### **Distribution Agreement**

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Fawaz Saror Alrasheedi

Date

# Measles Trends in the Kingdom of Saudi Arabia, 2002-2012

By

Fawaz Saror Alrasheedi Master of Public Health

Hubert Department of Global Health

Scott J. N. McNabb, Ph.D., M.S. Thesis Committee Chair

# Measles Trends in the Kingdom of Saudi Arabia, 2002-2012

By

Fawaz Saror Alrasheedi

M.D., Al Qassim University, 2009

Thesis Committee Chair: Scott J. N. McNabb, Ph.D., M.S.

An abstract of

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health

2013

## Abstract

**Purpose**: The Kingdom of Saudi Arabia (KSA) aims to achieve measles elimination by 2015. Since the beginning of elimination efforts in early 2000, there has not been a study tracking the national incidence over time. Thus, we described the distribution and incidence rates (IR) of measles in all 13 provinces of KSA from 2002 - 2012. This should give policymakers a clear picture about how to improve measles surveillance and accelerate elimination efforts.

**Methods**: Using the national measles notification data reported to the Ministry of Health from 2002 through 2012 from all 13 provinces of KSA, trends in annual measles IR in KSA were determined and described by age, gender, nationality, province, month, and immunization status.

**Results**: There were 9,643 confirmed cases of measles reported in KSA from 2002 - 2012. Most were reported from Makkah (21.9%) and were among the age group 0 - 14 years of age. Madinah province showed a continuous IR increase from 2009. Baha province has been measles free since 2008.

**Conclusion:** KSA could eliminate measles by 2015 by maintaining high vaccination coverage in the population and improving public health surveillance.

#### Keywords

Measles, Elimination, KSA, Vaccination, Immunizable disease

#### IN THE NAME OF ALLAH, MOST GRACIOUS, MOST MERCIFUL

# Measles Trends in the Kingdom of Saudi Arabia, 2002 - 2012

By

Fawaz Saror Alrasheedi

M.D., Al Qassim University, 2009

Thesis Committee Chair: Scott J. N. McNabb, Ph.D., M.S.

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health

2013

#### Acknowledgements

I would like to thank all of my family, especially my mother and father. I would like to express my appreciation to my wife, who has helped me a lot over the course of my studies. Special thanks to my oldest brother, Fayez, and to my uncle, Abdullah, and to all of the friends and family members who have cared for me over this journey. This paper is dedicated to my son, Ali, and my daughter, Alaa.

I would like to thank the Ministry of Health, Kingdom of Saudi Arabia, for their endless support. Also, I would like to thank Prabhjyot Singh Saini for assistance teaching me data cleaning, translation, and SAS coding. Jessica Gleason offered valuable support by sharing Saudi population census data that she collected from the Ministry of Economy and Planning, Central Department of Statistics and Information in KSA.

# **Table of Contents**

Chapter 1: Introduction	1
History of Saudi Arabia	1
Location	
Administrative Structure of the Kingdom	
Key Indicators	
Economy	
Education	2
Healthcare	
The First Stage: 1925-1941	
The Second Stage: 1941-1951	
The Third Stage: 1951-1981	
The Fourth Stage: 1981- Present	
Measles Immunization Program in KSA	5
Chapter 2: Literature Review	6
What Is Measles?	
Causative Organism	
Signs and Symptoms	
Measles Case Definitions	
Clinical Case Definition	
Criteria for Laboratory Diagnosis	
Case Classifications	
Discarded Cases	
Measles Complications	
Who Is at Risk?	
Transmission and Spread	
Treatment of Measles	
Measles Prevention	
Global Measles Elimination Efforts	
Measles Elimination Efforts in KSA	
Chapter 3: Manuscript	
Abstract	
Introduction	
Methods	
Data Source	-
Data Analysis	
Ethics	
Results	
Discussion	
Limitations	
Recommendations	29
Competing interests	
Chapter 4: Conclusions and Recommendations	
Immunization Coverage	
Public Health Surveillance (PHS)	

