes	2008	
Greece	HIC	Yes	2008	
Greenland	HIC	Yes	2008	
Guernsey		Yes	2015	May have been introduced in 2015
Hungary	HIC	Yes	2014	

Iceland	HIC	Yes	2011	
Ireland	HIC	Yes	2010	
Isle of Man	HIC	Yes	2009	
Italy	HIC	Yes	2007	
Bailiwick of Jersey		Yes	2008	
Kazakhstan	UMIC	Yes	2013	
Kosovo	LMIC			No data found on HPV immunization program
Kyrgyz Republic	LMIC	No		No nationwide HPV immunization program
Latvia	HIC	Yes	2010	
Liechtenstein	HIC	Yes	2007	Approved for use in 2007
Lithuania	HIC	Yes	2016	
Luxembourg	HIC	Yes	2008	
Macedonia, FYR	UMIC	Yes	2009	
Moldova	LMIC	Yes	2012	Introduced in November 2017
Monaco	HIC	Yes	2011	
Montenegro	UMIC	No		No nationwide HPV immunization program. The HPV vaccine not been registered for use as at March 2018
Netherlands	HIC	Yes	2010	
Norway	HIC	Yes	2009	
Poland	HIC	No		No nationwide HPV immunization Program. The vaccine has been introduced in some territorial self-government Units
Portugal	HIC	Yes	2008	
Romania	UMIC	No		No nationwide HPV immunization program. Voluntary immunization campaigns held in 2008 to 2010, but campaigns were discontinued due to low acceptance and uptake
Russian Federation	UMIC	Yes	2009	
San Marino	HIC	Yes	2008	
Serbia	UMIC	No		No nationwide HPV immunization program
Slovak Republic	HIC	Yes	2014	
Slovenia	HIC	Yes	2009	
Spain	HIC	Yes	2007	
Sweden	HIC	Yes	2010	
Switzerland	HIC	Yes	2008	
Tajikistan	LIC	No		No nationwide HPV immunization program
Turkey	UMIC	No		No nationwide HPV immunization program
Turkmenistan	UMIC	Yes	2016	
Ukraine	LMIC	No		No nationwide HPV immunization program
United Kingdom	HIC	Yes	2008	
Uzbekistan	LMIC	Yes	2015	

Latin America and the Caribbean				
Anguilla	HIC	Yes	2016	Introduced in April 2016
Antigua and Barbuda	HIC	Yes	2018	Nationwide HPV immunization begun in July 2018
Argentina	HIC	Yes	2011	
Aruba	HIC	No		No nationwide HPV immunization program
Bahamas, The	HIC	Yes	2015	
Barbados	HIC	Yes	2014	
Belize	UMIC	Yes	2016	
Bolivia	LMIC	No		HPV vaccine demonstration projects rolled-out between 2009 - 2011
Brazil	UMIC	Yes	2014	
British Virgin Islands	HIC			No data found on HPV immunization program
Cayman Islands	HIC	Yes	2012	
Chile	HIC	Yes	2014	
Colombia	UMIC	Yes	2012	
Costa Rica	UMIC	No		No nationwide HPV immunization program
Cuba	UMIC	No		No nationwide HPV immunization program
Dominica	UMIC	No		No nationwide HPV immunization program
Dominican Republic	UMIC	No		HPV immunization campaign rolled-out in April 2017
Ecuador	UMIC	Yes	2015	
El Salvador	LMIC	No		No nationwide HPV immunization program
Grenada	UMIC	No		No nationwide HPV immunization program
Guatemala	UMIC	No		No nationwide HPV immunization program
Guyana	UMIC	Yes	2011	
Haiti	LIC	No		HPV vaccine demonstration projects rolled-out in 2009 - 2010 and 2018
Honduras	LMIC	Yes	2016	
Jamaica	UMIC	Yes	2017	Introduced in October 2017
Mexico	UMIC	Yes	2012	
Netherlands Antilles				No data found on HPV immunization program
Nicaragua	LMIC	No		No nationwide HPV immunization program
Panama	HIC	Yes	2008	
Paraguay	UMIC	Yes	2013	
Peru	UMIC	Yes	2011	
Puerto Rico	HIC	Yes	2006	
Sint Maarten (Dutch part)	HIC	Yes	2013	
St. Kitts and Nevis	HIC	No		No nationwide HPV immunization program. Introduction announced for 2018
St. Lucia	UMIC	No		No nationwide HPV immunization program
St. Martin (French part)	HIC			
St. Vincent and the Grenadines	UMIC	No		No nationwide HPV immunization program
Suriname	UMIC	Yes	2013	
Trinidad and Tobago	HIC	Yes	2013	

Turks and Caicos Islands	HIC			No data found on HPV immunization program
Uruguay	HIC	Yes	2013	
Venezuela, RB	UMIC	No		No nationwide HPV immunization program. Included in national immunization policy in 2015 but remains available through the NIP
Virgin Islands (U.S.)	HIC	Yes	2006	
Middle East and North Africa				
Algeria	UMIC	No		No nationwide HPV immunization program
Bahrain	HIC	No		No nationwide HPV immunization program
Djibouti	LMIC	No		No nationwide HPV immunization program
Egypt, Arab Republic	LMIC	No		No nationwide HPV immunization program
Iran, Islamic Rep.	UMIC	No		No nationwide HPV immunization program
Iraq	UMIC	No		No nationwide HPV immunization program
Israel	HIC	Yes	2013	
Jordan	UMIC	No		No nationwide HPV immunization program
Kuwait	HIC	No		No nationwide HPV immunization program
Gaza Strip	LMIC			No data found on HPV immunization program
Lebanon	UMIC	No		No nationwide HPV immunization program
Libya	UMIC	Yes	2013	
Malta	HIC	Yes	2012	
Morocco	LMIC	No		No nationwide HPV immunization program
Oman	HIC	No		No nationwide HPV immunization program
Qatar	HIC	Yes	2018	Introduced in April 2018
Saudi Arabia	HIC	No		No nationwide HPV immunization program
Syrian Arab Republic	LIC	No		No nationwide HPV immunization program
Tunisia	LMIC	No		No nationwide HPV immunization program
United Arab Emirates	HIC	Yes	2008	
West Bank	LMIC	No		No nationwide HPV immunization program
Western Sahara				No data found on HPV immunization program
Yemen, Rep.	LIC	No		No nationwide HPV immunization program
North America				
Bermuda	HIC	Yes	2016	
Canada	HIC	Yes	2007	
Guadeloupe				No data found on HPV immunization program
Martinique				No data found on HPV immunization program
Montserrat				No data found on HPV immunization program
St Pierre & Miquelon				No data found on HPV immunization program
United States	HIC	Yes	2006	
South East Asia				
Afghanistan	LIC	No		No nationwide HPV immunization program
Bangladesh	LMIC	No		HPV vaccine demonstration project launched in 2016 for 2 years

Bhutan	LMIC	Yes	2010	
India	LMIC	No		HPV vaccine demonstration project launched in 2009
Maldives	UMIC	No		No nationwide HPV immunization program
Nepal	LIC	No		HPV vaccine demonstration program was launched
Pakistan	LMIC	No		No nationwide HPV immunization program
Sri Lanka	LMIC	Yes	2017	Introduced in July 2017
Sub-Saharan Africa				
Angola	LMIC	Yes	2015	Announced for nationwide introduction in 2015
Benin	LIC	No		HPV vaccine demonstration project was launched
Botswana	UMIC	Yes	2015	
Burkina Faso	LIC	No		HPV vaccine demonstration project launched in 2015
Burundi	LIC	No		HPV vaccine demonstration project was launched
Cameroon	LMIC	No		HPV vaccine demonstration project launched between March 2010 - November 2012
Cape Verde	LMIC	No		No nationwide HPV immunization program
Central African Republic	LIC	No		No nationwide HPV immunization program
Chad	LIC	No		No nationwide HPV immunization program
Comoros	LIC	No		No nationwide HPV immunization program
Congo, Democratic Republic	LIC	No		No nationwide HPV immunization program
Congo Republic	LMIC	No		No nationwide HPV immunization program
Côte d'Ivoire	LMIC	No		HPV vaccine demonstration project launched in 2015
Equatorial Guinea	UMIC	No		No nationwide HPV immunization program
Eritrea	LIC	No		No nationwide HPV immunization program
Ethiopia	LIC	No		HPV vaccine demonstration project launched in December 2015 for 2 years. Nationwide introduction announced for 2019
Gabon	UMIC	No		No nationwide HPV immunization program
Gambia, The	LIC	No		HPV vaccine demonstration project launched in November 2014
Ghana	LMIC	No		HPV vaccine demonstration project launched in November 2013 for 2 years
Guinea	LIC	No		No nationwide HPV immunization program
Guinea-Bissau	LIC	No		No nationwide HPV immunization program
Kenya	LMIC	No		HPV vaccine demonstration project launched in 2013. Nationwide introduction announced for 2019
Lesotho	LMIC	Yes	2012	
Liberia	LIC	No		HPV vaccine demonstration project launched in April 2016
Madagascar	LIC	No		HPV vaccine demonstration project rolled-out between 2013 to 2015
Malawi	LIC	No		HPV vaccine demonstration project rolled-out between 2013 to 2016. Nationwide introduction announced for January 2019

