



**Measles in Rwanda:
Evaluation of decade (2006-2015) surveillance and immunization coverage
towards measles elimination goal by 2020.**

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DECLARATION

This study is an original report drafted by the author. It has not been submitted for publication to any journal or other publication.

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SIBOMANA Hassan

SUPERVISOR'S APPROVAL

AUTHORITY TO SUBMIT THE THESIS

Title of the thesis/Dissertation:

**Measles in Rwanda:
Evaluation of decade (2006-2015) surveillance and immunization coverage towards
measles elimination goal by 2020.**

I, Dr NZAYIRAMBAHOManassé, in my capacity, I do hereby authorize the student to submit his Thesis to the school ready for its defense.

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EXECUTIVE SUMMARY

The introduction of vaccines against measles has drastically reduced the incidence of measles in World Health Organization (WHO) Member States in the African Region, and substantial progress has been made towards measles mortality reduction and elimination goals. However, many countries are at risk for not meeting elimination goals by 2020 due to challenges in measles surveillance and inadequate immunization coverage that has resulted in a resurgence of measles in some countries.

A cross-sectional study was conducted to investigate national measles case-based surveillance and immunization data maintained by the Vaccine Preventable Disease Program, Rwanda Biomedical Center from 2006 to December 2015. The objective of the study was to identify characteristics of reported measles cases, geographic trends in measles and immunization rates, and to evaluate the achievement of performance indicators for surveillance and elimination targets.

Measles was confirmed in 301 of the 3,787 suspected cases reported, with the majority of cases occurring in 2010 (40.5%) alone. Children of under 5 age were the most affected (46%). Measles cases were most frequently reported from the Western province (40%), and in districts that shared a border with neighboring countries. From 2006 to 2015, national immunization rates were estimated at 95% for routine and ($\geq 100\%$) for supplementary immunizations. During the 10-year study period, Rwanda achieved 8 of the 11 WHO target indicators used in this study to evaluate performance towards measles elimination.

Despite progress from 2006 to 2015, inadequate immunization coverage and challenges with measles surveillance in Rwanda have delayed progress towards Rwanda's measles elimination goals. Improved measles surveillance, strengthened immunization strategies, and a renewed political and financial commitment are necessary to achieve elimination targets for Rwanda by the year 2020.

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GLOSSARY

Case definition: a set of standardised criteria applied to identify the individuals with a given disease or any other condition under investigation (cases).

Control: a reduction in the incidence, morbidity, or mortality of an infectious disease to a locally acceptable level.

Effectiveness: the extent to which a plan, a program, an intervention or a response achieves the defined objective for which it was initiated.

Elimination: a reduction to zero of the incidence of disease or infection in a defined geographical area.

Epidemiological Link: a case meeting the clinical case definition and is also linked epidemiologically to a laboratory confirmed case.

Eradication: the permanent reduction to zero of the worldwide incidence of infection.

Incidence: number of new cases or out breaking events within a given population for a given period.

Laboratory criteria for diagnosis: presence of measles-specific IgM antibodies.

Line List: aggregated data collected on suspected measles cases during an outbreak investigation.

Measles case definition: any person in whom a clinician suspects measles infection, or any person with fever and maculopapular rash (i.e. non-vesicular) and cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes).

Non-Measles Febrile Rash: all discarded cases that do not meet the laboratory or epidemiologically confirmation for measles.

Non-Measles Febrile Rash Illness Rate: the proportion of discarded cases divided by the national population annually.

Notification: compulsory communication to the health official of cases and deaths caused by communicable disease or diseases of public health importance.

Susceptible: a member of a population who is at risk of becoming infected by a disease.

Targeted population: a subgroup of population defined also as beneficiary/targeted by an intervention or a given service.

ABBREVIATIONS

AFR	African Region
AFRO	African Regional Office
CFR	Case Fatality Rate
CI	Confidence Interval
DRC	Democratic Republic of Congo
EPI	Expanded Program on Immunization
IDSR	Integrated Disease Surveillance and Response
JRF	WHO-UNICEF Joint Reporting Form
MCHW	Maternal and Child Health Week
MCV	Measles-containing Vaccine
MDG	Millennium Development Goal
MMR	Measles, Mumps, and Rubella
MOH	Ministry of Health
MR	Measles and Rubella
R_0	Reproductive Number
RBC	Rwandan Biomedical Centre
RED	Reaching Every District
SIA	Supplementary Immunization Activities
UNICEF	The United Nations Children's Fund
VPD	Vaccine Preventable Disease
VPDP	Vaccine Preventable Diseases Program
WHO	World Health Organization

I.INTRODUCTION

I.1 Context

Measles virus is highly infectious and, in the pre-vaccination period, >90% of individuals were infected by the age of 10 years, the majority with symptoms(1). Measles remains one of the leading causes of morbidity and mortality globally due to the highly communicable nature of the disease. Measles is highly communicable, with greater than 90% secondary attack rates among susceptible persons (2) and can infect populations in which fewer than 10% are susceptible (3) In 1980, before widespread vaccination, measles caused 2.6 million deaths each year, with the largest burden in children of five years of age or younger(4) In 2001, an estimated global total of >23 million disability-adjusted life years were lost as a result of measles. Fortunately, a safe, effective, and affordable vaccine has been made widely available in most countries through the Expanded Program on Immunization (EPI) provided through the World Health Organization (WHO). By the end of 1997, global measles mortality decreased by 85% compared to pre-vaccine era estimates (5) Measles deaths dropped to an estimated one million deaths worldwide, with over half of the deaths reported in sub-Saharan Africa (5) In Rwanda, the incidence of measles have been reduced since the creation of vaccination program in 1980, but there is still a lot to do for achieving measles elimination goal by 2020.

I.2 Background to the study

In Rwanda, Measles vaccination started in 1980 with vaccination program. Rwanda adopted the WHO strategy of accelerating control/elimination/eradication of EPI targeted diseases; measles, polio and NNT. In 1996, Rwanda has started polio eradication initiative using all strategies including polio SIAs. For measles, Rwanda introduced catch-up measles SIAs since 2003 followed by periodic follow-up SIAs. Only one dose of measles vaccine was being provided in routine immunization till 2014 where the second dose of measles vaccine was introduced in routine immunization preceded by a large catch up vaccination campaign covering children aged from 9 months to 15 years in March 2013. Considering much efforts and strategies put in place to eliminate measles, this study aims to evaluate if really the measles can be eliminated in Rwanda by 2020.

I.3 Problem statement

Accelerated immunization activities for measles have had a significant impact on the reduction of measles mortality in the African Region (AFR). In 2000, measles mortality was estimated at 750,000 globally, of which 395,000 (53%) were reported from the African Region(6). The WHO African Regional Office (AFRO) took on the goal to reduce measles mortality by $\geq 98\%$ between 2000 and 2012(5) Despite substantial progress, the 2012 pre-elimination goal was missed by nearly 10%, with a measles mortality reduction from 395,900 to 41,400 between 2000 and 2012 (5). The goal was not achieved due to large measles outbreaks that occurred in 2011 and 2012, where 89% of cases in 2011 were reported in four countries (Chad, DRC, Nigeria, and Zambia) and 88% of cases in 2012 were reported in five countries (Angola, Burkina Faso, DRC, Ethiopia, and Nigeria) respectively(5) Waning herd immunity, inadequate immunization coverage, and incomplete surveillance were identified as the leading causes of these outbreaks and other measles resurgence seen in countries throughout sub-Saharan Africa.

Measles deaths play a significant role in global child mortality as the disease predominantly affects children under the age of five-years-old. Between 2000 and 2008, child mortality decreased by 1.6 million, where 569,000 of that decline was attributed to averted measles deaths (7) Nearly a quarter of all lives saved annually were the result of progress towards reducing measles deaths. It is for this reason that measles vaccination coverage and measles mortality reduction was selected as an indicator of progress towards the Fourth Millennium Development Goal (MDG). MDG4 was aiming at reducing the under-five child mortality rate by two-thirds between 1990 and 2015 (8).

