Characterisation of national immunisation programmes in countries experiencing public health emergencies within the WHO Africa region

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CHPVIO001

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PREAMBLE

DECLARATION

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

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ABSTRACT

Background

The World Health Organisation (WHO) African region experiences multiple public health emergencies (PHEs) annually. PHEs have been documented to affect the provision of health services including immunisation. To our knowledge, there is a scarcity of studies characterising PHEs and the performance of national immunisation programmes (NIPs) in countries within the WHO Africa region that have experienced PHEs. This study assessed PHEs (armed conflicts, disasters, and disease outbreaks) and the performance of NIPs in the context of PHEs using global and regional immunisation targets.

Methods

Countries in the WHO Africa region that were reported to benefit from the African Public Health Emergency Fund (APHEF) were used as case studies. Data on PHEs and immunisation indicators recorded between 2010 and 2019 in the study countries were extracted from different electronic PHE databases (the Emergency Events database, the Uppsala Conflict Data Program, the WHO Emergency Preparedness and Response, and the Program for Monitoring Emerging Diseases Mail) and the WHO/UNICEF immunisation database, respectively.

The PHEs and immunisation indicators were stratified by country and summarised using descriptive statistics. The Mann-Whitney U test was carried out to determine the association between the frequency of PHEs and the performance of NIPs in the selected countries from 2010 to 2019. Statistical significance was defined at p-value < 0.05.

Results

Thirteen countries were included in this study. A total of 175 disease outbreaks, 288 armed conflicts, and 318 disasters were reported to have occurred within the 13 countries from 2010

to 2019. The Democratic Republic of Congo had the highest total PHE count (n=208), while Liberia had the lowest (n=20).

Only three of the 13 countries had a median coverage value for the third dose of the combined Diphtheria, Tetanus, and Pertussis vaccine (DTP3) that had attained the target for ≥90% immunisation coverage.

Higher counts of armed conflict and total PHEs were statistically significantly ($p<0.01$) associated with not meeting the immunisation targets for national DTP3 coverage of ≥90% and Maternal and Neonatal Tetanus (MNT) elimination, $p<0.01$. Higher disaster counts were also, significantly ($p=0.03$) associated with not attaining MNT elimination.

Conclusion

PHEs are prevalent in the WHO Africa region, irrespective of the level of a country's immunisation maturity. In absence of effective interventions, PHEs have the potential to derail the progress of NIPs in the WHO Africa region. As we enter the Immunisation Agenda 2030 era, this study advocates for the prioritisation of interventions to mitigate the impacts of PHEs on the NIPs.

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LIST OF ABBREVIATIONS

APHEF	African Public Health Emergency Fund
COVID-19	Coronavirus Disease
DoV	Decade of Vaccines
DTP1	First dose of the combined Diphtheria, Tetanus, and Pertussis Vaccine
DTP3	Third dose of the combined Diphtheria, Tetanus, and Pertussis Vaccine
EPI	Expanded Programme on Immunisation
GVAP	Global Vaccine Action Plan
HPV	Human Papillomavirus
JRF	Joint Reporting Form
MNT	Maternal and Neonatal Tetanus
NIPs	National Immunisation Programmes
NITAG	National Immunisation Technical Advisory Group
PCV	Pneumococcal Conjugate Vaccine
PHE	Public Health Emergency
RSPI	Regional Strategic Plan for Immunisation
UNICEF	United Nations Children's Fund
VACFA	Vaccines for Africa Initiative
VPDs	Vaccine-Preventable Diseases
WHO	World Health Organisation

GLOSSARY

Armed conflict- A dispute involving the use of armed force between two or more parties.

Disaster- A serious disruption of the functioning of a community or a society causing widespread human, material, economic or environmental losses which exceed the ability of the affected community or society to cope using its own resources. It can be either natural or technological.

Natural disaster- events brought about by natural hazards e.g., floods and earthquakes that seriously affect the society, economy, and/or infrastructure of a region.

Non-state armed conflict- The use of armed force between two organised armed groups, neither of which is the government.

One-sided violence- The deliberate use of armed force by the government or by a formally organised group against civilians.

State armed conflict- use of armed force between two parties, of which at least one is the government.

Technological disaster- Examples include transport accidents, multiple collisions, fires, and explosions.

Adopted from the following sources: The Emergency Events Database (EM-DAT)[1], the Uppsala Conflict Data Program (UCDP)[2] and the ReliefWeb Glossary of Humanitarian Terms[3].

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[1] https://www.emdat.be/Glossary. Accessed 12 November 2020.
[2] https://www.pcr.uu.se/research/ucdp/definitions/#tocjump_06798436313805123_33. Accessed 12 November 2020.
[3] https://reliefweb.int/sites/reliefweb.int/files/resources/4F99A3C28EC37D0EC12574A4002E89B4-reliefweb_aug2008.pdf. Accessed 12 November 2020.

ORGANISATION OF THESIS

This thesis is divided into three sections: Part A to Part C.

Part A- the research protocol outlines the background to the study with a literature review, the study rationale, study objectives, methods, and ethical considerations.

The journal manuscript (Part B) is formatted using submission guidelines of a selected peer-reviewed journal. This part summarises the background, outlines the methods used, presents, and discusses the results from the study, and the conclusions from the study.

Part C- the appendices section, includes the ethics documentation, submission guidelines for the selected journal used in formatting the manuscript, and an addendum material to the literature in the introduction part of the protocol. The referencing style used for the entire thesis is Vancouver, as outlined in the submission guidelines of the selected journal.

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PART A: RESEARCH PROTOCOL

PROTOCOL SYNOPSIS

Immunisation is recognised as one of the most effective public health interventions of modern time (1, 2). Immunisation not only saves lives but also, enhances the social and economic wellbeing of communities and countries (3).

Numerous benefits have been accrued from immunisation including global eradication of smallpox and a reduction in the mortalities caused by different vaccine-preventable diseases (VPDs) (1, 4). However, optimising the benefits of immunisation by achieving high coverage has proved evasive (4). For instance, in the World Health Organisation (WHO) African region, while immunisation coverage for the third dose of the combined Diphtheria, Tetanus and Pertussis vaccine (DTP3) has risen from 57% in 2000 to 74% in 2019, the past decade has, however, witnessed a stagnated coverage (5, 6). Furthermore, the region has lagged in meeting the 90% immunisation coverage target set for the decade between 2010 and 2020 (7).

Sub-optimal trends in immunisation coverage can be propagated by various factors, including the widespread occurrence of public health emergencies (PHEs) (8-10). From 2010 to 2019 the WHO Africa region has experienced various PHEs ranging from disease outbreaks, natural disasters, and human-induced hazards (11). The PHEs have been reported to put pressure on the already burdened and weakened health systems within WHO Africa region member states (12, 13). Generally, national immunisation programmes (NIPs) are embedded within the broader health system (14). The NIPs are, therefore, susceptible to the impact PHEs have on the entire health system (14). Where PHEs occur, the performance of NIPs may eventually be undermined (8, 13). Unfortunately, the impact of PHEs on the performance of NIPs in the WHO Africa region remains inadequately studied.

The proposed study aims to characterise the performance of NIPs in the WHO Africa region experiencing PHEs between 2010 and 2019. The African Public Health Emergency Fund

(APHEF), a solidarity fund instituted by the WHO Africa region in 2012 to aid in the mitigation of PHE occurrences (15), will be used as a reference in selecting countries to be included in the study. Countries reported to have benefited from the APHEF since its time of inception will be used as case studies. The study will utilise retrospective secondary data from relevant sources to gather information on the frequency of PHEs from 2010 to 2019. Target immunisation indicators outlined in both global and regional immunisation frameworks for the decade will be used as a reference in gauging immunisation performance between 2010 and 2019. This will be a low-risk study as no direct contact or involvement with human subjects during the conduct of the study will be established.

The WHO Africa region is simultaneously grappling with endemic PHEs and a range of NIP-related challenges (8, 10). The proposed study will generate results that will contribute to the body of evidence on the negative effects of PHEs to the NIPs in the WHO Africa region. The ongoing Coronavirus Disease (COVID-19) pandemic underscores the critical need for such evidence in designing evidence-based interventions to strengthen NIPs. During the COVID-19 pandemic, the provision of immunisation services has been negatively affected and it is estimated that a population of 80 million infants worldwide are at risk of contracting VPDs (16).

1. INTRODUCTION

1.1 Background

The establishment of NIPs within the WHO Africa region can be traced back to the institution of the Expanded Programme on Immunisation (EPI) in 1974 (1, 17). Since then, significant progress has been achieved through NIPs. The DTP3 coverage which is used as a proxy performance indicator for immunisation programmes has gradually increased, having begun with a mere 5% the WHO Africa region DTP3 coverage stood at 74% in 2019 (1, 6). However, despite such gains, the full benefits of vaccines are yet to be fully realised.

It is estimated that 1 in 5 children in the WHO Africa region still do not have access to life-saving vaccines, putting them at significant risk of VPDs (18). In 2015 alone, the WHO Africa region accounted for an estimated 33% of VPD occurrences among under-fives globally (10). These VPD incidences not only resulted in VPD-associated mortalities but also a substantive economic burden to the affected countries (10).

The drawbacks experienced by NIPs within the WHO Africa region have been attributed to various factors including limited resources, weak health systems and disease surveillance, low levels of immunisation advocacy and communication, emerging infectious diseases, and PHEs (9, 13, 19).

1.2 Public health emergencies

In 2007, the WHO identified the occurrence of PHEs as one of the major threats to global public health security (20). A PHE is described as a situation that impacts the lives and well-being of a large number of people and which often necessitates substantial multi-sectoral assistance; as it presents with a critical threat to the health, safety, and wellbeing of the people (21, 22). Briefly, PHEs may include infectious disease outbreaks, exposure to toxic and

hazardous materials, natural disasters (e.g., floods), and human-induced hazards (e.g., armed conflict, civil unrest, and terrorism) (21).

According to global estimates, in 2018, close to 1.4 billion people lived in fragile and conflict-affected settings due to PHEs (23). In the African context, 32 out of the 47 member countries within the WHO Africa region were reported to have at least one occurrence of a PHE by the turn of the decade in 2009 (11).

