DRIVERS OF VACCINE HESITANCY AND UNDERIMMUNIZATION AMONG CHILDREN OF HOIMA AND WAKISO DISTRICTS OF UGANDA

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Abstract

DRIVERS OF VACCINE HESITANCY AND UNDERIMMUNIZATION AMONG CHILDREN OF HOIMA AND WAKISO DISTRICTS OF UGANDA

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The inclusion of vaccine hesitancy among the 10 leading threats to public health worldwide highlighted the urgent need for interventions that can address the problem. Besides hesitancy, Wakiso and Hoima districts continue to report low immunization rates of coverage with vaccine preventable diseases continuing to be frequent and recurrent. This study set out to find out what is responsible for recurrence of these VPDs and low in Hoima and Wakiso Districts of Uganda and to identify possible interventions, approaches and strategies that can help address these problems.

This mixed methods study included quantitative and qualitative research methods comprising focus group discussions (FGDs) and in-depth interviews for caregivers of children that were eligible for immunization; face-to-face interviews for immunization focal health workers; key informant interviews (KIIs) for immunization focal persons and decision makers within the two districts; and a systematic review on vaccine hesitancy and underimmunization in sub-Saharan Africa. The study population included 643 caregiver interviews, 20 FGDs and 80 KIIs.

The drivers of hesitancy and underimmunization identified comprise geographical, community, caregiver, child and health system factors. These were access difficulties, geographical barriers, inadequate funding, cold chain inadequacies, inadequate social mobilization, vaccine stock outs, high training needs for health workers, and adverse events. Most vaccine hesitancy determinants listed on WHO matrix were applicable, including poor access to vaccines or to vaccination services, diminished trust in some vaccines, and diminished acceptance for some vaccines especially for children and HPV vaccines.

The ministry of health needs to train the Health Workers, enhance outreach services, social mobilization, and build trust in communities. It also needs to work with supervisors to avail more funding for district cold chain teams especially transportation required for mentorship, train and frequently supervise health workers, ensure a steadier supply of vaccines, injections, cold chain consumables, and record books. Additionally, the ministry of health needs to sensitize the community more, plan joint collaborated engagement activities, involve communities in organizing introduction of new vaccines and activities for catch up immunization campaigns to help improve the outputs of the immunization program.

Declaration

I declare that the thesis has been composed by myself and that the work has not been submitted for any other degree or professional qualification. I confirm that the work submitted is my own, except where work which has formed part of jointly-authored publications has been included. My contribution and those of the other authors to this work are explicitly indicated below. I confirm that appropriate credit has been given within this thesis where reference has been made to the work of others.

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Dedication

I dedicate this work to all caregivers who overcome so many challenges to ensure that they take their children for the scheduled immunization visits on the appointed date and time.

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May the LORD God bless you all abundantly.

List of abbreviations

ACIP - Advisory Commission on Immunization Practices

AEFIs - Adverse Events Following Immunization

ANC - Antenatal Care

BCG - Bacillus Calmette-Guérin

CBOs - Community-Based Organizations

CEPI - Coalition for Epidemic Preparedness Innovations

DTP - Diphtheria-Tetanus-Pertussis

ECAVI - East Africa Centre for Vaccines and Immunization

ELISA - Enzyme-Linked Immunosorbent Assay

EPI - Expanded Programme on Immunization

FDA - Food and Drug Administration

FGD - Focus Group Discussion / FGDs - Focus Group Discussions

GAVI - Global Alliance for Vaccines and Immunization

HBM - Health Belief Model

HC - Health Centre

HCWs – Health Care Workers

HPV - Human Papillomavirus

HSD - Health sub-District

ICCM - Integrated Community Case Management

IDI - In-Depth Interviews

IEC - Information, Education and Communication

KIIs - Key Informant Interviews

LC – Local Council

LMICs – Low and Lower Middle-income Countries

MBL - Mannose-Binding Lectin

MAC - Membrane Attack Complex

MDGs - Millennium Development Goals

MHC - Major Histocompatibility Complex

MOH – Ministry of Health

NESI - Network for Education and Support in Immunisation

NIH - National Institutes of Health

NMS - National Medical Stores

PAMPs - Pathogen Associated Molecular Patterns

PCV - Pneumococcal Conjugate Vaccine

PICO - Participants, Intervention, Comparator, and Outcome

PRRs - Pattern Recognition Receptors

RED - Reach Every District

RRH - Regional Referral Hospital

SAGE - Strategic Advisory Group of Experts

SDGs - Sustainable Development Goals

SIAs - Supplementary Immunization Activities

SOMREC - School of Medicine, Research and Ethics Committee of the College of Health Sciences, Makerere University.

SSA - Sub-Saharan Africa

TLRs - Toll-Like Receptors

TPP - Target Product Profile

Nations Children's Fund

UREC - Unicaf University Research Ethics Committee

VHT - Village Health Team

VPD - Vaccine Preventable Disease

Operational Definitions

A vaccine: referred to a suspension of live (attenuated/weakened) or inactivated microorganisms (e.g. bacteria, viruses) or fractions of microorganism administered to induce immunity and prevent an infectious disease or its complications.

Vaccination: giving an antigen to a person with the aim of provoking the person's system of immunity to generate a protective response against the antigen.

Coverage: referred to the percentage of children of age twelve to twenty-three months who had got the third dose of DPT (DPT 3) (currently given in Pentavalent 3) as per National Expanded Program on Immunization schedule expressed as a percentage of the children enrolled in the study.

Good coverage: referred to over ninety percent or more of the children having received DPT3 vaccine at the time they attain the age of one year.

Fully vaccinated: Any child of the age between twelve to the age twenty-three months, who was given 1 BCG dose, at least 3 doses of the pentavalent vaccine, 3 OPV doses, one measles vaccine dose, and 3 Hemophilus influenza type B doses before the child reaches the first birthday and measured by vaccination card.

Incomplete vaccinated: A situation where any one of the 8 recommended vaccines was missed when it was due.

Unvaccinated child: This refers to the case of a child who has not yet received any one dose out of the eight vaccines recommended in the immunization schedule.

Coverage by card only: refers to vaccination coverage as calculated with numerator based only on the documented dose, and excluding from the numerator those vaccinated by vaccination history.

Coverage by card plus history: refers to vaccination coverage as calculated with numerator based on the card and the mother's report.

Caregiver: referred to a person who looked after the child, physically or provides resources for most of the time.

Cluster sampling: This refers to referred to a survey method where groups (or clusters) of sampling units (not the individual units) are selected from a given population for analysis.

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CHAPTER 1: INTRODUCTION

The highest proportion of deaths and diseases occurring in poor and developing countries (also called LMICs) follow infectious diseases that are largely vaccine preventable (Anthony et al., 2009; Størdal & Lie, 2009; WHO, 2017a, 2020c, 2020f, 2021c). Immunisation is therefore regarded an important strategy to ensure children live to adulthood, and can avert 4 million deaths annually (Adekeye et al., 2015; WHO, 2019d) especially in the very poor or low income communities of the world (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). There are some interventions aimed at increasing availability of immunisation services around the world that have been added to the Abuja declaration on health whose theme was to promote allocation of resources to health (AbouZahr et al., 2015; Anthony et al., 2009; Blencowe et al., 2016; Szwarcwald et al., 2020; WHO, 2021c), and these resolutions mirrored those under the child survival action convention for political mobilization (Wolfson et al., 2008). These aims informed the health-leaning sections of the United Nations' Millennium Development Goals (MDGs), which were later replaced by the current Sustainable Development Goals (SDGs), which in their third goal focus on reducing the deaths of children of age under five years to less than 25 deaths for every 1000 live births by the year 2030. The hope therefore is over four million childhood deaths to be averted each year (Dicker et al., 2018; Jofiro et al., 2018; Murray et al., 2007; Ntukanyagwe, 2019).

A review of global trends from the 1980s onward reveals that there has been a rapid escalation in the rates of immunization coverage since the early years following roll out of the EPI until 1990s, and subsequently followed by a much slower pace of progress in the vaccine roll out and uptake until year 2010, and afterwards a gradual stagnation up to the year 2019 (Chopra et al., 2020; Decouttere et al., 2021; Diekema, 2005; Douglas & Samant, 2018; Hug et al., 2019; Igme, 2020; Kiely et al., 2018). Recent reports suggest that there has been a prolonged stagnation overall in the vaccination coverage levels across the world, with no vaccine shown to be exceeding 90 per cent coverage at the global level (Chopra et al., 2020; Decouttere et al., 2021; Diekema, 2005; Douglas & Samant, 2018; Hug et al., 2019; Igme, 2020; Kiely et al., 2018). This stagnation has raised major concerns regarding the strategies that are currently used (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016)and if there was additional interventions necessary to tip the scales and to move the world much closer to achieving the united nations Sustainable Development Goal 3.b.1, that targets universal vaccination coverage worldwide (Dicker et al., 2018; Lee et al., 2020; Liu et al., 2012; Liu et al., 2016; MacDonald et al., 2020).

An important strategy here would be to reduce missed opportunities against vaccination and fight the low acceptancy of vaccines owing to vaccine hesitancy and prevailing underimmunization (Dicker et al., 2018; Lee et al., 2020; Liu et al., 2012; Liu et al., 2016; MacDonald et al., 2020). Refusal and hesitancy to vaccines are now the central threats to national immunization programs meeting their targets. This is a bog health problem that led to the listing of vaccine hesitancy in the 10 biggest public health worldwide threats(Abbas et al., 2020; MacDonald et al., 2020; WHO, 2019c, 2020c, 2020f). The WHO through its group of experts define hesitancy as "a delay in the acceptance of or the refusal of vaccines by communities despite the availability of vaccination services" (Butler & MacDonald, 2015). This WHO's Strategic Advisory Group of Experts (SAGE) had a hesitancy working group. This group of experts identified 3 major factors that drive vaccine hesitancy. The three factors were 3Cs, put into what is now commonly referred to as the 3C's model. This model entails the following: 1. Confidence (in this case, there is neither trust in the vaccines nor in the health workers who give the vaccines); 2. Complacency (in this case the groups targeted by the vaccination program do not perceive the need for the vaccines or they in fact do not value the vaccination itself) and 3. Convenience (this concerns access to the vaccines being a problem or access to the vaccination services being inadequate) (MacDonald, 2015; WHO, 2014).

Vaccine hesitancy continues to pose a huge public health problem and a major barrier to immunization (Dicker et al., 2018; Diekema, 2005). It is widespread and context specific with identifiable variation in the various reasons given by caregivers for refusing to accept different vaccines, be it a single or be it multiple vaccines (Dratva et al., 2021; Dubé et al., 2015; Dubé et al., 2018; Francis et al., 2008). The WHO SAGE working group on vaccine hesitancy therefore designed a vaccine hesitancy matrix, which clearly categorize the reasons behind vaccine hesitancy into: individual and group factors, into contextual factors, and as well into vaccine or vaccination-specific factors (MacDonald, 2015). It has been however observed that most hesitant individuals tend to be largely reluctant following individual as well as group influences (Dratva et al., 2021; Dubé et al., 2015; Dubé et al., 2018; Ekirapa-Kiracho et al., 2021; Elizabeth et al., 2015; Eshetu & Woldesenbet, 2011; Eskola et al., 2015; Ezbakhe & Pérez-Foguet, 2020; Francis et al., 2008).

These factors include lack of adequate knowledge about the vaccines or the awareness regarding the vaccines and the vaccination services; bad/not so favourable experiences with past vaccination(Abbas et al., 2020; MacDonald et al., 2020; WHO, 2019c, 2020c, 2020f); a low level of trust owing to poor personal experience with the health care system and /or with the healthcare providers; individual or group knowledge, practices, and attitudes concerning health decisions and disease control/prevention through vaccination and what those who are targeted by the vaccines perceive of vaccination risks and the vaccination benefits (MacDonald, 2015; MacDonald et al., 2018; MacDonald & Dubé, 2018; Machado et al., 2021; Machingaidze et al., 2013; Magambo et al., 2020; Malande et al., 2019; Marshall & O'Leary, 2018). Contextual factors driving hesitancy include some religious and various cultural beliefs; includes socioeconomic factors for example the level of education of an individual, one's employment, one's income, a person's age, a person's gender, one's marital status and the ethnicity (MacDonald & Dubé, 2018; Malande et al., 2019; McAllister et al., 2019).

Other contextual factors are the media environment that usually allows the dissemination of misinformation, various conspiracy theories and rumors, the influence from various opinion leaders (for example the church, the community or traditional leaders) and certain geographical barriers (MacDonald, 2015; MacDonald et al., 2018; MacDonald & Dubé, 2018; Machado et al., 2021; Machingaidze et al., 2013; Magambo et al., 2020; Malande et al., 2019; Marshall & O'Leary, 2018). Vaccine hesitancy is also driven by vaccine and vaccine-specific factors, including caregiver safety concerns that include adverse events following immunization (AEFIs), or access related barriers (for example timely vaccine delivery and location, transportation costs), unusually long waiting times at the immunizing health facilities, inadequate or lack of time needed to go for vaccination services, the fear of needles/injections, the introduction of new vaccines into the program, concerns related to vaccine scheduling as well as the different mode of delivery of various vaccines (MacDonald & Dubé, 2018; Malande et al., 2019; McAllister et al., 2019; Mutua et al., 2021; Nabirye et al., 2020).

The recent widespread rise in the cases of vaccine hesitancy centers around the recently developed vaccines against COVID-19 disease (Poland et al., 2020; Roberton et al., 2020; Schwarzinger & Luchini, 2021; Sherman et al., 2021; Snape & Viner, 2020; Sun et al., 2020). The major concerns about Sars-Cov-2 targeting vaccines have largely been concerns with the fast speed in the clinical production process for these vaccines, the novel mRNA technique for some of the vaccines, the expedited process of approval of these vaccines and the apparent lack of clarity regarding adverse events against these vaccines (Morgan & Rose, 2020; Piché-Renaud et al., 2021; Poland et al., 2020; Roberton et al., 2020; Schwarzinger & Luchini, 2021; Sherman et al., 2021; Snape & Viner, 2020; Sun et al., 2020). These concerns have added fuel to the fire surrounding the pre-COVID misinformation, and myths and rumors that were spreading widely on various social media platforms (Morgan & Rose, 2020; Munster et al., 2020; Ogunkola et al., 2021). These rumors increased in the pandemic and post pandemic periods and there exists significant concerns about erosion of public's trust in vaccines, in the healthcare systems, in government initiatives, and in the vaccine manufacturers (Morgan & Rose, 2020; Piché-Renaud et al., 2021; Poland et al., 2020; Roberton et al., 2020; Schwarzinger & Luchini, 2021; Sherman et al., 2021; Snape & Viner, 2020; Sun et al., 2020).

Some vaccines, for example the HPV vaccine, have shown significant hesitancy and very poor performance of the second dose across the world (Hidle et al., 2018; WHO, 2020c; Wiysonge et al., 2012). The HPV vaccine related hesitancy usually more likely to be accompanied with social stigma, especially given that it targets adolescents and not younger population than the rest mainly given during infancy (Hidle et al., 2018; WHO, 2020c; Wiysonge et al., 2012). Several different factors influence HPV vaccine hesitancy, including stigma from sociocultural influences given that the virus is a sexually transmitted infection and the general lack of knowledge about HPV virus and vaccines, and the risks associated particularly among adolescents (Hug et al., 2019; Lin et al., 2020; Lin et al., 2019; Nabirye et al., 2020; WHO, 2019c). Recent rise in use of social media platforms have provided an avenue for those with antivaccine information and misinformation on HPV disease to rapidly spread their message and agenda targeting the adolescents, including long-term anti-fertility fears and rumors that the vaccination for young girls leads to increase in the risk of erosion of the trust and the confidence in HPV vaccine (Hug et al., 2019; Lin et al., 2020; Lin et al., 2019; Nabirye et al., 2020; WHO, 2019c).

Despite the obvious global progress achieved towards providing childhood vaccinations worldwide (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016), there are still many challenges especially in reaching the most vulnerable populations; the poorest communities, the most disadvantaged and vulnerable children in most remote communities of Africa (Hug et al., 2019; Igme, 2020; Lane et al., 2018). Inequalities and iniquities in immunization service provision and coverage still exist globally, with most being often masked by the national or the regional summarized immunization data that often does not reveal the true picture on the ground (Abbas et al., 2020; Alkema et al., 2016; Anthony et al., 2009).

Immunization coverage in most low-income and poor countries remains significantly much lower than the immunization levels seen in middle-income and high-income countries of the world (Abbas et al., 2020; Alkema et al., 2016; Anthony et al., 2009). The picture in countries with fairly high national immunization coverage rates and showing demonstrable improvement in their immunization still reveals evidence of some disparities in the immunization coverage owing to social economic differences within their communities given that immunization services there are provided at a cost (David et al., 2011; De Figueiredo et al., 2020; Dratva et al., 2021). Concerns about these disparities were behind the drive to set up the EPI program in 1974, that sort to increase the numbers of qualifying and targeted children across the world receive timely life-saving immunizations (Atouf et al., 2021; Blencowe et al., 2016; CDC, 2011; Douglas & Samant, 2018).

There is a rising concern and discomfort regarding the impact of hesitancy in vaccines and refusal of vaccines driving low vaccine uptake and opening doors for groups that promote negative messages and low public mood and confidence towards immunization and vaccine programs (Dicker et al., 2018; MacDonald et al., 2018; WHO, 2019c, 2019d). Low income and developing nations as well as the developed countries have been guided by WHO to device and pursue various measures and avenues to assess, review, quantify the magnitude of refusal of vaccines and hesitancy to vaccines within those nations, and come up with various recommendations and strategies that will help in addressing this problem. All countries including Uganda are affected, and has now spread to healthcare workers and end user communities, who should be target of new interventions for addressing this problem.

Statement of the Problem

Despite many previous efforts by various stakeholders in the immunization space, there remains a gap in the understanding of the reasons for low immunization rates and recurrence of vaccine preventable infections in Uganda, and the need for further recommendations about interventions that can help address this problem. It is true that there are reports from Uganda and around the region attempting to study and explain what makes many communities to not fully take up available vaccines in the region (Adekeye et al., 2015; Malande et al., 2019). These reports and the recommendations thereof have not adequately addressed the problem. Some of the barriers identified include difficulties in language thus hampering effective communication; a difficult terrain and poor road network making transportation difficult when trying to access the immunization centres for delivery of supplies or even for supervision and mentorship (Adekeye et al., 2015; Dicker et al., 2018; Igme, 2020; Malande et al., 2019; Nations, 2020). There are additional barriers affecting access or availability or acceptance of immunization services in Uganda and countries with similar contexts in sub Saharan Africa, including a large population with inadequate to low education level; a generally high number of adolescent or teenage pregnancy rates that end up in early parenthood; a restless conflict ridden border especially with DR Congo or South Sudan that has communities constantly on the moon and high numbers of refugees housed in Hoima District (Adekeye et al., 2015; Nations, 2020; Ntukanyagwe, 2019; Wiysonge et al., 2012).

Immunization is widely recognized by the WHO as only second to clean water in preventing communicable diseases, and is thus a cost-effective intervention needed to prevent the currently high morbidity and mortality caused by these infectious diseases, especially in high-endemic settings (David et al., 2011; De Figueiredo et al., 2020; Dratva et al., 2021). The efforts over the past two decades aimed at reducing child mortality have been commendable, much as a significant number (more than ten million) of persons below age of 5 die annually owing to vaccine preventable diseases (Dudley et al., 2020; Durrheim et al., 2019; Ezbakhe & Pérez-Foguet, 2020). Many reports show that most of these deaths are a results of causes preventable by vaccines take place in poor or developing countries of the world (Alkema et al., 2016; Anthony et al., 2009; Bangura et al., 2020; Bedford et al., 2018; Cascini et al., 2021; CDC, 2020; Chan, 2014).

It is noteworthy that vaccines prevent more than four million child deaths annually, with children who receive all the age appropriate recommended vaccinations by eighteen months of age showing less likelihood of dying by age five compared to those that do not complete their scheduled immunization (Alkema et al., 2016; Anthony et al., 2009; Bangura et al., 2020; Bedford et al., 2018; Cascini et al., 2021; CDC, 2020; Chan, 2014). The COVID pandemic adversely affected immunization, with over twenty five million children now not completing their immunization schedules, when compared to nineteen million two hundred thousand before the pandemic(González et al., 2022; Kabagenyi et al., 2022; Ndejjo et al., 2023; Rachlin et al., 2022; Summan et al., 2023). The most affected vaccines are measles containing vaccines, where about 5 million children in 2022 missed a measles containing vaccine (Rachlin et al., 2022). The other vaccines are pneumococcal conjugate vaccines, the cervical cancer vaccines for adolescent girls and DPT(González et al., 2022; Kabagenyi et al., 2022; Ndejjo et al., 2023; Rachlin et al., 2022; Summan et al., 2023). It is this impact of immunization that put it at the centre of the drive aimed at decreasing childhood mortality under the united nations Millennium Development Goal (MDG) 4 and now the united nations Sustainable Development Goal (SDG) 5; which targeted to achieve the reduction of under-five mortality rates in children by two-thirds by the year 2015 and SDG 3 which that aims to achieve a reduction of under-five deaths worldwide to less than 25 deaths per one thousand live births by the year 2030 (Dudley et al., 2020; Durrheim et al., 2019; Ezbakhe & Pérez-Foguet, 2020).

In sub-Saharan Africa, where Uganda falls, over 170 child deaths in every 1000 live births are reported under the age of five (Rachlin et al., 2022). Majority of these early child deaths are vaccine preventable, and follow vaccine preventable diseases including malaria, tuberculosis, diarrhea, influenza, group B streptococcus, measles and pneumonia (Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; WHO, 2017a, 2019c, 2020c). Iniquities and inequalities in the provision of and access to vaccines and in vaccine coverage in the poor communities of the globe have been reported as the underlying factors fuelling low immunization rates in various studies (Alkema et al., 2016; Anthony et al., 2009; Bangura et al., 2020; Bedford et al., 2018; Cascini et al., 2021; CDC, 2020; Chan, 2014). Other factors previously described include very low education level of caregivers, a young age of some of the caregivers owing to teenage pregnancies, poor or low social economic status of the caregivers, inadequate male partner or fathers' involvement among others (Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; González-Block et al., 2021; Hough-Telford et al., 2016; WHO, 2017a, 2019c, 2020c). A deeper and broader understanding of these factors associated with poor vaccination uptake is critical and urgent needed if we are to ensure improvement of vaccination uptake and coverage.

Over the years, there have been various interventions that have included the MDGs, the Abuja declaration on healthcare financing, the Alma Atta declaration of nineteen seventy eight, the SDGs and the child survival action convention for political mobilization to end preventable child deaths that have greatly improved child survival in most countries (Hilleman, 2000; Hug et al., 2019; Igme, 2020). Despite all these efforts, most countries, including Uganda, have not yet achieved the set targets, failing as well to achieve the MDGs, with the end of 2015 showing that 44 out of fifty developing countries carried only a twenty percent or less chance of achieving the Millennium Development Goal four. Most of these countries never achieved MDGs at the time they were replaced by the SDGs (Hilleman, 2000; Hug et al., 2019; Igme, 2020).

Uganda did make positive strides with the under-five mortality falling by 6.3% (167/1000 to 90/1000 live births) per year for the period nineteen ninety to two thousand and twenty (Igme, 2020). The country however did not gain the pace of 10% average annual reduction that was needed to help achieve the MDG under five mortality targets of less than fifty-six child deaths for every one thousand births by the year 2015. The National Uganda Expanded Program on Immunization (UNEPI) program covers the 8 major/core diseases including Polio, Tuberculosis (BCG vaccine), Diphtheria, Pertussis, Tetanus, (combined in the DTP vaccine), and more recently, the addition of the conjugated pneumococcal vaccine (PCV) launched in twenty twelve. The HPV vaccine for adolescent girls has been introduced as well. The most recent survey in Uganda (UDHS 2016), showed that only fifty five percent of eligible children aged twelve months to twenty-three months are fully vaccinated, with urban areas at sixty one percent slightly edging the rural areas (fifty percent).

The factors underlying the low coverage in Uganda require further study and examination. As mentioned, current and recent reports highlight low education level regarding vaccines, availability of vaccine related information being inadequate, the rising cases of groups that oppose vaccines and increasing access to internet and social media networks that promote vaccine refusal, rising poor health seeking behaviours that do not prioritise vaccination or abet missing of scheduled immunization appointments (Alkema et al., 2016; Anthony et al., 2009; Bangura et al., 2020; Bedford et al., 2018; Cascini et al., 2021; CDC, 2020; Chan, 2014). There have been published and print media reports regarding some local indigenous communities within Uganda that hold onto religious beliefs and cultural norms that influence perceptions on vaccines and immunization, where some promote hesitancy (Adekeye et al., 2015; Bangura et al., 2020; Budu et al., 2020; Dicker et al., 2018; Liu et al., 2012; Liu et al., 2016; Malande et al., 2019). The rising cases of negative messages against vaccines, many more communities fearing or refusing vaccines, many areas not able to access all vaccines when needed are additional driers of low immunization documented (Eshetu & Woldesenbet, 2011; van der Maas, 2018). Uganda has been running a national program on immunization for many years, but many districts, Hoima and Wakiso included, still continue to report significantly low immunization coverage and frequent reports of recurrent outbreaks of diseases including rotavirus diarrhea, measles, pneumonia, and posting a seventy three percent measles coverage in Wakiso and an average low of sixty eight percent nation-wide measles coverage (UBOS, 2016).

In the most recent review for Uganda, nationwide rates of full immunization rate stood at fifty five percent for children of age between twelve months to twenty three months, while the immunization coverage for urban centres was sixty one percent and fifty percent for rural areas (UBOS, 2016). The new concept of Vaccine hesitancy as defined by the WHO has yet to be adequately studied in Uganda, with clear need for additional studies, especially those that focus on designing affordable easy to implement strategies and recommendations to address the problem. There is need to quantify just how big the problem of vaccine refusal is, and to what extend the reported low caregiver and consumer confidence in vaccines is, including its contribution to the reported low utilization of immunization services in urban and rural Uganda.

Purpose of the Study, Research Aims, and Objectives

Purpose of the Study

This mixed method study explored drivers of low uptake and utilization of immunization services in the rural district of Hoima and the peri-urban district of Wakiso; to compare the identified drivers of underimmunization in these two districts and to identify and propose interventions, strategies and approaches that can help to address the problem of vaccine hesitancy and underimmunization in these districts. Deaths for children in poor or developing countries commonly follow sickness and illness from common vaccine preventable diseases, making this study all the more relevant and timelier. According to the WHO, immunization is listed as a key and important strategy that can help to save many early child lives, through the prevention of more than four million child deaths annually, especially in poorer and underdeveloped countries of the world.

There indeed have been several interventions that aimed at increasing the availability of immunisation services and vaccines worldwide. Some of these strategies have been partly implemented as an implementation of the Abuja declaration on healthcare financing that focused on allocating of 15^{th} of GDP resources of each county for healthcare in that country. Implementation of these strategies have been supported by the resolutions under the child survival action convention for political mobilization. To address the pending and unaddressed gaps in implementation of various remedial measures, and in general drivers of vaccine hesitancy and underimmunization, this study chose a mixed method approach, that combined quantitative and qualitative research methods of data collection. Triangulation was therefore achieved at the level of data collection. The goal was to attain as much variation and exhaustive examination of the barriers to immunization.

The methods entailed both quantitative and qualitative approaches to data collection. The qualitative arm of the study included focus group discussions (FGDs) for caregivers of the children who were eligible for immunization in Hoima and Wakiso districts and had been brought to the immunization centers. The quantitative arm entailed face-to-face in-depth interviews for the caregivers, key and the focal health care workers involved in immunization within Hoima and Wakiso districts; and key informant interviews for focal persons, decision makers, leaders and managers of immunization services within the two districts. This was done with the broadest reach to ensure that views from both caregivers, health workers, and community leaders and village health team members are all incorporated in the study. All these are players in the immunization cycle and program, and play a critical role in distribution or consumption of immunization services.

This study also did involve the collection of secondary data from the health information records at Wakiso and Hoima District health offices, from record offices at ministry of health and at the vaccination and immunization health centres within the two Hoima and Wakiso districts. In addition to these approaches, this study as well conducted a systematic review of research peer reviewed articles that have been published on vaccine hesitancy and underimmunization to establish a firm and a deep understanding of the current status, the causes, the motivating factors, and the promoters of vaccine hesitancy and underimmunization in Uganda and sub Saharan Africa. It assessed promoters and reasons behind vaccine hesitancy along the three main categories as identified and classified by the World Health Organization including the following focus areas: 1. Confidence of the communities in vaccination programs and vaccines (relates to situations where there is no trust in vaccines and in the healthcare providers of the vaccines); 2. Complacency of the communities and populations to vaccines and vaccination programs (relates to where target groups do not perceive the need for vaccination or they do not value vaccination) and 3. Convenience of the vaccination process as perceived by the communities and populations targeted by vaccination (deals with matters that relate to access to vaccines and access to vaccination services). These factors have driven hesitancy to being declared a threat to global health. These factors are of increasing concern especially as regards the diminishing public confidence in vaccines and in vaccination services as anti-vaccine movements and groups increasingly becomes stronger and stronger in their agenda.

This study intended to compare immunization indicators, status, performance and quality of services in rural Hoima and urban/peri-urban Wakiso Districts. The WHO therefore has tasked both developing and developed countries to ensure they aggressively and urgently institute measures necessary to assess and to quantify the magnitude of vaccine hesitancy and underimmunization in their specific contexts, and to design strategies and various measures needed to address this problem. Uganda, like many other nations is included in the region burdened with high child deaths numbers and rising cases of vaccine hesitancy as reported both among the health workers and target communities.

Urgent interventions are thus required to immediately address this problem. This is because Uganda, just like many other developing countries suffers inadequacies and many inequalities that greatly affect the immunization uptake, and completion of vaccination schedules (Adekeye et al., 2015; Bangura et al., 2020; Budu et al., 2020; Dicker et al., 2018; Liu et al., 2012; Liu et al., 2016; Malande et al., 2019). These factors include language barrier problems, cultural and communication barriers, inadequate or poor transport and poor road network, a very mobile and migrant border/refugee population, a very difficult geographical terrain that affects vaccine distribution (Adekeye et al., 2015; Bangura et al., 2020; Bulamu, 2021; CDC, 2011; Chan, 2014; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019). Additional drivers of underimmunization in Uganda include a poorly educated population, a significant proportion of which conceive while still teenagers thus leading to early parenthood, and religious groups and cults which affect immunization (Adekeye et al., 2015; Bangura et al., 2020; Budu et al., 2020; Dicker et al., 2018; Liu et al., 2012; Liu et al., 2016; Malande et al., 2019).

The problem of vaccine hesitancy and underimmunization with the underlying drivers/promoters in Uganda have not been fully studied, with very little data existing on this topic, especially strategies and initiatives that can be used to solve this problem in Hoima and

Wakiso Districts. This is a comparative and descriptive cluster randomized mixed method study of both qualitative and quantitative methods, using interviews and focus group discussions for caregivers of eligible children, and key informant interviews of focal persons involved in immunization in Hoima (rural) and Wakiso (urban) districts in Uganda. The study also included a systematic data review of peer-reviewed research articles that have been published on underimmunization and vaccine hesitancy. We aimed to establish a clear understanding of vaccine hesitancy and of underimmunization in Wakiso and Hoima districts of Uganda and also explore and examine published reports of drivers of vaccine hesitancy in Sub Saharan Africa. These findings were used to propose areas that require further research, suggest practical interventions and recommendations that can be used to address the problem of vaccine hesitancy and underimmunization in Uganda.

Research Aim

To estimate the level and factors associated with underimmunization in Hoima and Wakiso districts of Uganda, and describes barriers to immunization and the determinants of vaccine hesitancy and underimmunization in Uganda.

Research Objectives

1. To estimate the level of underimmunization in rural Hoima and urban/peri-urban Wakiso Districts of Uganda
2. To determine the factors associated with underimmunization in in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.
3. To determine and describe the barriers to the uptake and utilization of immunization services in rural Hoima and urban/peri-urban Wakiso Districts of Uganda.

4. To understand the causes and determinants of vaccine hesitancy in Sub Saharan Africa.
5. To compare and contrast the drivers of vaccine hesitancy and under-immunization in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.

Nature and Significance of the Study

Nature of the Study

This study used a mixed methods design, with an experimental approach, that combined both qualitative and quantitative data collection methods (Bekhet & Zauszniewski, 2012; Carter et al., 2014; David & Resnik, 2011; Glanz et al., 2015; Noble & Heale, 2019a). A blend of multi stage cluster sampling and consecutive sampling method was used in which the parish was used as a cluster. The data collection period was from October 2021 to April 2022.The qualitative component entailed Focus group discussions with care givers to children coming for immunization services and face to face interviews of both child caregivers and key immunization focal persons from Wakiso and Hoima districts. Focus group discussion participants were chosen through purposive sampling in order to achieve maximum variation in the sample. The Focus group discussions were conducted in the local language (or in the language spoken and understood by all participants) by a moderator and a note taker. The discussions were audio recorded and then later transcribed.

This study was built on the constructs of the health belief model (HBM) model, which suggests that people's beliefs regarding their health problems, and what they hope to gain or benefit from seeking solutions to those problems, and any hindrances or barriers to that particular action, and their self-efficacy (for either engaging or not engaging) are important and instrumental in whether they decide to embrace immunization, or take up a given vaccine and in combating vaccine hesitancy against various vaccines (Abraham & Sheeran, 2015; Eskola et al., 2015; Glanz et al., 2015; Janz & Becker, 1984). Based on this model, this study sought to test these principles in Hoima and Wakiso districts (Janz & Becker, 1984). In this study, the persisting problem of vaccine hesitancy, recurrent outbreaks of vaccine preventable diseases especially measles in these two districts, underimmunization, emerging and re-emerging vaccine preventable diseases and rising cases of anti-vaccine messaging and sentiments provide the stimulus (or the cue to action) [as described in the health belief model], necessary to address these problems (Adekeye et al., 2015; Bangura et al., 2020; Bulamu, 2021; CDC, 2011; Chan, 2014; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019).

While the health belief model theoretical constructs do find their origin from theories in Cognitive Psychology (Glanz et al., 2015), which opined that reinforcements usually work through affecting the expectations and not the behavior of individuals, this study however recognizes that the behavior of the caregivers in embracing immunization and taking up vaccines for themselves and their children is a function of the degree to which these caregivers attach value to the outcome or result anticipated (that is reduced numbers and rate of VPD occurrence & caregiver evaluation of expectation that rests upon them to ensure they attain the outcome of better health from avoiding or recovery from these diseases (Carpenter, 2010). It therefore follows that, an individual avoiding any sickness from infection with these vaccine preventable diseases is therefore of great value as an outcome of this model, and that the expectation that they accepting and embracing immunization can help the caregivers and communities reach this anticipated goal are important targets which the communities should therefore be empowered to embrace and appreciate (Glanz et al., 2015; Siddiqui et al., 2016).

Focus group discussion participants were different from those who had participated in the individual caregiver-child interviews to reduce the risk of bias and allow for variability in respondent views and opinions. Secondary data included in the study was sourced from the health information records at Wakiso and Hoima District Head Quarters, at immunization centres within Wakiso and Hoima Districts. This study included a systematic review of already published research work and research articles on vaccine hesitancy and underimmunization that were conducted in sub-Saharan Africa (Bekhet & Zauszniewski, 2012; Carter et al., 2014; David & Resnik, 2011; Glanz et al., 2015; Noble & Heale, 2019a).

The systematic review protocol used in this study was structured using the PICO (participants, intervention, comparator, and outcome) format for systematic reviews (Heale & Forbes, 2013; Larson et al., 2015; Noble & Heale, 2019a; Olsen et al., 2004; WHO, 2020c, 2020d). This study considered both quantitative (controlled before-and-after studies, randomized controlled trials, cohort studies, interrupted time series designs, cross-sectional studies, or case-control studies) and qualitative studies (containing in-depth interviews, focus group discussions, case studies, direct observation, action research and ethnography).

This study excluded interventional studies (for example clinical trials or vaccine efficacy/vaccine effectiveness studies or studies that were not designed to measure outcomes that were associated with vaccine hesitancy); systematic or narrative reviews, papers that were not peer reviewed, editorials among others like grey literature. The study population/participants were persons living in Africa and are vaccine hesitant, or that have chosen against being vaccinated recommended vaccines; including caregivers, children and other adults/adolescents. The main outcome was vaccine hesitancy determinants, which was the reasons the participants had given for not accepting or allowing their children or themselves to be vaccinated.

The study population consisted of caregiver-child pairs (a care giver with a child of age less than five years) from Wakiso and Hoima Districts attending vaccination services in any of the designated health facilities that offer immunization services. A study unit consisted of a caregiver-child pair with at least one child aged 9 - 59 months in their home in either Hoima or Wakiso District who fulfilled the inclusion criteria. Exclusion criteria was on caregivers that did not give informed consent or did not reside in the district (Wakiso/Hoima) for less than nine months. The dependent variable was the acceptance of immunization services, while the independent variables included among others age of the caregiver, marital status, religion, level of education, occupation, sex of the caregiver, distance to the health facility and waiting time before receiving immunization services at the facility or outreach site.

Quantitative data was collected from caregiver interviews using a pre-tested and piloted data collection tool. This researcher administered questionnaire comprises of four sections to capture socio-demographic information, information about the child, vaccine compliance and the child vaccination history. The focus group discussion recordings were transcribed into Word 2016 by research team that understood local language and English adequately, and then cross checked with an independent reviewer for correctness and consistency. Afrter completing the transcription process, the proceeds were exported to NVIVO 12, to identify and align emerging themes. The quantitative and secondary data findings was entered anonymously in a special Excel spreadsheet for cleaning and completion and after exported to Stata version 13. Stata was used to do regression and modified passion analysis. Descriptive analysis of the data was expressed as means ± standard deviation, percentages and frequencies, with associations between variables being analysed using chi-square test - differences between means were assessed using the Student's t-test.

Significance of the Study

The identification of vaccine hesitancy by WHO as a global health threat (WHO, 2019b) emphasized the need for urgent interventions to address this problem. Factors contributing to vaccine hesitancy vary from one place to another. With low immunization coverage and frequent outbreaks of vaccine preventable diseases in Hoima and Wakiso districts of Uganda, this study aimed to explore the reasons behind this problem (Adekeye et al., 2015; Bangura et al., 2020; Bulamu, 2021; CDC, 2011; Chan, 2014; Ezbakhe & Pérez-Foguet, 2020;

Malande et al., 2019). This study estimated the level of underimmunization, identified barriers to the uptake of immunization, reasons for underimmunization, drivers for vaccine hesitancy and reasons for low confidence in immunization in rural Hoima and (peri)urban Wakiso districts, and thus provided useful information for planning, forecasting, and addressing these recurrent problems that contribute to immunization coverage rates that have remained below the World Health Organization recommended targets.

This study generated and proposed educational recommendations and communication strategies and health system focused approaches that can help address the problem of vaccine hesitancy and underimmunization particularly in Uganda and Sub-Saharan Africa in general. This study generated important information on vaccine uptake, coverage, utilization of immunization services, refusal, and barriers to immunization within Uganda. This information is unique, because it emanates from both rural, peri-urban and urban communities in Uganda. The rural Hoima district information was enriched further by experiences of caregivers from a very mobile migrant border and refugee communities in Hoima district. This information is useful for the local health authorities in Wakiso and Hoima districts to improve their immunization health systems, and address the identified challenges/barriers to immunization, advocate for/lobby for more government investment in immunization and allocation of resources to health in line with the Abuja declaration on health financing.

The drivers of hesitancy identified were addressed at local, district and national levels. Experiences from addressing these drivers to hesitancy and underimmunization can then be shared with other districts, and African countries with similar contexts to be implemented in their nations for solving the problem of vaccine hesitancy. Some of the lessons have been included into ministry of health policy and strategic plans towards addressing vaccine hesitancy and underimmunization. This study provided relevant information useful in planning, forecasting, and addressing the recurrent outbreak of vaccine preventable diseases, the problem of underimmunization, the emerging problem of vaccine hesitancy and the persistently low immunization coverage rates in Uganda.

The findings of this study will be disseminated in University library, presented at local and international scientific and public health conferences and published in peer review scientific journals. This study findings will lead to generation of innovative educational interventions and new communication strategies or relevant health system approaches to help address the problem of vaccine hesitancy and underimmunization in Uganda and Sub-Saharan Africa at large.

Out of this study, we hope to see strengthened immunization services in Wakiso and Hoima districts; improved knowledge, communication and skills in the immunization service delivery by health workers as a way of encouraging parents to come for the services; enhanced community engagement, and participation in immunization, uptake of immunization services and empowerment to demand for immunization services and adhering to recommended immunization schedules; generation of guidelines and tools for assessing vaccine hesitancy and underimmunization; reduction in the out breaks and the occurrence/recurrence of common vaccine preventable disease in Wakiso and Hoima districts; writing of policy briefs and position papers which can be used to provide an evidence base for policy development and strategic planning; improved ministry of health and government funding and investment into immunization especially in fighting the problem of vaccine hesitancy and improved numbers of children who survive up to the fifth birthday, due to reduced morbidity and mortality as a result of vaccine preventable diseases following improved uptake and availability of immunization services in Hoima and Wakiso Districts.

Research Questions and Research Hypotheses

Research Questions

1. What are the levels of underimmunization in rural Hoima and urban/peri-urban Wakiso Districts of Uganda?
2. What are the factors associated with underimmunization in in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda?
3. What are the barriers to the uptake and utilization of immunization services in rural Hoima and urban/peri-urban Wakiso Districts of Uganda?
4. What are the causes and determinants of vaccine hesitancy in Sub Saharan Africa?
5. What comparisons and contrasts exist between the drivers of vaccine hesitancy and under-immunization in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda?

Research Hypotheses

1. Ugandan children fail to complete the recommended immunization schedule because the caregivers do not consider vaccines safe.
2. Ugandan children fail to complete the recommended immunization schedule due to lack of caregiver trust in vaccination.
3. Ugandan children fail to complete the recommended immunization schedule because the caregivers do not consider vaccines effective.
4. Ugandan children fail to complete the recommended immunization schedule due to poor immunization health services.

CHAPTER 2: LITERATURE REVIEW

Summary of the Purpose Statement

Vaccine preventable diseases are the main contributors to disease in poor countries of world (Anthony et al., 2009; Blencowe et al., 2016; Igme, 2020; WHO, 2017a). The WHO ranks immunization second to provision of safe water as regards strategies for preventing VPDs, with immunization projected to avert over 4 million deaths post pandemic especially in the sub-Saharan Africa (Brenzel, 2015; CDC, 2011; Roser et al., 2013).The United Nations' Sustainable Development Goals (SDGs) emphasize the role of immunization towards child survival and reduction of under 5 deaths, and implementing the “child survival action convention for political mobilization” resolutions (David et al., 2011; Igme, 2020). Common VPDs like measles, polio, tetanus, pneumonia, and diarrheal disease still require a lot of effort and investment to be completely eliminated or substantially reduced (Blencowe et al., 2016; Ntukanyagwe, 2019; Roser et al., 2013; WHO, 2021c).

Uganda, a developing country suffers inadequacies and major inequalities across all spheres of society and development, including immunization, language barrier, cultural beliefs, communication barriers, a very poor transport terrain, challenging road network, a very unsettled and highly mobile cross-border refugee population, a difficult land/ geographical terrain that affects the distribution of vaccine distribution in the district (Malande et al., 2019; Rudan et al., 2008). The other factors contributing to low immunization in Uganda are an inadequately educated general population, a high population of teenage pregnancies and teenage mothers, the presence of religious groups and populations that preach against vaccines and immunization, and fathers/male partners who make final decisions on vaccination and thus can deny the mothers permission to take children for vaccination, (Albers et al., 2022; Gonzales et al., 2021; Kaufman et al., 2021; Kimmel et al., 2007; Kuehn et al., 2022; Ntukanyagwe, 2019; Olusanya et al., 2021; Paul et al., 2022; Stratoberdha et al., 2022; Yang et al., 2023;

Yazdani et al., 2021) and the worldwide rising levels of negative vaccine sentiment, hesitancy, (Eshetu & Woldesenbet, 2011; van der Maas, 2018) and vaccine refusal due to rising internet access and use of social media platforms (Butler & MacDonald, 2015).

According to the Strategic Advisory Group of Experts (SAGE) of the World Health Organization, there major factor that underly vaccine hesitancy have been captured in the 3C's model of complacency, confidence and convenience (WHO, 2019c). Subsequent to this was the listing of hesitancy by the World Health Organization into the top ten threats to global health in 2019 (WHO, 2019c). The low rate of 55% national coverage of immunization for Uganda, and 61% in urban areas and 50% in rural Uganda is a worrying concern (Bulamu, 2021), where more than 26 districts have been documented to experience low immunization coverage and recurrent measles' outbreaks (UBOS, 2016).

Theoretical Framework

Introduction

The World Health Organization rates immunization only second to fresh water as an intervention for promoting health (Francis et al., 2008). The need to overcome underimmunization, and vaccine hesitancy are current pressing needs if developing countries are to realize the advantages of immunization (WHO, 2019c, 2019d). By including Vaccine hesitancy among the Ten major threats to global health (WHO, 2019c), the World Health Organization has restored focus on need for promoting greater vaccine uptake, especially with the pressing need to overcome unprecedented adverse outcomes from outbreak of COVID-19 which have left healthcare systems worldwide overwhelmed, with a real risk of erosion of gains previously made with the control of measles, polio, pneumonia among others (Albers et al., 2022; Gonzales et al., 2021; Kaufman et al., 2021; Kimmel et al., 2007; Kuehn et al., 2022;

Olusanya et al., 2021; Paul et al., 2022; Stratoberdha et al., 2022; WHO, 2019d; Yang et al., 2023; Yazdani et al., 2021).

It is the focus of this study to evaluate and determine drivers of both underimmunization and hesitancy in Hoima and Wakiso districts of Uganda, and suggest recommendations and interventions that could be implemented to address these problems. This study has the unique advantage to compare these two major problems in a rural (Hoima) versus an urban/peri-urban (Wakiso) district, and propose relevant educational interventions, communication strategies and health system modifications and improvements that can help solve these problems.

This study is built around the health belief model (HBM) model, that suggests that people's beliefs concerning their health problems, what they hope to gain from seeking solutions to these problems, any hindrances/barriers to that action, and self-efficacy (for engaging or not engaging) are important in the uptake of immunization services and combating hesitancy against vaccines in Hoima and Wakiso districts (Janz & Becker, 1984). In this study, the persisting problem of underimmunization, frequent recurrence of vaccine preventable diseases especially measles in these two districts, and rising cases of vaccine hesitancy provide the stimulus (or cue to action) to address these problems.

While the HBM theoretical constructs find their origin from theories in Cognitive Psychology (Glanz et al., 2015) which held that reinforcements worked through affecting expectations and not behavior, this study however recognizes that the behavior of people in embracing immunization is a function of the degree to which the caregivers attach value to the result (reduced vaccine preventable diseases [VPDs]) and the caregivers evaluation of the expectation upon them to attain the outcome of better health from these diseases (Carpenter, 2010). Avoiding sickness from vaccine preventable diseases is of great value as an outcome of this model, and the expectation that embracing immunization can help the communities reach this goal are important targets that communities should be empowered to embrace (Glanz et al., 2015; Siddiqui et al., 2016).

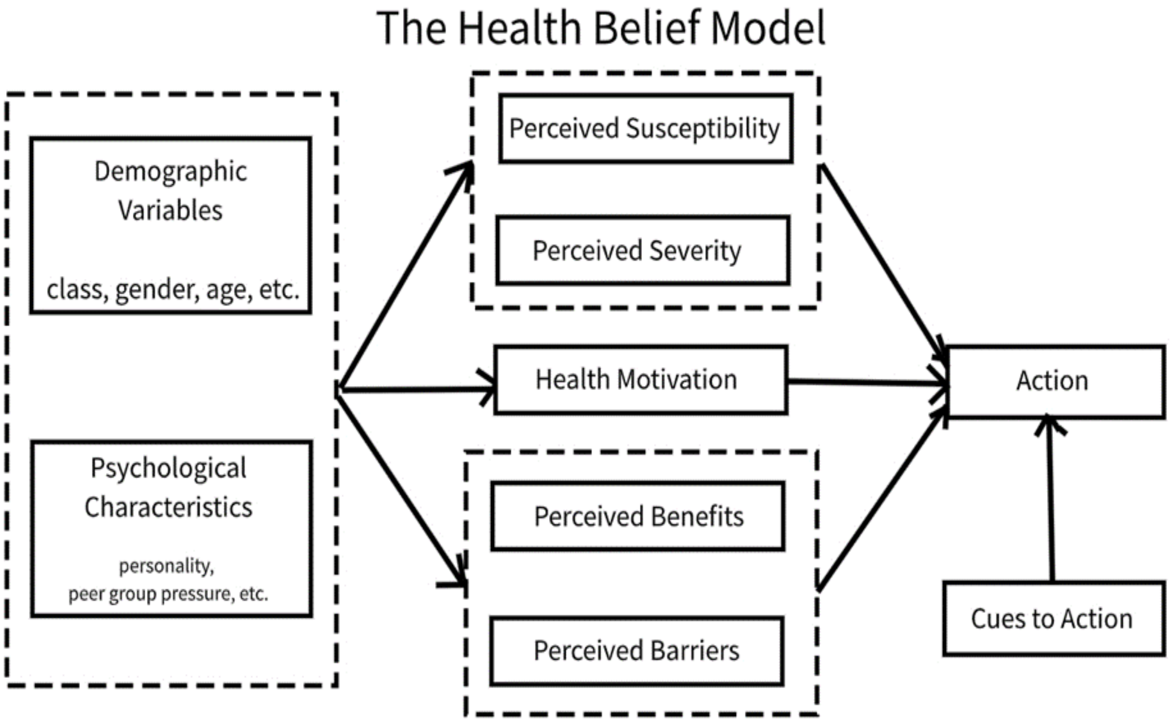

Figure 1: The illustration of the Health Belief
(Janz & Becker, 1984)

Perceived susceptibility

A big problem with communities uptake to vaccination is sometimes inadequate understanding of the benefits of immunization, a factor that affects “perceived susceptibility” as contemplated in the HBM – as subjective assessment of the communities risk of developing vaccine preventable diseases (Glanz et al., 2015). If communities are educated and empowered on the benefits of immunization, it is believed that they will understand their susceptibility to vaccine preventable diseases in the absence of immunization, and therefore embrace the need to have themselves and their children vaccinated thus reduce their risk of developing vaccine preventable diseases (Carpenter, 2010). Traditionally, it has been found that individuals who consider themselves to have low "perceived susceptibility" may consider that they are not at a big risk for contracting a certain disease, and so even engage in risky practices (Carpenter, 2010).

Some while acknowledging the likelihood of developing the disease, may still view that possibility as unlikely, while those who see their risk as high would likely engage in activities that reduce their possible risk of developing the vaccine preventable diseases (Carpenter, 2010). The perceived threat of vaccine preventable diseases – which is a factor of both perceived susceptibility and perceived severity is modified by level of knowledge about vaccines, about the preventive measures, the vaccine preventable diseases themselves among others (Glanz et al., 2015). The use of the HBM in this study therefore helped to predict if a higher perceived threat does as expected lead to a higher likelihood of embracing and taking up immunization services in Hoima and Wakiso districts.

Perceived severity

The subjective assessment by the communities of degree of severity of underimmunization and hesitancy and its possible outcomes in resulting in increased cases of vaccine preventable diseases is defined as "Perceived severity," under the HBM. In the HBM theory on which this study is anchored (Carpenter, 2010; Glanz et al., 2015), proposes that those who consider a given health problem (in this case hesitancy and underimmunization) as serious to their health are more likely to then engage in activities or behaviors that prevent the occurrence of the health problem (in this case high cases of vaccine preventable diseases) from occurring (or at the very least reduce the severity of the vaccine preventable diseases).

In the HBM theory and model, perceived seriousness entails beliefs held about the (VP) diseases themselves (that does the disease cause pain, disability or is it a threat to life) for example whether it is life-threatening or may cause disability or pain) including the other wider outcomes of the disease and social roles (Carpenter, 2010). A good example is measles, a disease that is very common and recurrent in Wakiso and Hoima districts – which while a child may recover from it, the caregiver may consider it serious based on the time he/she will spent away from work looking after sick affected child, the fact that it can spread and affect an entire household and child may end up will severe long term complications – a factor that then makes these caregivers consider this condition as serious.

Perceived benefits

The extent to which the residents of Wakiso and Hoima districts perceive immunization to be beneficial, determines how they respond to immunization initiatives within the districts (Glanz et al., 2015). In the HBM theory/model, these Perceived benefits relate to one's assessment of immunization's value or to the efficacy of taking up and embracing immunization activities to promote health and reduce the risks of vaccine preventable diseases (Carpenter, 2010). When the caregivers believe that embracing immunization activities will reduce their children's susceptibility to or the seriousness of vaccine preventable diseases, the caregiver then is more likely to embrace immunization without questioning the effectiveness of this intervention (Carpenter, 2010).

Perceived barriers

The immunization health behaviors in Wakiso and Hoima districts are as well a function of perceived barriers to immunization (Abraham & Sheeran, 2015) These barriers are based on the communities and caregiver's own assessment of the prevailing obstacles to change in their behaviour (Abraham & Sheeran, 2015). The HBM holds that in some circumstances, though individuals may perceive a given health condition as a threat to them and that some actions can effectively reduce that threat, prevailing barriers can prevent the engagement of the individual in behaviour that promotes health. In Hoima, a very rough geographical terrain hinders several community members from accessing immunization services, even if they embrace and desire vaccination for their children. In general, perceived benefits in the HBM theory should outweigh any perceived barriers if behaviour change is to occur (Abraham & Sheeran, 2015; Carpenter, 2010).

Modifying variables

An important factor to consider in determining drivers of underimmunization and hesitancy in Hoima and Wakiso districts is the realization that individual characteristics, for example structural, demographic, and psychosocial variables can all affect caregiver perceptions (for example benefits, perceived seriousness, barriers and susceptibility) that in turn impact on the immunization health-seeking behaviors (Glanz et al., 2015). There are (demographic) variables like sex, ethnicity, race, age, level of education, socioeconomic status among others that affect immunization uptake (Carpenter, 2010; Glanz et al., 2015).

Psychosocial factors/variables for example include an individual's social class, personality, peer group pressure and reference group pressure, whereas structural variables that affect immunization uptake include individual knowledge on a given disease as well as prior contact of the individual with the disease (Carpenter, 2010). As per the HBM, these modifying variables usually affect immunization health-related behaviours (indirectly) usually by affecting any perceived seriousness, or susceptibility, or benefits, and barriers to immunization (Abraham & Sheeran, 2015).

Cues to action

In the HBM, the cue/trigger, is required to prompt demand for or uptake of immunization services (Carpenter, 2010; Glanz et al., 2015). Internal cues to action may constitute disease eg to measles or pain of loss through death (Carpenter, 2010). External cues, which usually include some events or even information from close others, or from the media, or from health workers (Carpenter, 2010).

In the community, the immunization program uses different cues to action to promote immunization. These include the immunization card indicating the date of next appointment, short message reminders, media promotional messages, supplementary immunization campaigns and activities among others (Abraham & Sheeran, 2015). The speed and urgency with which one responds to the cues is determined by the intensity with which the cues advance the message about the illness to the targeted caregivers, and the perceived susceptibility, benefits, seriousness, and barriers (Glanz et al., 2015).

Self-efficacy

While the four major components of HBM are perceived susceptibility, benefits, severity, and barriers (Abraham & Sheeran, 2015), self-efficacy has been added – and defined as the perception of individual's on their competence to perform a given behavior successfully (Orji et al., 2012). Self-efficacy helps the HBM explain differences of individuals in health seeking behaviors (Orji et al., 2012). Self-efficacy plays a big role in explaining engagement in behaviors of a one-time nature for example cancer screening or immunization (Orji et al., 2012). Self-efficacy recognizes that confidence in a caregivers ability to prevent a vaccine preventable disease through immunization is important for immunization health seeking behavior change (Orji et al., 2012).

Conceptual Framework

The figure 2 and figure 3 below summarize a conceptual framework of factors that have been described to underly vaccine hesitancy (Phillips et al., 2018; Regassa et al., 2019; Roser et al., 2013; Rudan et al., 2008). These factors, that are likely drivers and determinants of vaccine hesitancy and underimmunization in Hoima and Wakiso districts include issues related to caregiver complacency, challenges with vaccine supply, transport, access, refusal of vaccines and low confidence in vaccines (WHO, 2019c). Other documented drivers of vaccine hesitancy and poor vaccine uptake include a difficult and poor geographical road terrain that then hinders success to most remote areas; unstable political climate especially along the Congo border in Hoima District, a very mobile refugee and border community in Hoima district, poverty and low/poor socioeconomic status (Francis et al., 2008; Malande et al., 2019).

Additional determinants of underimmunization as shown in Figure 2 include poor/low education levels (specifically about new and current vaccines) for health workers and caregivers; population displacements due to insurgencies and wars, inadequate vaccine stocks and supplies (Eshetu & Woldesenbet, 2011; Quinn & Andrasik, 2021; Schwarzinger & Luchini, 2021; Shen & Dubey, 2019; Siciliani et al., 2020; Stern & Markel, 2005; Størdal & Lie, 2009; Tamirat & Sisay, 2019), and dilapidated/inadequate cold chain equipment for vaccine storage and preservation (Acharya et al., 2018, 2019; Akyıldız et al., 2019; Anderson et al., 2020; Anthony et al., 2009; Atouf et al., 2021; Bambra et al., 2010; Bangura et al., 2020; Brenzel, 2015; Brewer et al., 2017; Budu et al., 2020; Malande et al., 2019).