Rwanda, through the Rwandan Biomedical Centre's (RBC) Vaccine Preventable Diseases Program (VPDP), was sharing the goal with the other 47 WHO AFRO Member States to contribute to progress towards MDG 4 through the implementation of measles mortality reduction and elimination efforts. The measles mortality reduction strategy, supported by the WHO, recommends that countries provide measles vaccinations as a part of routine immunization activities, secondary opportunity for measles vaccinations through mass supplementary immunization activities (SIAs) in countries with high case and death rates, monitoring of outbreaks through a case-based surveillance system, and improved management of measles cases (8).

In Rwanda, more than 80,000 measles cases were reported at the beginning of vaccination program in 1980. In 1994, after the tragedy of Genocide the entire health sector collapsed and the immunization coverage fell down which resulted to the measles outbreaks the following year (1995). After 2002 year, the measles immunization coverage started to increase beyond 80% and reached 98% in 2015 (9)(10). As long as the measles immunization coverage was increasing, the number of measles cases decreased notably and currently the country is reporting less than 1 measles case per 1,000,000 inhabitants. Even though, Rwanda has achieved remarkable results in terms of measles vaccination, much efforts have to be put in measles surveillance and strengthening immunization coverage to ensure the elimination of measles by 2020. With all strategies put in place to increase the immunization coverage and strengthening vaccine preventable diseases surveillance, Rwanda will be able to eliminate measles by 2020?

I.4 Purpose of the study

This study emphasizes the importance of measles case-based surveillance reporting and measles immunization coverage as an indicator of progress towards measles elimination. The aim of this study is to evaluate performance of the surveillance system and progress towards WHO AFRO elimination goals by analyzing case-based measles surveillance data and immunization data between 2006 and 2015. It is the ambition that this study will provide a description of the epidemiology of measles in Rwanda and offers recommendations on how to focus measles elimination efforts in the future to meet the 2020 targets.

I.5 Research Objectives

I.5.1. General Objective

The primary objective of the study is to evaluate measles case-based surveillance and national immunization coverage data.

I.5.2. Specific objectives

1. To describe epidemiological and descriptive characteristics of suspected and confirmed cases of measles.
2. To map trends in confirmed measles cases and immunization rates based on location and year reported.

3. To determine if the surveillance system for measles is performing according to WHO recommended guideline (Appendix 3: Performance indicators of quality of measles surveillance) .
4. To discuss progress towards meeting measles elimination goals established by WHO AFRO by the year 2020.

II. LITTERATURE REVIEW

II.1. Overview of the topic

II.1.1. Measles epidemiology

Measles is an acute viral disease that is transmitted from person-to-person via respiratory droplets in the air or on objects and surfaces. The basic reproductive number (R_0) is estimated at 16, meaning that 1 case of measles in a susceptible community will produce, on average, 16 secondary cases (11). The R_0 for measles is considerably higher than that for other infectious diseases, such as varicella, rubella, or poliomyelitis, which has an average R_0 of 11, 7, and 5, respectively(12). Clinically apparent measles begins with a prodromal phase characterized by the onset of a high fever, runny nose, a cough, conjunctivitis, and small white spots inside the cheeks called Koplik's spots(4). After several days, a rash appears which can spread from the face and neck to other parts of the body. The incubation period for measles, from exposure to the symptom onset, ranges from 7-18 days, with the onset of prodromal symptoms averaging at 10-12 days and the onset of a rash averaging at 14 days (2). Measles cases are communicable from approximately 4 days before until 4 days after rash onset (2). Measles communicability is often an issue for countries with limited surveillance and health infrastructure, as most cases of measles are clinically diagnosed after rash onset, allowing for the opportunity of an outbreak to occur within a community.

Recovery from measles begins soon after rash onset unless a case presents with complications. Complications occur in approximately 30% of reported measles cases (2), and the risk of complication increases by extremes of age and malnutrition (3) Case fatality is highest in infants and children under the age of five (3) The most severe complications include blindness, encephalitis, severe diarrhea and dehydration, ear infections, and severe respiratory infections such as pneumonia (5). Pneumonia is the most reported complication and the cause of the majority of measles-related deaths worldwide (3) The case-fatality rate for measles is approximately 15%, but can reach as high as 25% in populations with endemic malnutrition, especially those with Vitamin A deficiencies, and HIV/AIDS (2). Measles is the leading cause of blindness among children in Africa (2).

Measles is ubiquitous, having burdened all countries around the world. Cases of measles can occur throughout the year; however, cases are at its highest during dry seasons in tropical zones and during late winter and early spring in temperate zones (12)(13). No antiviral treatment exists for measles. Complications can be avoided through adequate nutrition and

fluid intake, as well as through an antibiotic regimen to prevent eye, ear, and respiratory infections (5). All children in developing countries are provided with two Vitamin A supplements given 24 hours apart to help prevent eye damage and blindness(5). Giving Vitamin A supplements to patients has been shown to reduce the number of measles-related deaths by more than 50% (5).

Measles can be prevented through vaccination. The WHO recommends that two doses of the measles containing vaccine (MCV) be given to children. Two doses of MCV help to guarantee immunity and prevent outbreaks. Nearly 15% of vaccinated children fail to develop immunity from the first dose of MCV alone (5). As of 2011, all 194 WHO Member States including Rwanda introduced or initiated introduction of a two-dose measles vaccination strategy delivered through routine immunization activities and/or SIAs(14). The majority also provided rubella-containing vaccines (RCVs) in the form of a combined measles and rubella (MR) or measles, mumps and rubella (MMR) vaccine (14).

II.1.2 The measles initiative

The Measles Initiative was launched in 2001. Only a year after, the World Health Assembly adopted its resolution to reduce global measles deaths by half compared with 1999 levels, from 2000 to 2005 (14). Today, efforts to reduce measles, rubella, and congenital rubella syndrome have been combined to form the Measles and Rubella (MR) Initiative. The MR Initiative is a global partnership with five spearheading partners—the American Red Cross, the United Nations Foundation, the United Nations Children’s Fund (UNICEF), the U.S. Centers for Disease Control and Prevention, and the WHO. The MR Initiative has been one of the driving forces behind efforts to accelerate measles mortality reduction worldwide through the delivery of technical and financial support to governments and communities(14). The initial aim of the measles mortality reduction strategy was control; once achieved, the focus shifted to outbreak prevention, regional elimination, and, finally, global eradication. Elimination of measles is not only biologically feasible, but also cost-effective and advantageous to health systems strengthening strategies.

The current goal of the MR Initiative is to reduce measles mortality worldwide by 95% between by 2015 compared to 2000 estimates, and to eliminate measles and rubella in at least five of six WHO regions by 2020 (14). Regional measles and rubella elimination goals for all

six of the WHO regions can be seen in Figure 1. The measles elimination goals are in black and the rubella elimination goals in red. Although all six of the WHO regions have made progress, towards measles elimination, some regions have yet to adopt rubella control or elimination goals. The Americas have consistently sustained measles elimination since 2002 (15). Additionally, the Western Pacific Region is on track to meet their 2015 goal (15). However, large outbreaks in countries from the remaining WHO regions jeopardize progress towards each regions respective elimination goals.

Figure 1: WHO regional goals (target years) for the elimination of measles and either the elimination or control of rubella.