# List of Tables and Figures

Figure 1. Incidence Rate of measles per 100,000 population in KSA and its (95% CI), 2002-
201221
Figure 2. Measles incidence rate in Medinah province, KSA 2002-2012
Table 1. Measles incidence rate per 100,000 population by nationality and year inKSA
Figure 3. Total number of confirmed measles cases by province, Saudi Arabia, 2002-2012
Table 2. Total confirmed measles cases by age group and year in KSA, 2002-2012
Figure 4. Total Number of confirmed measles cases by month in Saudi Arabia, 2002-2012
Figure 5. Measles Incidence Rate in Al-Joof province, KSA 2002-201224
Figure 6. Measles incidence rate per 100,000 by Gender in KSA, 2002-201225
Table 3. Measles cases count by Immunization status and province in KSA, 2002-2012
Table 4. Total confirmed measles cases by Immunization status and province in KSA,2002-2012
Figure 7. Measles Incidence Rate in Baha, KSA 2002-201227

## **Chapter 1: Introduction**

### **History of Saudi Arabia**

The Kingdom of Saudi Arabia (KSA) is the largest country in the Arabian Peninsula. The birthplace of Islam, the country is home to the two holiest Islamic cities of Makkah and Madinah. Abdul-Aziz Al-Saud founded the modern Saudi state in 1932, after a 30-year fight to unify most of the Arabian Peninsula. The King's official title is the Custodian of the Two Holy Mosques [1]. On September 23, 1932, the country was called the Kingdom of Saudi Arabia, and formally established as an Islamic state with Arabic as its national language and the Holy Qur'an as its only constitution [2].

#### Location

KSA is located in the Arabian Peninsula in the southeastern part of the Asian continent. The Kingdom occupies about 2,240,000 square km<sup>2</sup> of the Arabian Peninsula. It has 1,700 km of Western Coast along the Red Sea and 560 km of Eastern Coast along the Arabian Gulf. The sum of land borderlines in the South and in the North exceeds 2,700 km [3].

### Administrative Structure of the Kingdom

KSA is currently divided into 13 administrative provinces. Each one of them is divided into a number of different governorates, which vary in number from one province to another. Each governorate again is divided into multiple centers connected administratively to the governorate itself or to the Emirate. The Emirate, governorate or center includes a number of population settlements that are connected administratively to it [4].

#### **Key Indicators**

KSA has a population of 29 million; nearly 20 million are Saudis. The population growth rate is over 2.9%, and the demographic composition is very young [4]. Saudis comprise around 68.9% of the total population; 50.2% are male while 49.8% are female. In terms of age, 37.2% are under 15 years old and about 67.1% are under the age of 30 [5]. The need to find gainful employment for the youth of today weighs heavily on the government, and there is an understanding that fundamental steps must be considered to create the necessary jobs.

#### Economy

KSA is an oil-based economy with strong government controls over major economic activities. It holds about one-fifth of the world's proven oil reserves, ranks as the largest exporter of oil, and plays a principal role in OPEC. The oil sector accounts for roughly 80% of budget incomes, 45% of GDP, and 90% of export wages. According to a 2012 estimate, the GDP was \$25,000 per capita, with 6% real growth rate. Saudi officials are particularly focused on utilizing the large youth population, which generally lacks the education and technical skills the private business sector needs [1].

#### Education

Education has been a priority for the government. Usually educational institutions are administered by the state, with private establishments playing a significant role only at the lower levels. King Abdulaziz Al-Saud implemented a rigorous program in 1945 to establish schools in the Kingdom. Six years later, in 1951, the country had 226 schools with almost 30,000 students [2]. The first university, King Saud University, was established in Riyadh city in 1957. In 1954, the Ministry of Education was established, followed by the Ministry of Higher Education in 1975 [2]. Girls and boys are educated separately. The first girls' school was established in 1964, and the number of schools grew rapidly to reach every part of the country by the end of 1990s [2]. Today, Saudi Arabia's education system includes 25,000 schools, 24 public and 8 private universities, and a large number of colleges and other institutions under the Ministry of Higher Education, and it continues to expand. The education system is open to all citizens, and provides students with free education, books and health services [2].