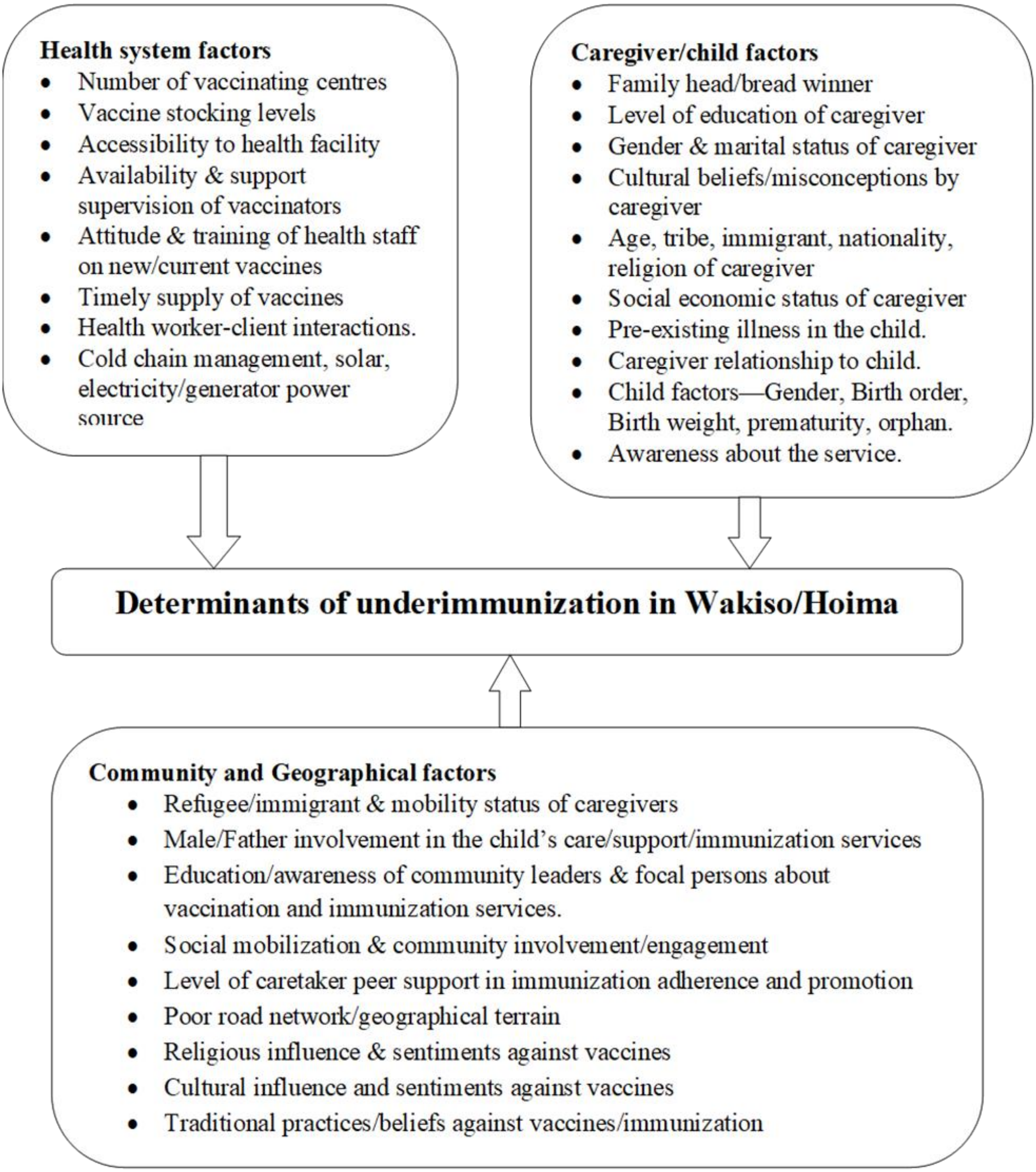

Figure 2: Conceptual Frame Work of the Determinants of underimmunization

The Vaccine Industry

The vaccine industry comprises companies engaged in: vaccine research, manufacture, development, marketing or sales, and vaccine distribution (Douglas & Samant, 2018). It depends on sale of vaccine products; and is smaller than the pharmaceutical industry, in slightly more than 50 countries worldwide, and was in 2013 estimated at more than $25 billion worldwide and over $35 billion in 2020 (WHO, 2021b). The growth of the industry over the last 20 years has been driven by new innovative vaccines, superior pricing strategies and increased uptake of additional vaccines by many countries into their national EPIs – including pneumococcal conjugate, varicella, rotavirus, hepatitis A, hepatitis B, shingles, meningococcal conjugate vaccine for A C, Y, W, human papillomavirus (HPV) vaccines, and now COVID-19 vaccines, with various combinations of these vaccines (Douglas & Samant, 2018).

Vaccine Development Opportunities

The vaccine development business is a capital-intensive business which requires substantial ongoing investment in manufacturing infrastructure, human resource, and scientists to maintain strict compliance with ever-increasing regulatory requirements (Douglas & Samant, 2018; WHO, 2020b). The departure of Baxter and Novartis in the early 2000's from the vaccine industry was an ominous sign on the continued financial pressure on major vaccine makers, and the support countries have given to COVID-19 manufacturing companies has been handy in steadying the ship. This has strengthened emergence of new alliances between the big four manufacturers and new emerging companies in India, Russia, China, and Brazil, to meet the growing need for vaccines.

Historically, the United States has been very successful in vaccine development and research, with over 20 new vaccines approved by the United States over the last 40 years. There have been newer combinations of some existing vaccines to simplify pediatric vaccination, like the penta and hexavalent vaccines including acellular pertussis vaccination (Douglas &

Samant, 2018). A polyvalent pneumococcal conjugate vaccine (PCV 7 and PCV 13) for infants worldwide introduced by Pfizer and later GlaxoSmithKline's (GSK) PCV 10, have proved major forces in vaccine business. Other vaccines licensed since 2006 include a combination of measles, mumps, and rubella (MMR) and varicella (MMRV); new vaccines against rotavirus, herpes zoster, hepatitis B, HPV, meningococcus, cholera, typhoid, rabies, influenza, among others (WHO, 2021b).

The newly manufactured and licensed COVID-19 vaccines for combating COVID-19 and the HPV vaccines that were developed by Merck/MSD and GlaxoSmithKline (GSK) significantly expanded the field of adolescent vaccines and confirmed market acceptance of premium pricing. This progress, over the last 10 years, has improved reliability of the vaccine industry (Pfizer, Biontec, Astra Zeneca, Moderna, Johnson & Johnson et). The problem of chronic shortages of the past has been resolved especially through modernized vaccine manufacturing, improved distribution infrastructure, assured funding from the GAVI alliance and better profitability of the new vaccine products (Douglas & Samant, 2018).

The decision to stockpile pediatric vaccines has helped alleviate concerns of critical/frequent shortages and interrupted interruptions in supply. A big challenge is dependence on single-sourced vaccines, for example COVAX dependence on serum institute of India for manufacture of vaccines for 92 poor and low-income countries (WHO, 2021a, 2021b). Improved regulation of industry and proactive development of solutions to this supply challenge is important to avoid future public health crisis resulting from shortages of vaccines and interrupted supplies (Douglas & Samant, 2018).

The Vaccine Development process

Vaccine development is a very difficult, tedious, complex, long, risky, and costly exercise; and goes through the clinical development phase, process development phase, and assay development phase – with many vaccine candidates failing to progress from preclinical to clinical or through the three main phases of clinical development, where less than 1 in 15 vaccine candidates enter Phase II clinical stage, or even phase III pre-licensure phase (Mitchell et al., 1993). This high failure rate is attributed to a poor understanding of the biology of protection; the lack of good animal models to be used to predict the behavior of the vaccine in humans; the unpredictability of the human immune system reactions to the antigens in the vaccines as it relates to immunogenicity or vaccine candidate safety; and the unpredictability of impact of combining various/multiple components in one vaccine (CDC, 2014).

The process of vaccine development (CDC, 2014; Mitchell et al., 1993; WHO, 2020b). requires strong systems, controls, skills and experience within the human resource involved (Douglas & Samant, 2018). Stakeholders involved in vaccine development are guided by the "target product profile" (TPP) document – which summarizes all the desired features and characteristics of the vaccine product under development, as well as key attributes of the vaccine showing its competitive advantage, and, also a topline roadmap of the nonclinical and the clinical studies that are required to evaluate the vaccine product's safety and efficacy in the target population (Douglas & Samant, 2018). The TPP thus provides all interested and concerned stakeholders with a statement of desired outcome of the vaccine product development program.

The development process must as well satisfy requirements related to preclinical toxicology testing, clinical lots plus analytical assessment, and scale-up methods to guide the manufacturing process. Part of the process entails three consecutive lots testing for immunogenicity (WHO, 2020b). At assay development stage, the specific methods for testing the purity of raw materials, the stability and potency of the vaccine product, and the immunologic/other criteria for predicting vaccine efficacy definition are tested. of to (CDC, 2014). All decisions at each stage are data driven, with integration of the clinical, process, tasks for the development of assays (WHO, 2020b). The Clinical development phase entails studies of vaccine effects on humans/patients for immunogenicity, safety, and efficacy through phase 1 (early safety and immunogenicity in small numbers); phase 2 (safety, dose ranging, and immunogenicity in 200 to 400 individuals); sometimes phase 2b (non-licensure, proof-of-concept trials for efficacy); and phase 3 – (safety and efficacy trials that permit licensure, which generally require thousands of subjects – and involves use of a placebo arm) (CDC, 2014; Douglas & Samant, 2018).

The process after clinical phase involves both bulk manufacturing and finishing operations. Bulk manufacturing stage includes process of cell culture or as well fermentation-based processing after which a variety of separation stages of vaccine purification follows (WHO, 2020b). After this, finishing is done, which entails formulation with addition of adjuvants and stabilizers and then vial or syringe filling is undertaken (Mitchell et al., 1993). Viral vaccines require lyophilization at this stage. After this, labeling and packaging are done, followed by controlled storage. The process towards licensure is costly since clinical studies progressively become larger, with scaling up of manufacturing, where costly infrastructure must be put in place. Post licensure studies in Phase 4 are necessary for efficacy and safety monitoring (WHO, 2020b).

GAVI – The Global Alliance for Vaccines and Immunizations

The GAVI Alliance, "(formerly the Global Alliance for Vaccines and Immunisation) is a global health partnership of public and private sector organizations dedicated to providing immunisation for all eligible populations" (WHO, 2021b). GAVI provides an opportunity for many partners to build consensus around various policies around vaccines, strategies, and priorities and serves to recommend the responsibility of implementation to the partner with the most experience and insight in the area of vaccines. GAVI alliance has developed many innovative approaches to promotion of international health and development. The GAVI alliance strategy aims to support its mission to save children's lives and to protect people's health through increasing the access to immunisation in poor countries of the world (WHO, 2021b).

GAVI has contributed significantly to the progress in achieving M/SDGs through focusing on the performance, outcomes and results of the programs. The partners of the Alliance provide funding for vaccines and the intellectual resources for advancement of care. The partners also contribute to the strengthening of the capacity of many health systems to deliver immunization and other related health services in a manner that is sustainable. GAVI draws on the strengths of its partners to make impact (WHO, 2021b). These include UNICEF, the World Bank and the Bill & Melinda Gates Foundation, the World Health Organization, advocacy groups, NGOs, professional and community associations, faith-based organizations and academia, private sector foundations and corporate partners, vaccine manufacturers, among others.

The COVAX Facility

COVAX is the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator. "COVAX is co-led by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and World Health Organization. Its aim is to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world"(WHO, 2021a). On 24 April, 2021, the World Health Organization (WHO) hosted the launch of the "Access to COVID-19 Tools (ACT) Accelerator – that is a new global collaboration for accelerating the development, the production, and the equitable access to current and future COVID-19 diagnostics, therapeutics, and vaccines. In this Accelerator, the Gavi, CEPI, and the World Health Organization together with other multinational and developing country manufacturers of vaccines worked on the COVAX (vaccine) Pillar, aimed at developing the COVAX Facility (WHO, 2021a).

The COVAX Facility provides for governments with this opportunity to be able to benefit from a large portfolio of new COVID-19 vaccines using a range of technology platforms, produced by an increasing pool of manufacturers across the world, with an assured bigger market to provide security of demand – often with a greater scope and muscle than governments or regional groups can be able to support on their own. Even in situations where governments do already have some access to a given portfolio of COVID vaccines, COVAX acts as a safe insurance policy through economies of scale and unique portfolio diversification. Through this CEPI's portfolio which will now be transferred to the new COVAX Facility, COVAX benefits from a rapidly growing number of new COVID-19 vaccines, and increasing manufacturing capacity (WHO, 2021a).

The COVAX Facility is also open to and actively seeking agreements with new vaccines from manufacturers emerging around the world not financed by CEPI (WHO, 2021a). COVAX provides additional insurance for many countries making deals with individual vaccine manufacturers provide vaccines in a very uncertain market. For Governments without bilateral agreements with manufacturers, COVAX offers a safe path for reliable vaccine supply. COVAX additionally contributes to the global scale-up and access to COVID vaccines and therefore contributes to controlling the pandemic. COVAX has estimated that the first phase that runs to end of 2021, the Facility targets to secure up to 2 billion doses of COVID vaccines. The second phase to run from 2022-2025 will sustain and ensure additional supply of vaccines (WHO, 2021a). The COVAX Facility is reinforced by the Gavi COVAX Advance Market Commitment (AMC) - an arm that provides funding for vaccines for poor/lower income countries, creating scale and as well making the Facility to be more attractive to the manufacturers who are assured an orderly market, and opportunities to tackle the COVID-19 pandemic around the world.

The Concept of Vaccines

The term vaccine (and vaccination) derives from Variolae vaccinae (which is term used for smallpox of the cow), and was devised by the scientist Edward Jenner (also called the father of vaccination, and developed the concept of vaccines and is credited for creating the first ever vaccine) to refer to cowpox (Plotkin, 2014). Edward Jenner used this phrase in the year 1798 as part of the title to his Inquiry into Variolae vaccinae that is Known as the Cow Pox, in which Edward Jenner described the possible protective effect of cowpox when used against smallpox.

It was not until 1881, when Louis Pasteur suggested that to honor Jenner, these terms be extended to use in describing the new protective inoculations under development then. Vaccinology then refers to the science of vaccine production and development (Plotkin, 2014). The process of vaccination refers to the administration of an antigen (referred to as a vaccine) in order to help an individual's immune system gain/develop protection against the disease from which the vaccination targets (Stern & Markel, 2005).

Vaccines contain an antigen which maybe a weakened or live or killed virus or even a protein component or toxin derived from a bacteria or virus (Hilleman, 2000; Plotkin, 2014). It is this antigen within the vaccine that stimulates the individual's adaptive immune system thus enabling it to prevent the body from acquiring an infectious disease. Vaccines artificially activate the immune system through priming it using an immunogen, a process called immunization (Stern & Markel, 2005). Vaccination thus entails administration of various immunogens, mostly before a patient has contracted a disease, but also sometimes after an individual has already contracted the disease (Hilleman, 2000; Ursula et al., 2016).

History of Vaccines

The beginning of vaccines and active immunization dates back to efforts to eradicate smallpox, led by the observation that body immunity could be induced through rubbing scabs of smallpox against the skin of an individual thus resulting in a mild form of disease called smallpox (Stern & Markel, 2005). Historically, there are several countries, including China and parts of Africa where the inoculation of susceptible subjects with infectious material obtained from people suffering from mild smallpox, with subsequent introduction in Britain and several American colonies in early eighteenth century (Plotkin, 2014). A few scattered cases of possible deaths from these inoculations led to several controversies on both risks and benefits of this procedure, thus driving the search for improved vaccines.

This research drive led to exploration of the finding that a vesicular eruption that occurred on cow udders (called cowpox), resulted in occurrence of small blisters then described as "milkers' nodes" on hands of the milk maids (Plotkin, 2014). Subsequently, health workers progressively discovered a chicken pox infected individual appeared to also be protected from suffering from smallpox, a discovery that resulted in the experiment by Edward Jenner in 1796. Jenner’s discovery of the small pox vaccine was widely embraced, with the USA formulating their first law to regulate its distribution, called the Vaccine Act of 1813 (Plotkin, 2014). The act provided for Presidential appointment of a federal agent to "preserve the genuine vaccine matter, and to furnish the same to any USA citizen" who has requested it.

This act was subsequently repealed in the year 1822, after the USA Congress decided that all vaccine regulation work should be left to concerned local authorities (Plotkin, 2014). These early smallpox vaccination efforts were successful, and encouraged scientists to broaden and intensify efforts to control infectious diseases. One of the famous scientists that grew this research path was French chemist, Luis Pasteur and his methods for active immunization to protect against rabies, that was first tested in 1885 (Plotkin, 2005).

The evolution of the history of immunization progressed to serum therapy, (now called antitoxin therapy), which began in early 1890s with discovery which showed that animals that are inoculated with heat-killed broth cultures of tetanus causing bacteria or diphtheria showed ability to survive subsequent (fatal) inoculations with these organisms (Plotkin, 2014). It was not immediately apparent that the supernatant of that broth culture, and not killed bacteria, is what led to immunity development. Later, it as well became clear that immunization derived protection could be transferred to other animals using body fluids via inoculation like use of serum from immunized individuals (Plotkin, 2014).

The antitoxin was first used for treating diphtheria in 1891 in Berlin Germany (Plotkin, 2014). This would later be followed by widespread production and use of diphtheria antitoxin in Germany and Britain by the mid-1890s, and in 1895 in the United States by the Mulford Company of Philadelphia that later became Merck Sharp & Dohme (Plotkin, 2014). As commercial manufacture of this antitoxin spread in several countries, concern shifted to regulation of uncontrolled production of vaccines, including the diphtheria antitoxin and smallpox vaccine, especially the possibility of defective preparations. In late 1894, New York city initiated plans to regulate purity, potency and control of profiteering by manufacturers of diphtheria antitoxin (Plotkin, 2005). These concerns led USA congress to appoint a commission to look into issues of diphtheria antitoxin treatment, especially driven by concerns regarding the deaths of 13 children from tetanus after receiving diphtheria antitoxin made from a horse which shortly died tetanus in St. Louis city (Plotkin, 2005, 2009).

Due to this tragedy, there was a lot of uproar leading to passage by USA congress of virus-toxin act by Congress of 1902 (Plotkin, 2009), with the establishment of a board in charge of licensing regulations for all antitoxins and vaccines producers. This board authorized inspection of vaccine and antitoxin manufacturing units by the Hygienic Laboratory of the Public Health Service, and either issue or revoke licenses of those that do not meet set efficacy and safety standards. Up to 13 diphtheria antitoxin smallpox vaccine licenses had been issued by this board by 1904 and up to 41 by 1921 (Plotkin, 2009).With the incorporation of the 1902 act into the Public Health Service Act of 1944, the National Microbiological Institute of the National Institutes of Health (NIH) was established and took over these roles.

Other developments in the 1950s included the reconstitution of the Public Health Service Hygienic Laboratory as the Division of Biologics Standards at the NIH. Around 20 years later, in 1972, the Food and Drug Administration (FDA) was established, that took over these roles, and has gone on to establish regulations for more than 80 different generic biological products used for both active and passive immunization, with the Bureau of Biologics being combined with the Bureau of Drugs within the FDA to then form the Center for Drugs and Biologics (Plotkin, 2014). The FDA subsequently developed procedures for the review of effectiveness, safety, and the labeling of biologics, partly through establishment of consultant panels, three of which focused on antitoxins and vaccines (Plotkin, 2014).

The consultant panels established by the FDA reviewed toxoids, vaccines, and the products that are used for passive immunization against bacterial diseases; those used against viral and rickettsial vaccines (Plotkin, 2005). They also reviewed products that are used for passive immunization against various viral diseases; and “bacterial preparations classified as those "without U.S. standards of potency" – meaning for example older products including "mixed respiratory vaccine (Plotkin, 2005). One of the assignments of the panels included evaluation of efficacy and generic safety of all immunoglobulins, vaccines, and antitoxins; and recommend early, emergency, or full licensure or revocation of licensure. In 1979, these panels submitted their final reports to the FDA (Plotkin, 2014).

In the early 1900s, there was rising confidence that lessons from smallpox vaccination and diphtheria antitoxin could be employed in most infectious diseases through similar immunologic prevention and therapy. The extensive and wide use of tetanus antitoxin in those wounded in World War I and II, and the development of the tetanus toxoid between the two wars was a great success, with it becoming obligatory within the French Army in 1940, to only 12 (Plotkin, 2009). The consolidation of these gains by late 1940s, led tetanus toxoid be recommended into the routine public health use for all children within the United States, to be administered in a combination with the diphtheria toxoid and the pertussis vaccine (Plotkin, 2014).

The lessons gained from the diphtheria toxins ability to induce protective immunity to diphtheria in animals using diphtheria toxin led to production of the first active immunization vaccine against diphtheria that was derived from a mixture of an antitoxin and a toxin in 1913 (Plotkin, 2014). This vaccine had some limitations relating to instability of the vaccine mixture as well as allergic reactions observed among some of the recipients of horse serum. Since its first production in early 1920s, the Diphtheria toxoid has been in use since though with minor modifications. As regards the pertussis vaccine, then made of whole, killed organisms, the earliest firm experiments with were carried out in the 1920s (Plotkin, 2009).

Whereas there have been progressive improvements made to this vaccine, including production of an acellular pertussis type, to date, the widely used vaccine still contains the whole, killed causative organism (Plotkin, 2014). The post-World War II period saw great advances in vaccine development for many diseases, aided by greater understanding of disease-causing organisms, immunological advances, and better viral/bacterial culture techniques. of vaccines for other diseases (Plotkin, 2014). These advances led to production of vaccines for measles, poliomyelitis, varicella (chicken pox) virus, rotavirus, mumps, rabies, rubella, and meningitis.

The licensure and use of these vaccines have been seen in eradication of small pox, and significant reduction in current reported cases and deaths from rubella, measles, mumps, diphtheria, tetanus, Paralytic poliomyelitis and pertussis among others (Plotkin, 2005). The enormous impact of these vaccines with their supporting enabling legislation and now widely employed as public health interventions has reduced the morbidity and mortality due to vaccine preventable illnesses and improved overall under five child survival (Zimmermann et al., 2019). Currently, there are over 20 different vaccines against various infectious diseases on the market, some in combinations (Guo et al., 2013; Zimmermann et al., 2019).

There are some of these vaccines (including against poliomyelitis viruses 1, 2, and 3; against pertussis; against measles virus; against rubella virus: and against mumps virus; and against the diphtheria and tetanus toxoids) which are now recommended for use in routine immunisation among children (Abu Raya et al., 2021; Guo et al., 2013). There are as well those that are primarily intended to be used among groups of individuals that are at a special risk to certain infections due to their prevailing circumstances for example exposure risk, age, underlying health problems and life-style (Zimmermann et al., 2019). An example is vaccine for anthrax recommended for persons working with animal hides and at-risk laboratory personnel.

Newer vaccines are those that have been recently produced against COVID-19 (Bettini & Locci, 2021; Creech et al., 2021). There are many other infections that could be effectively prevented through vaccination, with various potential vaccines going through different stages of vaccine development (Lee et al., 2020; Poland et al., 2020). Vaccines for cytomegalovirus, herpes simplex infections, COVID-19, group B streptococci and gonorrhea are currently in progress (Creech et al., 2021). The production and development of vaccines against parasitic infections such as schistosomiasis and malaria have been slow in development, but on steady course (Dudley et al., 2020; Poland et al., 2020).

Advances in medicine, microbiology and immunology with better understanding of cell biology, molecular genetics and immunity, and current stratification of new target patient populations, (e.g., post bone marrow/organ transplant patients) are developments that offer promise for future control and immunologic prevention of many vaccine preventable and infectious diseases (Dudley et al., 2020; Hacisuleyman et al., 2021; Lukusa et al., 2018; Navaratna et al., 2021). These new vaccines are being made to reflect the changes in life-style, in hygiene, and other environmental factors and shifts in the current patterns of infectious disease occurrence (Bettini & Locci, 2021; Hacisuleyman et al., 2021).

Immunization Against Infectious Diseases

In literature, you will often find the word vaccination and immunization in interchangeable use. Either process involves administration of a particular antigento offer protection, or the use of a person’s natural defense ability to offer protection to a person targeting a particular organism. The two are not same as inoculation, a process that entails using live unweakened pathogens to produce immunity against a given pathogen (Mackin & Walker, 2020). Immunization may be classified as passive and active, where by passive type is characterised by are preformed antibodies that are usually transferred or given to an individual that does not have immunity, therefore conferring some short-lived type of immunity to the individual against the organism or toxin to which immunity targets. If and when the preformed antibodies are destroyed, the immunity is lost (Koichi et al., 2002). Passive type of immunity has been divided into two forms: natural form (for example the passage of maternal antibodies from an expectant mother to a foetus trough the placenta) or it can be artificial form of passive immunity (for example the administration of an antivenin or administration of pooled human immune gamma globulin to a person to provide some temporary immunity in the individual against a given disease or a given venom (Hilleman, 2000).

It is the transfer of protective preformed antibodies specific to a particular disease or illness given to a non-immune individual that characterizes passive immunization (Spits & Cupedo, 2012). Passive immunization may as well be conferred through injection of an immune individual’s serum or antisera or even the injection of partially purified extract of serum from an immune into a non-immune person. The inclusion of antitoxins against particular bacteria are examples, and these have been used for diseases like hepatitis, diphtheria and against tetanus. In the case of diphtheria for example, the passive immunization through the antitoxin serves two roles – it provides prevention against the disease and also serves as a treatment measure (Abu Raya et al., 2021). It is important to recognise the temporary and transient nature of passive immunity.

Active immunization on the other hand is a result of exposing a person to the pathogen that causes disease, and in turn the individual's own immune system starts to develop protection against that pathogen (Spits & Cupedo, 2012). It is for this reason that active immunization process leads to immunity that is long-term since it stimulates the persons immune system. There are situations were active immunization can be conferred through administering a pathogen that has been specially modified or even a section or part of a given pathogen with the aim of stimulating the individual's immunity with the aim of producing required protection but avoiding the result of symptoms of the disease. The following are examples of these preparations that can cause active immunity. (Plotkin, 2014):

1. In some cases, inactivated or whole or killed pathogens or even components of some pathogens can be included in vaccines. An example is vaccine against polio, pneumonia, meningitis, influenza, pertussis and hepatitis B (Leuridan & Van Damme, 2011).
2. In other instances, toxoids are used to generate immunity, as occurs in the case of tetanus toxoid and diphtheria toxoid. This process involves use of special toxins that have been modified in order not to produce signs of clinical disease, but they have the capacity to generate immunity that is effective.
3. The use of attenuated vaccines like the case of viruses grown and cultures in labs repeatedly thus weakening them leading to the loss of the ability of these viruses to cause clinical disease and yet they induce or produce significantly strong response in the individual's immunity. This has been demonstrated in vaccines for polio, rubella, mumps, measles, and yellow fever.

The inactivated vaccine against influenza is usually produced by the process of destruction of the influenza virus by use of chemical radiation or use of heat or use of radiation (Abu Raya et al., 2021). Through this process, the inactivation of the microorganism is aimed at making the vaccine to be more stable, and makes the cold chain process of transporting and storing them much easier even in a freeze-dried form (Spits & Cupedo, 2012). The challenge with these vaccines is that they produce a weaker response of the immune system and therefore do require the use of booster shots in order to sustain the immunity generated. In the case of subunit vaccines, for example the recombinant vaccine for hepatitis B, this contain epitopes only. The epitopes consist of parts of the antigens which when they are introduced into the human body, they lead to the production of antibodies or they are recognized by T-cells which in turn bind onto them. The epitopes therefore stimulate the recipient's immune system. The advantage with these vaccines is that the side effects are substantially reduced be the vaccines using few specific antigens, much as this high specificity unfortunately increases the challenge of identifying the antigens that the vaccine should cover (Spits & Cupedo, 2012).

The innate and adaptive immune systems

The role of the immune system is to defend one's body against diseases. It is made up of the innate, (also called general) immune system and the specialized/or adaptive immune system (Koichi et al., 2002). For effective functioning, these two immune systems must work closely together (Fearon, 2000; Plotkin, 2014). Since the innate system responds in a similar way to all offending pathogens, it is also called the "nonspecific" immune system. The innate system acts very quickly, though it is limited in its overall effectivity. It broadly comprises the protection provided by the skin and mucous membranes and the protection offered by the cells and proteins of the immune system (Koichi et al., 2002; Ursula et al., 2016).

The skin and mucous membranes form a physical barrier against invading organisms. There are chemical substances like enzymes, acid, mucus (that prevent viral/bacterial entry) and hair-like structures in some body parts like bronchi (also called cilia) and propelling muscular function that expel viral particles and stop them from settling within the body (Fearon, 2000; Koichi et al., 2002). Apart from anatomic barriers, the innate immune system of the body also includes various physiologic barriers for example body temperature, or fever, lysozyme, or gastric acidity, collectins, and interferon (Fearon, 2000). The usual normal body temperature inhibits various microorganisms; while fever does inhibit various pathogenic organisms (Hilleman, 2000). The gastric acid in the stomach as well helps to eliminate many different microorganisms ingested with food.

There are scavenger cells (also called phagocytes) that stop viruses and bacteria from invading the body (Spits & Cupedo, 2012). Different proteins help the cells of the innate immune system in their function through marking invading pathogens as targets for scavenger cells, attracting other cells of the immune system from bloodstream, destruction of bacteria cell walls or viral envelopes thus destroying them (Kumar et al., 2011). The natural killer cells specialize in identification of infected cells for destruction using cell toxins.

The complement system belongs to the innate form of immune system, and is made up of three different pathways that work together, (Fujita et al., 2004; Walport, 2001) – namely: “the classical pathway which is triggered when IgM antibodies or some IgG antibody subclasses bind to antigens or surface markers on microorganisms; the alternative or properdin complement pathway that is triggered by deposition of complement protein called C3b onto microbial surfaces (this pathway does not require use of antibodies for activation); and the lectin complement pathway that is triggered by the attachment of plasma mannose-binding lectin (MBL) to various microbes (this also does not require antibodies for its activation)” (Carroll, 1999; Kumar et al., 2011; Rus et al., 2005; Walport, 2001). The three complement pathways usually merge into one common pathway that leads to formation of the membrane attack complex (MAC) that has ability to form pores in the cell membrane of targeted cells (Fujita et al., 2004; Rus et al., 2005; Walport, 2001). The complement system pathways are as well integral in opsonization (or the increased susceptibility) of various particulate antigens to phagocytosis and also play a role in triggering of a localized inflammatory response (Carroll, 1999; Rus et al., 2005; Walport, 2001).

There is as well another innate type of immunity that uses an inflammatory response - which allows the products of the immune system to enter into infected area producing cardinal features of inflammation, that include heat, redness, swelling, pain, and loss of function (Fujita et al., 2004; Spits & Cupedo, 2012). There exists as well a pattern recognition receptors (PRRs), which though not specific to any particular pathogen or antigen, can provide a rapid immune response to invading antigens (Carroll, 1999). PRRs, also classified as membrane proteins (due to association with cell membrane) - can be found in all cell membranes of immune system cells; and have genes encoded in the cell germline that ensures limited variability within their molecular structures (Fujita et al., 2004; Spits & Cupedo, 2012).

Some examples of these PRRs include pulmonary surfactant protein, MBL, toll-like receptors (TLRs), C-reactive protein, NOD, C-Type lectin, and MX. These PRRs recognize pathogen associated molecular patterns (PAMPs) that trigger cytokine release (Vijay, 2018). Various examples of these PAMPs include lipoproteins (bacterial capsules) and LPS (endotoxin) among others (Spits & Cupedo, 2012; Vijay, 2018). These antigens are usually produced by microbal cells and not by the human cells. The recognition of these PAMPs by the PRRs leads to complement activation, then opsonization, cytokine release, and also phagocyte activation (Fujita et al., 2004; Spits & Cupedo, 2012; Vijay, 2018).

The mononuclear phagocytes cells and the granulocytic cells help to link the innate immune response to adaptive immune response (Vijay, 2018). The mononuclear phagocytes include monocytes (which circulate in blood) and macrophages (found in the tissues) (Spits & Cupedo, 2012). The macrophages and monocytes play a major role in antigen presentation, in phagocytosis, in cytokine production, and also perform antimicrobial and cytotoxic activities (Spits & Cupedo, 2012). After their maturity, monocytes circulate in the blood from seven to ten hours before moving into the tissues where they then become specific tissue macrophages and in other cases they become dendritic cells (Spits & Cupedo, 2012). Different dendritic cells are involved in various immune functions, including antigen presentation to T-helper cells (Carroll, 1999). Follicular dendritic cells are usually found only within the lymph follicles and usually participate in binding of antigen–antibody complexes within lymph nodes (Spits & Cupedo, 2012).

The granulocytic cells involved in immune system include neutrophils, basophils/mast cells, and eosinophils. The neutrophils are highly active in phagocytosis arrive first at the inflammation site. The eosinophils are phagocytic cells as well, and are more important in the resistance to parasites. The basophils (present in the blood) and the mast cells (found in the tissues) release histamine (plus other substances) and are very important in the development of allergies. The innate system can eradicate pathogenic agents without assistance from the adaptive immune system or it may stimulate the adaptive immune system to help in the eradication of the pathogenic agents. The adaptive immune system, unlike the innate immune system, is specific to a given pathogenic agent (Spits & Cupedo, 2012). It therefore involves a longer response. It has memory, meaning that the adaptive immune system responds more quickly to the same pathogen with every successive exposure (Spits & Cupedo, 2012).

The adaptive immune system usually takes over when the innate immune system fails to destroy the offending invading pathogen (Plotkin, 2014; Spits & Cupedo, 2012). As stated above, the difference is that the adaptive immune system is specific, so it specifically targets the invading pathogen, after identifying it, making it a slower but precise system (Koichi et al., 2002). A key feature of adaptive immunity therefore is the ability to keep memory, thus making any response to future encounters with the same pathogen quicker and more efficient (Mackin & Walker, 2020). This memory provides for future immunity for some diseases, thus conferring long term protection.

The adaptive immune system comprises T lymphocytes, B lymphocytes and antibodies in the blood and other body fluids. The B–cells and antibodies form the humoral immunity or also called antibody-mediated immunity; while the T-cells compose cell-mediated immunity (Spits & Cupedo, 2012). It is important to note that natural killer cells also come from the lymphocyte lineage like B–cells and T-cells; through natural killer cells are only involved in the innate immune responses. The T lymphocytes (also called T cells) are produced in bone marrow and then migrate to the thymus through the bloodstream, where they mature. They serve as chemical messengers for activating other immune system cells for starting the adaptive immune system (also called T helper cells); detecting infected cells or tumorous cells and then destroy them (also called cytotoxic T cells) and some T helper cells also become memory T cells after an infection is cleared (also called memory T cells) (Koichi et al., 2002; Spits & Cupedo, 2012).

The first arm of adaptive immune system is the humoral immunity, which functions against toxins and extracellular pathogenic agents. The B lymphocytes (B cells) are as well made in the bone marrow and mature there to become specialized. Unlike T-cells, the B–cells can recognize antigens in their native form meaning that the B–cells can recognize antigens without the need for the antigen to be processed by an antigen-presenting cell and after be presented by a T-helper cell. These antigens are referred to as T-independent antigens because they do not require T-cell activation. Some examples of these T-independent antigens are lipopolysaccharide, bacterial polymeric flagellin, and dextran (Spits & Cupedo, 2012).

These antigens are large polymeric molecules with repeating antigenic determinants. These antigens induce activation of numerous B–cells; though through a weaker immune response and weaker memory induction than with activation through T-helper cells. On the contrary, activation of B–cells through T-helper cell activation leads to a much better immune response that has more effective memory. This long-term, effective response of the immune system is the goal for immunizations. When the antigen binds to the Fab region on receptor of B–cells and the secondary signaling from the cytokines released by the T-helper cells, the B–cells then begin somatic hypermutation at the Fab region thus further increasing the corresponding fit established between the Fab region and the antigen (Spits & Cupedo, 2012).

This is the process that stimulates the B–cells to mature into plasma cells, leading to production of specific antibodies with the appropriate corresponding fit to the targeted antigen. It is this stimulated B-cells from which clones of B-cells having specificity for a given antigen are formed. Progressively, these cells progress to become plasma cells leading to production of antibodies or memory cells that remain in the lymph nodes thus stimulating a new immune response to the specific antigen – a process that occurs following the primary immune response the first time the immune system is exposed to that particular antigen. While “T” in T cells stands for Thymus, the "B" in B cells stand for "bone marrow." There are very many types of B cells, and B cells are activated by the T helper cells thus causing them to multiply and to transform into plasma cells (Mackin & Walker, 2020).

It is these plasma cells that in turn produce large amounts of antibodies that are then released into the blood circulation. The B cells produced are antigen specific, hence only the precise antibodies will be produced. Some activated B cells do transform into memory cells and thus form part of the adaptive immunity "memory" (Koichi et al., 2002). The process of clonal selection and the expansion takes days to happen, and usually involves production of IgM, which is the first antibody to be produced during a primary immune response. The progression of the immune response is followed by production of activated plasma cells which produce IgG specific to the specific antigen (Spits & Cupedo, 2012).

While IgM is a much larger antibody that is first to be produced, the IgG has better neutralizing activity, binds more effectively to antigens and also aids in the process of opsonization. The other antibodies that can be produced by plasma cells are IgA, IgD, and IgE. The IgD is usually found as a receptor bound to the surfaces of mature B–cells. The IgA is found in secretions like mucous, tears, saliva, and breast milk, while IgE is involved in allergic reactions and response against parasitic infections. Vaccines in general largely work through production of IgG. Due to the resulting memory cells from the primary immune response, the succeeding exposures to that antigen results in a more rapid and effective secondary immune response – that comes with a quicker, larger, reaction primarily composed of IgG (Spits & Cupedo, 2012).

The other arm of adaptive immunity, called the cell-mediated immunity, functions mainly against intracellular pathogens. The T-cells mature in the thymus after which they are released into the bloodstream. The two main types of T-cells are the CD4 cells and CD8 cells. The CD4 cells or the T-helper cells have on them the CD4 co-receptor and usually recognize only the major histocompatibility complex (MHC) II protein. This MHC II protein is normally found on all the immune cells and thus acts as a marker for the immune cells (Spits & Cupedo, 2012). The CD4 cells are the essential cells for antibody-mediated immunity and help B–cells to control extracellular pathogens. The CD4 cells have two subsets, the Th1 and Th2. The Th1 help to promote cell-mediated immunity while the Th2 cells help promote antibody-mediated immunity.

The CD8 cells (T-cytotoxic cells) have a CD8 co-receptor and only recognize MHC I protein. This protein is found on all the nucleated body cells except mature erythrocytes and usually acts as a marker of body cells. The CD8 cells are used for CMI and help control intracellular pathogens. Unlike for B-cells, the T-cells can only recognize an antigen that has been already processed and presented by the APCs. One initial type of antigen processing involves attaching the intracellular antigens along with the MHC I proteins to surface of APCs, which usually occurs with viral antigens and tumor cells (Spits & Cupedo, 2012).

The other type of antigen processing usually involves attaching the extracellular antigens along with the MHC II proteins onto the surface of APCs; which normally occurs with parasitic and bacterial antigens. Once activated by APCs, the T-cells begin to carry out their functions. Just like for B-cells, the activated T-cells also undergo clonal expansion that produces additional effector T-cells useful for the current infection and for memory T-cells required for future infections with this or similar antigen. The communication within the cells of the adaptive immune system is done directly or through soluble chemical messengers like cytokines. Antibodies attack/neutralize pathogens, activate proteins and other immune cells and as well support the innate immune system (Koichi et al., 2002).

Vaccine correlates of protection

Correlates of protection therefore refers to measurements of immune system parameters that enable prediction of the degree or level of protection one generates against infection or disease that's induced by a given pathogen (WHO, 2013). The level of functioning of the immune system in producing desired impact of vaccines is measured by estimating the immune responses to these vaccines that correlate with protection. These are called correlates of protection (WHO, 2013). Indeed, the current vaccines work through antibodies that are found in serum or on the mucosa and thus block infection or counter bacteremia or viremia, hence providing a correlate of protection. The resulting functional attributes and the numbers of the antibodies is important, since the antibody can be highly correlated to the protection or be synergistic with other immune functions (WHO, 2013).

An important correlate is immune memory, where effector memory is generated after a short-incubation disease while central memory is developed after long-incubation diseases. Cellular immunity usually acts in order to kill or to suppress intracellular pathogens, though it may as well synergize with antibody function. There are some vaccines for which no clear correlates have been established, and thus useful surrogates are determined for protective responses that may be unknown (WHO, 2013). Vaccination just like natural infection can protect an individual through multiple mechanisms. The immune memory that is induced by vaccination is critical to protection, especially in long-incubation diseases, like hepatitis B virus infection.

While concerns exist that antibody protection after vaccination may be lost in some cases, the central memory that is established by vaccination is usually sufficient under most circumstances to confer protection to the vacinee. Correlates of protection may thus vary qualitatively and quantitatively depending on individual characteristics, such as gender, age, and the major histocompatibility complex (MHC) group of the individual; and depending on whether the goal is to prevent systemic infection from the pathogen, mucosal infection, or uncomplicated disease, or severe disease (WHO, 2013).

Protection against encapsulated bacteria is based on the existence of an anticapsular antibody or of antitoxin antibody (WHO, 2013). The challenge occurs when there is no capsule on the bacteria or toxins from the bacteria, it becomes difficult. The bacteremic disease pneumococcus, Haemophilus influenzae type b (Hib), and meningococcus, the defined correlates include bactericidal or opsonophagocytic antibodies, much as binding antibodies are often used as surrogate markers for protection (Plotkin, 2010). For example, binding antibodies are usually used to define protection against H. influenzae, where a 0.15 μg/ml antibody cut off level is used, though concentrations of 0.03- 0.1 μg/ml are protective against bacteraemia (Plotkin, 2010).

Important observations made about protection against H. influenzae are that "(i) that anamnestic responses are insufficient and that the antibody must be present at the time of exposure, (ii) that the antibodies must be of high avidity in order to protect, and (iii) that with the T-cell-dependent response reduced by protein conjugates, a 1ower concentration may be protective"(Plotkin, 2010). For pneumococcus, the pneumococcal antibodies are measured using enzyme-linked immunosorbent assay (ELISA), and the protective level of antibody lies between 0.18 and 0.35 μg/ml. It is however important to note that a recent analysis from Africa, (a setting with lower vaccine efficacy), a correlate of 2.3 μg/ml was reported; a scenario attributed to a compressed vaccine schedule usually used in Africa or it may be due to a higher challenge dose of pneumococci; thus suggesting that the protective concentration varies depending on the serotype, the population, and the set clinical end point (Plotkin, 2010; WHO, 2013). While humoral responses to meningococcus may be measured by ELISA, only the bactericidal tests correlate with adequate protection. This protective bactericidal antibody level is >1/8 (even >1/4) in human serum in all serogroups in children and 2 μg/ml in adults (Plotkin, 2010).

Vaccine Preventable Disease Burden

Background

Vaccination and use of vaccines are now central to prevention of infectious diseases globally (CDC, 2011; Chan, 2014; Ngwa et al., 2021), with about 2-3 million lives saved from common infections annually through routine vaccination (Peck et al., 2019; WHO, 2019c, 2020c). From the development of the concept of vaccines, to smallpox vaccination by Edward Jenner, to the rollout of global immunization efforts when WHO established the EPI program in May 1974, vaccines have now been embraced across all targeted groups, that includes children, to adolescents, and also adults (Chan, 2014; WHO, 2019c).

While the initial focus was on 6 major vaccine preventable diseases - tetanus, poliomyelitis, pertussis, tuberculosis, diphtheria, and measles; the programme has grown to cover over 116 million eligible children who are annually vaccinated against more than 20 vaccine-preventable diseases (Libwea et al., 2019; MacDonald et al., 2020; WHO, 2019c). This success has partly been achieved through adopting the Reach Every District (RED) World Health Organization strategy for improving vaccination coverage (Tekle et al., 2020). This strategy has five components " (1) 're-establishing outreach' services for immunization such as the use of mobile teams to extend regular services to all communities, (2) 'Supportive supervision' which involves providing onsite supervision to health staff at district levels during regular supervision meetings, (3) 'Linking services with communities' as a participatory approach to service delivery and identification of defaulters and drop-outs, (4) 'Monitoring and use of data' to assess progress and solve problems and finally, (5) 'Planning and management of resources' involving a context based plan at the district level for the implementation of the EPI" (MacDonald et al., 2020).

The implementation of the RED strategy though beneficial, has not eliminated all problems related to immunization, with well over 13 million children not receiving any vaccine in 2019 (Hayir et al., 2020; Libwea et al., 2019; MacDonald et al., 2020). It is this disparity in vaccination that continues to drive morbidity and mortality due to vaccine preventable diseases (McAllister et al., 2019). The true burden and actual data on burden of vaccine preventable diseases is incomplete or lacking many countries in the SSA region (Muhindo et al., 2016). In this section, we review some of the available data on the burden of the more common vaccine preventable diseases currently driving ongoing morbidity and mortality in Africa, including measles, pneumonia, and COVID-19.

Measles

Measles is a very contagious viral infection, and causes marked morbidity and mortality, leading to close to 2.6 million deaths annually worldwide (Haston & Pickering, 2020). The reproduction number for measles virus is 12 – 18, a figure that is the highest amongst all respiratory viruses, even higher than that of SARS-CoV-2 coronavirus that causes COVID-19 disease (Durrheim et al., 2019; Olugbade et al., 2019). The measles vaccination was one of the first to be included into the EPI program at the onset in the 70s, but its eradication has faced numerous bottlenecks (Chan, 2014; Portnoy et al., 2019). Even though this effective vaccine against measles virus has been available for a long time, many countries continue to experience frequent measles outbreaks (Dabbagh et al., 2017; Durrheim et al., 2019). There are five countries with the highest number of children who are not vaccinated against measles, including Pakistan, Tanzania, Yemen, India and Nigeria (Portnoy et al., 2019).

In the year 2019, 413,308 measles confirmed cases and 207,500 deaths were reported, a sharp increase from the 140,000 measles deaths in 2018, 110,000 in the year 2017, and 89,780 measles-related deaths in 2016. In the year 2000, almost 1,300 cases of measles were reported in 31 states in the U.S. in 2019— the greatest number since 1992" (CDC, 2021). While the early vaccine roll-out was accompanied by a significant reduction of measles deaths in the 80s and 90s, recent resurgence in the last decade have heightened concern and fears of recurrent outbreaks (Malande et al., 2019; Ngwa et al., 2021).

Table 1: Table showing the Top 10 Countries with Global Measles Outbreaks

Rank	Country	Number of Cases
1	Nigeria	5,300
2	Pakistan	4,868
3	India**	1,865
4	Niger	1,583
5	Democratic Republic of the Congo	1,495
6	Burkina Faso	1,243
7	Afghanistan	1,129
8	Bangladesh	917
9	United Republic of Tanzania	902
10	Côte d'Ivoire	888

Source: (CDC, 2021)

It is believed that persistent and recurrent sporadic measles outbreaks in many SSA countries are related to persistent failure by many countries to meet the immunization coverage targets for measles (Nabirye et al., 2020; Ngwa et al., 2021). In general, the global measles burden and mortality have steadily decreased, except in 2015 when the global milestones were not met, and recent setbacks have increased the incidence of measles globally (WHO, 2019d). through the period 2000 - 2018, the WHO tracked the progress towards the elimination of measles in the 6 World Health Organization regions; focusing on measles vaccination coverage, measles disease incidence and measles mortality based on these milestones and targets of the World Health Assembly (WHA) (WHO, 2020f):

1. **First milestone: To increase the measles vaccine coverage with the first dose given to children by/at 1 year of age**

This milestone aimed at increasing this measles containing vaccine (MCV)1 national vaccine coverage to children to equal to or over 90% in every country; and district coverage set at equal to or over 80%. By year 2000, only 45% of the target countries attained 90% or higher national MCV1 coverage, but with only 9% of countries from the African World Health Organization region and the highest was noted in the Americas where 63% of the countries met the national target (De Broucker et al., 2020). While the overall national average increased to 61% in 2018, with largest increases observed in the African region (9% to 30%), none of the World Health Organization regions achieved coverage of 90% or higher in all its countries (Cochi & Schluter, 2020; Durrheim et al., 2019; Holt, 2019; Patel et al., 2020).

2. **Second milestone 2: To reduce global measles incidence**

The second goal of the WHA aimed to reduce the overall global measles incidence to less than 5 cases per 1 million people population. This goal has not been met, with the total number of 353,236 cases in 2018 (Portnoy et al., 2019). Over the last 2-5 years, each of the 6 World Health Organization regions has reported an increase in number of cases during the past two years, with exception of the Western Pacific region (WHO, 2017a).

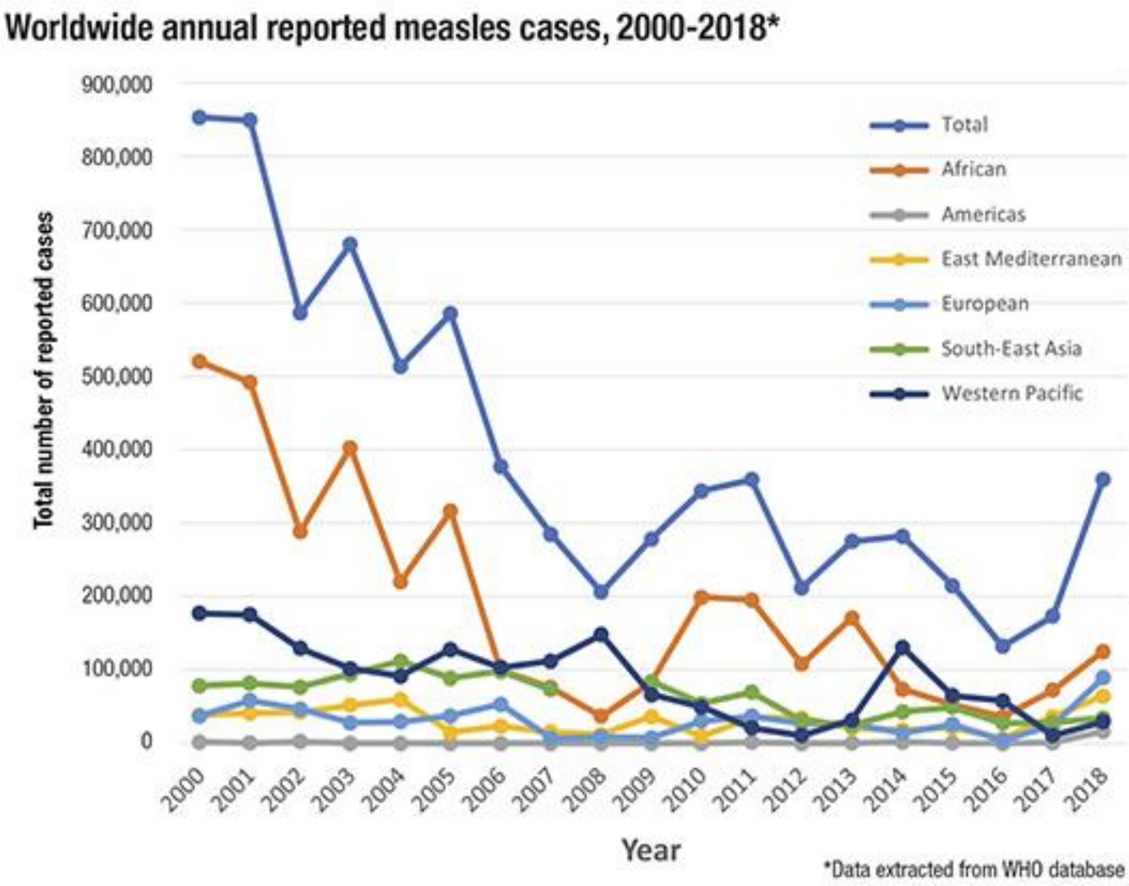

Figure 3: Worldwide annual reported measles cases, 2,000 – 2018

Source: (Haston & Pickering, 2020)

1. Third Milestone: To reduce global measles mortality

The third WHA milestone focused on reducing measles related mortality. There was a 73% reduction since 2010 in measles-related mortality, and while the goal of 95% reduction was not achieved, measles vaccination is estimated to have led to over 23.2 million deaths averted deaths between the year 2000 and 2018 (Dabbagh et al., 2017). In general, trends in the previous rapid gains in reduction of measles burden globally have not been sustained in last two years. Some mitigating factors strengthening the in-country immunization programs, identifying immunity gaps in the countries, vaccinating travellers adequately and improving surveillance efforts (Durrheim et al., 2019).

Pneumonia and Diarrheal diseases

Pneumonia and diarrhoea are two leading infectious causes of childhood disease and mortality. In 2010, over 1·731 billion episodes of diarrhoea in children (36 million severe episodes) and over 120 million episodes of pneumonia (Libwea et al., 2019; Peyrani et al., 2019; Rudan et al., 2008; Walker et al., 2013). The following year 2011 saw 700 000 diarrhoea episodes and 1·3 million pneumonia cases led to childhood deaths, most of these occurring in those under 2 years of life (72% following diarrhoea and 81% for pneumonia deaths) (Liu et al., 2012; Liu et al., 2016; You et al., 2010). Most deaths from pneumonia and diarrhoea occur in children below 2 years of age, with both being associated with high child mortality, poverty and occurring mainly among populations situations undergoing crisis (You et al., 2010).

The overlap in pneumonia and childhood diarrhoea epidemiology is partly due to shared risk factors, for example suboptimum breastfeeding, undernutrition, and zinc deficiency (Liu et al., 2012). Vitamin A deficiency increases risk of severe diarrhoea and mortality following diarrhoea mortality; though it is not a major risk for the incidence of pneumonia or diarrhea, or even pneumonia-related mortality (Liu et al., 2012). Water and sanitation related risk factors (including poor water quality and unwashed hands) have been described to contribute to diarrhea-related morbidity and mortality; while pneumonia is higher is situations with overcrowding, exposure to indoor air pollution among others. Rotavirus is the commonest cause of severe vaccine-preventable diarrhoea (in 28% of cases), while Streptococcus pneumoniae (in 18·3% of cases) is largest cause of vaccine-preventable severe pneumonia (Liu et al., 2012).

There's been studies examining whether pneumonia and diarrhoea each are independent risk factors for increasing simultaneous or sequential infection risk with each other. In Ghana, India and Nepal, studies showed that "as daily prevalence of diarrhoea increased, the risk of a subsequent acute lower-respiratory-tract infection increased by 1·08 per day of diarrhoea."(You et al., 2010) In Brazilian children, this association did not hold. Measles has for long been associated with increased cases of diarrhoea disease and mortality; while pneumonia is the largest cause of mortality from measles (linked to 56–86% of measles deaths), with case fatality of severe pneumonia with measles being over twice more than CF of severe pneumonia without measles, - to a large extend being due to immunosuppressive and other systemic effects of measles infection with secondary bacterial superinfection (You et al., 2010).

Acute diarrhoeal and respiratory infections are commonest childhood diseases and causes of attendance at most health centres in developing countries where together with measles, HIV/AIDS, measles and pneumonia contribute a significant inpatient population among children in those countries and up to thirty percent of all-cause mortality among children globally. It has been recently estimated that close to 2 million pneumonia childhood deaths occur annually especially arising from Africa and South-East (Rudan et al., 2008; Walker et al., 2013). The WHO estimates show that "Pneumonia is largest infectious disease leading to child deaths globally, and was responsible for 15% of all child deaths before the 5th birthday in the year 2018 (McAllister et al., 2019; WHO, 2019a). The commonest causes of pneumonia are *Streptococcus pneumoniae*, *Haemophilus influenzae* type b (which is the second commonest cause of bacterial pneumonia), RSV and *Pneumocystis jiroveci* - the most common cause of pneumonia in infants infected with HIV (McAllister et al., 2019).

In the year 2015, the incidence rate of pneumonia in children was 1603 and 2509 per 100 000 children in Africa and Southeast Asia, higher than the global average incidence of 1419 per 100 000 (Ferreira-Coimbra et al., 2020; Troeger et al., 2017). It was estimated in 2015 that over 102 million cases of pneumococcal disease occurred in children under-five, and over 700,000 of these died (McAllister et al., 2019). Annually, pneumonia is responsible for over 450 million infections and over 4 million deaths, and affects more children than TB, HIV and malaria combined (Ekirapa-Kiracho et al., 2021; Ferreira-Coimbra et al., 2020; Hug et al., 2019).

Hepatitis B infection

Hepatitis B virus causes hepatitis B infection and leads to significant morbidity and mortality worldwide, especially in Africa. Globally, close to two billion people are considered exposed to Hepatitis B virus infection, with 296 million chronic carriers of the hepatitis B surface antigen reported worldwide (Akyıldız et al., 2019; Bilounga Ndongo et al., 2018; Bwogi et al., 2009; Chiesa et al., 2020; Rugaatwa Ndibarema et al., 2022; Tsague et al., 2019; Zampino et al., 2015). Epidemiologically, the Western Pacific Region of the world has the highest burden of close to 116 million, followed next by the burden in the African Region, where about 81 million people have chronic disease. In the year 2019, about 820,000 deaths were reported to be associated with hepatitis B infection, occurring mainly following hepatocellular carcinoma and liver cirrhosis.

The Hepatitis B virus is a double stranded, enveloped DNA virus that contains an icosahedral nucleocapsid. The hepatitis B virus may be spread through vertical transmission (from mother-to-child), or be spread horizontally when one is exposed to body fluids, products, and blood of an individual infected with the virus (saliva, vaginal fluids, seminal fluids, etc), or through needle stick injury, or body fluid splashes, or through sexual intercourse commonly among individuals with multiple sexual partners (Leuridan & Van Damme, 2011; Zampino et al., 2015). The hepatitis B virus can as well spread through blood transfusion, but the incidence of this type of spread has greatly reduced since the intensification of widespread routine screening of blood products before transfusion.

Hepatitis B virus infection is a self-limiting condition in over 90% of patients that acquire Hepatitis B virus infection in adulthood. The condition becomes chronic in less than five percent of cases, and only one percent experience a fulminant acute hepatitis course which can sometimes be fatal. Hepatitis B infection puts the infected persons and attending health workers infected to serious and severe morbidity risks like primary liver cancer and liver cirrhosis (Leuridan & Van Damme, 2011; Zampino et al., 2015). Though some reports suggest that about seventy percent of worlds global Hepatitis B virus infection burden is found in Africa (precisely SSA), HBV infection has as well been found to be prevalent outside the Sub Saharan Africa region, with about 15% prevalence in Asia, and 8-40% burden occurring in the rest of Africa population outside Sub Saharan Africa (Chiesa et al., 2020; Coste et al., 2019; Joseph et al., 2019; Leumi et al., 2020; Leuridan & Van Damme, 2011; Zampino et al., 2015).

A recent Cameroon study put the country paediatric Hepatitis B virus infection prevalence at 12% in 2019 (Tsague et al., 2019). Similar patterns of distribution have been reported in Tanzania, Ethiopia, Democratic republic of Congo, and Malawi (Leumi et al., 2020; Leuridan & Van Damme, 2011; Singh & Lewin, 2020; Tsague et al., 2019; Zampino et al., 2015). The relatively lower to moderate rate of paediatric Hepatitis B virus infection prevalence in Cameroon may be attributed partly to the wide and broad paediatric coverage of the vaccine against Hepatitis B virus infection in children in Cameroon. It is now appreciated globally that rising rates of universal vaccination among children and infants against hepatitis B has decreased the HBsAg prevalence rates in children who are younger than age 5 years from rates of 5% in the pre-vaccination era (of the 1980s to the early 2000s) to rates of around one percent in the year 2015 (Leumi et al., 2020; Leuridan & Van Damme, 2011; Singh & Lewin, 2020; Tsague et al., 2019; Zampino et al., 2015).These figures should however be seen in context, since several studies in Cameroon had reported an eight percent prevalence of HBV infection among pregnant women in the year 2012, and eleven percent within the general population in the year 2016. Both these prevalence rates are high when one factors in the recommended WHO's threshold rate.

Vaccination against HBV infection was introduced into the Expanded Programme on Immunization in 1982, with the expectation that between 90 to 100% protection level would be achieved progressively against the hepatitis B virus infection (Schmit et al., 2021; Zampino et al., 2015). There was the goal to globally eliminate viral hepatitis infection that was adopted during the World Health Assembly with a target of 90% reduction in new infections and 65% reduction in mortality. Uganda is among countries with very high seroprevalence of Hepatitis B virus infection (Akyıldız et al., 2019; Bwogi et al., 2009; Coste et al., 2019; Leuridan & Van Damme, 2011; Zampino et al., 2015). As reported from the 2005 Uganda National Hepatitis B Sero-survey, the prevalence of HBV infection was reported to be ten percent. A few years later, in 2018, the seroprevalence of HBV infection was reported to have dropped to 4.3% (broken as 5.6% among Ugandan men and 3.1percent among Ugandan women).