(CDC, 2014)

WHO AFRO adopted measles mortality reduction goals in 2001 following strategies recommended by WHO and UNICEF (16). Measles mortality reduction strategies reduced the estimated number of measles deaths in the region by 92% between 2000 and 2008 (16). Despite significant reductions, WHO AFRO still accounted for 36% of all measles deaths in 2010(14). In 2011, the 60th Regional Committee of the WHO adopted a goal of measles elimination in the African Region by the year 2020 (17), which includes the following objectives (16):

- (a) to reduce measles incidence in all countries;

- (b) to increase access to immunization services in all districts;
- (c) to improve coverage during all scheduled measles SIAs and outbreak response immunization activities;
- (d) to improve the quality of measles surveillance, as well as the epidemiological and virological investigation of measles outbreaks in all countries.

To achieve these objectives by 2020, all countries in the AFR will have to achieve and maintain the following targets (16):

- (a) measles incidence of less than 1 case per million population at national level;
- (b) at least 95% measles immunization coverage at national level and in all districts;
- (c) at least 95% coverage in all scheduled measles SIAs, and in outbreak response immunization activities;
- (d) at least 80% of districts investigating one or more suspected measles cases within a year,
- (e) and a non-measles febrile rash illness rate of at least 2 per 100 000 population at national level.

By the end of 2012, 15 African countries out of 46 (32%) Member States are on track to meet the measles elimination targets by 2020 (17). However, 16 countries (35%) are at risk of failing to reach 2020 elimination targets unless country capacity to deal with the burden of measles is strengthened considerably (17). The Ministry of Health (MOH) of Rwanda has approved and subscribed to all WHO recommendations aimed at measles elimination. In 2013, Rwanda became the first sub-Saharan African country to introduce the combined MR vaccine in routine immunization schedule and SIAs (18). Measles SIAs are normally conducted once every 2 to 3 years targeting children aged 9 months to 14 years with target coverage rates above 95% (19). Also, Rwanda introduced a second dose of the measles vaccine (MCV2) in routine immunization in 2014. The current immunization schedule established that the first dose of MCV should be given to children at 9 months old (Rwanda Immunization schedule to be put on Annex 1). In 2015, the MR vaccine started to be administered to both children aged 9 months and 15 months old.

II.2. Determinants or summary of factors associated with measles

The severity of measles varies widely, depending on a number of host and environmental factors. The risk of developing severe or fatal measles increases for those aged <5 years, living in overcrowded conditions, who are malnourished (especially with vitamin A deficiency), and those with immunological disorders, such as advanced HIV infection. In developing countries, case-fatality rates among young children may reach 5–10% (1). In industrialized countries, deaths from measles are rare, although severe forms of the disease and even death may occur in previously healthy individuals. Relatively common complications of measles include otitis media, laryngo-tracheobronchitis and pneumonia. In children, otitis media occurs in 5–15% of cases and pneumonia in 5–10%. In developing countries, persistent diarrhoea with protein-losing enteropathy may ensue, particularly in infants. Post-infectious measles encephalitis occurs in about 1/1000 cases, and sub-acute sclerosingpanencephalitis, a slowly progressing infection of the central nervous system, occurs in about 1/10 000–100 000 cases (1).

III. METHODS

III.1. Study design

The study design is cross sectional. It has been chosen for this study because it aims at evaluating the current status of measles case based surveillance and routine immunization coverage.

III.2. Source of data

Data for measles surveillance were analyzed from the Measles surveillance database managed by RBC/VPDP while measles immunization coverage data were extracted from annual Joint Report Form (JRF) for WHO and UNICEF.

III.3. Study participants

All suspected cases of measles reported in the database from 2006 to 2015 were part of our study. In total 3,787 cases were analyzed after cleaning the database.

III.4. Data collection and instruments development procedures

Data were collected retrospectively from two secondary sources. The first source was the national measles case-based surveillance data collected through measles surveillance system by the RBC VPDP. The second was immunization coverage rates collected by the UNICEF-WHO Joint Reporting Form.

Disease Surveillance is a key component of control programs and serves as the means of monitoring program success. In routine surveillance systems, data on individual patients, which are recorded in patient registers, are used to calculate the number of cases of reportable diseases diagnosed by health facility staff over a certain period of time. These data are periodically reported to district authorities who compile and send them to higher administrative levels. This process of detecting and reporting information on diseases that bring patients to the health facility is known as passive surveillance. Passive surveillance yields only limited data because many sick people do not visit a health facility and because those cases may not be correctly classified, recorded, or reported.

One way to overcome the limitations of passive surveillance and obtain more reliable and accurate data about the disease burden in the community is for surveillance officers to regularly visit the most utilized health facilities and traditional health care service delivery points. These visits will help to ensure that all cases are notified and reported in time. Surveillance officers can also look for cases of a specific disease at community level. This

process is known as active surveillance. Since passive surveillance has limitations due to its lack of access to some groups within the population, active surveillance is often used to enhance the completeness of a passive surveillance system.

When there is a suspected case of a disease targeted for eradication/ elimination (such as polio or neonatal tetanus or measles) or during suspected outbreaks of epidemic-prone diseases, health workers conduct case-based investigations to learn more about a specific disease pattern. In such cases, health workers use the epidemiologic case definitions to identify suspected cases, and proceed to record detailed information such as the patient's name, age, vaccination status, district and village of residence, date of disease onset, and to take appropriate specimens for laboratory confirmation if necessary. All measles samples collected are sent at National Referral laboratory for confirmation and feed-back should be given to health facilities within 7 days.

III.5. Ethical considerations

Case-based surveillance data for suspected measles cases is collected through Rwanda's national IDSR system managed by the RBC VPDP. Additionally, the RBC VPDP also manages immunization data from the WHO-UNICEF JFR conducted annually. It is for this reason that explicit review by an ethics committee was deemed unnecessary. Instead, permission to use secondary data was sought and obtained from the management of the RBC VPDP before initiating analysis. Names and other personal identifiers were removed from the data to ensure confidentiality of cases.

III.6. Measures (description of main variables)

Study variables include age, sex, and measles vaccination status, date of onset, laboratory results, and symptoms.

III.7. Data analysis

This report provides details on the implementation of Rwanda's measles elimination strategies and assesses progress towards elimination goals stipulated by WHO AFRO. The analysis includes an epidemiological review of measles trends from January 2006 to December 2015; looking specifically at case characteristics, and performance indicators for surveillance and elimination goals.

The investigator performed a descriptive analysis for both suspected and confirmed measles cases looking specifically at age, gender, vaccination history, hospitalization status, location

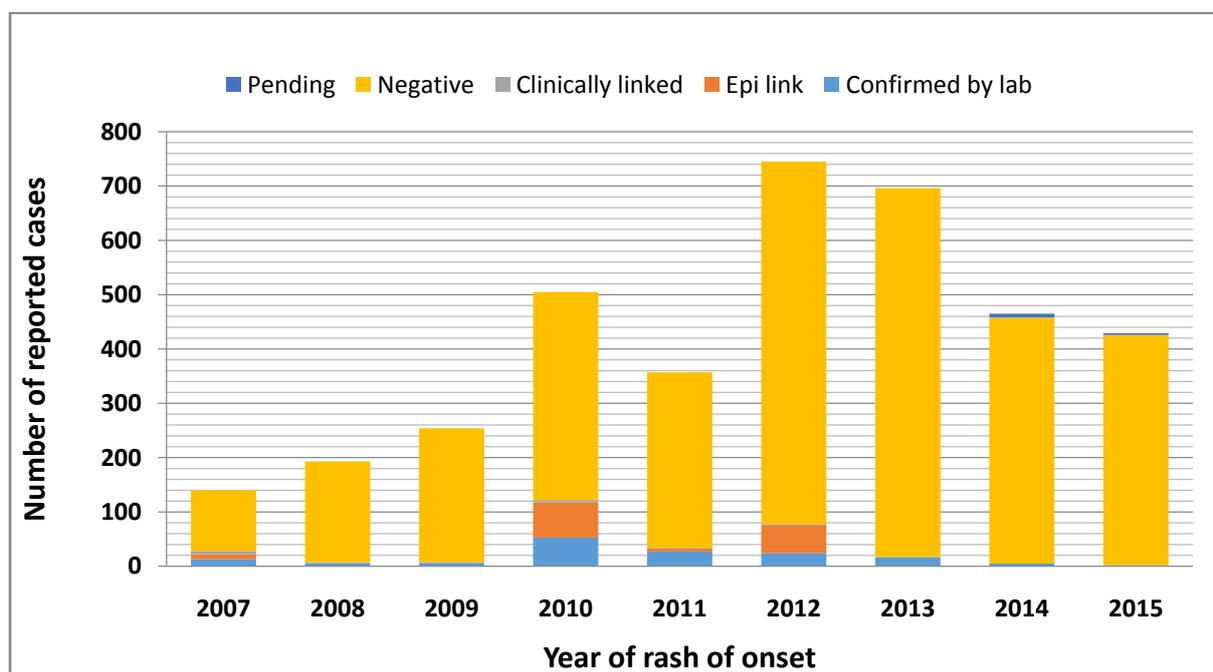
of residence by rural or urban status, and reporting province. STATA statistical software, version 11 was used in this study to calculate age mean within a 95% confidence interval (CI) and frequencies for all variables. Mapping the immunization coverage and distribution of measles cases were performed using QGIS while Excel 10 was used to show the trends of suspected and measles cases over the years.