Mali	LIC	No		HPV vaccine demonstration project was launched
Mauritania	LMIC	No		HPV vaccine demonstration project was launched
Mauritius	UMIC	Yes	2016	Announced in August 2016
Mayotte				No data found on HPV immunization program
Mozambique	LIC	No		HPV vaccine demonstration project launched in 2014
Namibia	UMIC	No		No nationwide HPV immunization program
Niger	LIC	No		HPV vaccine demonstration project rolled-out between 2013 to 2015
Nigeria	LMIC	No		HPV vaccine demonstration project was launched. Nationwide introduction planned for 2019
Réunion				No data found on HPV immunization program
Rwanda	LIC	Yes	2011	
Saint Helena				No data found on HPV immunization program
São Tomé and Príncipe	LMIC	Yes	2016	
Senegal	LIC	Yes	2016	
Seychelles	HIC	Yes	2014	
Sierra Leone	LIC	No		HPV vaccine demonstration project launched in 2012 for 2 years
Somalia	LIC	No		No nationwide HPV immunization program
South Africa	UMIC	Yes	2014	
South Sudan	LIC	No		No nationwide HPV immunization program
Sudan	LMIC	No		No nationwide HPV immunization program
Swaziland	LMIC	No		No nationwide HPV immunization program
Tanzania	LIC	Yes	2018	
Togo	LIC	No		HPV vaccine demonstration project was launched
Uganda	LIC	Yes	2012	
Zambia	LMIC	No		HPV vaccine demonstration project launched in 2013
Zimbabwe	LIC	Yes	2018	Introduced in May 2018

Source; Author, (drawing on data from <http://www.hpvcentre.net>, WHO 2018a; Gallagher et al. 2018; LaMontagne et al. 2017; Herrero et al. 2015)

Notes: NIP = National Immunization Program; LIC = Low-Income Country; LMIC = Lower Middle-Income Country; UMIC = Upper Middle-Income Country; HIC = High-income Country.

Country income ranking as defined by the World Bank (<http://data.worldbank.org/about/country-and-lending-groups>). Where the income ranking is not indicated, the information could not be confirmed.

Where nationwide HPV immunization programs have not been identified, it may be that the vaccine is available in the private health sector.

Appendix 2: Literature Search Strategy

Query #	Search Term
#1	"Immuni* Program"
#2	"National Immuni* Program" OR NIP OR "Expanded Program on Immuni*" OR EPI OR "Universal Immuni* Program" OR UIP OR Immuni* OR "Vaccination" OR "Vaccine Administration" OR Vaccine OR "Vaccine/Introduction" OR "Immuni*/Pilot*" OR "Immuni*/Demonstration Project" OR "Immuni* Program/Communication" OR "Immuni* Program/Community and Partnership" OR "Immuni* Program/Economics" OR "Immuni* Program/Finance" OR "Immuni* Program/Instrumentation" OR "Immuni* Program/Legislation" OR "Immuni* Program/Workforce" OR "Immuni* Program/Organization and Administration" OR "Immuni* Program/Management" OR "Immuni* Program/Supply and Distribution" OR "Immuni* Program/Performance" OR "Immuni* Program/Strengthen*"
#3	#1 OR #2
#4	"Health System"
#5	"Global Health" OR "Health Service" OR Hospital OR Clinic OR "School Health" OR "Adolescent Health" OR "Health Policy" OR "Health Governance" OR "Health Workforce" OR "Health Worker" OR "Health Care Worker" OR "Health Provider" OR Nurse OR "Medical Products" OR "Medical Technologies" OR "Service Delivery" OR "Health Care" OR "Health Care Delivery" OR "Health Information" OR "Health Financing" OR "Health System/Constraints" OR "Health System/Limitations" OR "Health System/Restrictions" OR "Health System/Barriers" OR "Health System/Challenges" OR "Health System/Facilitators" OR "Health System/Enablers" OR "Health System/Drivers" OR "Health System/Building Blocks" OR "Health System/Strengthen*" OR "Health System/Function*" OR "Health System/Capacity"
#6	#4 OR #5
#7	#3 AND #6
#8	"Sub-Saharan Africa" OR "West Africa" OR "East Africa" OR "Central Africa" OR "Southern Africa"
#9	Algeria OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR Cameroon OR "Cape Verde" OR "Cabo Verde" OR "Central African Republic" OR Chad OR Comoros OR Comores OR Comoro OR Congo OR "Congo-Brazzaville" OR "Congo Republic" OR "Republic of the Congo" OR "Côte d'Ivoire" OR "Democratic Republic of the Congo" OR "DR Congo" OR DRC OR "Congo-Kinshasa" OR Djibouti OR "Equatorial Guinea" OR Eritrea OR Ethiopia OR Gabon OR Gambia OR "The Gambia" OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR "Sao Tome and Principe" OR "São Tomé and Príncipe" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "South Africa" OR "South Sudan" OR Sudan OR Swaziland OR Togo OR Uganda OR "United Republic of Tanzania" OR Tanzania OR Zambia OR Zimbabwe
#10	#8 OR #9
#11	"Human Papillomavirus/Vaccine" OR "HPV/Vaccine" OR "Cervical Cancer/Vaccine" OR Gardasil OR Cervarix OR "Human Papillomavirus/Vaccination" OR "Human Papillomavirus/Immuni*" OR "HPV Vaccination" OR "HPV/Immuni*"
#12	#7 AND #10 AND #11
Filters	Abstract (Available); Full text (Available); published in last 10 years; Humans; English

Source; Author

Appendix 3: Critical Appraisal Skills Programme (CASP) Appraisal Tool



10 questions to help you make sense of qualitative research

How to use this appraisal tool

Three broad issues need to be considered when appraising a qualitative study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is “yes”, it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a “yes”, “no” or “can’t tell” to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

These checklists were designed to be used as educational pedagogic tools, as part of a workshop setting, therefore we do not suggest a scoring system. The core CASP checklists (randomised controlled trial & systematic review) were based on JAMA 'Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL, and Cook DJ), and piloted with health care practitioners.

For each new checklist a group of experts were assembled to develop and pilot the checklist and the workshop format with which it would be used. Over the years overall adjustments have been made to the format, but a recent survey of checklist users reiterated that the basic format continues to be useful and appropriate.

Referencing: we recommend using the Harvard style citation, i.e.:

Critical Appraisal Skills Programme (2017). CASP (insert name of checklist i.e. Qualitative Research) Checklist. [online] Available at: *URL*. Accessed: *Date Accessed*.

©CASP this work is licensed under the Creative Commons Attribution – Non Commercial-Share A like. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-sa/3.0/> www.casp-uk.net

Screening Questions

1. Was there a clear statement of the aims Yes Can't tell No

of the research?

HINT: Consider

What was the goal of the research?

Why it was thought important?

Its relevance

2. Is a qualitative methodology appropriate? Yes Can't tell No

HINT: Consider

If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants

Is qualitative research the right methodology for addressing the research goal?

Is it worth continuing?



Detailed questions

3. Was the research design appropriate to address the aims of the research? Yes Can't tell No

HINT: Consider

If the researcher has justified the research design (E.g. have they discussed how they decided which method to use)?

4. Was the recruitment strategy appropriate to the aims of the research?

 Yes

 Can't tell

 No

HINT: Consider

- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)

5. Was the data collected in a way that addressed the research issue?

 Yes

 Can't tell

 No

HINT: Consider

- If the setting for data collection was justified
- If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
- If the researcher has justified the methods chosen
- If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
- If methods were modified during the study. If so, has the researcher explained how and why?
- If the form of data is clear (e.g. tape recordings, video material, notes etc)
- If the researcher has discussed saturation of data

6. Has the relationship between researcher and participants been adequately considered?

 Yes

 Can't tell

 No

HINT: Consider

- If the researcher critically examined their own role, potential bias and influence during
 - (a) Formulation of the research questions
 - (b) Data collection, including sample recruitment and choice of location
- How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

7. Have ethical issues been taken into consideration? Yes Can't tell No

HINT: Consider

If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained

If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)

If approval has been sought from the ethics committee

8. Was the data analysis sufficiently rigorous? Yes Can't tell No

HINT: Consider

If there is an in-depth description of the analysis process If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data?

Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process

If sufficient data are presented to support the findings

To what extent contradictory data are taken into account
Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation

9. Is there a clear statement of findings?

 Yes

 Can't tell

 No

HINT: Consider

If the findings are explicit

If there is adequate discussion of the evidence both for and against the researchers arguments

If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst)

If the findings are discussed in relation to the original research question

10. How valuable is the research?

HINT: Consider

If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g. do they consider the findings in relation to current

practice or policy?, or relevant research-based literature?