#### Healthcare

KSA invests greatly in healthcare, and healthcare facilities are usually financed directly by the government through its establishment of hospitals and clinics and its liberal encouragement and support of private sector institutions. Public health and disease control have been among the government's top priorities since the modern state of KSA was first founded. In 1925, King Abdulaziz established the Public Health Department in Makkah. Later that year, the Public Health and Ambulance (PHA) department was established to meet the needs of the Kingdom's health and environmental divisions [6]. This department was responsible for sponsoring and monitoring free health care for the population and pilgrims by the establishment of a number of hospitals and health centers across the Kingdom [5].

Healthcare services in the Kingdom were funded with limited resources and delivered through small clinics, which gradually have become highly modern hospitals, medical cities and centers [7]. I can outline the development and improvement of healthcare in KSA by dividing it into four main stages:

#### The First Stage: 1925-1941

The main events during this stage were the establishment of the Public Health and Ambulance (PHA) department. Due to lack of resources and facilities during this stage, health services were poor and most of the population was dependent on traditional medicine [8].

#### The Second Stage: 1941-1951

The commercial introduction of oil during this stage contributed significantly to improving the quality of health services, which led to an increase in access to healthcare. The Kingdom also introduced policies for hospital capacity building and preventive health practices during this stage [8].

#### The Third Stage: 1951-1981

The major event during this stage was the establishment of the Ministry of Health (MOH), which was created in 1951. During the 1960s, due to economic wealth and the presence of foreign companies, work-related insurance coverage became more common. Human and financial resources increased in both public and private sector hospitals; in addition, the expenditures increased for improving healthcare service quality and preventive care programs. In 1978, the Alma Alta Declaration (Health For All) on primary healthcare was approved to expand healthcare coverage and improve the overall health status of the population [8].

#### The Fourth Stage: 1981- Present

The MOH remains responsible for healthcare service provision to the population including general and specialized hospital care. The Ministry coordinates with several other governmental agencies in health service delivery: hospitals of the National Guard, the Ministries of the Interior, Defense and Aviation, and the Royal Commission for Jubail and Yanbu. These organizations provide healthcare services not only to their employees but also to other Saudi citizens in special circumstances. Other government agencies including the Saudi Red Crescent Society provide emergency services and medical assistance to the Saudi population as well as to the many pilgrims who visit every year [8].

#### **Measles Immunization Program in KSA**

Measles immunization efforts in KSA are divided into two main phases: the control and elimination phases [9]. The control phase was started in 1974 by introducing a single measles vaccine dose (Schwarts) that targeted children in age group of 1-9 years [10]. Before the introduction of the control phase, children in KSA would usually become immune to measles by the age of 5. At the beginning of control phase, the vaccination was not mandatory. Then, in order to increase the vaccination coverage rate, a royal decree was issued in 1982 that made the measles vaccine a mandatory requirement for all infants in order to obtain the national birth certificate [10].

As a result, the measles vaccination coverage rate increased from 8% in 1980 to 80% in 1984, exceeding 90% in 1990 [9]. In the early 1990s, the Edmonston-Zagreb Measles Vaccine and the two-dose strategy were implemented to reduce primary measles vaccine failure due to persistent maternal antibodies after the administration of the Schwarts vaccine [9]. The main goal of this phase was to reduce the measles mortality and morbidity rates. The elimination phase started in 1998 and has continued until the present. In 2001, the introduction of lab confirmation strengthened the measles surveillance system [9].

The goal of this study is to provide information to Saudi policymakers about measles trends from 2002 through 2012, to track the progress toward the goal of elimination, and to improve future policies in this field. These trends will be described mainly by age, sex, nationality and province.

5

#### Chapter 2: Literature Review

"A child that gets out of measles is a child that is reborn" (Arabic) [11].

#### What Is Measles?

Measles is a highly viral infectious disease that can cause severe illness, permanent complications and death [12]. Before the introduction of measles vaccines, measles was one of the most overwhelming infectious diseases and caused millions of deaths and disabilities worldwide each year [13]. The measles virus, which is also known as rubella, infects only humans [14]. Measles is believed to have first affected human beings 5,000–10,000 years ago, and in the 10th century, Rhazes, a Persian philosopher and physician, was the first scholar who described and differentiated between measles and smallpox

#### **Causative Organism**

The measles virus is a spherical, enveloped, non-segmented, single stranded RNA virus and a member of the paramyxoviridae family. The measles virus RNA genome encodes eight proteins and consists of about 16,000 nucleotides [13].