IV. RESULTS

IV.1 Epidemiological Characteristics

A total of 3,784 suspected measles cases with rash onset were notified through the IDSR in Rwanda from January 2007 to December 2015, and included 3,625 (95.7%) case-based and 149 (4 %) line list reports. Figure 2 shows the distribution of notified cases by confirmed, Epidemiological link and measles cases diagnosed clinically for the 9-year period (2006 data were not available).

Figure 2: Distribution of suspected cases and confirmed measles cases in Rwanda, 2006-2015.



Measles was confirmed in 301 of the 3,784 suspected cases reported. Of which, 152 (50.4%) were laboratory confirmed by blood specimen and 149 (49.5%) were confirmed by either epidemiological link or clinically. A total of 3,483 cases were discarded, because of a negative or undetermined measles-specific IgM test result. The measles-specific IgM test was conducted on 3,625 suspected cases. Of which; 3,483 cases were discarded, making the overall positivity rate for the measles antibody 4 %.

IV.2 Demographic Characteristics

Table 1 shows the suspected and confirmed measles cases by gender, age group, vaccination history, hospitalization status, household location, and reporting province.

Table 1: Socio-demographic characteristics of both suspected and confirmed measles cases in Rwanda, 2007-2015.

Characteristics	Suspected (n=3787)		Confirmed (n=301)	
Gender		%		%
Male	1998	53%	162	54%
Female	1789	47%	139	46%
Age group		%		%
> 1 an	212	6%	51	17%
1-4 ans	1466	39%	87	29%
5-9 ans	325	9%	44	15%
10-14 ans	54	1%	6	2%
15-19 ans	1681	44%	107	36%
20+	49	1%	6	2%
Vaccination history		%		%
0 dose received	210	6%	74	25%
1 dose	2032	54%	130	43%
2+	1336	35%	33	11%
Unknown/Unsure	209	6%	64	21%
Hospitalization status		%		%
Yes	435	11%	149	50%
No	3352	89%	152	50%
unknown	209	6%	64	21%
Household location		%		%
Rural	3157	83%	263	87%
Urban	602	16%	38	13%
unknown	28	1%	0	0%
Province		%		%
Est	952	25%	100	33%
North	380	10%	4	1%
West	886	23%	121	40%
South	1054	28%	46	15%
Kigali City	515	14%	30	10%

There were a larger percentage of male patients (53%) suspected of having measles reported by the health facilities. Children were the most effected by measles, with 51 (17%) of patients less than 1 years old and 87(29%) between 1 and 4 years old. The median age for both suspected and confirmed measles cases was 5.0 (95% CI: 5.36-5.67) and 5.2 (95% CI: 4.7-5.7), respectively. Fewer than 2% of patients were above the age of 20.

The vaccination status for MCV was known for 94.4% (3,578) of all patients that reportedly had measles. A total of 3,368 (89%) suspected cases were vaccinated with at least one dose of MCV. Of the 3,368 suspected cases that were vaccinated, 2,032(60.3%) of the patients had received only one dose and 1,336 (39.6%) had received two or more doses of MCV. The vaccination status varied slightly for confirmed measles cases. The majority of confirmed cases had prior vaccination history of at least one dose (43%). A total of 74 (25%) of the 301 confirmed cases had no history of MCV vaccination, and 64 of the cases (21%) their vaccination status was unknown.

Hospitalization rates varied significantly for suspected and confirmed measles cases. A large majority of all patients were not hospitalized 3352 (89%). Only 435 of the 3787 suspected cases reported being hospitalized for complications. Of the 435 suspected cases that were hospitalized, only 149 (34.2%) patients were confirmed for having measles and this figure represent 50% of all measles cases reported during the period. 152 (50%) of the 301 patients with measles were not hospitalized. The data provided no information on the cause of hospitalization or the severity of their condition and outcome of the disease.

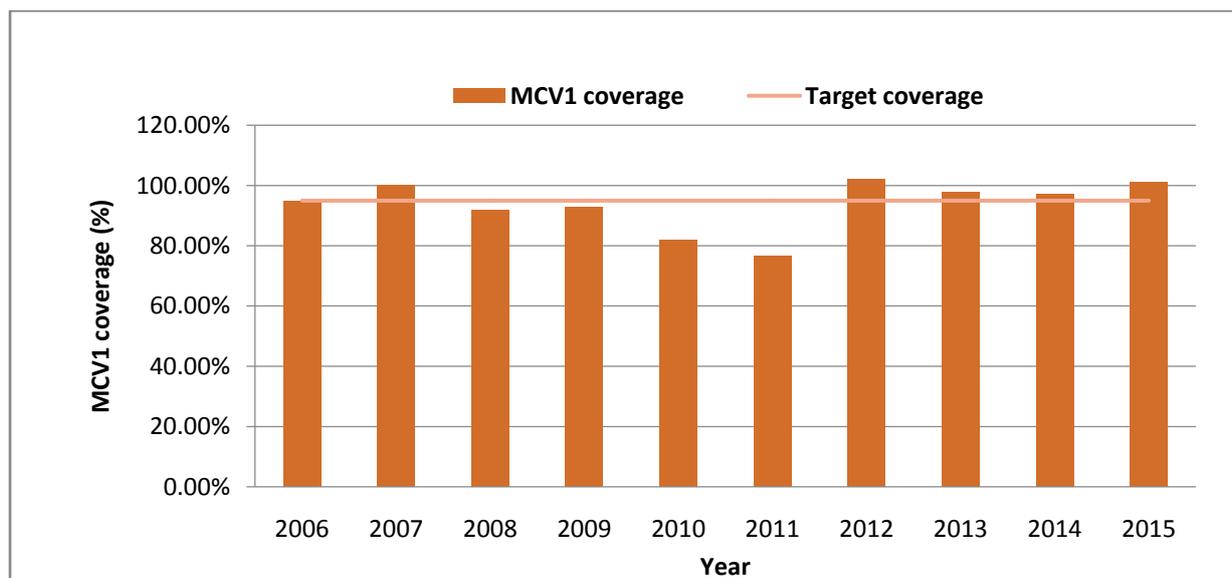
The majority of patients were from rural area (83%), which is expected because approximately 83% of the total population in Rwanda lives in rural areas. When stratified by province, the largest proportion of patients was from the Southern province with 1,054 (28%) suspected and 46 (15%) confirmed cases. The Eastern province accounted for the second largest proportion of suspected cases with 952 (25%), followed by the Western province with 886 (23%) suspected cases but with a big number of confirmed cases 121 (40%) of the total measles cases, Kigali City with 30 (10%), and the Northern province with only 4 (1%) cases.