If they identify new areas where research is necessary

If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

Appendix 4: Data Extraction Table

Study No.	Study Details			Context		Data Extraction					
	Author and Year	Title	Country	Underlying Context	Availability / Type of HPV Immunization Program	Main Theme	Health Systems Constraint	Health Systems Facilitator	Comment 1	Comment 2	Comment 3
1	Audu et al. 2015	Awareness and perception of human papilloma virus vaccine among healthcare professionals in Nigeria	Nigeria	Not Applicable	Not Available	Health Workers	Inadequate training of health workers		91.0% were aware of HPV while 44.0% knew about the HPV vaccine. 81.0% would allow their teenage daughters to be vaccinated	Reasons given for refusing HPV vaccination: lack of knowledge about the safety of the vaccine, immorality, doubt about vaccine potency	Nurses and midwives were the least aware about the HPV vaccine (p = 0.001)
2	Ayissi et al. 2012	Awareness, acceptability and uptake of human papilloma virus vaccine among Cameroonian school-attending female adolescents	Cameroon	Socio-demographic	Demonstration Project	Information / Community Engagement		Appropriate communication and sensitization strategies	34.2% of the respondents had been vaccinated against HPV infection	75.9% were aware that that HPV vaccine is important in preventing HPV infections and cervical cancer	62.9% heard about HPV from a nurse. There was a high acceptability of HPV vaccination
3	Bardaji et al. 2018	Awareness of cervical cancer and willingness to be vaccinated against human papillomavirus in Mozambican adolescent girls	Mozambique	Not Applicable	Demonstration Project	Information / Community Engagement		Appropriate health education and sensitization about HPV vaccine	Increased acceptability of HPV vaccine among adolescent girls was associated with level of education		
4	Botha et al. 2015	The Vaccine and Cervical Cancer Screen (VACCS) project: Acceptance of human papillomavirus vaccination in a school-based programme in two provinces of South Africa	South Africa	Socio-economic	Demonstration Project	Information / Community Engagement		Appropriate communication and sensitization strategies	High acceptance rate following better information underlines the importance of clear, direct communication with parents	Parents who received complete information on the HPV vaccine demonstrated a very high acceptance rate	Appropriate information contributed significantly to vaccine uptake

5	Botwright et al. 2017	Experiences of operational costs of HPV vaccine delivery strategies in Gavi-supported demonstration projects	African Countries	Socio-economic	Demonstration Project	Health Financing	Non-integration of HPV immunization programs within existing routine immunization programs	Planning appropriate delivery strategies based on local context. Evidence-based social mobilization	Social mobilization, information, education, and communication (IEC) and service delivery each comprised the greatest financial cost	Countries incurring the greatest financial costs also had the highest social mobilization/IEC costs	School-based delivery had the highest service delivery cost per dose due to transportation costs and health worker per diems
6	Chigbu et al. 2017	The impact of community health educators on uptake of cervical and breast cancer prevention services in Nigeria	Nigeria	Socio-economic	Demonstration Project	Health Workers		Educating and training nurses on the HPV vaccination schedule and technique	The intervention was house-to-house cervical and breast cancer prevention education by trained health workers	At baseline, only 2 (0.9%) children had received HPV vaccination. This increased to 33.2% after the intervention (p<0.001)	Education of mothers improves the uptake of HPV vaccination of children
7	Coleman et al. 2011	HPV vaccine acceptability in Ghana, West Africa	Ghana	Socio-economic	Available in Private Sector Only	Information / Community Engagement	Lack of awareness, poor knowledge about cervical cancer and HPV vaccine	Education, social mobilization, communication about HPV and the vaccine	Although majority of the women had heard about cervical cancer (87%) and Pap test (63%) before the survey, fewer women had heard about the HPV vaccine (40%)	Participants proved very accepting of the HPV vaccine, both for themselves and their daughters (94% each)	Those less likely to accept the vaccine had significantly lower level of income
8	De Groot et al. 2017	Knowledge, attitudes, practices and willingness to vaccinate in preparation for the introduction of HPV vaccines in Bamako, Mali	Mali	Socio-economic	Demonstration Project	Information / Community Engagement		Education and communication about HPV, cervical cancer and HPV vaccination	Before the educational session, awareness about HPV was low; 8.6% knew that HPV was transmitted by sexual contact	Knowledge of the participants significantly increased after the education session.	The education session increased the HPV vaccine acceptance in all groups, especially among adolescents

9	DiAngi et al. 2011	A cross-sectional study of HPV vaccine acceptability in Gaborone, Botswana	Botswana	Socio-economic	Available in Private Sector Only	Information / Community Engagement		Education and communication about HPV, cervical cancer and HPV vaccination	Prior to the survey, few (9%) respondents had heard of HPV vaccine, and most (75%) wanted more information about it	80% percent of respondents said they would obtain the HPV vaccine for their adolescent daughters	
10	Francis et al. 2011	A qualitative analysis of South African women's knowledge, attitudes, and beliefs about HPV and cervical cancer prevention, vaccine awareness and acceptance, and maternal-child communication about sexual health	South Africa	Socio-economic	Available in Private Sector Only	Information / Community Engagement	Poor access to information about HPV, cervical cancer and HPV vaccine		Majority of participants knew little about HPV, cervical cancer, and the HPV vaccine, and they expressed interest in learning more about these topics	Participants agreed that vaccinations would keep their children healthy, but they worried about long-term side effects	Most participants thought the government should offer the vaccine for free as part of the country's immunization program
11	Francis et al. 2010	Examining attitudes and knowledge about HPV and cervical cancer risk among female clinic attendees in Johannesburg, South Africa	South Africa	Socio-economic	Not Available	Information / Community Engagement	Poor access to information about HPV, cervical cancer and HPV vaccine		39% of participants had not heard of cervical cancer while 71% had never heard of HPV	Almost half of participants were very likely to vaccinate if their health provider recommended it	Commonly cited barriers to vaccinating included inadequate information, fear of side effects, cost of vaccine.
12	Friedman et al. 2014	Preparing for human papillomavirus vaccine introduction in Kenya: implications from focus-group and interview discussions with caregivers and opinion leaders in Western Kenya	Kenya	Socio-cultural	Not Available	Information / Community Engagement	Poor access to information about HPV, cervical cancer and HPV vaccine	Effective Community sensitization about HPV vaccination through culturally appropriate strategies	Majority of caregivers and opinion leaders had not previously heard of cervical cancer	Apart from health and media experts (n = 3), none of the participants had heard of the HPV vaccine	Participants identified cultural beliefs as potential barriers to vaccination

13	Harries et al. 2009	Preparing for HPV vaccination in South Africa: key challenges and opinions	South Africa	Not Applicable	Available in Private Sector Only	Service Delivery	Health resource constraints. Logistical challenges with vaccine delivery	Appropriate health promotion strategies. Partnerships between Departments of Education + Health, private + public health sectors	Policy influencers and health providers expressed strong support for the HPV vaccine	Participants acknowledged the difficulties of introducing a new technology in a health system with limited capacity and resources - especially where school health is concerned	Opposition could be countered by providing comprehensive information and communication with all stakeholders about the benefits of the HPV immunization
14	Hoque 2015	Acceptability of human papillomavirus vaccination among academics at the University of KwaZulu-Natal, South Africa	South Africa	Socio-economic	Available through NIP	Information / Community Engagement	Poor knowledge about safety and effectiveness of the vaccine	Adequate knowledge about HPV, cervical cancer and HPV vaccine	Almost all (96%) the academics had heard of cervical cancer and all had heard about HPV	After reading information on cervical cancer and HPV, the vaccine acceptability rate increased from 80% to 89%	Those who still did not want to vaccinate their daughters cited the "newness" of the vaccine and fear of side-effects.
15	Hoque 2016	Factors influencing the recommendation of the Human Papillomavirus vaccine by South African doctors working in a tertiary hospital	South Africa	Not Applicable	Available through NIP	Health Workers	Low level of knowledge on HPV infection and vaccination among Doctors		75.3% of Doctors indicated not knowing the effectiveness of the HPV vaccine	Only one doctor (of 320) agreed that the vaccines should be given to girls before sexual debut	96.3% of the Doctors indicated willingness to recommend the vaccines to their patients
16	Hoque et al 2013	Human Papillomavirus vaccination acceptability among female university students in South Africa	South Africa	Not Applicable	Available in Private Sector Only	Information / Community Engagement	Low level of knowledge on HPV infection, cervical cancer, and HPV vaccine		Overall, awareness of cervical cancer and HPV was low	Of the 163 students who reported never having had sex, 127 (77.3%) were willing to accept HPV vaccination	Reasons for non-acceptance, included fear of injection (78.9%), side-effects (15.8%), and pain (5.3%)

17	Hutubessy et al. 2012	A case study using the United Republic of Tanzania: Costing nationwide HPV vaccine delivery using the WHO Cervical Cancer Prevention and Control Costing Tool	Tanzania	Not Applicable	Not Available	Health Financing	Financial costs of social mobilization and HPV vaccine delivery		Excluding vaccine procurement, social mobilization and IEC contributed to the largest share of costs, followed by service delivery	Substantial funding is required to facilitate HPV vaccine delivery	Recurrent costs per dose would be higher for a school-based compared to health facility-based delivery because of transportation costs and health worker per diems
18	Kanya et al. 2017	Evaluating global health partnerships: A case study of a Gavi HPV vaccine application process in Uganda	Uganda	Political	Available through NIP	Governance / Policy	Weak involvement Ministries of Education and Finance	Clear governance and management structures and processes. Political champions (First Lady). Advocacy by NGOs (PATH)	Respondents agreed that partnerships increased country ownership and improved the effectiveness and efficiency of the GAVI application process	Potential drawbacks of the partnership, included an unnecessary management burden on organization	Network mapping identified the absence of the Ministries of education and Finance
19	Katz et al. 2013	A qualitative analysis of factors influencing HPV vaccine uptake in Soweto, South Africa among adolescents and their caregivers	South Africa	Socio-economic	Available in Private Sector Only	Health Workers		The influence of health workers	Health workers at the adolescent clinic were serves as "adult proxies" and positively influenced HPV vaccine uptake	High HIV endemicity, sexual violence, poverty, and an abundance of female-headed households influenced vaccine uptake	
20	Ladner et al. 2012	Assessment of eight HPV vaccination programs implemented in lowest income countries	Lesotho and Cameroon (non-African countries included)	Socio-economic	Demonstration Project	Service Delivery		Use of mixed vaccine delivery models; school and health facility -based strategies	Health-facility model had a lower vaccine coverage (77.1%) compared to the school-based (93.0%) or mixed model (93.8%) ($p = 0.74$)	With regards to adherence to the vaccine doses, the mixed model was the most effective	In Cameroon, intensive IEC strategies were facilitators to the success of HPV vaccination campaigns