The sero-survey reported that hepatitis B sero-prevalence was found to be highest in the Northern region of Uganda with about 4.6% rate reported in mid-Northern part of the country, 4.4% in the North-eastern part and 3.8% in the West Nile region of the country(Apecu et al., 2018; Rugaatwa Ndibarema et al., 2022; Zampino et al., 2015). Hepatitis B infection sero-prevalence rates was found to be lower in most of the rest of the country, ranging from 0.8% in Southwest region of the country to 2.7% in East Central parts of the country. These figures were lower than what Ochola et al had reported earlier that indicated up to 17.6% sero-prevalence in the Northern part of Uganda around Gulu that had Hepatitis B virus infection. They reported a lifetime exposure of about 72.4 percent in the same region. There was also a report of a household cross-sectional study in the south western Kiruhura district of Uganda that found a Hepatitis B virus infection sero-prevalence of 4.1percent (Apecu et al., 2018; Rugaatwa Ndibarema et al., 2022; Zampino et al., 2015).

An outpatient investigation at Mbarara Regional Referral Hospital in southwestern part of Uganda, found that 5.5% of the participants were sero-positive (Rugaatwa Ndibarema et al., 2022). This as seen earlier, was a higher prevalence than the 3.8% previously reported by Bwogi et al in their nationwide population-based sero-prevalence cross-sectional survey that involved adults aged between 15–59 years in Uganda and in children aged less than 5 years (Bwogi et al., 2009). The Mbarara Hospital findings were as well higher than that of the national sero-prevalence of 4.3 percent that was reported in the results mentioned earlier from of Uganda Population-based HIV Impact Assessment Survey conducted in the year 2016 (Akyıldız et al., 2019; Bwogi et al., 2009; Rugaatwa Ndibarema et al., 2022; Zampino et al., 2015).

The Mbarara survey was much lower than 7 percent sero-prevalence reported among the fishing communities living around the Lake Victoria (Rugaatwa Ndibarema et al., 2022). The findings of the survey in south-western Uganda by Apecu et al found a fairly low prevalence of HBV at around 4.1 percent in a household district wide cross-sectional survey in Kiruhura district (Apecu et al., 2018). It is noteworthy that since this was a hospital-based survey, the HBV disease burden found is indeed expected to be much higher when compared to community based or household surveys. In this hospital-based cross-sectional study, the respondents' gender and the district of origin were independently associated with positive hepatitis B infection seroprevalence among outpatients attending Mbarara Regional Referral Hospital (Rugaatwa Ndibarema et al., 2022). In the same study, male respondents showed a higher likelihood of testing positive for hepatitis B infection when compared to female participants (Joseph et al., 2019; Leuridan & Van Damme, 2011; Rugaatwa Ndibarema et al., 2022; Singh & Lewin, 2020; Zampino et al., 2015).

All these findings on Hepatitis B virus infection sero-prevalence indicate the clear need for a comprehensive and an effective strategy to interrupt the spread of HBV within the population (Akyıldız et al., 2019; Bilounga Ndongo et al., 2018; Bwogi et al., 2009; Chiesa et al., 2020; Rugaatwa Ndibarema et al., 2022; Tsague et al., 2019; Zampino et al., 2015). These strategies must pay specific attention to rural settings and some regions of the country especially those with high sero-prevalence of HBV infection. The ministry of health Uganda has made various attempts to design strategies for Hepatitis B virus infection prevention including vaccination for young children since 2002 under the UNEPI. The Ministry of Health should ensure that it scales up routine hepatitis B testing and treatment at regional referral hospitals. The ministry should as well engage adult males in hepatitis B routine provider-initiated testing alongside other control programs including vaccination and the sensitization against hepatitis B to minimise the chances of hepatitis transmission. Other strategies are community engagement, community education, social mobilization, strengthened cold chain systems, ensuring steady supply of vaccines and combating vaccine hesitancy (Akyıldız et al., 2019; Bilounga Ndongo et al., 2018; Bwogi et al., 2009; Chiesa et al., 2020; Rugaatwa Ndibarema et al., 2022; Tsague et al., 2019; Zampino et al., 2015).

Coronavirus disease 2019 (COVID-19)

It was observed that paediatric population were affected by non-pharmaceutical public-health measures, school closures, decrease in social care and interactions, feeding and health provision disruptions (CDC et al., 2020; Durrheim et al., 2019; Durrheim et al., 2021; Durrheim & Crowcroft, 2017; Hillis et al., 2021; Snape & Viner, 2020). The pandemic has so far caused 194,183,287 cases and 4,159,273 deaths in over 200 countries (BBC, 2021). The pandemic has had serious effects on childhood immunization uptake and coverage, with all the six World Health Organization Regions reporting disruptions on both routine immunization and mass vaccination campaigns (including outreach services and surveillance services)

(Alsuhaibani & Alaqeel, 2020; Danese & Smith, 2020; Frederiksen et al., 2020; Hillis et al., 2021; Williams et al., 2021). Childhood immunization is indeed one of the routine health services significantly disrupted by coronavirus disease 2019 (COVID-19) in Africa, since this system relies mainly on functioning healthcare facilities and stable socio-economic communities to function effectively (Abbas et al., 2020; Adamu et al., 2020; Amadori et al., 2020; Billon-Denis & Tournier, 2020; Bramer et al., 2020).

This disruption in immunization has the risk of leading to increases in numbers of cases of vaccine-preventable diseases, and related deaths (David et al., 2021; Decouttere et al., 2021). Many regions have experienced decreased reporting from their EPI programs and re-emergence of vaccine preventable diseases, partly due to the effects of COVID-19 pandemic and associated containment measures (Danese & Smith, 2020; Morgan & Rose, 2020). The COVID-19 pandemic has led to severe worldwide social, economic, infrastructural, social and health disruption, not forgetting the largest ever global recession maybe since the Great Depression of the nineteen thirties (Bernal et al., 2020; Hillis et al., 2021; Lieneck et al., 2021; WHO, 2021d).

There has been pressure on healthcare system due to increased challenges of COVID-19 pandemic affecting health system effectiveness in measuring and responding to the pandemic (Abbas et al., 2020; Colombo et al., 2020; Ogunkola et al., 2021; Ombere, 2021; Shakespeare et al., 2021). This has worsened the problems of healthcare systems in Africa which already face many challenges including poor funding, low numbers of healthcare workforce, inequitable distribution and allocation of resources to health, very high disease burden, poor political will, poor leadership that does not prioritize healthcare and very outdated health infrastructure. These weak systems have been worsened in many areas by the pressure brought by the COVID-19 pandemic on healthcare in Sub-Saharan Africa (Colombo et al., 2020; Hoang et al., 2020; Khalil et al., 2020; Roberton et al., 2020; Vousden et al., 2021).

Not only has immunization programs suffered effects of COVID-19, but as well other services like an increase in preventable causes of childbirth mortality and pregnancy in low and middle-income countries (Buja et al., 2021; Cascini et al., 2021; das Neves Martins Pires et al., 2021). Maternal mortality levels have continued to remain high in Sub-Saharan Africa (SSA), with poor access to good antenatal care (ANC) services, with 52% of women having at least 4 ANC visits in many parts of SSA (Adelekan et al., 2021; Juan et al., 2020; Tardiolo et al., 2021). The lack of funds, access difficulties, corruption, shortage of workers, generally poor infrastructure, counterfeit drugs, low budgetary allocations to the health in many nations and changing medical needs of the population (Hui et al., 2020; Kwok et al., 2020; Munster et al., 2020; Shakespeare et al., 2021). The impact of COVID-19 on health sector, coupled with impact of containment measures, overstretched health centres, limited supply of commodities due to the disrupted supply chain, the shortage of adequately skilled health workers, redirection or reduction of funds and focus on health by governments, by donors, and stakeholders towards COVID-19 containment (Bedford et al., 2020; Kwok et al., 2020; R. Lu et al., 2020; X. Lu et al., 2020; Wang et al., 2020).

The COVID-19 pandemic has also led to the widespread supply shortages in commodities, that were exacerbated by agricultural disruption, panic buying and food shortages (Ji et al., 2020; Lieneck et al., 2021; Zoumpourlis et al., 2020). In many societies, numerous educational institutions, social recreation halls and public areas/amenities have been partially or even fully closed, with many events either cancelled or postponed (Binagwaho et al., 2012; Morgan & Rose, 2020). There has been misinformation that has seen incorrect information widely circulated through social media platforms and mass media (Binagwaho et al., 2012; Makoni, 2020). There has as well been issues of possible racial discrimination, health inequity, wealth inequality and the balance between public health imperatives and individual rights

(Chan et al., 2020; Ogunkola et al., 2021; Pallangyo et al., 2020; Sun et al., 2020; Umviligihozo et al., 2020).

Expanded Programme on Immunization (EPI)

Historical Background of the EPI

In the year 1974, encouraged by the success gained from the efforts to eradicate smallpox, the Expanded Programme on Immunization (EPI) was established with the aim of expanding the immunization programmes around the world, to cover additional antigens within the umbrella of immunizable diseases and make sure that each child around the world can access life-saving vaccines(Chan, 2014). This was followed in the 1977 by setting goals of availing immunization against pertussis, diphtheria, tetanus, polio, tuberculosis and measles to every eligible child in the world by the year 1990(WHO, 2017a). In 1984, the World Health Organization (WHO) then established a standardized vaccination schedule for the four original EPI vaccines: - Bacillus Calmette-Guérin (BCG) vaccine, diphtheria-tetanus-pertussis (DTP) vaccine, oral polio vaccine, and measles vaccine (Lukusa et al., 2018).

Progressively, these available vaccines have been added and expanded to now include additional vaccinations that can protect older children, adolescents and adults. It was the eradication and certification of eradication of smallpox in the world that showed the power of vaccines, and their lasting potential impact to change world health promotion and provision (WHO, 2020f). This progress has elevated immunization to being only second to clean water for interventions with the largest public health impact for control of communicable diseases, with now each country in the world having a recognized organized immunization Programme(Chan, 2014; WHO, 2017a).

At the time when the EPI was formed in 1974, fewer than five percent of eligible children were receiving recommended 3 doses of DPT and polio vaccines in infancy. In this progress, the number of public health vaccines that are being used for the universal protection against vaccine preventable diseases has more than doubled since the year 1974, and now, almost all member countries include the vaccines against HBV and Hib type b bacteria in addition to the other original six vaccine preventable diseases in 97% of all member countries(Chan, 2014). Today, the coverage levels for DPT3 has on average surpassed 50% of all eligible children in developing countries, with more diseases and deaths due to Vaccine Preventable diseases (VPDs) averted (Yaya et al., 2019).

It is estimated that by 1987, the introduction of measles vaccine had helped prevent over 700,000 measles deaths in developing countries. This success has also been seen with introduction of tetanus vaccine during pregnancy that has significantly reduced cases of neonatal tetanus and associated deaths worldwide (Siciliani et al., 2020). The efforts towards Polio eradication through immunization have been outstanding, since Rotary International's launch of a global effort to immunize all the world's children against polio in the year 1985, with subsequent establishment of the GPEI in the year 1988. At the start of the GPEI, poliomyelitis was estimated to paralyze more than 1000 children in the world daily.

Since the initiation of the GPEI, over 2.5 billion eligible children have now been immunized against poliomyelitis in over 200 countries (Siciliani et al., 2020). Currently, Today, wild poliovirus remains endemic in only two countries of Afghanistan and Pakistan, and the global incidence of poliomyelitis cases has decreased by over 99%. This success has also been replicated in the in eradication of certain strains of the polio virus; whereby, of the three types of wild polioviruses (WPVs), the last case of type 2 polio virus was reported in 1999 with its eradication being declared in September 2015.

Before the EPI was initiated in the 70's, child vaccination coverage for BCG, pentavalent, pertussis, pentavalent then estimated that only about 5% targeted by four vaccines

(Chan, 2014; Yaya et al., 2019). This has now risen to 83%, with some low-income countries reaching 99% immunization coverage, and the vaccines under the Programme have increased, with the Programme now expanded to include vaccines for Haemophilus influenzae type B, Hepatitis B, rubella, yellow fever, mumps, rubella, tetanus, pneumococcal (PCV), rotavirus diarrhea, human papilloma virus (HPV) vaccines and soon to be introduced vaccines for COVID-19 (Li et al., 2020; Liu et al., 2012; Lukusa et al., 2018). The impact of this increased vaccination is noteworthy, with measles related deaths decreasing by 60% worldwide between the year 999 and 2005, and poliomyelitis deaths and paralysis reduced with eradication of Type 2 and 3 wild polio viruses (Lukusa et al., 2018; Yaya et al., 2019).

In 1999, GAVI was created with the goal of improving child health through immunization in the poor countries of the world by extending the reach of the EPI. A grand coalition was put together in establishing the GAVI - includes the three UN agencies/institutions (the WHO, the UNICEF, the World Bank), various public health institutes, the Bill and Melinda Gates Foundation, the donor and implementing countries, and The Rockefeller Foundation, the vaccine industry, non-governmental organizations (NGOs) among others. The creation of the GAVI has helped to speed up response to increasing vaccine demand for emerging and re-emerging vaccine preventable diseases worldwide.

The goals of the EPI

The EPI has the following goals(WHO, 2017b):

1. to ensure full immunization of children under one year of age in every district,
2. to globally eradicate poliomyelitis,
3. to reduce maternal and neonatal tetanus to an incidence rate of less than one case per 1,000 births by 2005,
4. to cut in half the number of measles-related deaths that occurred in 1999, and

5. to extend all new vaccine and preventative health interventions to children in all districts in the world.

To speed up and focus the implementation of these goals, the GAVI set up specific milestones (WHO, 2017b):

1. By 2010 all countries have routine immunization coverage of 90% of their child population
2. Hepatitis B vaccine be introduced in 80% of all countries by 2007
3. That 50% of the poorest countries have Hib vaccine by 2005.

Implementation of the EPI

Each member state and country within the United Nations was requested to create and to implement their health policies on vaccination in adherence to the guidelines set by WHO on EPI (WHO, 2017b). The World Health Organization offered technical and institutional support for setting up of country immunization programs in a multifaceted complex structure with many components that includes setting up a reliable system of cold chain, a clear functional transport network for vaccine delivery, a system for vaccine stock maintenance, health worker training, monitoring and evaluation, establishment of outreach educational/health promotional programs for local communities, social mobilization and sensitization systems, a system for record keeping, documentation and storage, and a system for management of AEFIs (WHO, 2017b).

Whereas the World Health Organization helped countries to set up the general structure for the EPI, each region has slightly variations in the ways of operationalizing and implementing their various immunization programs as based on their individual level of health infrastructure and organization. There are areas with fixed/static sites for vaccination

(vaccination centers within designated health facilities) while others have either mobile vaccination teams running an outreach component or a blend of both outreach and static services.

In some under-developed hard to reach communities, countries have adopted ‘pulse immunization’ approach, where ‘pulses’ of vaccines are usually given to eligible children during annual vaccination campaigns. In urban and per-urban centres with high numbers of populations in informal settlements, door-to-door canvassing, “also referred to as channeling,” has been used to increase the uptake of immunization services, and is usually blended with periodic national-level mass supplementary immunization activities (SIAs) vaccination campaigns (WHO, 2017b).

Bottlenecks in the roll out of the EPI

The implementation of the EPI around the world has not been without challenges. Some of the problems that have been encountered in this process include a lack of public awareness of the scope and burden/seriousness of the targeted vaccine preventable diseases(VPDs), lack of an effective approach to the management of the EPI programmes; poor health worker and overall health force skills and equipment for handling, storage and handling of vaccines; a weak/poor infrastructure for maintaining cold chain infrastructure for vaccine storage and transport for vaccines from storage centres to immunization points (Bailey et al., 2016; Malande et al., 2019; Troeger et al., 2017).

Other barriers to implementation of an effective EPI Programme include language barriers, frequent vaccine stock outs, inadequately trained health workers, poor road network and difficult geographical terrain, nomadic/migrant refugee populations that find it hard to complete scheduled vaccines, political instability, poverty, inadequate allocation of funds by governments to health, an insufficient infrastructure for monitoring the EPI Programme and the now emerging problem of vaccine hesitancy and vaccine refusal (Bailey et al., 2016; Malande et al., 2019; Troeger et al., 2017).

Evaluation of the EPI

Monitoring and evaluation is an important aspect of running an effective EPI. In each country running an EPI, immunization programs are usually monitored using two methods - an administrative method and also through use of community-based surveys (Chan, 2014; WHO, 2017b). The administrative method of monitoring uses immunization data sourced from private, public, and non-governmental immunization centers. The limitation with this method is that the accuracy and reliability of the reports from these facilities may not be guaranteed (WHO, 2017b). This method applies in areas where government services and ministries deliver the immunizations and vaccines directly in their facilities or deliver supplies and vaccines to the non-governmental facilities (WHO, 2017b).

Countries without this type of infrastructure are better served through community-based surveys to estimate immunization coverage. These community-based surveys utilize a modified cluster sampling method that was developed by the World Health Organization (WHO, 2017b). In this approach, Vaccine coverage is usually evaluated using a 2-stage sampling study approach in which there are 30 clusters and seven children allocated to each cluster (Machingaidze et al., 2013; WHO, 2017b). It is simplified to allow health workers with little or limited background in health statistics and sampling techniques to perform data collection with some minimal or basic training.

This kind of survey allows for collection of information from areas lacking a reliable data source and allows for validation of reported vaccine coverage estimates within a 10 percent margin. The use of surveys or questionnaires helps to improve the quality of administrative reports on vaccine uptake and coverage. In someone situations during data collection, home-based records when available, can aid in determining vaccination status and dates of vaccination reviewed on the records to determine if the vaccines were given at the ideal age and in the recommended appropriate intervals (WHO, 2017b). This helps in identification of missed immunizations, and update vaccination be done either at static or through outreach services.

Lessons from the EPI

The World Health Organization estimates that immunization programmes currently save up to 2·5 million lives each year while protecting many millions more lives from disability and illness (Peck et al., 2019; WHO, 2017a). The certification of WHO's S.E Asia Region as polio-free, it is noteworthy that over 80% of the current world's population live in a country in which polio has now been eradicated (Bailey et al., 2016; Liu et al., 2016). Indeed, the prevention of these childhood deaths helps create momentum within individual member countries and within the international community to rally support for immunization programmes. Vaccine delivery can carry on even in the absence of perfectly functioning health systems (Troeger et al., 2017).

In the last four decades, EPI has fostered international cooperation, sourcing for more funding, encouraged innovation in technology, with better systems for disease surveillance and monitoring (Hug et al., 2019). EPI is also credited for strengthening of fundamental in country public health capacities with the accreditation of over 700 laboratories, in 164-member countries, which are now accredited by the World Health Organization to perform measles and other VPD lab surveillance (Ezbakhe & Pérez-Foguet, 2020). As observed earlier, the establishment of the GAVI vaccine Alliance in 2000 was helpful, with UNICEF, World Health Organization, and the GAVI Alliance working together to change market dynamics for vaccines, supporting increased vaccine supplies, making vaccines stocking more predictable, plentiful and affordable through collaborations with pharmaceutical vaccine manufacturing industry with focus on product designs and better formulations that have simplified vaccine administration and safety in resource-constrained settings (McAllister et al., 2019; Peck et al., 2019).

One of the biggest drivers of the EPI is a commitment to fairness in supply of current and new vaccines (Hug et al., 2019). To their credit, the GAVI alliance, with help from the World Health Organization, the UNICEF, and other stakeholders, has increased equitable access to vaccines through the rapid introduction of the newer vaccines into the routine EIP programmes of low-income countries (Ezbakhe & Pérez-Foguet, 2020). For example, in the year 1997, only 29 countries used Hib in their EPI; but as at the end of 2014, the number had risen to 190 countries, especially including most low-income countries (Peck et al., 2019).

It is noteworthy that the financial sustainability for most national EPI programmes remains a major concern (Hug et al., 2019). It is estimated that close to 20 million children eligible for vaccines are still unreached by immunization programmes (Liu et al., 2016; McAllister et al., 2019). The GVAP aims to extend full benefits of immunization to all eligible populations, has focused its attention beyond the foreseeable eradication of polio, followed by targeted elimination of measles, of rubella, and of neonatal tetanus, and a clear call to all countries to try to reach 90% national immunization coverage and up to 80% vaccine coverage in every district, and the provision of essential vaccines, especially those against pneumococcal disease and rotavirus diarrheal disease (Hug et al., 2019). These initiatives, its hoped, should avert an estimated 24 to 26 million child deaths by the year 2020 (Masters et al., 2019).

As previously observed by Margaret Chan, “the future of global health can benefit from the pioneering work done by EPI in many respects—for example, finding new ways to secure and increase funding, fostering cooperation between multiple partners to work together with shared yet flexible strategies, stimulating industry innovation, and promoting country ownership through the streamlining of programmatic demands. Above all, EPI carved out pathways and strategies to achieve universal access to immunization services. This legacy provides guidance for reforms that move health systems towards universal coverage, another worthy ambition for the future."(Chan, 2014)

The Burden of Underimmunization

Over time, immunization and vaccination have played a major role in the control and prevention of VPDs, by >95% - for every paediatric vaccine currently recommended for routine immunization before the year 1990 (Bailey et al., 2016; Victora et al., 2016). Despite this progress, about 19 million children in the world are not fully immunized (Alkema et al., 2016). It is thought that postimmunization adverse events could be a contributor to this problem – whether they be coincidental or vaccine-related, thus the increase in focus on vaccine safety (WHO, 2017a). The concerns about vaccine safety may affect caregiver decisions to have their children immunized, leading to delayed vaccinations, or decreased vaccine coverage and increase in disease outbreaks (WHO, 2019c). Delayed vaccination contributes to public health risks for vaccine preventable disease acquisition (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016) for the affected individual and transmission of the vaccine preventable disease in the community since children remain highly susceptible to vaccine preventable diseases and reservoirs for the vaccine preventable diseases for prolonged periods (Albers et al., 2022; Alkema et al., 2016; Gonzales et al., 2021; Kaufman et al., 2021; Kimmel et al., 2007; Kuehn et al., 2022; Olusanya et al., 2021; Paul et al., 2022; Stratoberdha et al., 2022; Ursula et al., 2016; Yang et al., 2023; Yazdani et al., 2021).

Delays in vaccination often increase the likelihood of involved children missing subsequent doses of scheduled vaccines or even dropping out of the recommended schedule all together before concluding the full series of their vaccines before the second birthday (Alkema et al., 2016; Kiely et al., 2018; Mutua et al., 2021). Evaluation of vaccination timeliness is critical in order to identify age-specific risks of targeted vaccine preventable diseases and design programmatic interventions for timely vaccination (Alkema et al., 2016; Janusz et al., 2021). Recent studies suggest that dose-specific delays in vaccination are common, and they lead a much higher probability of children dropping off the vaccination schedule, thus leading to prolonged susceptibility of the children to specific vaccine preventable diseases way beyond the first year of life (Kiely et al., 2018; Masters et al., 2019; Masters et al., 2018)

Additionally, reports from both low-income and high-income settings show significant risk of dropouts associated with delayed initiation of infant vaccination at birth (Masters et al., 2019; Masters et al., 2018; Mutua et al., 2021). These studies have proposed the need for education and design of outreach programs to improve community demand for on-time vaccination services (Janusz et al., 2021; Mutua et al., 2021). This they maintain would lessen the burden of follow-up, that often sees children falling behind in the schedules, and therefore reduce the risk of undervaccination, while intensifying outreach and catch-up immunization campaigns to help bring eligible children up to date on their vaccination (Janusz et al., 2021; Kiely et al., 2018; Masters et al., 2019; Masters et al., 2018; Mutua et al., 2021).

This pattern has been seen in SSA, where many child deaths (more than 100 deaths per 1,000 live births) coincide with observation that less than a third of countries in SSA reporting completion of immunization schedules for infants by >60% (Alkema et al., 2016; Victora et al., 2016). In parts of Europe as well as in Japan, there was concern regarding the safety of whole-cell pertussis vaccine which led to substantial reduction in the coverage of the vaccine and outbreaks of pertussis. Elsewhere in France, 3 people suffering from multiple sclerosis were compensated by the government due to purported association of the disease with the hepatitis B vaccine. Another problem followed the false associations the MMR vaccine and occurrence of inflammatory bowel disease and autism (Alkema et al., 2016; Masters et al., 2019; Masters et al., 2018; Victora et al., 2016).

Considerable progress has indeed been made in reducing under-five mortality, which globally declined by 53% from the year 1990 to 2015 (Alkema et al., 2016; Chan, 2014; Victora et al., 2016). Sub-Saharan Africa (SSA) has h6owever experienced much slower progress on th6is front, with 6 only 8 of 43 countries in the SSA region reported to have et or even exceeded the United Nations Millennium Development Goals (UN-MDGs) related to childhood survival by 2015 (Alkema et al., 2016; Chan, 2014; Victora et al., 2016). Inequities in rates of vaccination are a big contributor to disparities currently seen in childhood health and survival (Chang et al., 2018; Victora et al., 2016). In poor countries, under-immunization largely contributes to the over 10 million children die before reaching age of 5 (Chang et al., 2018).

The recently launched United Nations Sustainable Development Goal 3 (SDG 3), immunization is hoped to contribute greatly to reducing childhood deaths to < 25 per 1,000 live births by the year 2030, thus hopefully contribute to reduction of about 4 million under-five deaths per year (Bergen et al., 2022; Bhadoria et al., 2019; Chan, 2014; Chang et al., 2018; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). The factors driving underimmunization in poor countries include transportation and difficult terrain, language difficulties, migrant refugee communities, inadequate caretaker and health care education (Malande et al., 2019; McAllister et al., 2019). Additional factors are religious and cultural beliefs against immunization, adolescent or young caregivers, and increasing anti-vaccine messages (Malande et al., 2019). Additionally, frequent poor or low stocks of vaccines and supplies of vaccines for health facilities, and poor socio-economic status and health-seeking behaviors of caretakers also contribute to underimmunization (Malande et al., 2019; McAllister et al., 2019).

Zero-Dose Children

The focus of SDGs has been to ensure equity, and to make sure no one is left behind. There have been critics wo suggest that marginalized communities should be more of the focus and not country averages for coverage rates (Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). Some of areas requiring renewed focus have been ending HIV/AIDS epidemic, reducing infant and neonatal and under five child and maternal mortality, reducing deaths due to TB, malaria, and the renewed focus on neglected tropical diseases, accompanied with the ever-rising costs of essential services making them inaccessible to the vast majority of communities in need (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016).

Poor countries have many hard to reach areas where the burden of health care provision is profound. Immunization as an intervention ranks only second to fresh water as a public health intervention to prevent deaths and diseases(Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). It as well offers significant benefits for economies and for health, especially when you consider that 50 million deaths were projected to be averted through immunization related initiatives (Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). The economic benefits are because of averted costs of sickness and illness thus easing pressure on the health care system especially in poorer countries with weak infrastructure (Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016).

Despite the obvious justification in favor of immunization, over 18 million infants in 2021 are reported to have missed the first dose of DPT vaccine. These are defined as zero-dose children, and are indicators of missed communities, which also happen to be the ones facing multiple deprivations, and many iniquities and inequalities; especially when you note than 2/3 of zero-dose children come from families living below the recognized international poverty line that is defined at a cut off of USD 1.90 per day(Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016). There is an urgent need for strategies to reacg these children. This is because reaching them and providing to them the needed vaccines and immunization services is necessary to connect them to the health ecosystem.

In poor countries, an immunization visit also provides an opportunity for growth assessment and monitoring and provision of deworming and needed vitamin A supplements. Offering treatment to this critical mass of children will offer future economic and societal benefits including reducing poverty (as envisaged in SDG1), providing improved nutrition (as envisaged in SDG2), provision of better education and related outcomes (as envisaged in goal SDG4), and the overall benefit of reductions in existing inequalities (as seen in SDG10). Clear focus on Zero dose children is a door to addressing targets of Immunization Agenda 2030 (IA2030)(Bergen et al., 2022; Bhadoria et al., 2019; Cata-Preta et al., 2021; COVID, 2021; Galles et al., 2021), one of which is the reduction of zero-dose children by 50% by the year 2030 and the benefit of strengthening attainment of SDGs- especially the target to ensure no one is left behind.

One of the key points in addressing these children has been defining “zero-dose child.” There is now clarity that this is a “child who has failed to receive any routine immunizations”. This has been simplified for the purposes of monitoring as an infant has received DPT 1 vaccine. Note that this definition focuses on routine as opposed to campaign-based immunizations, because it aims to estimate the reach of the measured immunization services, and its performance in the communities (Galles et al., 2021; Johri et al., 2021; Lindstrand et al., 2023; Portnoy et al., 2021; Santos et al., 2021). The ultimate goal is to reach all communities. While one could consider other vaccines as proxies, DTP is often preferred one for the global IA2030 monitoring, especially given that measurement of other vaccines like polio or measles coverage usually through household indicator surveys could contain a mix of the routine and those campaign-delivered vaccine doses(Portnoy et al., 2021; Santos et al., 2021; Summan et al., 2021; UNICEF, 2020; Wendt et al., 2022; Wigley et al., 2022).

There is no doubt that many countries and many EPI programs have improved immunization coverage rates over the last decade. The gains have been seen in the reduction in deaths due to meningitis, pneumonia, measles and diarrhea(Bergen et al., 2022; Bhadoria et al., 2019; Chatterjee et al., 2021; Galles et al., 2021; Lindstrand et al., 2023; Summan et al., 2021; UNICEF, 2020; WHO, 2016), clearly showing that more and more children worldwide are as a result protected from many VPDs. The challenge however is that in the year 2021, over 25 million children did not complete recommended vaccines, shown by those who did not get DPT3 vaccine(UNICEF, 2020; Wendt et al., 2022; WHO, 2016; Wigley et al., 2022). It is important to remember however that of these 25 million children, seventy three percent (18.2 million children) are zero-dose children (COVID, 2021; Santos et al., 2021; UNICEF, 2020; WHO, 2016). The high proportion of zero dose children therefore emphasizes the reason why urgent strategies to address the zero-dose problem are long overdue. It is clear that reaching the zero-dose children can serve as a catalyst to cascade uptake of further vaccinations for children. This is because recent surveys have shown that children either missed all vaccines or received 3 or 4 doses of vaccines, meaning that the initiation of dose 1 of DPT offers promise that other doses will be received(UNICEF, 2020; Wendt et al., 2022; WHO, 2016; Wigley et al., 2022). This clearly shows that reaching the zero-dose children must be a big focus of any immunization program that is seeking to ensure that it increases the immunization coverage for that country to expected targets, now that the children that receive at least one dose of the scheduled vaccines will most certainly be able to receive the other doses of vaccinations.

One glaring fact is that majority of zero-dose children are found in poor or low- and lower-middle-income countries; that account for eighty seven percent of the worldwide total of 18.2 million zero dose children (COVID, 2021; Santos et al., 2021; UNICEF, 2020; WHO, 2016). In the 2021 report, 6 countries with large-populations contributed a large proportion of Zero dose children – namely India at 2.7 million children, Nigeria at 2.2 million children, Indonesia at 1.1 million children, Ethiopia at 1.1 million children, Philippines at one million children, and the DRC at seven hundred thousand children. These countries accounted for over half of all the zero-dose children in 2021(COVID, 2021; Lindstrand et al., 2023; Santos et al., 2021; UNICEF, 2020; WHO, 2016; Wigley et al., 2022). These countries have many poor communities, low literacy levels, and poverty with some ridden with conflict or post conflict communities. The presence of informal settlements and slums is also a driver for high Zero dose numbers, with an urgent need to quantify what proportion of zero dose children are from slums. It has been hypothesized that children who reside in slums could have better access to immunization services than children from rural communities, but whether this translates to higher uptake and utilization of the services is unknown (Cata-Preta et al., 2021; COVID, 2021; Galles et al., 2021; Lindstrand et al., 2023; Santos et al., 2021; UNICEF, 2020; WHO, 2016; Wigley et al., 2022). Other barriers to access, including long distances to health facilities, poor road network, lack of male partner support, cultural and religious barriers all need to be assessed for their impact on Zero dose numbers (Bergen et al., 2022; Cata-Preta et al., 2021; Johri et al., 2021; Lindstrand et al., 2023; Portnoy et al., 2021; Santos et al., 2021; Summan et al., 2021; UNICEF, 2020; Wendt et al., 2022; WHO, 2016; Wigley et al., 2022). Given that a zero-dose child is likely to face many different barriers to access to immunization services, there is need to understand the various social, or political or economic situations and contexts in which zero-dose children or their families exist (Cata-Preta et al., 2021; COVID, 2021; Galles et al., 2021; Lindstrand et al., 2023; Santos et al., 2021; UNICEF, 2020; WHO, 2016; Wigley et al., 2022).

Recent reports and empirical studies have shown that zero-dose children and the caregivers to these children go through and experience many different barriers to access of immunization services and the fact that they are so many is a clear sign that significant iniquities exist (Cata-Preta et al., 2021; COVID, 2021; Galles et al., 2021; Lindstrand et al., 2023; Santos et al., 2021; UNICEF, 2020; WHO, 2016; Wigley et al., 2022). Besides stigma, there exist gender-based barriers to provision and the access of immunization services. Children from families where the mothers or female caregivers are educated and emancipated tend to not likely be in zero dose category. Another observation has been that children from very poor families or households are likely to fall in the zero-dose category when compared to those from wealthy family backgrounds (Portnoy et al., 2021; Santos et al., 2021; Wendt et al., 2022; Wigley et al., 2022).

There have been recent reports suggesting that the ethnic and religious backgrounds of caregivers affect if the child will end up in the Zero dose category or not. Concerns continue to persist that some religious groups promote messages and views that do not support the immunization efforts. Ethnic background has as well been reported to affect occurrence of Zero dose. Ethnicity and cultural influences are predominant in low income and poor nations of the world. This finding maybe coincidental, but is so predominant that it invites further exploration (Portnoy et al., 2021; Santos et al., 2021; Wendt et al., 2022; Wigley et al., 2022). This is because, some reports have observed that differences in the numbers of zero-dose children and their prevalence as rated by ethnicity were persistent even after the studies controlled for wealth, or maternal education, or location/area of residence as confounders; therefore suggesting that there could be several other factors that may be linked to ethnicity as a factor, and that drivers of observed immunization inequalities and underimmunization in several countries require further interrogation. Even in some countries where ethnicity is a possible factor, variations exist between smaller ethnic groups and bigger ethnic groups (Portnoy et al., 2021; Santos et al., 2021; Wendt et al., 2022; Wigley et al., 2022). Even religion as a factor, seems to show variation from country to country, and from community to community within the same country. This variation as well exists between predominant majority religions and existing minority religions. This inter-religion variability and inter-ethnic variabilities require additional and further interrogation. What is clear however is that zero dose drivers are multifactorial and strategies to address them will require a broad based multi-pronged approach to better solve the problem (Bergen et al., 2022; Cata-Preta et al., 2021; Johri et al., 2021; Lindstrand et al., 2023; Portnoy et al., 2021; Santos et al., 2021; Summan et al., 2021; UNICEF, 2020; Wendt et al., 2022; WHO, 2016; Wigley et al., 2022).

There exists the major gap especially as regards the evidence or literature base regarding the zero-dose category of children (WHO, 2020a). This gap is constituting the understanding of patterns among special groups for example the refugee, the migrant, and the nomadic groups or populations (Causey et al., 2021; Nnaji et al., 2021; WHO, 2020a). Recently, the WHO commissioned a review that found that over twenty six million people, in this case refugees in the year 2020 and over forty million people that are in the internally displaced categorization as a result of variants like violence as well as conflict in the year two thousand and twenty one, and that whereas some of the populations in question experience much lower immunization coverage rates, all these determinants are context-specific, often times with very unclear patterns (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).What has not been adequately quantified are the numbers of children that miss vaccines among these special groups. It is hard to estimate the size or numbers of the nomadic, or the displaced, or even the migrant populations, since this is very dynamic. Secondly, this is usually or maybe exacerbated by all or any forms of conflicts, or of food shortages, or natural calamities, or of climate shocks, and even the loss of personal/individual incomes (Causey et al., 2021; Nnaji et al., 2021; O'Brien et al., 2021; O'Brien et al., 2022; WHO, 2020a). The constant mobility of nomads in the context of conflicts may in turn lead to the increase in the numbers of the children that are missed by routine immunization services or by household demographic surveys that are designed usually to measure the immunization percent coverage in that population (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).

Besides the fact that there exist inequalities as a result of problems of access to immunization services, the zero-dose children including the families they come from do face very many forms of deprivations that are related to enjoyment of healthcare and that of several aspects of development (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). When you consider or compare to several other maternal care and child health services, the children under zero-dose category and their caregivers or mothers are about two to two and half times as or more likely to fail to get antenatal services and to access possibility of institutional delivery of their pregnancy. The contrast lies in the fact that only about twenty percent of them are less likely to be able to access the care of the childhood illnesses or of the symptoms (Causey et al., 2021; Nnaji et al., 2021; O'Brien et al., 2021; O'Brien et al., 2022; WHO, 2020a). Results were recently published of an increased analysis that considered broader and wider indicators of development for individuals.

This analysis found that the lack of a given vaccination or the failure to get this vaccine is associated more strongly with lower accessibility to improved fresh water and to better sanitation, and of higher rates of occurrence of childhood stunting, or of lower levels of numbers of maternal education, and of lower levels of cases of maternal demand among respondents for family planning as satisfied with most of the modern methods (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). There was an ecological analysis that showed that similar patterns to the ones described above were as well observed in spread across many countries and also across several subnational regions or provinces within those countries. An important aspect analyzed that looked at these variables of deprivation revealed that nearly all the zero-dose categorized children tend to be within the highest level of deprivation quintile. This means that when a zero-dose defined child is found, then it is very highly likely in this case that this child is facing multiple levels or forms of deprivations (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). It is therefore not surprising that in India, one geospatial statistical analysis of the time trends observed in zero-dose children seen in India from the year 1992 up to the year 2016 returned similar results, with the zero-dose categorized children being more likely to fall in the poor category, or to have mothers or caregivers without any formal education, or themselves at risk of stunting or severe stunting, and as well to live in the less developed or poorly serviced and poorly developed states and regions/districts (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).

It has been shown in the Immunization Agenda 2030 plus other related documents and reports like the Gavi strategy for two thousand and twenty one to two thousand and twenty five report (Causey et al., 2021; Nnaji et al., 2021; O'Brien et al., 2021; O'Brien et al., 2022; WHO, 2020a), both have very aggressive and ambitious set targets aimed at reducing the total number of estimated zero-dose children by twenty five percent by the year two thousand and twenty five and fifty percent by the year two thousand and thirty, when you compare to the two thousand and nineteen levels. The focus of the targets within these reports become much more daunting if you consider that for the two years two thousand and twenty and two thousand and twenty-one entailed significant backsliding affecting vaccination coverage that resulted in additional five million children classified as zero-dose children worldwide. These declines were made worse by the COVID-19 related disruptions. These disruptions affected coverage, especially following widespread lockdowns across very many countries, that affected roll out of new vaccines, affected supplementary immunization activities and catch up activities for immunization (Causey et al., 2021; Nnaji et al., 2021; O'Brien et al., 2021; O'Brien et al., 2022; WHO, 2020a). The clearest are measure of these declines have been clear impact shown with rise in number of zero dose children, declining coverage numbers, the rise in the overall numbers of unimmunized or incompletely immunized from nineteen million two hundred thousand children to twenty five million, two hundred thousand children, whereby it is clear that the 95% (and above) that reflects rise in numbers of the under-immunized children in the low-income and the lower-middle-income countries has been as a result of the increase observed in the numbers of zero-dose children (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018; Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021).

The Big Catch Up

It is the annual practice of the WHO and UNICEF during the months of July to release the estimates of the latest National Immunization Coverage also called WUENIC for all the 195 listed member states (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). The estimates that they release are the total culmination of a very comprehensive and detailed collection of the available health data, especially involving the immunisation program staff involved in each country, with the data that is validated against very large-scale surveys and system assessment of vaccine stock-outs or other aspect of health system delivery (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). In 2012, the WUENIC estimates confirmed what has been widely reported that COVID-19 pandemic led to major disruptions in the routine immunisation programs (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). This decline has been very severe, occasioning many losses in immunisation that had never been seen before, hampering eradication efforts for polio, provoking recurrent outbreaks and resurgence of yellow fever and measles, pertussis and diphtheria (Bigouette et al., 2023; Causey et al., 2021; Nnaji et al., 2021; O'Brien et al., 2021; O'Brien et al., 2022; Shet et al., 2022; WHO, 2019b, 2020a, 2022).

A major concern has surrounded the reduction and delays in vaccination targeting cervical cancer using the vaccine against human papillomavirus (WHO, 2020c, 2020f, 2022; Zoumpourlis et al., 2020). This particular vaccine has been performing poorly, even before the pandemic. The biggest fear is that we may end up with higher cases of cervical cancer not prevented as a result, with girls and women mainly from poor and middle to low-income countries being burdened (Cartmell et al., 2019; Lin et al., 2020; Lin et al., 2019; Massey et al., 2021; Nabirye et al., 2020). These declines are made more pronounced by the low levels of screening, with poor surveillance capacity and inadequate funding towards treatment. HPV infection numbers being high and low vaccine uptake worsen an already precarious situation occasioned by high numbers of people living with HIV in these poor countries (Cartmell et al., 2019; Lin et al., 2020; Lin et al., 2019; Massey et al., 2021; Nabirye et al., 2020; WHO, 2022).

The most recent publication by UNICEF and WHO has shown that there has been a major decline in the immunization program ever witnessed in over thirty years of the EPI program. In the period between two thousand and nineteen to two thousand and twenty-one, there was a five percent drop from eighty-six to eighty-one for dose three of DPT vaccine, that is used for measuring vaccine coverage (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). Because of this drop, over twenty-five million children did not complete the recommended three doses of DPT vaccine in the year 2021. Curiously, this figure is two million more children that the children who did not complete in two thousand and twenty, and six million more children in twenty nineteen. Of the twenty-five million children who did not complete immunization schedules in 2022, there was eighteen million who never received the first dose of DPT (called DPT 1), and eight million three hundred thousand of these are from Africa (Anthony et al., 2009; COVID, 2021; Organization, 2020; UNICEF, 2020; WHO, 2019b; WHO, 2016; Wolfson et al., 2008).

The figure of 25 million constitutes 2 million children more than the number of children that missed out on completing the schedule in 2020 and as well comprises more than six million additional children who did not complete in the year 2019 (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). This worrying decline highlights the worrying and growing number of not fully immunized children who are at risk due to the devastating impact of these preventable diseases (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). There have been hypothesis around reasons for the decline, some of which include an increase in the number of the children wo are living in unstable conflict and volatile and fragile areas where access to immunization is usually very challenging; the increase in misinformation and the outcome related to the COVID-19 pandemic including but not limited to service provision challenges and major disruptions in the supply chain, and the diversion of budgeted resources now repurposed to response to pandemic control, and the other measures use din pandemic containment that limited the access to immunization services to the vast majority of at risk comminutes (Anthony et al., 2009; COVID, 2021; Organization, 2020; UNICEF, 2020; WHO, 2019b; WHO, 2016; Wolfson et al., 2008).

The worrying thing about this decline has been the fact that this is the largest drop witnessed in many years, arguably since the inception of the EPI program. While there is indeed the concern that COVID played a big part in getting to this state, it is important to realize that these problems existed before COVID. Indeed 19.2 million children did not complete their immunization in 2019 (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). COVID pandemic made the situation worse. The bigger worry is not the fact that COVID disruptions and lock downs caused delays and declines in immunization numbers, but that we continue to see this decline continuing (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). We need immunization catch-ups for the missing millions or we will inevitably witness more outbreaks, more sick children and greater pressure on already strained health systems." Whereas it is important to increase the number of children starting immunization and thus reduce the Zero dose numbers, there is the greater need to catch up on the numbers of eligible children who already missed vaccines (WHO, 2020c, 2020f; Zoumpourlis et al., 2020).

These are the children targeted in the Big catch up. The Zero dose numbers were largely contributed to by Nigeria, India, Ethiopia, Indonesia and the Philippines who recorded the largest proportions of the 18 million Zero dose numbers (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). Mozambique and Myanmar comprise countries with largest numbers of eligible children that did not receive a single dose of the recommended vaccines between the years two thousand and nineteen to two thousand and twenty-one. The global outlook shows that more than one quarter of roll out of the HPV cervical cancer vaccine was attained in the year twenty nineteen (Cartmell et al., 2019; Lin et al., 2020; Lin et al., 2019; Massey et al., 2021; Nabirye et al., 2020). The unfortunate observation is that worldwide, more than twenty five percent of the HPV vaccine coverage that had been achieved in the year 2019 has now been lost, thus reversing earlier gains and effort that had been invested into the Epi programs. This loss compounds an existing problem, with global coverage for first dose standing at only 15 percent at fifteen years into the program, and thus putting may girls and women at risk of cervical cancer (Cartmell et al., 2019; Lin et al., 2020; Lin et al., 2019; Massey et al., 2021; Nabirye et al., 2020).

Majority of health economists and EPI programs had hoped that the year two thousand and twenty-one would provide opportunity for recovery of most programs from the impact of the COVID pandemic (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). The hope was that the year 2021 would provide opportunity for those who missed vaccines in 2021 catch up. Unfortunately, however, in the year two thousand and twenty-one, the decline continued further, with DPT3 coverage hitting the lowest level seen since the year two thousand and eight. Alongside DPT3 decline, all other basic vaccines have declined, with HPV, PCV and Measles containing vaccines all declining in big ways (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). Confounding this decline is the worrying rising numbers of cases of severe malnutrition in children. These children with weakened and poor nutrition have body systems that cannot mount effective immune responses and them missing vaccines compounds an already precarious situation. These are the children who would most likely die of these vaccine preventable diseases (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).

There was a ray of hope and encouragement to the gloom around COVID-19 pandemic, because a few countries are reported to have held off declines in immunization services (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). A case in point is Uganda, which relatively maintained a high level of immunization coverage and performance of routine immunization programmes, as it rolled out COVID vaccines, whose initial priority was health care workers (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). Another country is Pakistan, which was reported to have returned back to its pre-pandemic immunization and coverage levels, a plus that is attributed to very high commitment level of the government and very significant efforts towards catch-up efforts targeting the immunization program and pandemic enforced gaps. These two countries should be applauded for the great performance (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).

There will need to be great efforts in order to achieve universal immunization attained coverage levels and sustain pandemic and outbreak prevention and enhance preparedness. The ensuing and recurrent outbreaks have resulted from poor or inadequate pandemic preparedness (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). The prevalent and inadequate levels of coverage have been the main drivers of recurrent VPD occurrence especially polio (vaccine derived) and measles in 2021, thus once again highlighting the need for sustained performance of immunization programs (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). The measles containing vaccines were the most affected antigens post pandemic, with dose one of Measles containing vaccines dropping to eighty one percent in two thousand and twenty-one, the lowest level it has been since the year two thousand and eight (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). What this means is that, twenty-four million seven hundred thousand children missed their first measles dose in two thousand and twenty-one, a figure that was five million, three hundred thousand more than the figure in 2019 (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008).

Not only was the first dose missing a concern, but that a further fourteen million seven hundred thousand children went without receiving the second dose of measles containing vaccine (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). The 2019 data also revealed that six million, seven hundred thousand children missed their 3rd dose of the oral polio vaccine, and that three million, five hundred thousand children missed their first HPV vaccine dose, putting many girls at risk of cervical cancer (Cartmell et al., 2019; Lin et al., 2020; Lin et al., 2019; Massey et al., 2021; Nabirye et al., 2020). It is concerning to note that this decline in those two years papers over cracks on a decade of severe stall in progress on immunization uptake, clearly highlighting the important need to plan ahead of and to prepare well for disruptions often occasioned by pandemics and the underlying impact of chronically weak and overwhelmed immunization programs for childhood and adolescent vaccines (WHO, 2020c, 2020f; Zoumpourlis et al., 2020).

The underlying goals of the global Immunization Agenda 2030 (IA2030), that was prepared by the WHO and with UNICEF in conjunction with Gavi and other partners is to ensure they deliver than important strategy covering all countries and incorporating the relevant worldwide partners and stakeholders to ensure they achieve the set goals towards preventing the spread and occurrence of diseases through the use of immunization and the delivery of vaccines to all eligible children in the whole world regardless of age: leaving no one behind (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). In the IA2030, the above partners and stakeholders have called on concerned governments as well as the relevant players and actors to: make sure they intensify the efforts for ensuring catch-up vaccination for all eligible children in order to address or stop the ongoing backsliding and stagnations affecting the routine immunization programs, and to expand the outreach services in the EPI programs thus expanding access of needed vaccines to the underserved areas of the population to reach all the missed children and also implement timely campaigns to help prevent occurrence of outbreaks (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018; Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021).

Additional expectations are for countries to implement and put in place evidence-based, and people-centered and deliberately tailored plans and strategies aimed towards building the trust in the vaccines and the immunization program as a whole, and to counter misinformation thus increasing the uptake of vaccines for the most vulnerable communities (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008); to ensure that the current pandemic preparedness efforts and response plans as well as the global health infrastructure and architecture for strengthening these efforts can be directed to lead towards investment in key primary health care (PHC) centered services, with clear support geared towards strengthening and sustaining all essential immunization service; to ensure there is strong political will/commitment from all national governments and there is increased domestic resource provision/allocation needed to strengthen and to sustain the immunization programs within PHC (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008); to make sure they prioritize health management information systems and strengthen disease surveillance systems towards effective provision of required data and for monitoring that is needed in the programmes in order to have the best impact; and finally to make sure they leverage and that they increase the investment in new research needed to develop and to improve necessary and new and or existing vaccines platforms and immunization services that are necessary to achieve community requirements/needs and therefore give the programs the best chance to deliver on the IA2030 goals (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008).

The commitment embedded within the Immunization Agenda 2030 (IA2030), which all the countries within the membership ratified in the year two thousand and twenty committed towards reducing by fifty percent the world's proportion of zero-dose children and ensuring that no child is left behind (as an indicator of equity). In their plans, GAVI, the UNICEF and WHO together with other partner, selected the year two thousand and twenty-three as the year for intensified effort and action referred to as “The Big Catch-Up” (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008). This calls for identifying and locating all children who missed any vaccination, and included in the twenty-five million two hundred thousand children who did not complete immunisation and providing immunisation for them, and also helping strengthen immunization programs and services to at the very least to pre-pandemic levels, and as well strengthening the current and planned immunization services to be able to achieve IA2030 set targets (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008).

IA2030 calls for target-driven, evidence-informed, and experience-based accountability approach by immunisation programs and partners and EPI programmes and partners for the implementation needed to achieve the tough commitments made by countries on improving immunisation coverage and ensuring equity is made by all the member countries (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). It is for this reason that the Big Catch-Up’ was selected as the theme for this year’s 2023 World Immunization Week. The intention was to emphasize the need for catching-up on high numbers of children that missed on the recommended and routine immunizations and vaccines during the COVID-19 pandemic (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). In addition to the recent WHO and UNICEF publication that showed that worldwide there was a five percent drop in DPT3 coverage between 2019 – 2021 to eighty percent, there was an additional UNICEF report that as well showed that sixty seven million children worldwide did miss out on either all or some of immunization in the routine program between 2019 and 2021 and forty eight million children that did not receive any single dose recommended during that particular time period (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008).

The great decline in the last two years up to a decade shows that there should be greater investment in the area of primary health care (PHC) entailed services, and adequate support offered to strengthen, fasten and sustain all essential scheduled immunization services (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). In the past three years, the resources and the personnel in many countries were diverted, therefore essential needed healthcare services, together with immunization, and efforts for COVID-19 treatment and vaccination tasks are needed (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). The challenge associated with this is the reduction in demand vaccines needed in routine immunization thus heightening the risk for VPDs, especially outbreaks with weaker pandemic preparedness efforts and therefore likelihood of recurrence of diphtheria, yellow fever, measles, and polio (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). There is therefore need for intensified pandemic response efforts with corresponding allocation of resources and energy to support the rapid and deliberate scale-up and the delivery of necessary vaccines, surveillance, cold chain capacity, health worker training and social mobilization. This is the time to strengthen primary health care services and routine immunization as the main integral component of pandemic preparedness (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008).

Without effective planning and preparation, including securing and allocating needed financing, data management and advocacy, the programs will continue to lag behind (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). In the future, programs will continue to eb strained due to shrinking budgets and low numbers and poorly motivated health work force. As we emerge from the COVID-19 pandemic and emergency, the projections paint a worrying picture, with countries having falling budgets with lesser and lesser revenue generated and higher borrowing (Abbas et al., 2020; Adamu et al., 2020; Alsuhaibani & Alaqeel, 2020; Billon-Denis & Tournier, 2020; David et al., 2021; González et al., 2022; Hillis et al., 2021; Hoang et al., 2020). The recent World Bank projections show that up to forty countries (where twenty-nine are in middle- and low-income category) may never even manage to go back to the levels before pandemic even if by the year two thousand and twenty-six (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008). This will affect government planning and domestic budgets and the PHC especially immunization.

It should be recognized that countries will require to find or device ways for protecting allocated finances towards PHC targets, with immunization central to it as a major public health intervention (WHO, 2020c, 2020f; Zoumpourlis et al., 2020). The protection of government finance allocations set aside for immunization and for ensuring that the money is actually spent as planned in an efficient way. A recent primary health financing Global Health Commission by Lancet proposed that policy makers for health can use several categories below of policy tools that can protect resources to support PHC, and especially immunization (Anthony et al., 2009; COVID, 2021; WHO, 2017a, 2020c; Wolfson et al., 2008). The tools entail those related to budget allocation, which include mainly program budgeting, that provides the visibility and the transparency for country immunization support. Secondly, there are tools that relate to the budget implementation that includes how the health services are procured and later paid for (Alkema et al., 2016; Anthony et al., 2009; WHO, 2019b, 2020a, 2020c, 2020f; Wigley et al., 2022; Wolfson et al., 2008). There was a recent trial published in a Nigerian paper that has found that direct facility financing (DFF) and performance-based financing (PBF) are both more effective and efficient than input-based financing when it comes to financing for increased DTP3 coverage. Thirdly, the Service delivery tools or levers would include – the transparency and the clarity needed around vaccines provided, and the service delivery norms, especially the number of the immunization health staff per functional unit population density (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018; Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021).

Another approach is for countries to ensure that they have in place structures and processes for prioritizing the country immunization program in financial planning, investment planning and budget prioritization. Harnessing the National Immunization Strategy (NIS) as a framework may be a good starting point (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018; Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021). This strategy focus should entail evidence-based decision making for new vaccine introductions, for selection of products and for delivery of the same; ensuring that the very top level of government is involved in these allocation decisions thus embedding NIS into the wider sectoral planning/prioritization; and that budgeting process centrally reflects support for NIS and immunization in particular (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018;

Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021). These efforts can be tied to improved efficiency in accountability and austerity in use of available resources to ensure value for money. These efforts may lead to reforms that target efficiency is use of resources, especially in tender award and monitoring, reducing wastage and leakage of funds, addressing corruption related concerns, and ensuring internal auditing, monitoring and evaluation (AbouZahr et al., 2015; Alkema et al., 2016; AlShurman et al., 2021; Bambra et al., 2010; Barker et al., 2015; Bergen et al., 2022; Betsch et al., 2018; Blencowe et al., 2016; Brenzel, 2015; Buja et al., 2021).

Immunization Coverage in Uganda

Uganda, a developing country reported that 64 children in every 1,000 live births die though a GAVI alliance report suggested an improvement to 79 in 2018 with 84% of districts reporting a DPT 3 coverag5e of more than 80%; while 43 out of every 1,000 live births suffer from frequent vaccine-preventable diseases (VPDs) among all Ugandan children under 5 years of age (UBOS, 2016; WHO, 2020c). Uganda is included among 10 countries that contribute 81% of unvaccinated infants in Africa (WHO, 2017a). A recent World Health Organization report showed that, in Uganda, 90 out of 112 districts (or 80% of districts) recorded poor immunization performance (WHO, 2020d). The report further showed that in only 20% of the districts in Uganda, at least 80% of the targeted illegible children had received all the doses of the recommended childhood vaccines (WHO, 2020d).

While the number of under-five deaths in Uganda fell by 6.3% each year over a 10-year period from 167 death6s/1000 live births in 1990 to 90 deaths /1000 live births in 2012 (UBOS, 2016), only 55% of children aged 12-23 months are fully vaccinated and full vaccination coverage is relatively higher in urban areas (61%) than rural areas (50%), as shown in the 2016 report of the Uganda Demographic and Health Survey (UDHS) (UBOS, 2016). The country reported that only 55 percent of children of age between 12 and 23 months completed the recommended vaccination schedule (UBOS, 2016). The fact that only slightly over 50% of children were fully immunized could in part be due to the ignorance of caregivers on vaccines and immunization schedules and dosing protocols. Maternal education contributes to completion of childhood immunization, enhancing demand for vaccines, promoting changes in beliefs, in attitudes, and increasing autonomy and the control over household resources, behavior and traditions that improve healthcare-seeking (WHO, 2020c).

In many parts of rural Uganda, poor road networks negatively affect provision of immunization services, especially during rainy seasons, where both vaccine transport to facilities and movement of caregivers and eligible children to vaccination centres is affected (Malande et al., 2019). An inevitable outcome of the low immunization coverage rates has led to frequent cases of vaccine-preventable diseases, including measles, pneumonia, polio, diarrhea among others (Machingaidze et al., 2013). For example, in March 2019, 26 districts that experience recurrent measles outbreaks were identified by the Uganda Ministry of health (WHO, 2019d). This led to the Uganda Ministry of Health and Uganda Parliament initiating a measles action plan for combating the re-emergence of measles in these districts. Listed among these districts was Wakiso and Hoima.

Recent reports have provided useful insights into additional factors associated with failure to attain full childhood immunization in Uganda (Malande et al., 2019; Masters et al., 2019; Masters et al., 2018). These reports have recommended efforts that enhance caregiver education and gender parity; the need for strengthening of village outreach programmes aimed at the establishment of well stocked village-level clinics with adequate vaccine stocks to overcome regional disparities (Chopra et al., 2020; WHO, 2020c). Additional recommendations focus on need for media outreach among the community, for dissemination of up to date information on vaccination, scheduling and doses of childhood immunization (Masters et al., 2019; WHO, 2020c). Measures that enhance access, improved transport network, provision of maternal support healthcare services during pregnancy, breastfeeding and immunization (Chopra et al., 2020). The caregivers should be educated on immunization cards, their importance and additional useful information contained on the card (Chopra et al., 2020; Masters et al., 2019; WHO, 2020c).

Immunization Coverage Among Children of Hoima and Wasiko Districts of Uganda

While Uganda operates an active National Immunization Program (UNEPI), Hoima (rural) and Wakiso (peri]/urban), have always posted figures of coverage below targets and show frequent outbreaks of VPDs (UBOS, 2016). These two districts continue to report cases of measles, rotavirus diarrhea and pneumococcal disease. These districts also report high numbers of pneumonia in children. Over the last decade, Hoima and Wakiso have not attained a steady recommended DPT3 immunization coverage of more than 90%, with the districts DPT3 and measles vaccination coverage averaging between 70-75% for DPT3 and 65-70 % for (Magambo et al., 2020; UBOS, 2016). In March 2019, these two districts were listed by the Uganda Ministry of health among the 26 districts within Uganda that experience recurrent measles outbreaks (WHO, 2019d).

Hoima is a rural district, with many hard to reach arrears, due to difficult geographical terrain and poor road network (Magambo et al., 2020). Hoima has refugee dominated regions, which are frequently affected with low levels of vaccination, since the refugee population is highly mobile (Magambo et al., 2020; Malande et al., 2019; UBOS, 2016). Drivers of inequalities in the coverage of vaccines across these districts include low level of education on importance of immunization for caregivers, prohibitive cultural or religious beliefs, young age of caregivers, difficult to access health facilities (Magambo et al., 2020; Malande et al., 2019; UBOS, 2016). Wakiso district, being both urban and peri-urban, around Kampala city, has a large informal settlement population, who as well experience high levels of underimmunization and poor vaccine coverage.