PHEs have major impacts on various facets of society including the health, economic stability, political standing, and social aspects (21). The impact of PHEs on the health of affected populations cannot be understated, given the widespread disruption they cause to both provision of health services and the broader health system (8, 19). The effect of PHEs on public health is fuelled by varying factors such as the destruction of health infrastructure, fragile health workforce, massive population displacements, reduced health budget, and a decline in the use of preventative programmes including immunisation (24, 25). There is, however, limited evidence on the interactions between PHEs and immunisation programmes within the WHO Africa region.

1.3 Immunisation programmes in the context of PHEs

During PHEs, the performance of immunisation programmes has been noted to be among the first to be mostly affected (19, 26). It is estimated that on average, PHE affected countries, have 20% lower immunisation coverage rates compared to countries not experiencing PHEs (4, 27).

The suboptimal immunisation coverage rates experienced in countries affected by PHEs have been attributed to different factors including reduced access to immunisation services, destroyed vaccine logistic systems and infrastructure, depleted, and diverted financial and human resources for immunisation, and reduced trust towards immunisation services (8, 13, 19, 26). A survey done in 2015 in Syria- a country where civil war and progressive collapse

of health services has been experienced, is illustrative of how such aforementioned factors contribute to sub-optimal immunisation performance (28). The low vaccine coverage rates consistently reported in the country were linked to population displacements, attacks meted on health institutions, and the exodus of healthcare workers during war (28). Similarly, a study in Afghanistan by Mashal *et al.* indicate that regardless of the availability of immunisation resources the presence of protracted conflicts and insecurity can negatively affect the achievement of national immunisation coverage goals (29).

The occurrence of the Ebola Virus Disease (EVD) outbreak between 2014 and 2018 (30, 31) is also a clear case in point on the impact PHEs have on immunisation coverage in the WHO Africa region. A study conducted in Liberia, at the peak of the EVD outbreak, that occurred from March 2014, reported on decreasing immunisation coverage rates (32) that were experienced in the country. While the national DTP3 coverage was estimated to be 91% before the outbreak, the value decreased to 47% during the EVD outbreak (32). The reasons reported for the marked decline included a decrease in the use of health services by the communities for fear of contracting EVD, immunisation health workers being repurposed to deal with the epidemic, and constraints in vaccine logistical supplies (32).

Similarly, a significant decline in immunisation coverage was reported to occur in the Democratic Republic of Congo during the 2018 EVD outbreak (30). With the country already subject to protracted conflicts (31), the EVD outbreak served to worsen the widespread mistrust in the health system and shortages in vaccine supply (30, 31). As a result, the country is reported to have experienced one of the largest measles outbreaks in the African continent with more than 6000 deaths reported over a period spanning less than two years (28, 33-35).

The challenges brought by PHEs on immunisation is also topical, given that in 2020, the world is grappling with an unprecedented COVID-19 pandemic. Preliminary reports indicate that immunisation programmes are one of the most affected health services during the pandemic

(35). Following the global onset of the pandemic, the WHO in March 2020 recommended its member states to suspend mass immunisation campaigns (37, 38) in line with the physical distancing measures aimed at decreasing transmission of SARS-CoV-2, the virus that causes COVID-19 (37). In many settings, it was reported that many caregivers with children due for immunisation refrained from attending immunisation clinics for fear of contracting COVID-19 (39). Additionally, disruptions in the vaccine supply chain, owing to lockdown measures and control of border points instituted to curb the pandemic, further, contributed to the interruption of immunisation services (40). With the disruptions of NIPs, it is predicted that possible VPD outbreaks would occur should immunisation services not improve (37).

With such outlined frailties in NIPs that are occasioned by PHE endemicity, the WHO Africa region has lagged in meeting global and regional immunisation targets set for the decade.

1.4 Global and regional immunisation targets

In May 2012, the World Health Assembly adopted the Global Vaccine Action Plan (GVAP), as a blueprint for achieving the Decade of Vaccines (DoV) from 2011 to 2020 (7). The mission of GVAP is to "… improve health by extending by 2020 and beyond the full benefits of immunisation to all people, regardless of where they are born, who they are, or where they live." The immunisation goals and indicators used in the GVAP framework to gauge progress are shown in **Table 1**.

Table 1. Goals and indicators for the GVAP

Goals/ strategic objectives	Indicators
1. Meet vaccination coverage targets in every region, country, and community	1.1 Reach 90% national coverage and 80% in every district or equivalent unit with three doses of diphtheria, tetanus, and pertussis containing vaccine
	1.2 Reach 90% national coverage and 80% in every district or equivalent unit for all vaccines in national programmes, unless otherwise recommended
2. Develop and introduce new and improved vaccines and technologies	2.1 Number of low-income and middle-income countries that have introduced one or more new or underutilised vaccines
	2.2 Licensure and launch of at least one platform delivery technology
3. Meet global and regional elimination targets	3.1 Maternal and Neonatal Tetanus (MNT) elimination
	3.2 Measles elimination
	3.3 Rubella/ Congenital Rubella Syndrome (CRS) elimination
4. Establishment of National Immunisation Technical Advisory Group (NITAG)	4.1 Countries with an existing NITAGs
	4.2 Countries with functional NITAGs
5. Achieve a world free of poliomyelitis	5.1 Interrupt wild poliovirus transmission globally
	5.2 Certification of poliomyelitis eradication
6. Exceed Millennium Development Goal 4 target for reducing child mortality	6.1 Reduce under-five mortality rate

Adopted from the Global Vaccine Action Plan: Secretariat Annual Report 2013 (7)

In response to the GVAP, the WHO Africa region immunisation framework (2014 – 2020) referred to as the Regional Strategic Plan for Immunisation (RSPI) was developed. Its mandate is to actualise the contextualised regional immunisation goals using the GVAP as a reference (41).

To accelerate the efforts toward the achievement of the two DoV immunisation frameworks the WHO in 2018 came up with the "Business case for WHO immunisation activities on the

African continent." One of its key agenda is to offer tailored support to countries in the region based on their immunisation maturity grid (10). The immunisation maturity grid constitutes of six rating components namely **(A)** programme management and financing, **(B)** immunisation service delivery and new vaccine introduction, **(C)** disease surveillance and VPD outbreak management, **(D)** data management and analytics, **(E)** vaccine quality, safety, and regulation and **(F)** community engagement (**Appendix 1)** and is used in rating immunisation systems and identifying gaps in immunisation programmes that the WHO can support (10). It is a scaled indicator with four levels which include **level 1-**countries with very weak immunisation systems, **level 2**- countries with significant deficiencies in immunisation service delivery. **Level 3-**countries with targeted areas for improvement in their immunisation programmes and **level 4-**countries with strong and robust immunisation systems (10).

In this study, selected immunisation indicators in the DoV and the classification outlined by the immunisation maturity grid, will be used to gauge the performance of NIPs in countries experiencing PHEs within the WHO Africa region.

The WHO Africa region has not only invested in a regional immunisation framework but has also made effort to institute a regional emergency fund named the African Public Health Emergency Fund.

1.5 The African Public Health Emergency Fund

The African Public Health Emergency Fund (APHEF) was established by the WHO Africa region and the African Union in 2012. Developed as a solidarity fund, its main aim is to provide financial support to WHO Africa region countries experiencing PHEs (15).

Since its inception, the fund has provided financial support to different countries to support their relief efforts during PHEs (42). The PHEs that the APHEF has supported include disease outbreaks, natural disasters, and armed conflicts (42).

The APHEF will be used as a reference point in selecting countries for the case studies, aimed at characterising the performance of NIPs in the WHO Africa region in the presence of PHEs.

1.6 Problem Statement

Whilst efforts have been made by the WHO to have a collective data source that reports on various national immunisation indicators, evidence on the interactions between NIPs and PHEs in the WHO Africa region remains limited. To understand how these interactions, unfold characterisation of immunisation performance will be an important step towards the development of policies aimed at mitigating the negative impacts PHEs have on NIPs.

Optimal strengthening of NIPs in the WHO Africa region requires an understanding of the interactions between the endemicity of PHEs and immunisation. Therefore, evidence-based immunisation recommendations in the region will need context-specific data on the weak points in immunisation caused by PHE prevalence in the region. Such data is currently limited.

Advocacy and communication to enhance commitment by political and public health leaders and as well as to mobilise resources, are critical in cushioning NIPs from disruptions caused by PHEs. Despite the existence of the APHEF, meagre support has been accorded to the fund to dispense its mandate (15). Contributions have perennially been at an all-time low, with only 13 out of the 47 WHO Africa region countries ever contributing to the fund between 2012 and 2016 (15). Also, the insufficient investment by governments in tackling immunisation supply challenges has persisted, therefore, failing to reach the underserved and marginalised populations in PHE settings (43). Evidence to implore national governments and stakeholders in the WHO Africa region to support initiatives like the APHEF needs to be backed up by generated data which is currently sparse.

As the world shifts towards Universal Health Coverage (UHC) (44), improving coverage and equity in NIPs is instrumental in ensuring that vaccines are accessible to all people (7). This

would be key in augmenting efforts aimed at fulfilling commitments embodied by the DoV and other regional and global goals. It is, therefore, important for the region's policy and decision-making to be informed by emerging evidence on the performance of NIPs in PHE contexts, to facilitate progress towards regional and global goals. However, such evidence still remains scanty.

2. STUDY AIMS AND OBJECTIVES

2.1 Research question

How do NIPs within the WHO Africa region perform during PHEs?

2.2 General objective

To characterise immunisation programmes in countries within the WHO Africa region that have benefited from the APHEF and experienced at least one PHE between 2010 and 2019.

2.3 Specific objectives

1. To describe the PHEs reported between 2010 to 2019 in countries that have benefited from the APHEF.

2. To assess the performance of NIPs between 2010 to 2019 in countries that have benefited from the APHEF using selected DoV immunisation indicators.

3. To assess how the frequency of PHEs is associated with the performance of NIPs among beneficiary countries of the APHEF.

2.4 Hypothesis

The occurrence and frequency of PHEs negatively affect the performance of NIPs within the WHO Africa region.

3. METHODS

3.1 Study design

A case study of selected countries in the WHO Africa region using secondary data analysis review.

3.2 Study population

The APHEF will be used as a reference in selecting countries for the study. Countries reported to have benefited from the fund will be used as case studies.

3.3 Data sources

Data to be utilised in the study will be collected retrospectively for the past ten years from 2010 to 2019 using various relevant sources to answer the research question. The specified period is based on the DoV's implementation timeline. Also, the APHEF, which will be used as criteria for selecting countries into the study was instituted in 2012 and is synchronous in timing with that of the DoV.