21	Ladner et al. 2014	Performance of 21 HPV vaccination programs implemented in low and middle-income countries, 2009-2013	Cameroon, Kenya, Lesotho, Tanzania and Uganda (non-African LMICs included)	Socio-economic	Demonstration Project	Service Delivery		Use of school-based delivery models. Community engagement. Adequate communication, especially on vaccine safety and efficacy	School-based vaccine delivery and program management by an NGO (vs MoH) each had a positive and statistically significant impact on vaccine uptake rates	Community involvement appeared to have a positive impact on the vaccine uptake rate	Inclusion of key messages regarding the safety and efficacy of the vaccine had a positive impact on vaccine uptake
22	LaMontagne et al. 2011	Human papillomavirus vaccine delivery strategies that achieved high coverage in low and middle-income countries	Uganda (non-African LMICs included)	Socio-economic	Demonstration Project	Service Delivery	Use of age-based vaccine delivery models. Low level of awareness about HPV vaccine and vaccination program	Use of grade-based vaccine delivery models. Parents' perceived benefits of HPV vaccine due to sensitization and trust in existing NIP	High HPV vaccination coverage was achieved with the grade-based compared to the age-based vaccine delivery strategy in Uganda	The most frequently cited reasons for non-vaccination was a lack of awareness of the immunization programme	Difficulty in determining girl's eligibility was the mainly challenge with the age-based vaccine delivery model
23	Levin et al. 2013	Delivery cost of human papillomavirus vaccination of young adolescent girls in Peru, Uganda and Viet Nam	Uganda (non-African LMICs included)	Socio-economic	Demonstration Project	Health Financing	Cost of delivering vaccines to adolescents is higher than that of routine childhood immunization	Investments in community mobilization and sensitization increases vaccine acceptance and uptake	School-based vaccine delivery incurred a higher economic cost than the health facility-based or integrated outreach models	The average incremental economic cost per fully immunized girl was highest with school-based delivery model	Community mobilization and IEC activities accounted for approximately 40% of start-up costs
24	Mabeya et al. 2018	Uptake of three doses of HPV vaccine by primary school girls in Eldoret, Kenya; a prospective cohort study in a malaria endemic setting	Kenya	Disease Epidemiology	Demonstration Project	Service Delivery	Low level of awareness about HPV. Distance to health facility.		Of those who received the first dose of HPV vaccine (3026), 63.8% returned for the second dose, and 39.1% for the third dose	Administration of the 2 nd dose and caregiver's knowledge of HPV were predictors of uptake of the 3 rd dose	Distance to the health facility was a significant barrier to uptake of subsequent doses of the HPV vaccine

25	MacPhail et al. 2013	Using HPV vaccination for promotion of an adolescent package of care: Opportunity and perspectives	South Africa	Socio-economic	Available in Private Sector Only	Information / Community Engagement	Poor access to information about HPV, cervical cancer and HPV vaccine		Participants expressed demand for information about the HPV vaccine	Community members echoed adolescents' demands for information about the HPV vaccine	There was an expressed need for integrating other adolescent health programs with HPV immunization
26	Makwe and Anorlu 2011	Knowledge of and attitude toward human papillomavirus infection and vaccines among female nurses at a tertiary hospital in Nigeria	Nigeria	Not Applicable	Not Available	Health Workers	Low level of knowledge on HPV, cervical cancer prevention and HPV vaccine		99.4% had heard of cervical cancer and 84.8% had heard of HPV infection. Only 13% knew it could be prevented through vaccination	Most (74.7%) of the respondents had never heard of the HPV vaccines	Reasons for not recommending HPV vaccination included: young age, poor knowledge of risk factors and vaccine safety
27	Masika et al. 2015	Knowledge on HPV vaccine and cervical cancer facilitates vaccine acceptability among school teachers in Kitui County, Kenya	Kenya	Socio-economic	Demonstration Project	Information / Community Engagement	Lack of information about HPV and HPV vaccine. poor road networks to schools	Effective social mobilization. Engaging teachers at the outset of the HPV immunization program	95% of participants knew that the HPV vaccine prevents cervical cancer, but they had very little information about HPV infection and cervical cancer	89% would allow their daughter or close relative to receive the vaccine.	Vaccine refusal was mainly associated with concerns about vaccine safety
28	Massey et al. 2017	Human papillomavirus (HPV) awareness and vaccine receptivity among Senegalese adolescents	Senegal	Socio-economic	Demonstration Project	Information / Community Engagement	Low level of awareness about HPV and HPV vaccine. Poor socio-economic status	Appropriate health worker re-recommendation on HPV vaccine	27% of participants had heard of HPV. Only 28% of those who had heard about HPV indicated willingness to vaccinate	Health providers' re-recommendations were strongly associated with willingness to vaccinate	As socio-economic status increased, the odds of having heard of HPV also increased

29	Moodley et al. 2013	High uptake of Gardasil vaccine among 9 – 12-year-old schoolgirls participating in an HPV vaccination demonstration project in KwaZulu-Natal Province, South Africa	South Africa	Not Applicable	Available in Private Sector Only	Service Delivery	Use of paper-based vaccine records	School-based vaccine delivery strategy. Well-trained school health team. Intensive community mobilization and sensitization	99.7% received their first dose of vaccine, 97.9% received their second dose, and 97.8% received their third dose.	High uptake of the vaccine depends on parental or caregiver consent	Using predominantly paper-based vaccine records was cited as a barrier to real-time monitoring and evaluation of the program
30	Morhason-Bello et al. 2015	Willingness of reproductive-aged women in a Nigerian community to accept human papillomavirus vaccination for their children	Nigeria	Not Applicable	Available in Private Sector Only	Information / Community Engagement	Low level of awareness about HPV and HPV vaccine	Free, universal HPV vaccination	64.3% strongly agreed that HPV vaccination should be made mandatory to all female children	Concerns about the vaccine included: cost (10.2%) and fear of encouraging promiscuity (9.9%), early sexual debut (6.7%), infertility (6.3%), and side-effects (6.0%)	88.6% women were willing to vaccinate their children
31	Msyamboza et al. 2017	Implementation of a human papillomavirus vaccination demonstration project in Malawi: successes and challenges	Malawi	Not Applicable	Demonstration Project	Service Delivery	Use of health facility-based or community outreach delivery models. Low level awareness about the safety of the vaccine	Using a school-based vaccine delivery strategy	23,831 (89.0%) of school girls and 403 (52.7%) out-of-school girls aged 9–13 years were fully vaccinated	Reasons cited for no or partial vaccination included girls transferring out of the district, dropping out of, and absence from school, and caregivers' dissent	

32	Mugisha et al. 2015	Feasibility of delivering HPV vaccine to girls aged 10 to 15 years in Uganda	Uganda	Not Applicable	Demonstration Project	Service Delivery	Use of age-based vaccine delivery strategy	Use of grade-based vaccine delivery strategy. Active participation by teachers. Government endorsement of the vaccine	Use of the grade-based strategy achieved higher vaccination coverage compared to the age-based strategy	Establishing eligibility was easier with the grade-based compared to the age-based strategy	The dropout rate between the 1 st and 3 rd dose was higher using the age-based model
33	Ndizeye et al. 2018	Knowledge and practices of general practitioners at district hospitals towards cervical cancer prevention in Burundi, 2015: A cross-sectional study	Burundi	Not Applicable	Not Available	Health Workers	Low level of knowledge about HPV vaccination among General Practitioners (GPs)		Of 131 GPs, 89% knew that HPV infection is associated with most cervical cancer cases	55% of GPs were aware that the HPV vaccine can prevent invasive cervical cancer	Only 10.7% knew the target age group for HPV immunization and 3.1% knew the required doses
34	Ngabo et al. 2017	A cost comparison of introducing and delivering pneumococcal, rotavirus and human papillomavirus vaccines in Rwanda	Rwanda	Socio-economic	Available through NIP	Health Financing	High financial cost of HPV vaccine delivery due to greater resource requirements		The financial cost of delivering the HPV vaccine was significantly higher compared to other routine childhood vaccines	HPV vaccine introduction costs were higher due to greater social mobilization and training requirements	Recurrent costs were greater for the HPV vaccine than for routine childhood vaccines
35	Oduyemi et al. 2018	Effect of nursing intervention on mothers' knowledge of cervical cancer and acceptance of human papillomavirus vaccination for their adolescent daughters in Abuja - Nigeria	Nigeria	Not Applicable	Available in Private Sector Only	Health Workers	Lack of education on HPV, cervical cancer and HPV vaccination. Cost of vaccination	Adequate education and communication from nurses about HPV, cervical cancer and HPV vaccination	Prior to the intervention 74% in the experimental arm and 83.1% in the control group had heard about cervical cancer	85.5% of the respondents cited lack of information as a deterrent to vaccinating their daughters	HPV vaccine acceptance increased after the intervention