Vaccine Hesitancy

Background

In the last century, vaccinations have contributed significantly to reduction in morbidity and mortality especially among children with immunization now considered only second to clean water for interventions of greatest impact towards control of infectious diseases (Chan, 2014; Panatto et al., 2018). Despite these enormous successes, especially in developed countries, there is a growing concern about vaccine safety, which has an effect of undermining progress of vaccination programs (Janusz et al., 2021; Vivier et al., 2000).. These caregivers or persons are therefore considered to be vaccine hesitant (Diekema, 2005; Guess et al., 2020; Jama et al., 2019).

There is a real fear among public health EPI programs that a sustained decline in the uptake of vaccination programs may drop to levels below the "herd immunity" even among well performing programmes thus possibly leading to free circulation of previously controlled pathogens (Ezbakhe & Pérez-Foguet, 2020). The USA recently experienced a return of some vaccine-preventable diseases (VPDs), where compared to the 2001 to 2008 median of 56 (range: 37–140) cases of measles reported to Centers for Disease Control and Prevention annually, this number rose to 9143 cases in California alone in 2010 - the highest it's been in the last 63 years (Durrheim et al., 2019).

In Europe, measles surveillance reported 9579 cases for the 12-month period (April 2013 - March 2014) with 26.5% of these cases recorded in Italy alone, a country that also reported the lowest rate for measles vaccination over the last decade (CDC, 2020; Cochi & Schluter, 2020; Dabbagh et al., 2017). These developments followed decisions made in the 1990s when the National Vaccination Program in Italy introduced a project that gradually abolished compulsory vaccination for the period 1997–2000 (Dabbagh et al., 2017; Diekema, 2005; Hough-Telford et al., 2016; Panatto et al., 2018).

In the years that followed, the following mandatory objectives were implemented: "starting information campaigns about vaccine safety; setting up electronic databases; including vaccine-adverse events; achieving high vaccination rates in the population; promoting education for health practitioners" (O'Leary et al., 2020). Subsequently, the Italian government abandoned the distinction between "mandatory and recommended vaccines" in their EPI (S. Fernández-Basanta et al., 2021; O'Leary et al., 2020).

Elsewhere in Europe, The French government in 1998 suspended all their hepatitis B immunization programs for adolescents "because of a suspected correlation with multiple sclerosis," even though the World Health Organization (WHO) advised otherwise (O'Leary et al., 2020; WHO, 2017a, 2017b). After later finding no evidence to support their decision, the hepatitis B vaccination program was then reinstated but suffered deficiency of support due to widespread and unjustified concerns (Chiesa et al., 2020; Coste et al., 2019; O'Leary et al., 2020).

Due to increasing pressure from anti-vaccine groups and resistance to compulsory vaccinations, an increasing number of countries have therefore removed cumulative penalties and then introduced a conscience clause in the vaccination programmes, thus allowing parents and caregivers the option to refuse or reject immunization for their children and even be able to a certificate of exemption from vaccination (Ashfield & Donelle, 2020; Marshall & O'Leary, 2018; O'Leary et al., 2020). A common message of these anti-vaccine groups is their deliberate promotion of their unfounded concerns that vaccination involves the injection of foreign material into an individual's body, and that this carries a lot of risks.

As global immunization programmes continue to expand, the understanding and addressing of vaccine hesitancy especially for both implementers and communities will be crucial to the successful implementation of EPIs (Giordano et al., 2021; O'Leary et al., 2020; Rucoba, 2019; Zucker et al., 2020). This section reviews the history and drivers of vaccine hesitancy, recent studies on this topic and suggests possible approaches to help reduce hesitancy and strengthen vaccine acceptance.

Historical Context

Way before Edward Jenner started developing a smallpox vaccine in the nineteen seventies, variolation (inoculating an uninfected individual with pus from a person with smallpox) was in use for many years in preventing disease in India, China, Africa, and the Ottoman Empire (Boylston, 2012). Documented reports of Onesimus, an African slave is reported to have taught the Puritan pamphleteer Cotton Mather about variolation in 1706 (Boylston, 2012). The other documented report is of Lady Mary Wortley Montagu that introduced variolation to the United Kingdom after witnessing it in Turkey in 1717.

Mary went on to encouraged the UK government to allow inoculation of children against small pox, a move that fuelled a great debate supporting or opposing the practice. It is reported that "Pro-inoculators tended to write in the cool and factual tones encouraged by the Royal Society, with frequent appeals to reason, the modern progress of science and the courtesy subsisting among gentlemen. Anti-inoculators purposely wrote like demagogues, using heated tones and lurid scare stories to promote paranoia."(Wolfe, 2002) Years later, Edward Jenner's vaccine against smallpox replaced the process of variolation, which though much safer, many people objected vociferously to its use.

There was increasing resistance stemming from the decision by the British government aimed at making smallpox vaccination mandatory for young children, and compelling the population to comply through enacting severe fines that could also accumulate with each refusal. It was shortly after passage of Great Britain's Vaccination Act of 1853, that the Anti-Vaccination League was created, and was followed by another protest movement called the Anti-Compulsory Vaccination League (formed after the age requirements were raised to include children of 14 and below) (Boylston, 2012)

Details from historical accounts document that opponents to smallpox vaccine in the 19th century claimed that the vaccine didn't work; that it would make recipients sick and it contained poisonous chemicals (carbolic acid) and that mandatory vaccinations were a form of medical despotism (Plotkin, 2014). The opponents, instead of providing empirical evidence opted to push alternative medical practices, that included and homeopathy and herbalism, as they distributed their own literature that warned people of the "dangers" of vaccination (Boylston, 2012). Concurrently, during this period, there were anti-vaccination leagues that started operating.

As early as the 1850s, resistance to vaccines was reported from the time some members of public considered smallpox mandates as violations to liberties (Peck et al., 2019; Plotkin, 2014). In the year 1879, the Anti- Vaccination Society of America was established in response to the attempts of the USA to enforce vaccinations for smallpox that followed an epidemic of smallpox (Ahmad et al., 2020). The introduction of vaccines and the roll of the Expanded Program on Immunization in the second part of the 1900s has led to a substantial decrease in occurrence of VPDs, and reduction in resulting mortality and morbidity (Ahmad et al., 2020; Chan, 2014).

In Europe, the movement against vaccines (and subsequent spread to other countries), especially as regards compulsory vaccination started in the 1970s in the United Kingdom (UK), when there were questions on safety of the whole cell pertussis vaccination (Chan, 2014). In the year 1998, Andrew Wakefield made a publication full of errors linking the MMR vaccine and occurrence of autistic spectrum disorder, thus leading to a worldwide crisis of antivaccine crusade, fuelled by increase in the access to and use of the internet (Gostin et al., 2020). Globally, the increasing rates of vaccine-preventable diseases (VPDs) with concurrent lower and lower vaccination rates remains a big concern (Gostin et al., 2020). In the post pandemic period, number of incompletely vaccinated children rose from 19.2

million to 25 million, and 18 million are xero dose cases, in an era where some learning institutions have ongoing exemption from kindergarten school entry vaccine mandates programs (Fernández-Basanta et al., 2021). The USA has recently, due to rising vaccine hesitancy, experienced pertussis and measles outbreaks that were linked directly to rising undervaccination, where children that are unvaccinated children are 8 times or more likely to suffer from pertussis when compared to vaccinated children (D'Errico et al., 2021; Deem et al., 2018).

Defining Vaccine Hesitancy

The WHO defines vaccine hesitancy as "a delay in the acceptance of or the refusal of vaccines by communities despite the availability of vaccination services" (Butler & MacDonald, 2015; Dubé et al., 2018; MacDonald et al., 2020). Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence." The WG identified three key factors that underly or drive vaccine hesitancy, and designated them into 3C's model (MacDonald, 2015) described as: "1. Confidence (where there is no trust in vaccines and in healthcare providers of vaccines); 2. Complacency (where target groups do not perceive the need for vaccination or they do not value vaccination) and 3. Convenience (deals with access to vaccines and access to vaccination services)"(MacDonald, 2015; WHO, 2014) [See figure 4 below] As reported by the SAGE working group, "in the "3 Cs" model, confidence is defined as trust in (i) the effectiveness and safety of vaccines; (ii) the system that delivers them, including the reliability and competence of the health services and health professionals and (iii) the motivations of policy-makers who decide on the needed vaccines."

The SAGE working group reviewed the available to establish if a definition, whether it was negative to use the term 'hesitancy', with 'confidence' the more positive word found. They observed that: "while confidence covers a range of issues such as trust in vaccines including concerns about vaccine safety, and trust in health-care workers delivering the vaccine and in those making the decisions to approval of vaccines for a population, confidence is still narrow in scope covering only one category of factors that affect vaccination acceptance decisions."(MacDonald, 2015) They also noted other terms like 'vaccine acceptance' and 'uptake' but excluded them arguing that those did not capture the concept breadth (where one might indeed accept a vaccine yet delay in accepting the vaccine thus not going by schedule. The working group thus settled for Hesitancy and provided further guidance on the factors entailed in the definition (MacDonald, 2015).

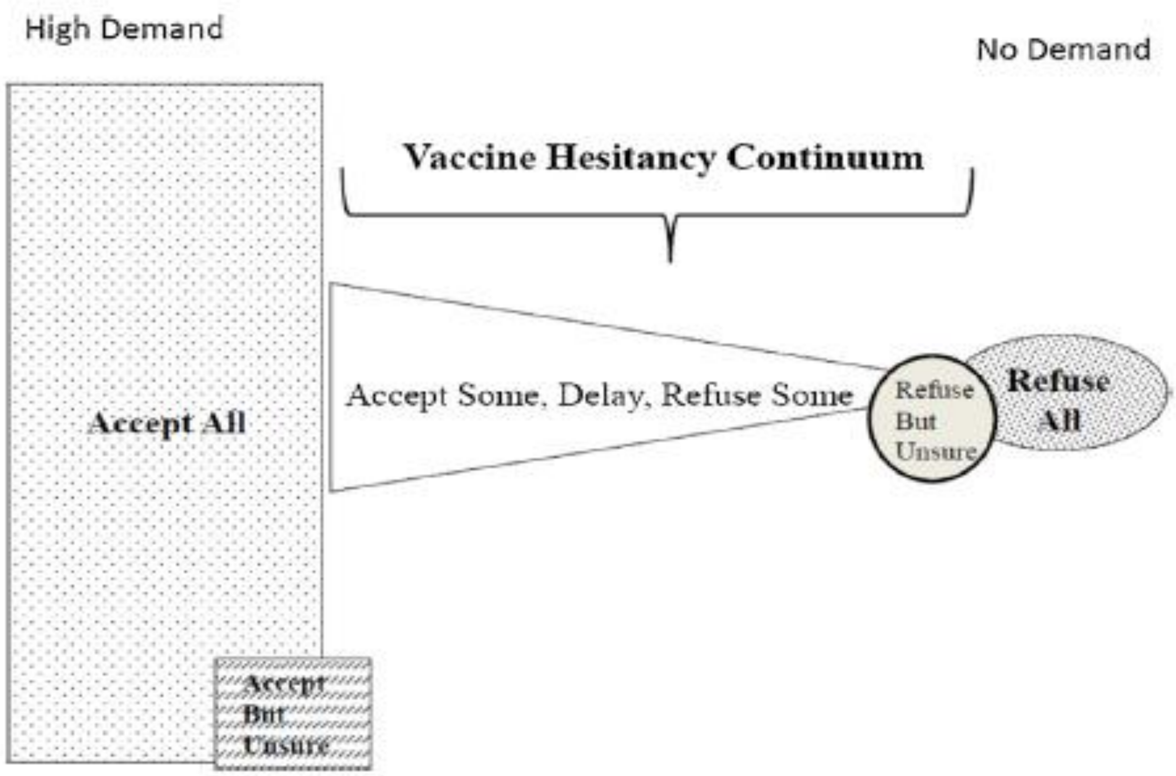

Figure 4: The continuum of vaccine hesitancy (from acceptance to outright refusal) of vaccines Source: (MacDonald, 2015)

Another matter the working group considered was 'the concept of 'vaccine hesitancy' versus 'vaccination hesitancy', where vaccine hesitancy "implies that the core issue is vaccine related" while vaccination hesitancy covers "a much wider range of factors such as immunization time, immunization services, and place where it is done, the recipients fear of injections, the lack of concern about vaccine preventable diseases among others (MacDonald, 2015).

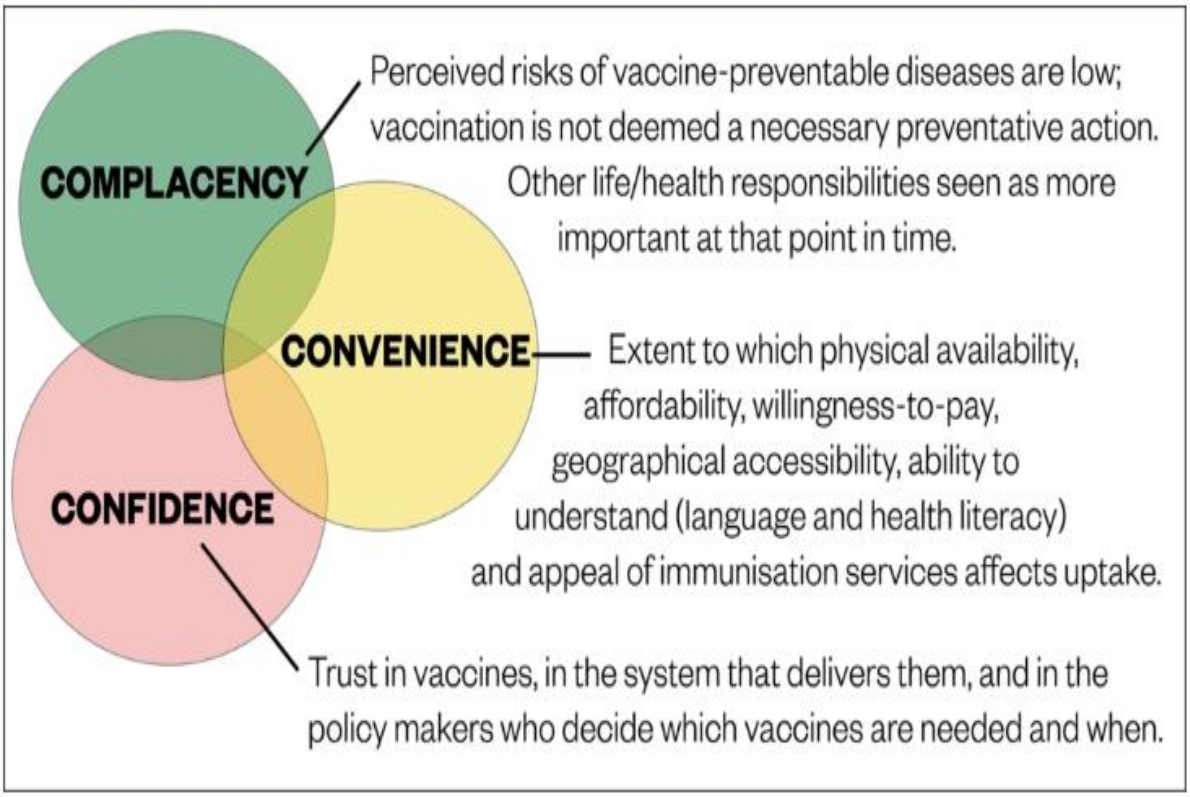

Figure 5: Three Cs" model of vaccine hesitancy
Source: (MacDonald, 2015)

It was observed that some people accept some vaccines and refuse others, and some accept oral vaccines and refuse injectable ones. The variation from vaccine to vaccine shows that considerations are not only individual based, but also vaccine based. Hesitancy therefore is a continuum, either refusing all, or accepting some, or accepting all, thus putting vaccine hesitant individuals in a heterogeneous group lying between these two extremes. This was thus described by the working group as the continuum on which vaccine hesitancy" exists as influenced by various factors (Costantino et al., 2020; Eskola et al., 2015; Schuster et al., 2015). These factors are "vaccine and context specific "and are measured against an expectation of reaching a specific goal, depending on available immunization services (MacDonald, 2015).

There is the concern that Vaccine hesitancy may occur in situations where there is low vaccination uptake due to health system failures, that relate to poor supply of vaccines, stock-outs, poor infrastructure and vaccination centres wars, instability and conflict, and thus hesitancy is not the main explanation for there being unvaccinated or under-vaccinated populations (Goldstein et al., 2015; Larson et al., 2015). This difference therefore needs to be clearly outlined to better define the degree of vaccine hesitancy in the population.

The working group also discussed the relationship between vaccine demand and vaccine hesitancy. Hesitancy has been shown to occur on the continuum between one high demand on one hand and no demand on the other extreme for the available vaccines on offer. The WG noted that an individual or a person or a community may indeed fully accept vaccination as a concept without hesitancy yet they may not demand the vaccination or a particular or specific vaccine. Since hesitancy undermines vaccine demand, if countries are to achieve the vaccine demand goal in the Global Vaccine Action Plan, they need to act to counter vaccine hesitancy. In order to achieve a high individual and high community vaccine demand, the context, community and the vaccine specific strategies that exceed those aimed at addressing vaccine hesitancy should be developed.

As shown in Table 2, there is concern about growing numbers of hesitant individuals with varying degrees of indecision regarding different vaccines and in some cases with vaccines in general (MacDonald & Dubé, 2018; WHO, 2014, 2017a). This leads to vaccine refusal and in some cases active lobbying and recruiting of like-minded individuals who would join their anti-vaccine movement (MacDonald et al., 2018; Wang et al., 2021). With these rising concerns in mind, and resurgence of vaccine preventable diseases like measles and pertussis in the face of rising hesitancy, coupled with the diminishing level of public confidence in immunization that the World Health Organization then listed vaccine hesitancy one of the top ten threats to global health (MacDonald et al., 2018; Sherman et al., 2021).

The WG also came up with a 'Vaccine Hesitancy Determinants Matrix' with these factors grouped into three categories: individual, contextual, and group and vaccine or vaccination-specific influences. This Matrix includes determinants that have been identified from various research studies, from experiences of the WG members in the field, and from discussions with various experts working in this area. This matrix is shown in Table 2 below.

Table 2: Working Group on Vaccine Hesitancy Determinants Matrix

CONTEXTUAL INFLUENCES	
Influences arising due to historic, socio-cultural, environmental, health system/ institutional, economic or political factors	a. Communication and media environment
	b. Influential leaders, immunization programme gatekeepers and anti- or pro-vaccination lobbies
	c. Historical influences
	d. Religion/culture/gender/socio-economic
	e. Politics/policies
	f. Geographic barriers
	g. Perception of the pharmaceutical industry
INDIVIDUAL AND GROUP INFLUENCES	
Influences arising from personal perception of the vaccine or influences of the social/peer environment	a. Personal, family and/or community members' experience with vaccination, including pain
	b. Beliefs, attitudes about health and prevention
	c. Knowledge/awareness
	d. Health system and providers – trust and personal experience
	e. Risk/benefit (perceived, heuristic)
	f. Immunization as a social norm vs. not needed/harmful
VACCINE/ VACCINATION	
specific issues Directly related to vaccine or vaccination	a. Risk/benefit (epidemiological and scientific evidence)
	b. Introduction of a new vaccine or new formulation or a new recommendation for an existing vaccine
	c. Mode of administration

	d. Design of vaccination programme/Mode of delivery (e.g., routine programme or mass vaccination campaign)
	e. Reliability and/or source of supply of vaccine and/or vaccination equipment
	f. Vaccination schedule
	g. Costs
	h. The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals

Source: (MacDonald, 2015)

Building upon expertise from multiple fields, including the behavioral theory, bioethics, social psychology, and behavioral economics, several models (that integrate relevant cultural, social, personal and political factors that impact vaccine decision-making) have now been designed to describe the heterogeneity of the problem of vaccine hesitancy (González-Block et al., 2021; Lane et al., 2018). In the systematic review by Leask et al, a spectrum of parent attitudes on vaccination was identified, and consequently 5 groups were identified including " hesitant parents, late or selective acceptors, unquestioning acceptors, cautious acceptors, and those who refuse all vaccines (Brewer et al., 2017; Lane et al., 2018; Leask et al., 2012).

Though there is a very small number of parents that refuse all vaccines for their children, and also very many caregivers who accept vaccines, there as well many families who fall in between these two extremes and who express some degree of vaccine hesitancy (Jama et al., 2019; Wang et al., 2021; Wong et al., 2020). This group of hesitant caregivers is the focus of recent and current research focusing on coming up with strategies to address and increase vaccine acceptance (Kaufman et al., 2018; Sherman et al., 2021; Wong et al., 2020)

Empirical Studies on The Drivers of Vaccine Hesitancy and Under-Immunization Among Children

Factors contributing to vaccine hesitancy

There are different factors, now clearly linked to vaccine hesitancy. The decisions of parents decisions to vaccinate are influenced various factors, including previous experience with vaccine preventable diseases, previous relationship with the health system, community related factors including social norms; and external factors, like vaccine policy (Dubé et al., 2018) (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018). Vaccine decision-making has to a large extent been influenced by access to vaccine information and misinformation, since not all information that caregivers access is accurate and may contribute to misperceptions that later influence vaccine acceptance (Dubé et al., 2018). There is increasing access to media, and some sources have negative stories on vaccine safety, a factor that may influence caregiver knowledge and attitudes towards immunizations (Dubé et al., 2018; Dudley et al., 2020).

The considerations of caregivers whether to accept vaccines is often based upon their perceived risk of contracting vaccine preventable diseases. There are many   who do not have any experience with vaccine preventable diseases, and this may make them more afraid of the vaccine than the vaccine preventable diseases (Adekeye et al., 2015; Bangura et al., 2020; Bulamu, 2021; CDC, 2011; Chan, 2014; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019). The continued success of vaccines therefore means lesser risk of obtaining a vaccine preventable disease and thus lower motivation of parents to have their children immunized but more parental focus on vaccine safety and concerns about possible short and long-term adverse events following vaccinations (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Dubé et al., 2018; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018).

It has been observed that health workers are essential promoters of vaccine acceptance. While there is information from various sources, caregivers still prefer and respect health workers as sources of guidance and information on vaccines (Deem et al., 2018). It is thus important for health providers to be well informed about vaccines and equipped to communicate with caregivers and patients on specific concerns often raised by a families, especially regarding the immunization schedule, vaccine safety and adverse events, with the aim of encouraging the patients to embrace vaccination (Deem et al., 2018; Dubé et al., 2018).

The public health system as well can affect vaccine acceptance through influencing vaccine policy such as school entry mandates; the development and implementation of immunization recommendations; and the monitoring of vaccine safety (Lane et al., 2018; Machado et al., 2021; Smith, 2010). In the US for example, the Advisory Commission on Immunization Practices (ACIP) develops recommendations on all vaccines, which provide important guidance and reference point for caregivers to cross check any conflicting information and doubts on vaccines (CDC, 2020; Smith, 2010). Additionally, it is the role of the public health system to educate and sensitize the public about current and new vaccines and emergence and re-emergence of vaccine preventable diseases, and to ensure the general public embrace vaccination (Lane et al., 2018; Lee et al., 2020).

Since vaccine safety is a leading concern among caregivers, the establishment of many agencies that monitor and ensure vaccine safety has been a positive move (Dubé et al., 2018; Piché-Renaud et al., 2021). There are additional surveillance initiatives and programs like the Vaccine Injury Compensation Program that provide financial compensation to families and patients who may have experienced vaccine-associated adverse events, a factor that helps build confidence in immunization programs (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018). In the unfortunate event of miscommunication from any of the public health agencies regarding vaccines, this can have the effect of reducing public confidence in vaccines and their safety and in turn increase cases of vaccine hesitancy (Dubé et al., 2018; Smith, 2010).

Another factor that influences parents' motivation to accept vaccines and vaccinate their children is social norms and religious beliefs – these refer to rules that a given group employs to monitor appropriate or inappropriate values, social beliefs, their attitudes and behaviors (Atouf et al., 2021; Bambra et al., 2010). It is for this reason that in most communities, having a child vaccinated is considered a positive parental/caregiver decision and a social responsibility; and likewise, if the community has many caregivers that are hesitant about vaccination, the reverse may be true (Butler & MacDonald, 2015; D'Errico et al., 2021).

In the U.S, 48 of 50 states have religious exemptions accepted from school entry mandates (Lane et al., 2018). There are faith groups that eschew all medical interventions while there are others with specific beliefs that target specific components on some vaccines (Leask et al., 2012). It is often time very difficult to move or change strongly held religious beliefs, even when providers make available information about certain vaccine facts (Lane et al., 2018; Leask et al., 2012).

Another determinant of parental vaccine acceptance is trust in vaccines (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Fernández-Basanta et al., 2021; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018). The emergence of internet, social media, education and rising literacy levels has made access to false and true information easy, such that rapid-fire dissemination of information means that it is very easy for caregivers to hear inconsistent and incorrect messages on vaccines or vaccination, which may have the effect of eroding trust in vaccines, in the providers and even in the entire health system (Bedford et al., 2018; Butler & MacDonald, 2015; Deem et al., 2018; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018). Lack of trust in vaccines thus is a major gap in vaccine-confidence, and is also determined by how trustworthy the source of vaccine information is (D'Errico et al., 2021).

Origins and Emergence of Anti-vaccination Movements

Promotion of myths and fear of vaccines and vaccine opposition dates as far back as early 18th century (Spinney, 2021; Vincent, 2021). There are examples of sermons by Reverend Edmund Massey in England who described vaccination as "diabolical operations" in his 1772 sermon titled: "The Dangerous and Sinful Practice of Inoculation" In this sermon, he described vaccines as "an attempt to oppose God's punishments upon man for his sins." Elsewhere, Reverend John Williams in Massachusetts in his writings cited similar reasons to advance opposition to vaccines, describing them as the devil's work (Spinney, 2021; Vincent, 2021).

Opposition to vaccination manifested outside religious circles following the discovery of smallpox vaccine in the 1800s - with formation of anti-vaccination leagues (Hussain et al., 2018; Vincent, 2021). In the early 1800s, there was widespread opposition to Edward Jenner's cowpox experiments and subsequent discovery of vaccine against small pox (Hussain et al., 2018; Spinney, 2021). This criticism included religious, sanitary, political and scientific objections. For some, the smallpox vaccine itself induced fear and to some protests. Some local clergy insisted that the small pox vaccine was "unchristian" since it came from an animal, while antivaxxers advanced a general distrust in Jenner's ideas and medicine about disease spread (Spinney, 2021; Vincent, 2021).

There were also those who said that the vaccine violated personal liberty, especially following the 1853 Vaccination Act that ordered "mandatory vaccination for infants up to 3 months old", and the 1867 Act that "extended this age requirement to 14 years" (Hussain et al., 2018). The resistance to these laws led to formation of the Anti-Vaccination League and the Anti-Compulsory Vaccination League with subsequent production of many anti-vaccination journals and many antivaccine rallies especially in Leicester city (Spinney, 2021;

Vincent, 2021).

In 1885, there was the most notorious demonstration ever against vaccines in Leicester city, where 80,000-100,000 anti-vaccinators with banners marched with an effigy of Jenner and a child's coffin (Spinney, 2021). These demonstrations and rising opposition to vaccines lead to the formation of commission specifically designed to study vaccination. Subsequently, in 1896, the commission ruled that "vaccination protected against smallpox, but also suggested removing penalties for failure to vaccinate" (Hussain et al., 2018). The Vaccination Act of 1898 subsequently removed all penalties and as well included a "conscientious objector" clause, so that caregivers who did not believe in efficacy or safety of vaccines could obtain a certificate of exemption (Hussain et al., 2018; Spinney, 2021; Vincent, 2021).

Besides the highly publicized false allegations against linking measles vaccine to autism, the refusal by British caregivers to vaccinate their children late 20th century against pertussis following a 1974 report associating 36 neurological adverse reactions to whole-cell pertussis vaccine was equally notable, since it led to significant (81% in 1974 to 31% in 1980) decrease in the uptake of the pertussis vaccine in the United Kingdom (UK) (Hussain et al., 2018). This decline is blamed for the pertussis outbreak that followed in the UK. The publication of the national reassessment of (pertussis) vaccine efficacy helped reaffirmed the vaccine's benefits and raised vaccine uptake levels to normal, with financial incentives implemented for general practitioners who achieved the set target for vaccine coverage.

The Lancet publication by a former 'British doctor and researcher,' Andrew Wakefield had suggested a causal relationship between MMR vaccine and autism (Hussain et al., 2018). Several researchers later published various studies that disproved the existence of any causal association between MMR vaccine and autism (Hussain et al., 2018; MacDonald et al., 2018; MacDonald & Dubé, 2018), with additional revelations of conflict of interest regarding Wakefield's publication following receipt of funding from known litigants against vaccine manufacturers, that he had not disclosed to his co-workers/medical authorities (MacDonald et al., 2018). These discoveries led to Lancet retracting the publication with Lancet editor declaring that the contents were “utterly false” (Hussain et al., 2018). Consequently, Wakefield was struck off the UK Medical Registry, and was barred from practicing medicine in the United Kingdom, due to "abuse of his position of trust" and "bringing the medical profession into disrepute" through the studies that he carried out (Hussain et al., 2018; MacDonald et al., 2018; Marshall & O’Leary, 2018).

In current times, the internet has become an influential medium of informing parents about immunizations. Recent surveys show that about 15% of the people interviewed sourced immunization information from internet and more than half (52%) of users ‘believe almost all or most” information found on health sites to be credible (Hussain et al., 2018; Janusz et al., 2021; Vivier et al., 2000). The same survey found that parents who refuse vaccines most likely found their information from internet, with widespread fears that “vaccines might cause harm or overload the immune system”; or believing that their child was “not at risk for the disease or that the disease was not dangerous”; while others believe that it was “better to develop immunity naturally rather than from vaccines or that the vaccines might not work” (Hussain et al., 2018; Schwarzinger & Luchini, 2021).

The most common arguments concern “the safety of vaccines, the promotion of treatments superior to vaccination (e.g., homeopathy), defense of civil liberties, fear of pharmaceutical and government conspiracies, and morality and religion” (Hussain et al., 2018). A recent analysis of YouTube regarding immunization revealed that 32% of the videos opposed vaccination and that these videos had higher ratings and recorded more views than pro-vaccine videos (Hussain et al., 2018; Spinney, 2021). A separate analysis of MySpace blogs regarding HPV immunization against cervical cancer found that up to 43% of blogs portrayed immunization in negative light and up to 60% searches promoted anti-vaccine sentiments

(Hussain et al., 2018; Spinney, 2021). These findings were similar to those of a study which examined content of the first 100 anti-vaccine sites that were found after searching for "immunization" and "vaccination" on Google which found that 43% of the websites were anti-vaccine (Hussain et al., 2018; Spinney, 2021). These observations point to existence of huge masses of data online against vaccination that is a great risk for the general public leading them to make misinformed decisions regarding vaccination without cogent scientific knowledge (Shen & Dubey, 2019; Spinney, 2021; Williamson & Glaab, 2018).

Repercussions of declining vaccination rates

Antivaccine sentiments have affected immunization and vaccination worldwide. The MMR controversy in the UK led to drop in measles vaccination from 92% in the year 1996 to 84% in the year 2002 (Dabbagh et al., 2017). By 2003, the measles immunization rate had dropped to a low of 61% in some parts UK in London, way below the rate required in order to avoid a measles epidemic (CDC, 2021; Shen & Dubey, 2019). In the UK, in 1998, 56 people suffered measles; and 449 in first 5 months of, and come 2008, measles in the UK was declared endemic for the first time in 14 years (Dabbagh et al., 2017; Quinn & Andrasik, 2021).

The same case was replicated in Ireland where national vaccination coverage levels in 1999-2000 fell below 80% with Northern Dublin reporting 60%. And outbreak occurred in the year 2000 in Ireland with 1,500 cases and three deaths reported. In the USA, MMR uptake dropped by 2% in 1999 and 2000 (CDC, 2021; Quinn & Andrasik, 2021). In 2008 – 2011, France reported more than 22,000 cases of measles, while in the United States, 2014-2015 saw a major outbreak, with reports of as low as 50% MMR vaccination rates among the exposed population in which secondary cases have occurred might be as low as 50% and likely no higher than 86% (CDC, 2021; Schwarzinger & Luchini, 2021; Shen & Dubey, 2019).

Addressing Vaccine Hesitancy

There are several suggestions for addressing the problem of vaccine hesitancy, as shown in Figure 6 below (Dubé et al., 2014; Marti et al., 2017; Singh et al., 2022). One is the use of tailored messaging that are based upon where a caregiver is on the vaccine hesitancy spectrum and use celebrity Immunization Champions that are trustworthy, likeable, and share common goals with the audience (Chou & Budenz, 2020; Frank et al., 2015; Hoffman, 2019). Another method proposed by Shelby and Ernst is use of storytelling as an important method for disseminating messages in a way parents easily relate to and can employ to counter antivaccine sentiments (Cartmell et al., 2019; Massey et al., 2021; Shelby & Ernst, 2013).

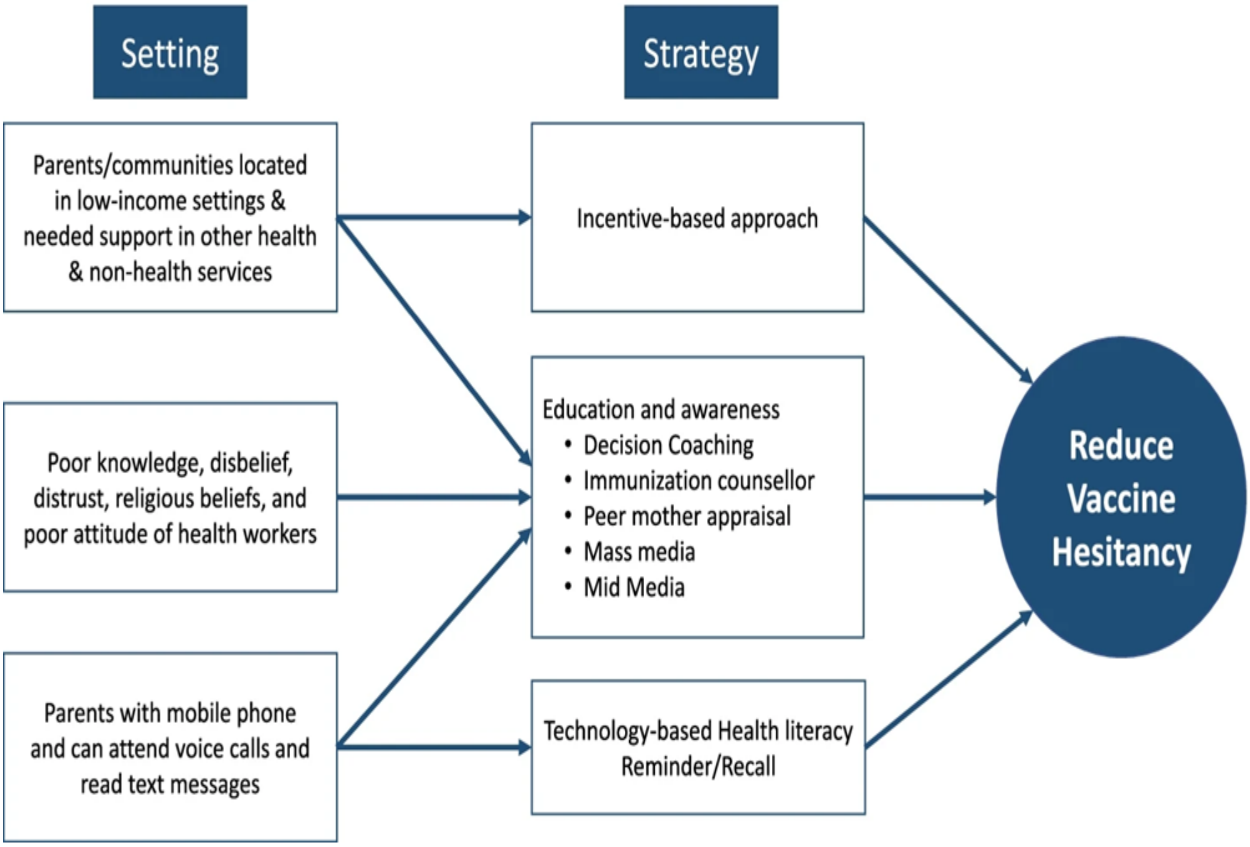

Figure 6: Strategies to address the problem of vaccine hesitancy

Source: (Singh et al., 2022)

It is important that providers show confidence in vaccine efficacy and safety and be able to translate this confidence to caregivers (Bambra et al., 2010; Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018; Massey et al., 2021). The caregivers should ask open ended questions and aim at addressing the questions and worries of caregivers, and communicate the need for vaccination, allay fears regarding vaccine safety and provide comprehensive answers (Shelby & Ernst, 2013). The providers should be equipped with resources that keep them up to date, for this as well helps them have their own questions answered. Information, communication and education (IEC) resources should be made available to parents especially when there is inadequate time for in depth discussions (Cartmell et al., 2019; O'Donnell et al., 2017; Odone et al., 2015; Oduwole et al., 2019; Orenstein et al., 2018; Organization, 2006). Having their own questions answered helps providers to lead by example, and to comply with the immunization recommendations that they promote (Chou & Budenz, 2020; Shelby & Ernst, 2013).

Beyond focusing on provider-patient relationship, additional initiatives should focus on health policy with aim to increase rates of immunization (Shen & Dubey, 2019). A good example is school entry mandates with fewer personal belief/religious exemptions for these mandates (Shelby & Ernst, 2013). Caution however should be exercised, especially since previous experience shows that "tightening exemption policies can make it more difficult for vaccine hesitant parents to delay or refuse vaccination… and future exploration of stricter exemption laws, economic incentives for those who are vaccinated, restrictions on social activities, and stricter mandates may be necessary to protect public safety" (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018; Quinn & Andrasik, 2021).

In addition, vaccination providers should balance a desire to maintain their relationship with caregivers and the desire to provide what is considered as standard of care as they strive to protect other families/caregivers in their practice (Bedford et al., 2018; Butler & MacDonald, 2015; Dubé et al., 2015; Eskola et al., 2015; Goldstein et al., 2015; Kulkarni et al., 2021; Lane et al., 2018; Shen & Dubey, 2019). It is important to develop a clear policy that guides the response of providers in the context of vaccine refusal, including the provision of vaccine education, the signing declination forms dismissal in the event these efforts fail. In the end, implementing a consistent policy would likely send a stronger message to caregivers that vaccination is a key strategy for child survival (Julia C. Haston & Larry K. Pickering, 2020; Rucoba, 2019; Shen & Dubey, 2019).

It is important that ongoing research focuses on development of effective strategies to enhance vaccine acceptance (Hayman, 2019; Hidle et al., 2018; Hilleman, 2000; Hough-Telford et al., 2016). These will need a multi-faceted approach, focusing on “national and regional municipality laws, school level laws and parent-centred education (Wong et al., 2020). The focus should not only be on reducing prevailing knowledge gaps to change behavior, but as well focus on determining how caregivers make decisions regarding immunization; to what extent their attitudes and their beliefs influence their decisions on immunization; and what are their source(s) of information on immunization (O'Donnell et al., 2017; Odone et al., 2015; Oduwole et al., 2019; Orenstein et al., 2018; Organization, 2006; Shen & Dubey, 2019). When developing effective community-based interventions, focusing on a health care visit may help elucidate the most effective communication strategies on presenting information and process of negotiating with hesitant parents, while the focus on communities that are most at-risk for high rates of hesitancy on the other hand can help identify the socio-cultural factors influencing decision-making on vaccines (Hayman, 2019; Hidle et al., 2018; Hilleman, 2000; Hough-Telford et al., 2016; Williamson & Glaab, 2018).

Summary

Vaccine preventable diseases contribute most childhood diseases and deaths in the developing world. That has made immunization to be ranked only second to safe water as an intervention to prevent these diseases, and up to 3 million annual deaths; and a major intervention towards attainment of the UN-SDGs. With most of these deaths occurring in sub Saharan Africa, Uganda needs to put in place measures to address the underlying inadequacies and inequalities affecting immunization uptake. These include language barrier, cultural and communication barriers, poor transport and road network, a highly mobile border/refugee population, a difficult terrain (geographical) affecting vaccine distribution. Other drivers of underimmunization in Uganda including a generally poorly educated population, a significant proportion of which conceive while teenagers leading to early parenthood, and religious groups and cults which affect immunization.

The rising levels of negative vaccine information and sentiments, vaccine refusal, hesitancy and promotion of incorrect information against vaccines are a major concern. Uganda has a 55% national coverage of immunization, with over 26 districts experiencing perennially low immunization coverage and recurrent outbreaks of measles. This problem of vaccine hesitancy and underimmunization with the underlying drivers/promoters in Uganda needs to be studied, especially strategies and initiatives that can be used to solve this problem in Hoima and Wakiso Districts.

CHAPTER 3: RESEARCH METHODS AND DATA COLLECTION

Introduction to the Section

Immunization is regarded as only second to clean water as a public health intervention for prevention of communicable diseases, and is therefore as a result regarded a very cost-effective intervention for prevention of early child deaths (Chopra et al., 2020; De Figueiredo et al., 2020). These interventions involving use of vaccines prevent up to 4 million child deaths annually post-pandemic, with the bigger burden being pneumonia, malaria, diarrheal disease and measles (Chopra et al., 2020; De Figueiredo et al., 2020; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019). The largest majority of these under five deaths in these take place in low income or developing countries.

As earlier observed above, vaccines and immunization help prevent more than four million child deaths annually, with higher survival rates among children who complete their immunization schedules. The COVID pandemic adversely affected immunization, with over 25 million children now not completing their immunization schedules, when compared to 19.2 million before the pandemic. The most affected vaccines are measles containing vaccines, where about 5 million children in 2022 missed a measles containing vaccine. The other vaccines are pneumococcal conjugate vaccines, the cervical cancer vaccines for adolescent girls and DPT (González et al., 2022; Kabagenyi et al., 2022; Ndejjo et al., 2023; Rachlin et al., 2022; Summan et al., 2023). It is this impact of immunization that put it at the Centre of the drive aimed at decreasing childhood mortality under the united nations Millennium Development Goal (MDG) 4 and now the united nations Sustainable Development Goal (SDG) 5(Chopra et al., 2020; De Figueiredo et al., 2020; Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019; WHO, 2017a, 2020c, 2021c).

In sub-Saharan Africa, where Uganda falls, over 170 child deaths in every 1000 live births are reported under the age of five years of age. Majority of these deaths are vaccine preventable, and follow vaccine preventable diseases including malaria, diarrhea, measles, tetanus and pneumonia (Chopra et al., 2020; De Figueiredo et al., 2020; Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019; WHO, 2017a, 2020c, 2021c).

Iniquities and inequalities in the provision of vaccines and in vaccine coverage in the poor communities have been reported as the underlying factors in various studies. Other factors previously described include very low education level of caregivers, a young age of some of the caregivers owing to teenage pregnancies, poor or low social economic status of the caregivers, inadequate male partner or fathers' involvement among others (Chopra et al., 2020; De Figueiredo et al., 2020; Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; Malande et al., 2019; WHO, 2017a, 2020c, 2021c). A deeper and broader understanding of these factors associated with poor vaccination uptake is critical and urgent needed if we are to ensure improvement of vaccination uptake and coverage.

Over the years, there have been many interventions that have included the MDGs, the Abuja declaration on healthcare financing, the Alma Atta declaration of 1978, the SDGs and the child survival action convention for political mobilization to end preventable child deaths that have greatly improved child survival in most countries (Chopra et al., 2020; Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; WHO, 2017a). Despite all these efforts, most countries, including Uganda, have not yet achieved the set targets, failing as well to achieve the MDGs, with the end of 2015 showing that 44 out of 50 developing countries carried only a 20% or less chance of achieving the Millennium Development Goal four. Most of these countries never achieved MDGs at the time they were replaced by the SDGs (Chopra et al., 2020; Dudley et al., 2020; Ezbakhe & Pérez-Foguet, 2020; WHO, 2017a).

The factors underlying the low coverage in Uganda have not been exhaustively studied. Recent reports highlight an inadequate caregiver understanding on vaccines, inadequate awareness of immunization services available, long distances to the immunization service delivery points, poor health seeking behaviour are some of the barriers driving under immunization (Braka et al., 2012; Bulamu, 2021; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002). Additionally, there are communities in Uganda that experience religious beliefs and cultural practices that affect the way they view or whether they take up immunization. There additionally are some parts of the country that are increasingly experiencing negative sentiments against vaccines, rising cases of vaccine refusal, and other factors that promote vaccine hesitancy (Alsuhaibani & Alaqeel, 2020; Chopra et al., 2020; Dudley et al., 2020; Umviligihozo et al., 2020; Wong et al., 2020).

Uganda is a country with a national immunization program in place but rural Hoima district, and Wakiso, a peri-urban/urban District of Uganda, often report poor immunization coverage and recurrent outbreaks of measles, with a low Hoima immunisation coverage of below 73% and measles coverage below 68% (UBOS, 2016). Nationally, only 5.5/10 children between 12-23 are fully immunized, with a 61% urban and 50% average rural immunization coverage respectively (UBOS, 2016). Vaccine hesitancy problem in Uganda has not been adequately studied thus very little data exists. The magnitude of vaccine refusal, and to what extent low confidence in vaccination contributes to this poor performance of immunization services is unknown; and a comprehensive analysis of hesitancy, comparing rural and (peri)urban Uganda has not been explored.

The identification of vaccine hesitancy among ten leading threats to public health put emphasis on need for urgent interventions to address this problem. The factors contributing to vaccine hesitancy vary from one place to another. With low immunization coverage and frequent outbreaks of vaccine preventable diseases in Hoima and Wakiso districts of Uganda, studies to explore the reasons behind this problem are necessary. The problem therefore that this study addresses is that underimmunization and vaccine hesitancy in Uganda have not been adequately studied. There are some barriers to the effective immunization that have been described, including barriers to access of services, language, communication thanks in great part to a poor road network or a difficult geographical terrain (Braka et al., 2012; Bulamu, 2021; Hillis et al., 2021; Igme, 2020; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002; Walker et al., 2013; WHO, 2019c, 2020e, 2020f). This has hindered effective and timely delivery of vaccines, of health staff and cold chain equipment to the vaccinating centres and difficulties in conducting outreach services to communities that are located far from district headquarters.

Additional barriers to provision of immunization services in Uganda and in most poor countries include large populations that have a very low level of education owing to low prevailing literacy levels, adolescent and teenage pregnancies with young mothers who are not well educated and informed on child care and child survival strategies, low health worker knowledge on new and current vaccines, poor father/male partner involvement in the health of the child, poverty and a low socio economic status, negative messaging and anti-vaccine sentiments driving vaccine hesitancy (Braka et al., 2012; Bulamu, 2021; Hillis et al., 2021; Igme, 2020; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002; Walker et al., 2013; WHO, 2019c, 2020e, 2020f).

There are some interventions aimed at increasing availability of immunisation services worldwide which have been partly implemented following the Abuja declaration that focused on allocating resources for healthcare, supported by the resolutions under the child survival action convention for political mobilization (Braka et al., 2012; Bulamu, 2021; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002). To address these gaps in implementation of remedial measures, and in general drivers of vaccine hesitancy and underimmunization, this study chose a mixed method approach, that combined quantitative and qualitative research methods of data collection. Triangulation was therefore achieved at the level of data collection. The goal was to attain as much variation and exhaustive examination of the barriers to immunization.

The methods described in this chapter entailed use of both quantitative and qualitative study designs, comprising focus group discussions (FGDs) for caregivers of the children who are eligible for immunization; face-to-face interviews for the caregivers and the health care workers involved in immunization; and key informant interviews for focal persons, decision makers, leaders and managers of immunization services within the two districts. This was done with the broadest reach to ensure that views from both caregivers, health workers, and community leaders and village health team members are all incorporated in the study. All these are players in the immunization cycle and program, and play a critical role in distribution or consumption of immunization services.

The study also involved the collection of secondary data from health information records at Wakiso and Hoima District offices and records from vaccination centres within the two districts. Additionally, the study as well conducted a systematic review of research articles that have been published on vaccine hesitancy and underimmunization, to build a firm and a deep understanding of the causes, the motivating factors, and the promoters of vaccine hesitancy and underimmunization. The goal was to compare immunization indicators and services in rural Hoima and urban/peri-urban Wakiso Districts and identify barriers to the uptake of services in the districts. These two were chosen in consultation with the ministry of health immunization program, as two large, cosmopolitan districts, with a blend of both rural, urban, peri-urban, migrant, refugee, and border districts that provide the most varied populations with recurrent occurrence of VPDs. The WHO therefore has tasked both developing and developed countries to ensure they aggressively and urgently institute measures necessary to assess and to quantify the magnitude of vaccine hesitancy and underimmunization in their specific contexts, and to design strategies and various measures needed to address this problem. Uganda, like many other nations is included in the region burdened with high child deaths numbers and rising cases of vaccine hesitancy as reported both among the health workers and target communities.

The problem of vaccine hesitancy and underimmunization with the underlying drivers/promoters in Uganda have not been fully studied, with very little data existing on this topic, especially strategies and initiatives that can be used to solve this problem in Hoima and Wakiso Districts. The goal of this study was therefore to find out and establish a clear understanding of vaccine hesitancy and of underimmunization in Wakiso and Hoima districts of Uganda and also explore and examine published reports of drivers of vaccine hesitancy in Sub Saharan Africa. These findings were used to propose areas that require further research, suggest practical interventions and recommendations that can be used to address the problem of vaccine hesitancy and recommend the design of a tool for assessing vaccine hesitancy that can be adopted and implemented within and beyond Uganda especially during national and supplementary immunization activities and vaccination campaigns.

An additional focus area was to identify interventions, strategies and approaches that can help address the problem of vaccine hesitancy and underimmunization in these districts. This section includes details of the methodological approach to the study; the Research Approach and Design, the description and size of study sample, the materials and the instrumentation of research tools, the operational Definition of study variables, the study Procedures and Ethical Assurances and the process of data collection.

Research Approach and Design

Research Approach

The vast majority of diseases and deaths in developing countries follow communicable diseases that are vaccine preventable (Anthony et al., 2009; Størdal & Lie, 2009; WHO, 2017a, 2020c, 2020f, 2021c). It is for this reason that immunisation is considered a key strategy for child survival, that can prevent 2-3 million deaths per year, (Adekeye et al., 2015; WHO, 2019d) especially in poor communities where over 10 million annual deaths occur that affect children under the age five (AbouZahr et al., 2015; Anthony et al., 2009; Blencowe et al., 2016; Szwarcwald et al., 2020; WHO, 2021c).

There are some interventions aimed at increasing availability of immunisation services worldwide which have been incorporated into the Abuja declaration that focused on allocating resources for healthcare and the resolutions under the child survival action convention for political mobilization (Wolfson et al., 2008). These targets are included in the current Sustainable Development Goals (SDGs), with the third goal of the SDGs focusing on the reduction of these deaths of children under-five to < 25 deaths for every 1000 live births by the year 2030, and hopefully lead to saving the deaths of over 3 million children annually (Dicker et al., 2018; Jofiro et al., 2018; Murray et al., 2007; Ntukanyagwe, 2019). A rapidly emerging threat to the success of immunization programs worldwide is vaccine hesitancy, (Butler & MacDonald, 2015), with World Health Organization identifying 3 main factors thought to underly vaccine hesitancy. These factors are included in the 3C's model described as: 1. Confidence (where there is no trust in vaccines and in healthcare providers of vaccines); 2. Complacency (where target groups do not perceive the need for vaccination or they do not value vaccination) and 3. Convenience (deals with access to vaccines and access to vaccination services) (WHO, 2014).

It is with these factors in mind, and the increasing concern about diminishing public confidence in vaccines/vaccination as anti-vaccine movements/groups becomes stronger that hesitancy is a serious threat (Dicker et al., 2018; MacDonald et al., 2018; WHO, 2019c, 2019d). WHO therefore has tasked developing and developed countries to aggressively and urgently pursue measures to assess and quantify the magnitude of vaccine hesitancy in their contexts, and design strategies and measures to address this problem. Uganda is not spared, with hesitancy reported both among health workers and target communities. Urgent interventions are thus required to immediately address this problem.

Vaccine preventable diseases contribute majority of diseases in the developing world (Anthony et al., 2009; Blencowe et al., 2016; Braka et al., 2012; Bulamu, 2021; Igme, 2020; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002; WHO, 2017a). This is the reason why immunization is now ranked only second to safe water as an intervention to prevent these diseases, and up to 3 million annual deaths, more so in sub-Saharan Africa where over 10 million deaths occur among children under five years of age (Brenzel, 2015; CDC, 2011; Roser et al., 2013).The SDG's child survival under the resolutions of this child survival action convention for political mobilization (David et al., 2011; Igme, 2020) puts immunization as a key pillar. Diseases like Polio, measles, pneumonia, tetanus and diarrheal disease feature prominently among these vaccine preventable diseases targeted for control with the hope of preventing up to 3 million annual childhood deaths (Blencowe et al., 2016; Ntukanyagwe, 2019; Roser et al., 2013; WHO, 2021c).

Uganda, like many developing countries is affected by inadequacies and inequalities that affect immunization uptake, including language barrier, cultural and communication barriers, poor transport and road network, a highly mobile border/refugee population, a difficult terrain (geographical) affecting vaccine distribution (Braka et al., 2012; Bulamu, 2021; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Rudan et al., 2008; Tugumisirize et al., 2002). There are other drivers of underimmunization in Uganda including a generally poorly educated population, a significant proportion of which conceive while teenagers leading to early parenthood, and religious groups and cults which affect immunization (Braka et al., 2012; Bulamu, 2021; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002). Recently, Uganda, like many other parts of the world is facing a high rate of negative vaccine information and sentiments, vaccine refusal , hesitancy and promotion of incorrect information against vaccines (Eshetu & Woldesenbet, 2011; van der Maas, 2018).

The problem this study addressed was vaccine hesitancy in Uganda which had not yet been fully studied. Traditionally, some challenges to the provision of immunization have been described, including language and communication barriers, problems with accessing means for transport to immunizing health centres and a poor road network or geographical terrain that hampers the access of communities to health service centres while making it hard for government officials to deliver and to distribute vaccines and immunization consumables to immunization health centres (Adekeye et al., 2015; Dicker et al., 2018; Igme, 2020; Malande et al., 2019; Nations, 2020). Other barriers to accessing immunization services in Uganda include the fact that a significant proportion of Ugandan population have a low level of education, in a population with high rates of teenage pregnancies which result in early parenthood; while some communities are very mobile - especially the refugee within Hoima District (Adekeye et al., 2015; Nations, 2020; Ntukanyagwe, 2019; Wiysonge et al., 2012).

Additionally, there are communities in Uganda that experience religious beliefs and cultural barriers that affect the way they view or take up immunization; and other parts of the country are increasingly experiencing negative sentiments against vaccines, rising cases of vaccine refusal, and other factors that promote vaccine hesitancy (Braka et al., 2012; Bulamu, 2021; Eshetu & Woldesenbet, 2011; Magambo et al., 2020; Malande et al., 2019; Ntukanyagwe, 2019; Phillips et al., 2018; Tugumisirize et al., 2002; van der Maas, 2018). Uganda is a country with a national expanded immunization programme (EPI), but rural Hoima district, and Wakiso, a peri-urban/urban District of Uganda, often report poor immunization coverage and recurrent outbreaks of measles, with a low Hoima immunisation coverage of below 73% and measles coverage below 68% (UBOS, 2016).

Nationally, only 5.5/10 children between 12-23 are fully immunized, with a 61% urban and 50% average rural immunization coverage respectively (Uganda Bureau of Statistics, 2016). Vaccine hesitancy problem in Uganda has not been adequately studied thus very little data exists. The magnitude of vaccine refusal, and to what extent low confidence in vaccination contributes to this poor performance of immunization services is unknown; and a comprehensive analysis of hesitancy, comparing rural and (peri)urban Uganda has not been explored. With a 55% coverage of immunization for Uganda where 61% is in the urban and 50% in rural areas (Bulamu, 2021), with over 26 districts experiencing perennially low immunization coverage and recurrent outbreaks of measles (UBOS, 2016).

Research Design

This was an experimental mixed method study (Bekhet & Zauszniewski, 2012; Carter et al., 2014; Casey & Murphy, 2009; Singh et al., 2022). The experimental arm focused on identifying the barriers to uptake and utilization of immunization services, that involved the conduct of primary research in Hoima and Wakiso districts. The systematic arm reviewed vaccine hesitancy and underimmunization in sSA. The experimental study was a mixed method study, with both quantitative and qualitative arms. The quantitative arm entailed structured interview administered questionnaires through in-depth interviews (IDI) of child caregivers and Key informant interviews (KIIs) who were mainly focal vaccination personnel from Wakiso and Hoima districts. Focus groups and KIIs comprised main sources of qualitative data, while further additional data came from records at district and national offices in the ministry of health. The systematic review of published work on vaccine hesitancy and under-immunization in sub-Saharan Africa (SSA) was aimed at establishing a deep understanding of the problem of vaccine hesitancy and under-immunization in SSA; and assembling a firm and deep understanding of vaccine hesitancy in SSA. This review was important in consolidating the contextual aspects and drivers of vaccine hesitancy in the African context.

Justification of the research design

This study utilised experimental mixed methods design, with a cross-sectional approach. Sampling blended cluster and consecutive sampling methods using a parish as a cluster. The quantitative component included in-depth interviews for caregivers and interviews for key informants. There was also collection of secondary quantitative data from the ministry of health records. The qualitative component entailed focus group discussions (FGDs) with care givers to children coming for immunization services and face to face interviews of both child caregivers and key immunization focal persons from Wakiso and Hoima districts. Purposive sampling ensured variation in focus group sample population. The FGDs were conducted in the local language (or in the language spoken and understood by all participants). The discussions were audio recorded and then later transcribed. Focus group discussion participants were different from those who had participated in the individual caregiver-child interviews. Secondary data included in the study was sourced from the health information records at Wakiso and Hoima Districts and at the ministry of health. This study included a systematic review of already published research work and research articles on vaccine hesitancy and underimmunization.

This review excluded interventional studies, narrative reviews, papers that were not peer reviewed, editorials among others like grey literature. The review only included studies published in English language. The study population/participants were persons living in Africa and are vaccine hesitant, or that had chosen against being vaccinated recommended vaccines; including caregivers, children and other adults/adolescents. The main outcome was vaccine hesitancy determinants, which was the reasons the participants had given for not accepting or allowing their children or themselves to be vaccinated.

Justification of use of triangulation for this mixed methods study

Triangulation refers to a research design which combines the qualitative and quantitative research methods in data collection and analysis (Carter et al., 2014; Heale & Forbes, 2013; Noble & Heale, 2019b). Triangulation or sometimes referred to as “concurrent triangulation" derives its meaning from three recognized concurrent levels for testing in various triangulation research studies, which include quantitative level (this includes interviewing and/or observation), or the qualitative level (this may be a survey and/or a statistical analysis of generated data) and thirdly quantitative analysis which usually involves incorporation of findings from the two other tests (Heale & Forbes, 2013; Johnson et al., 2017).

This study selected triangulation because it is the best suited for mixed method studies. The quantitative component will be especially important in investigating the barriers to vaccination that drive hesitancy and underimmunization while the qualitative component will help to investigate the drivers underlying the barriers to underimmunization and the factors that underlie hesitancy in Wakiso and Hoima districts.