3.3.1 Data on PHEs

A single and complete reference database for all PHEs occurring in the WHO Africa region has not been in existence before 2017. Various key data sources will, therefore, be used to corroborate information on PHEs experienced between 2010 to 2019. These sources will include

1. The Emergency Events Database (EM-DAT) of the Centre for Research on the Epidemiology of Disasters (45), which is a database with curated information on natural and technological disasters (***for the definition of disaster terms see glossary***) that have occurred globally since the year 1900.

2. The Uppsala Conflict Data Program (UCDP) which collates data on the various types of armed conflicts experienced globally namely state conflicts, one-sided violence conflicts and, non-state conflicts (***for the definition of armed conflict terms see glossary***) (46).
3. The WHO emergency preparedness and response (47) which is an integrated global alert and response system that reports on occurrences of disease outbreaks and will be corroborated with the Program for Monitoring Emerging Diseases Mail (PROMED-Mail) (48) to abstract data on disease outbreaks reported in the selected countries.

3.3.2 Data on immunisation

Country reports made to the WHO and the United Nations Children's Fund (UNICEF) using the joint reporting form (JRF), will be utilised to extract immunisation data from various reporting sources as follows:

1. Data on the administrative national DTP3 coverage, drop-out rate between DTP1 and DTP3, establishment of national immunisation technical advisory groups (NITAGs), and country maternal and neonatal tetanus (MNT) elimination status will be obtained from the immunisation indicator selection centre (49, 50).
2. Information on the introduction and use of new and under-utilised vaccines accessed from the vaccine introduction database (51).
3. The immunisation maturity grid of each country will be obtained from the 2018 report of the Business case for WHO immunisation Data (10).

3.4 Variables

Table 2 displays all the study variables that will be obtained from the outlined data sources.

Table 2. List of variables to be utilised in the data analysis

Variable name	Variable type
National DTP3 coverage estimates	Numerical-continuous
Drop-out rate between DTP1 and DTP3	Numerical-continuous
Introduction of new and underutilised vaccines	Numerical-continuous
Country MNT elimination status	Categorical-Binary (Yes or No)
Immunisation maturity grid	Categorical (category 1, category 2, category 3, and category 4)
Country has an existing NITAG	Categorical-Binary (Yes or No)
Country has a functional NITAG	Categorical-Binary (Yes or No)
PHE occurrences:	
1. Disease outbreaks	Numerical-continuous
2. Armed conflicts	Numerical -continuous
3. Disasters	Numerical- continuous
Total PHE count	Numerical- continuous

3.5 Data management and analysis

Data extracted from the above-mentioned sources will be captured into a research database using Microsoft Excel, 2016 software. All data exploration and analysis will be conducted using R software version 4.0.2 (R Core Team, 2020).

3.5.1 Univariate and bivariate analysis

Once imported into the R software, univariate statistical analysis for numerical-continuous variables will be done using the mean/standard deviation (SD) or the median/inter-quartile range (IQR), based on their normality distribution, as determined using the Shapiro-Wilk test.

While descriptive statistics for binary and categorical variables will be done using frequency distributions and their proportions.

Bivariate analysis will be performed to compare the counts of the three types of PHEs and the total PHEs across the outlined DoV immunisation target indicators during the study period from 2010 to 2019, using the Two-sample t-test for independent samples and /or the Two-sample Wilcoxon rank-sum test (Mann-Whitney U) depending on the distribution in count for the three different types PHEs and the total PHEs.

All statistical significance tests conducted will be two-tailed and statistical significance tests will be defined at the 5% alpha level.

4. ETHICAL CONSIDERATION

The secondary data to be utilised in the study are available in the public domain. There will be no direct contact or involvement with human subjects when conducting the study. For this reason, no formal ethical clearance will be required to conduct this study. The University of Cape Town, School of Public Health and Family Medicine Departmental Research Committee will be notified of the low risk of the study and requested for approval to waive formal ethics application. All information and data sources to be used in the study will be given due acknowledgment. Disclosure of findings will be made available through the online platform provided by the University of Cape Town Library and will be published in a peer-reviewed, internationally accredited journal.

4.1 Risks and benefits of the study

Being a secondary data analysis review, this will be a low-risk study. We do, however, recognise that the study may highlight the poor performance of some of the NIPs. As mentioned previously, all data sources to be utilised in the study will have been obtained from various public domains that these countries frequently report to.

It is anticipated that the study will directly contribute to the limited knowledge base by describing the various PHEs experienced within the WHO Africa region and the possible impacts they have on the performance of NIPs. The anticipated findings of the study may inform the design of future research into the complex relationships that exist between PHEs and NIPs through the identification of gaps in the field. Finally, it also anticipated that the evidence generated will support key stakeholders in developing policies that will aid in promoting and sustaining optimal performance of NIPs in the presence of PHEs like the COVID-19 pandemic.

4.2 Limitations of the study

The use of secondary data sources may introduce limitations on data quality and completeness. The two sources of data utilised in estimating immunisation coverage as recommended by the WHO are the administrative coverage and immunisation coverage survey methods (52). These two sources of immunisation data have their limitations, which may lead to discrepancies in coverage estimates obtained. While administrative coverage data may be convenient and timely, they sometimes may overestimate or underestimate coverage if there are inaccuracies in the number of vaccine doses administered (numerator) or inaccuracies in the population count (denominator) (52, 53). On the other hand, immunisation coverage surveys are prone to recall bias in the absence of vaccination cards (53).

In as much as the study aims at corroborating information from multiple sources to generate a comprehensive database on immunisation and PHEs, this may still be limited by issues of missing data and inconsistencies in the reporting mechanisms from some of the countries.

Using the APHEF as a reference in selecting countries as case studies may limit the scope of the study. Countries excluded from this study based on this criterion may have experienced relevant PHEs and possess immunisation trends that may have relevance to the study. However,

given the scope of the study, it may not be pragmatic to include all 47 countries in the WHO Africa region. Instead, findings from the countries selected will serve as a set of "lessons learned" for countries with similar contexts.

4.3 Milestones

Figure 1 displays the expected time frame towards the completion of the thesis.

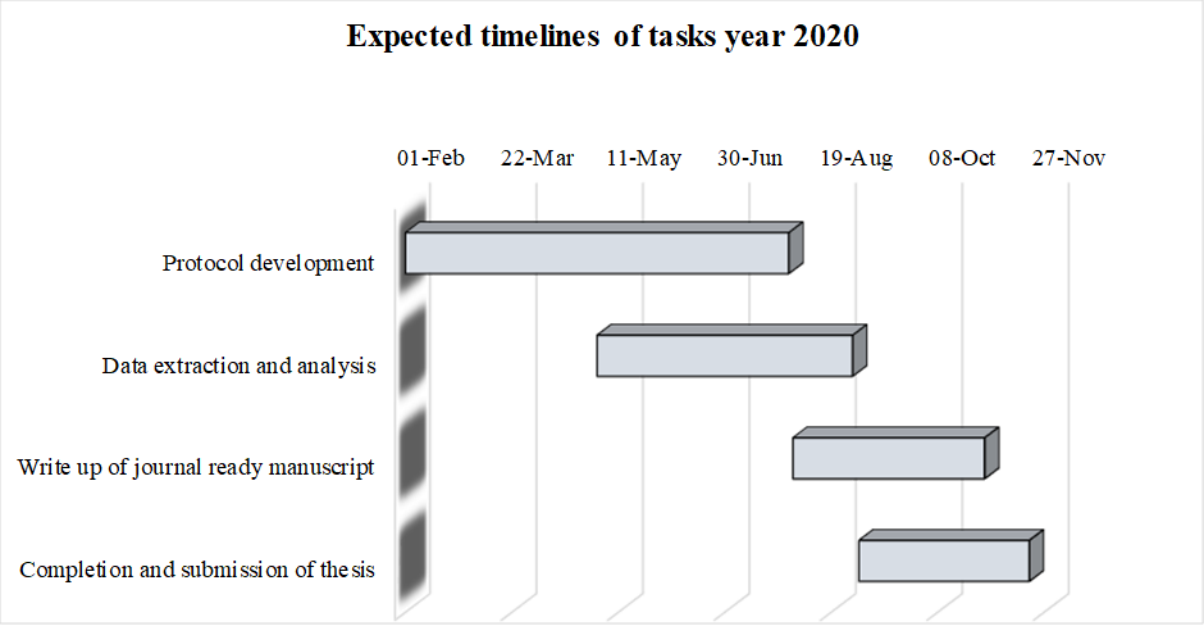

Figure 1. Schedule for the completion of the thesis

4.4 Research budget

All the research activities for the study will be self-funded and undertaken in the primary author's country of residence in partial fulfilment of requirements for a Master of Public Health degree. As the study utilised secondary data, there will be no anticipated direct costs arising from conducting the research. **Table 3** gives an overview of the expenditures, that will be undertaken in facilitating the research.

Table 3. Estimated research budget

Item	Units	Unit Cost (Rands)	Total Cost
Pens	5	5.00	25.00
Pencils	5	5.00	25.00
Notebooks	5	10.00	50.00
Printing (two copies of research protocol and the final thesis)	200	3.50	700.00
Incidental expenses	___	1000.00	1000.00
Total		1023.50	1800.00

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PART B: JOURNAL MANUSCRIPT

Characterisation of National Immunisation Programmes (NIPs) in the context of Public Health Emergencies (PHEs): A case study of 13 countries in the WHO Africa region

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[1] The target peer reviewed journal chosen to guide the formatting of this manuscript is the **Biomed Central (BMC) : Conflict and Health**. The journal submission guidelines for authors are included in **Part C** of the thesis in **appendix 3**. For the purposes of this thesis the student is the sole and first author, the co-authors contributions are recognised in the acknowledgements section of the thesis.

ABSTRACT

Background

In the World Health Organisation (WHO) African region, multiple public health emergencies (PHEs) are experienced annually. PHEs have been documented to affect the provision of health services including immunisation. To our knowledge, there is limited information on the characterisation of PHEs and the performance of national immunisation programmes (NIPs) in countries within the WHO Africa region that experience PHEs. This study assessed PHEs (armed conflicts, disasters, and disease outbreaks) and the performance of NIPs within PHE contexts using global and regional immunisation targets.

Methods

Countries recorded to have benefitted from PHE mitigation funds from the African Public Health Emergency Fund (APHEF) were used as case studies.

Data on PHEs and immunisation indicators between 2010 and 2019 in the selected countries were extracted from different PHE electronic databases and the WHO/UNICEF immunisation database, respectively.