36	Ogembo et al. 2014	Achieving high uptake of human papillomavirus vaccine in Cameroon: Lessons learned in overcoming challenges	Cameroon	Socio-economic	Demonstration Project	Service Delivery	Negative media reports about the side-effects and interference in HPV immunization program	Use of mixed vaccine delivery models. Adequate community sensitization. Community engagement, especially with municipal and religious leaders	Low vaccine uptake despite adequate social mobilization was linked with false reports by a newspaper article claiming the vaccine had serious side effects including death	The use of mixed vaccine delivery models involving school-based and community outreach approaches was feasible	Wealthy community members subsidized the cost of immunization for those who could not afford to pay
37	Okunade et al. 2017	Knowledge and acceptability of human papillomavirus vaccination among women attending the gynaecological outpatient clinics of a university teaching hospital in Lagos, Nigeria	Nigeria	Socio-demographic	Available in Private Sector Only	Information / Community Engagement	High cost of vaccination. Poor knowledge of the safety of the vaccine. Limited access to the HPV vaccine		36.5% of the respondents had heard about genital HPV infection and 18.9% were aware of the existence of HPV vaccines	81.8% of the respondents expressed their willingness to vaccinate their daughters	Reasons unwillingness to vaccinate were high cost (55.6%) concerns about side-effects (48.1%), and poor availability (25.9%) of the vaccine
38	Poole et al. 2013	A cross-sectional study to assess HPV knowledge and HPV vaccine acceptability in Mali	Mali	Socio-cultural	Not Available	Information / Community Engagement	Low level of knowledge about HPV and cervical cancer		Participants exhibited low level of knowledge about HPV and cervical cancer	100% of participants said they would like the HPV vaccine to be available in Mali	There was a high level of willingness to vaccinate
39	Ports et al. 2013	Barriers and facilitators to HPV vaccination: Perspectives from Malawian women	Malawi	Socio-cultural	Not Available	Information / Community Engagement	Long distance to health facilities. Inadequate IEC strategies about HPV, cervical cancer and HPV vaccine	Health worker re-recommendation on HPV vaccine. Adequate IEC and community engagement	Participants' knowledge about HPV and cervical cancer was limited. None of the women had heard of the HPV vaccine	Long distance to health facilities negatively influenced women's ability to access health services and their decision to vaccinate	All participants were accepting of the vaccine once informed about it and were willing to recommend the vaccine to others

40	Quentin et al. 2012	Costs of delivering human papillomavirus vaccination to schoolgirls in Mwanza Region, Tanzania	Tanzania	Socio-economic	Demonstration Project	Health Financing	Using an age-based vaccine delivery strategy – less cost effective	Using a class or grade-based vaccine delivery strategy – more cost-effective	Marked difference in the costs of delivering HPV vaccines to girls between age-based and class-based deliver	The cost per fully-immunized schoolgirl using a class-based delivery strategy was lower	
41	Remes et al. 2012	A qualitative study of HPV vaccine acceptability among health workers, teachers, parents, female pupils, and religious leaders in northwest Tanzania	Tanzania	Not Applicable	Not Available	Information / Community Engagement	Low level of awareness about HPV, cervical cancer and HPV vaccine. Fragile health worker capacity and limited health resources	Appropriate community sensitization	Nurses' knowledge was limited. None of the parents, teachers, religious leaders or the girls had heard about HPV or the vaccine.	Most respondents welcomed the vaccine. Almost all parents indicated they would vaccinate their daughters. All the girls wanted to be vaccinated	Health workers were concerned about staff shortages and lack of transport if the HPV immunization program was to be introduced in the country
42	Tchounga et al. 2012	Cervical cancer prevention in reproductive health services: Knowledge, attitudes and practices of midwives in Côte d'Ivoire, West Africa	Côte d'Ivoire	Socio-demographic	Available in Private Sector Only	Health Workers	Low level of knowledge about cervical cancer and HPV vaccine	Appropriate training of health workers on cervical cancer and cervical cancer prevention	Only 298 midwives (50.3%) were aware of the HPV vaccine and knew that it protects against cervical cancer	38.5% of the midwives knew that the vaccine was already available in Côte d'Ivoire	Factors associated with appropriate knowledge were professional experience, training
43	Torres-Rueda et al. 2016	HPV vaccine introduction in Rwanda: Impacts on the broader health system	Rwanda	Socio-economic	Available through NIP	Service Delivery		Appropriate training, supervision, planning, partnerships, and political will. Strengthening surveillance	HPV vaccine-specific supervision was reported by 10/27 health facilities and were said to have taken place before and during immunizations	Surveillance of adverse events following immunization was emphasised during planning and formed part of training of health workers	A cold chain inventory was carried out before the introduction of the HPV vaccine

44	Tuhiro et al. 2014	Effect of school-based human papillomavirus (HPV) vaccination on adolescent girls' knowledge and acceptability of the HPV vaccine in Ibanda District in Uganda	Uganda	Socio-demographic	Demonstration Project	Information / Community Engagement	Mis-information about the side-effects of the HPV vaccine	Pre-immunization sensitization	Vaccinated girls who were sensitized during the demonstration project had a higher level of knowledge about cervical cancer and the HPV vaccine	Motivation for HPV vaccine acceptability was related to appreciation of its preventive role against cervical cancer	Introduction of the HPV vaccine triggered several rumours which threatened acceptability of the vaccine
45	Tuhiro et al. 2017	Perceptions of human papillomavirus vaccination of adolescent schoolgirls in western Uganda and their implications for acceptability of HPV vaccination: A qualitative study	Uganda	Socio-cultural	Demonstration Project	Information / Community Engagement	Mis-information about the benefits of the HPV vaccine	Existing perceptions that vaccination in general prevents disease due to the availability of a well-functioning NIP	Following IEC and community mobilization, respondents perceived the HPV vaccine to be beneficial	Misconceptions potentially threatened acceptance; Some believed that the vaccine prevented HIV and pregnancy	Misconceptions about safety of the HPV vaccine persisted despite dissemination of information about vaccine safety
46	Ugwu et al. 2013	Acceptability of human papilloma virus vaccine and cervical cancer screening among female health-care workers in Enugu, Southeast Nigeria	Nigeria	Socio-demographic	Available in Private Sector Only	Health Workers	Non-availability of the vaccine in the NIP and high cost of the vaccine		85.9% were aware of cervical cancer and 84.2% knew that HPV was the causative agent	62.7% respondents were aware of the HPV vaccine and 91% of them were willing to recommend it	Reasons for non-vaccination included cost (92%) and limited access to the vaccine (76%)
47	Umeh et al. 2016	Mothers' willingness to pay for HPV vaccines in Anambra state, Nigeria: A cross sectional contingent valuation study	Nigeria	Socio-economic	Available in Private Sector Only	Health financing	High cost of the HPV vaccine	Availability of GAVI funding and support	Demand for HPV vaccine was high. A total of 91.6% of mothers were willing to pay for the HPV vaccine	Majority of the mothers were willing to pay an average of US\$ 11.68 to get their daughters fully vaccinated	At the GAVI vaccine price, up to US\$ 7.58 is needed to augment the cost of the vaccine
48	Urasa and Darj 2011	Knowledge of cervical cancer and screening practices of nurses at a regional hospital in Tanzania	Tanzania	Socio-demographic	Available in Private Sector Only	Health Workers	Inadequate knowledge on HPV vaccination. Inadequate training		Only 31 (22.6%) of the respondents were aware of the HPV vaccine	Of these, 7 (22.6%) knew that vaccination should be done before sexual debut	Only 2.9% and 8% had attended relevant training seminars

49	Venturas and Umeh 2017	Health professional feedback on HPV vaccination roll-out in a developing country	Zambia	Socio-economic	Demonstration Project	Health Workers	Inadequate training of health workers Disparities in education levels of urban vs rural communities. High cost of the vaccine		Misconceptions and myths surrounding the vaccine translated into a fear of the HPV vaccine within the community	Health workers who were not directly involved in the pilot program were not given HPV vaccine training	Low level of education was reported as a barrier to effective vaccine communication
50	Vermande et al. 2015	Implementation of an HPV vaccination program in Eldoret, Kenya: Results from a qualitative assessment by key stakeholders	Kenya	Socio-cultural	Demonstration Project	Information / Community Engagement	Inadequate IEC and engagement with fathers and male teachers. Misconceptions about vaccines. Health facility-based vaccine delivery	Appropriate communication about cervical cancer and HPV vaccination as a preventive measure	Few fathers had heard about the past HPV vaccination program and when they had, it was mostly through their children and wives. Health care providers failed to sensitize all teachers	There was a general low level of understanding about the potential side effects of the vaccine which negatively impacted on promotional activities	Once participants were fully informed about cervical cancer and the HPV vaccine, they were accepting the vaccine
51	Vermande et al. 2014	Determinants of acceptance and subsequent uptake of the HPV vaccine in a cohort in Eldoret, Kenya	Kenya	Socio-demographic	Demonstration Project	Information / Community Engagement	Weak IEC strategies on the HPV vaccine		Up to 59.4% considered a lack of information as potentially preventing them from vaccinating their daughter. Older mothers were more likely to accept the vaccine	Baseline acceptance was associated with subsequent uptake of the vaccine. Being well-informed increased the odds of immunization	Barriers-faced leading to non-uptake: poorly informed regarding where and when immunization was to take place; fear of side effects