The five justifications for mixed method approach include the validation of results of research from diverse research methods (in this case quantitative and qualitative methods) executed to study a given research problem; the complementarity through which one desires to improve and to clarify his research findings from using the two approaches; and thirdly, the development showing how one’s research findings can help him to build knowledge on results from other methods (Heale & Forbes, 2013; Noble & Heale, 2019b). The last two justifications entail the initiation that discovers any presence of contradictors that sometimes make’s an author to restructure or reframe a given research question and lastly the expansion where a different approach may be used by the researcher in order to grow his research (Carter et al., 2014; Johnson et al., 2017).

This study combined aspects of concurrent triangulation and concurrent nested triangulation approaches. The “Concurrent Triangulation” method is characterized by either two or more research methods that are used to confirm, or to cross-validate, or to corroborate the research findings within a given study, with concurrent data collection (Carter et al., 2014; Noble & Heale, 2019b). It is aimed at using one method to complement and overcome weaknesses of another method. The “Concurrent Nested” method takes a nested approach which prioritizes one method to guide the research project, while the second method is “embedded or is “nested.”

In this approach, the nested study method was used to address a different research question than the main/dominant method or can be used to seek additional information from other levels (Heale & Forbes, 2013; Noble & Heale, 2019b). The systematic review component of this study filled nested component of study design. The advantages of triangulation are that it is the best approach that will provide this study with valid and reliable findings (Heale & Forbes, 2013; Johnson et al., 2017). This is because mixed methodology allows for synthesis of the entire data collection, data analysis, and allows for the incorporation of both qualitative and quantitative data.

Mixed methodology approaches have been associated with generation of answers with greater accuracy, a better testing of the hypothesis and a more comprehensive answer to the research question since the angles at which the research question is approached are varied and different (Johnson et al., 2017). Triangulation is of additional benefit since it increases the confidence in one’s research data due to the different views taken; it creates innovative ways for one to understand a given research concept or occurrence; it allows for unique or unusual revelation of findings; it allows for integration or for one to challenge existing theories; and it provides one with a clearer and deeper understanding of the research problem" (Heale & Forbes, 2013; Noble & Heale, 2019b). The use of (in-depth) interviews together with the use of questionnaires helps to add depth to research results, something that would non-have been possible if one utilized only a single-strategy in the study, a factor that therefore improves the utility and validity of the given research findings.

Another major advantage of triangulation relates to cross validation (Noble & Heale, 2019b), since triangulation designs when used in research studies have the ability to help find agreement and find validation of research results since a wide variety of different research methods are used (Heale & Forbes, 2013). When different research methods utilized arrive at the same conclusions or outcomes, a researcher becomes more confident and assured that the research results are a true reflection or image of the situation being studied or that is taking place and that the findings are not just a reflection of the study method of testing utilized in data collection (Noble & Heale, 2019b).

Triangulation also helps to achieve balance between two different research methods (Noble & Heale, 2019b). Qualitative research methods usually focus on either stories, or on exploration, or on contextualizing, or introspection and also on theory construction (Heale & Forbes, 2013). This methodology utilizes small(er) sample size(s) like in focus group discussions and in-depth study (like in in-depth interviews) or in-depth observation of single occurrences in time. On the other hand, quantitative research methodology focuses on (a) large group(s), or on trends and patterns of occurrence of events (Heale & Forbes, 2013; Johnson et al., 2017).

When one combines these two methods, the researcher is able to establish and identify trends and even inconsistencies in the findings through quantitative research methods, and then use qualitative research methodology to delve deeper into those identified issues, and find out or establish why they occur and also learn the thoughts or motivations behind the individuals involved in the occurrence of these events (Johnson et al., 2017).

In summary, due to employing two or more techniques, triangulation helped this study to collect reliable data which enabled the study to compensate for any research bias (inter-observer bias) and therefore they guard against the different assumptions one researcher would have had that could then influence results of a given study (Noble & Heale, 2019b). Triangulation therefore confirms and validates the quality of research results. Through use of multiple sources and multiple methods, any inadequacies in one research approach or research process can therefore be minimized. Besides, triangulation allows for more insights to be obtained or generated through the use of multiple methodology (Heale & Forbes, 2013; Noble & Heale, 2019b). It also ensures that any inconsistency in the data and findings is recognized and therefore removed. It thus increases and also strengthens the research data credibility and data validity thus leading to strong research design and methodology.

Population and Sample of the Research Study

Uganda is a country that neighbours are Kenya to the East, South Sudan to the North, Democratic Republic of Congo to the west, Rwanda to the south-west and Tanzania to the south (Parliament, 1995). Lake Victoria as well occupies a substantial portion of the southern border. The country lies within the East African Plateau, between 4°N and 2°S and 29° and 35°E longitudes; and averages 1,100 meters (or 3,609 ft) above sea level and covers a total area of 241,038 sq km (land covers 197,100 sq km and water mass is 43,938 sq km) (Parliament, 1995). The country has a population of about 45 million people, with a 183.3 population per km², a male life expectancy of 60.7 years, female life expectancy of 65.2 years, with a 38.1% birth rate, 6.6% death rate, male: female ratio of 49.7%:50.3%; with a median age of 15.8, and a 58.7% of the population being below age 20 years and life expectancy of 62.9 years (WorldData, 2020).

Uganda lies in the Nile basin region, and generally experiences an equatorial climate. A protracted civil war against militants of the Lord's Resistance Army group affecting mainly the Northern Region of the country left many northern districts dilapidated, many people died, others were displaced and most of the basic infrastructure was destroyed. While official languages are English and Kiswahili, Luganda is the central local language, with other regions speaking Runyankole, Acholi, Luo, Lango, Rukiga, Runyoro and Lusoga among others (UBOS, 2016). Uganda has large untapped natural gas and crude oil reserves.

Figure 7: The Map of Uganda showing Districts
(Source: https://images.app.goo.gl/35vGMudtFtkAd5c59)

Agriculture largely accounts for 55 – 60% of the economy, mainly through exports of coffee, maize, fish, tea, cocoa beans, flowers, sugar, tobacco, hides and skins among others (WorldData, 2020). Recently, the service sector has experienced progressive increase in its contribution to the GDP. Recovery has been slow but steady from the days of unrest and civil conflict, through the World Bank in 2012 listed Uganda on the list of Heavily Indebted Poor Nations. Uganda is a poor country, with over 37.8 people living below the poverty line (WHO, 2010). And over 80% of the population living in the poor, remote and rural areas (Healthcare, 2020). These rural populations largely depend on farming (mostly subsistence or peasant farming) as their main source of income (Musoke et al., 2014).

It has been estimated that over 90% of all rural Ugandan women work in the agricultural sector in the rural areas. These rural women are often caregivers for their families, spending an average 9 hours per day on family domestic chores/tasks like fetching water, fetching firewood, preparing clothing and food. The rural women as well engage in small scale activities in entrepreneurship including selling farm produce to generate income. Women on average work 15 hours (range 12 – 18 hours) while men work on average 9 hours (range 8-10 hours) (Musoke et al., 2014).

Due to high levels of poverty, inability of parents to effectively look after and educate their children, most children, especially girls drop out of school and engage in domestic work, child labour or early marriages, increasing the risk of early/teenage pregnancies and sex work, factors that have contributed to the high rates of HIV infections especially in the informal settlements (Abebe et al., 2019). The country has high poverty levels, and a high maternal, under five, infant and neonatal mortality (UBOS, 2016), and is one of the countries that did not attain the UN Millennium Development Goals by 2015 (Jones et al., 2003; Ntukanyagwe, 2019; WHO, 2010).

Various factors contributing to this high mortality include poor socio-economic status, prematurity, complicated deliveries, teenage mothers, illnesses during pregnancy, high rates of home deliveries and new-born illnesses, with only 30% of pregnant mothers starting their antenatal care (ANC) visits on time in first trimester and only 60-70% completing the recommended 4 ANC visits, and more than 40% delivering at home (Eshetu & Woldesenbet, 2011; Mason et al., 2014). Only 50% of these mothers and their new born babies after delivery receive recommended postnatal check-up within the first 2 days after delivery, thus increasing chances of maternal mortality while decreasing likelihood of initiating immunization schedule on time (UBOS, 2016). Some of the barriers that also affect immunization include geographical inaccessibility/difficult terrain, lack of means for transport, low education levels, poor health and social infrastructure, prevalent gender inequalities, cultural beliefs that affect health seeking behaviour, negative religious influence and a large refugee population fleeing the neighbouring countries experiencing conflicts (Eshetu & Woldesenbet, 2011; Healthcare, 2020).

STUDY SETTING

Wakiso District

Wakiso, the fastest growing District in Uganda, is located in Central region, and occupies 736.2 square miles with a population of over two million people of largely urban and peri urban communities (UBOS, 2017). The district has two counties (Kyadondo and Busiro) and a municipality (Entebbe); 15 sub counties, 146 parishes and 704 villages. The inhabitants are mainly of bantu origin (Ankole, Baganda, Banyakitara, Basoga, Gishu, etc) and the Nilotic (the Luo and Acholi subtribes) (WorldData, 2020). The district is divided into 7 health sub-districts (Busiro South, Entebbe, Busiro East, Busiro North, Kyadondo, Kyadondo North, South and Kyadondo East) (Healthcare, 2020).

Wakiso district has 105 Government aided public health facilities - 68 of which are fully Government owned and operated while the remaining 37 facilities are Private Not for Profit (PNFPs) health institutions. Close to 45% of Wakiso district population live within 5km distance from a health facility) (UBOS, 2016). To support community access to care, Wakiso district has about 2,800 Village Health Team (VHT) members that are trained in offering the basic health package (at least 4 VHT members per village) and about 1400 VHT members are trained in integrated community case management (ICCM) for sick children (Vandelaer et al., 2008).

They are involved in health promotion and disease prevention activities that include mosquito net distribution, health education, community mobilization especially on child health days, support for supplementary immunization activities, contact tracing, community fever management, home-based care activities, nutrition, deworming and distribution of treated mosquito nets among others.

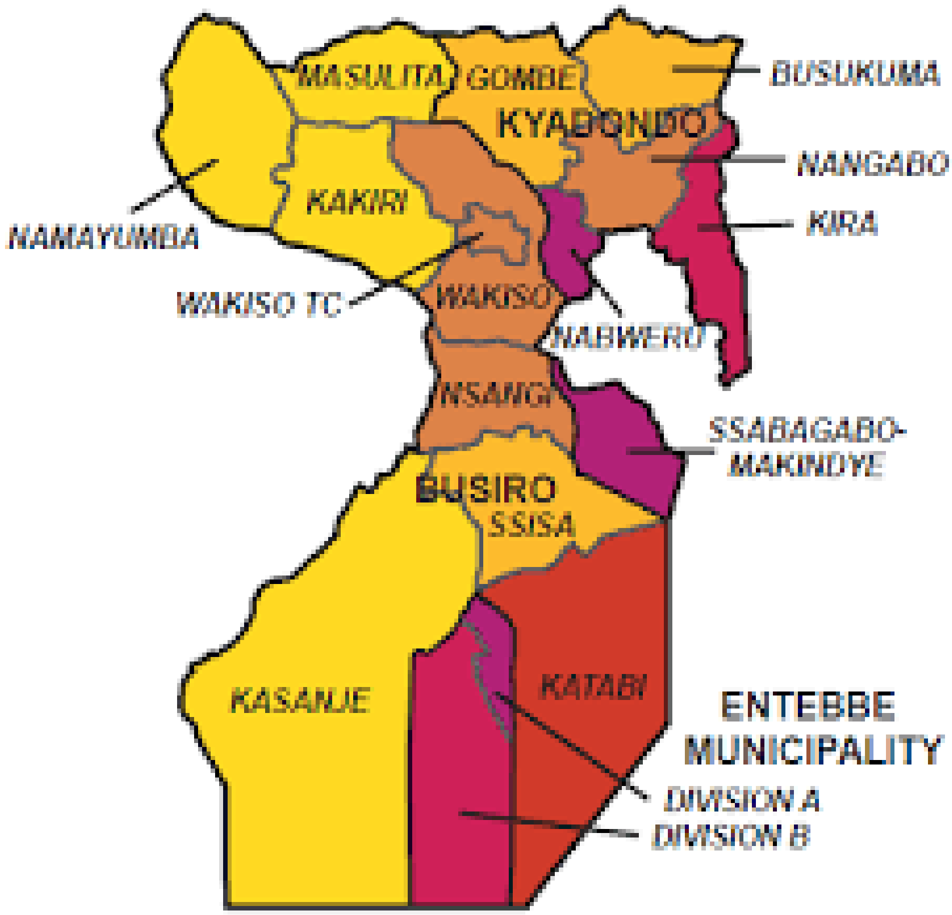

Figure 8: Map of Wakiso District

Source: Google Wakiso District Map https://images.app.goo.gl/c1mgtmJqSZT2bQEJ7

About 40% of Wakiso population are self-employed/skilled laborers in small businesses and around 30 – 40% are unemployed/peasant farmers and fishermen while the other 20-30% hold white collar job in public service. Most residents are either Catholics or protestants while the remaining are of either Muslim or Hindu faith.

Hoima District

Hoima District is located in Western Uganda in the Bunyoro-kitara region. It borders Buliisa to the North, Kibaale district to the South, Ntoroko district to the Southwest, Masindi district to the North East, the Lake Albert to the west and Kyankwanzi district to the Eastern side (Parliament, 1995). The population of Hoima district is estimated at 617,600 people inhabiting 14,144.7 square miles (UBOS, 2017; WorldData, 2020). Hoima district is made of thirteen sub-counties, of fifty-four parishes, which comprise six hundred and forty-three villages. The district is as well divided into 2 HSDs and has fifty four government owned treatment facilities (MOH, 2019).

The predominant tribe in Hoima district is the Banyoro, and comprises over 92 clans. Hoima is a border town, neighboring Congo DRC across the Albert lake, thus has many other communities from Congo who cross in across the lake. Majority of the population are farmers and fishermen (UBOS, 2016). Most of the population are Christians (of Catholic or protestant faith) while the remaining are mainly of Islam faith (Burton et al., 2009).

Figure 9: Map of Hoima District

Source: Google Hoima Map https://www.google.com/search?q=hoima+uganda+map

Study population

The study population consisted of caregiver-child pairs (care giver with a child less than five years of age 9-59 months) from Wakiso and Hoima Districts attending vaccination services in any of the designated study health facilities that offer immunization services. Excluded were caregivers that did not consent or that had not resided within the district for at least 9 months.

Target population

A caregiver and a child aged 9 months to 59 months residing in Wakiso/Hoima district.

Accessible population

All caregiver-infant pairs of children aged 9 – 59 months in Wakiso/Hoima district during the study period.

Eligible Population

Caregiver-infant pairs made of children aged 9- 59 months in Wakiso/Hoima district who have resided in Wakiso/Hoima District for at least 12 months.

Study Unit

A caregiver-infant pair with at least one child aged 9 - 59 months in their home in either Hoima or Wakiso District who fulfill the inclusion criteria.

Sampling (size and technique)

The WHO 30 cluster sampling technique was used to determine sample size . This technique for immunization coverage uses a cluster survey design and assigns the minimum number of target populations that should be sampled and surveyed in order to provide statistically valid data (Bennett et al., 1991; Henderson & Sundaresan, 1982; Hoshaw-Woodard, 2001; Lwanga & Abiprojo, 1987). This Expanded programme on immunization (EPI) Cluster Survey Design recommends the use of 30 clusters taking at least 7 respondents from each cluster giving a total of 210 quantitative samples (Harris & Lemeshow, 1991; Henderson & Sundaresan, 1982).

In this study, to allow for none response, 3 respondents were added per cluster. This gave a total of 300 minimum quantitative sample size per district. Hoima district has 13 sub counties, 54 parishes, and 643 villages, while Wakiso district has 15 sub counties, 146 parishes and 704 villages. Using the sub counties as clusters, six sub counties in Wakiso were considered (three urban, three peri-urban for Wakiso, and all six rural for Hoima) to provide an even distribution of respondents, with 50 minimum caregiver-child pairs from each of the 6 sub-counties.

Study Design and Approach

<table>
<tr><th>No.</th><th>Research Objective</th><th>Design</th><th>Approach</th></tr>
<tr><td>1</td><td>To estimate the level of underimmunization in rural Hoima and urban/peri-urban Wakiso Districts of Uganda</td><td>Quantitative</td><td>Cross sectional study design</td></tr>
<tr><td>2</td><td>To determine the factors associated with underimmunization in in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.</td><td>Quantitative</td><td>Cross sectional study design</td></tr>
<tr><td>3</td><td>To understand the causes and determinants of vaccine hesitancy in Sub Saharan Africa.</td><td colspan="2">Systematic review</td></tr>
<tr><td>4</td><td>To determine and describe the barriers to the uptake and utilization of immunization services in rural Hoima and urban/peri-urban Wakiso Districts of Uganda.</td><td rowspan="2">Mixed methods – quantitative and qualitative</td><td rowspan="2">Cross sectional</td></tr>
<tr><td>5</td><td>To compare and contrast the drivers of vaccine hesitancy and under-immunization in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.</td></tr>
</table>

Materials/Instrumentation of Research Tools

Data Collection Tool

This is an experimental mixed method study with both quantitative and qualitative arms (Carter et al., 2014; Heale & Forbes, 2013; Johnson et al., 2017; Noble & Heale, 2019b). The experimental arm focused on identifying the barriers to uptake and utilization of immunization services, that involved the conduct of primary research in Hoima and Wakiso districts. The quantitative arm entailed structured interview administered questionnaires through in-depth interviews (IDI) of child caregivers and Key informant interviews (KIIs) who included focal vaccination personnel from Wakiso and Hoima districts. Focus group discussions and KIIs made the qualitative data. Additional data was from records at district and at the ministry of health. The systematic review of published work on vaccine hesitancy and under-immunization in sub-Saharan Africa (SSA) was aimed at establishing a deep understanding of the problem of vaccine hesitancy and under-immunization in SSA.

1. Primary objective of the systematic review

To identify, understand and describe the drivers of vaccine hesitancy in Sub Saharan Africa.

2. Study design for the systematic review

The systematic review utilized participants, intervention, comparator, and outcome (PICO) approach to design the study.

3. study participants for the systematic review

The participants comprised persons living in Sub Saharan Africa and opting or not choosing not to get vaccinated with World Health Organization -licensed recommended or scheduled vaccines as at August 2022. These may include parents, patients, caretakers, guardians, children, adolescents and adults. They had to be studies from publications or articles in English language.

4. Study settings for the systematic review

Studies that were conducted in any of the countries in the Sub Saharan African region and published in English.

5. Intervention in the systematic review

There was no specific intervention by the researchers. However, in those studies, the important commonality had to be studies that deal with or report vaccine refusal or vaccine acceptance, or uptake or utilisation of immunization services within SSA.

6. Comparator in the systematic review

The use of comparator was not applicable in this systematic review.

5. Defining the outcome in the systematic review

To define what constitutes an outcome, the study identified variables and factors listed within the WHO's WG on Vaccine Hesitancy to identify the drivers of interest.

6. Inclusion and exclusion criteria for the systematic review

The included studies were quantitative studies (including randomized controlled trials, interrupted time series designs, among others), also included qualitative studies. As for randomized control studies, only those that specifically sought to address vaccine hesitancy and underimmunization or both were included. In the case of interventional studies, for example clinical trials or studies that tested only vaccine effectiveness or vaccine. Additionally, non-peer-reviewed articles or research papers were excluded, same to literature, narrative and systematic reviews. This study excluded interventional studies.

7. Search strategy for the systematic review

The PICO elements were used to build a search strategy. Databases searched included: PubMed, Cochrane Central Register of Controlled Trials (COCHRANE CENTRAL), Scopus, Web of Science, Africa Wide, and CINAHL as shown in table 4.

8. Study selection

Before study selection was done, optimization of the search strategy was undertaken in PubMed database, given that this database is comprehensive and extensive and allows medical subject headings (MeSH) to be searched. The optimization of the Search strategy included the first author applying the search query in order to get the outputs, and then screening the titles and the abstracts to identify ten studies considered relevant. It is out of these studies that the full articles were then read while looking out for key terms which had been omitted from initial search and they were consequently added.

There was further optimization that included evaluating the specificity/sensitivity by systematically adding or systematically omitting synonymous search terms, and then followed by assessment of outputs. After optimization of questions for search, all identified databases were searched and results imported into EndNote citation manager. The Duplicates were then removed. A PRISMA diagram was generated showing flow of the entire process, how studies were selected, which ones were either included or excluded, and what reasons for this. Once this was completed, the proceeds were entered into Microsoft office Excel 2019 for cleaning and further removal of any remaining duplicates.

9. Data extraction and dealing with missing data

A specially designed and customized form was used in extraction of data, after selection of eligible studies. The form utilised had been initially piloted to make it appropriate for extraction of data using a Ms office Excel standardized code-frame. In situations where a selected study was found to be missing data, effort was made to contact the study correspondent author with request for the data. Where this failed, these studies were excluded. The systematic review was structured using the PICO (participants, intervention, comparator, and outcome) format.

SAMPLING TECHNIQUE

This study utilised a comparative and descriptive cluster randomized mixed methods design, that combined both qualitative and quantitative data collection methods (Carter et al., 2014; Heale & Forbes, 2013; Johnson et al., 2017; Noble & Heale, 2019b). Both cluster and consecutive sampling methods were used in which parish was used as a cluster. The qualitative component entailed focus group discussions (FGDs) with care givers to children coming for immunization services and face to face interviews of both child caregivers and key immunization focal persons from Wakiso and Hoima districts. The sampling selection of participants of focus groups was purposive. The FGDs were conducted in the local language (or in the language spoken and understood by all participants). The discussions were audio recorded and then later transcribed. The WHO technique used allows a small number of target populations to be sampled while providing data that is statistically valid, was used.

The Standard EPI Cluster Survey Design recommends use of 30 clusters taking at least 7 respondents from each of the clusters giving a total of 210 quantitative samples. To allow for none response, 3 respondents were added per cluster giving a minimum of 300 participants each for Hoima and Wakiso. Additionally, 10 FGDs and 40 Key informants per District were required. Focus group discussion participants were different from those who had participated in the individual caregiver-child interviews. Secondary data included in the study was sourced from the health information records at Wakiso and Hoima District Head Quarters and immunization centres within Wakiso and Hoima Districts.

Table 3: The outline of data collection methods and tools

STUDY METHOD	DATA COLLECTION TOOLS	DETAILED EXPLANATIONS
Quantitative data collection methods	Structured interview administered questionnaires through in-depth interviews (IDI)	Fixed response questions in interviews of child caregivers from Wakiso and Hoima districts.
	Meta-analysis	A systematic review of published work on vaccine hesitancy and under-immunization in sub-Saharan Africa (SSA) was aimed at establishing a deep understanding of the problem of vaccine hesitancy and under-immunization in SSA.
	Secondary data	From immunization records at Wakiso and Hoima District Head Quarters, the national EPI Health records office, and from vaccination health centres within Wakiso and Hoima Districts.
Qualitative data collection Methods	Focus group discussions (FGDs)	These were discussions with child caregivers from Wakiso and Hoima districts.
	Key informant interviews (KIIs)	These were Key informant interviews (KIIs) involving focal vaccination personnel from Wakiso and Hoima districts.
Systematic Review	This review was structured using the PICO (participants, intervention,	The systematic review considered both quantitative (controlled before-and-after studies, randomized controlled trials, cohort studies,

	comparator, and outcome) format.	interrupted time series designs, cross-sectional studies, or case-control) and qualitative studies. This study systematic review excluded interventional studies (for example clinical trials or vaccine efficacy and vaccine effectiveness studies or studies that were not designed to measure vaccine hesitancy or outcomes that are associated with vaccine hesitancy or underimmunization; systematic or narrative reviews, papers that are not peer reviewed, editorials among others like grey literature. The study population or participants had to be persons living in Sub Saharan Africa and are vaccine hesitant, or persons that have chosen against receiving the World Health Organization recommended vaccines; including children, caregivers, adolescents and adults. The main outcome is vaccine hesitancy and underimmunization drivers. These constitute the reasons the participants have given for not allowing their children to be vaccinated or for not accepting themselves to be vaccinated.

Operational Definition of Variables

Study variables

Independent variables

Predictor variables: age of the caregiver, marital status, religion, level of education, occupation, sex of the caregiver, distance to the health facility and waiting time before receiving immunization services at the facility or outreach site.

Dependent variable: The outcome variable is acceptance of immunization services.

Selection criteria

Inclusion criteria for quantitative study arm

1. A caregiver with at least one child (9 - 59 months); a resident of Hoima/Wakiso district; can give the required information.
2. Caregiver of a child aged 9- 59 months in Wakiso and Hoima districts who have resided in the district for at least 12 months.
3. Caregiver of a child aged 9- 59 months able to give the required information.
4. A caregiver who consents for his/her child to participate in the study.
5. A caregiver who can has a vaccination book record/ vaccination card on the day of interview

Exclusion criteria for quantitative study arm

1. A Caretaker of a child aged 9 - 59 months in their home who does not consent or who is unable to give the required information due to mental/other incapacity.

Study Procedures and Ethical Assurances

Sampling procedure

A blend of multi stage cluster sampling and consecutive sampling method was used in which all the sub-counties per district were the clusters. From each of the randomly selected six clusters, the main public immunizing health facilities were selected, peri-urban and urban facilities for Wakiso, while for Hoima all the six facilities will be considered, based on the standard Uganda demographic economic indicator grading(MOH, 2019). At least two facilities and at most three facilities from each of these clusters were randomly selected.

Where only two or three facilities exist per cluster, then they all were used. In the study, effort was made to ensure uniform distribution of facilities and population distribution economically and based on how busy the immunization is based on secondary data at the District offices. The researcher visited the facilities to familiarize with the staff and work programs a week to two weeks to the commencement of the study. A plan was drawn in consultation with heads of the immunization centers. On the day data collection, every consenting alternate child-caregiver pair was enrolled into the study and taken through the interview administered questionnaire until the required sample for the site is attained. The caregivers for the focus groups were different from those from whom the interviews were conducted.

Study procedure

The principal investigator contacted the District Health Officer Wakiso and Hoima districts and introduced the study to the district focal team members of the DHT and other relevant focal persons and leaders in the district, including the Resident District Commissioner of Wakiso and Hoima districts from whom permission to conduct the study in the districts was sought. The principal investigator also visited the district immunization focal persons, including cold-chain technicians to identify all active immunization centers in the Districts. The PI introduced himself and the purpose of the study and sought informed consent from the facility heads, the health workers in charge of immunization and from caregiver-child pairs to be included in the study. The caregiver's informed consent was acknowledged by either thumb printing or signing an informed consent document. The required information on immunization and vaccination was obtained from caregivers using interviewer administered pre-tested questionnaire, which included collecting relevant data from the immunization card for the eligible child. Vaccination was validated with a vaccination card, and assessed by vaccination card and caregiver history.

A child's immunization status was considered up to date/completed as per the Uganda National Expanded programme on immunization (UNEPI) schedule and or if the child has received: a dose of Bacille Calmette Guerin (BCG), three doses of oral polio (OPV), three doses of diphtheria, pertussis and tetanus (DPT), three doses of hepatitis B (HB), three doses of Pneumococcal conjugate vaccine (PCV), one dose of injectable polio vaccine, and one dose of measles vaccine by the time of data collection, and as fitting to the expected immunization status corresponding to the age of the child.

After identifying eligible caregivers, appointments for focus group discussions at agreed venues were made. The focus group discussions were conducted in the local language (or in the language spoken and understood by all participants) by a moderator and a note taker. The discussions were audio recorded and then later transcribed. Focus group discussion participants were different from those who had participated in the individual caregiver-child interviews, to reduce the risk of bias and allow for variability in respondent views and opinions.

Focus group discussions

Focus group discussion participants were chosen through purposive sampling from caregivers visiting immunization facilities but who did not participate in the in-depth interviews, in order to achieve maximum variation in the sample. The number of focus groups was pre-determined at 6 (one from each cluster), but saturation on most themes must be achieved. Where saturation was not achieved on the occurring themes, further focus group discussions were conducted until the desired saturation is achieved. The focus groups discussions were conducted by the PI with assistance of well- trained research assistants. In each data collection session, there was a moderator and a note-taker. Detailed notes and audio-taping were done by the research team.

The PI and lead research assistants were responsible for moderation by guiding the focus group, using a topic guide to facilitate the interviews. Appropriate translation and back translation procedures were used in developing the guides. The guides were designed a priori, to explore the concept of community perceptions, knowledge, uptake, attitude and practices regarding vaccination. These tools were developed with reference to the existing literature and the researchers' professional experience. Structured demographic profile of participants was taken before each session using a structured questionnaire.

Focus Groups were conducted at community halls or locations away from the immunization center, and each focus group discussion lasted between 60- 80 minutes. Each focus group discussion was conducted in the appropriate language (Lunyoro or Tooro or Luganda or English as appropriate), audio recorded, and the trained note-takers recorded all gestures, expressions, and non-verbal information in their field books. The use of appropriate language facilitated a richer understanding of the terminology and framing that the community uses to describe perceptions, knowledge, uptake, attitude and practices on vaccination.

Systematic Review

This section of the study reviewed studies from sub Saharan Africa. There were quantitative studies, qualitative studies, and topic specific randomized control studies. Those studies were included. The review excluded interventional studies that tested vaccine efficacy or effectiveness alone. Other excluded studies were those that were not peer reviewed. To build a search strategy, the study used PICO. The study searched Scopus, PubMed, Africa Wide, COCHRANE CENTRAL, CINAHL and Web of Science, as shown in table 4 below

Table 4: Systematic Review Search Strategy

DATABASE	SEARCH STRING	RESULTS
PUBMED	(Vaccine hesitancy [Title/Abstract] OR Vaccination Hesitancy [Mesh Terms] OR under immunization [Title/Abstract] OR barriers to immunization [Title/Abstract] OR vaccine delay [Title/Abstract] OR Vaccination Delay [Title/Abstract] OR vaccine delay*[Title/Abstract] OR Vaccination Delay*[Title/Abstract] OR Vaccine Hesitancies [Title/Abstract]) (Children [Title/Abstract] OR child [Title/Abstract] OR child [Mesh Terms] OR patients [Title/Abstract] OR parents [Mesh Terms] OR guardians [Title/Abstract] OR caregivers [Title/Abstract] OR adolescents [Title/Abstract]) Angola[Title/Abstract] OR Benin[Title/Abstract] OR Botswana[Title/Abstract] OR Burkina Faso[Title/Abstract] OR Burundi[Title/Abstract] OR Cabo Verde[Title/Abstract] OR Cameroon[Title/Abstract] OR Central African Republic[Title/Abstract] OR Chad[Title/Abstract] OR Comoros[Title/Abstract] OR Congo[Title/Abstract] OR Democratic Republic of Congo[Title/Abstract] OR Ivory Coast[Title/Abstract] OR Equatorial Guinea[Title/Abstract] OR Eritrea[Title/Abstract] OR Eswatini[Title/Abstract] OR Ethiopia OR Gabon[Title/Abstract] OR Gambia OR Guinea[Title/Abstract] OR Guinea-Bissau[Title/Abstract] OR Kenya[Title/Abstract] OR Lesotho[Title/Abstract] OR Liberia[Title/Abstract] OR Madagascar[Title/Abstract] OR Malawi[Title/Abstract] OR Mali[Title/Abstract] OR	1241

	Mauritania[Title/Abstract] OR Mauritius[Title/Abstract] OR Mozambique[Title/Abstract] OR Namibia[Title/Abstract] OR Niger[Title/Abstract] OR Nigeria[Title/Abstract] OR Rwanda[Title/Abstract] OR Sao Tome[Title/Abstract] AND Principe[Title/Abstract] OR Senegal[Title/Abstract] OR Seychelles[Title/Abstract] OR Sierra Leone[Title/Abstract] OR Somalia[Title/Abstract] OR South Africa[Title/Abstract] OR South Sudan[Title/Abstract] OR Sudan[Title/Abstract] OR Tanzania[Title/Abstract] OR Togo[Title/Abstract] OR Uganda[Title/Abstract] OR Zambia[Title/Abstract] OR Zimbabwe[Title/Abstract] OR sub-Saharan Africa[Title/Abstract] OR Sub Saharan Africa[Title/Abstract] OR Africa, South of the Sahara[Title/Abstract]	
COCHRANE CENTRAL	Vaccine hesitancy OR under immunization OR barriers to immunization OR vaccine delay OR Vaccination Delay OR vaccine delays OR Vaccination Delay OR Vaccine Hesitancy OR Vaccine Hesitancies Children OR child OR patients OR parents OR guardians OR caregivers OR adolescents Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cabo Verde OR Cameroon OR Central African Republic OR Chad OR Comoros OR Congo OR Democratic Republic of Congo OR Cote D'ivoir OR Ivory Coast OR Equatorial Guinea OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR	310

	Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR Sao Tome And Principe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Sudan OR Tanzania OR Togo OR Uganda OR Zambia OR Zimbabwe OR sub-Saharan Africa OR Sub Saharan Africa OR Africa, South of the Sahara	
SCOPUS	TITLE-ABS-KEY (“Vaccine hesitancy” OR “under immunization OR barriers to immunization” OR “vaccine delay” OR “Vaccination Delay” OR “vaccine delays” OR “Vaccination Delay” OR “Vaccine Hesitancies”) ALL (Children OR patients OR parents OR guardians OR caregivers OR adolescents) ALL(Angola OR Benin OR Botswana OR “Burkina Faso” OR Burundi OR Cabo Verde OR Cameroon OR “Central African Republic” OR Chad OR Comoros OR Congo OR “Democratic Republic of Congo” OR Cote D’ivoir OR “Equatorial Guinea” OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia 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 Senegal OR Seychelles OR “Sierra Leone” OR Somalia OR South Africa OR “South Sudan” OR Sudan OR Tanzania OR Togo OR Uganda OR Zambia OR Zimbabwe OR “sub-Saharan Africa” OR “Sub Saharan Africa” OR “Africa South of the Sahara”)	111

GOOGLE SCHOLAR	(“Vaccine hesitancy” OR under-immunization OR “barriers to immunization” OR “vaccine delay” OR “Vaccination Delay” OR “Vaccine Hesitanc*”) AND (Children OR patients OR parents OR guardians OR caregivers OR adolescents) AND “sub-Saharan Africa” OR “Sub Saharan Africa”)	50 (1st 5 pages)
WEB OF SCIENCE	Vaccine hesitancy OR under immunization OR barriers to immunization OR vaccine delay OR Vaccination Delay OR vaccine delays OR Vaccination Delay OR Vaccine Hesitancy OR Vaccine Hesitancies Children OR patients OR parents OR guardians OR caregivers OR adolescents Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cabo Verde OR Cameroon OR Central African Republic OR Chad OR Comoros OR Congo OR Democratic Republic of Congo OR Ivory Coast OR Equatorial Guinea OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia 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 Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Sudan OR Tanzania OR Togo OR Uganda OR Zambia OR Zimbabwe OR sub-Saharan Africa OR Sub Saharan Africa	86
CINAHL	AB (Vaccine hesitancy OR under immunization OR barriers to immunization OR vaccine delay OR Vaccination Delay OR vaccine	31

delays OR Vaccination Delay OR Vaccine Hesitancy OR Vaccine Hesitancies)	
AB (Children OR patients OR parents OR guardians OR caregivers OR adolescents)	
AB(Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cabo Verde OR Cameroon OR Central African Republic OR Chad OR Comoros OR Congo OR Democratic Republic of Congo OR Cote D'ivoir OR Equatorial Guinea OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia, Theghana 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 Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR South Sudan OR Sudan OR Tanzania OR Togo OR Uganda OR Zambia OR Zimbabwe OR sub-Saharan Africa OR Sub Saharan Africa OR Africa, South of the Sahara)	
TOTAL SEARCHES	**1829**
DUPLICATES REMOVED	**195**
TOTAL SCREENED	**1634**

Assessment of the risk of bias

This study used the "Critical appraisal skills program qualitative checklist" in order to appraise qualitative studies. The mentioned Critical Appraisal Skills Program (CASP) tool has been designed to be used to organize the approach necessary for reviewing the merits of an article based on a yes response, a no response or can't tell for each question posed. In the score, each “yes” response merits to be awarded a score of one. For the cross-sectional, longitudinal cohort, and case-control studies risk of bias was assessed in this study using appropriate UNHLBI checklists for cross-sectional, observational cohort and case-control respectively. These assessment tools offer the possibility to the researcher to appraise the methodological quality of the articles, based on given specific criteria. The tools contain a list of the items and allows one to record ‘yes,’ or ‘no,’ or ‘don’t know’ for each of the criterion as well as to add some short comments.

Ethical Assurances

Ethical Principles in this study

The Belmont, USA Report released in 1978 on “ethical principles and guidelines” regarding human subject’s protection helped define ethics in research and followed public uproar and public concern due to Tuskegee study of 1932- 1972, involving more than 400 study subjects (NCPHS, 1978). The study subjects comprised mainly men of poor African-American descent who were denied medical treatment given that the study intended to “monitor the natural history or course of a given disease” (Barrow et al., 2021; Beauchamp & Childress, 1994; Bedford et al., 2018; Bekhet & Zauszniewski, 2012; Carter et al., 2014; Casey & Murphy, 2009; Singh et al., 2022). It was a product of the Belmont Report, that three principals emerged: the respect for persons (ie autonomy), justice and beneficence (Marshall & O’Leary, 2018; Muhindo et al., 2016; Plotkin, 2014; Wolfe, 2002). In 1983, principles of biomedical ethics book by Beauchamp and Childress adopted these three ethics principles and added a 4th principle called non-maleficence (Beauchamp & Childress, 1994). The four principles are explained below:

Beneficence.

Beneficence has been applied in this study through showing “compassion and showing kindness” with the main aim of benefitting others. (David B. and Resnik, J.D, 2019). In this study, beneficence was shown in both the patient and patient's family's view. This was especially applied where the researcher and interviewer disagreed or did not support the respondent's responses, yet these responses are accepted and incorporated (Marshall & O'Leary, 2018; Muhindo et al., 2016; Plotkin, 2014; Wolfe, 2002). The study team were therefore guided by the view that the respondent's views are important, supreme and must be respected, especially in situations where one is dealing with hesitancy and vaccine refusal or uptake that may affect vaccine promoter or provider (Purdy & Wadhwani, 2006). The beneficent approach of this study was to explore further the reasons why the respondent made the choice they did regarding the vaccine preference, and educate and provide more information to them with a view to equip them with correct information to better guide their choices (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018).

The principle of Nonmaleficence means that one should not do harm to the study subjects (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). Where as in this study we ensured beneficence as involving the action the respondents take, this study ensured nonmaleficence is observed by avoiding performing any actions that may cause harm or its effects thereof to them (Barrow et al., 2021). One of the goals of this study is to promote vaccines, some which may be new modalities of care for which respondents may have concerns of possible long-term medical side effects (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). The study went to exhaustive length to reassure the students about the current recognized safety of the vaccines and any prevailing concerns. The researcher weighed the balance of the considerations of choosing some vaccines against the fears and concerns of the respondents and available evidence of research in order to better guide the respondents. This was considered important because not only does nonmaleficence in conduct of research come into play when benefit is considered, but as well when recommend vaccine or approach or decision may be viewed as futile (Barrow et al., 2021).

The presence of an oversight ethics committee that approved and guided the tools for the conduct of this study was important to ensure that the principle of nonmaleficence is observed, especially the growing leaning towards need for respecting patients or respondents autonomy and that the respondents play a more (or even broader) active role in the final decision making regarding their uptake of the vaccines and when this needs to be done (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). In this study, beneficence involved striking a balance between the value and the benefit of the programs and vaccines being recommended to respondents against costs and associated risks where as non-maleficence focused on researcher making sure to avoid anything or any action that could cause harm (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018).

One thing the study took cognisance of is that all medical modalities, vaccines and new inventions all involve some degree (even if minimal) of possible harm, and so the researcher had to have this in mind as we engaged the respondents in the face to face interviews and focus group discussions (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). This means that in routine care, and recommendation of new vaccines and approaches, while health workers try to respect the choices of patients or caregivers, there will arise situations where health workers may have to give a medication or a treatment modality that is not easily chosen by the respondent in order to prevent a more adverse future complication or outcome. Risk stratification is therefore very much an important segment in application of the nonmaleficence principle (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). The most important step is to exhaustively discuss all and any likely form of harm that may occur, whether in the immediate or long-term use of any vaccine, provided that medical errors are avoided and kept to the minimum as far as is humanly possible, and health workers must commit to reducing and limiting harm when serving their patients.

This study paid a keen attention to the application of an ethical research principle of autonomy. This principle is based on the concept that each person involved in the research has the right for dignity and the need to be respected (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). This study ensured that all participants were respected and all study subjects' right to self-determination was honoured, including veracity, the correct disclosure of information with informed consent, ensure and observe confidentiality, and that promises made are kept. This principle had its challenges in application especially bearing in mind that vaccines involve infants and new-born babies as subjects, and consent of caregivers were required (Barrow et al., 2021). This is because very young subjects cannot make autonomous decisions; and the ethics committee provided for the caregivers to provide consent (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). One way in which this was mitigated and any disagreements was to make sure as much information as possible was provided to the caregivers, to bring them on board and to empower them to make as well-informed decisions as possible.

The fourth principle this study took into attention is justice in research; a principle that emphasizes that the researcher must reflect fairness in all the aspects of the research being conducted (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011). In this study, every aspect was as much as possible conducted with compassion and fair understanding and allocation of any risks, all resources and benefits to all the subjects. No subject was denied vaccination for opting out of the study. All participants were offered equal amount of transport refund, all got refreshments of equal cost, e also refers to fair allocation of services and resources.

The study recognized that there may be situations where scarcity or limits on the available resources can create some ethical conflicts around the topic of justice in research (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018). Justice principle required that the moral obligation of this study was to act and to offer fair adjudication for all participants. This study observed fairness, observed entitlement and observed equality for all the subjects in fairness. The elements included "fair distribution of scarce resources especially transport refund (distributive justice), the respect for the participants rights (rights-based justice) and the respect for all morally acceptable laws in research (legal justice)" (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011).

One issue that this study observed was that there are two elements to the justice principle: equality and equity (Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011).This study ensured that all subjects were accorded the right to equal treatment, same vaccines, from same source, and for the same indication; and ensured equal access to any benefits and any risks from the study. It is noteworthy that different factors affect access to immunization services, including the place of residence, the social status, the age of child, the culture, the sexual preferences, the ethnic background, any disability, legal capacity, among others (Barrow et al., 2021; David & Resnik, 2011). The study ensured that none of the subjects, as much as possible, did not feel that they have in any way not been treated with equal or same degree of respect as the rest of the participants (Amarasinghe et al., 2013; Atouf et al., 2021; Barrow et al., 2021; Beauchamp & Childress, 1994; David & Resnik, 2011; Purdy & Wadhwani, 2006; Williamson & Glaab, 2018).

Study Approval

The study was approved by UNICAF University Research Ethics Committee (UREC – Ref: REAF_DSPA - VERSION 1.0)) and Makerere University medical school REC (REC REF 2017-077), UNCST (SS4245).

Informed Consent for the study

Informed consent was sought and obtained before every focus group discussion, key informant interview and individual caregiver face-face interviews and/or interview recording. Additionally, institutional and facility approval from the head of health facility or unit or immunization Centre was obtained before the conduct of the study. Study participants were free and informed that they could leave the study at any point in time during the study and that any withdrawal does not affect their inherent rights to be served or attended to in their workplaces or communities.

Risks to the participants

There were no direct risks to the participants in this study, and there were no invasive medical procedures on study participants, or any direct harm to infants in the study, or to pregnant mothers or to any live subjects in the study. The Declaration of Helsinki was adhered to during the study.

Confidentiality

The questionnaire responses were transferred into data sheets that will are password protected during and after analysis. The hard copies of the questionnaires along with the informed consent forms are stored in lockable cupboards at the ECAVI offices in Kampala. For the focus group discussion, the recordings will be destroyed once the discussion has been transformed into the data sheets or entered into the data capture tool and the data will be analyzed and password protected. The information collected from the research will be kept anonymous and only the research team has access.

Participants of focus group discussion were asked to keep confidentiality about the content in the group discussions from outsiders. Participants of interviews were asked not to talk to people outside the group about what was said inside the group. However, the findings will anonymously be used in scientific publications and to provide recommendations to the concerned district and national health authorities in Uganda. At all steps, the identity of the participants will not be disclosed in the published research articles as well as when providing recommendations.

Conflict of Interest

There was no conflict of interest.

Benefits to participants

There was a transport refund and refreshments provided to participants based on the prevailing recommended World Health Organization Uganda rates an equivalent of UGX 10,000/= per participant. The findings of this study will be used to improve provision of immunization services and combat the problem of hesitancy to vaccines and underimmunization, thus benefiting the participants and other residents of Hoima and Wakiso districts and Uganda in general.

Dissemination of study findings

Findings from this study will be disseminated to Wakiso & Hoima districts as applicable, Ministry of Health Uganda, Uganda National Expanded Program on Immunization, World Health Organization (WHO), UNICAF University and Makerere University. The investigators undertake to publish the findings in peer reviewed scientific journals and presented in scientific conferences.

Data Collection and Analysis

Data collection tools

Quantitative data was collected using a pre-tested self-developed tool based on the WHO SAGE template. This tool was piloted through a test-retest approach on two segments of 5 and 6 in Hoima and 8 each in per-urban and 8 each in urban Wakiso each at different times and it returned satisfactory desired results. It is these total 11 for Hoima and 32 for Wakiso that produced the additional sample added to the target sample of 300 for each district giving a final sample of 311 for Hoima and 332 for Hoima District. These additional sample results were added to the results and analyzed. The data collection tool was a researcher administered questionnaire comprising of four sections to capture socio-demographic information, information about the child, vaccine compliance and the child vaccination history. Qualitative data was collected through focus group discussions using preset interview guides for caregivers.

Data Management for Qualitative Component of the study

The focus group discussion recordings were translated into English and transcribed and saved into Microsoft Word version 2016. These were then entered into NVIVO 12 to identify and align the themes utilizing standard thematic analysis techniques. Th research team, comprising investigator and assistants jointly reviewed the transcripts and identified coding frame. After these, they performed transition from open codes to themes; and the definitions and relationships between the latter.

Data Management for Quantitative Component of the study

Data from the pre-coded case report forms were entered into the computer using Excel 2019. Data were subsequently transferred into STATA version 14 for analysis where bivariate analysis and multivariate logistic regression was done. Descriptive analysis of the data is expressed as means ± standard deviation, percentages and frequencies, with associations between variables being analyzed using chi-square test - differences between means was assessed using the Student's t-test. Respondents' responses on different variables, especially on vaccine confidence, trust, safety, effectives and misgivings were described as proportions. P values of below 0.05 were considered significant and confidence intervals of 95% were used.

All factors with a P-value less than 0.2 at bivariate analysis were entered into a model designed for logistic regression. This was aimed at determining independent or multivariable association with coverage, defined by those who received DPT 3 vaccine dose. These findings were further refined through Poisson analysis to determine health system factors independently associated with completion of immunization schedules. Data was summarized in tables. The data sheets used were assigned identifiers and unique study numbers that enabled the researchers to check any information from the different research data collectors and study centers. The unique study numbers (and NOT names of the individual study respondents) were entered into an electronic database for further anonymous analysis. At all times, deliberate efforts were put in place to make sure no unauthorized person accessed the data. The study filled data tools were kept safe lockable containers and soft copies protected by passwords in data storage devices. All study quantitative data (including secondary data from the ministry of health at national and district levels) was entered anonymously in a customized Excel spreadsheet and then exported to Stata version 14 for further analysis.

Table 5: Data Collection Summary/ Details

Type of Survey (i.e. Questionnaire or Interview OR Both)	Both Questionnaire, interviews and systematic review
Distribution Method (i.e. Hand Administered/ online, face to face etc)	Quantitative (self-administered questionnaires) and Qualitative (Face to Face [key informant] Interviews & Focus Group discussions)
Date survey was issued/ commences	October 2021 to April 2022 – Dates for the entire process of finalizing data collection tools, seeking approvals, collecting data
Number of respondents participated	311 Hoima and 332 Wakiso district caregiver questioners, additionally 10 FGDs and 40 Key informants per District were conducted.
Type of respondents (i.e. Students of secondary education, accountants etc)	Respondents in the questionnaires and focus groups included 18-65-year-old caregiver with at least one child (9 - 59 months); a resident of Hoima/Wakiso district; who can give the required information; provides informed consent & who has carried the child's vaccination book record/vaccination card.
Location of respondents	Wakiso and Hoima districts of Uganda
Date survey was completed/ ended	31st April 2022

Summary

The identification of vaccine hesitancy as a threat to global health emphasized the need for urgent interventions to address this problem. With low immunization coverage and frequent outbreaks of vaccine preventable diseases in Hoima and Wakiso districts of Uganda, studies to explore the reasons behind this problem are necessary. The purpose of study was to determine the barriers to the uptake and utilization of immunization services in (rural) Hoima and (peri-urban) Wakiso Districts of Uganda; to compare the drivers of vaccine hesitancy and underimmunization in these districts and to identify interventions, strategies and approaches that can help address the problem of vaccine hesitancy and underimmunization in these districts.

This was a mixed methods study that combined quantitative and qualitative methods of data collection. These methods entailed 10 focus group discussions (FGDs) per district, for caregivers of children who are eligible for immunization; over 300 face-to-face interviews for caregivers per district, and 40 key informant interviews for focal persons, decision makers and managers of immunization services in each of the two districts. The study involved collection of secondary data from health information records at Wakiso and Hoima District offices, record offices and vaccination centres within the two districts.

Additionally, the study includes conduct of a systematic review of research articles published on vaccine hesitancy and underimmunization in sub-Saharan Africa. This study sought to establish a firm and deep understanding of vaccine hesitancy and underimmunization in Uganda and the reasons for recurrent outbreaks of vaccine preventable diseases.

CHAPTER 4: FINDINGS

Introduction

The results presented here arise from this mixed method study (Carter et al., 2014) that combined both qualitative and quantitative data collection methods (Carter et al., 2014; Heale & Forbes, 2013; Johnson et al., 2017; Noble & Heale, 2019b). Both cluster, purposive and consecutive sampling methods were used, with the parish being a cluster. Secondary data to be included in the study was sourced from the health information records at Wakiso and Hoima District Head Quarters, and from the immunization centres within Wakiso and Hoima Districts (MOH, 2022). These findings as well include a systematic review of published research work and research articles on vaccine hesitancy and underimmunization. When parents opt not to vaccinate themselves or their children, various factors may be at play. These include their previous interaction with the health system, their previous experience with Vaccine Preventable Diseases, various community practices and factors like social norms; and other factors that are more external for example availability of vaccines, vaccine policy among others (Dubé et al., 2018). Decision-making regarding vaccines, has largely been influenced by concerns around access to vaccine information and to misinformation, since caregivers access information that is inaccurate and that may contribute to misconceptions and misperceptions which later influence their vaccine acceptance (Dubé et al., 2018). The increasing access to media networks and information, some of which is negative and deliberately against vaccine safety, these factors do influence the knowledge and the attitudes of caregivers towards vaccines and immunizations (Dudley et al., 2020).

The systematic review explores the prevailing thinking that parent's perception on the use and uptake of vaccines is premised on their fear and perceived risk of suffering from Vaccine Preventable Diseases (Dudley et al., 2020). There may be or are many caregivers who do not have any experience of suffering from Vaccine Preventable Diseases (VPDs), and this could make the caregivers more afraid of being vaccinated than of the Vaccine Preventable Disease. Due to continued success of vaccination and vaccines, there is thus a much lesser risk of suffering from a Vaccine Preventable Disease and in the process may lower motivation of the caregivers to have their children vaccinated but more parental focus on vaccine concerns and safety and about possible long and short -term adverse events that follow vaccinations (Dudley et al., 2020).

This study, in Hoima and Wakiso and in the systematic review focused as well on the role played by health workers in vaccine uptake. It is widely accepted that health workers play an essential role in promoting vaccine acceptance. Indeed, as it will be seen in this study's results, the public may well have access to a lot of information from various different sources, however, caregivers have consistently shown that they still prefer and have respect for health workers as the preferred sources of information and guidance on vaccines (Deem et al., 2018). This study will show the role that health care providers play in running immunization programs, their level of knowledge about vaccines, their attitudes around vaccines and delivering them to caregivers, their nature and effectiveness of their communication with caregivers on their specific worries and concerns about vaccines and immunization in general.

This section of the thesis highlights important aspects of the results. It discusses the trustworthiness of the data this study has collected, that the data is clear, and can be trusted now and in the future. Trustworthiness of this data includes its credibility, especially given that its mixed methods study, with coded data that does not in any way reveal the participants names or impinge on their privacy; that the data is transferable and comparable to other settings of similar demography; the dependability of the data, in the sense that the overlap between different styles/approaches to collection of data and conformability of the study especially as regards admission of the study researcher’s assumptions and beliefs, and acknowledge limitations and strengths of the study.

An important part is ensuring that the results are valid, in both an internal and an external way, an important requirement if one is to analyze the meaningfulness, appropriateness, and usefulness of the findings of this study. Validity is an important part of reliability of this study, that as well focuses on the consistency of this research that are shown from the use of the qualitative and quantitative data collection tools used in this study and a positive test-retest reliability of the study. This section also includes a systematic presentation of the results per research question with the structure of analysis being parallel to structure of introduction and the methods section. The results are presented in Tables and figures as a representation of the outputs of the data analysis. Included in this section is a brief report of what the study findings mean.

Trustworthiness of Data

This study employed triangulation to ensure the data is cogent and trustworthy (Casey & Murphy, 2009; Heale & Forbes, 2013). This allows one design to fill gaps left by the former. When you consider that this study did this, and went further to add a systematic review of the concepts around the study topic, this strengthened the study methodology. Three levels of triangulation were employed in this study was “concurrent triangulation" that included quantitative level (this included in-depth and key informant interviewing), qualitative level and also quantitative analysis level which involved the incorporation of findings from the two, with refining in the focus group discussions (Bekhet & Zauszniewski, 2012; Noble & Heale, 2019a).

This study employed triangulation in order to ensure the validation of the results using both qualitative and quantitative method; complementarity of the methods especially where the qualitative component helped to answer some questions that were not adequately addressed in the quantitative component; identification of contradictors and incongruence in responses and using further exploration to address these; and expansion especially where the focus group discussions helped to grow themes and explore further ideas noted in the quantitative component (Bekhet & Zauszniewski, 2012; Heale & Forbes, 2013; Olsen et al., 2004).

This study blended "Sequential Explanatory triangulation method" – where quantitative data collection and quantitative data analysis were followed by qualitative data collection and data analysis, thus enabling the qualitative data results to help and assist the explaining and interpretation of the findings from the quantitative study component and filling of gaps that emerge and "Concurrent Triangulation," where the two research methods were from time to time utilized to confirm and to cross-validate, and to corroborate the findings of the research in this study (Heale & Forbes, 2013; Olsen et al., 2004). This helped to make sure the methods complement and as well overcome the weaknesses of each other.

This study chose triangulation to provide as much as possible reliable and valid findings through allowing synthesis of the study's entire data collection and analysis while blending both qualitative and quantitative research data, and thus establish deep understanding of vaccine hesitancy and underimmunization (Bekhet & Zauszniewski, 2012; Casey & Murphy, 2009; Heale & Forbes, 2013; Noble & Heale, 2019a; Olsen et al., 2004). This helped improve the accuracy, a more robust testing of the hypothesis and give as comprehensive as possible answers to the research questions. Triangulation in this study increased the confidence in this research data and allowed for a unique or an unusual revelation of the study findings in real time from original research added more depth to the research results, thus improving the validity and utility of these research findings (Bekhet & Zauszniewski, 2012; Casey & Murphy, 2009; Heale & Forbes, 2013; Noble & Heale, 2019a; Olsen et al., 2004).

Due to triangulation, cross validation was made possible in this research, since the qualitative component helped in finding agreement and finding validation of the research results by use of a wide variety of different research methods to arrive the same conclusions and outcomes, making the findings a true reflection and true image of vaccine hesitancy and underimmunization data (Bekhet & Zauszniewski, 2012; Casey & Murphy, 2009; Heale & Forbes, 2013; Noble & Heale, 2019a; Olsen et al., 2004). Through triangulation, the study achieved an important balance between the different research methods used and thus overcome bias thus guarding against different assumptions between researchers. Triangulation thus confirmed and validated the quality of the research results, compensated for any inadequacies in the research approach, allowed for more insights to be generated and ensured clearing of inconsistencies in the data generated (Bekhet & Zauszniewski, 2012; Casey & Murphy, 2009; Heale & Forbes, 2013; Noble & Heale, 2019a; Olsen et al., 2004).

The purpose of study was to determine the barriers to the uptake and utilization of immunization services in (rural) Hoima and (peri-urban) Wakiso Districts of Uganda; to compare the drivers of vaccine hesitancy and underimmunization in these districts and to identify interventions, strategies and approaches that can help address the problem of vaccine hesitancy and underimmunization in these districts. The design of this study was mixed methods, with a cross sectional approach. These methods involved the use of focus group discussions (FGDs) for caregivers of children who are eligible for immunization; face-to-face interviews for caregivers; key informant interviews for focal persons and health care workers involved in immunization, decision makers and managers of immunization services within the two districts.

This study also involved the collection of secondary data from health information records at Wakiso and Hoima District record offices and at the vaccination centres within the two districts. Additionally, the study conducted a systematic review of research articles published on vaccine hesitancy and underimmunization in sub-Saharan Africa. This study sought to establish a firm and deep understanding of vaccine hesitancy and underimmunization in Uganda and the reasons for recurrence of VPDs. The findings of this study will be used to design practical interventions and solutions to vaccine hesitancy and design a tool for assessing vaccine hesitancy that can be adopted and implemented within and beyond Uganda especially during national and supplementary immunization activities and vaccination campaigns.

The protocol for this study received approval from the UNICAF University Research Ethics Committee (UREC – Ref: REAF_DSPA - VERSION 1.0) and the School of Medicine, Research and Ethics Committee of the College of Health Sciences, Makerere University. SOMREC (REC REF 2017-077), UNCST (SS4245). Each participant provided informed consent before every focus group discussion, key informant interview and individual caregiver face-face interviews and/or interview recording. Additionally, institutional and facility approval from the head of health facility or unit or immunization centre was obtained before the conduct of the study. Study participants were free and made aware that they could leave at any time during the study and that any withdrawal does not affect their inherent rights to be served or attended to in their workplaces or communities.

In this study, there were no direct risks to the participants in this study, and there were no invasive medical procedures on study participants, or any direct harm to infants in the study, or to pregnant mothers or to any live subjects in the study. The Declaration of Helsinki informed the conduct of the study. The questionnaire responses were transferred into data sheets that are password protected during and after analysis. The hard copies of the questionnaires along with the informed consent forms are stored in lockable cupboards.

For the focus group discussion, the recordings have been safely stored and will be destroyed based on the guidance and protocols of the ethics committee. Soon after the discussion was transformed into the data sheets, it was entered into the data capture tool and the data was then analyzed and password protected. The information collected from the research has been kept anonymous and only the research team allowed access. Participants of focus group discussion were asked to keep confidentiality about the content in the group discussions from outsiders.

Participants of interviews were asked not to talk to people outside the group about what was said inside the group. However, these findings will anonymously be used in scientific publications and to provide recommendations to the concerned district and national health authorities in Uganda. At all steps, the identity of the participants will not be disclosed in the published research articles as well as when providing recommendations.

Reliability and Validity of Data

This study employed triangulation with use of a comparative and descriptive cluster randomized mixed methods design, cross sectional approach; to ensure that the data is detailed and rich to exhaustively address the study questions. This was important because while majority of the questions could be qualitatively addressed, the quantitative component was necessary as well to cover the broader quantitative aspects of the study. The study employed a blend of multi stage cluster sampling and consecutive sampling techniques in which the parish was used as a cluster.