The PHEs and immunisation indicators were stratified by country and summarised using descriptive statistics. The Mann-Whitney U test was carried out to determine the association between the frequency of PHEs and the performance of NIPs. Statistical significance was defined at p-value < 0.05.

Results

Between 2010 and 2019 there were a total of 175 disease outbreaks, 288 armed conflicts, and 318 disasters in the 13 countries selected as case studies. The Democratic Republic of Congo had the highest total PHE count (n=208), while Liberia had the lowest (n=20). Only three of the 13 countries had a median coverage value for the third dose of the combined Diphtheria,

Tetanus, and Pertussis vaccine (DTP3) that had attained the target for ≥90% immunisation coverage.

Higher counts of armed conflict and total PHEs were associated with not meeting the immunisation targets for national DTP3 coverage of ≥90% and Maternal and Neonatal Tetanus (MNT) elimination, $p<0.01$. Higher disaster counts were also associated with not attaining MNT elimination, $p=0.03$.

Conclusion

PHEs are prevalent in the WHO Africa region, irrespective of the level of a country's immunisation maturity. In absence of effective interventions, the PHEs have the potential to derail the progress of NIPs in the WHO Africa region. As we transition towards the Immunisation Agenda 2030, we recommend that the WHO Africa region prioritises interventions to mitigate the impacts of PHEs on the NIPs.

Keywords

public health emergencies, national immunisation programmes, decade of vaccines, WHO Africa region

1. BACKGROUND

Public Health Emergencies (PHEs) are recognised as one of the major threats to global public health security (1). Globally, numerous countries experience different types of PHEs which range from infectious disease outbreaks, natural disasters (e.g., floods) and human-induced hazards (e.g., armed conflicts) (2). In the WHO Africa region, more than 100 PHEs are reported to occur annually (3, 4). A PHE is described as a situation that impacts the lives and well-being of a large number of people and which often necessitates substantial multi-sectoral assistance; as it presents with a critical threat to the health, safety, and wellbeing of the people (2, 5). In 2020, the unprecedented occurrence of the Coronavirus Disease (COVID-19) pandemic, which is classified as a PHE of international concern (6), has highlighted more than ever that PHEs do transcend international boundaries and have negative impacts on various facets of society including public health (2, 3). The impact PHEs have on public health cannot be understated, given they cause widespread disruption to both the broader health system and provision of health services (7-9) including that of immunisation (10, 11).

The disruption to national immunisation programmes (NIPs) experienced in countries with PHEs has been associated with suboptimal immunisation coverage rates (7, 12, 13). The plummeting coverage witnessed during PHEs is facilitated by reduced access to immunisation services, destroyed and disrupted vaccine logistic systems, depleted and diverted financial and human resources for immunisation, and reduced trust towards immunisation (7, 12, 13). Many of these factors have eminently featured during the COVID-19 pandemic (14-16). The sub-optimal immunisation coverage rates, also, create large pockets of unimmunised and under-immunised children and adults thereby lowering herd immunity (17-19). The compromised herd immunity acts together with other PHE co-existing factors like poor sanitation and overcrowding to provide ideal conditions for outbreaks of Vaccine-Preventable Diseases (VPDs) (19-22). Due to such frailties, countries affected by PHEs are reported to lag in meeting

global and regional immunisation targets aimed at control, elimination, and eradication of VPDs (23, 24).

The Global Vaccine Action Plan (GVAP) was developed in 2011 to actualise the vision of the Decade of Vaccines (DoV) for having a world where individuals and communities will be able to enjoy lives free from VPDs (25). The Regional Strategic Plan for Immunisation (RSPI) is a WHO Africa region contextualised immunisation framework adopted from the GVAP with goals for attainment by 2020 (26). Although, through the two immunisation frameworks the WHO Africa region has achieved substantive gain in immunisation e.g., the successful eradication of wild poliovirus disease (27), many targets remain unmet, owing to amidst other factors the prevalence of PHEs (28). During the DoV there has been growing concern on the possible role PHEs play in delaying achievement for set immunisation targets (24, 28, 29). According to reports by the WHO, Strategic Advisory Groups of Experts in immunisation (SAGE), PHEs are recognised as one of the major shifts during the decade and a key driver of inequity in immunisation access between and within countries in the region (24, 29). In cognisance of PHE prevalence in the WHO Africa region, including the COVID-19 pandemic, and the end in sight of the DoV in 2020, there is need to take stock of immunisation performance in countries experiencing PHEs. The evidence generated would advance the understanding that is critical in strengthening NIPs in the context of PHEs.

In as much PHEs have been recognised to have repercussions on NIPs, inadequate focus has been given on synthesising evidence in PHE affected settings in the WHO Africa region. A limited number of studies have attempted to describe immunisation in countries affected by PHEs, however, a majority are restricted to single types of PHEs, especially armed conflict and single immunisation indicators (7, 9, 12, 30). To the best of our knowledge this will be the first study that aims to characterise NIPs in the WHO Africa region experiencing PHEs; using three

different types of PHEs (armed conflicts, disease outbreaks, and disasters) and the DoV immunisation targets to account for performance of NIPs.

2. METHODS

2.1 Study design

Retrospective case study using secondary data on immunisation indicators and PHEs.

2.2 Study population

Countries in the WHO Africa region that have received funding from the African Public Health Emergency Fund (APHEF) between 2012 and 2019 were used as case studies.

2.3 General objective

To characterise immunisation programmes in countries within the WHO Africa region that have benefited from the APHEF and experienced at least one PHE between 2010 to 2019.

2.4 Specific objectives

1. To describe the PHEs reported between 2010 to 2019 in countries that have benefited from the APHEF.

2. To assess the performance of NIPs between 2010 to 2019 in countries that have benefited from the APHEF using selected DoV immunisation indicators.

3. To assess how the frequency of PHEs is associated with the performance of NIPs among beneficiary countries of the APHEF.

2.5 Data sources

The study utilised secondary data from different sources available as of July 2020 and reported from 2010 to 2019 (**Figure 1**).

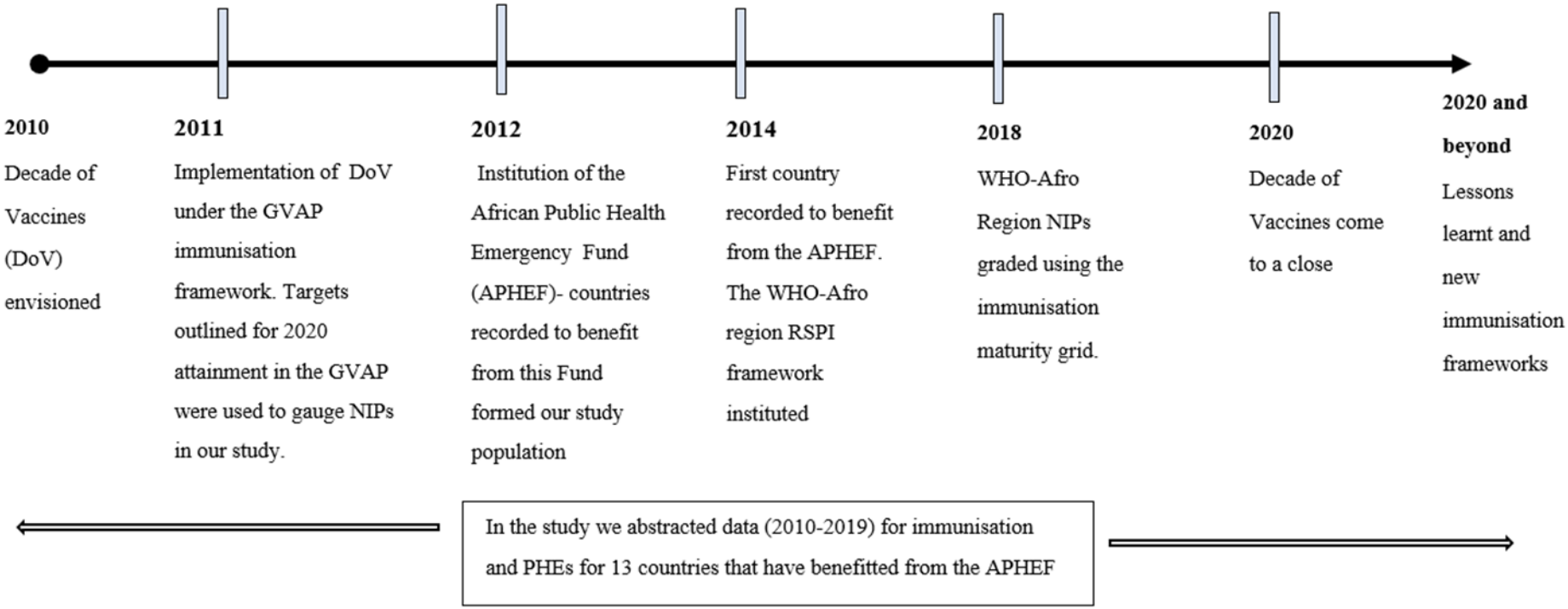

Figure 1. A conceptual framework of initiatives used to inform the choice of the study variables

Data on immunisation indicators outlined in the DoV were obtained through country reports made to the World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF) using the Joint Reporting Form (JRF) (31).

The APHEF had supported three types of PHEs namely armed conflict, disasters, and disease outbreaks (32). Data was collated from different electronic databases reporting on these three types of PHEs. The databases used were:

1. The Emergency Events Database (EM-DAT) from the Centre for Research on the Epidemiology of Disasters which reports on natural and technological disasters, for the study these two disaster subtypes were collectively referred to as disasters (33).
2. The Uppsala Conflict Data Program (UCDP), a database that curates data on various types of armed conflicts namely state conflicts, one-sided violence conflicts and non-state conflicts (34).
3. The WHO Emergency Preparedness and Response an integrated global alert and response system that reports on occurrences of disease outbreaks (35), which was corroborated with data from the Program for Monitoring Emerging Diseases Mail (PROMED- Mail) (36).

2.6 The determinant variables

The counts of the three types of PHE namely disasters, armed conflicts, and disease outbreaks, and the total PHE count (the cumulative total count of the three PHE types) were used as the main determinant variables.