With 89 cases reported, Rusizi district in the Western province had the highest percentage of cases reported within the province (74.1%) and among all districts (29.5%) in Rwanda between 2007 and 2015. Gatsibo and Nyagatare districts in the Eastern province had the second and third large percentage of cases among all districts with 49 (16.2%) and 36 (11.9%), respectively. Nyarugenge District of Kigali city was the fourth one to have a big number of measles cases 28 (9.3%). The remaining districts reported less than 25 cases during the 9-year period; 22 from Gisagara in the Southern province, 20 from Nyamasheke in the Western province, 18 from Nyaruguru in the Southern province, 6 cases from Kirehe District in Eastern province and 5 or less from the remaining 22 districts.

IV. 4 Immunization Activities

IV.4.1 Routine Immunization Activities

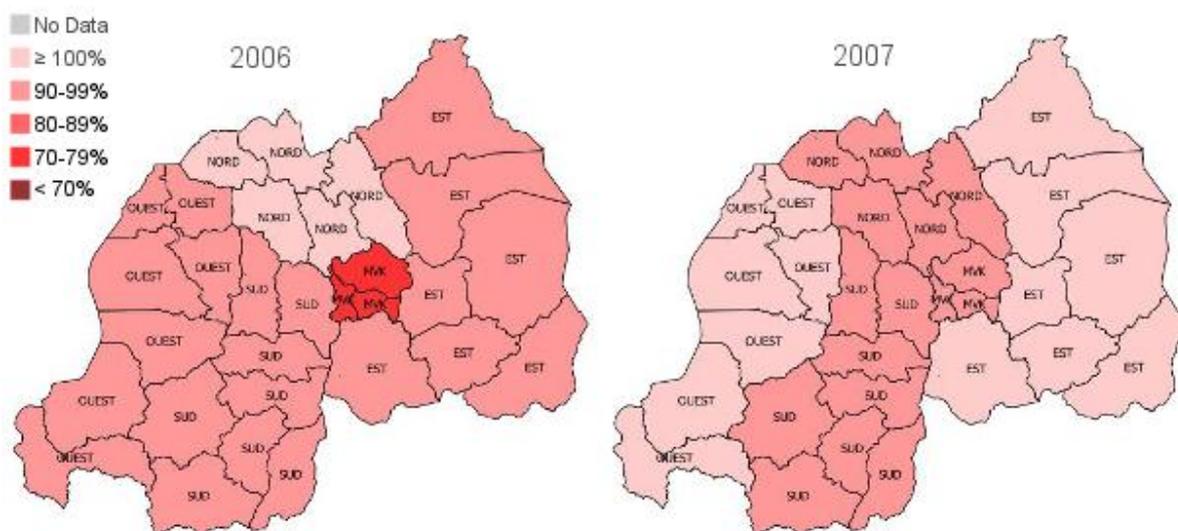
Figure 4: MCV coverage rates (1 dose of MCV) by year compared to target coverage in Rwanda, 2006-2015.



National coverage rates of the first dose of MCV are shown in figure 7 for the period 2006-2015. Coverage rates in Rwanda have fluctuated between 76% and 102% during the period. The target coverage rate of 95% was achieved in five years; in 2007 with 100%, in 2012 with 102%, in 2013 with 98%, in 2014 with 97% and in 2015 with 101% coverage. All years were consistently above 90% coverage, with exception to 2010 and 2011, which reported 82% and 77% coverage, respectively.

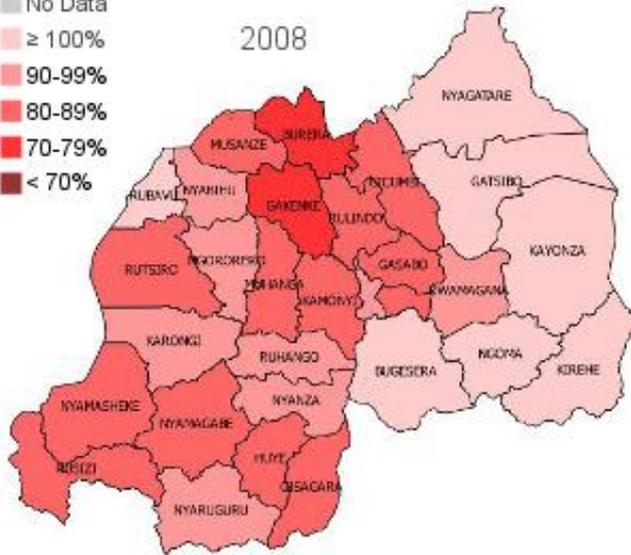
Wide differences can be seen among districts within a given year. Thus, it is important to map trends in immunization rates for each district and province. Figure 8 illustrates the trend in immunization rates by province and district from 2006 to 2015 in Rwanda. Immunization rates are provided by the JFR, which has evolved significantly within the 10-year study period as to how data is analysed and presented. In 2006 and 2007, immunization data was only stratified according to province. Immunization data began to be stratified by all 30 districts within Rwanda by 2008. Thus, the maps below are stratified according to how data was presented in the JFR for a given year. Immunization rates for the period 2006-2007 are aggregated by province, whereas immunization rates for the period 2008-2015 is aggregated by district.

Figure 5: Immunization coverage rates by province and district in Rwanda, 2006-2015