The qualitative component of the study included focus group discussions (FGDs) with the care givers to children coming for immunization services; face to face interviews of child caregivers; and key informant interviews of key immunization focal persons from Wakiso and Hoima districts. The Focus group discussion participants were chosen through purposive sampling in order to achieve maximum variation in the sample interviewed. To ensure internal validity, this study used a multi stage cluster sampling technique, and considered all sub counties in the two districts, with parishes as clusters, to ensure variability, uniformity and that every population was included. From each of the selected clusters, the immunizing health facilities were selected. Each parish selected also provided a village health team member per village and local council leaders from whom the required number for KII were randomly selected. The distribution of health facilities selected, caregivers, key informants and focus health workers was randomly done and evenly distributed across the clusters.

After obtaining ethical approval to conduct the study, the principal investigator contacted the District Health Officer for Hoima and for Wakiso districts, district who then introduced him to the respective Chief Administrative Officers and Local Council five chairmen (LCV) of each respective district. The Local council chairmen offered permission to conduct the study in the districts. The principal investigator also contacted both political, religious, cultural and technical heads in the sub-counties from which parishes had been selected to seek for permission to conduct the study in their areas and to inform them about the study. The administrative leaders of the sub county linked the principal investigator with the Local Council II leaders and parish chiefs of the selected parishes, who in turn linked the principal to the Local Council I chairmen of villages from the identified parishes.

The principal investigator together with the research assistants introduced themselves and the purpose of their visit and then sought and obtained informed consent which the caregivers visiting immunizing centres within the selected parishes. The caregivers and child pairs had to be residents of either Wakiso or Hoima districts. The required information on immunization, vaccines, level of utilization of immunization services and reasons for failure to meet schedule as recommended from caregivers was obtained using interviewer administered pre-tested questionnaire, which involved requesting for the immunization card for the eligible child.

In this study, the status of vaccination was confirmed by use of a validly completed vaccination card. While DPT 3 was the variable for determining vaccination coverage, completing immunization coverage required a child to have gotten all vaccines recommended at birth, at 6 weeks, at 10 weeks, at 14 weeks, and at 9 months. To achieve maximum randomization, if a caregiver had two eligible children for vaccination, only one child was chosen by simple random sampling. The caregivers of the children who were eligible but did carry the immunization cards were asked some questions that correspond to the periods when the particular vaccines are given to the child and the number of vaccinations received and if correct was also be recorded. This child was however excluded if any of the responses generated doubt as to the veracity of the information or the ability of the caregiver to correctly remember. An assistant identified the caregivers to participate in FGDs who had to be different from those who participated in the interviews. These were then identified and appointments for discussions at agreed venues made. The FGDs were conducted in the local language or in the language best understood by the participants. The moderator and a note taker were needed for each group. Discussions were audio recorded and later transcribed later. Similarly, the KIs were identified and approached and interviewed from an agreed venue. Focus group discussion participants were different from those who had participated in the individual caregiver-child interviews, to avoid bias.

The review was structured using the PICO (participants, intervention, comparator, and outcome) format. The study considered both quantitative and qualitative studies in line with the overall triangulation design. It excluded interventional studies (for example clinical trials or vaccine efficacy/vaccine effectiveness studies); systematic or narrative reviews, papers that were not peer reviewed, editorials among others like grey literature. The study population/participants had to be persons living in Africa and are vaccine hesitant, or that had chosen against being vaccinated recommended vaccines; including caregivers, children and other adults/adolescents. The main outcome was vaccine hesitancy determinants, which are the reasons the participants had given for not accepting or allowing their children or themselves to be vaccinated.

The study population for this study consisted caregiver-child pairs (a care giver with a child of age less than five years) from Wakiso and Hoima Districts attending vaccination services in any of the designated health facilities that offer immunization services. A study unit consisted a caregiver-child pair with at least one child aged 9 - 59 months in their home in either Hoima or Wakiso District who fulfil the inclusion criteria. Exclusion criteria consisted caregivers that did not give informed consent or that did not reside in the district (Wakiso/Hoima) for less than nine months. The dependent variable was acceptance of immunization services, while the independent variables included among other things age of the caregiver, marital status, religion, level of education, occupation, sex of the caregiver, distance to the health facility and waiting time before receiving immunization services at the facility or outreach site.

Quantitative data was collected using a pre-tested and piloted data collection tool. This researcher administered questionnaire comprised of four sections to capture socio-demographic information, information about the child, vaccine compliance and the child vaccination history. The focus group discussion recordings were transcribed into Word 2016 by bi-coordinate bilinguals, then transferred to NVIVO 12 for aligning themes. Quantitative data cleaning in Excel spreadsheet and analysis/regression in Stata version 13 were done. Descriptive analysis of the data was expressed as percentages and frequencies.

RESULTS

Objective 1: To estimate the level of underimmunization in rural Hoima and urban/peri-urban Wakiso Districts of Uganda [DPT3 (14 Weeks)]

Table 6 showing Prevalence of underimmunization in Hoima and Wakiso Districts

HOIMA	Yes	252	81%
	No	59	19%
WAKISO	Yes	182	75%
	No	82	25%

Table 6 above shows that both Wakiso and Hoima Districts had immunization overage and uptake below the 90% target, with rural Hoima at 81% and urban/peri-urban Wakiso at 75%. Both Districts are under-immunized, with the peri urban and urban areas being more prone to under-immunization.

Assessing Vaccine confidence and acceptance

The table 7 below shows that 91% of respondents consider vaccines safe, 85% consider vaccines effective, over 95% have complete trust in vaccines and would readily accept them to be given to their children, and only 13% have some misgivings regarding vaccines. These misgivings centred around fears of what they consider side effects/adverse events following vaccines – including pain, fever, risk of convulsions and abscess formation at injection sites.

Table 7 showing factors assessing Vaccine confidence and acceptance

Variable (N = 643)	Percent (Yes)	Percent (No)	Percent (I don't know)
I believe Vaccines are safe	91.57	3.61	4.82
I believe Vaccines are effective	85.24	12.35	2.41
I have full trust in vaccines and would readily accept my child to be vaccinated	95.11	3.06	1.83
I have some fears and misgivings about vaccines	13.86	86.14	

Objective 2: To determine the factors associated with underimmunization in in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.

Modified Poisson regression multivariable model for association of DPT 3 Vaccine completion in table 17 shows the factors found to be independently associated with underimmunization. These factors include low trust in vaccines, being single parent caregiver, those who do not believe that vaccine are safe, relying on social media as source of vaccines information, those who did not receive any medical education on vaccines during visit to immunization centres, and those who have misgivings about vaccines.

Table 8 showing Modified Poisson regression multivariable model for association of DPT 3 Vaccine completion

	Crude prevalence ratio (PR)			Adjusted prevalence ratio (PR)		
	PR (SE)	**95% CI**	**p-value**	**PR (SE)**	**95% CI**	**p-value**
Residence						
Rural	Reference					
Semi-urban	1.19(.16)	0.82 - 1.55	1.18	1.19 (.18)	0.89 - 1.61	0.24
Urban	1.06 (.19)	0.75 - 1.51	0.74	0.87 (.16)	0.60 - 1.26	0.45
Level of education						
None	Reference					
primary	0.89 (.26)	0.50 - 1.58	0.70	0.89 (.26)	0.50 - 1.58	0.69
secondary	0.94 (.26)	0.54 - 1.63	0.82	0.86 (.25)	0.49 - 1.52	0.61
Tertiary	0.89 (.27)	0.49 - 1.62	0.71	0.97(.31)	0.52 - 1.81	0.92
Marital status						
Married	Reference					
Single	1.27 (.18)	0.97 - 1.66	0.09	1.33 (.18)	1.02 - 1.73	**0.03***
Never married	1.44 (.33)	0.92 - 2.27	0.12	1.51 (.45)	0.85 - 2.70	0.17
Source of vaccine information						
Official Media	Reference					
Family/Friends	0.80 (.15)	0.55 - 1.18	0.27	0.66 (.23)	0.33 – 1.32	0.24
Community leaders	0.96 (.06)	0.84 – 1.10	0.59	0.82 (.21)	0.65 – 1.20	0.42
Teachers	1.01 (.27)	0.68 - 1.79	0.68	0.54 (.14)	0.33 – 0.89	**0.01***
Social Media	1.68 (.11)	1.45 - 1.90	**0.01***	0.60 (.21)	0.30 – 1.21	0.16
Others	0.48 (.28)	0.15 - 1.54	0.22	0.35 (.43)	0.03 – 3.74	0.39

Employment						
Formally Employed			Reference			
Unemployed	0.93 (.10)	0.75 - 1.16	0.54	0.95 (.11)	0.76 – 1.18	0.63
Self employed	0.85 (.60)	0.21 - 3.41	0.81	0.55 (.29)	0.20 – 1.54	0.26
Religion						
Moslem			Reference			
Catholic	1.03 (.07)	0.74 - 1.43	0.85	0.98 (.17)	0.70 - 1.40	0.93
Protestant	0.94 (.15)	0.68 - 1.28	0.69	0.95 (.16)	0.68 – 1.32	0.75
Others	1.71 (.24)	1.30 – 2.26	**0.01***	1.52 (.38)	0.93 – 2.47	0.09
How did you access immunization Centre						
Walked			Reference			
Bicycle	0.74 (.33)	0.30 - 1.78	0.45	0.90 (.40)	0.37 - 2.16	0.81
Vehicle	0.70 (.13)	0.67 - 1.19	0.45	0.88 (.14)	0.65 – 1.20	0.42
Bodaboda	1.15 (.30)	0.69 - 1.91	0.60	1.12 (.33)	0.63 – 2.00	0.70
Others	1.12 (.15)	0.85 - 1.48	0.42	1.27 (.20)	0.93 – 1.73	0.13
Did you receive health education before vaccination						
Yes			Reference			
No	1.37 (.60)	0.58 - 3.25	0.47	0.93 (.12)	0.72 - 1.21	0.58
I don't know	0.26 (.16)	3.05 - 5.23	**0.01***	0.26 (.22)	0.48 – 0.45	**0.01***
Vaccines are safe						
Yes			Reference			
No	1.27 (.05)	1.16 - 1 .39	**0.01***	1.06 (.34)	0.56 - 2.00	0.86
I don't know	0.28 (.18)	0.08 - 1.00	**0.05***	0.50 (0.34)	0.13 – 1.92	0.32
Vaccines are effective						
Yes			Reference			
No	0.97 (.11)	0.76 - 1.22	0.78	0.91 (.36)	0.13 – 1.98	0.82
I don't Know	0.25 (.09)	0.29 - 0.47	**0.01***	1.73 (.34)	1.18 – 2.53	**0.01***
Do you trust vaccines						
Yes			Reference			
No	1.25 (.30)	0.77 - 2.01	0.37	0.99 (.25)	0.60 – 1.63	0.96
I don't know	0.35 (.31)	0.06 - 2.02	0.24	0.43 (0.37)	0.08 – 2.27	0.32
I have misgivings about vaccines						
Yes			**Reference**			
No	1.06 (.17)	0.76 (1.47)	**0.72**	0.93 (.15)	0.68 – 1.27	0.63
I don't know	0.55 (.08)	0.40 (0.74)	**0.01***	0.40 (.29)	0.09 – 1.69	0.21

Objective 3. To determine and describe the barriers to the uptake and utilization of immunization services in rural Hoima and urban/peri-urban Wakiso Districts of Uganda.

This section of the objective was achieved by conducting a mixed method study with both quantitative and qualitative research methods of data collection in Hoima and Wakiso districts. Table 9 shows the distribution of caregivers per Health Facility that participated in the study, while Table 10 shows the characteristics of caregivers in the study.

Table 9: Distribution of caregivers per Health Facility in Hoima considered in the study

Health facility	**Frequency of caregivers**	**Percentage**
Buhanika HC III	5	1.6%
Munteme HC II	9	3%
Mukabara Health Center III	41	13%
Mparangasi HC III	30	9.8%
Hoima Regional Referral Hospital	29	9.3%
Kikube Health Centre III	38	12.2%
Kigorobya HC IV	20	6.4%
Kabwoya Health centre III	12	3.8%
Dwooli Health Centre III	30	9.6%
Butema Health Centre III	49	15.7%
Buhimba health centre III	25	8%
Buseruka Health Centre III	20	6.4%
Kyangwali Health Centre III	3	1%
Total	**311**	**100%**

Table 10: Characteristics of caregivers in Hoima District

Variable	**Frequency (N=311)**	**Percentage (%)**
Relationship to the participant child		
Parent	309	99.3%
Others	2	0.7%
Age		

<=25	184	59.1%
26-30	63	20.2%
31-35	32	10.2%
36-40	21	6.7%
>40	11	3.6%
Sex		
Male	16	5.1%
Female	295	94.9%
Religion		
Muslim	13	4.2%
Catholic	137	44.1%
Protestant	116	37.3%
Pentecostal	39	12.5%
Traditional (Bisaka)	3	1%
SDA	3	1%
Marital status		
Married	273	87.8%
Single	19	6.1%
Widowed	3	1%
Divorced	16	5.1%
Occupation		
Housewife	13	4.2%
Peasant farmer	199	64%
Employed/professional/others	22	7%
Self-employed	69	22.2%
None	8	2.6%
Education level		
None	18	5.8%
Primary	191	61.4%
Secondary	86	27.7%
Tertiary	16	5.1%
Is the caretaker household head		
No	249	80%
Yes	62	20%
Occupation of household head		
Professionals	25	8%
Self employed	61	19.6%
Peasant farmer/housewife	163	52.5
None	62	20
Sex of the household head		
Male	270	86.8
Female	41	13.2

To assess for completion of immunization schedule, the study enrolled a further 311 child-caretaker pairs randomly from among the caregivers that maintained a well-kept vaccination book and who had attained age 12 months. These were expected to have completed the schedule that ends at 9 months immunizations. Table 11 and Table 12 show the immunization completion rates among these participants.

Table 11: Immunization coverage for children over 12 months of age in Hoima District

Antigen	Frequency (N=311)	Age at Vaccination	Percentage (%)
BCG		Birth	
Yes	296		95%
No	15		5%
OPV0		Birth	
Yes	299		96%
No	12		4%
DPT1		6 Weeks	
Yes	291		93%
No	20		7%
DPT2		10 Weeks	
Yes	263		84.5%
No	48		15.5%
DPT3		14 Weeks	
Yes	252		81%
No	59		19%
Measles		9 Months	
Yes	204		65.5%
No	107		34.5%

From the 311 caregiver/child pairs that were enrolled, 95% (295/311) were female; and belonged mainly to either catholic or protestant religion (33.4% vs 28.9%). As regards individual vaccine completeness as per the recommended immunization schedule, 95% had got BCG vaccine, 96% for bOPV0, 93% DPT1, 84.5% DPT2, 81% DPT3 and 65.5% for measles (see Table 11 and 12). This study found that 87.8% (273/311) of the caregivers were married. The rest of the caregiver characteristics are described in table 10. Of the children surveyed belonging to these caregivers, 46% (145/311) were of age less than 3 months; 33.8% (105/311) were 3-12 months, while 19.6% (151/311) were of aged above 12 (13-60) months.

This study also found that 84.9% (264/311) of the children were born at a health facility, and 12.9% (40/311) were home deliveries with the remaining 2.3% (7/311) being born on the way to hospital. This study also revealed that 53.7% (167/311) of the respondents had their child assessed for immunization status during a previous visit to a health center. This study also found that the vast majority [99% (308/311)] of respondents sought treatment from a health facility when sick (20% sought from hospital, 73% sought from a dispensary/health Centre, while 19% sought from private clinics). Secondary data was sourced from the HMIS records at Hoima District offices, and also from vaccination data within Hoima District for both static and outreach.

Table 12: Immunization coverage for children over 12 months of age in Wakiso District

Name of Vaccine	**Response**	**Frequency**	**Percentage**
DPT1	Yes	315	94.9
	No	17	5.1
DPT2	Yes	290	87.9
	No	42	12.7
DPT3	Yes	250	75.3
	No	82	24.7
BCG	Yes	284	85.3
	No	48	14.4
IPV1	Yes	221	66.4
	No	111	33.3
OPV1	Yes	208	62.5
	No	124	37.2
OPV2	Yes	220	66.1
	No	112	33.6
OPV3	Yes	195	58.6
	No	137	41.1
Measles vaccine	Yes	171	51.4
	No	161	48.3

Table 13: Details for Health workers as Key Informants in Hoima District

Sub county	Health facility name	Position	Number of KIIs
Hoima municipality	Hoima Regional Referral Hospital	Cold chain Focal Person	1
	Hoima Regional Referral Hospital	Head of immunization	1
	Hoima Regional Hospital	In charge Hoima Regional Hospital	1
	Bujumbura HC III	In charge Bujumbura HC III	1
	Bujumbura HC III	Head of Immunization	1
	Buchayaya HC III	In charge Buchayaya HC III	1
	Butema HC III	Head of Immunization	1
	Mparangasi HC II	Assistant Head of Immunization	1
	Kyakapeya HC II	EPI Focal Person	1
	Buhanika HC III	Head of Immunization	1
Bugahya	Kigorobya HC IV	Health Assist Kigorobya HC IV	1
	Buseruka HC III	Assistant Incharge	1
	Tonya HC II	In charge of Tonya HC II	1
	Sebigoro HC III	Assist Incharge Sebigoro HC III	1
	Dwooli HC III	EPI Focal person	1
	Dwooli HC III	In charge Dwooli HC III	1
Buhaguzi	Mukabara HC II	In charge of Mukabara HC II	1
	Mukabara HC II	Head of Immunization	1
	Kyangwali III	Head of Immunization	1
	Kabwoya III	Focal Person Immunization	1
	Munteme II	Head of Immunization	1
	Rwenyawawa HC III	In charge Rwenyawawa HC III	1
	Kikube Health Centre	Immunization Focal person	1
	Buhimba HC II	Immunization Focal person	1
TOTAL NUMBER OF KEY INFORMANT INTERVIEWS WITH HEALTH WORKERS			**24**

Table 14: Details of immunization focal persons interviewed as Key informants

Location of placement	Position	Number of Years	Sex
Kabwooya	Former LC III Chairman	10	Male
Munteme	LC I Committee Member (Treasurer)	5	Male
Buhimba East	VHT	10	Male
Nyangambi	VHT	1	Male
Butema HC III	VHT	1	Female
Buhimba East	LC 1 Secretary	10	Male
Kikube HC III	VHT	5	Male
Mparangasi Sub county	LC III	1	Male
Kiragura Parish	Parish Chief	3	Male
Buhanika HC II	Parish coordinator and VHT	3	Female
Bujumbura HC III	VHT	3	Female
Hoima Referral	VHT	4	Male
Bujumbura West	LCI	4	Male
Hoima Hospital Cell	LCI	5	Male
Mparangasi	LCI	10	Female
	Total 16 Key informants		

Table 10 showcased that majority of the caregivers were in the age bracket 21-25 representing 127(38.4%), followed by respondents between 26-30 who were 96(29%). The age bracket 16-20 had 56(16.9%) followed by respondents between 31-35 who were 38(11.5%). The least number of caregivers were in the age bracket of more than 35 years representing 3.6% and less than 16 years representing 0.60%. The gender category consisted had majority 327

(98.5%) caretaker respondents who were females. This means that majority of the caregivers are female which is not surprising considering it’s the main role of females to take care of the children in Uganda.

Majority respondents resided in the semi urban 182(54.8%), followed by those who resided in the rural setting 92(27.7%). The least number of respondents resided in the 58(17.5%). Majority of the respondents were protestant in terms of religion representing 170(51.4%), followed by Catholics who were 108(32.6%). Moslem religion had the least number of caregivers 49(14.8%). In terms of marital status majority of the caregivers were married representing 286(86.7%), this was followed by single caregivers 37(11.2%). The least number of caregivers had ever married and widowed representing 7(2.1%). It was interesting to note that majority caregivers were employed accounting to 197(59.3%), which was followed by the unemployed caregivers who were 133(40.1%). Majority of the respondents had attained secondary education qualifications who were 182(55%). This was followed with respondents who had attained primary qualification level who were 92(27.2%). The least number of respondents had attained tertiary qualification 49(14.8%) while only 10(3%) had no qualification at all.

In terms of monthly income, majority of the respondents had incomes less than 300,000 representing 171(56.3%), followed by 66(21.7%) who were between 300,000 to 500000. The number of caregivers between 33(10.9%) who were between shs 500,000 to 900,000. The least were 9(8.2%) who had a monthly income of above shs 900,000. It was interesting to note that 25(8.2%) of the care takers didn’t know their monthly income.

Draft analysis for number of children, caretaker relationship and main caregiver

Table 15, 16, and 17 reveal that majority of caretaker families had an average of 283(85.8%), followed by families with 4-6 children representing 42(12.7%). The least number of caretaker families had seven children and above who were 5(1.50%). In terms of relationship of caretaker to the child, majority were mothers representing 317(96.1%). They were a few fathers who had brought their children for immunisation who were 7(2.10%). The responsibility of main care giver was dominated by fathers as expected in a Ugandan setting where men are supposed to take care of their families. Fathers who were the main caregivers were 245(75.2%), followed by mothers who were 63(19.3%). The other relatives represented 5(1.50%).

Table 15: Socio Demographic information for caregivers from Wakiso District

Age category	**Frequency**	**Percentage**
Less than 16	2	0.60%
16-20	56	16.90%
21-25	127	38.40%
26-30	96	29.00%
31-35	38	11.50%
more than 35	12	3.60%
Sex of the caretaker		
Male	5	1.50%
Female	327	98.50%
Residence		
Rural	92	27.70%
Semi-Urban	182	54.80%
Urban	58	17.50%
Religion		
Moslem	49	14.80%
Catholic	108	32.60%
Protestant	170	51.40%
Others	4	1.20%
Marital status		
Married	286	86.70%
Single	37	11.20%
Ever married	7	2.10%
Occupation		

Employed	197	59.30%
Unemployed	133	40.10%
Others	2	0.60%
Education level		
None	10	3.00%
Primary	90	27.20%
Secondary	182	55.00%
Tertiary	49	14.80%
Family income		
<Shs 300000	171	56.30%
Shs 300000-500000	66	21.70%
Shs 500000-900000	33	10.90%
>Shs 900000	9	3.00%
I don't know	25	8.20%

Table 16: Additional caregiver factors from Wakiso District

Number of children in the family	Frequency	Percentage
1-3	283	85.80%
4-6	42	12.70%
7 and above	5	1.50%
Valid total	**330**	**100.00%**
Relationship of child to caretaker		
Father	7	2.10%
Mother	317	96.10%
Others	6	1.80%
Valid total	**330**	**100.00%**
Main caregiver		
1. Father	245	75.20%
2. Mother	63	19.30%
3. Both parents	13	4.00%
4. Others	5	1.50%
Valid total	**326**	**100.00%**

Table 17: Most frequent source for you obtain the health-related information

Source of health-related information	1st Source		2nd Source		3rd source	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Official media (newspapers, radio and television)	182	55.0	56	16.8	10	3.0
Family and friends	40	12.0	47	14.1	42	12.6
Religious and community leaders	24	7.2	63	18.9	27	8.1
General practitioners	60	18.0	39	11.7	22	6.6
School teachers	9	2.7	30	9.0	25	7.5
Social media	3	.9	4	1.2	16	4.8
Others	8	2.4	2	.6	2	.6
Missing	5	1.5	92	27.6	188	56.5
Total	**332**	**100**	**241**	**100**	**332**	**100**

Table 18: Different sources of health-related information that you trust

Trusted		Frequency	Percent
Source 1		6	1.8
	1. Official media (newspapers, radio and television)	158	47.4
	2. Family and friends	26	7.8
	3. Religious and community leaders	23	6.9
	4. General practitioners	74	22.2
	5. School teachers	30	9.0
	6. Social media	7	2.1
	7. Others (Hospitals, posters and VHTs)	8	2.4
Total		**332**	**100.0**
Trusted source 2		**Frequency**	**Percentage**
	1. Official media (newspapers, radio and television)	61	18.3
	2. Family and friends	55	16.5
	3. Religious and community leaders	54	16.2
	4. General practitioners	37	11.1
	5. School teachers	21	6.3

	6. Social media	2	.6
	7. Others (Hospitals)	1	.3
Total		**332**	**100**
Trusted source 3		**Frequency**	**Percentage**
	1. Official media (newspapers, radio and television)	20	6.0
	2. Family and friends	40	12.0
	3. Religious and community leaders	32	9.6
	4. General practitioners	15	4.5
	5. School teachers	6	1.8
	6. Social media	12	3.6
	7. Others	1	.3
Total		**332**	**100.0**

Table 19: Summary findings from Focus group discussions (for Caregivers)

No.	Focus group question	SUMMARY OF THE RESPONSES
1	Why do you think children are given vaccines/immunization?	In general mothers said that immunization is given to prevent children them from getting diseases
2	Are there situations when you failed to bring your child for immunization? What were the reasons?	The major reasons included laziness from mothers, Long distances, some religions do not believe in immunization, Ignorance of mothers, Fear of side effects and unclear immunization schedules are not clear.
3	Do you think that most parents from your area accept taking their children for immunization? Are there those who do not? What are some of the reasons why they	Generally, most parents in the area accept however they were a few cases where parents don't accept which included the Bisaaka people who do not immunize their children, though I do not know the reason to why they don't take their children for immunization, Some old people have a perception that they have lived without

	opt not to take the children for immunization?	being immunization, and that the vaccines are the ones that have shortened people's life spans, some it's because of ignorance, because someone will say that you are taking your child for western medicine it will spoil your children's lives.
4	Are there days you went to a health facility and found when there were no vaccines? Which vaccine was it? And what did you do to get your child vaccinated?	Almost all the mothers who participated in the focus group discussion said that they are days when they did not find vaccines, apart from mothers from Rwenyawawa HC IV. After we find they are no vaccines sometimes they advise us to try other Health Centres or come back on the next day that is always given by the Health workers. BCG was the most lacking vaccine, others said the vaccine they inject on the both thighs at 3 months and the polio vaccine.
5	Are there any side effects to vaccines? Has your child or a child you know of ever got those side effects? What did the parent or caretaker do to help the affected child?	All the mothers reported that they were side effects of vaccines, which included fever, swelling, excessive crying from the child and failure to breastfeed. The solution that was given included giving panadol, using an onion and bottle on the swelling, taking the child to the hospital
6	Are there any religious groups or cultural groups you know of that do not encourage or promote immunization for children? If	There were mixed reactions most of the mothers said they didn't know any however in some areas near Kagadi district mothers at the Health facilities mentioned that the people of Bisaka religion do not immunize their children

	yes, what are their reasons for being against immunization?	
7	What is the first thing the government does when they want to introduce a new vaccine to your area? Do they educate the community enough? Do they usually get feedback from the community?	The government normally first announces in churches, in villages, in markets, in schools so that all the local people are aware and involved. Yes, they announce enough because we all get to know about it. However sometimes, the health workers just write on our cards and sometimes we do not know what they have written. We used to get one inject for the child but now they are given two and we do not know why? Most respondents noted that they don't give feedback because there is no concern in that when the child get any side effects, most of us know how to get a cloth, dip it in water and cool the child's temperature and the child becomes ok.
8	In what ways do you think parents/mothers from your locality can be better empowered to demand for or access immunization services?	They should arrest those who resist the policy of the government They should continue to advertise. We should be told the importance of immunization. Should stock more vaccines in the health facilities The people should be educated well on the vaccines and medicines that they introduce because some people have poor perceptions on the medicines and drugs.

Table 20: Summary findings from KIIs (for focal persons)

No.	KII Question	RESPONSES
1	How many facilities in your area offer immunization?	Most community leaders said that there was at least one health facility offering static and outreach immunisation services in their area of service
2	Do these facilities always have vaccines? If there are any stock outs, what do you think are possible reasons?	While most facilities have vaccines, some community leaders especially from Kabwoya HC said that vaccines are inadequate; and the reason for the stock out given was delays from the national medical stores and sometimes-delayed funds; and that Kabwoya population is large yet the vaccines given out are few -- – *"there is a period when immunization is taking place and the people are more than the available vaccines for that particular day."* *"there are many migrations to this place, therefore the data that was captured by the census is not the actual number at the ground, therefore when the government is planning for this area, we are given less than we deserve."*
3	Do you think that most parents from your area accept taking children for immunization? What are some of the	Most parents bring their children for immunisation however in Buhimba, not all parents accept because some are not willing that need a little push. Some parents believe that immunization is not important because they have grown up without being immunized. *"The biggest percentage does not know the importance of immunization. Before we had a challenge where some people*

	reasons why some opt not to?	*thought that vaccines are harmful to children but we have tried to educate the people and people are now okay, also there are some people who believe that immunizing your child weakens the child and may die."*
4	Are there any religious or cultural groups you know of that do not encourage immunization?	Some religions exist that believe that people should not take their children for immunization *"we have done our best to teach our people against these groups that teach that even Jesus wasn't immunized and are dangerous."*
5	What is the first thing the government does when they want to introduce a new vaccine? Do they educate the community enough? Do they usually get feedback from the community?	Generally, most community leaders said that government firsts carries out sensitization through the media; the staff at the health facilities are communicated to and the health assistant at the sub county are informed to sensitize VHTs because they are more connected to the community. *They do educate the community because it's not only the VHTs who are involved, we have religious and cultural leaders are brought on board. We have the local leader, councilors and chairpersons who also are educated.* However, government does not get feedback, because the community is illiterate. Some feedback is given during trainings and seminars with stakeholders, except situations where there is no follow up in the community from VHTs.
6	What are the key things that make it easy for you to provide	The community leaders said that if the roads should be worked on because during the rainy season, the health workers cannot easily

	immunization services to children in your catchment area/facility?	reach to the community for outreach services, this either delays the service or hinders the service provision. More health centres should be constructed, most vaccines should be made available, and we need well-trained health staff. We have VHTs and LCs on the mobilizing team and staff at the facility who are readily available and we also have outreach.
7	What would you say are the major barriers to fully immunize their children in your catchment area?	**The following barriers were given by the community leaders;** "We have few health centres, and many mothers wanting to deliver or have their children immunized, but the lack of enough health centres is a big problem." *"some people say you have brought vaccines to spoil our children "leave us alone", you have your own personal motives for bringing the vaccines."*
8	In what ways do you think people from your locality can be better empowered to demand for immunization services?	***The following ways were given by community leaders;*** *"Whenever we have a health challenge in this area, the people are alert and vigilant, they report the issue at hand. I would like to thank our DHO because every time we report, he responds by sending surveillance. Our people also report and demand for services."* *"The community should be sensitized to know what services they are entitled to so that they can be able to demand for these services."* *"It depends when the mother is still pregnant and attends ANC, it is easier to enroll in the immunisation process since they are sensitized during the ANC. This makes them aware and empowered."*

		"In my village setting, accessibility of vaccines is key, if information passed on time, the people are always willing."
9	What should be done to improve immunization coverage in your catchment area/facility?	**The following suggestions were given as ways of improving immunisation coverage by community leaders:** "*The people should be educated about the importance of immunization."* *"Through community sensitization, the people need to know that a healthy body is a healthy mind. Our children need to be immunized so that they are healthy and able to perform well academically."* *"People should be taught their right to access health services, and that it's their right to demand for it because it is the duty of the government to provide health services."* *"We also need to continue sensitization considering all the education levels of people."* *"I would like to ask the government to put up more facilities in the parishes so that the services are closer to the people."* *"I would also like to request any NGO or government to facilitate outreach services if the facilities are not up."*
10	Do you have any other comment or questions you would like us to talk about in relation to immunization services for children?	**These are some of the comments we received from community leaders;** *"In future, there is need for facilitation. LC1 leaders get 120,000 shillings annually. This can't help given that its limited funding for the kind of monitoring we do,"* *"And the community is positive towards immunization."*

	"I also want to have VHTs who have been influential in the routine and mass immunization."
	"I want to thank all the NGOs that have supported immunization in my community."

SECONDARY DATA FROM HMIS

Table 21 below shows the national performance of the immunization program for Uganda from 2018 to 2023 August. The performance of all the antigens for immunization currently under the expanded program on immunization are shown.

Table 21: Uganda Ministry of Health immunization performance average for 2018 - 2023

Antigen	**2018-2019**	**2019-2020**	**2020-2021**	**2021-2022**	**2022/2023-August**
BCG	88%	79%	83%	**85%**	**80.8%**
DPT1	103%	92%	97%	**98%**	**90.1%**
DPT2	95%	87%	91%	**92%**	**87.2%**
DPT3	93%	85%	91%	**92%**	**86.4%**
IPV	88%	73%	90%	**91%**	**94.0%**
Measles	87%	80%	90%	**91%**	**89.5%**
PCV 1	100%	92%	97%	**99%**	**92.9%**
PCV 2	94%	87%	91%	**93%**	**90.3%**
PCV 3	92%	85%	91%	**93%**	**88.9%**
Polio 0	74%	72%	77%	**79%**	**65.9%**
Polio 1	103%	98%	97%	**98%**	**94.1%**
Polio 2	94%	97%	91%	**93%**	**88.2%**
Polio 3	92%	84%	91%	**93%**	**87.6%**
Rotavirus 1	96%	90%	94%	**94%**	**89.4%**
Rotavirus 2	88%	84%	87%	**86%**	**86.3%**
HPV1	115%	95%	96%	**105%**	**34.9%**

HPV2	65%	38%	56%	**56%**	**18.6%**
Td2+_Preg Women	75%	58%	64%	**58%**	**58.7%**

(N/B – Source – Ministry of Health HIMS, Uganda, 2022)

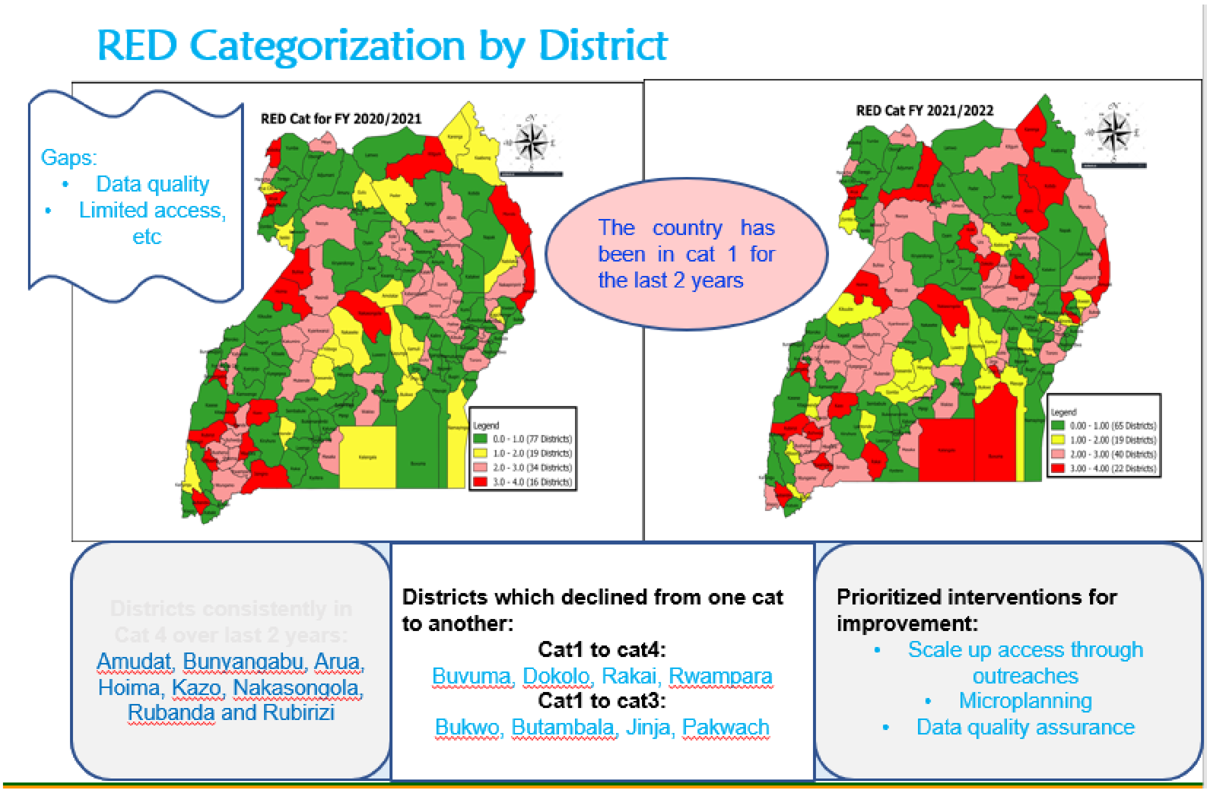

Figure 10 showing Uganda Red Categorization by District for 2020 - 2022

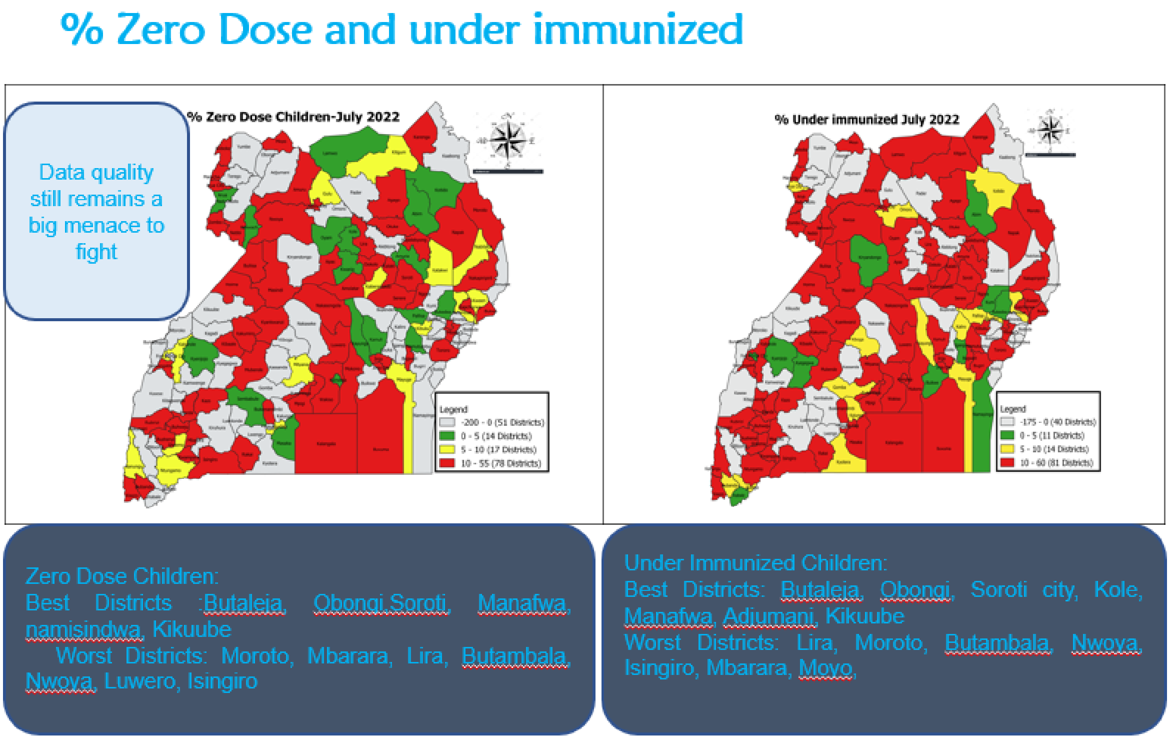

Figure 11showing Uganda Zero dose and under-immunized for 2022

Objective 4: To understand the causes and determinants of vaccine hesitancy in Sub Saharan Africa

This reviewed published research work and research articles on vaccine hesitancy and underimmunization, to establish and assemble a deeper and broader understanding of the rapidly emerging problem of hesitancy and underimmunization. The protocol was structured using the PICO (Methley et al., 2014) format - participants, intervention, comparator, and outcome. It considered controlled before-and-after studies, randomized controlled trials, and qualitative studies. The systematic review excluded interventional studies, systematic or narratives, editorials, papers that are not peer reviewed among others like grey literature. The study population or participants had to be persons that were living in Sub Saharan Africa and are vaccine hesitant, or under vaccinated and had chosen against being vaccinated recommended vaccines; including caregivers, children and other adults/adolescents. The main outcome is vaccine hesitancy and underimmunization determinants, which are thought to be the reasons why the participants were not vaccinated or were not accepting or allowing themselves or their children to be vaccinated.

Table 4 shows the search strategy, figure 10 shows the PRISMA diagram of the systematic review and Table 5 lists the 95 studies finally included and the countries from Sub Saharan Africa from where the studies were published. The reported drivers for hesitancy to vaccination align with the SAGE Determinants Matrix. Complaints or dissatisfaction with health system especially delays, access, long waiting time or lines at facilities and poor attitude of health workers. While knowledge did not contribute significantly, the beliefs or attitudes regarding health prevention. In this study, vaccine specific issues contributed slightly over a quarter of drivers of vaccine hesitancy, especially availability, cold chain, delivery, stock outs and storage challenges.

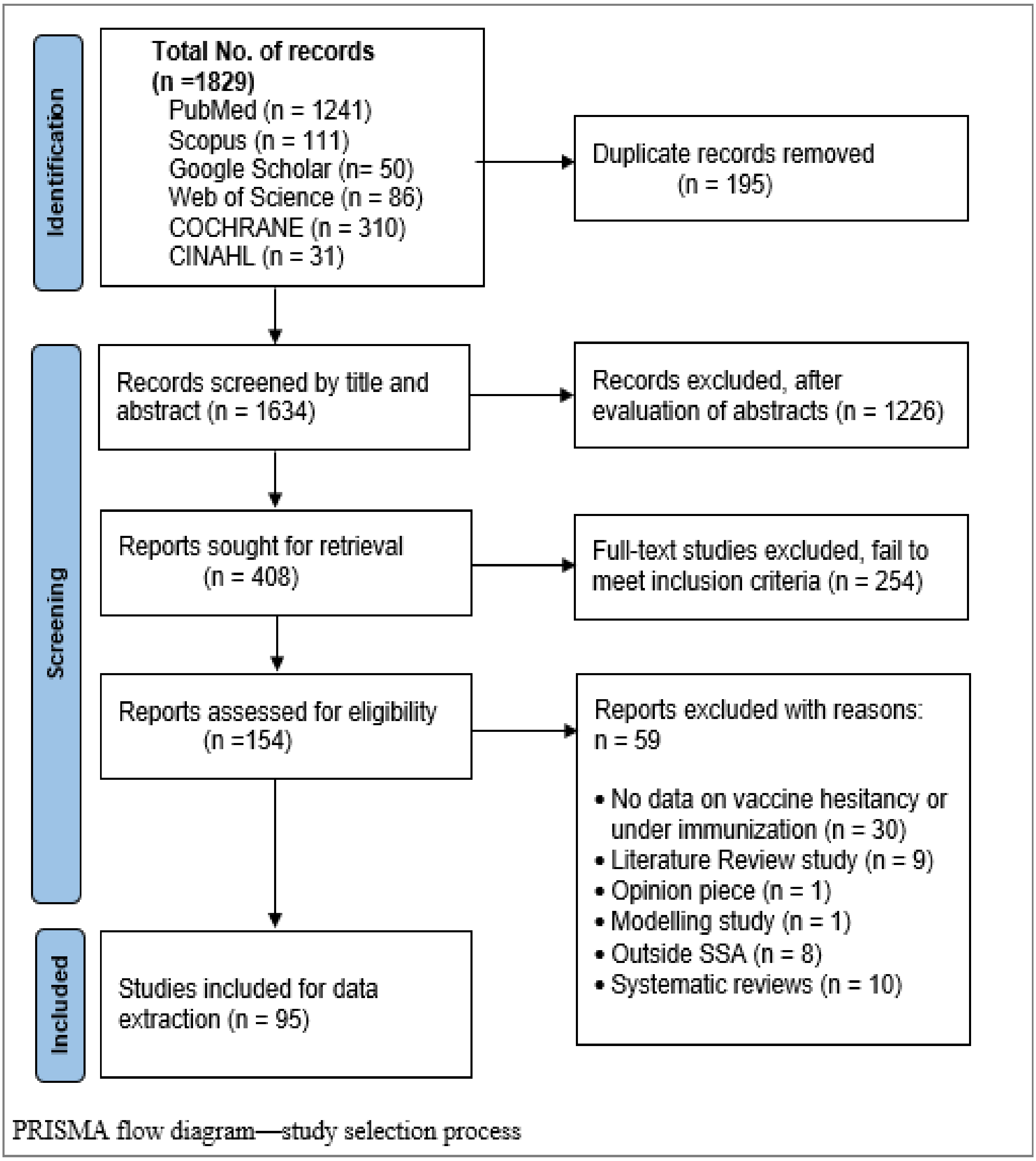

Figure 12: PRISMA Flow diagram showing study selection process.

Table 22: Table showing studies included into the systematic review

	ARTICLE TITLE	COUNTRY
1.	Abadura, S. A., Lerebo, W. T., Kulkarni, U., & Mekonnen, Z. A. (2015). Individual and community level determinants of childhood full immunization in Ethiopia: a multilevel analysis. *BMC public health*, *15*(1), 1-10.	Ethiopia
2.	Abdulraheem, I. S., Onajole, A. T., Jimoh, A. A. G., & Oladipo, A. R. (2011). Reasons for incomplete vaccination and factors for missed opportunities among rural Nigerian children. *Journal of Public Health and Epidemiology*, *3*(4), 194-203.	Nigeria
3.	Acharya, P., Kismul, H., Mapatano, M. A., & Hatløy, A. (2018). Individual-and community-level determinants of child immunization in the Democratic Republic of Congo: a multilevel analysis. *PloS one*, *13*(8), e0202742.	Congo
4.	Addo, P. C., Kulbo, N. B., Sagoe, K. A., Ohemeng, A. A., & Amuzu, E. (2021). Guarding against COVID-19 vaccine hesitance in Ghana: analytic view of personal health engagement and vaccine related attitude. *Human Vaccines & Immunotherapeutics*, *17*(12), 5063-5068.	Ghana
5.	Adetokunboh, O. O., Uthman, O. A., & Wiysonge, C. S. (2018). Non-uptake of childhood vaccination among the children of HIV-infected mothers in sub-Saharan Africa: A multilevel analysis. *Human Vaccines & Immunotherapeutics*, *14*(10), 2405-2413.	Sub-Saharan Africa
6.	Adeyanju, G., Betsch, C., & Sprengholz, P. (2021). Understanding Drivers of Vaccine Hesitancy among Pregnant Women in Nigeria: A Longitudinal Study.	Nigeria
7.	Adeyanju, G. C., Betsch, C., Adamu, A. A., Gumbi, K. S., Head, M. G., Aplogan, A., ... & Essoh, T. A. (2022). Examining enablers of vaccine hesitancy toward	Malawi

routine childhood and adolescent vaccination in Malawi. *Global health research and policy*, *7*(1), 1-10.

8. Amuzie, C. I., Odini, F., Kalu, K. U., Izuka, M., Nwamoh, U., Emma-Ukaegbu, U., & Onyike, G. (2021). COVID-19 vaccine hesitancy among healthcare workers and its socio-demographic determinants in Abia State, Southeastern Nigeria: a cross-sectional study. *The Pan African Medical Journal*, *40*. Nigeria

9. Aregawi, H. G., Gebrehiwot, T. G., Abebe, Y. G., Meles, K. G., & Wuneh, A. D. (2017). Determinants of defaulting from completion of child immunization in Laelay Adiabo District, Tigray Region, Northern Ethiopia: a case-control study. *PloS one*, *12*(9), e0185533. Ethiopia

10. Arnaud EMD. Immunization Coverage and Factors Associated with the Non-Completeness of Vaccination of Children from 12 to 23 Months of the Health District of Djoungolo-Cameroon in 2012. Texila Int J Public Heal. 2020;8(1):164–8. Cameroon

11. Asfaw, A. G., Koye, D. N., Demssie, A. F., Zeleke, E. G., & Gelaw, Y. A. (2016). Determinants of default to fully completion of immunization among children aged 12 to 23 months in south Ethiopia: unmatched case-control study. *Pan African Medical Journal*, *23*(1). Ethiopia

12. Adeyanju, G., Betsch, C., & Sprengholz, P. (2021). Understanding Drivers of Vaccine Hesitancy among Pregnant Women in Nigeria: A Longitudinal Study. Senegal

13. Babalola, S. (2011). Maternal reasons for non-immunisation and partial immunisation in northern Nigeria. *Journal of paediatrics and child health*, *47*(5), 276-281. Nigeria

14. Babirye, J. N., Engebretsen, I., Rutebemberwa, E., Kiguli, J., & Nuwaha, F. (2014). Urban settings do not ensure access to services: findings from the Uganda

	immunisation programme in Kampala Uganda. *BMC health services research*, *14*(1), 1-12.	
15.	Bhopal, S., & Nielsen, M. (2021). Vaccine hesitancy in low-and middle-income countries: potential implications for the COVID-19 response. *Archives of Disease in Childhood*, *106*(2), 113-114.	Sub-Saharan Africa
16.	Brown, J., Djogdom, P., Murphy, K., Kesseng, G., & Heymann, D. (1982). Identifying the reasons for low immunization coverage. A case study of Yaounde (United Republic of Cameroon). *Revue d'epidemiologie et de sante publique*, *30*(1), 35-47.	Cameroon
17.	Chido-Amajuoyi, O. G., Wonodi, C., Mantey, D., Perez, A., & Mcalister, A. (2018). Prevalence and correlates of never vaccinated Nigerian children, aged 1–5 years. *Vaccine*, *36*(46), 6953-6960.	Nigeria
18.	Chutiyami, M., Salihu, D., Bello, U. M., Winser, S. J., Gambo, A. A., Sabo, H., ... & Kannan, P. (2022). Are Fear of COVID-19 and Vaccine Hesitancy Associated with COVID-19 Vaccine Uptake? A Population-Based Online Survey in Nigeria. *Vaccines*, *10*(8), 1271.	Nigeria
19.	Cockcroft, A., Usman, M. U., Nyamucherera, O. F., Emori, H., Duke, B., Umar, N. A., & Andersson, N. (2014). Why children are not vaccinated against measles: a cross-sectional study in two Nigerian States. *Archives of Public health*, *72*(1), 1-10.	Nigeria
20.	Cutts, F. T., Rodrigues, L. C., Colombo, S., & Bennett, S. (1989). Evaluation of factors influencing vaccine uptake in Mozambique. *International journal of epidemiology*, *18*(2), 427-433.	Mozambique

21.	du Loû, A. D., & Pison, G. (1994). Barriers to universal child immunization in rural Senegal 5 years after the accelerated Expanded Programme on Immunization. *Bulletin of the World Health Organization*, *72*(5), 751.	Senegal
22.	Ekouevi, D. K., Gbeasor-Komlanvi, F. A., Yaya, I., Zida-Compaore, W. I., Boko, A., Sewu, E., ... & Landoh, D. E. (2018). Incomplete immunization among children aged 12–23 months in Togo: a multilevel analysis of individual and contextual factors. *BMC Public Health*, *18*(1), 1-10.	Togo
23.	Engelbrecht, M., Heunis, C., & Kigozi, G. (2022). COVID-19 Vaccine Hesitancy in South Africa: Lessons for Future Pandemics. *International Journal of Environmental Research and Public Health*, *19*(11), 6694.	South Africa
24.	Etokidem, A. J., & Ndifon, W. (2013). Myths and misconceptions as barriers to uptake of immunization services in Nigeria. *J Vaccines Vaccination*, *4*(7), 204.	Nigeria
25.	Ettarh, R. R., Mutua, M. K., & Kyobutungi, C. (2012). Ethnicity and delay in measles vaccination in a Nairobi slum. *Tropical medicine and health*, *40*(2), 59-62.	Kenya
26.	Evans, D. R., Yemeke, T. T., Kiracho, E. E., Mutebi, A., Apolot, R. R., Ssebagereka, A., & Ozawa, S. (2019). Trust in vaccines and medicines in Uganda. *Vaccine*, *37*(40), 6008-6015.	Uganda
27.	Faye, S. L. B., Krumkamp, R., Doumbia, S., Tounkara, M., Strauss, R., Ouedraogo, H. G., ... & Fusco, D. (2022). Factors influencing hesitancy towards adult and child COVID-19 vaccines in rural and urban West Africa: a cross-sectional study. *BMJ open*, *12*(4), e059138.	West Africa
28.	Ghinai, I., Willott, C., Dadari, I., & Larson, H. J. (2013). Listening to the rumours: what the northern Nigeria polio vaccine boycott can tell us ten years on. *Global public health*, *8*(10), 1138-1150.	Nigeria

29.	Gibson, D. G., Ochieng, B., Kagucia, E. W., Obor, D., Odhiambo, F., O'Brien, K. L., & Feikin, D. R. (2015). Individual level determinants for not receiving immunization, receiving immunization with delay, and being severely underimmunized among rural western Kenyan children. *Vaccine*, *33*(48), 6778-6785.	Kenya
30.	Janusz, C. B., Frye, M., Mutua, M. K., Wagner, A. L., Banerjee, M., & Boulton, M. L. (2021). Vaccine delay and its association with undervaccination in children in sub-Saharan Africa. *American Journal of Preventive Medicine*, *60*(1), S53-S64.	Sub-Saharan Africa
31.	Jegede, A. S. (2007). What led to the Nigerian boycott of the polio vaccination campaign?. *PLoS medicine*, *4*(3), e73.	Nigeria
32.	Kabudi, A. M., Lutala, P. M., Kazadi, J. M., & Bardella, I. J. (2015). Prevalence and associated factors of partially/non-immunization of under-five in Goma city, Democratic Republic of Congo: a community-based cross-sectional survey. *Pan African Medical Journal*, *20*(1).	Democratic Republic of Congo
33.	Kapp, C. (2004). Nigerian states again boycott polio-vaccination drive. *The Lancet*, *363*(9410), 709.	Nigeria
34.	Khosa, L. A., Meyer, J. C., Motshwane, F. M., Dochez, C., & Burnett, R. J. (2022). Vaccine hesitancy drives low human papillomavirus vaccination coverage in girls attending public schools in South Africa. *Frontiers in Public Health*, *10*.	South Africa
35.	Yenit, M. K., Assegid, S., & Abrha, H. (2015). Factors associated with incomplete childhood vaccination among children 12–23 months of age in Machakel Woreda, East Gojjam Zone: aCase-controlStudy. *Journal of Pregnancy and Child Health*, *2*(4), 180.	Ethiopia

36.	Landoh, D. E., Ouro-Kavalah, F., Yaya, I., Kahn, A. L., Wasswa, P., Lacle, A., ... & Soura, A. B. (2016). Predictors of incomplete immunization coverage among one to five years old children in Togo. *BMC Public Health*, *16*(1), 1-7.	Togo
37.	Le Polain de Waroux, O., Schellenberg, J. R. A., Manzi, F., Mrisho, M., Shirima, K., Mshinda, H., ... & Schellenberg, D. M. (2013). Timeliness and completeness of vaccination and risk factors for low and late vaccine uptake in young children living in rural southern Tanzania. *International health*, *5*(2), 139-147.	Tanzania
38.	Li, A. J., Tabu, C., Shendale, S., Okoth, P. O., Sergon, K., Maree, E., ... & Ogbuanu, I. U. (2020). Qualitative insights into reasons for missed opportunities for vaccination in Kenyan health facilities. *PloS one*, *15*(3), e0230783.	Kenya
39.	Machekanyanga, Z., Ndiaye, S., Gerede, R., Chindedza, K., Chigodo, C., Shibeshi, M. E., ... & Kaiser, R. (2017). Qualitative assessment of vaccination hesitancy among members of the apostolic church of Zimbabwe: a case study. *Journal of religion and health*, *56*(5), 1683-1691.	Zimbabwe
40.	Magodi, R., Mmbaga, E. J., Massaga, J., Lyimo, D., Mphuru, A., & Abade, A. (2019). Factors associated with non-uptake of measles-rubella vaccine second dose among children under five years in Mtwara district council, Tanzania, 2017. *The Pan African Medical Journal*, *33*.	Zimbabwe
41.	Mahachi, K., Kessels, J., Boateng, K., Achoribo, A. E. J. B., Mitula, P., Ekeman, E., ... & Gabrielli, A. F. (2022). Zero-or missed-dose children in Nigeria: Contributing factors and interventions to overcome immunization service delivery challenges. *Vaccine*.	Nigeria
42.	Malande, O. O., Munube, D., Afaayo, R. N., Chemweno, C., Nzoka, M., Kipsang, J., ... & Owino-Okongo, L. (2021). Adverse events following immunization reporting and impact on immunization services in informal	Kenya

settlements in Nairobi, Kenya: a prospective mixed-methods study. *The Pan African Medical Journal*, *40*.

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The inability to access the vaccination centres due to the illness, or financial problems or handicap of caregivers or child were the most reported determinants. About 15% of reasons were contextual influences as drivers of vaccine hesitancy, and these comprise religious, cultural, socioeconomic and gender barriers, as well as political and geographic issues. There were family related caregiver cross cultural issues that relate to male involvement or family head/father refusal to consent for vaccination. Geographical and contextual barriers also relate to poor geographical terrain, refugee status, residents of migrant communities and ever mobile populations that have problems finishing or completing the recommended immunization schedules.

The majority of studies included focused on routine childhood immunisation, and the studies included caregivers as main participants who gave responses on their hesitancy to current vaccines and their use in children. The drivers/determinants from these studies related to group and individual influences. These factors related to their lack of satisfaction with the health system, poor male partner support to facilitate attendance of immunization visits, forgetting to attend scheduled visits, low or inadequate knowledge or awareness regarding vaccine and scheduling, and competing interests especially the interruption of where they have to attend other activities like their own work or farm duties.

The vaccine factors included adverse events following immunization especially fever, pain, swelling at injection site and malaise. The pentavalent and pneumococcal vaccines were largely attributed to most AEFIs causing failure to attend subsequent immunization visits. Among study participants who were making their own independent decision to or not to vaccinate themselves, the most common/frequently reported reason(s) for vaccine refusal were the individual fear of side effects, the inability to access vaccination sites, interruption of the time that is normally used for other activities like work etc, long waiting hours, short immunization site open hours and the low trust when vaccines are offered for free.

One other factor identified to be a driver of hesitancy were Contextual issues within campaigns, especially those related to religious or cultural or gender or socioeconomic and political factors. Politicians can be a potent source of messages that can hinder vaccine uptake. Supportive political messages and sentiments by influential political leaders can play a major role as a driver for vaccine uptake, especially during immunization campaigns for both introduction and catch up vaccination programs. Political and cultural leaders play a key role of shaping opinions, and religious leaders to a great extent influence individual participant’s in making their decision on vaccines. This influence cuts across, whether these caregivers were independently making their decision to or not to get themselves vaccinated, or making the decision as to whether a caregiver should let their child or his/her dependent to get vaccinated.

Objective 5: To compare and contrast the drivers of vaccine hesitancy and under-immunization in rural (Hoima) versus urban/peri-urban (Wakiso) Districts of Uganda.

In the table below, the comparisons and contrasts that exist in drivers of hesitancy in Hoima and Wakiso districts are highlighted. Majority of the determinants are similar and cut through both the rural and the urban/peri-urban districts.