2.7 Outcome variables

The following selected immunisation indicators implemented for the DoV (**Figure1**) were used as the study outcome variables:

1. The combined Diphtheria, Tetanus, and Pertussis vaccine (DTP) coverage rates which were used as proxies to gauge the strength and reach of routine immunisation programmes (25) including:

   i) Having ≥90% national coverage for the third dose of the DTP (DTP3)

   ii) Drop-out rate between the first dose of the DTP (DTP1) and DTP3
2. Introduction of new and underutilised vaccines (25); three vaccines were considered for study and used as proxies, they included two childhood vaccines- the Rotavirus vaccine and the Pneumococcal Conjugate Vaccine (PCV), and one adolescent vaccine- the Human Papillomavirus (HPV) vaccine.
3. The attainment status for elimination of Maternal and Neonatal Tetanus (MNT) which is one of the targeted VPDs for regional and global elimination (25).
4. The establishment of national immunisation technical advisory group (NITAG); which was used to gauge immunisation prioritisation and country ownership for NIPs. Data for this variable was obtained on both the existence and functionality of a NITAG. The functionality of a NITAG is pegged on an existing country NITAG meeting 6 minimum criteria as outlined by the WHO including the **(A)** administrative basis for the advisory group, **(B)** formal written terms of reference, **(C)** at least five different areas of expertise represented among NITAG core members, **(D)** at least one meeting per year, **(E)** circulation of the agenda documents at least one week before meetings, and **(F)** the mandatory disclosure of any conflict of interest. Each of the 6 outlined criteria needs to be satisfied for a country's NITAG to be merited as functional (43).

5. Immunisation maturity grid which is a six-component tool used to rate immunisation systems and identify gaps in the performance of NIPs. The six components used to rate the immunisation maturity grid include (**A)** programme management and financing, **(B)** immunisation service delivery and new vaccine introduction, **(C)** disease surveillance and VPD outbreak management, **(D)** data management and analytics, **(E)** vaccine quality, safety, and regulation and **(F)** community engagement (**Appendix 1)** (37).

2.8 Data synthesis and analysis

To establish any underlying trends in the total PHE count for each of the study countries, the study duration was stratified into three-time points in 2010 at the beginning of the study, in 2014 after five years, and in 2019- ten years and the end of the study.

The three types of PHEs were stratified by country using stacked bar plots in each of the study years to establish both the overall prevalence for each of the three types of PHEs and identify the individual country-specific prevalence for a given PHE.

All the statistical analysis and visualisation of study data were done using the R software version 4.0.2 (R Core Team, 2020). The selected DoV immunisation indicators were stratified by country and summarised using descriptive statistics such as the mean (Standard Deviation (SD)) and/or the median (Interquartile range (IQR)) for numerical continuous variables depending on their normality distribution, and counts and proportions, used for categorical variables. The results were presented in a table. We also used, a line graph to establish the temporal trends in the national and regional DTP3 coverage indicator.

Two groups were created for the target immunisation indicators outlined in the DoV. The two groups were based on the number of years from 2010 to 2019 that each of the selected countries had either met a specific target or had failed to meet the target. Labels used for the two target groups were “target met”- Yes, and “target not met”- No. The distribution of the three types of

PHEs and the total PHE counts were compared across the two groups using the Mann-Whitney U group-comparison test, as the data had a non-normal distribution. Statistical significance for the tests was defined at p-value < 0.05. The distribution of the total PHE count in the selected countries from 2010 to 2019 was also, compared across the two immunisation target groups using boxplots.

3. RESULTS

3.1 Countries benefiting from the APHEF

As of 2017, the APHEF had supported 13 countries within the WHO Africa region. The 13 countries were Burundi, Zimbabwe, the Central African Republic, South Sudan, Guinea, Cameroon, Liberia, Sierra Leone, Democratic Republic of Congo, Malawi, Niger, Angola, and Ethiopia.

3.2 PHEs reported between 2010 and 2019

Between 2010 and 2019 PHEs were present in each of the study population countries and varied in count across the countries (**Figure 2**).

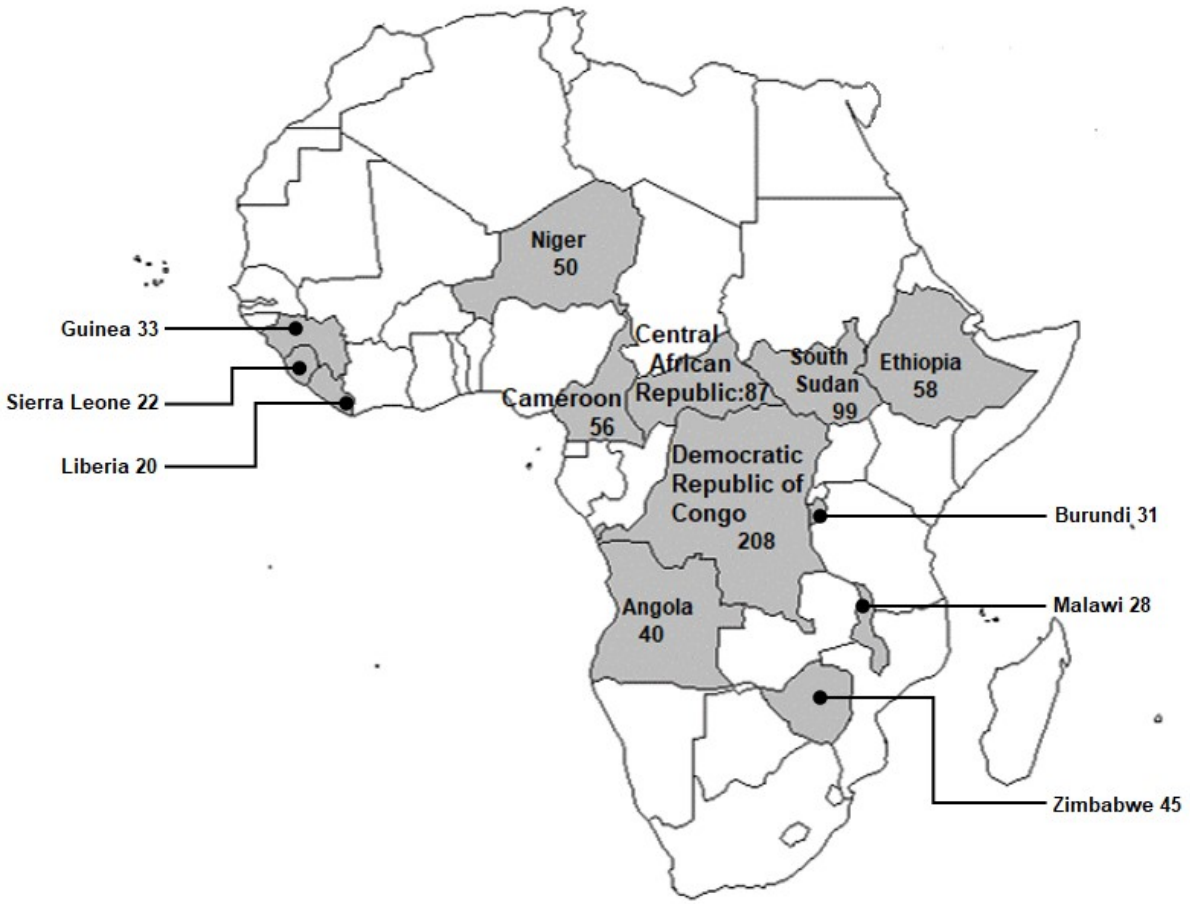

Figure 2. Distribution of total PHE counts by country from 2010 to 2019

The highest total PHE count was recorded in the Democratic Republic of Congo (n=208), while the lowest total PHE count was recorded in Liberia (n=20) (**Figure 2**). Despite being the youngest country in the WHO Africa region, South Sudan (gained independence in 2011), had the second-highest total PHE count at (n= 99).

3.2.1 Total PHE counts across three time periods

A snapshot of the total PHE count in the 13 countries in 2010, 2014, and 2019 showed the individual country trends at the beginning of the study period in 2010, after five years, and at ten years in 2019. The PHE counts fluctuated across the study periods. While eight countries witnessed a decrease in the PHE count in 2014 compared to 2010, nine countries in 2019 recorded an increase in the PHE count compared to 2014 (**Table 1**).

Table 1. Total PHE counts stratified by year in 2010, 2014, and 2019

Country	2010	2014	2019
Angola	5	1	4
Burundi	3	2	6
Cameroon	7	4	6
The Central African Republic	3	10	9
Democratic Republic of Congo	20	22	36
Ethiopia	5	2	11
Guinea	4	4	2
Liberia	2	1	1
Malawi	2	0	3
Niger	3	3	7
Sierra Leone	3	2	2
South Sudan[a]		8	13
Zimbabwe	6	5	2

Key
Increase in PHE count
Decrease in PHE count
PHE count constant
No data

[a] South Sudan gained independence in 2011. As such data for 2010 is unavailable

3.2.2 Types of PHEs

Three types of PHEs namely armed conflicts, disasters, and disease outbreaks were extracted from databases and summarised (**Figure 3**). In the 13 countries and from 2010 to 2019, a total count of n=175, n=288, and n=318 for disease outbreaks, armed conflicts, and disasters were recorded respectively.

A summary of the annual distribution of the three types of PHEs occurring in each country during the study period is shown (**Figure 3**).

Figure 3. Three types of PHEs recorded in 13 WHO Africa region countries between 2010 and 2019

Overall, counts of armed conflicts (n=89), disasters (n=91), and disease outbreaks (n=28) were highest in Democratic Republic of Congo (**Figure 3**). In general, and with exception of the Democratic Republic of Congo, armed conflicts and disease outbreaks were majorly prevalent in all other countries for the entire study period (**Figure 3**).

3.3 Performance of NIPs in the period of PHEs

The target immunisation indicators for the DoV were used to assess the performance of NIPs in the study countries from 2010 to 2019.

3.3.1 National DTP3 coverage

The DTP3 coverage was used as a proxy indicator for the performance of NIPs in meeting national and regional immunisation coverage targets.

The recorded trend in the annual national DTP3 coverage estimates in each of the 13 countries points to fluctuating patterns during the entire study period (**Figure 4**).