- No Data
- ≥ 100%
- 90-99%
- 80-89%
- 70-79%
- < 70%

2008

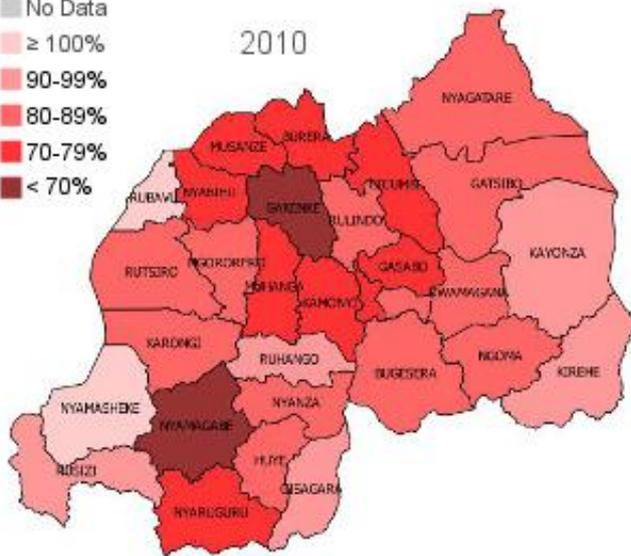


2009



- No Data
- ≥ 100%
- 90-99%
- 80-89%
- 70-79%
- < 70%

2010

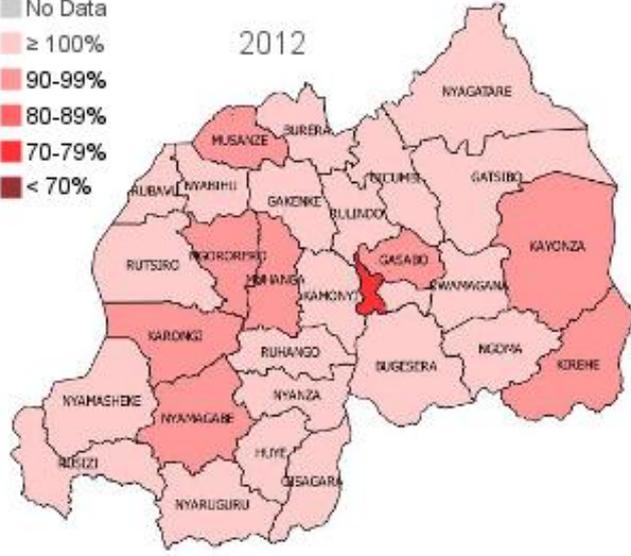


2011



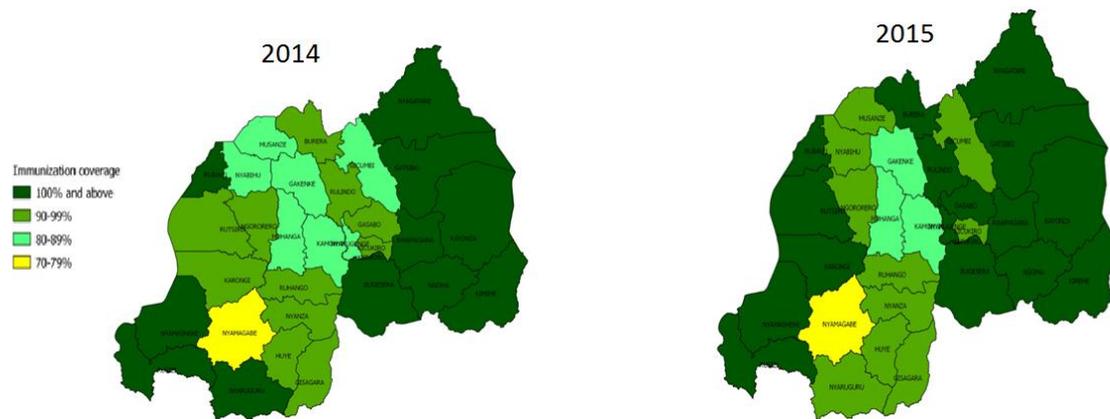
- No Data
- ≥ 100%
- 90-99%
- 80-89%
- 70-79%
- < 70%

2012



2013





Stratifying by district and province provides a clearer picture of immunization rates in Rwanda. Immunization rates fluctuate throughout the 10-year period with no consistency in any province or district. Both 2006 and 2007 had high immunization rates for each province (> 90%), with exception of Kigali City province, which reported 75% coverage in 2006. All rates improve between 2006 and 2007, with exception of the Northern province, which saw a 4% decrease in coverage. Coverage in Kigali City province improved between 2006 and 2007 by 22%.

Between 2008 and 2015, all districts consistently reported immunization rates above 70%, except for 2 districts in 2010 and 7 districts in 2011, which reported rates as low as 60%. Immunization rates improved substantially in 2012 in all districts with exception of Nyarugenge district in Kigali City province, which saw a 8% drop in coverage, from 85% to 77%. Rates started to decline again by 2013 in 21 of the 30 districts. The largest decline was noted in Burera district of the Northern province with a 26% drop from 111% to 86%.

Gakenke district in the Northern province reported the lowest immunization rates for the entire period with an average of 77.5% coverage (ranging from 60% to 100%). Rubavu in the Western province reported the highest immunization rates for the period, from 98% to 122%, with an average of 105% coverage. Interestingly, Gakenke district reported no measles cases from 2006 to 2015, while Rubavu consistently reported measles cases for the same time period.

IV.4.2 Supplemental Immunization Activities

From 2006 to 2015, two SIAs were planned and executed for all districts in Rwanda; one from the 6th to the 10th of October 2009 and one from the 12th to the 15th of March 2013. A

total of 1,350,125 children in 2009 and 4,391,081 million children in 2013 were immunized during nation-wide SIAs during each year. The increased coverage in 2013 is due to a larger targeted age range (9 months to 14 years) than during the first SIA in 2009, which only targeted children 9 months to 5 years old. Coverage rates for both SIAs were above 100% (101% in 2009 and 103% in 2013) compared to target estimated coverage. No information is provided on specific coverage rates for each district or province.

The SIA conducted in 2009 was a targeted measles campaign with the MCV, whereas the SIA conducted in 2013 was included in a more comprehensive Maternal and Child Health week (MCHW) in Rwanda. The MCHW campaign not only targeted measles and rubella with the MR vaccine, but also provided vaccine coverage against Human Papilloma virus to adolescent girls, Vitamin A supplements to pregnant women and children, iron folic supplements to pregnant women, and mebendazole for deworming to pregnant women and children.

IV.5 Performance of the Surveillance System

The quality of data was analyzed by looking at the completeness and timeliness of reporting for measles through the IDSR system. The study uses six indicators, recommended by the WHO AFRO, to evaluate the completeness and timeliness of Rwanda's measles surveillance system. Table 2 identifies the 6 indicators used to evaluate measles surveillance, and provides information on the target and cumulative achievement for each indicator for the 10-year study period.

Table 2: Indicators to evaluate the quality of measles surveillance in Rwanda, 2006-2015.

Indicators for quality of measles surveillance	Target	Achievement
% of reported cases* containing core data (i.e. age, gender, vaccination status).	$\geq 80\%$	99.97%
% of cases* notified ≤ 48 hours after rash onset.	$\geq 80\%$	28,8%
% of notified cases from whom blood specimens have been collected.	$\geq 80\%$	95.6%
% of cases* with adequate specimen** and laboratory results within 7 days.	$\geq 80\%$	95%
% districts that have reported at least 1 suspected case of measles with a blood specimen per year.	$\geq 80\%$	100%
% of confirmed cases with source of infection identified.	$\geq 80\%$	-

*All cases that meet the clinical case definition.

**An adequate specimen is a blood specimen collected within 28 days of the onset of rash.

Age, gender, and vaccination status was used as variables to analyze completeness of reported data. Each case reported to the IDSR system should, at minimum, contain these three core variables. From 2006 to 2015, 78 cases were missing one or more core variables. Of the 3,787 reported cases, all of them contained data on gender, 3,738 contained data on age, and 3,758 contained data on vaccination history. In total, 99,97% of all cases reported from the period contained data on gender, age, and vaccination history.

Suspected measles cases should be notified within 48 hours of rash onset. The performance indicator target of $\geq 80\%$ for cases notified within 48 hours of rash onset was not met.

Reported cases were evaluated to determine the percentage of cases that were adequately investigated. According to WHO standards, $\geq 80\%$ of reported cases should be investigated with a blood specimen. A total of 3,622 cases reported collecting a blood specimen, and 149 cases reported not collected a blood specimen due to being epidemiologically linked to a laboratory confirmed case. The target was achieved, 95.6% of cases were investigated with a blood specimen.

Confirmed measles cases with blood specimens collected were evaluated to determine if the specimen was adequate and if results were reported within 7 days. A total of 152 of the 301 confirmed measles cases were investigated with blood specimens. The 149 remaining cases were epidemiologically linked to a laboratory confirmed measles case, and thus were removed from the denominator. Of the 152 cases investigated with a blood specimen, 95% (144) cases had both adequate lab specimens and were notified with results within 7 days. On average, it took 4.7(95% CI: 4.5-4.9) days for the district to be notified with a result for the blood specimen.

It is important for each district to report suspected measles cases. The WHO recommends that each district should report at least 1 suspected measles case with blood specimen per year. The number of districts reporting at least 1 suspected measles case with blood specimen per year was analyzed cumulatively considering the period of study between 2006 and 2015. Cumulatively, 100% of districts reported at least 1 suspected measles case with blood specimen.

Source of infection could not be identified because the measles case-based surveillance system in Rwanda does not collect information on this variable.

IV.6 Progress Towards Elimination Goals

Table 3: Indicators to evaluate progress toward measles elimination in Rwanda, 2006-2015.