Table 23: Drivers of vaccine hesitancy and underimmunization in rural (Hoima) versus urban (Wakiso) Districts

Variable	**Hoima District**	**Wakiso District**
Immunization coverage	They were daily static immunization days carried out on the Hoima regional referral hospital, Most of the HC II and HC III s were carrying out static immunization once in a week Most of HC II, HCIII, HC IV had at least one day of outreach immunization services in a week Most of the HC IV were carrying out static immunization services twice in a week Regional Hospital was immunizing at least 1000 children in a month, HC IV at least 500, HC III at least 300 and HC	They were daily static immunization days carried out at Wakiso and Entebbe level B hospital, Most of the HC II and HC III s were carrying out static immunization once in a week Most of HC II, HCIII, HC IV had at least one day of outreach immunization services in a week Most of the HC IV were carrying out static immunization services twice in a week

	II like 80 children in a month in both static and outreach	
Staffing and staff training needs affecting static, support supervision and outreach activities	Most of the Health Facilities were understaffed which negatively affected carrying out immunization outreach services for instance Kyangwali Health Centre IV, Buchayaya HC III, Munteme HC II and Rwenyawawa Health Centre III. Concerns around very high workload due understaffing were reported in Rwenyawawa Health Centre III, Munteme HC II and Kyangwali Health Centre IV in Hoima District and in Entebbe, Kiira HC IV, Wakiso HV IV, and Namayumba HC IVin Wakiso District. The district immunization teams would love to do regular support supervision for the immunizing sites in Hoima and Wakiso districts, but inadequate funding and transport facilitation remains the biggest challenge to this.	
Child factors – including being an orphan and preexisting illness	It emerged from the focus group discussions and KIIs that children who are orphaned and therefore not having stable parental care; or children who have a pre-existing chronic illness like cerebral palsy or cancer or mental illness are likely to miss vaccination scheduled visits or appointments in both Hoima and Wakiso. The same applies to children born pre-mature or with existing congenital disorders. This however did not vary in children based on gender or birth order.	
Reporting of AEFIs	Caregivers reported that they were AEFIs. The major AEFIs reported by mothers were fever and swellings. Some Health facilities have a reporting tool/booklet for reporting these cases, but reporting is poor. Ndwooli HC III	Caregivers reported AEFIs, especially attributed to MR vaccine introduction. The major AEFIs reported by mothers were fever, pain, swelling at injection site and alleged neurological sequalae.

	and Buhimba Health Centre have no AEFI tools.	
Vaccine storage, supply, stock outs and challenges	Health centres were getting supplies from UNCHR, District stores; BCG vaccine had the most stock outs especially in Kigorobya HC IV, Buhimba HC II and Dwooli HC III and Mende. Most of the times supply of vaccines at the district stores is inadequate, Most Health centres have cold chain system and use gas for power, use fridges to keep the vaccines but they reported issues of breakdowns. Wakiso has problems with electricity supply	
Transport and long-distance barriers	Most caregivers struggle due to lack of funds to access some facilities, some have no easly available transport means to access some facilities eg Butema Health Centre III, Kikube Health Centre, Sebigoro Health Centre III, Tonya Health Centre II and Butema Health Centre III, Mende HCIII.	
Location of the area	Facilities on the far periphery including within refugee camps and on Congo Border eg Kyangwari and Rwenyawawa find it hard to monitor and complete immunization	Only far located facilities like Mende HC III were affected
Language barrier and immigrant or refugee status of caregivers	Due to a very cosmopolitan and migrant population within the district, language barrier is a big challenge and a barrier to immunization services delivery as reported in areas especially with a lot of refugees like Rwenyawawa Health Centre III, Sebigoro Health Centre III and Tonya	N/A While language barrier may not be a big challenge in Wakiso – low level of caregiver education poses significant challenge to caregivers in understanding the available vaccines, the immunization schedule and the rationale behind immunization.

	Health Centre II. In such facilities they mainly speak Kiswahili, Runyarwanda and Alur which is hard for health workers	
Limited sensitization about immunization and its benefits and caregiver peer support	Caregivers and community focal persons complained about the lack of adequate community education and social mobilization on the benefits and importance of immunization. These were reported in Entebbe, Kiira HC IV, Namayumba HC IV, and Namulonge HC IV in Wakiso and Butema HC III, Buhimba HC III in Hoima District. It was reported in the focus group discussions that participants with good peer support were more likely to bring their children for immunization and were more likely to be receptive to new vaccines.	
Attitudes of Health workers	Though the health workers are doing their best, often time sin very difficult circumstances, caregivers did complain about negative attitude of health workers as a barrier to access and uptake of immunization services. These were reported in Kiragura Parish and Mparangasi HC III and Buhimba HC III.	
Cultural and religious barriers	The study discovered that in Buhimba East, Buhanika and Kikube HC III there is a religion of Owobusobozi in which their God (owobusobozi) that discourage their followers from taking their children for immunization. In Kabwooya HC, it was reported also some clans believe that they shouldn’t be immunized.	No cultural barriers identified, but religious barriers thought to exist.

Limited support from fathers/male partners; gender; marital status and age of caregiver	In Kigorobya HC IV, and several other HCs in Wakiso and Hoima, caregivers gave examples of fathers/male partners failed to provide transport money or permission or consent for mothers to take their children for immunization. There was no big difference in marital status and gender as drivers of hesitancy and underimmunization, though available data favored being married with a supportive male partner as a facilitator to uptake of immunization services. In both studies, teenage mothers or children cared for by elderly grandmothers were more likely to miss scheduled immunization visits.
Caregiver attitude towards immunization	Caregivers reported that fellow mothers at different health facilities, which include Kigorobya HC IV, believe that all those injections given at 6, 10- and 14-weeks vaccination "are meant to kill our children." It was also reported in Kabwoya Health Centre III that most times mothers who get pregnant and deliver without visiting the hospital for antenatal are unlikely not bring their children for immunization.

Evaluation of Findings

The study evaluated the barriers to the uptake and utilization of immunization services in Wakiso and Hoima districts, and possible drivers of underimmunization and hesitancy based on the WHO SAGE working group recommended matrix for determinants (see table below). The table shows which determinants returned a positive/yes outcome from the findings, meaning that it was found to apply to the study population, or NO, meaning it either did not apply to the respondents or that on the balance of available information from the study, the researcher could not adequately strongly associate the finding to the WHO Working Group on Vaccine Hesitancy Determinants Matrix.

Table 24: Vaccine Hesitancy Determinants Matrix as compared to results from the districts and systematic review

	Determinants	**Hoima**	**Wakiso**	**Systematic Review**
CONTEXTUAL INFLUENCES				
Influences arising due to historic, socio-cultural, environmental, health system/institutional, economic or political factors	a. Communication and media environment	Yes	Yes	Yes
	b. Influential leaders, immunization programme gatekeepers and anti- or pro-vaccination lobbies	Yes	Yes	Yes
	c. Historical influences	Yes	Yes	Yes
	d. Religion/culture/gender/socio-economic	Yes	Yes	Yes
	e. Factors dependent on political stability and policy	Yes	Yes	Yes
	f. Geographic barriers	Yes	Yes	Yes
	g. Perception of the pharmaceutical industry	No	No	Yes
INDIVIDUAL AND GROUP INFLUENCES				

Influences arising from personal perception of the vaccine or influences of the social/peer environment	a. Personal, family and/or community members' experience with vaccination, including pain	Yes	Yes	Yes
	b. Beliefs, attitudes about health and prevention	Yes	Yes	Yes
	c. Knowledge/awareness	Yes	Yes	Yes
	d. Health system and providers – trust and personal experience	Yes	Yes	Yes
	e. Risk/benefit (perceived, heuristic)	Yes	Yes	Yes
	f. Immunization as a social norm vs. not needed/harmful	Yes	Yes	Yes
VACCINE/ VACCINATION				
specific issues Directly related to vaccine or vaccination	a. Risk/benefit (epidemiological and scientific evidence)	No	No	Yes
	b. Introduction of a new vaccine or new formulation or a new recommendation for an existing vaccine	Yes	Yes	Yes
	c. Mode of administration	Yes	Yes	Yes
	d. Design of vaccination programme/Mode of delivery (e.g., routine programme or mass vaccination campaign)	Yes	Yes	Yes
	e. Reliability and/or source of supply of vaccine and/or vaccination equipment	No	No	Yes
	f. Vaccination schedule	Yes	Yes	Yes
	g. Costs	No	No	Yes
	h. The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals	Yes	Yes	Yes

Additionally, besides the summary of findings being aligned to the matrix table, the study further explored the quantitative research findings using the qualitative methods through triangulation and aligned them along the following themes:

Theme I: The Knowledge, the attitudes and the perceptions of caregivers towards immunization

a) Knowledge about immunization

The focus groups revealed a satisfactory level of knowledge about immunization:

Immunization prevents occurrence of VPDs

Most caregivers understood that immunization protects their children from diseases. A few further understood that an immunized child may still get sick even if vaccinates, but they will suffer from a weak manifestation of the disease and immunized individuals are protected from disabilities arising from VPDs like polio.

> *"... vaccines are important in prevention of illnesses and diseases like being lame due to polio."* (FGD in Buseruka; Single mother with two children but no formal education)

Some caregivers thought that vaccines offer full protection, while some said that immunization does not provide 100% protection hence no complete guarantee of protection from diseases.

> *"……. If a child has received immunization, he has a lot of energy when compared to a non-immunized child..."* (FGD in Tonya, Married mother two children)
>
> "… *immunization and vaccines are very important, since vaccinated children may get no infection or only mild infection."* (FGD – Kyangwari, single mother of three children)

Theme II: State of Immunization Services in Hoima And Wakiso Districts

Availability and quality of immunization services

Caregivers were asked for their view regarding the overall delivery of immunization services. Diverse respondents had different responses about this matter as shown below.

The Buhimba HC II EPI focal person had this to say about their immunization coverage, he noted that;

"We do static immunization on Tuesday and outreach on Thursday but for babies of the mothers who have just delivered, they receive immunization in the hospital on day one. In a month we immunize at least They rage 150-200 and some who come from very far miss out on the immunization services."

An immunization in charge in Rwenyawawa pointed out that;

"Vaccination is done once in a week and we immunize approximately 300 children in a month. It is usually done on Tuesday. We do conduct immunization outreaches. We usually go to Kangoma and Ketomi depending on the need. Usually the outreach is done on Mondays".

The EPI focal person in Tonya HC II had this to say;

"Approximately in a month we immunize may be like 80 plus, Static we have once a week, outreach it also depends but we go once a week. We are all seven-health workers at the facility. Approximately four cover immunization clinics."

The Chairman LC 3 Mparangasi said:

"We have 4 parishes and one parish has a health centre III, we have 5 facilities that offer immunization services but we have one more under Bunyoro- Kitara diocese by maternity international. So we have six facilities offer immunization".

The Hoima Referral Hospital EPI focal person responded:

"*We do static immunization daily, we don't do any outreach, we immunize 450 children in a week, and reach 1000 babies on average in a month."*

Staffing and staff training needs

The study also aimed at finding out the status of staffing and staff training needs in Hoima district, the respondents had diverse expressions about staffing as shown below.

The Hoima Regional referral EPI Focal person had this to say about staffing;

"We have a shortage but we rotate so in this unit, we have 1 senior nursing officer, 4 nursing officers, 2 enrolled midwives and 2 nursing assistants. So they are nine. But right now, we usually have one person in the clinic."

The In-charge Rwenyawawa Health Centre III had this to say about staffing;

"We are about 30 staff including the non-health staff, the cleaner and the security. Currently, there midwives are the one in charge of immunization and they are 4 midwives and they rotate according to the schedule. We have someone specifically in charge of immunization."

On the matter of staffing, the Buhimba HC II EPI focal person pointed out that;

"We have 14 staff at this facility, including medical and non-medical staff, and 2 nurses are assigned to run the immunization clinic".

Status of cold chain in Hoima district Health facilities

Ideal temperature monitoring and regulation is an integral part of the vaccine or the immunization supply chain. The cold chain consists of a series of links that are designed to keep vaccines within World Health Organization recommended temperature ranges, from the point of manufacture to the point of administration. In order to maintain a reliable vaccine cold chain at the peripheral level, the following key procedures must be observed: store vaccines and diluents within the required temperature range at all sites, pack and transport vaccines to and from outreach sites according to recommended procedures and keep vaccines and diluents within recommended cold chain conditions during immunization sessions.

To establish the status of the cold chain system in the district, health workers were asked questions about whether they had cold chain system in place to prevent vaccine spoilage, the source of power for the refrigerator and whether they experience malfunctioning of equipment's. If so, how often? What measures are taken to correct this? How long does it take for the system to be fully operational after breakdown?

An EPI focal person from Dwooli Health Centre III had this to say about the current cold chain system;

"Yes we have; We have a fridge, we monitor the temperatures, we have vaccine control books, we have child registers, so we are able to make our system. Power supply is gas but has a problem of inconsistent supply. It can go off, it's at night or weekend and you don't have transport to get what to replace it yet it's supposed to. Even our fridge is old model. It goes off even when gas is still on. About 3 times since 2013 when I came here. We have reported that and they are planning replacement of a solar fridge. It freezes so easily too so you have to keep defrosting. It takes about a day to fix".

An EPI focal person from Bujumbura Health Centre III had this to say on the cold chain;

"Yes, we have a cold chain system. We have Electricity and solar for powering the fridge. The fridge has been disturbing us. We called the district officers and they came and worked on it and it has stabilized. They also promised to get us a new refrigerator. It took a month to have the system worked upon. We had another fridge where we kept the vaccines until the refrigerator was worked upon".

A health Assistant in-charge of Sebigoro Health Centre III had this to say about the cold chain at the facility;

"Yes, we do have the cold chain system, which is powered by solar; so far we have not had any malfunctioning of the equipment. We have contacts of the people who are in charge of the cold

chain system. They tell us that in case of any challenge, we call them within the shortest time possible".

They were some good reports made by some health workers on the cold chain system, for instance the Kabwoya Health Centre Immunization focal person said;

"Yes we do have a cold chain system. The refrigerator is powered by electricity. It has never failed to work".

From Butema Health Centre III, the Immunization focal person said;

"We are updated on immunization schedules because they are pinned on the notice board, everyone is aware of the cold chain system. The communication is communicated to the in charge who communicated to us during staff meetings".

The EPI focal person in Munteme Health Centre II said;

"Not all staff are updated only the ones that cover the immunization clinic, we have never been updated".

In line with the report from Munteme Health Centre, the Head of Immunization from Mparangasi said that;

"We are all updated. We get communication from support supervision. We rarely get communications on update".

A focal person from Buchayaya Health Centre III had some concerns;

"Yes, we have a cold chain system our source of power is gas. We experience malfunctioning of the system occasionally. We call the cold chain people, because gas had issues. The

refrigerator we have, at times the temperatures get so low and like in the morning, it has frozen and when you tamper with it, the temperatures get to alarm. Sometimes to reads zero. When there is breakdown in the system, it takes a week for to be worked on".

Record keeping

The focal persons and health workers were asked about record keeping, health information management and transmission of immunization data.

The EPI Buhimba Health Centre II had this to say about record keeping;

"Because of very few health staff, we have asked the record personnel to assist cover the immunization outreach service"

Health assistant Kigorobya HC IV stressed that;

"Sometimes record keeping about immunization is not consistent. In most cases in outreaches, they offer transport and per-diem is given so no problems though it delays to come".

The Health Assistant of Kigorobya had this to say;

"Sometimes record keeping about immunization is not consistent."

The Hoima Hospital cell LCI leader had this to say about record barriers, he noted that;

"It is hard to have records of who has already immunized or not for follow up."

Ways in which the communities can be encouraged to demand for immunization services

The demand creation for Immunization services is a crucial issue; therefore, respondents were asked about ways that the communities could be promoted to enhance demand creation.

LC I Secretary Buhimba County had this to say:

"They mobilize announce and sensitize and keep telling mothers to take children for immunization and ask for vaccination and deworming for children".

Similar to caregivers from Kikube HC III, those interviewed in the FGD held at Munteme HC II had this to say;

"People should be sensitized on the dangers of not immunizing and the importance of immunization. The health facilities are far, the government should come to the villages to teach us how we should take care of our children."

Findings from focus group discussions among caregivers attending Buseruka Health Centre III stressed that;

"Health workers should educate people about the vaccines that available and how they help the children. We need outreach services and if possible, they can provide transport."

Findings from the FGD held at Hoima Regional Referral Hospital, caregivers pointed out the following measures for immunization services demand creation they had this to say;

"We should get more sensitization about the value of immunization may be the people who are reluctant about immunization can also get involved. The hospital should invite all the people with children and pregnant mothers and put a law that everyone should immunize their children."

Both the LC I Secretary and Chairman LC 3, Mparangasi sub county had this to say;

"We as local leaders should continue to sensitize the community to empower them demand for these services".

A VHT member Buhimba had this to say;

"We need to educate the mothers on why they should immunize children so that they know the importance of immunization because educating and learning never stops".

In line with the previous respondent, a VHT member of Kabwoya Health Centre III had this to say;

"We as the people e need to mobilize ourselves, we need to go through the leaders have elected from the as low as the LC I up to the top leaders".

He also added that;

"We need to sensitize and health educate the people about immunization so that people know why its done".

Findings from the FGD held with mothers from Buchayaya Health Centre III revealed that;

"Health workers should continue to advertise. We should be told the importance of immunization. Health facilities should stock more vaccines in the health facilities. The people should be educated well on the vaccines and medicines that they introduce because some people have poor perceptions on the medicines and drugs".

In the same line the FGD held with mothers immunizing from Kikube HC III, they suggested the following methods to promote immunization services in the community. They had this to say;

"They should sensitize and educate them. They should give outreach service. They should be lured like giving them incentives to make them bring their children for immunization."

Findings from the FGD held at Tonya Health Centre II suggested the following measure to create demand for immunization services, they noted;

"They should mobilize the community and informing them of immunization dates. Health workers do not have transport to do outreach services; this facility has 9 villages under it. The government should give health workers transport".

Mothers immunizing from Bujumbura HC III who attended the FGD suggested the following measures to improve demand for immunization services, they pointed out that;

"They should find us in the villages and educate us about immunization because in the villages people don't know the importance of immunization. Increase outreach programs so that the people may be sensitized and minimize the transport challenges."

The LC 1 Secretary Buhimba East emphasized about outreaches that;

"We should also have outreach service weekly to help in reaching all mothers. The government should also put a way to ease transport to encourage mothers to get to the facility in time so that they do not have any excuse."

Theme III: Gaps in immunization service provision promoting low vaccine uptake or completion of recommended schedules

Transport and long-distance barriers

The Sebigoro Health Centre III, Assistant Clinical officer had this to say;

"The challenge is actually transportation like travelling to Hoima is expensive in times of emergencies".

In the same line the in charge from Kikube Health Centre had this to say;

"The challenge we face at the facility is lack of transport and the staff who go for outreach are women and cannot ride boda boda".

The challenge of transport was also mentioned by the Butema Health Centre III, he had this to say;

"When we go for out reaches transport is not enough and the funds do not come in time(EPI Focal person for Immunization."

The LC1 Secretary Buhimba East had this to say on transport barriers, she noted that;

"There is a challenge of long distances the villages are wide. It's hard for mothers to make it to the facility to immunization due to the long distances"

The VHT from Butema Health Centre III stressed that;

"Some of them complain about the long distances and that why we introduce outreach services".

One respondent from Tonya Health Centre II, had this to say on transport costs, she stressed that;

"Health workers don't have transport to do outreach services, this facility has 9 villages under it and therefore the government should give health workers transport".

The EPI focal person at the Hoima Regional Hospital had this to say about transport, she pointed out that;

"We have a problem of transport especially when the vaccines are finished. We need to book early enough because the hospital has few. We also have that challenge of vaccines running out at the district."

In line with the previous respondent, the VHT Kabwooya HC III had this to say on the transport issues;

"There is barrier on distance; there is a long distance from people's home to the facility, for example from my village to the facility is 10,000 so it's hard for someone to pay that money just for immunization."

Location of the area

The VHT Kikube HC III highlighted the geographical location of the area as a barrier to immunization services, he pointed out that;

"Hoima is located at the shores of lake Albert, it had many outlets, there is free entry from Congo, so you find many people come in. during immunization days, there are few people who have negative attitude and they don't take it serious to go for immunization, they keep saying I will go on the last day and even on the last day they get another program and end up missing immunization. So they cause our target not be 100%."

The LCI Hoima Hospital Cell had this to say about the location of the area;

"Because Hoima is on the border, we have many people coming from Congo, you find after delivering, you find a woman after three months they have not had immunization because they go back to Congo and don't turn up for immunization".

Limited health facilities

The LC III Kabwoya had this to say related to transport challenges, he pointed out that;

"The parents are willing and they love to bring their children for immunization apart from a few because of distances to the facilities. The other reason for not turning up for immunization is that the sub county is as big as some districts in the country yet we have one serving health facility so because of long distances some mothers don't turn up".

In line with the previous respondent, the Chairman LCI Munteme had this to say about health facility shortage;

"We need more facilities. Otherwise we are okay; the people are involved in immunization here."

Vaccine stock outs and inadequate supply problems

The Incharge of Buchayaya Health Centre III had this to say on vaccine supply;

"The district stores supply us. I would say yes, the supply is adequate but at times we get stock out of BCG which can last for a month and at times and measles. Like a month ago, the whole district did not have BCG vaccine. And in some month, we never had measles vaccine."

The Incharge from Rwenyawawa HC III which is located in the refugee camp had this to say on vaccine matters;

"We usually get the vaccines from the UNCHR store, which supplies us. The supply is adequate because I have not had any stock out except currently we have a challenge with diluents. We don't know how they miss out because they are supposed to come with the vaccines. We mostly do not have the measles diluents."

The Assistant Incharge of Sebigoro Health Centre III located near the Lake Albert landing site had this to say about vaccines;

"The district, Hoima district supplies the vaccines and yes, the supply is adequate unless the vaccines are not out of stock nationwide."

The EPI focal person from Buhimba Health Centre II, had this to say about vaccine matters;

"Actually, we don't have suppliers; we pick the vaccines from the district by ourselves. From the district, the supply is not adequate because currently there are some vaccines we are missing and we have missed them for quite some time now i.e. BCG. I cannot tell how often but the affected drugs are IPV, BCG and HPV."

The EPI focal person of Kabwoya Health Centre III said that;

"I have been picking the vaccines from the DVS, and generally we have had vaccines except for some months when BCG and OPV were out of stock."

The immunizing nurse in Butema Health Centre III had this to say about vaccine matters;

"We pick the drug by ourselves from the district stores. We sometimes do not get them because they say they don't have transport or they have stock outs. The supply is inadequate. It's a challenge that when one doesn't get the first immunization, they don't easily come back, they come back when it's too late. We have a challenge in BCG, polio and measles vaccines."

The Head of Immunization Munteme Health Centre II had this to say;

"The supply is not adequate because we have gone there three consecutive times and we don't have measles vaccine. Measles vaccine, BCG and IPV are often stocked out. The stock out happens almost every month. It's a challenge because when a mother doesn't get the vaccine for two consecutive visits, they don't come back."

The Assistant Head of Immunization Mparangasi Health Centre III, had this to say;

"We have experienced vaccine stock outs. BCG normally gets out of stocks because you cannot keep it. IPV also sometimes gets out of stock".

The VHT Kabwooya HC III had this to say about vaccine supply and stock outs;

"The vaccines are inadequate, because sometimes mothers come and don't find the vaccines. We get outreach services every Saturday. Sometime some mothers transport themselves up to Kabwooya HC III and still don't find the vaccines hence decide to wait until the outreaches are carried out. The vaccines come late and by the time they vaccines come, some people are busy and some are past the date of immunization then the drugs also get expired and the health workers can't tell us that vaccines are expired but instead say that the drugs are done."

The immunization in charge, Kyangwali Health Centre III said;

"Last week we did not have vaccines and this week we don't have vaccines. The mothers get discouraged to keep coming for immunization and they don't find vaccines".

Language barrier

LC Chairperson from Rwenyawawa said:

"there are many communities, some speak Runyakole, others Rukiga and others Rutoro. This can be a big communization and health education barrier."

While the head of Tonya Health Centre said;

"Most of our patients originate from Alur and do not speak Runyoro. A few speak Kiswahili. This makes communication a big problem".

Sebigoro Health Centre III Assistant in charge had this to say on the language barrier issue;

"We have a challenge of language barrier, they don't know English or Kiswahili so we keep asking them tactfully like how many months does this child have, we have different outreaches, we realize these people keep taking their children for all immunization outreaches which comes up and end up confusing mass immunizations with the routine immunization".

Limited sensitization about immunization and its benefits

On the issue of limited sensitization about immunization and its benefits, the VHT Butema HC III noted that;

"Some families are not well sensitized, they complain because they don't know side effects and importance of immunization.

The LC1 Secretary Buhimba had this to say on the issue of limited sensitization she emphasized that;

"Not all parents accept because some are not willing that need a little push. The biggest percentages do not know the importance of immunization. Before we had a challenge where some people thought that vaccines are harmful to children but we have tried to educate the people and people are now okay".

Understaffing and staff work load

The VHT from Rwenyawawa said;

"We have work overload. We have 30 staff but they are not enough just simply because the number of patients is too much and work is too much, for example we have OPD, the lab, we have the art clinic, there is immunization. We have four nurses but they should be six midwives in the sense that one if off, when she goes, she goes for leave and you have two midwives on duty, so we also have PMTC. Majorly its work overload".

In the same line the Munteme HC II, Head of immunization had this to say;

"There is understaffing, like if when one person is not around we cannot carry out outreach".

The EPI focal person Hoima regional referral hospital in line with staffing challenges pointed out;

"We have a shortage but we rotate so in this unit, we have 1 senior nursing officer, 4 nursing officers, 2 enrolled midwives and 2 nursing assistants. So they are 9. But right now, we usually have one person in the clinic."

In agreement to Munteme HC II, the Incharge of Buchayaya HC III had this to say;

"We are understaffed, like during outreaches, it's a challenge to do outreach when we are two staff".

The EPI focal person from Kyangwali Health Centre IV had this to say about workload;

"We have a big population, that even when we think we are doing a lot, there is a bigger population that is not accessing the services. Last week we did not have vaccines and this week we don't have vaccines. The mothers get discouraged to keep coming for immunization and they don't find vaccines".

Attitudes of Health workers

VHT Kiragura Parish had this to say on some health workers;

"Some doctors make immunization schedules and do not show. This annoys the people in communities and causes them to miss immunization the next time. The drugs sometimes do not come in a timely manner. People lose the morale when they bounce on health centers because of know drugs.

In the same line the VHT Mparangasi HC III had this to say on Health workers;

"When the health workers are not hospitable to the mothers or when you go there, they are slow…. the health workers speak rudely to the mothers, the health workers should be told on how to handle mothers not to talk to them rudely so that parents don't get discouraged to come for immunization."

In line with the previous respondent, the VHT Buhimba has this to say on the behaviour of Health workers he pointed out that;

"The health workers speak rudely to the mothers; the health workers should be told on how to handle mothers not to talk to them rudely so that parents don't get discouraged to come for immunization."

Limited facilitation for Health workers

There was also a barrier of inadequate financial facilitation for health workers to carry out outreach services. The EPI focal person Hoima regional referral hospital said;

"We don't conduct out reaches. We have left that for the district to perform. We lack funds to facilitate outreach activities. We would have loved to go to schools for TT but we lack funds. We have a health facility even around this place so we have left out reaches for these health facilities."

Cultural and religious barriers

In relation to culture, the VHT Buhimba East had this to say about some of the barriers that limit immunization services.

"We don't have such religion but we I have heard in another village that because God has told them not to take their children for immunization and to school."

The LCI Secretary Buhimba East on the matter of religious barriers pointed out that;

"A local group says that even Jesus was not immunized so there is no need for immunization for their children."

The VHT Buhanika had this to say about religious barriers;

"There is a religious cult called "egiri ya Yesu" that teaches against immunization and vaccines."

The VHT Kabwooya HC had this to say on the cultural barriers, he noted that;

"The major thing is cultural barrier and some clans believe that they shouldn't be immunized. The people have poor perspectives on immunization. The people are illiterate".

The VHT Kabwooya had this to say on cultural and religious barriers;

"The seventh day adverts because out reaches are done on Saturdays and adverts will not bring their children for immunization because it's a Saturday. In Kibale district, there was religion that encouraged their believers not immunize their children because if they did, the children will die earlier. But I don't understand the religion well."

One respondent from an FGD, who was immunizing at Bujumbura HC III, pointed out that;

"There are some religions that don't encourage mothers to come for immunization; they say that immunization makes children get more diseases. There are men who don't give women transport to go to hospital yet the hospital is far."

In the same line, the VHT Mparangasi HC III had this to say about religious barriers;

"In this area, we do not have them but in other places they are there. For example the "BISAKA" Faith do believe in immunization but we don't have that faith in our area."

The LCI Committee Chairman also had this to say about religious barriers;

"All other people accept taking their children for immunization apart from "abaikiriza". I don't know the reason why they don't take their children for immunization."

In line with the issue of religion barriers the VHT Butema HC III noted that;

"We have a few people who don't accept like the Abaikiriza from the bishaka religion they don't accept to take their children for immunization because they believe in using herbs. But sometimes the sub county chiefs and LCI talk to them and they accept."

The parish chief Kiragura parish also had a lot to say on cultural beliefs that have become cultural barriers to immunization, he pointed out that;

"For those that do not take their children for immunization is because of cultural beliefs. There are some people who believe that immunizing your child weakens the child and may die. Some parents believe that immunization is n t important because they have grown up without being immunized."

He added on the matter of religious barriers that;

"I heard about one sometime but I don't remember when there was religious group that was against immunization. They gave their lives to God so they did not think immunization was relevant."

Limited support from fathers or male partners to female caregivers

One respondent from Hoima referral Hospital had this to say;

"Some husbands stop their wives from bringing the children because they don't want their children immunized."

Vaccine stock outs

The VHT Buhanika also mentioned something about vaccines and their supply in the district and health centre at large, she pointed out that;

"Sometimes we don't have the vaccines. The nurse tells us that she did not find vaccines at the stores and the population is higher than the vaccines supplied".

The Hoima Regional Hospital EPI focal person said this about Vaccines;

"Recently I got to know that these vaccines are under National Medical Stores when we were getting several stock outs. From there they come to our district stores and the we go and pick

them from there. The most affected vaccines are IPV which went missing in March for a month, I got to know it was a national problem."

The former LC III Kabwoya had this to say about vaccines challenges, he pointed out that;

"The vaccines are not adequate, because immunization date of this facility is on Tuesday but sometimes you meet mothers who are coming from the health facility and they tell you that they did not receive immunization for their children. We have stock outs because we are being underserved, i.e. the population is large yet the vaccines given out are few. There is when immunization is taking place and the people are more than the available vaccines for that particular day. The other reason is that since this area has oil, there are a lot of migrations to this place, therefore the data that was captured by the census is not the actual number at the ground, therefore when the government is planning for this area, we are given less than we deserve".

Mother's attitude towards immunization

In the data from Kigorobya Health Centre IV, one respondent had this to say;

"Some mothers believe that all those injections are meant to kill our children".

The VHT Buhanika mentioned something related to mothers attitude, he pointed out that;

"Yes the parent accept to take the children but when we are mobilizing for immunization some parents have doubts on bringing the children for immunization, we convince them to bring the children for immunization. There is rumor that when the child is immunized they get fever, they might die or get problems or get lame."

One respondent from Kabwoya Health Centre III pointed out that;

"The mothers who get pregnant and deliver without visiting the hospital for antenatal are likely not bring their children for immunization."

The VHT Bujumbura West mentioned a statement related to mothers attitude towards immunization, he pointed out that;

"The mothers somehow bring difficulty in the service by refusing to bring children for immunization. As I told you some people say you have brought vaccines to spoil our children "leave us alone", you have personal motives you are searching for". He added that;

"Mothers refuse to come for immunization because of busy schedules also because these are town people as you know. Some say how can I take a child for immunization instead of looking for 100 shillings."

The VHT Buhanika HC II mentioned some matter about the attitudes of mothers during the interview she said that;

"Sometimes the mothers don't remember the immunization dates, they need follow up."

The VHT Kabwooya had this to say about the perception of some mothers about immunization he stressed that;

"Some mother accept immunization but some don't accept. They do not refuse because they do not have time but because of the perception that immunization is not important. It's a big challenge that mothers skip immunization series because they don't consider it important."

One respondent from the FGD, which was held at Munteme Health Centre II, pointed out that;

"Some mothers don't immunize because they don't believe in immunization, some say that they were not immunized yet they have been able to grow. I would say it is because of ignorance, because someone will say that you are taking your child for western medicine it will spoil your children's lives.

Some mothers, who attended the FGD from Buseruka Health Centre III, pointed out that;

"Some women are lazy, some wait for outreach services because it's far and some claim that the vaccines are not good for the children."

"We have an issue of lack of cooperation from the patients. The mothers think everything is free and we must serve them tooth and nail despite the added work - because dealing with these people who are psychologically tortured, who have seen their mothers die, and relatives die is hard".

In the same line, the LCI from Butema HC III had this to say about caregiver attitude towards immunization;

"Parents especially mothers are lazy and claim to be busy, they don't care that the children are not immunized".

Theme IV: Ways in Which the Capacity of Health Workers in Hoima And Wakiso Districts Can Be Strengthened in Order to Reach At Least 90% Of the Unvaccinated Children

Setting up more facilities

Linking people with existing health care services is a role of any effective and efficient health care delivery system. The former LC III Kabwoya had this to say about ways of strengthening capacity of Health workers.

"*I would like to ask the government to put up more facilities in the parishes so that the services are closer to the people."*

Sensitization and mobilization of mothers

Sensitization about a program is one of the most effective way of getting communities respond to a program from the government or acquire knowledge about what it is about. The LCI Hoima Hospital Cell had this to say about sensitization;

"The VHT systems should help to sensitize the people about immunization in communities."

The VHT Kikube HC III had this to say about mobilization and sensitization of mothers, he said that;

"They should facilitate us to reach all corners in the days of immunization. Of recent we have been using house to house mobilization and it's not effective, some people are not reached. Even the days we are given to mobilize are less for mass immunization and for outreaches, they should put more points."

The Hoima Regional Hospital cell had this to say about sensitization and mobilization;

"Through mobilization and sensitization of the people in the villages and it should be done by the health staff therefore we need to increase the health staff in the district".

Facilitation of health workers

The current LC 3 Chairperson Mparangasi sub county said that;

"We need to facilitate health facilities, like earlier mentioned that they do not have transport.

In line with the Mparangasi LC 3 Chairperson, the Community Leader Dwooli Parish had this to say;

"The staff in a facility should be well facilitated in terms of transport and should also be motivated".

Facilitation of VHTs

Nationally, VHTs are expected to carry out general tasks in all PHC core areas which include home visiting, mobilization of communities for utilization of health services, health promotion and education, management of common illnesses, follow-up of pregnant mothers and newborns, follow-up of discharged patients and those on long-term treatment and community information management.

The VHT Hoima Referral Hospital stressed the importance of working with VHTs. He said that;

"Improving VHT allowance, the allowance is too low, though we are doing voluntary work, we are squeezed to the wall, we need transport, water and a meal, and they should cater for the VHTs, which will improve on the services we provide for our people. Because when we do one on one, the parents feel obligated to go for immunization".

The VHT Buhanika Health Centre III had this to say on ways to improve immunization he stressed that;

"If the mothers were sensitized and the VHTs were funded, it would be easy to provide immunization services".

The VHT from Buhimba East in line with the previous VHTs had this to say;

"We VHTs, should be involved in immunization because we are closer to the community. Sometimes we just hear rumors. We should also be facilitated with some money. We should also be given time to sensitize and mobilize the people."

The VHT Buhanika mentioned something related to VHT facilitation, he noted that;

"If the mothers were sensitized and the VHTs were funded, it would be easy to provide immunization services."

Establishment of outreach programs

Outreach immunization sessions are held in a location other than a health facility, from which health workers can go out and return the same day. They are held periodically, at intervals of one, two or three months, or even twice a year. Successive outreach sessions in a community should be held in the same place (for example, the school), on the same day of the week and at the same time, to maximize the likelihood that people will remember to attend. Outreach immunization services (OIS) are an important tool for increasing childhood immunization coverage. The services ensure that immunization is available to children who are unable to access a general practice in a timely fashion for their immunization events.

The former LC III Chairman mentioned a statement emphasizing outreaches;

"I would also like to request any NGO or government to facilitate outreach services if the facilities are not up."

The VHT Butema also emphasized the need for outreaches he said that;

"We need to introduce more outreaches to cover more areas".

Transport facilitation for health workers

The VHT Kiragura parish had this to say on transport issues for health workers, he pointed out that;

"We need to support these health workers because transport is poor. It causes time delay and so forth for these health workers".

THEME V: Identification, Reporting and Management of AEFIs

Respondents were asked whether any of their children had experienced any adverse events following immunization, and health workers asked if the caregivers attending their facility had noticed or recorded any AEFIs; if so, how often does this happen, what would you attribute it to, do you have a reporting system for AEFIs; is this system standardized; is there a reporting tool available for this and what are the measures taken to prevent this from recurring.

The EPI focal person from Kigorobya Health Centre IV had this to say about AEFIs she had this to say;

"We receive reports about adverse events. Recording and reporting rarely occurs. Health workers need to be trained better on reporting".

In contrast, the EPI Focal person from Ndwooli HC III stressed that;

"No AEFIs have been registered yet. We normally report directly to the district but it has never happened as the procedure. No reporting tool I think. We use the right drugs, monitor temperatures well; all these help us to archive no AEFIs".

The nurse in Charge of Immunization also added that;

"No AEFIs so far but we have measures in place. We have surveillance forms, tools and focal persons to identify diseases that follow such illnesses on routine. So we pick samples and send. That is the system in place".

The Incharge Buchayaya Health Centre III had this to say about AEFIs;

"No, we have not experienced any adverse effects, we have a reporting system and we have the tool for reporting. It depends on the type of adverse effect, some we can manage, but if it is severe, I call my bosses but we should also write them down for easy reporting".

The Incharge of Bujumbura Health Centre III had this to say about the AEFIs matters;

"We have not faced any adverse effects. I think we have a reporting system. I don't know if it's standardized".

The matters of AEFIs were clearly articulated by the Assistant Incharge Sebigoro Health Centre, he had this to say about the matters;

"It only happened once in one month, it was attributed to DPT, I believe the focal person reported about it. Yes, we have reporting system, we discussed it in our meeting and we hope reporting improves".

According to the Incharge Buhimba Health Centre he had this to say;

"We have not experienced anything of the sorts. We might have (sounds not sure) but it's just dormant. It may not be standardized; we don't have any tool for".

The Head of Immunization Mparangasi HC II had this to say about AEFIs;

"They happen, like some do get swellings though it is a rare occurrence. We have a book where we report to the national Drug authority."

In line with AEFIs, the Health Assistant of Kigorobya had this to say;

"No. We have never received any problem of AEFIs. Apart from meningitis in January which occurred for few people. I was once just in that week. There is a reporting tool/booklet for reporting these cases. I don't know of any measures taken."

The EPI Focal Person Hoima regional referral hospital had this to say about AEFIs, she noted that;

"We have not faced any AEFIs. We normally talk about the like reactions for children after immunization and give advice on what to do but we have not had any AEFIs. We have an emergency tray because as long as we give an injection, we expect any. So they emergency tray is to help us in sorting out any effects. Those at home, we advise they come to the hospital very fast. Our main emphasis is educating the mothers."

Summary

What interventions, strategies and approaches can help to address the problem of vaccine hesitancy and underimmunization in Uganda?

This study identified main barriers to effective immunization that drive underimmunization in Hoima District to be grouped under community, geographical, caregiver, child and health system factors. In general, Hoima District has adequate number of health facilities to provide required immunization services, but these facilities suffer shortage of health worker numbers, vaccine stock outs, stable electricity supply, and inadequate financial resources to ensure outreach programs. Vaccine stock outs have been attributed to unreliable vaccine supply, while the prevailing difficulties in accessing health facilities which offer immunization services are linked to transportation related difficulties, very long rough distances that are hard for vehicles or motor cycles to navigate. The cold chain team is very committed, motivated and well mapped out to cover the district.

Besides frequent vaccine stock outs especially affecting BCG and oral polio and rota virus oral vaccines, some of the health facilities in Hoima have no vaccine fridges and therefore have to depend of other neighbouring health facilities for storage of vaccines, a factor that becomes difficult because some of the facilities with working fridges are located far away, a situation that is worsened by the district's poor road terrain. Examples of Some of these facilities without fridges include Buraru, Kisiha, Nsozi Health Centres. The problem of lack of fridges is complicated by poor access to gas supplied for the fridges.

The communities in the two districts accept vaccines and immunization. The health workers as well were found to be hard working, committed, but overwhelmed with work. The numbers of caregivers served by each health worker is very high. This low numbers affect the ability of the health facilities to offer outreach services. The lack of adequate funding, especially for fuel and transport makes this problem even more profound. Some outreach sites are very far from the facilities, some are hard to reach due to a hilly narrow road that are difficult to use in rainy seasons. This problem as well affects the caregivers, who find it difficult to take their children to the Health Facilities or outreach sites for immunization.

The drivers of poor immunization can be grouped into community, geographical, caregiver, child and health system factors. In general, Wakiso District lacks adequate number of health facilities to provide required immunization services, and the facilities suffer shortage of health worker numbers, vaccine stock outs, stable electricity supply, and inadequate financial resources to ensure outreach programs. Vaccine stock outs have been attributed to unreliable vaccine supply, while the prevailing difficulties in accessing some far located health facilities which offer immunization services are linked to inadequate transport finances. The cold chain team is committed, motivated and well mapped out to cover the district. Besides frequent vaccine stock outs especially affecting BCG and oral polio and rota virus oral vaccines, some of the health facilities in Wakiso lack adequate vaccine fridges. The problem of lack of fridges is complicated by unstable electricity supply to facilities in Wakiso district.

The health teams are not well versed with program for managing AEFIs. The ministry does have a program, but the implementation has not been done, with very few health workers having knowledge how to implement it. The launch of measles – rubella (MR) vaccines was associated with marked antivaccine sentiments and hesitancy, especially fears around alleged autism and convulsions and neurological sequalae. There are cults and religious groups in Wakiso that have been linked to anti vaccine messages and sentiments. The impact of these groups on hesitancy needs to be studied further.

CHAPTER 5: IMPLICATIONS, RECOMMENDATIONS AND CONCLUSIONS

Introduction

The identification of vaccine hesitancy as a public health threat (WHO, 2019b) highlighted need for urgent interventions to address this problem. Factors contributing to vaccine hesitancy vary from one place to another. With low immunization coverage identified in this study, and frequent outbreaks of vaccine preventable diseases in Hoima and Wakiso districts of Uganda, this study’s aim was to explore the reasons behind this problem. This study has identified barriers to the uptake of immunization, prevailing underimmunization, drivers for under-immunization and vaccine hesitancy and reasons for low confidence in immunization in rural Hoima and (peri)urban Wakiso districts, and thus provides useful information for planning, forecasting, and addressing these recurrent problems that contribute to immunization coverage rates that have remained below the World Health Organization recommended targets.

This study hypothesised that : Ugandan children are under immunized due to low caregiver confidence in immunizations, due to poor immunization health systems, due to inadequate caregiver awareness on immunization and due to unavailability or unreliable supply of vaccines and poor geographical terrain and poor road network that results in vaccines supply not being able reach all eligible children within the country.

This section of the thesis discusses the results from this study as they relate to the local context, compares with other published findings from other settings within Uganda and Africa, and goes further to generate and propose educational interventions, tools, communication strategies and health system focused approaches that can help address the problem of vaccine hesitancy and underimmunization particularly in Uganda and Sub-Saharan Africa in general.

This section therefore discusses important information on vaccine uptake, coverage, utilization of immunization services, refusal, and barriers to immunization within Uganda. This information generated in this study is unique, because it emanates from both rural, peri-urban and urban communities in Uganda. The rural Hoima district information is further enriched by experiences of caregivers from a very mobile migrant border and refugee communities in Hoima district. This information will help the local health authorities in Wakiso and Hoima districts to improve their immunization health systems, and address the identified challenges/barriers to immunization, advocate for/lobby for more government investment in immunization and allocation of resources to health in line with the Abuja declaration on health financing.

There are very many reasons and factors that affect why people or communities will accept or reject a given vaccine (Albers et al., 2022; Gonzales et al., 2021; Kaufman et al., 2021; Kimmel et al., 2007; Kuehn et al., 2022; MacDonald, 2015; Olusanya et al., 2021; Paul et al., 2022; Stratoberdha et al., 2022; Yang et al., 2023; Yazdani et al., 2021). These reasons have now been shown to vary from place to place, from one vaccine to another, from person to person and even from one health worker to another (Acharya et al., 2018; Adekeye et al., 2015; Amarasinghe et al., 2013; Anthony et al., 2009; Atouf et al., 2021; Bangura et al., 2020; Barker et al., 2015). In an effort to increase surveillance around hesitancy, in the period 2002–2005, a pilot question was added to yearly form for joint reporting [Joint Reporting Form (JRF)] with the aim of monitoring and understanding the increasing cases of vaccine hesitancy (Marti et al., 2017). This JRF form was sent to the national immunization managers around the world and sought to establish if they had yet noted and come up with a response to media coverage through the year regarding vaccines and their vaccination programs (Marti et al., 2017). The resulting data revealed that there was negative media coverage from countries represented in all World Health Organization reporting regions a decade ago.

The Global Vaccine Action Plan (GVAP) for the recent Decade of Vaccines (DoV) spanning 2011–2020 identified six Strategic immunization Objectives for the coming decade, and proposed indicators needed to monitor and to evaluate the progress of achieving these objectives (Marti et al., 2017). These are to be implemented alongside two SAGE recommended indicators geared towards objective 2 with a finer focus on communities targeted by vaccinations and individuals that should comprehend value of vaccination as a responsibility and as a right. (Larson et al., 2015; MacDonald, 2015). These indicators were as follows: "1) Identify the three major explanations for vaccine refusal in the past year and whether the response was opinion or assessment-based and 2) Whether an assessment (or measurement) of the level of confidence in vaccination had taken place at national or subnational level in the previous 5 years" (MacDonald et al., 2020; MacDonald, 2015). The global launch of the indicators was done in 2015 JRF aiming to collect country data for the year 2014.

The goal of including these indicators in the JRF aimed to provide for the identification of reasons that are driving vaccine hesitancy around the world and to evaluate the countries that have conducted assessment for level of confidence. The early and initial inclusion of the indicators was successful in determining the three main drivers of hesitancy in the year 2014 and in establishing percentage of the countries which have conducted the assessment (Marti et al., 2017). These indicators were also useful in facilitating monitoring of the changes and the progress over a given time.

From findings of the 2014 JRF survey, vaccine hesitancy does vary by place, time, and by the individual vaccine (Marti et al., 2017). It is not unusual for people to avoid going to hospitals to get Ebola vaccine for example due to fear of contacting Ebola (Kieny et al., 2014). In countries with very low rates of infectious diseases, the population perceived risk is low, thus may fuel complacency to uptake of immunization, as has been seen in the European and western world; which as a result has recently started reporting re-emergence of these vaccine preventable diseases (VPDs) especially measles, pertussis and mumps despite presence of existing reliable programs of vaccination (Acharya et al., 2018; Adekeye et al., 2015; Amarasinghe et al., 2013; Anthony et al., 2009; Atouf et al., 2021; Bangura et al., 2020; Barker et al., 2015). These experiences show that hesitancy to vaccines is very context specific (Larson et al., 2014; Muscat, 2011).

The documented reasons for hesitancy to vaccines were linked to either vaccine product concerns or vaccination issues; including risk or benefit determinants; fears around vaccine safety; and concerns related to AEFIs. Another major reason identified for vaccination hesitancy related to awareness and knowledge of the vaccine and vaccination programs within the country. Another factor is cultural and religious factors issues. The drivers of hesitancy identified will be addressed at local, district and national levels. Experiences from addressing these drivers to hesitancy and underimmunization can then be shared with other districts, and

African countries with similar contexts to be implemented in their nations for solving the problem of vaccine hesitancy. Some of the lessons will be included into ministry of health policy and strategic plans towards addressing vaccine hesitancy and underimmunization. This study provides relevant information useful in planning, in forecasting, and in addressing the recurrent outbreak of vaccine preventable diseases, the problem of underimmunization, the emerging problem of vaccine hesitancy and the persistently low immunization coverage rates in Uganda.

The findings of this study will be disseminated in University library, presented at local and international scientific and public health conferences and published in peer review scientific journals. This study findings will lead to generation of innovative educational interventions and new communication strategies or relevant health system approaches to help address the problem of vaccine hesitancy and underimmunization in Uganda and Sub-Saharan Africa at large.

Out of this study, we expect to see strengthened immunization services in Wakiso and Hoima districts; improved knowledge, communication and skills in the immunization service delivery by health workers as a way of encouraging parents to come for the services; enhanced community engagement, and participation in immunization, uptake of immunization services and empowerment to demand for immunization services and adhering to recommended immunization schedules; generation of guidelines and tools for assessing vaccine hesitancy and underimmunization; reduction in the out breaks and the occurrence/recurrence of common vaccine preventable disease in Wakiso and Hoima districts; improved ministry of health and government funding and investment into immunization especially in fighting the problem of vaccine hesitancy and improved numbers of children who survive up to the fifth birthday, due to reduced morbidity and mortality as a result of vaccine preventable diseases following improved uptake and availability of immunization services in Hoima and Wakiso Districts.

Implications

Barriers to the uptake and utilization of immunization services in Hoima District, and Wakiso District, Uganda.

This study identified major barriers to effective immunization that drive underimmunization in Hoima District to include vaccine stock outs (due to unreliable vaccine supply), problems with access to health facilities that offer immunization services (due to transportation related difficulties, very long distance that clients have to travel to health facilities and a very difficult geographical terrain that is hard for vehicles or motor cycles to navigate). Across many areas of SSA, terrain and transport difficulties have been documented are significant drivers of poor immunization service uptake(Bangura et al., 2020). The caregivers may desire to have their children vaccinated, but the access barriers pose a real threat to immunization schedule completion. In Uganda, this problem is widespread, and has been reported in other parts of the country, especially Yumbe district in far north western part of the country along Congo Border, and were as well reported in studies in Nigeria and Kenya(Bangura et al., 2020; Tugumisirize et al., 2002; WHO, 2020c; Wiysonge et al., 2012).

The findings from Hoima district reveal that the district has adequate Health Facilities to provide required immunization services. Indeed, the ratio of facility to population has been previously described as satisfactory; however, the lack of adequate staff numbers and cold chain infrastructure capacity remains a big driver of under immunization. Some of the health facilities have no vaccine refrigerators or have refrigerators that are mal functional. These facilities have to depend of other neighbouring health facilities for storage of vaccines; only that these supporting facilities are located very far away, and coupled with the district’s poor road terrain, provides a major barrier to movement of the vaccines to the vaccination centres and back for storage.

Some of the health facilities without refrigerators include Buraru, Kisiha, Nsozi Health Centres (Bangura et al., 2020; Durrheim & Crowcroft, 2017; Malande et al., 2019; Tugumisirize et al., 2002; WHO, 2020c; Wiysonge et al., 2012). The greater concern therefore is that this is a widespread problem in Uganda, and contributes to missed opportunities for immunization and contributes to long waiting time at both static and outreach centres of immunization, a factor that is recognized as a major driver of underimmunization. Previous reports have attributed this problem to inadequate supply of vaccines, lack of vaccine storage and inadequate numbers of health workers to operate the immunization services (Plotkin, 2005; Tugumisirize et al., 2002; Vivier et al., 2000). These supply and access barriers have been described widely in studies in sub Saharan Africa, where the failure of countries to allocate 15% of their GDP to immunization as per the Abuja declaration has left them stretched in their effort to balance pressing demands(Bangura et al., 2020).

In Wakiso, an urban/peri-urban set up for example, the problems of inadequate staff numbers at health facilities, the unsteady supply of vaccine (Acharya et al., 2018; Adekeye et al., 2015; Alkema et al., 2016; Bangura et al., 2020; Bedford et al., 2018)stocks, and long waiting hours are comparable to rural Hoima. Wakiso however relies more on electricity than gas to power the vaccine refrigerators, and the unstable electricity supply, coupled with inadequate allocation of financial resources to effectively run the immunization programs remains a big barrier. This was similar to reports in Yumbe, and elsewhere in SSA. The commitment of health workers in both Wakiso and Hoima though laudable, is frustrated by poor transport infrastructure and terrain in Hoima or poor allocation of transport finances in both districts, thus making it difficult even for central district immunization officers to supervise and mentor and support health facilities.

This study found that the level of acceptance of immunization services and vaccines in general among communities in Wakiso and Hoima districts are satisfactory, with caregivers being receptive to both old and new vaccines, even for those who would get vaccination from outreach centres. The large turn out and long lines of caregivers waiting for vaccination at the outreach centres is testimony of acceptable levels of vaccine acceptance that needs to be sustained. Demand creation and sustainability requires deliberate efforts by the government and ministry of health and other key stakeholders to ensure they support and equip the immunization program with the required enabling infrastructure(Acharya et al., 2018; Adekeye et al., 2015; Alkema et al., 2016; Bangura et al., 2020; Bedford et al., 2018).

The rationale for having outreach programs was to help expand access to the immunization programs, especially for communities and populations that would for one reason or another not travel to static immunization centres. The lack of adequate funding to support this program, especially provision of transport for staff and vaccines, coupled with the difficult to navigate geographical terrain greatly hampers the provision of an effective immunization program. This barrier affects both health workers and caregivers, who struggle to access health facilities, and often give up. Caregivers reported that they would rather stay home and run their own businesses or go to the farms than report to facilities where they will find vaccine snot available or very long lines with extended waiting hours.

There are additional drivers of underimmunization identified in Hoima and Wakiso that relate to inability of children (with long-term illnesses, orphans, children born premature, children catered for by elderly grandmothers as caregivers) to attend immunization visits or scheduled appointments. The challenge involved in transporting these children to the facilities are enormous to these poor parents, tied to the high levels of poverty and financial need, factors that jointly affect effective delivery of immunization services. These are the populations that would be best served by an effective mobile outreach program, that can deliver vaccines as close to their residence as possible.

Another barrier to immunization and driver of hesitancy identified in both Hoima and Wakiso districts was the impact of Adverse Events Following Immunization (AEFIs). It was clear from the districts that the ministry of health has a program in place to address this problem, only that it has not been effectively implemented. It also emerged that most health workers were not familiar with the identification of AEFIs, their management and reporting system. The caregivers notice their children experiencing fever, pain, swelling at injection site, convulsions among others, yet they don't know who they can report to.

In Wakiso district, the launch of measles – rubella (MR) vaccines was associated with marked antivaccine sentiments and hesitancy, especially fears around alleged autism and convulsions and neurological sequalae. This problem was compounded by presence of cults and religious groups in both Hoima and Wakiso districts that have been linked to anti vaccine messages and sentiments. The impact of these groups on hesitancy needs to be studied further(Cooper et al., 2018; Elizabeth et al., 2015; Nolna et al., 2018; Tadesse et al., 2009; Zewdie et al., 2016). It is also possible that the impact of these antivaccine groups in promoting anti vaccine sentiments and vaccine hesitancy in these districts has been reduced over time by the ministry of health new laws promoting immunization and the sustained and competing immunization promotion programs around the country. The introduction of health promotion and education sessions for caregivers at health facilities before immunization sessions are progressively improving the understanding of vaccines and immunization programs in the country and helping fight hesitancy (Braka et al., 2012; Tobin-West & Alex-Hart, 2012; Yenit et al., 2018; Zewdie et al., 2016).

Reviewing the determinants of vaccine hesitancy and underimmunization in Uganda (focusing on Hoima and Wakiso Districts) and Sub Saharan Africa

The systematic review only included studies from SSA, a region that generally has low research output when compared to its potential and size and population. That generally means that the data available maybe sub optimal or skewed to a few counties in a very wide region. A major part of the studies were from Nigeria (Adekeye et al., 2015; Bangura et al., 2020; Tobin-West & Alex-Hart, 2012). The WHO designed a model with three main factors that underly vaccine hesitancy; that include what is now referred to as the 3C's model that includes: "1. Confidence (where there is no trust in vaccines and in healthcare providers of vaccines); 2. Complacency (where target groups do not perceive the need for vaccination or they do not value vaccination) and 3. Convenience (deals with access to vaccines and access to vaccination services)(WHO, 2014).

It is informative to note that both the systematic review and the study in Hoima and Wakiso found that over a half of the drivers of vaccine hesitancy in this study were Convenience related, and largely reflected problems related to both the caregivers, the health workers and supervisors to access vaccines or immunization sites. Majority of Sub Saharan communities are poor, and face similar challenges to accessing immunization services, including barriers related to language and communication, barriers of transport to health centres, a very poor often hard to use road network, complicated by very unfavorable geographical terrain. This geographical related problem makes it difficult even for ministry of health staff to deliver or to distribute the necessary vaccines or consumables to vaccination sites (Adekeye et al., 2015; Dicker et al., 2018; Igme, 2020; Malande et al., 2019).

A recent study in Ethiopian showed that over 85% of caregivers who attend immunization centres travel on foot to access these sites; and over 70% take between 30 minutes to one-hour walking; and over 75% of respondents spent more than an hour at the immunization centres. These findings are comparable to rural Hoima results, and suggest a multi factorial cause to access problems in immunization. Distance from facility, especially when far away therefore can be a major driver of hesitancy and poor uptake of immunization; especially in a community that has very low level of education, with very high rates of teenage pregnancies – a major cause of early parenthood. (Adekeye et al., 2015; Ntukanyagwe, 2019; Wiysonge et al., 2012).

From the 3 C's model, Confidence (where there is no trust in vaccines and in healthcare providers of vaccines) is not a very major barrier to immunization in Sub Saharan Africa, but there is no doubt that recent concerns about Measles-Rubella vaccine and COVID-19 vaccines coupled with rising numbers of anti-vaccine groups are likely to change the outlook. The recent measles rubella vaccine roll out in Uganda was associated with widespread negative sentiment in Wakiso district. This concern was highlighted both in the focus groups and individual interviews with both caregivers and key informants. Studies have additionally reported communities in the SSA region (Dicker et al., 2018)with religious groups that have beliefs against immunization, and communities that have cultural practices that affect uptake of immunization services. These groups promote negative messaging against vaccines, vaccine refusal, and sometimes outright rejection of some or all vaccines (Eshetu & Woldesenbet, 2011; van der Maas, 2018).

Vaccine acceptance is a key factor in ensuring many children get vaccinated and that vulnerable and unreached communities are helped to fight vaccine-preventable diseases. The COVID-19 pandemic revealed that many adults and populations manifest vaccine hesitancy to various degrees(Altmann et al., 2020; Cooper et al., 2018; OLAYINKA S Ilesanmi et al., 2020; Olayinka Stephen Ilesanmi et al., 2020; Marti et al., 2017; Olson et al., 2020), even among healthcare workers, who struggle to voice vaccine-related concerns and worries due to organizational, government, and societal pressures and restrictions (Tuckerman et al., 2022). It has been shown that Vaccine hesitancy is influenced by the way people think and how they feel about vaccines as well as the social processes that may underpin vaccine acceptance. This means that, from one environment to another, from one group to another, from one context to another, from one culture to another, the level of acceptance of a given vaccine will vary.

One of the weaknesses of approaches to address vaccine hesitancy is that, the interventions aimed at increasing vaccine uptake in communities are often tested in general population, instead of only targeting the vaccine-hesitant individuals, with a strong evidence on which strategies are effective often lacking for the specific groups tested. It has been reported in emerging reports that interventions that are based on a “knowledge-deficit” approach, such as education or information that are not tailored to addressing values or worries which underpin vaccine decision-making, may actually increase vaccine uptake but are certainly unlikely to address vaccine hesitancy (Tuckerman et al., 2022). There are behavioral ‘nudges,’ for example reminder or recall interventions that have now been shown to increase childhood, or adolescent and adult immunization or vaccination uptake in the general population, but the appropriateness of these in reducing vaccine hesitancy remains unclear.