52	Wamai et al. 2013	Awareness, knowledge and beliefs about HPV, cervical cancer and HPV vaccines among nurses in Cameroon: An exploratory study	Cameroon	Socio-economic	Demonstration Project	Health Workers	Low level of knowledge about the safety of the vaccine among health workers		90.8% of the nursing staff surveyed acknowledged that cervical cancer is caused by HPV infection	78.9% recognized HPV vaccine as an important means of prevention against HPV infections and 78.9% believed the vaccine is safe	69.7% of the nurses stated that they would often recommend the HPV vaccine although, 63.9% of them said they were concerned about the side-effects
53	Watson-Jones et al. 2015	Access and attitudes to HPV vaccination amongst hard-to-reach populations in Kenya	Kenya	Socio-economic	Demonstration Project	Service Delivery	Poor physical access to schools and health facilities. Inadequate information about HPV vaccine	Community health workers as source of information and drivers of social mobilization. Adequate and appropriate sensitization for hard-to-reach communities	Barriers to school-based delivery: long distances (up to 10km) and concerns about encountering wildlife on the way were cited as non- or delayed enrolment or absence from school	Barriers to health facility-based delivery: physical inaccessibility, complaints about the quality of care, a preference for traditional medicine	Most parents were willing for their daughters to be vaccinated after being sensitized
54	Watson-Jones et al. 2012	Reasons for receiving or not receiving HPV vaccination in primary schoolgirls in Tanzania: A case control study	Tanzania	Socio-economic	Demonstration Project	Information / Community Engagement	Inadequate IEC about the HPV vaccine, its safety and efficacy		Reasons for refusing to vaccinate: absence from school, caregivers' dissent, girls' dissent	Vaccine acceptance was associated with an understanding of the benefits of the vaccine in preventing cervical cancer	Fear of side effects, infertility and insufficient knowledge about the vaccine was associated with vaccine refusal

Source; Author

Appendix 5: Health Policy and Planning Journal Guidelines

Instructions for Authors

Health Policy and Planning improves the design, implementation and evaluation of health policies in low- and middle-income countries through providing a forum for publishing high quality research and original ideas, for an audience of policy and public health researchers and practitioners. *HPP* is published 10 times a year.

HPP has a double-blinded peer-review policy. All types of papers are peer reviewed and all article abstracts from each issue are translated into French, Spanish and Chinese.

Before you submit please make sure you have followed all the relevant instructions. A checklist for authors is available [here](#).

Not sure which section to submit to? Read our Section Summaries [here](#).

- [Guidance](#)
 - i. [Improving chances of publication](#)
 - ii. [Manuscript format and style for all articles](#)
- [Types of papers](#)
- [Submission process](#)

Guidance

Improving chances of publication

As well as the high overall quality required for publication in an international journal, authors should take into consideration:

- Addressing *HPP*'s readership: national and international policy makers, practitioners, academics and general readers with a particular interest in health policy issues and debates.
- Manuscripts that fail to set out the international debates to which the paper contributes, and to draw out policy lessons and conclusions, are more likely to be rejected, returned to the authors for redrafting prior to being reviewed, or undergo a slower acceptance process.
- Economists should note that papers accepted for publication in *HPP* will consider the broad policy implications of an economic analysis rather than focusing primarily on the methodological or theoretical aspects of the study.
- Public health specialists writing about a specific health problem or service should discuss the relevance of the analysis for the broader health system. Those submitting health policy analyses should draw on relevant bodies of theory in their analysis, or justify why they have not, rather than only presenting a narrative based on empirical data.
- Primarily focus on one or more low- or middle-income countries.

The editors cannot enter into correspondence about papers considered unsuitable for publication and their decision is final. Neither the editors nor the publishers accept responsibility for the views of authors expressed in their contributions. The editors reserve the right to make amendments to the papers submitted although, whenever possible, they will seek the authors' consent to any significant changes made. The manuscript will not be returned to authors following submission unless specifically requested.

Should you require any assistance in submitting your article or have any queries, please do not hesitate to contact the editorial office at hpp.editorialoffice@oup.com.

Manuscript format and style for all articles

Only articles in English are considered for publication.

Prepare your manuscript, including tables, using a word processing program and save it as a **.doc**, **.rtf** or **.ps** file. Use a minimum font size of 11, double-spaced and paginated throughout including references and tables, with margins of at least 2.5 cm. The text should be left justified and not hyphenated.

The **title page** should contain:

- Title - please keep as concise as possible and ensure it reflects the subject matter
- Corresponding author's name, address, telephone/fax numbers and e-mail address
- Each author's affiliation and qualifications

- Keywords and an abbreviated running title
- 2-4 Key Messages, detailing concisely the main points made in the paper
- Acknowledgements
- A word count of the full article

In the **acknowledgements**, all sources of funding for research must be explicitly stated, including grant numbers if appropriate. Other financial and material support, specifying the nature of the support, should be acknowledged as well.

Figures should be designed using a well-known software package for standard personal computers. If a figure has been published earlier, acknowledge the original source and submit written permission from the copyright holder to reproduce the material. Colour figures are permitted but authors will be required to pay the cost of reproduction.

Please be aware that the requirements for online submission and for reproduction in the journal are different: (i) for online submission and peer review, please upload your figures separately as low-resolution images (.jpg, .tif, .gif or .eps); (ii) for reproduction in the journal, you will be required after acceptance to supply high-resolution .tif files. Minimum resolutions are 300 d.p.i. for colour or tone images, and 600 d.p.i. for line drawings. We advise that you create your high-resolution images first as these can be easily converted into low-resolution images for online submission.

Figures will not be relettered by the publisher. The journal reserves the right to reduce the size of illustrative material. Any photomicrographs, electron micrographs or radiographs must be of high quality. Wherever possible, photographs should fit within the print area or within a column width. Photomicrographs should provide details of staining technique and a scale bar. Patients shown in photographs should have their identity concealed or should have given their written consent to publication. When creating figures, please make sure any embedded text is large enough to read. Many figures contain miniscule characters such as numbers on a chart or graph. If these characters are not easily readable, they will most likely be illegible in the final version.

Certain image formats such as .jpg and .gif do not have high resolutions, so you may elect to save your figures and insert them as .tif instead.

For useful information on preparing your figures for publication, go to <http://cpc.cadmus.com/da>.

All **measures** should be reported in SI units, followed (where necessary) by the traditional units in parentheses. There are two exceptions: blood pressure should be expressed in mmHg and haemoglobin in g/dl. For general guidance on the International System of Units, and some useful conversion factors, see 'The SI for the Health Professions' (WHO 1977).

Manuscript file must include text body. Title Page, Figures and Tables should be uploaded separately.

Manuscript Preparation

Page 1: **Title Page** – as above.

Page 2: **Abstract**. The abstract should be prepared in one paragraph, no headings are required. It should describe the purpose, materials and methods, results, and conclusion in a single paragraph no longer than 300 words without line feeds.

Page 3: **Introduction**. The Introduction should state the purpose of the investigation and give a short review of the pertinent literature, and be followed by:

Materials and methods. The Materials and methods section should follow the Introduction and should provide enough information to permit repetition of the experimental work. For particular chemicals or equipment, the name and location of the supplier should be given in parentheses.

Results. The Results section should describe the outcome of the study. Data should be presented as concisely as possible, if appropriate in the form of tables or figures, although very large tables should be avoided.

Discussion. The Discussion should be an interpretation of the results and their significance with reference to work by other authors.

Abbreviations. Non-standard abbreviations should be defined at the first occurrence and introduced only where multiple use is made. Authors should not use abbreviations in headings.

All **measures** should be reported in SI units, followed (where necessary) by the traditional units in parentheses. There are two exceptions: blood pressure should be expressed in mmHg and haemoglobin in g/dl. For general guidance on the International System of Units, and some useful conversion factors, see 'The SI for the Health Professions' (WHO 1977).

References. References must follow the Harvard system and must be cited as follows:

Baker and Watts (1993) found...

In an earlier study (Baker and Watts 1993), it...

Where works by more than two authors are cited, only the first author is named followed by 'et al.' and the year. The reference list must be typed double-spaced in alphabetical order and include the full title of both paper (or chapter) and

journal (or book), thus:

Baker S, Watts P. 1993. Paper/chapter title in normal script. Journal/book title in italics **Volume number in bold** : page numbers.

Baker S, Watts P. 1993. Chapter title in normal script. In: Smith B (ed). *Book title in italics*. 2nd edn. Place of publication: Publisher's name, page numbers.