Indicators for measles elimination	Target	Achievement
Measles incidence at the national level.	< 1 case per 1,000,000 population	3.25
Measles immunization coverage at national level and in all districts.	≥ 95%	95%
Coverage in all scheduled measles SIAs, and in outbreak response immunization activities.	≥ 95%	102%
Districts investigating one or more suspected measles cases within a year.	≥ 80%	100%
Non-measles febrile rash illness rate at national level.	≥ 2 cases per 100,000 population	3.8

The cumulative incidence during the 9-year study period was calculated as 3.25 per 1,000,000 population (92407432 of as of December 31, 2015). The year 2006, was excluded from the analysis for the performance indicator for measles incidence because there was no data related to Measles surveillance. The true cumulative incidence was calculated at 3.25 per 1,000,000 population. The performance indicator for measles incidence did not achieve its target of less than 1 case per 1,000,000 population.

High immunization coverage is key to achieve and maintain the elimination of measles. The WHO has established a target of 95% of higher coverage for all routine and supplementary immunization activities. National measles immunization coverage for the first dose of MCV provided through routine immunization activities was calculated at 93.6% for the period 2006-2015. Coverage ranged from 77% to 102% nationally, and from 60% to 122% at the district level. The performance indicator for immunization at the national level was achieved 5 out of the 10 reference years. However, the indicator was not achieved at the district level for any year during the study period. During the same time period, two SIAs were conducted at the national level with reported coverage rates of 101% and 103%. The cumulative

coverage rate for SIAs was calculated at 102%, which satisfies the target of 95% of higher coverage.

In an elimination setting, a single measles case constitutes an outbreak, and each case should be minimally investigated with a blood specimen. 100% of districts investigated at least 1 case with a blood specimen. The performance indicator of $\geq 80\%$ was achieved for all 9 years, and the cumulative rate was calculated at 100%

Between the years 2006 and 2015, the performance indicator ‘a non-measles febrile rash illness rate of ≥ 2 cases per 100,000 population’ was met. The incidence of non-measles febrile rash illness varied from 1.3 to 6.4 per 100,000 population for the period, with a cumulative rate of 3.8 per 100,000 population.

V. DISCUSSIONS

V.1 Specific results

In 2003, Rwanda implemented a case-based surveillance system that improved the quality of data collected for suspected measles cases. For the period 2007-2015, only 3.9% of cases were reported as a line list. This suggests that the system is improving in its capacity to detect and notify potential measles cases. The positivity rate for measles is 4.0%. The majority of suspected cases are discarded as non-measles. Surveillance needs to be strengthened to better evaluate the sources of infection among non-measles rash febrile cases.

Measles cases remained significantly low from 2007 to 2015, with exceptions to 2010 and 2012, which saw peaks in measles incidence as high as 12.2/1,000,000 and 7.4/1,000,000, respectively. Measles cases were reported in all provinces and were dispersed among 25 of the 30 reporting districts. The majority of cases were reported from districts bordering the DRC, Burundi, and Uganda. The highest proportion of cases (57.8%) was reported from three districts—Rusizi, Gatsibo and Nyagatare. Findings suggest that the high peaks in measles cases could be the result of imported cases. However, the proportion of cases imported or linked to imported cases cannot be determined using the current surveillance system. Understanding the importation status of cases is important to predict outbreaks in the future, and, thus, should be included in future surveillance efforts.

A large proportion of patients with measles were not hospitalized 3352 (89%). Only 435 of the 3787 suspected cases reported being hospitalized for complications. There was no information on the number of complications, if any, among patients that were hospitalized or if there was deaths due to measles.

Although there is complete reporting among all districts, it is likely that some measles-related cases and deaths will go undetected by the surveillance system for several reasons. First, the surveillance system can only detect cases that actively seek medical attention. Second, some measles deaths may occur at home after medical attention is sought. Most measles cases are not investigated after the initial visit to the health care facility to determine if further complications or death follows. Finally, deaths may not be reported as being attributed to measles if the primary cause of death is due to a measles-related complication such as pneumonia. It should be assumed that these biases exist in order to effectively plan measles elimination and mortality reduction strategies. If possible, measles cases should be investigated with home visits to determine if further complications or deaths occur.

Measles has traditionally been a disease that disproportionately affects young children. This study confirmed the high attack rate among children, with the largest proportion of measles cases reported among children 9 years or younger (61%), and the highest burden among those under 5 years of age (46%). This suggests that under 9 year age group is a high risk population for contracting measles, and immunization activities need to be targeted at this group. Measles is also more common in boys (54.%) than girls. Additionally, measles cases were reported mostly from the Western province (40%). Further studies are required to establish the relationship between these variable (age, gender, and reporting province) and susceptibility to infection.

Immunization rates need to be maintained at 95% or higher to prevent measles resurgence. Target rates were only achieved during five of the study years, with reported national rates as low as 76%. Routine immunization rates varied significantly by district and year with little consistency and the lowest rates were reported during 2010 and 2011. The peaks in measles outbreaks may be due to the highly varied immunization coverage. Rubavu district was the only district with consistently high coverage rates.

Routine immunization rates ranged from 60% to 122% from 2006 to 2015 among the districts. Two SIAs were conducted during the period with national coverage rates above 100% (101% in 2009 and 103% in 2013). Rates calculated above 100% for routine and supplementary immunization activities indicate that the population immunized was larger than the target population. This is likely due to an underestimation of the denominator for the target population. Population censuses were conducted in 2002 and then again in 2012. Population estimates for the remaining years in-between censuses are based on population projections. It is important for Rwanda to conduct an Immunization coverage survey (ICS) to determine if immunization rates are being overestimated or if the target population is being over-vaccinated.

The IDSR system provides action against infectious disease threats, and it is important for the system to be regularly evaluated to ensure timely and complete reporting. The case-based system achieved most of the WHO recommended indicators of measles surveillance performance (Annex 4), with exception of the percent of cases notified within 48 hours of rash onset. It took an average of 3.9 days for a health facility to report a suspected measles case. Timeliness of reporting for other indicators was achieved, including getting feedback for blood specimens within 7 days (median 4.7 days). Calculations for the achievement of

indicators may be slightly skewed due to a small percentage of cases with dates that were missing or entered incorrectly.

Completeness of reported data was also high, with 99% of cases containing data on age, gender, and vaccination history. Although impressive, the surveillance system is not reporting the source of infection for confirmed measles cases, which is a minimum requirement according to the WHO. This is an important variable for a land-locked country like Rwanda, where there is a high potential for importation of cases from bordering countries.

From 2006 to 2015, Rwanda satisfied four of the five criteria for declaration of elimination defined by WHO AFRO (Annex 3). Not one of the study years achieved all elimination indicators. Rwanda did not satisfy the indicator for less than one measles case per 1,000,000 population. Cumulative incidence was calculated at 3.25/1,000,000. Rwanda has made significant progress in the last decade since aligning with global measles elimination efforts. Despite not meeting all performance indicators for the study period, Rwanda is still on track to achieve elimination goals by 2020. Evaluation of performance indicators should be conducted annually in order to align public health efforts with the needs of the country.

V.2. Limitations of the study

There are several limitations to the study that need to be addressed. Firstly, the study relies primarily on self-reported data through a paper-based reporting system. Participants may have recalled information inaccurately or provided responses they felt were desirable to the health care provider, opening the data up to potential recall biases. Secondly, the study relies on already collected data and the researcher could not come up with definitive answers to certain anomalies in the data. For instance, a common issue observed when analyzing vaccination history was that the variable '9' and '99' presented frequently among the cases. The codebook identified '99' as the variable for cases with no vaccination history, while '9' is not an identified variable in the codebook. Thirdly, a small proportion of the data had missing or wrongly entered data on important variables that might have skewed the result. This is an indication of important gaps in the data collection and management system that need to be addressed. The current passive surveillance system is not capturing cases that aren't actively seeking medical attention. Because of this, a true depiction of the burden of measles cannot be determined because not all cases are being captured by the surveillance system. Finally, measles cases reported through the surveillance system typically represent only a fraction of the true number of cases due to the underreporting of individuals that do not actively seek medical treatment or were misdiagnosed when treatment was sought. Additionally, there is a lack of follow-up on measles cases after their case was notified. So, unless measles cases were hospitalized for complications, it was not possible to get accurate information on the outcome of the cases.