One of the issues identified in the systematic review was the need to clearly define how to measure vaccine hesitancy. Estimating the problem is critical in guiding strategies to address the problem. There are various tools that have been developed by various experts to measure parental and societal hesitancy towards childhood vaccination, even though they don’t specifically address parent vaccine hesitancy especially towards adolescent vaccination (González-Block et al., 2021; MacDonald, 2015; MacDonald et al., 2018; MacDonald & Dubé, 2018; Marshall & O’Leary, 2018). The adult 5C scale, that was published in 2018, is a psychometrically validated tool which assesses a set of five psychological antecedents of vaccination (complacency, confidence, constraints, collective responsibility and calculation), which capture an individual’s attitudinal and one’s behavioral tendencies (Betsch et al., 2018). It is my considered view that the World Health Organization SAGE 3C’s model remains the most elaborate, broad and balanced approach available for measuring vaccine hesitancy (MacDonald, 2015; MacDonald et al., 2018; MacDonald & Dubé, 2018; Machado et al., 2021).

Another aspect of hesitancy that emerged was the need to clearly define population-specific drivers that affect vaccine uptake. This can be attained through distinguishing vaccine hesitancy from other external barriers to vaccination uptake, such as access barriers. The tools for measuring these aspects have not been fully developed (González-Block et al., 2021; MacDonald, 2015; MacDonald et al., 2018; MacDonald & Dubé, 2018; Marshall & O'Leary, 2018). One of these is the Vaccine Barriers Assessment Tool, that will measure acceptance as well as access-related barriers to vaccination in children, piloted in Australia and in New Zealand. This tool can be adopted in many other settings especially both low income, middle income countries, and other more developed communities (Dubé et al., 2015). This is similar to that by the Working Group on the Behavioural and Social Drivers of Vaccination, that developed standardized qualitative and quantitative tools that measure social and behavioral drivers of vaccination. These tools will prove critical in measuring the emerging trends in ensuring accessibility to vaccines and acceptance of vaccination program(De Figueiredo et al., 2020).

Broadly, the systematic review did not reveal any historical or major political factors or drivers that drive hesitancy in sub Saharan Africa. However, there was widespread concern that governments need to allocate more resources to support health systems that relate to immunization (Abbas et al., 2020; Adamu et al., 2020). Political instability, as seen in Northern Nigeria, has been disruptive, and affected the entire immunization program. COVID-19 pandemic, Ebola outbreak and other recent pandemics greatly affected provision of routine immunization services, and contributed to stock outs, supply problems and have driven negative sentiments riding on many questions that followed COVID-19 vaccine roll out. The historical context of Nigeria, linked to the low rates of uptake of childhood immunisation have been affected by the impact of the 2003 boycott of the polio vaccination rollout in the country (Elizabeth et al., 2015; Malande et al., 2019; Tugumisirize et al., 2002; Zewdie et al., 2016).

Broadly speaking, the study found that the least number of studies showed Complacency (where target groups do not perceive the need for vaccination or they do not value vaccination) as a driver of hesitancy in sub Saharan Africa. In general, most SSA countries and communities do appreciate and support vaccination. There have been incidences where health system inadequacies and health provider attitudes have driven lack of trust in vaccines, especially among caregivers with previous unfavorable personal experiences. These negative experiences fuel dissatisfaction with the immunization program and health system as a whole, which then lead to poor completion of immunization schedules and in some cases complete failure to take up vaccines.

It is noteworthy that the Gavi Alliance has made a lot of contribution to ensuring access to immunization services for all parts of the world. The Alliance has been fairly successful despite the geographic, access, health system and communication barriers identified above. The Alliance has helped lessen the burden of cost of vaccines for a vast majority of LMICs, but the supporting infrastructure to deliver the vaccines remains a major river of underimmunization and vaccine hesitancy. Even when the vaccines are availed, caregivers have to cover the cost of transport to health facilities, which in itself is a major hinderance for the poor caregivers (Babirye et al., 2011; Miyahara et al., 2016; Pertet et al., 2018; Zewdie et al., 2016).

A major area that drives hesitancy and underimmunization is AEFIs. The studies revealed that about 20-30% of children who experience an AEFI were unlikely to come back for the subsequent scheduled vaccine. In identified studies, incidents where the AEFIs are less severe and generally self-resolving may go unreported (Babirye et al., 2011; Barker et al., 2015;

Malande et al., 2019; Wiysonge et al., 2012). Challenges in reporting AEFIs have been linked to health workers not being well versed with the reporting and management system for AEFIs. In most studies, health workers are not well versed with the system for AEFI handling. This is therefore a big gap since health workers are important in pharmacovigilance(Amarasinghe et al., 2013; WHO, 2012), post-marketing vaccine surveillance and identification of new adverse reactions not previously described (Parrella et al., 2013).

The improvement of AEFI reporting can thus play a role in pharmacovigilance strengthening. Most SSA countries don’t have efficient and robust pharmacovigilance infrastructure, a role that HCWs could play (Olsson et al., 2015). The WHO 2015 review of vaccine safety database revealed that less than 1% of AEFI reports worldwide originate from Africa, where only 10 countries contribute over 97% of these reports(Lei et al., 2018). While the International Drug Monitoring (PIDM) program by the World Health Organization started operations in 1968, African countries started joining in 1992, and though the number now stands at 35 out of 54 countries by 30th September 2015, their impact and prominence can be improved (Olsson et al., 2015).

African participation could definitely be better. There is need to improve the chain of supply, better enabling laws, continuous health worker training in pharmacovigilance, improved access to good medication, improved financial support and backing for investors, and investment in human resource capacity. Lessons from this program can be extended to AEFI management. These lessons extend to the eight strategic objectives of the WHO Global Vaccine Safety Blueprint, including “AEFI identification, utilizing the correct methods and approaches and tools, adequate investigation of safety signals, better framework for regulation, improved communication on safety and AEFIs, provision of technical support, ensuring the exchange and sharing of information between public and private stakeholders and global analysis and response” (Bangura et al., 2020; WHO, 2012).

INTERVENTIONS, STRATEGIES AND APPROACHES THAT CAN HELP ADDRESS THE PROBLEM OF VACCINE HESITANCY AND UNDERIMMUNIZATION IN UGANDA.

Recommendations for Application

There is need for the ministry of health to support the outreach component of immunization in Hoima district in terms of transportation, mentorship and ensuring timely supplies. Without effective transport, the vaccines cannot reach the health centres from the district vaccine stores. More importantly, support supervision would be hampered. Response during emergency situations, especially when the cold chain system malfunctions or power outages is a serious concern that depends on ability of technical staff to access the facilities quickly. The hard to reach areas in Hoima district especially Bunyawawa refugee camp, Tonya, Kyangwari and the whole Albertine Lake region can best be served by numerous and frequent supplementary immunization outreach activities as compared to other regions with a better terrain. These could be done as scheduled outreach immunization clinics and mobile services to hard to reach areas. Speed boats are a reliable approach that could be explored to reach the islands. This is key in ensuring catch up for all children who miss to go through the routine static immunization program at health facilities. This can then be replicated in other districts in Uganda with similar topography.

There is need for the ministry of health and the stakeholders in immunization to always train health professionals on current and new vaccines. This training should also target focal persons involved in immunization, village health teams and health promotion officers within the community and communication to caretakers. Training should not only target vaccines, but extend to cover vaccine economics, vaccine supply and cold chain, reporting, data and record management, reporting and vaccine monitoring. Training in communication and social community engagement is very important. Health workers and community leaders should be able to communicate the various recommended strategies for immunization. It is important to source for and allocate more funding to the cold chain infrastructure.

There is also need for the ministry of health trainings to also target primary and high school teachers, so that they communicate the right messages to students and parents, and enhance uptake of school-based immunization programs. The reach every child approach has been criticized for focusing more on service provision to the child than training and equipping the child. Targeting educators with information, who can then transmit this to the students is extremely effective as a strategy to involve the younger generation early in life. In addition, there is a need to design and develop a simple and easy to implement an effective program that targets focal trainers at lowest level of the community and educate and empower caregivers during immunization sessions. This approach can be helped by translating available IEC materials into local languages that can easily be understood by local communities.

The ministry of health through UNEPI should educate and engage the health workers on the currently existing system for identifying, recording, treating and reporting AEFIs. Additional interventions should target to train health workers with new or refresher courses to cover the basics of adverse events identification and diagnosis, adverse events reporting and adverse events following immunization management, and how to improve communication and trust among health workers and caregivers. Tied to this initiative is the need for community mobilisation and sensitization on the identification, and reporting of adverse events following immunization. This study further recommends the robust implementation of the existing EPI program confidence building in the community on fears around adverse events following immunization as a driver for vaccine hesitancy.

Vaccines and immunization have clearly been demonstrated to be beneficial and effective in fighting infections, and as a public health intervention, World Health Organization rates immunization only second to fresh water and sanitation. Indeed, immunization and vaccination is considered a very successful and very cost-effective public health intervention that improves health outcomes, and through which countless lives have been saved and health care improved worldwide, especially when effectively and widely deployed. The challenge has remained the fact that high vaccination uptake rates are required if we are to sustain improved health and prevention of deaths from vaccine preventable diseases. These desired high vaccination coverage and uptake rates are dependent on many other factors, especially a good population understanding of the value of vaccination for the target and general population; knowing were to get the vaccines from, understanding the schedule and times to best go for vaccines, the role of campaigns promoting vaccines and need to have all children vaccinated.

One of the factors that is becoming increasingly important in determining how much vaccination coverage can be achieved is vaccine hesitancy, that usually results in the delay or the refusal of immunization or vaccination by communities and individuals; either the delay in the acceptance of either one or more vaccines on offer to the complete refusal of all the vaccinations offered in the expanded immunization programme. Examples of the impact of hesitancy has been that affecting influenza vaccine among pregnant women in the Americas that aimed to combat strong evidence about increased mortality and morbidity and due to influenza among pregnant women, the reluctance of communities to embrace measles vaccine in parts of Europe, poor uptake of human papillomavirus vaccine in India and Japan, and hesitancy against polio vaccination campaigns in Pakistan and Nigeria.

Vaccine hesitancy is a complex problem requiring a multipronged approach to address it, and countries or populations seeking to address it must appreciate the magnitude and the setting of this problem and the need for a broad-based approach to root cause diagnosis for vaccine hesitancy. The identification by immunization stakeholders and funders of tailor-made evidence-based effective strategies for addressing the root causes of vaccine hesitancy, and the need exists for them to evaluate the impact of interventions and monitor the acceptance of vaccines or recurrence of hesitancy through routine ongoing surveillance. It was because of these concerns regarding hesitancy and the resulting poor vaccine uptake with declining or stagnating national expanded immunization programmes, a thorough review on hesitancy was carried out and several recommendations proposed on dealing with vaccine hesitancy and the determinants thereof. In October 2014, the Working group's final recommendations to the public health community, focal persons, funders and to World Health Organization member states remain relevant to date.

These recommendations are of three categories: The need for UNEPI and stakeholders involved in immunization to educate Ugandans on reasons for low uptake of vaccines, about the rapidly changing nature of challenges arising from vaccine hesitancy; the organizational capacity and the structures needed in order to decrease vaccine hesitancy and to increase vaccine acceptance globally, at local and at national levels; and thirdly sharing lessons that have been learned and the best practices arising out of experiences of countries including the development, the validation, and the implementation of new tools for addressing vaccine hesitancy. The SAGE-WG on hesitancy as well proposed a list of various subjects' categories on vaccine hesitancy that need urgent focus. The WG as well designed a matrix of determinants of hesitancy that can help with root cause analysis on vaccine hesitancy.

It is critical that the ministry of health puts in place interventions aimed at reducing opposition to vaccines and vaccine refusal specific to different communities and contexts. This should focus on better communication, use of social media, religious influences, enabling culture, gender disparities hindering immunization, political stability and support, and improving road network and access to facilities. Much as complacency and confidence issues were not major barriers, the convenience factors identified must be addressed based on the specific context. Some additional areas that need addressing relate to categorising influences that are influenced at individual level and at group level, and factors that drive them, that may relate to practices, to beliefs, to public health promotion and overall disease prevention strategies.

There is need for immunization stakeholders and UNEPI to reach the unreached through strengthening of immunization health systems and the expanding of sites for immunization delivery in both urban and hard-to-reach areas. This can be achieved through use of e-tracker support (equipment, offline or online platforms), enhancing capacity of communities, use of outreach or mobile clinics, and running mop up and catch services. Another approach would involve enhanced training and Supportive Supervision for the immunization health workers (some may require on-the-job training, improvements in supportive supervision, prioritize health facilities for knowledge and skill support, identification of strategies for remote areas supervision, identification of decision-support tools for HCWs to improve performance, update of pre-clinical curriculum and new hire orientation materials in line with EPI policies/guidelines on immunizations, liaise with training institutions [e.g. nursing schools] to share updated EPI information and materials for use in the classroom).

Another area that needs focus is by the ministry, vaccine manufacturers and other stakeholders is demand Generation – through development of localized (i.e. sub-national level) strategies to improve demand for services; engaging non-health stakeholders and community leaders with information and talking points to promote vaccination; the use of events, such as festivals, to screen vaccination cards, make referrals, and communicate messages child health interventions; employment of multiple strategies needed to reach the unreached, and especially in urban communities (e.g., container clinics in high traffic areas, door to door). The other areas are improvement of awareness among daycare/crèche proprietors; the use of simple and clear messages that indicate timing and services available and harmonization of messages across partners – tailor these messages to different groups (e.g. inform men directly about services and the role they play in getting their children vaccinated); working hard to avoid misconceptions (e.g. phrases like "up to 18 months" resulted in children being turned away or never coming for vaccines after 18m of age).

It is critical for UNEPI and the communication department at the ministry of health to address the matter of vaccine information communication and community engagement. Efforts towards community mobilization and social engagement are critical. While current strategies for vaccine information campaigns that influence vaccine attitudes within communities are helpful, there is need for tailored communication in order to reach high-risk and vulnerable populations. Vaccine communication therefore should be made evidence-based, and context-specific, with deliberate efforts for culturally appropriate and purposefully tailored approaches targeting the individual and his views or position on the continuum that is vaccine hesitancy. Efforts should target specific groups and attempt to address their concerns and fears against vaccines.

The efforts that aim at improving vaccine communication should leverage the critical role played by the providers to vaccinate, since this is critical for ensuring vaccine uptake. Some providers promote presumptive communication that presumes that the people are willing and ready to vaccinate; while others opt for participatory communication which usually asks people whether they want to take the vaccine or their overall view on vaccination. Communities may opt for the presumptive approach which has been associated with fairly higher levels of vaccine uptake. Communication should target motivational interviewing which offers a much more structured approach of counseling that is designed to provide people a guide towards change through exploring the enhancement of internal motivation. u

Another community engagement strategy UNEPI could employ is the use of vaccine champions especially when employed together with communication campaigns or with evidence-based community based interpersonal communication. There should be clear health worker training to make them champions. Others who can be champions includes community leaders, faith focal persons and vaccine industry leaders that can be trained to discuss vaccination and also address vaccine misinformation. These vaccine champions can be used to deliver training sessions and deliver advocacy tailored messages in their communities and their workplaces, and eventually they can have positive impact on social norms.

There is need for UNEPI to ensure more enhanced community participation in immunization campaigns and SIAs. This can be achieved through involvement of the community stakeholders in vaccines such as traditional chiefs, community heads, focal opinion leaders, and religious or cultural leaders, who are key community mobilizers for vaccination. Community mobilization has played a key role in COVID-19 vaccine uptake and confidence enhancement and provision of health education about benefits of COVID-19 vaccines. Beyond cultural, focal and religious leaders, community pharmacists, community health workers (CHWs), community-based organizations (CBOs) and patent medicine vendors also can play a critical role in patient education and community mobilization, and enhancement planning for structure and the modalities necessary for availing vaccines and enabling vaccine collection point location.

An important component in improving vaccine uptake initiatives is the provision of positive feedback and motivation for religious and community focal persons and leaders that participate in immunisation programmes and campaigns by UNEPI. The gratitude and appreciation given to vaccinators and supervisors of vaccination campaigns and SIAs and community focal persons improve community participation and uptake of vaccines. This could be achieved through public praise, public acknowledgement, acknowledgement letters, appreciation award giving meetings in town halls and award of gifts for active and high achieving community leaders.

As derived from the SAGE-WG review, the World Health Organization needs to develop key capabilities centrally, regionally and at country level, in order to gain important behavioral insights necessary for combating vaccine hesitancy. This effort requires a multisectoral approach, with integrated skills and the knowledge of behavioral scientists, sociologists, anthropologists, psychologists, and experts in community or social mobilization. To effectively address the required behavior, change for overcoming vaccine hesitancy, all the different experts from different sectors are required working in coordinated efforts to achieve effective reduction in hesitancy. Besides the use of experts, the World Health Organization should engage key stakeholders, partners, and civil society organizations, at both global, at regional and at country levels, to combat hesitancy and to mobilize support for immunization uptake.

Through this collaboration and multisectoral approach, low income countries that have gained a lot of experience in dealing with these problems can share lessons and experiences with high and the middle-income countries in overcoming vaccine hesitancy. A major stakeholder is UNICEF, which has worked with World Health Organization to increase immunization uptake. These two organizations can work together to address and to coordinate efforts against vaccine hesitancy and the demand creation for vaccination and immunization services. These efforts should include a coordinated and concerted cross-cutting approach aimed at counteracting hesitancy globally, through building of regional capacity needed to support various countries in combating vaccine hesitancy.

An initiative that has worked well in COVID vaccine roll out was deliberate promotion and emphasis on multisectoral collaboration that leveraged scarce and little available resources in most LMICs in African. This collaboration can be promoted in both public and private health sectors by UNEPI. The use of community informants could play a role of notifying sectoral representatives working in local governments or countries to make sure false information on vaccines is countered quickly. Multi-sectoral stakeholder collaboration can also be used to promote and enhance research on vaccines and vaccine acceptance in communities. This research is important in generation of new knowledge and approaches for promoting vaccine uptake and combating vaccine hesitancy.

It has been reported that successful interventions to overcome hesitancy must directly focus on the unvaccinated or the under-vaccinated communities or populations; and should focus on increasing vaccination knowledge and vaccination awareness; or aim at improving convenience or the access to vaccination services; or must targeted very specific target populations (for example heath care workers); and should seek to engage important special groups for example religious or cultural leaders who influence community decisions on vaccination. The goal to improve knowledge and attitudes or awareness could focus on education initiatives that embed new knowledge on vaccines into routine immunizations and similar routine medical practices.

Recommendations for Future Research

The following recommendations relate to areas requiring further research to deal with drivers of hesitancy and underimmunization:

1. There is need for universities, UNEPI, and other stakeholders in vaccination to design, to pilot and to implement novel teaching and training approaches for focal persons in immunization for education and mobilisation of communities and caregivers to be run during static and outreach immunization activities. This program should emphasize the need for effective communication and community engagement. This aspect of research should be premised on repeated findings in this and other recent research that show that caregivers trust the views and opinions of the health workers and community health leaders above all other sources of information on immunization. The caregivers and communities would trust and prefer to follow the guidance and opinion of the health worker especially on matters related to risk and harm that may relate to accepting a given vaccine.
2. There is need for universities, UNEPI, and other stakeholders in vaccination to initiate additional research to pilot and develop new tools or translate the current available tools and Information Education and Communication materials on immunization into local languages, widely and broadly understood by majority of African communities, for use in remote areas facing language barrier as a driver of underimmunization. The literacy levels in most African communities is low, and English or French is not widely spoken. Kiswahili is a rising and growing language, especially around East Africa and great lakes region, and would be the closest to a unifier for widest spoken language for the region. Local communities have their languages that are spoken widely in communities, schools, churches, village meetings and common work areas and farms in which piloting of translated IEC materials can be done, and if successful, escalated to cover more and more communities.
3. There is need for universities, UNEPI, and other stakeholders in vaccination to initiate further investigation of the impact of cultural/traditional or religious leader involvement

in decisions of populations on immunization, especially those that have a low uptake of vaccination. This investigation would address the role of misconceptions and lack of trust by communities in vaccines. The focus of this intervention would be to seeking out the community religious and cultural leaders while encouraging open community dialogue. Many communities have been found to easily embrace oral polio vaccine while being hesitant to embrace campaigns promoting injections for measles vaccine. The reasons for this disparity need to be further interrogated.

4. There is need for universities, UNEPI, and other stakeholders in vaccination to implement additional context specific studies across various African communities to define Vaccine hesitancy in their context and identify best approaches relating to addressing hesitancy and low uptake of vaccines. A vast majority of communities are affected by different factors, including but not limited to confidence in vaccines, perception of risk; lack of trust or the mistrust of communities in public services (such as healthcare, due to historical issues or contemporary perceptions of segregation and institutional racism), access barriers, barriers related to inconvenience, varying and different socio-demographic contexts, communication or language barriers, religious barriers, cultural factors relating to lack of endorsement of vaccines by cultural or community leaders, inadequate stocks and vaccine unavailability, poor community engagement and lack of adequate communication from the trusted health providers and community health leaders on vaccines.
5. There is urgent need for universities, UNEPI, and other stakeholders in vaccination to conduct studies to test specific interventions in Wakiso and Hoima districts, that can then be escalated to other districts in Uganda, and extending to:

a. Mobilising and educating communities on the advantage of vaccination; both at caregiver level, village health teams' level, cultural and religious leaders and influencers, and health worker level.
b. Training health workers with information on current and new vaccines – these trainings should be regular, frequently updated, to incorporate new and old vaccines, and extend to cold chain, vaccine storage and transport, and record keeping.
c. Implementation of an easy to use and understand system for identifying AEFIs; and the way proper education and communication around adverse events following immunization can help reduce any hesitancy that follows this concerned topic.
d. The implementation of joint approaches for delivery of vaccination services through the "reach every child approach" that covers both routine and outreach and mobile immunization activities.
e. Designing and piloting more novel training programs using newer technologies and techniques that align to new changing landscape due to wider internet availability.

Conclusions

This study filled a critical gap in knowledge by identifying and defining the drivers of poor immunization in Hoima and Wakiso Districts and classifying them into community, geographical, caregiver, child and health system factors. The biggest problems identified centred around access difficulties, inadequate funding, geographical barriers, vaccine stock outs, Cold chain inadequacies, high training needs for health workers and inadequate social mobilisation. While Hoima lacks adequate gas and refrigerators for vaccine, Wakiso lacks stable electricity and experienced higher rates of reported AEFIs than Wakiso.

This study also identified vaccine stock outs (due to unreliable vaccine supply), problems with access to health facilities that offer immunization services (due to transportation related difficulties, very long distance that clients have to travel to health facilities and a very difficult geographical terrain that is hard for vehicles or motor cycles to navigate). In general, Hoima District has adequate Health Facilities to provide required immunization services. However, some of the facilities have no vaccine fridges and therefore have to depend of other neighbouring Health facilities for storage of vaccines, some of which are located far away, due to the district's poor road terrain. Some of these facilities without fridges include Buraru, Kisiha, Nsozi Health Centres.

While the districts have gas supplied from the national government, delivery is affected by poor road network and unsteady fuel supply. The communities want the vaccines, they generally believe the program is helpful and beneficial and protective of VPDs. This positive attitude can be enhanced by continuous engagement and mobilisation efforts. The health workers could be better trained on social mobilisation, community engagement and health promotion strategies. It is clear that the static immunization program is not adequate. Investment in the mobile and outreach approaches is needed. These avenues need strengthening to ensure a two-pronged approach to access of services. Tis will mean provision of fuel, of mobile vans, of vaccine carriers, and additional health worsens to run the program.

This study found that there is a big problem with the poor understanding, identification and reporting of AEFIs because Adverse Events Following Immunization are now central as drivers of reduced uptake of vaccines and caregivers opting out of accepting some vaccines over others. This problem has not been previously robustly studied nor thoroughly described in literature. It has been demonstrated in both Hoima and Wakiso that some parents who embraced oral polio vaccines during campaigns reacted Measles Rubella injectable vaccines during campaigns. Jinja city for example reported a 37% uptake of MR vaccine in the campaign while two weeks it produced a result of above 110% for oral polio vaccines 2nd dose. The fears and hesitancy around Measles-Rubella vaccines due to perceived chances of their children experiencing adverse or unwanted effects have not been justified.

The potential influence and impact of cults has been speculated about, but had not been robustly tested in a study. This study made attempts to inquire into this question, and considerable difficulties were faced in adequately answering this question. There exist pockets of populations that still avoid vaccines due to influence from these cults, but the magnitude is much less. The apparent low impact may be attributed to increasing efforts of education and sensitization of masses and communities on need to take up vaccines and utilise immunization services. We did not observe similar aggressive anti vaccine movements driven by religious and cultural groups in Wakiso district. If they exist, then they are occult at best. The study however noted that there is inadequate social education and community engagement around this topic, and more needs to be done. This is an area requiring close attention both for Hoima and Wakiso districts.

Additionally, immunization centres could offer more education on vaccines to caregivers visiting vaccination centres. This process requires the hiring of additional health workers to support the immunization health promotion agenda and training them on community engagement and education and communication. These sessions would ideally be offered before the immunisation session starts or concurrently as some centres have done. Community engagement especially for caregivers and adolescent girls may help improve the observed low uptake of HPV II (2nd dose) vaccine in both Hoima and Wakiso district. It was observed that while the vaccine is available in both Hoima and Wakiso districts, most girls do not get the second dose, an observation that was also noted in the systematic review, where half or more adolescent girls that already got dose one of cervical cancer vaccine HPV do not turn up for the second dose. The myths, fears, concerns and worries around HPV vaccine in general need to be aggressively dispelled.

There is need to support the outreach component of immunization in Hoima and Wakiso districts in terms of transportation, mentorship and ensuring timely supplies. The hard to reach areas in Hoima district especially Bunyawawa refugee camp, Tonya, Kyangwari and the whole Albertine Lake region can best be served by numerous and frequent immunization outreach activities as compared to other regions with a better terrain. This is key in ensuring catch up for all children who miss to go through the routine static immunization program at health facilities. This can then be replicated in other districts in Uganda. Traditionally, the use of campaigns, especially SIAs has really helped immunization programs fill gaps for the missed children to be vaccinated. These campaigns are very expensive, but when well-coordinated, they can achieve overwhelming and great results. An area of need that requires urgent address is health worker training. This maybe formal pre-service training, or refresher and updates on what they already know. Adverse events, especially ability and knowledge on how to look out for them, how to diagnose them, how to manage them are areas these trainings should also cover.

As regards vaccine hesitancy, assessed based on the 3 C's model of vaccine hesitancy by the SAGE committee of the World Health Organization, Convenience (deals with access to vaccines and access to vaccination services) factors predominated the systematic review and main study as compared to Confidence (where there is no trust in vaccines and in healthcare providers of vaccines); and Complacency (where target groups do not perceive the need for vaccination or they do not value vaccination) factors. There is need to urgently address these factors to solve the contribution of vaccine hesitancy to underimmunization in Uganda and Sub Saharan Africa. There is urgent need to conduct studies to test specific interventions in Wakiso and Hoima districts, that can then be escalated to other districts in Uganda because the challenges faced across board are similar.

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APPENDICES

Appendix A: Data Collection Sheet

Study Topic: Drivers of Vaccine Hesitancy and Underimmunization Among Children of Hoima And Wakiso Districts of Uganda

ID No: ☐☐☐ Health facility:……………………………………...

Date of Interview: _____/_____/________

Day/Month/Year

Interviewer Initials: ☐☐☐ Start Time: End Time:

A. Socio-demographic information				
	QUESTION	**VARIABLE**		**CODE**
1	What is your age?	AGE		
2	What is your gender?	GENDER	1. Male 2. Female	
3	How will you describe your residence?	RESIDE	1. Rural 2. Semi-Urban 3. Urban	
4	What is your religion?	RELIGION	1. Moslem 2. Catholic 3. Protestant 4. Others (specify) …………………. 5. Prefer not to say	
5	What is the marital status?	STATUS	1. Married 2. Single	

			3. Ever married (Divorced/Widow) 4. Prefer not to say	
6	What is your occupation?	OCCUPC	1. Employed 2. Self employed 3. Peasant farmer 4. Home keeper 5. Others (specify) ……………………..	
7	What is your level of education?	EDUC	1. None 2. Primary 3. Secondary 4. Tertiary	
8	Monthly Family Income level	INCOME	1. <Shs 300000 2. Shs 300000- Shs 500000 3. Shs 500000- Shs 900000 4. >Shs 900000 5. Prefer not to say	
9	How many of children in the family?	CHILD		
10	What is the age of all the children?	AGECH		
11	What is your relationship with the child?	RELATION		

12	Who is the main caregiver in the family?	CARE		
B. Resources on health information and medical care				
14	Please arrange the source of health related information you trust the most? From high to low	TRUST	1. Official media (newspapers, radio and television) 2. Family and friends 3. Religious and community leaders 5. General practitioners 6. School teacher 7. Social media 8. Others (specify) ………………….	
14 a	Has distance, timing of clinic, time needed to get to clinic or wait at clinic and costs to get to health facility prevented you from getting your child immunized?	PREVAC1	1. Yes 2. No	
b	From the reasons listed above, which one bother you the most?	PREVAC2		
15 a	Do you pay anything extra in the process of vaccination?	PAYVAX1	1. Yes 2. No	

b	If yes, what is it?	PAYVAX2		
16	Before administering the vaccine, my healthcare worker always provides me with enough information on the side effects that might follow immunization.	INF	1. Yes 2. No	
17	My healthcare worker provides me with all the information I need to my questions on immunization.	QUESTION	1. Yes 2. No	
18 a	Have you ever felt healthcare workers, government, local authorities are pushing you into a vaccination decision you did not fully support?	PRES1	1. Yes 2. No	
b	If yes, which one? And why?	PRES2		
19 a	Has your healthcare worker ever advised you that a certain vaccine was not necessary or had too many side effects?	ADVISE1	1. Yes 2. No	
b	Which one? And why?	ADVISE2		
20 a	Did healthcare workers ever treat you without respect (e.g. in regard to your appearance, education or cultural	BEHAVE1	1. Yes 2. No	

	background) that you will hesitate to return to the healthcare facility?			
b	Is yes, what is the reason they treated you without respect?	BEHAVE2		
C. Vaccine compliance and confidence				
21	Do you think vaccine are safe?	SAFE	1. Yes 2. No	
22	Do you think vaccines are effective?	EFFECTIVE	1. Yes 2. No	
23	Do you believe that if you vaccinate your child, others are protected as well?	VACPRT	1. Yes 2. No	
24 a	Do you believe that there are better ways to prevent diseases which can be prevented by vaccine?	PREVENT1	1. Yes 2. No	
b	If yes, what are the ways?	PREVENT2		
25	Do you think that most parents like you have their child vaccinated with all the recommended vaccination?	RECOM	1. Yes 2. No	
26	Do you think it is possible to receive too many vaccines at one time?	MANYV	1. Yes 2. No	
27 a	Are there other pressure in your life that prevent you from getting your child vaccinated?	PRESSU1	1. Yes 2. No	
b	If yes, what are the pressures?	PRESSU2		

28 a	Have you ever received or heard negative information about vaccination?	NEGATIV1	1. Yes 2. No	
b	If yes, what are they?	NEGATIV2		
29	Do you remember any events that you experienced in the past would discourage you from getting a vaccine(s) for yourself or your children?	NEG	1. Yes 2. No	
30	Do leaders (religious / political leaders, teachers, healthcare workers) in your community support vaccinations for infants and children?	SUPPORT	1. Yes 2. No	
31 a	Does your religion/ philosophy/ culture recommend against (a certain) vaccination?	RELIGON1	1. Yes 2. No	
b	If yes, which/all vaccines? What is the reason?	RELIGON2		
32	Did you ever disagree with the choice of vaccine recommendation provided by your government?	CHOICE1	1. Yes 2. No	
b	If yes, which/all vaccines? What is the reason?	CHOICE2		

33	If you had another child, would you want him/her to get all the recommended shots?	VACCINATE	1. Yes 2. No	
D. Child vaccine history				
34 a	Have you vaccinate your child with all the vaccines recommended in the National Immunization program?	VACNIP	1. Yes 2. No	
b	If no, why you don't vaccinate?	REASON		
35 a	Have you ever been reluctant or hesitant to get a vaccination for your child?	HESITANT1	1. Yes 2. No	
b	If yes, which vaccine(s) and why?	HESITANT2		
36 a	Have you ever refused vaccination for your child?	REFUSE1	1. Yes 2. No	
b	If yes, which vaccine(s) and why?	REFUSE2		
37 a	Are there any reasons you can think of why children should not be vaccinated?	CHVAXNO1	1. Yes 2. No	
b	If yes, what are the reasons?	CHVAXNO2		
38	Do you fear the pain to your child when receiving a vaccine make you hesitate to be immunized?	FEAR	1. Yes 2. No	
39	Is the vaccination process welcoming?	WELCOME	1. Yes 2. No	

40 a	Are there any things that could be done to make it easier for you to get vaccines (on time) for yourself or your children?	EASY1	1. Yes 2. No	
b	If yes, what are they?	EASY2		
41 a	Have you ever been sent home from the health facilities due to lack of vaccine?	LACK1	1. Yes 2. No	
b	If so, did you go again to receive it?	LACK2	1. Yes 2. No	
C. Indicate your level of agreement for the following statements (1=Strongly Agree, 2=Agree, 3=Neither Agree nor disagree, 4=Disagree, 5=Strongly Disagree)				
42	Childhood vaccines are important for my child's health.			
43	Measles is not common where I live. That's why I don't think it is necessary to vaccinate.			
44	All childhood vaccines offered by the government program in my community are beneficial.			
45	Generally, I do what my healthcare worker recommends about vaccines for my child/children.			
46	The information I receive about vaccines from the immunization program is reliable and trustworthy			
47	I am concerned about serious adverse effects of vaccines			
48	My child/children does or do not need vaccines for diseases that are not common anymore			
49	It is better for my child to develop the immunity by getting sick rather than to get a shot.			

50	I think I have enough knowledge on vaccine and vaccination.	
51	I think the vaccine will overload the immune system.	

APPENDIX B: Guide for Focus Group Discussions

Purpose of the FGD: Understanding caregivers' beliefs toward vaccine and vaccination

Participants: All caregivers, who are visiting the health facilities, have at least one child of 1 month to 10 years old and are living in Wakiso district. Each FGD should have at least 8 participants (8-12), with a moderator and note taker, recording to be done; consent must be sought before FGDs

Describe participants – mothers, fathers, caretakers, number of kids

Campaigns related

1 Do you know the purpose of the vaccination campaigns? How do you get information on vaccination campaign?

2 Did you feel any difference with new immunization campaign (MR vaccine introduction) compare with the old immunization campaigns? (Process, reaction, information).

Vaccination related

1 Why do you think children are given vaccines/immunization?

2 Do you know what is the current national immunization schedule? Did your child receive all the dose on time?

3 Can we see the vaccination card? Can we take some photos of it?

3.1 Is there any notification for receiving the next vaccination?

4 Do you think that most parents from your area accept taking their children for immunization? Are there those who do not? What are some of the reasons why they opt not to take the children for immunization?

5 Are there situations when you failed to bring your child for immunization? What were the reasons?

5.1 Is there other difficulties that you have to put it in the top priority than vaccination?

6 Are there days you went to a health facility and found when there were no vaccines? Which vaccine was it? And what did you do to get your child vaccinated?

7 What is your experience of vaccine administration? (Good/ Bad)

7.1 Are there any side effects to vaccines? Has your child or a child you know of ever got those side effects? What did the parent or caretaker do to help the affected child?

8 Are there any religious groups or cultural groups you know of, (maybe not from your area) that do not encourage or promote immunization for children? If yes, what are their reasons for being against vaccines/immunization?

9 What is the first thing the government does when they want to introduce a new vaccine formulation (MR vaccine) to your area? Do they educate the community enough? Do they usually get feedback from the community?

10 What can be done or in what ways do you think parents/mothers from your locality can be better empowered or helped to demand for or access immunization services?

Measles related specific questions

1 Do you know what is measles?

1.1 What may be the consequences of measles?

2 Did your child ever experienced measles infection?

3 Do you think the measles vaccine is safe and effective?

APPENDIX C: Key Informant Guide - Health Workers

A. General information

Record identifiers

Position	Gender	Duration of work at the facility	Roles in immunization.

1. The level of health facility…………….

2. How many staff do you have in this facility, (give numbers by cardre)… 1) Doctor 2) C/Officers… 3) Nursing officer… 4) E/Nurses 5) N/assistants … 6) others…………..

3. Does this facility open 24hours and 7 days a week 1) Yes 2) No

If No why……………………………………………………………………………….

4. Do you have a functional cold chain …………………………………………………

5. Have you had any stock out of vaccines and supplies in the last 3 months? 1) Yes 2) No.

Which vaccine/vaccines………………………………………………

6. Is this facility supervised by the HSD and DHT? 1) Yes 2) No

7. How many supervisions have you had in the last 3 months …………………………………

Verify by copy of report (s) or supervision book.

8. What kind of immunization services do you offer (1) Static services only (2) both static and out reaches. Does this facility conduct immunization outreaches in the community? Why or why not?

9. Do you offer static immunization services daily? 1) Yes 2) No

If no, how many times in a week and why? ……………………………………..

How do you pass information to the community regarding the services you offer in immunization?

10. Have conducted all the planned outreach services in the last quarter 1) Yes 2) No

If No Why…………………………………………………………………………..

If yes, how many times do you run outreach services in week……………………………

B. Facilitators and Barriers to utilization of immunization services:

11. What is the first thing you want to know when a new vaccine is introduced or announced?

b) Would you rather wait and see what other people do?

12. Do you know of a child with a serious disease/ disability because they were not vaccinated?

12. What are the key things that make it easy for you to provide immunization services to children in your catchment area/facility?

(**Probe for facilitators at:**

-Health facility/ Community for outreach services levels

13. What would you say are the major barriers /things that make it difficult for care takers to fully immunize their children in your catchment area?

(**Probe for barriers at:**

-Health facility/ Community levels.

14. What should be done to improve immunization coverage in your catchment area/facility?

Probe for what should be done at;

-Family level/ Community level/ Health facility level.

C : Vaccine Supply and Cold Chain maintenance

15. Which agency supplies this facility with vaccines? Would you say that the supply is adequate?
16. Do you experience vaccine stock outs? If so, how often?
17. Which vaccines are the most affected by shortage in supply?
18. What are some of the strategies you employ to ensure there is adequate supply in the facility?

19. Do you have a cold chain system in place to prevent vaccine spoilage? What is your source of power for the refrigerator?
20. How consistent is power availability? Do you have a back - up generator in the event of a power blackout?
21. How efficient is the cold chain system that has been put in place?
22. Do you experience malfunctioning of equipment? If so, how often? What measures are taken to correct this? How long does it take for the system to be fully operational after a breakdown?

D - Adverse Events Following Immunization (AEFIs)

23. Have you experienced any AEFIs in your facility? If so, how many?
24. How often does this happen? What would you attribute it to?
25. Do you have a reporting system for AEFIs? Is this system standardized?
26. Is there a reporting tool available for this?
27. What are the measures taken to prevent this from recurring?
28. Do you have any other comment or questions you would like us to talk about in relation to immunization services for children?

Thank you very much for your time and sharing with us.

APPENDIX D: Key Informant Interview Guide - District and Community Leaders

A. General information;

Record identifiers e.g. position and gender, Duration of work in that role, roles as far as immunization is concerned…………………………………

1. How do you rate immunization performance in your area 1) Good 2) Average 3) Poor

Why? ....

2. What in your opinion are health facility factors facilitating utilization of immunization services………………………………………………………………………………………

3. What in your opinion are community factors barring utilization of immunization services…………………………………………………………………………………………

4. Is there anything in your opinion you think needs to be done to maintain or improve immunization services in your area…………………………………………………………

5. Do you know of a child with a serious disease/ disability because they were not vaccinated?

6. Do you experience vaccine stock outs? If so, how often? If yes, which vaccines are the most affected by shortage in supply? What are some of the strategies that can be employed to ensure there is adequate supply in the facilities?

7. What is the first thing you want to know when a new vaccine is introduced or announced?

8. Do you know of a child with a serious disease/ disability because they were not vaccinated?

9. What are the key things that make it easy for you to provide immunization services to children in your community?

10. What would you say are the major barriers /things that make it difficult for care takers to fully immunize their children in your catchment area?

11. What should be done to improve immunization coverage in your community?

12. Do you have any other comment or questions you would like us to talk about in relation to immunization services for children?

Thank you very much for your time and sharing with us.

Appendix E: Unicaf University Research Ethics Committee Decision

UNICAF UNIVERSITY

UREC Desision, Version 2.0

Unicaf University Research Ethics Committee Decision

Student's Name: Oliver Ombeva Malande

Student's ID #: R1903D7960792

Supervisor's Name: Dr Victor Adamu

Program of Study: UU-DOC-900-3-ZM

Offer ID /Group ID: O29349G30803

Dissertation Stage: DS 3

Research Project Title: Drivers of Hesitancy and Underimmunization Among Children in Uganda: A Case Study of Hoima District

Comments: 5b - Inclusion criteria: caregiver with at least one child (1 - 59 months). However in the Focus group discussion stated the following: have at least one child of 1 month to 10 years old. Please be consistent.

Decision*: B. Approved with comments for minor revision

Date: 25-Nov-2021

*Provisional approval provided at the Dissertation Stage 1, whereas the final approval is provided at the Dissertation stage 3. The student is allowed to proceed to data collection following the final approval.

Appendix F: Gatekeeper letter

UNICAF UNIVERSITY

UU_GL - Version 2.0

Gatekeeper letter

Address: BOX 3040, KAMPALA

Date: 01-Oct-2021

Subject: INTRODUCTION LETTER TO CONDUCT RESEARCH

Dear District Health Officer, Wakiso/Hoima District, Uganda,

I am an/a **doctoral [PhD]** student at Unicaf University **Zambia**.

As part of my degree I am carrying out a study on **Drivers of Vaccine Hesitancy and Underimmunization Among Children of Hoima and Wakiso Districts of Uganda.**

I am writing to **request for your support and permission to recruit and carry out this study in your district.**

Subject to approval by Unicaf Research Ethics Committee (UREC) this study will be using **interviews and focus group discussions for caregivers of children and key informant interviews of focal immunization persons within the district.**

My Supervisor is Prof Victor Adamu. This study has both quantitative and qualitative arms. The Quantitative data collection methods will entail Structured interview administered questionnaires of child caregivers from Wakiso and Hoima districts; a systematic review meta-analysis of published work on vaccine hesitancy and under-immunization in sub-Saharan Africa (SSA) aimed at assembling a firm and deep understanding of and consolidating the contextual aspects and drivers of vaccine hesitancy in the Africa; and collection of secondary data sourced from immunization records at Wakiso and Hoima District Head Quarters, the national EPI Health records office, and from vaccination health centres within Wakiso and Hoima Districts. The Qualitative data collection Methods will include Focus group discussions (FGDs) with child caregivers (not involved in the IDIs) from Wakiso and Hoima districts and Key informant interviews (KIIs) involving focal vaccination personnel from Wakiso and Hoima districts.

Thank you in advance for your time and for your consideration of this project. Kindly please let me know if you require any further information or need any further clarifications.

Yours Sincerely,

OLIVER OMBEVA MALANDE

Student's Name: OLIVER OMBEVA MALANDE
Student's E-mail: ombevaom@gmail.com
Student's Address and Telephone: Box 3040, Kampala, Tel: +256774068762
Supervisor's Title and Name: PROF VICTOR ADAMU
Supervisor's Position: FACULTY, UNICAF University, Lusaka, Zambia
Supervisor's E-mail: v.adamu@unicaf.org

Appendix G: Unicaf informed Consent Form

UNICAF UNIVERSITY

UU_IC - Version 2.1

Informed Consent Form

Part 1: Debriefing of Participants

Student's Name: OLIVER OMBEVA MALANDE

Student's E-mail Address: ombevaom@gmail.com

Student ID #: R1903D7960792

Supervisor's Name: PROF VICTOR ADAMU

University Campus: Unicaf University Zambia (UUZ)

Program of Study: UUZ: PhD Doctorate of Philosophy

Research Project Title: DRIVERS OF VACCINE HESITANCY AND UNDERIMMUNIZATION AMONG CHILDREN OF HOIMA AND WAKISO DISTRICTS OF UGANDA

Date: 13-Oct-2021

Provide a short description (purpose, aim and significance) of the research project, and explain why and how you have chosen this person to participate in this research (maximum 150 words).

We are doing a project to find out the immunization status of your child, whether the child developed any undesired reactions following the immunization and what caregivers do when such reactions occur. This new information may help improve immunization services in future. You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join, or withdraw your consent to be in the study without penalty. You may not receive any direct benefit from being in the research study. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, or your health care provider or determine if your child receives health care during your immunization visit. You may ask any member of the research team, any questions you have about this study at any time.

The above named Student is committed in ensuring participant's voluntarily participation in the research project and guaranteeing there are no potential risks and/or harms to the participants.

Participants have the right to withdraw at any stage (prior or post the completion) of the research without any consequences and without providing any explanation. In these cases, data collected will be deleted.

All data and information collected will be coded and will not be accessible to anyone outside this research. Data described and included in dissemination activities will only refer to coded information ensuring beyond the bounds of possibility participant identification.

I, OLIVER OMBEVA MALANDE **, ensure that all information stated above is true and that all conditions have been met.**

Student's Signature: ____________________

UU_IC - Version 2.1

Informed Consent Form

Part 2: Certificate of Consent

This section is mandatory and should to be signed by the participant(s)

Student's Name: OLIVER OMBEVA MALANDE

Student's E-mail Address: ombevaom@gmail.com

Student ID #: R1903D7960792

Supervisor's Name: PROF VICTOR ADAMU

University Campus: Unicaf University Zambia (UUZ)

Program of Study: UUZ: PhD Doctorate of Philosophy

Research Project Title: DRIVERS OF VACCINE HESITANCY AND UNDERIMMUNIZATION AMONG CHILDREN OF HOIMA AND WAKISO DISTRICTS OF UGANDA

I have read the foregoing information about this study, or it has been read to me. I have had the opportunity to ask questions and discuss about it. I have received satisfactory answers to all my questions and I have received enough information about this study. I understand that I am free to withdraw from this study at any time without giving a reason for withdrawing and without negative consequences. I consent to the use of multimedia (e.g. audio recordings, video recordings) for the purposes of my participation to this study. I understand that my data will remain anonymous and confidential, unless stated otherwise. I consent voluntarily to be a participant in this study.

Participant's Print name:

Participant's Signature: ____________________

Date:

If the Participant is illiterate:

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had an opportunity to ask questions. I confirm that the aforementioned individual has given consent freely.

Witness's Print name:

Witness's Signature: ____________________

Date:

Appendix H: UNICAF University Research Ethics Application Form Doctoral Studies Provisional Approval

UNICAF UNIVERSITY

REAF_DSPA - Version 1.0 AP

UNICAF UNIVERSITY
RESEARCH ETHICS APPLICATION FORM
DOCTORAL STUDIES PROVISIONAL APPROVAL

The Provisional Approval - Research Ethics Application Form (REAF) should be completed by Doctoral level candidates enrolled on Dissertation stage 1.

This form is a **provisional approval** which means that the UREC committee has accepted the initial description of the project but this is conditional as changes may have to be implemented following Dissertation Stage 2 and piloting in Dissertation Stage 3.

This is a conditional offer and acceptance of the project needs to be verified and confirmed upon completion of the Research Ethics Application Form in Dissertation Stage 3.

Important Notes:

- An electronic version of the completed form should be uploaded by the student to the relevant submission link in the VLE. Student's supervisor will then review the form and provide feedback commentary. Once supervisor's initial approval is given then the supervisor will forward this to doctoral.studies-aa@unicaf.org, for provisional approval by the Unicaf University Research Ethics Committee (UREC).
- Please type your answers and **do not** submit paper copy scans. Only *PDF* format documents should be submitted to the committee.
- If you need to supply any supplementary material, not specifically requested by the application form, please do so in a separate file. Any additional document(s) should be clearly labelled and uploaded in the relevant VLE link.
- If you have any queries about the form, please address them to your dissertation or project supervisor.

OLIVER OMBEVA MALANDE R1903D7960792 1

UNICAF UNIVERSITY
RESEARCH ETHICS APPLICATION FORM
DOCTORAL STUDIES PROVISIONAL APPROVAL

UREC USE ONLY:
Application No:
Date Received:

Student's Name: OLIVER OMBEVA MALANDE

Student's E-mail Address: ombevaom@gmail.com

Student's ID #: R1903D7960792

Supervisor's Name: PROF VICTOR ADAMU

University Campus: Unicaf University Zambia (UUZ)

Program of Study: UUZ: PhD Doctorate of Philosophy

Research Project Title: DRIVERS OF VACCINE HESITANCY AND UNDERIMMUNIZATION AMONG CHILDREN OF HOIMA AND WAKISO DISTRICTS OF UGANDA

1. **Please state the timelines involved in the proposed research project:**

Estimated Start Date: 01-Sep-2021 Estimated End Date: 30-Sep-2022

2. **The research project**

a. **Project Summary:**

In this section please fully describe the purpose and underlying rationale for the proposed research project. Ensure that you pose the research questions to be examined, state the hypotheses, and discuss the expected results of your research and their potential.

It is important in your description to use plain language so it can be understood by all members of the UREC, especially those who are not necessarily experts in the particular discipline. To that effect please ensure that you fully explain / define any technical terms or discipline-specific terminology (maximum 300 words +/- 10%).

Immunization, a strategy identified to ensure child survival can prevent over two million deaths annually, especially in poor countries like Uganda (Wolfson LJ, 2008) (Rutherford ME, 2009). Vaccine hesitancy, declared in 2017 by WHO as one of the top ten threats to global health, is partly driven by poor education levels for health workers and caretakers; poor geographical terrain hindering access to remote areas; political instability, wars and displacements; mobile refugee status and poor supply of immunization services (Burton A, 2009). The vaccination coverage in urban (61%) and rural (50%) Uganda have remained below recommended levels of 90% (UDHS, 2016) despite the country running a stable national expanded immunization programme (EPI). Rural Hoima and (peri)urban Wakiso districts with low coverage frequently report outbreaks of vaccine preventable diseases (UDHS, 2016). It is our hypothesis that in rural Hoima and (peri)urban Wakiso districts of Uganda, most children fail to complete the recommended immunization schedule due to factors related to hesitancy, vaccine refusal, low confidence in immunization, and inadequate supply of immunization services. This study will initially seek to answer the question: what are the determinants of vaccine hesitancy and underimmunization in sub-Saharan Africa? This systematic review will provide crucial information of the impact of hesitancy on immunization uptake in SSA which does as well apply to Uganda. The study will also additionally answer these questions: What are the barriers to the uptake and utilization of immunization services in rural Hoima District, Uganda; What are the barriers to uptake and utilization of immunization services in urban and peri-urban Wakiso District, of Uganda and finally how do the drivers of vaccine hesitancy in rural (Hoima) versus Urban/peri-urban (Wakiso) Districts of Uganda compare. In answering these questions, the study will identify and propose educational interventions, communication strategies and health system approaches that can help address the problem of vaccine hesitancy and underimmunization in Uganda.

b. Significance of the Proposed Research Study and Potential Benefits:

Outline the potential significance and/or benefits of the research (maximum 200 words).

The identification of vaccine hesitancy as a threat to global health emphasized the need for urgent interventions to address this problem. Factors contributing to vaccine hesitancy vary from one place to another. With low immunization coverage and frequent outbreaks of vaccine preventable diseases in Hoima and Wakiso districts of Uganda, studies to explore the reasons behind this problem are necessary. This study will identify barriers to the uptake of immunization, reasons for underimmunization, drivers for vaccine hesitancy and reasons for low confidence in immunization in rural Hoima and (peri)urban Wakiso districts, and thus provide useful information for planning, forecasting, and addressing these recurrent problems that contribute to immunization coverage rates that have remained below the WHO recommended targets. This study will generate and propose educational interventions, tools, communication strategies and health system focused approaches that can help address the problem of vaccine hesitancy and underimmunization particularly in Uganda and Sub-Saharan Africa in general.

3. <u>Project execution:</u>

a. Type of project. The following study is an:

- [x] experimental study (primary research)
- [x] desktop study (secondary research)
- [ ] desktop study using existing databases involving information of human/animal subjects
- [ ] Other

If you have chosen 'Other' please Explain:

The experimental arm on barriers to uptake and utilization of immunization services will involve conduct of primary research in Hoima and Wakiso districts. Additionally, a systematic review (meta-analysis/meta-synthesis) of published work/articles on vaccine hesitancy and underimmunization in sub-Saharan Africa will be undertaken, to establish and assemble a firm and deep understanding of vaccine hesitancy in SubSaharan Africa.

b. Methods. The following study will involve the use of:

Method	Materials / Tools
☑ Qualitative	☑ Face to Face Interviews ☐ Phone Interviews ☑ Face to Face Focus Groups ☐ Online Focus Groups ☐ Other*
☑ Quantitative	☑ Self-administered Questionnaires ☐ Online Questionnaires ☐ Experiments ☐ Tests ☑ Other *

*If you have chosen 'Other' please Explain:

A systematic review (meta-analysis/meta-synthesis) of published work on vaccine hesitancy and under-immunization in sub-Saharan Africa (SSA). This will establish a deep understanding of the problem of vaccine hesitancy and under-immunization in SSA.

4. Participants

a. Does the Project involve the recruitment of participants?

☑ YES **If YES, please complete all following sections.**

☐ NO **If NO, please directly proceed to Question 5.**

Note: The definition of "participation" includes active participation, such as when participants knowingly take part in an interview or complete a questionnaire.

b. Relevant Participant Details of the Proposed Research

Please state the number of participants you plan to recruit, and describe important characteristics such as: demographics (e.g. age, gender, location, affiliation, level of fitness, intellectual ability etc). It is also important that you specify any inclusion and exclusion criteria that will be applied (e.g. eligibility criteria for participants).

Number of participants: 600

Age range: From 18 To 65

Gender:
- ☑ Female
- ☑ Male

Eligibility Criteria:

- Inclusion criteria: A caregiver with at least one child (1 - 59 months); a resident of Hoima/Wakiso district; can give the required information; provides informed consent & who has carried the child's vaccination book record/vaccination card.

- Exclusion criteria: A Caretaker of a child aged 1 - 59 months in their home who does not consent or who is unable to give the required information due to mental/other incapacity.

Disabilities: They will be included provided they satisfy the inclusion criteria and consent for the study

Other relevant information (maximum 100 words):

The WHO's 30 cluster sampling technique for immunization coverage cluster survey design, which allows a small number of target populations to be sampled while providing data that is statistically valid, will be used. The Standard EPI Cluster Survey Design recommends use of 30 clusters taking at least 7 respondents from each of the clusters giving a total of 210 quantitative samples. To allow for none response, 3 respondents will be added per cluster giving a minimum of 300 participants each for Hoima and Wakiso. Additionally 10 FGDs and 40 Key informants per District will be required.

c. Recruitment Process for Human Research Participants:

Please clearly describe how the potential participants will be identified, approached and recruited (maximum 200 words).

The principal investigator (PI) will visit Hoima & Wakiso District Health Offices for permission to conduct the study & introduction of study team to members to district immunization focal persons & heads of active immunization centers. The target population are caregivers with children 1-59 months old visiting immunization centers for vaccination. Research assistants/PI will introduce themselves, seek permission from the caregivers to participate in the study, conduct advocacy/approval visits to health centers & sensitize participants on data collection process. Informed consent will be acknowledged by thumb print or signing informed consent document. Data will be obtained from caretakers using pre-tested questionnaire, plus collecting relevant data from the child's immunization card. Vaccination will be validated with a vaccination card, and assessed by vaccination card and caretaker history. After identifying eligile caretakers, focus group discussions will be done at agreed venues in (local) language spoken and understood by all participants. The discussions will be audio recorded and then later transcribed.

d. Relationship between the principal investigator and participants:

Is there any relationship between the principal investigator (student), co-investigators(s), (supervisor) and participant(s)? For example, if you are conducting research in a school environment on students in your classroom (e.g. instructor-student).

☐ YES ☑ NO

If YES, please specify (maximum 100 words).

5. Further Approvals

Are there any other approvals required (in addition to ethics clearance from UREC) in order to carry out the proposed research study?

☑ YES ☐ NO

If YES, please specify (maximum 100 words).

The study protocol will be submitted to the School of Medicine, Research and Ethics Committee of the College of Health Sciences, Makerere University for scientific/ethical review and approval. Where applicable, additional research and ethical approval may be sought and obtained from the National Uganda National Council for Science and Technology (UNCST), especially as regards access to secondary data on immunization.

6. Potential Risks of the Proposed Research Study

Are there any potential risks, psychological harm and/or ethical issues associated with the proposed research study, other than risks pertaining to everyday life events (such as the risk of an accident when travelling to a remote location for data collection)?

☐ YES ☑ NO

If YES, please specify (maximum 150 words):

7. Application Checklist

Please mark √ if the study involves any of the following:

☐ Children and young people under 18 years of age, vulnerable population such as children with special educational needs (SEN), racial or ethnic minorities, socioeconomically disadvantaged, pregnant women, elderly, malnourished people, and ill people.

☐ Research that foresees risks and disadvantages that would affect any participant of the study such as anxiety, stress, pain or physical discomfort, harm risk (which is more than is expected from everyday life) or any other act that participants might believe is detrimental to their wellbeing and / or has the potential to / will infringe on their human rights / fundamental rights.

☐ Risk to the well-being and personal safety of the researcher.

☐ Administration of any substance (food / drink / chemicals / pharmaceuticals / supplements / chemical agent or vaccines or other substances (including vitamins or food substances) to human participants.

☐ Results that may have an adverse impact on the natural or built environment.

8. Final Declaration by Applicants:

(a) I declare that this application is submitted on the basis that the information it contains is confidential and will only be used by Unicaf University and Unicaf University Research Ethics Committee (UREC) for the explicit purpose of ethical review and monitoring of the conduct of the research proposed project as described in the preceding pages.

(b) I understand that this information will not be used for any other purpose without my prior consent, excluding use intended to satisfy reporting requirements to relevant regulatory bodies.

(c) The information in this form, together with any accompanying information, is complete and correct to the best of my knowledge and belief and I take full responsibility for it.

(d) I undertake to abide by the highest possible international ethical standards governing the Code of Practice for Research Involving Human Participants, as published by the UN WHO Research Ethics Review Committee (ERC) on http://www.who.int/ethics/research/en/ and to which Unicaf University aspires to.

(e) In addition to respect any and all relevant professional bodies' codes of conduct and/or ethical guidelines, where applicable, while in pursuit of this research project.

(f) I understand it is my responsibility to submit a full REAF application during Dissertation Stage 3 to UREC. If a REAF application is not submitted my project is not approved by UREC.

(g) I fully acknowledge that this form does not constitute approval of the proposed project but it is only a provisional approval.

☑ **I agree with all points listed under Question 8**

Student's Name: OLIVER OMBEVA MALANDE

Supervisor's Name: PROF VICTOR ADAMU

Date of Application: 15-Sep-2020

Important Note:
Please now save your completed form (we suggest you also print a copy for your records) and then submit it to your UU Dissertation/project supervisor (tutor). **In the case of student projects, the responsibility lies with the Faculty Dissertation/Project Supervisor.** If this is a student application, then it should be submitted via the relevant link in the VLE. Please submit only electronically filled in copies; **do not** hand fill and submit scanned paper copies of this application.

☑ **Before submitting your application, please tick this box to confirm that all relevant sections have been filled in and the information contained is accurate to the best of your knowledge.**