Tables All tables should be on separate pages and accompanied by a title - and footnotes where necessary. The tables should be numbered consecutively using Arabic numerals. Units in which results are expressed should be given in parentheses at the top of each column and not repeated in each line of the table. Ditto signs are not used. Avoid overcrowding the tables and the excessive use of words. The format of tables should be in keeping with that normally used by the journal; in particular, vertical lines, coloured text and shading should not be used. Please be certain that the data given in tables are correct. Tables should be provided as Word or Excel files.

Types of papers

Health Policy and Planning welcomes submissions of the following article types:

- [Original research](#)
- [Review articles](#)
- [Methodological musings](#)
- [Innovation and practice reports](#)
- [Commentaries](#)
- ['How to do \(or not to do\)...'](#) [for example, see [Hutton & Baltussen, HPP, 20\(4\): 252-9](#)] and
- ['10 best resources'](#) [for example, see [David & Haberland, HPP, 20\(4\): 260-3](#)].

ORIGINAL RESEARCH

Manuscripts should preferably be a **maximum** of **6,000** words, excluding tables and figures/diagrams.

The manuscript will generally follow through sections: Title page (as [above](#)), Abstract (no more than 300 words), Introduction, Methods, Results, Discussion, Conclusion, Acknowledgements, References. However, it may be appropriate to combine the results and discussion sections in some papers. Tables and Figures should not be placed within the text, rather provided in separate file/s.

For the reporting of statistical analyses please consider the following additional points:

- Focus the statistical analysis at the research question.
- Provide information about participation and missing data.
- As much as possible, describe results using meaningful phrases (e.g., do not say "beta" or "regression coefficient", but "mean change in Y per unit of X"). Provide 95% confidence intervals for estimates.
- Report the proportions as *N* (%), not just %.
- Report *P* values with 2 digits after the decimal, 3 if <0.01 or near 0.05 (e.g., 0.54, 0.03, 0.007, <0.001, 0.048). Do not report *P* values greater than 0.05 as "NS".
- Always include a leading zero before the decimal point (e.g., 0.32 not .32).
- Do not report tests statistics (such as chi-2, T, F, etc.)."

For [acknowledgements](#), [figures](#) and [measures](#) see above.

REVIEW ARTICLES

Manuscripts should preferably be a **maximum** of **10,000 words**, excluding tables, figures/diagrams and references.

Reviews may be invited. They generally address recent advances in health policy, health systems and implementation. **Systematic reviews are particularly welcomed**, but may not be appropriate for every topic. If authors are submitting a review article that is not a systematic review then the paper should explain why a systematic review was not feasible/desirable, and the review methods should be described in a way that is as clear and as replicable as possible.

The manuscript will generally follow through sections: Abstract (no more than 300 words), Introduction, Methods, Results, Discussion, Conclusion, References. However, it may be appropriate to combine the results and discussion sections in some papers. Tables and Figures should not be placed within the text, rather provided in separate file/s.

Checklists have been developed for a number of study designs, including randomized controlled trials (CONSORT), systematic reviews (PRISMA), observational studies (STROBE), diagnostic accuracy studies (STARD) and qualitative studies

(COREQ, RATS). We recommend authors refer to the EQUATOR Network website (<http://www.equator-network.org>) for further information on the available reporting guidelines for health research, and the MIBBI Portal for prescriptive checklists for reporting biological and biomedical research where applicable. Authors are requested to make use of these when drafting their manuscript and peer reviewers will also be asked to refer to these checklists when evaluating these studies.

COMMENTARIES

Short commentaries on topical issues in health systems are welcomed - [please email the editorial office prior to submission](#). Most such commentaries are commissioned by the editors, but the journal will also consider unsolicited submissions. Commentaries should of broad interest to readers of *Health Policy and Planning*, and while they are not research papers, they should be well substantiated. Manuscripts should preferably be a **maximum of 1,200 words**, excluding tables, figures/diagrams and references.

The manuscript will generally contain a short set of key take-home messages. Tables and Figures should not be placed within the text, rather provided in separate file/s.

HOW TO DO...OR NOT TO DO

This series is meant to explain how to use a particular research or analytical method (e.g. social network analysis, discrete choice experiment etc.). The research or analytical methods discussed should be well accepted and clearly defined: this category of paper is not meant to address methodological debates but rather to help disseminate and promote the use of well-accepted methodologies.

Manuscripts should preferably be a **maximum of 3,000 words** excluding tables, figures/diagrams and references.

- The sections must be arranged as follows: i) Title page (as [above](#)), ii) Abstract, iii) Introduction, iv) Body of the paper, and v) References. Main sections should be coordinated by the author, and inserted between Introduction and Reference sessions. Please contact our office before submitting a manuscript in this category.

Tables and Figures should not be placed within the text, rather provided in separate file/s.

10 BEST RESOURCES

This 10 best is a series of articles that identify and outline the 10 most useful resources from a range of sources to help facilitate a better understanding of a particular issue in global health.

We often commission these articles but we also hear unsolicited suggestions.

For [acknowledgements](#), [figures](#) and [measures](#) see [above](#).

METHODOLOGICAL MUSINGS

This series is meant to address methodological issues in health policy and systems research, where there is currently a lack of clarity about accepted research methods. This series is intended to support the development of the health policy and systems research field, through supporting methodological discussion.

Manuscripts should preferably be a **maximum of 3,000 words**, excluding tables, figures/diagrams and references.

- The sections must be arranged as follows: i) Title page (as [above](#)), ii) Abstract, iii) Introduction, iv) Body of the paper, and v) References. Main sections should be coordinated by the author, and inserted between Introduction and Reference sessions. Please contact our office before submitting a manuscript in this category.
- For [acknowledgements](#), [figures](#) and [measures](#) see [above](#).

INNOVATION AND PRACTICE REPORTS

These short reports are narratives from the perspective of health managers operating at the national or sub-national level which focus on innovative approaches to strengthen health systems. Papers should highlight the practical experience of health managers or practitioners involved in taking action to strengthen health systems through innovative activities and new practices. The new activities and practices should preferably have been implemented for a sufficiently long time to allow authors to demonstrate the potential for sustained improvement or change in the health system. Examples might include practices to build capacity, develop new partnerships or restructure relationships within health systems. Papers should identify 2-4 key messages or lessons for consideration in other settings. We will not consider clinical and pharmaceutical innovations and practices. Manuscripts should be a **maximum of 2,000 words**.

The manuscript will generally follow through sections: Key Messages, Abstract (no more than 300 words), Introduction, Methods, Results, Discussion, Conclusion, References. However, it may be appropriate to combine the results and discussion sections in some papers. Tables and Figures should not be placed within the text, rather provided in separate

file/s. In the main body of the paper, sub-headings may be useful to signal key elements of the experience reported. Reports must be led by local practitioners, managers or policy-makers.

Submission process

- [Pre-submission language editing](#)
- [Authorship](#)
- [Originality](#)
- [Online submission](#)

PRE-SUBMISSION LANGUAGE EDITING

HPP asks all authors to ensure that their papers are written in as high a standard of English as possible before submission to the journal. If your first language is not English, to ensure that the academic content of your paper is fully understood by journal editors and reviewers, you may want to consider using a language editing service. Language editing does not guarantee that your manuscript will be accepted for publication. For further information on this service, please click [here](#). Several specialist language editing companies offer similar services and you can also use any of these. Authors are liable for all costs associated with such services. If your first language is not English, to ensure that the academic content of your paper is fully understood by journal editors and reviewers is optional. Language editing does not guarantee that your manuscript will be accepted for publication. For further information on this service, please click [here](#). Several specialist language editing companies offer similar services and you can also use any of these. Authors are liable for all costs associated with such services.

AUTHORSHIP

All persons designated as authors should qualify for authorship. The order of authorship should be a joint decision of the co-authors. Each author should have participated sufficiently in the work to take public responsibility for the content. Authorship credit should be based on substantial contribution to conception and design, execution, or analysis and interpretation of data. All authors should be involved in drafting the article or revising it critically for important intellectual content, must have read and approved the final version of the manuscript and approve of its submission to this journal. An email confirming submission of a manuscript is sent to all authors. Any change in authorship following initial submission would have to be agreed by all authors as would any change in the order of authors.

ORIGINALITY

Manuscripts containing original material are accepted for consideration with the understanding that neither the article nor any part of its essential substance, tables, or figures has been or will be published or submitted for publication elsewhere. This restriction does not apply to abstracts or short press reports published in connection with scientific meetings. Copies of any closely related manuscripts should be submitted along with the manuscript that is to be considered by HPP. HPP discourages the submission of more than one article dealing with related aspects of the same study. For further information on the prior publication policy see https://academic.oup.com/heapol/pages/Prior_Publication.

During the online submission procedure, authors are asked to provide:

- information on prior or duplicate publication or submission elsewhere of any part of the work;
- a statement of financial or other relationships that might lead to a conflict of interest or a statement that the authors do not have any conflict of interest;
- a statement that the manuscript has been read and approved by all authors (see also section on [authorship](#));
- name, address, telephone and fax number of the corresponding author who is responsible for negotiations concerning the manuscript;
- copies of any permissions to reproduce already published material, or to use illustrations or report sensitive personal information about identifiable persons.