V.3. Recommendations

This study provides data on the burden of measles and progress towards measles elimination in Rwanda. Despite significant efforts, Rwanda is at risk of not meeting their target elimination goals by 2020 due to inconsistent immunization rates and inefficient reporting of measles outbreaks. The period from 2016 to 2019 presents an opportunity to improve strategies to reach measles elimination goals. Efforts need to target children and high burden districts, which this study has proven to be disproportionately affected by measles. Additionally, the surveillance system must be strengthened with special focus on timely reporting and the collection of additional data (i.e. immigration status). The following recommendations are presented as priority actions for Rwanda based on the results of this report:

1. **Determine Under-notification Rate:** A survey should be conducted to determine the proportion of cases that do not seek medical attention/use traditional healers. The current passive surveillance system is not capturing cases that aren't actively seeking medical attention. Because of this, a true depiction of the burden of measles cannot be determined because not all cases are being captured by the surveillance system.
2. **Strengthen Immunization Strategies:** Immunization coverage levels of 95% need to be sustained, using the reaching every district (RED) approach. This involves a complete scale up of routine and supplementary immunization nationally. Coverage gaps between districts should be minimized in order to maintain low measles incidence, especially among districts that are deemed high risk (i.e. Rusizi, Nyagatare, Gatsibo and other border districts).
3. **Improve Data Quality and Management:** Audits of the surveillance system should be conducted to address potential problems with data collection and management. Several anomalies in the data were addressed in the study, such as missing data, incorrectly entered dates, and variables presented in the database that were not explained by the codebook.
4. **Conduct National Immunization Coverage Survey (ICS):** A national census needs to be conducted to address potential inaccuracies in immunization coverage (coverage exceeding 100%) for target populations.
5. **Identify Source of Infection:** The WHO recommends that "source of infection identified" be used as a variable in a measles surveillance system. It was observed in the analysis that the majority of measles cases occur in bordering districts, especially

in the Western province. This suggests that peaks in outbreaks could be due to imported cases from bordering countries. Identifying the source of infection is critical to understanding the true trend in measles cases, and will help identify strategies for measles elimination.

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VII. APPENDIXES

Appendix 1: Immunization Schedule in Rwanda

Vaccines	Total doses	Age at administration
BCG	1	Birth
OPV	4	Birth, 6, 10, 14 weeks
DTP or DTP-HepB-Hib	3	6, 10, 14 weeks
Pneumococcal	3	6, 10, 14 weeks
Rotavirus (Rota Teq)	3	6, 10, 14 weeks
MR	2	9, 15 months
Tetanus toxoid (pregnant women)	2	During pregnancy
HPV	2	12 years old girls

Appendix 2a: Case investigation form for Measles

NOTIFICATION OBLIGATOIRE, PRIERE DE REMPLIR CETTE FICHE POUR CHAQUE CAS

Officiel Numéro

Epidnumber Reçu, le / /

Pays **Province** **District** **Année début** **N° du cas**

1. IDENTIFICATION

Hôpital de district :Province :Formation sanitaire la plus proche :

District administratif.....Secteur.....Cellule..... 1 : Urbain
2 : Rural

Nom(s) du patient.....Père/Mère.....Sexe : 1 : Masculin

Date de naissance...../...../..... Ou âge.....ans ou si < 1 an âge.....(mois) 2 : Féminin

Si la date de naissance n'est pas connue

2. NOTIFICATION/ENQUETE

Date où le centre de santé a vu le patient :...../...../..... Cas notifiés par :.....

Date où le centre de santé a notifié le cas au district :...../...../.....Date de l'enquête...../...../.....

3. HISTORIQUE DE LA MALADIE

Date du début de l'éruption (**rush**) :/...../....., **Issue** : 1 : vivant 1 : oui
2 : décédé **Hospitalisé** : 2 : non
3 : inconnu 3 : inconnu

Nombre des valide de **VAR**

Date de la dernière vaccination :...../...../.....

4. ECHANTILLON DE SANG

Date de prélèvement :...../...../..... Date d'expédition vers le niveau national...../...../.....

Date de réception au labo :...../...../....., Date de réception des résultats au PEV :...../...../.....

Condition d'arrivée des échantillons : 1 : adéquate
2 : non

Résultats de **IgM rougeole** : 1 : Positif **IgM Rubéole** : 1 : Positif

Sérologie : 2 : Négatif 2 : Négatif

3 : Indéterminé 3 : Indéterminé

Autres résultats : _____

Date d'expédition des résultats du labo au district qui a envoyé l'échantillon :...../...../.....

5. CLASSIFICATION FINALE DU CAS :

1 : cas confirmé par le labo

2 : cas confirmé par lien épidémiologique avec 1 cas
confirmé par le labo

3 : compatible (tests de labo non réalisés)

4 : Exclu/IgM négative

5 : Résultats en attente

6. SOURCE DE L'INFECTION IDENTIFIEE :

1 : Oui

2 : non

Si le test de confirmation IgM rougeole est positif, investigation communautaire faite? 1 : Oui

2 : non

Si oui, décrire le résultats de
l'investigation

—

7. ENQUETEUR :

Nom :Titre :Unité.....Téléphone.....

.

Adresse.....

Appendix 2b: IDSR case-based laboratory reporting form

DSR case based laboratory Reporting Form		
<i>Part I. Referring health worker to complete this form and send a copy to the laboratory with the specimen</i>		
	Variables	Answers
1	Date of specimen collection (day/month/year)	
2	Suspected Disease or Condition	
3	Specimen type *	
4	Specimen unique identifier **	
5	Patient Name (s)	
6	Sex (M= Male F= Female)	
7	Age (...Years/...Months/...Days).	
8	Date Specimen sent to laboratory (day/month/year)	_____\
<i>Part II. Laboratory to complete this section and return the form to district and clinician</i>		
	Variables	Answers
1	Laboratory Name and location	
2	Date laboratory received specimen (dd/mm/yyyy)	_____\
3	Specimen condition: (Adequate/Not adequate)	
4	Type of test(s) performed	
5	Final Laboratory Result(s)	
6	Date (dd/mm/yyyy) laboratory sent results to district	_____\
7	Date Results sent to the clinician (dd/mm/yyyy)	_____\
8	Date district received laboratory results (dd/mm/yyyy)	_____\
<p>* Blood, Plasma, Serum, Aspirate, CSF, Pus, Saliva, Biopsy, Stool, Urethral/Vaginal discharge, Urine, Sputum, food/water samples</p> <p>** Same as the patient's identifier in the IDSR immediate case based reporting form</p>		

Appendix 3: Indicators for progress towards measles elimination.

Indicators for measles elimination by 2020	Target
Measles incidence at the national level.	< 1 case per 1,000,000 population
Measles immunization coverage at national level and in all districts.	≥ 95%
Coverage in all scheduled measles SIAs, and in outbreak response immunization activities.	≥ 95%
Districts investigating one or more suspected measles cases within a year.	≥ 80%
Non-measles febrile rash illness rate at national level.	≥ 2 cases per 100,000 population

Indicators of quality of measles surveillance	Target
% of reported cases* containing core data (i.e. age, gender, vaccination status).	≥ 80%
% of cases* notified ≤ 48 hours after rash onset.	≥ 80%
% of notified cases from whom blood specimens have been collected.	≥ 80%
% of cases* with adequate specimen** and laboratory results within 7 days.	≥ 80%
% districts that have reported at least 1 suspected case of measles with a blood specimen per year.	≥ 80%
% of confirmed cases with source of infection identified.	≥ 80%

*All cases that meet the clinical case definition.

**An adequate specimen is a blood specimen collected within 28 days of the onset of rash.