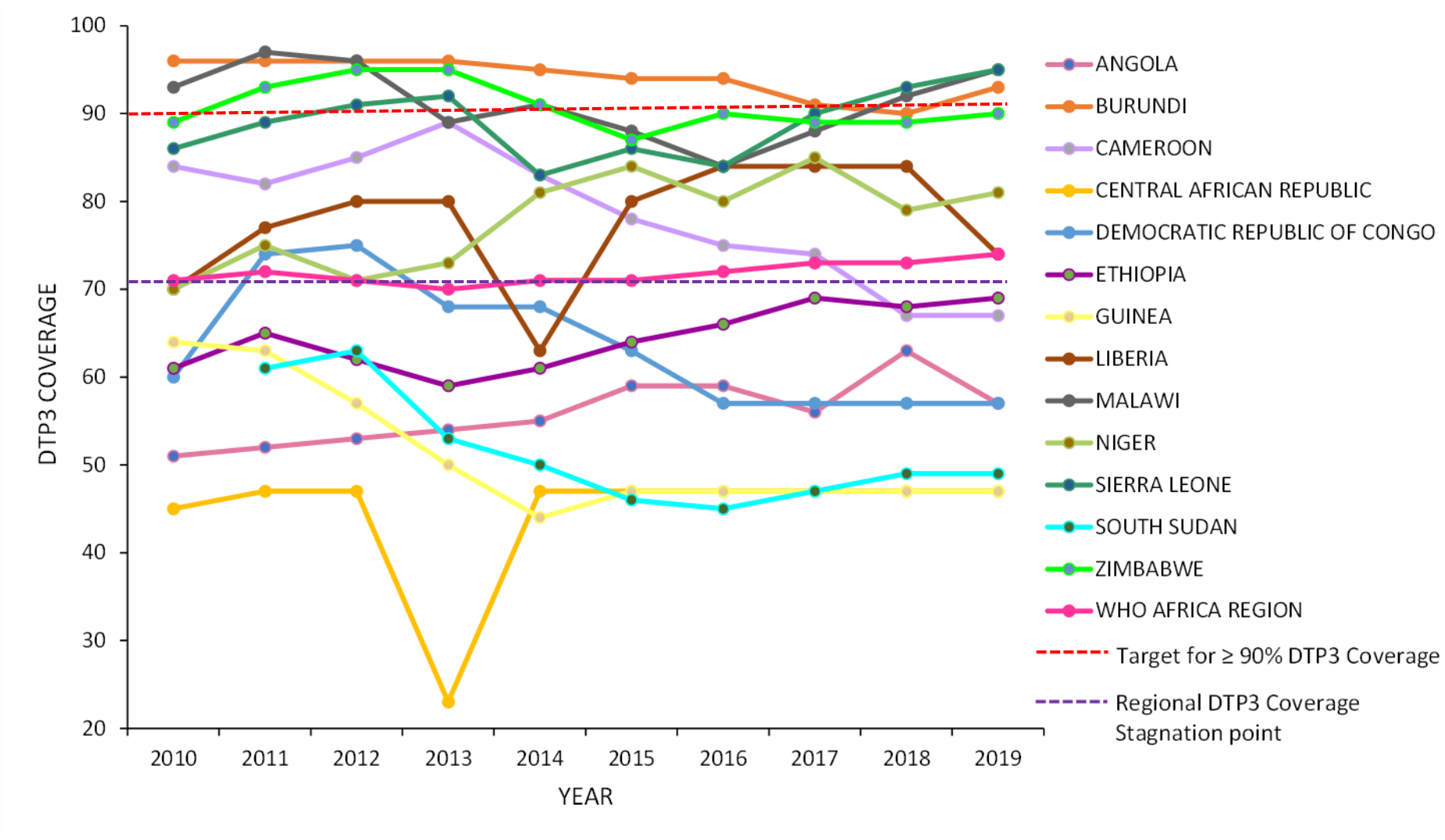

Figure 4. Annual DTP3 coverage trends between 2010 and 2019 for the 13 countries and the WHO Africa region

Only three (Burundi, Malawi, and Zimbabwe) of the 13 countries had a median national DTP3 coverage value that had met the ≥90% immunisation coverage DoV target (**Table 2**). In addition to this, Burundi's annual DTP3 coverage rates were found to supersede the ≥90% immunisation coverage target during the entire study period (**Figure 4**).

The WHO Africa region DTP3 coverage between 2010 and 2019 stagnated at around the average 72% mark (**Figure 4**). Six countries, (the Central African Republic, the Democratic Republic of Congo, South Sudan, Guinea, Angola, and Ethiopia) had national DTP3 coverage rates below the regional DTP3 stagnation point in the entire study period (**Figure 4**). While four countries maintained a coverage rate above that of the region including Burundi, Malawi, Zimbabwe, and Sierra Leone. The remaining three countries (Liberia, Cameroon, and Niger) had fluctuating immunisation coverage rates.

Two countries were recorded to have major dips, followed by major increases in their national DTP3 vaccine coverage in some of the study years; they were the Central African Republic and Liberia, these dips occurred in 2013 and 2014 respectively (**Figure 4**).

3.3.2 Percentage drop-out rates between DTP1 and DTP3

To gauge accessibility and utilisation of immunisation services we used drop-out rates between DTP1 and DTP3. Three countries (The Central African Republic, South Sudan, and Angola) had drop-out rates above 10%. The highest drop-out rate in the ten-year study period was recorded in the Central African Republic, with a median [IQR] of 24.00 [9.50] (**Table 2**).

Table 2. Descriptive summary of NIP related immunisation indicators between 2010 and 2019 stratified by country

	Angola	Burundi	Cameroon	CAR[a]	DRC[b]	Ethiopia	Guinea	Liberia	Malawi	Niger	Sierra Leone	South Sudan[c]	Zimbabwe
	Number of years data was obtained												
Immunisation indicators	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=10	n=9	n=10
DTP3 national coverage %:													
Median	55.50	94.50	80.00	47.00	61.50	64.50	47.00	80.00	91.50	79.50	89.50	49.00	90.00
[IQR]	[5.25]	[2.75]	[9.50]	[0.00]	[11.00]	[6.25]	[8.25]	[8.25]	[6.25]	[7.50]	[5.75]	[6.00]	[3.50]
Percentage drop-out rate between DTP1 and DTP3:													
Median	15.00	3.00	8.00	24.00	6.00	5.00	6.00	8.50	4.50	7.50	5.50	17.00	4.50
[IQR]	[1.75]	[0.75]	[0.75]	[9.50]	[3.50]	[2.50]	[9.00]	[4.50]	[2.50]	[5.50]	[3.25]	[14.00]	[1.75]
Total number of new and underutilised vaccines introduced as of 2019 (Rotavirus, PCV and HPV vaccines)	2	2	2	1	2	3	0	3	3	2	2	0	3
Number of years a country has had an existing NITAG:													
Years (%)	6 (60)	1(10)	5 (50)	1(10)	4 (40)	7 (70)	2 (20)	0 (0)	5 (50)	8 (80)	4 (40)	7 (77.80)	10 (100)
Number of years a country has had a functional NITAG:													
Years (%)	0 (0)	0 (0)	2 (20)	0 (0)	2 (20)	4 (40)	1 (10)	0 (0)	3 (30)	2 (20)	3 (30)	3 (33.30)	4 (40)
Has country eliminated MNT	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes
Number of years a country has been MNT free within the study period	0	10	8	0	2	2	0	9	10	0	7	0	10

[a] **CAR** Central African Republic [b] **DRC** Democratic Republic of Congo

[c] South Sudan gained independence in 2011 hence data obtained were for 9 years

3.3.3 Introduction of new and underutilised vaccines

To gauge the progress of countries in the introduction of new vaccines in their NIPs three vaccines: The Rotavirus, PCV, and the HPV vaccines were considered. The PCV and the Rotavirus vaccine were first introduced in the WHO Africa region between the years 2008 and 2009, while the HPV vaccine was first introduced in 2014. Among the thirteen countries, eleven countries had introduced PCV, while seven countries had introduced the Rotavirus vaccine to their immunisation schedule between 2010 and 2014. Only four countries had introduced the HPV vaccine in the second half of the study period (2015-2019). The HPV vaccine is the newest to be introduced in the NIPs of countries in the WHO Africa region.

Ethiopia, Liberia, Malawi, and Zimbabwe had introduced all three vaccines by 2019. While Guinea and South Sudan were yet to introduce any of the three vaccines in their NIPs by 2019 (**Table 2**).

3.3.4 Elimination of MNT

To monitor the performance of countries in meeting global and regional elimination targets for key VPDs the elimination of MNT was considered. As of 2019, 8 of the 13 countries had attained MNT elimination. Countries yet to eliminate MNT by 2019 were Angola, the Central African Republic, Guinea, Niger, and South Sudan (**Table 2**).

3.3.5 Establishment of NITAGs

To gauge progress towards country ownership of NIPs and immunisation prioritisation, the establishment of NITAGs in the study countries were examined during the entire study period.

Except for Zimbabwe, none of the countries had an existing NITAG for the entire ten-year study period. Niger, South Sudan, Ethiopia, and Angola had existing NITAGs for over half of the study period. The remaining countries had existing NITAGs for less than half of the study

period, apart from Liberia which had no existing NITAG for the ten-year study period (**Table 2**).

All the 13 study countries had functional NITAGs for less than half of the study period (**Table 2**).

3.3.6 Immunisation maturity Grid

The immunisation maturity grid is a six-component tool developed by the WHO aimed at attaining control, elimination, and eradication of key VPDs in the African continent. As of 2018 the NIPs of the 13 countries were classified into four maturity levels as shown in **Table 3**.

Table 3. Classification of countries according to their immunisation maturity grid

Immunisation maturity grid	Countries in the maturity grid	Rating criteria[a]
Level 1	The Central African Republic, South Sudan, Sierra Leone, and Liberia	Countries with very weak immunisation systems
Level 2	Guinea, Angola, and the Democratic Republic of Congo	Countries with significant deficiencies in immunisation service delivery
Level 3	Cameroon, Niger, Ethiopia, and Malawi	Countries with targeted areas for improvement in their immunisation programmes
Level 4	Burundi and Zimbabwe	Countries with strong and robust immunisation systems

[a] Adopted from the Business case for WHO immunisation activities on the African continent 2018 (37)

3.4 The association between PHEs and NIP performance

We compared the distribution in count for the three types of PHEs and the total PHEs across the two groups created from the DoV immunisation targets.

In the 13 countries from 2010 to 2019, higher armed conflict counts were associated with not meeting the immunisation targets for national DTP3 coverage of ≥90% and MNT elimination, $p<0.01$, (**Table 4**).

Higher disaster counts were also, associated with not meeting the target for MNT elimination, $p=0.03$, (**Table 4**).