All papers submitted to HPP are checked by the editorial office for conformance to author and other instructions all specified below. Non-conforming manuscripts will be returned to authors.

If authors are unsure about the originality of their manuscript or any part of it, they should contact the editorial office at hpp.editorialoffice@oup.com.

ONLINE SUBMISSION

Prior to submission please carefully read instructions on each type of paper and closely follow instructions on word count, abstract, tables and figures and references. This will ensure that the review and publication of your paper is as efficient and quick as possible. The Editorial Office reserve the right to return manuscripts that are not in accordance with these instructions.

All material to be considered for publication in Health Policy and Planning should be submitted in electronic form via the journal's online submission system. Once you have prepared your manuscript according to the instructions below, instructions on how to submit your manuscript online can be found by clicking [here](#).

CONFLICT OF INTEREST

Authors must declare any conflicts of interest during the online submissions process. The lead author is responsible for confirming with the co-authors whether they also have any conflicts to declare.

ETHICAL APPROVAL

A requirement of publication is that research involving human subjects was conducted with the ethical approval of the appropriate bodies in the country where the research was conducted and of the ethical approval committees of affiliated research institutions elsewhere. A clear statement to this effect must be made in any submitted manuscript presenting such research, specifying that the free and informed consent of the subjects was obtained.

FUNDING

The following rules should be followed:

- The sentence should begin: 'This work was supported by ...'
- The full official funding agency name should be given, i.e. 'the National Cancer Institute at the National Institutes of Health' or simply 'National Institutes of Health' not 'NCI' (one of the 27 subinstitutions) or 'NCI at NIH' - [see the full RIN-approved list of UK funding agencies](#) for details
- Grant numbers should be complete and accurate and provided in brackets as follows: '[grant number ABX CDXXXXXX]'
- Multiple grant numbers should be separated by a comma as follows: '[grant numbers ABX CDXXXXXX, EFX GHXXXXXX]'
- Agencies should be separated by a semi-colon (plus 'and' before the last funding agency)
- Where individuals need to be specified for certain sources of funding the following text should be added after the relevant agency or grant number 'to [author initials]'.

An example is given here: 'This work was supported by the National Institutes of Health [P50 CA098252 and CA118790 to R.B.S.R.] and the Alcohol & Education Research Council [HFY GR667789].

Oxford Journals will deposit all NIH-funded articles in PubMed Central. See [Author self-archiving policy](#) for details. Authors must ensure that manuscripts are clearly indicated as NIH-funded using the guidelines above.

PERMISSIONS

Authors are reminded that it is their responsibility to comply with copyright laws. It is essential to ensure that no parts of the submission have or are due to appear in other publications without prior permission from the copyright holder and the original author. Materials, e.g. tables, taken from other sources must be accompanied by a written statement from both author and publisher giving permission to HPP for reproduction.

COPYRIGHT

Upon receipt of accepted manuscripts at Oxford Journals authors will be invited to complete an online copyright licence to publish form.

Please note that by submitting an article for publication you confirm that you are the corresponding/submitting author and that Oxford University Press ("OUP") may retain your email address for the purpose of communicating with you about the article. You agree to notify OUP immediately if your details change. If your article is accepted for publication OUP will contact you using the email address you have used in the registration process. Please note that OUP does not retain copies of rejected articles

It is a condition of publication in Health Policy and Planning that authors assign licence to publish to Oxford University Press. This ensures that requests from third parties to reproduce articles are handled efficiently and consistently and will also allow the article to be as widely disseminated as possible. In assigning licence to publish, authors may use their own material in other publications provided that the Journal is acknowledged as the original place of publication, and Oxford University Press is acknowledged as the original Publisher.

THIRD-PARTY CONTENT IN OPEN ACCESS PAPERS

If you will be publishing your paper under an Open Access licence but it contains material for which you **do not** have Open Access re-use permissions, please state this clearly by supplying the following credit line alongside the material:

Title of content

Author, Original publication, year of original publication, by permission of [rights holder]

This image/content is not covered by the terms of the Creative Commons licence of this publication. For permission to reuse, please contact the rights holder.

PRIOR PUBLICATION POLICY

Please review our [prior publication policy](#). We expect authors to disclose any prior dissemination including via a website or at national meetings.

OFFPRINTS

All authors are supplied with a free URL linking you to a press-ready PDF version of your article. If you wish to order offprints please visit the Oxford Journals Author Services site.

CHANGE OF ADDRESS

Please notify the editors of any change of address. After manuscript acceptance, please also notify the publishers: Journals Production Department, Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK. Telephone +44 (0) 1865 556767 , Fax +44 (0) 1865 267773.

IMPORTANT NOTES TO AUTHORS

The manuscripts will not be returned to authors following submission unless specifically requested.

PROOFS

Authors are sent page proofs by email. These should be checked immediately and corrections, as well as answers to any queries, returned to the publishers as an annotated PDF via email or fax within 3 working days (further details are supplied with the proof). It is the author's responsibility to check proofs thoroughly.

PERMISSION TO REPRODUCE FIGURES AND EXTRACTS

Permission to reproduce copyright material, for print and online publication in perpetuity, must be cleared and if necessary paid for by the author; this includes applications and payments to DACS, ARS and similar licensing agencies where appropriate. Evidence in writing that such permissions have been secured from the rights-holder must be made available to the editors.

It is also the author's responsibility to include acknowledgements as stipulated by the particular institutions. Please note that obtaining copyright permission could take some time. Oxford Journals can offer information and documentation to assist authors in securing print and online permissions: please see the Guidelines for Authors section at https://academic.oup.com/journals/pages/access_purchase/rights_and_permissions.

Should you require copies of this then please contact the editorial office of the journal in question or the Oxford Journals Rights department on journals.permissions@oup.com.

For a copyright prose work, it is recommended that permission is obtained for the use of extracts longer than 400 words; a series of extracts totalling more than 800 words, of which any one extract is more than 300 words; or an extract or series of extracts comprising one-quarter of the work or more. For poetry: an extract of more than 40 lines; series of extracts totalling more than 40 lines; an extract comprising one-quarter or more of a complete poem.

SUPPLEMENTARY DATA

Supporting material that is not essential for inclusion in the full text of the manuscript, but would nevertheless benefit the reader, can be made available by the publisher as online-only content, linked to the online manuscript. The material should not be essential to understanding the conclusions of the paper, but should contain data that is additional or complementary and directly relevant to the article content. Such information might include more detailed methods, extended data sets/data analysis, or additional figures.

It is standard practice for appendices to be made available online-only as supplementary data. All text and figures must be provided in suitable electronic formats. All material to be considered as supplementary data must be submitted at the same time as the main manuscript for peer review. It cannot be altered or replaced after the paper has been accepted for publication, and will not be edited. Please indicate clearly all material intended as supplementary data upon submission and name the files e.g. 'Supplementary Figure 1', 'Supplementary Data', etc. Also ensure that the supplementary data is referred to in the main manuscript where necessary, for example as '(see Supplementary data)' or '(see Supplementary Figure 1)'.

OXFORD OPEN ACCESS

HPP authors have the option to publish their paper under the [Oxford Open](#) initiative; whereby, for a charge, their paper will be made freely available online immediately upon publication.

After your manuscript is accepted the corresponding author will be required to accept a mandatory licence to publish agreement. As part of the licensing process you will be asked to indicate whether or not you wish to pay for open access. If you do not select the open access option, your paper will be published with standard subscription-based access and you will not be charged.

Oxford Open articles are published under Creative Commons licences. Authors publishing in *Health Policy and Planning* can use the following Creative Commons licences for their articles:

- Creative Commons Attribution licence (CC BY)
- Creative Commons Non-Commercial licence (CC BY-NC)
- Creative Commons non-Commercial No Derivatives licence (CC BY-NC-ND)

Please click [here](#) for more information about the Creative Commons licences.

You can pay Open Access charges using our Author Services site. This will enable you to pay online with a credit/debit card, or request an invoice by email or post. The open access charges applicable are:

- Regular charge - £1680/\$2678/€2205
- Health Systems Global member charge - £1260/\$2048/€1628
- Reduced Rate Developing country charge* - £840/\$1139/€1103
- Free Developing country charge * - £0/\$0/€0

*Visit our [Developing Countries](#) page for a list of qualifying countries. Qualifying discounts will be applied automatically and are dependent on the address of the [corresponding author](#) of the submitted paper.

Please note that these charges are in addition to any colour/page charges that may apply.

Orders from the UK will be subject to the current UK VAT charge. For orders from the rest of the European Union, OUP will assume that the service is provided for business purposes. Please provide a VAT number for yourself or your institution, and ensure you account for your own local VAT correctly.

ETHICS

Health Policy and Planning is a member of the Committee on Publication Ethics (COPE), and strives to adhere to its code of conduct and guidelines.

Authors are encouraged to consult <http://publicationethics.org/resources/guidelines> for more information.

In reports of investigations in humans or animals, authors must explicitly indicate (in the appropriate section of the Methods) their adherence to ethical standards and note the approval of an ethics committee when this is relevant.

CROSSREF FUNDING DATA REGISTRY

In order to meet your funding requirements authors are required to name their funding sources, or state if there are none, during the submission process. For further information on this process or to find out more about the CHORUS initiative please click [here](#)