Table 4. A Comparison of PHE count across two target groups of immunisation indicators outlined in the DoV

	Target for ≥90% national DTP3 coverage			**Target for MNT elimination**			**Target to have a functional NITAG**			**Target to introduce at least one new or underutilised vaccine [b]**		
	Target not met	Target met	p-value	Target not met	Target met	p-value	Target not met	Target met	p-value	Target not met	Target met	p-value
	n[a]=102	n[a]=27		n[a]= 71	n[a]= 58		n[a]= 105	n[a]= 24		n[a]=103	n[a]=24	
PHE type												
Armed conflict												
Median	1	0	<0.01*	1	0	<0.01*	0	0.5	0.40	1	0	0.05
[IQR]	[5]	[0]		[5.5]	[1]		[3]	[5]		[3]	[1]	
Disaster												
Median	2	2	0.90	2	1	0.03*	2	2	0.30	2	2	0.60
[IQR]	[2]	[2]		[2.5]	[2]		[2]	[1]		[2]	[2]	
Disease outbreak												
Median	1	1	0.10	1	1	0.90	1	2	0.40	1	1	0.60
[IQR]	[2]	[1.5]		[2]	[2]		[2]	[3]		[2]	[1]	
Total PHEs[c]												
Median	5	3	<0.01*	5	3	<0.01*	4	5	0.10	5	5	0.06
[IQR]	[6]	[2]		[7]	[3]		[5]	[6.5]		[3]	[3]	

*p-value significant

a Between 2010 and 2019 each of the 13 countries contributed 10 years, except for South Sudan (gained independence in 2011), which contributed 9 years, hence, the total number of years for all the 13 countries was 129.

b For this target two years had no data as two countries had already introduced all the three new vaccines examined in the study in their preceding years

c This variable is a function of the total count of the armed conflict, disaster, and disease outbreak variable

Higher total PHE counts were associated with not meeting immunisation targets for national DTP3 coverage of ≥90% and not attaining MNT elimination, $p<0.01$, (**Table 4**).

Higher counts of armed conflicts, disasters, disease outbreaks, and total PHEs were not associated with meeting the DoV immunisation targets for introducing new vaccines and the presence of functional NITAGs, $p>0.05$ (**Table 4**).

4. DISCUSSION

The primary intent of the study was to characterise the NIPs of countries within the WHO Africa region experiencing PHEs using immunisation targets outlined for the DoV as proxy indicators. We found that PHEs were endemic during the entire study period and the performance of NIPs in the PHE endemic countries was variable, although mostly suboptimal. Additionally, higher total PHE and armed conflict counts were associated with not achieving the immunisation targets for ≥90% national DTP3 coverage and MNT elimination. Higher disaster counts were also associated with not eliminating MNT.

The endemicity of PHEs observed during the study period, agree with other reports on the recurrent and diverse nature of PHEs experienced in the WHO Africa region (4, 38). While armed conflict and disasters were found to have the highest cumulative count in our study, contrary, trends were observed in the WHO Africa region, with a majority of reported PHEs being that of disease outbreaks (3, 38, 39). The discrepancy can be explained by findings from other studies done in similar settings, where disease outbreaks were noted to occasionally go unrecorded as they occur as twin PHEs, in the context of armed conflicts and disasters (2, 40).

Regardless of the immunisation maturity level, the overall performance of NIPs in the PHE endemic countries was variable but predominantly suboptimal. The fluctuating and the low national DTP3 coverage rates below the WHO Africa region DTP3 coverage stagnation point are synonymous with DTP3 coverage reports in other NIPs in the region during PHEs (12, 23). As outlined by Grundy *et al.* in their study, other WHO Africa region countries like Nigeria and Somali that have experienced constant civil unrest and yet have not benefited from the APHEF, were reported to have sub-optimal DTP3 coverage rates (7). Similarly, the high DTP vaccine drop-out; classified as ≥10% (26), recorded in some of the NIPs, concur with findings from a study by Mugali *et al.* (41) in Afghanistan where high DTP drop-out rates were associated with conflict and insecurity.

The introduction of the PCV and the Rotavirus vaccines into the NIPs of the study countries was high compared to the HPV vaccine. These findings are comparable to those in the region as 86%, 76%, and 8% of GAVI eligible countries had introduced the PCV, Rotavirus, and the HPV vaccines respectively by 2017 (42). Delay in HPV vaccine introduction has been attributed elsewhere to the poor adoption of life-course immunisation, vaccine supply constraints, and pricing issues (17, 24) which stand exacerbated by PHEs (7). The outlier countries yet to introduce any of the three selected vaccines are potential key pointers to the contributing role PHEs play in delaying vaccine introductions into NIPs as raised by Grundy *et al.* in their study (7).

Despite the positive progress in NITAG establishment in the WHO Africa region (43), a non-consistent pattern in their existence and functionality simultaneously existed. Such inconsistent trends have been attributed in previous reports to the lack of political commitment and country ownerships of NIPs and the low NITAG financial investments, in general, and during PHEs (43, 44).

The elimination target for MNT was not met in countries with high counts of PHEs like South Sudan, the Central African Republic, Niger, Guinea, and Angola. The enlisted five countries constitute nearly 50% of the remaining global MNT elimination priority countries (45) and have similar trends with other MNT priority countries like Afghanistan and Yemen, where the presence of protracted PHEs have been blamed on delaying elimination (46).

Having higher armed conflict and total PHE counts were associated with not attaining the target for ≥90% national DTP3 coverage. These findings are comparable to those from studies conducted in similar contexts where armed conflicts were reported to be associated with poor immunisation coverage outcomes (7, 12, 30). Conversely, while the Democratic Republic of Congo had the highest PHE count, its national DTP3 coverage was not the poorest. As

described elsewhere, this finding in the Democratic Republic of Congo could be partly attributed to the humanitarian aid in the country (47). In addition, there have been recent specific plans developed by the government of the Democratic Republic of Congo in collaboration with technical and financial partners such as WHO and GAVI, The Vaccine Alliance to strengthen the NIPs in the country (48).

The findings further show that periods of higher counts of armed conflicts, disasters, and total PHEs were also associated with not eliminating MNT. Elimination of MNT in the WHO Africa region has been evasive to some extent, with most of the countries prioritised for MNT elimination being affected by PHEs (49-51). In other PHE endemic contexts, where MNT elimination remains unattained, low tetanus vaccine coverage among women of reproductive age, unhygienic birth practices, delayed treatment, and inadequate MNT surveillance have been cited to delay progress (50, 52, 53).

Higher counts of all the three types of PHEs and the total PHEs were not associated with meeting the immunisation targets of having functional NITAGs or the introduction of new vaccines. The lack of consistency in the existence and functionality of NITAGs is not uncommon as observed in other PHE prone contexts in the region (43). On the other hand, during PHEs, whereas the functionality of NITAGs may be compromised (44), the WHO recommends humanitarian immunisation teams to utilise the unique expertise and local knowledge of existing NITAG members (19). For the target to introduce new vaccines, a possible caveat may exist in interpreting association, as within the scope of this study, only three vaccines were selected out of a pool of new vaccines. Conversely, we equally recognise that despite PHE endemicity, most of the case study countries had performed relatively well in this target which is also credited as one of the WHO Africa region DoV successes (24, 29) owing to political commitment and strong immunisation investments (49). Arguably, such

progressive performance noted in this DoV target, can offer a lesson; that the link between PHEs and immunisation performance may not be always absolute.

In summation, it is imperative to note that central to the attainment of the discussed DoV targets and "health for all" as embodied under Sustainable Development Goal 3 (SDG 3) is the presence of peace and stability in a country which is a critical pillar to SDG 16 namely "peace justice and strong institutions" (54, 55). This will reciprocally ensure that every individual regardless of their background will have access to vaccines in a timely manner (55).

Our results should be interpreted in light of certain caveats. First, our study was limited to three broad types of PHEs, that may not be exhaustively representative of all types of PHE experienced in the study countries. Furthermore, the severity of the PHEs could not be accounted for as this level of data was not available. The WHO conventional PHE grade system for grading PHE severity was first availed for use in the WHO Africa region in 2017, which was towards the end of the study period. It should be noted that PHEs often overlap in the real-world context and it may be challenging to identify how a single PHE may have impacted the performance of immunisation programmes. Additionally, we may be unable to determine how previous PHEs experienced before the start of the study period in 2010 may have affected the NIPs in the selected countries.

Secondly, we used country generated reports from the WHO/UNICEF JRF to abstract data on DoV immunisation indicators. It is, possible that potential inaccuracies in the country data may have influenced the outcome of our study. However, this could not be avoided within the scope of this study. Data quality issues from country reports have been constantly highlighted as one of the major concerns by the WHO, SAGE in their annual DoV immunisation reports (24, 28, 29).

Lastly, while associations between the occurrence of PHEs and the performance of immunisation programmes were inferred we cannot rule out with certainty the influence of other determinants of immunisation programme performance. It was also not possible to account for emergency responses aimed at providing immunisation services during PHEs. As such, our estimated results may represent a lower bound for the true effect of PHEs on immunisation.

Future research investigations should address these limitations to broaden the scope of evidence on the interactions that exist between PHEs and immunisation performance. We propose that future studies should further explore (1) how other types and grades of PHEs may variably impact immunisation performance, (2) immunisation performance at the sub-national level using immunisation data from localised communities where PHEs are recorded to occur, and (3) other determinants that may act together with PHEs to influence immunisation performance.

5. CONCLUSION

PHEs are endemically present in the WHO Africa region and form part of the eco-system in which NIPs exist. With the goal of extending immunisation to all individuals, countries experiencing PHEs within the WHO Africa region may be excluded from reaping the full benefits of immunisation owing to unmet targets. Immunisation performance in countries where PHEs are endemic are largely suboptimal and not at par with envisioned immunisation targets for the DoV. As the DoV comes to an end in 2020 and as the Immunisation Agenda 2030 nears its launch, PHEs like the COVID-19 pandemic, armed conflicts, and disasters are a major threat to NIPs. Therefore, priority should be given in developing evidence-based interventions to mitigate the impacts of PHEs on NIPs. Such interventions may include the commitment by governments in the WHO Africa region to strengthen the resilience of NIPs against PHE challenges by investing in PHE prevention and mitigation initiatives like the

APHEF. Characterising the performance of NIPs in PHE contexts is undoubtedly elemental in bridging the gap to equitable access to immunisation for all populations, irrespective of where they live, thus enabling the collective achievement in shared goals like the DoV, SDG 3 and 16, and the Immunisation Agenda 2030, thereby, enhancing regional health outcomes.

6. LIST OF ABBREVIATIONS

APHEF	African Public Health Emergency Fund
COVID-19	Coronavirus Disease
DTP1	First dose of the combined Diphtheria, Tetanus, and Pertussis Vaccine
DTP3	Third dose of the combined Diphtheria, Tetanus, and Pertussis Vaccine
EM-DAT	Emergency Events Database
GVAP	Global Vaccine Action Plan
HPV	Human Papillomavirus
JRF	Joint Reporting Form
MNT	Maternal and Neonatal Tetanus
NIPs	National Immunisation Programmes
NITAG	National Immunisation Technical Advisory Group
PCV	Pneumococcal Conjugate Vaccine
PHE	Public Health Emergency
PROMED	Program for Monitoring Emerging Diseases
RSPI	Regional Strategic Plan for Immunisation
UCDP	Uppsala Conflict Data Program
SAGE	Strategic Advisory Groups of Experts in Immunisation
SDG	Sustainable Development Goal
UNICEF	United Nations Children's Fund
VPDs	Vaccine-Preventable Diseases
WHO	World Health Organisation
WHO-AFRO	World Health Organisation Africa region

7. DECLARATIONS

7.1 Ethics

Ethical clearance to conduct this study was granted by the University of Cape Town, Faculty of Health Sciences, Human Research and Ethics Committee (**Appendix 2**).

7.2 Consent for publication

Not Applicable.

7.3 Availability of data and materials

The datasets used during the current study are available from EM-DAT repository (https://www.emdat.be/)**,** UCDP repository (https://ucdp.uu.se/), PROMED-Mail repository (https://wwww.promedmail.org/eafr), WHO Emergency Preparedness and Response database (https://www.who.int/csr/don/archive/year/en/) and the WHO/UNICEF JRF immunisation database (https://www.who.int/immunization/monitoring_surveillance/data/en/)

7.4 Competing interests

The author has no competing interests to declare.

7.5 Funding

Not Applicable.

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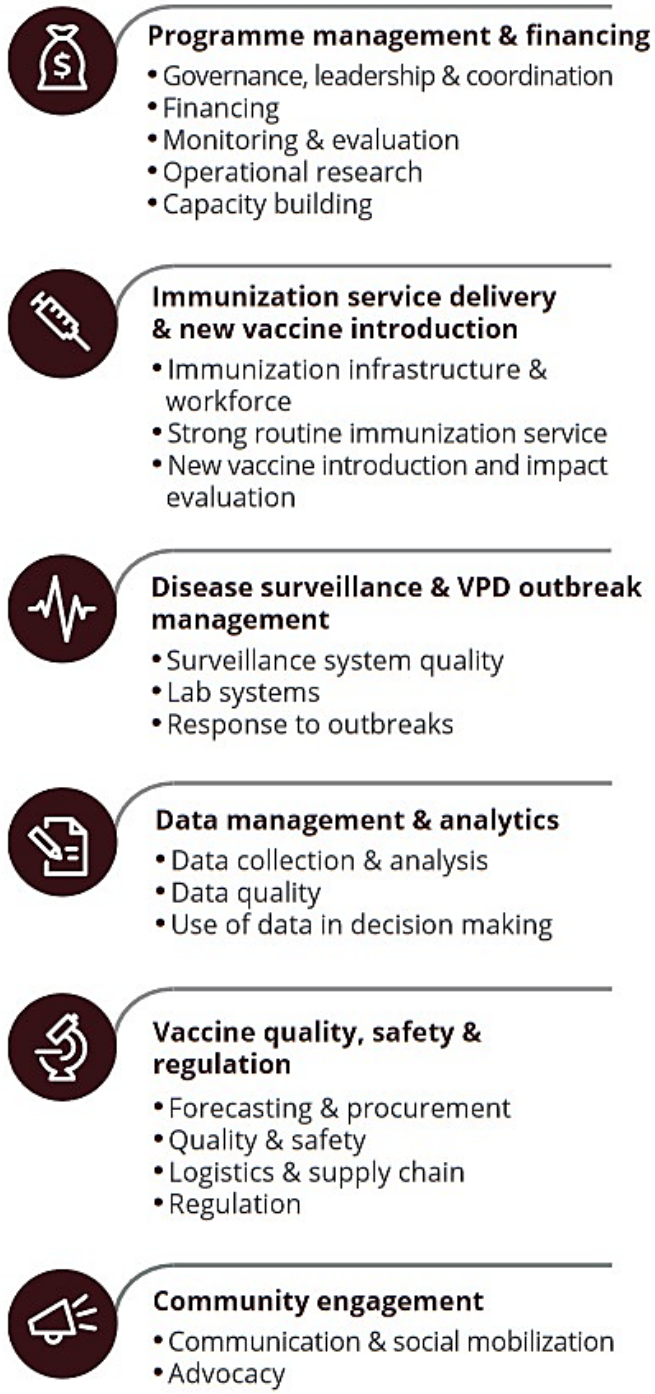
PART C: APPENDICES

1. APPENDIX 1 : IMMUNISATION MATURITY GRID COMPONENTS



Adopted from the Business case for WHO immunisation activities on the African continent 2018

Figure 1. Six components used to assess a country's immunisation maturity grid

2. APPENDIX 2: ETHICS APPROVAL DOCUMENTS

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

25 September 2020

HREC REF: 583/2020

Dr Bejamin Kagina
Public Health and Family Medicine
Wernher & Beit North Building, IDM
Anzio Road
Observatory
7925
Email: Benjamin.kagina@uct.ac.za
Student email: chpvio001@myuct.ac.za

Dear Dr Kagina

PROJECT TITLE: CHARACTERISATION OF IMMUNISATION PROGRAMS ON COUNTRIES EXPERIENCING PUBLIC HEALTH EMERGENCIES WITHIN THE WHO-AFRO REGION-MASTERS CANDIDATE-MISS VIOLA CHEPKURUI

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 and 06 July 2020, found on the following website link:
http://www.health.uct.ac.za/fhs/research/humanethics/about

Approval is granted for one year until the 30 September 2021.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Ms Viola Chepkurui will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC 355/2020 le

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC 355/2020 le

3. APPENDIX 3: JOURNAL SUBMISSION GUIDELINES

BMC: Conflict and health

Research article

Criteria

Research articles report original findings from individual studies (or groups of studies). They may be based on qualitative or quantitative data and may involve experimental or non-experimental designs.

Conflict and Health strongly encourages studies that make use of data, infrastructure or personnel in a foreign country to involve at least one local researcher from that country as an author.

Conflict and Health also strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's information on recommended repositories.

Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page

The title page should:

- present a title that includes, if appropriate, the study design e.g.:

    - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"
    - or for non-clinical or non-research studies a description of what the article reports
- list the full names and institutional addresses for all authors
    - if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the “Acknowledgements” section in accordance with the instructions below
- indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the CONSORT extension for abstracts. The abstract must include the following separate sections:

- **Background:** the context and purpose of the study
- **Methods:** how the study was performed, and statistical tests used
- **Results:** the main findings
- **Conclusions:** brief summary and potential implications
- **Trial registration:** If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration

number and date of registration should be in stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words 'retrospectively registered'. See our editorial policies for more information on trial registration

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

Methods

The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

Results

This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.

Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

Conclusions

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

List of abbreviations

If abbreviations are used in the text, they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information (optional)

Please see below for details on the information to be included in these sections.

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

Ethics approval and consent to participate

Manuscripts reporting studies involving human participants, human data or human tissue must:

- include a statement on ethics approval and consent (even where the need for approval was waived)
- include the name of the ethics committee that approved the study and the committee's reference number if appropriate

Studies involving animals must include a statement on ethics approval and for experimental studies involving client-owned animals, authors must also include a statement on informed consent from the client or owner.

See our editorial policies for more information.

If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

Consent for publication

If your manuscript contains any individual person's data in any form (including any individual details, images, or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.

You can use your institutional consent form or our consent form if you prefer. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication).

See our editorial policies for more information on consent for publication.

If your manuscript does not contain data from any individual person, please state "Not applicable" in this section.

Availability of data and materials

All manuscripts must include an 'Availability of data and materials' statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.

Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
- Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.

More examples of template data availability statements, which include examples of openly available and restricted access datasets, are available here.

BioMed Central also requires that authors cite any publicly available data on which the conclusions of the paper rely in the manuscript. Data citations should include a persistent identifier (such as a DOI) and should ideally be included in the reference list. Citations of datasets, when they appear in the reference list, should include the minimum information recommended by DataCite and follow journal style. Dataset identifiers including DOIs should be expressed as full URLs. For example:

Hao Z, AghaKouchak A, Nakhjiri N, Farahmand A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. figshare. 2014.

http://dx.doi.org/10.6084/m9.figshare.853801

With the corresponding text in the Availability of data and materials statement:

The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number]

If you wish to co-submit a data note describing your data to be published in *BMC Research Notes*, you can do so by visiting our submission portal. Data notes support open data and help authors to comply with funder policies on data sharing. Co-published data notes will be linked to the research article the data support (example).

For more information please email our Research Data Team.

Competing interests

All financial and non-financial competing interests must be declared in this section.

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Funding

All sources of funding for the research reported should be declared. The role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript should be declared.

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Acknowledgements

Please acknowledge anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials.

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Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

References

Examples of the Vancouver reference style are shown below.

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Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

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Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

Article within a journal supplement

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.

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Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

Online First chapter in a series (without a volume designation but with a DOI)

Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. Top Curr Chem. 2007. doi:10.1007/128_2006_108.

Complete book, authored

Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

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Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. http://www.rsc.org/dose/title of subordinate document. Accessed 15 Jan 1999.

Online database

Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998. http://www.healthwise.org. Accessed 21 Sept 1998.

Supplementary material/private homepage

Doe J. Title of supplementary material. 2000. http://www.privatehomepage.com. Accessed 22 Feb 2000.

University site

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FTP site

Doe, J: Trivial HTTP, RFC2169. ftp://ftp.isi.edu/in-notes/rfc2169.txt (1999). Accessed 12 Nov 1999.

Organization site

ISSN International Centre: The ISSN register. http://www.issn.org (2006). Accessed 20 Feb 2007.

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Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, *et al.* Genome data from sweet and grain sorghum (Sorghum bicolor). GigaScience Database. 2011.

http://dx.doi.org/10.5524/100012.

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