#### Signs and Symptoms

The incubation period usually lasts 10 days from exposure to the onset of fever (with a range of 7-18 days) [15]. Clinically, measles symptoms begin with prodromal illness characterized by fever, tiredness, coryza, cough, runny nose, and painful red eyes. This is followed a few days later by the appearance of a maculopapular rash, which starts on the face and behind the ears, spreads down to the body, and lasts for 4-7 days [16]. The characteristic signs of measles are Koplik's spots, small red spots with white-centered lesions on the mouth's buccal mucosa, which may be visible during the onset of symptoms and allow for the diagnosis of measles before the onset of the rash [13].

#### **Measles Case Definitions**

The case definition of measles, based on WHO guidelines, may vary according to a country's current phase of measles control.

### **Clinical Case Definition**

A clinician may suspect the measles infection in any patient presenting with fever, maculopapular (non-vesicular) rash and concurrent cough, coryza (runny nose), or conjunctivitis (red painful eyes) [15].

### **Criteria for Laboratory Diagnosis**

- Presence of at least a four-fold increase in measles antibody titre, or
- Isolation of measles virus, or
- Presence of measles-specific IgM antibodies [15].

### **Case Classifications**

A clinically-confirmed case is a case that meets the clinical case definition [15]. A laboratory-confirmed case is one that meets the clinical case definition and is laboratory confirmed or epidemiologically linked to a laboratory-confirmed case. Lab confirmation is necessary for outbreak confirmation and during the measles elimination phase. Epidemiological linkage cases are defined as direct contact with a laboratory-confirmed measles case in which that rash's onset occurred 7-18 days before [15].

A suspected measles case that is not completely investigated for any reason should be reported as clinically confirmed. Since health providers suspect a measles infection and the possibility of a measles virus infection cannot be excluded, these cases cannot be rejected but are considered failures on the part of the surveillance system [15]. Possible reasons for the failure to confirm the case are that the patient received only a clinical diagnosis from a health care worker without laboratory investigation; the patient could not be located; the patient did not follow-up; or that the patient died before an investigation was completed.

The goal of the measles surveillance system in elimination programs is to decrease the number of clinically-confirmed measles cases as much as possible and conduct a complete epidemiological analysis on every reported suspected measles case. At least 80% of the total confirmed measles cases should be laboratory-confirmed [15].

#### **Discarded Cases**

A suspected measles case that has been completely investigated, including the collection of an adequate blood specimen, and lacks serological evidence of a measles virus infection is classified as discarded [15].

#### **Measles Complications**

One-third of those with measles develop complications due to secondary infections, leading to ear infections, diarrhea, dehydration and pneumonia, which may require hospitalization [16]. Complications are common in children under five or adults over the age of 20 [17]. The most dangerous complication is encephalitis (brain infection), which occurs in 1 out of 1,000 patients. Death was reported in 0.3% of all cases with complications [18].

Among populations with high levels of malnutrition and lack of access to adequate healthcare, 10% of measles cases result in death. A higher rate of complications and a higher death rate has been associated with low vitamin A levels, as this deficiency has related pathological effects on epithelial tissues and the immune system. The vast majority of measles deaths (98%) occur in developing countries, where vitamin A deficiency is common [15].

The measles mortality rate in girls was estimated to be 5% higher than in boys according to studies conducted primarily in the Americas and Europe [13]. Pregnant women with measles are at risk of developing severe complications, and their gestation may end in miscarriage or preterm delivery. Patients who recover from measles have lifelong immunity [19].

#### Who Is at Risk?

Unvaccinated children and pregnant women are at highest risk of measles and its complications, including death [19]. Those at the next highest risk for measles are AIDS patients and immune-compromised people (e.g., people undergoing chemotherapy or radiotherapy treatment or people taking high-dose steroids). This population is at risk even if they have been fully immunized or have had the measles infection before [16]. Measles is still endemic in many developing countries. More than 20 million people are affected by measles annually. The overwhelming majority of measles deaths (more than 95%) occur in countries with low incomes and fragile healthcare infrastructures [19].

#### **Transmission and Spread**

The measles virus is an airborne, highly contagious disease spread by sneezing and coughing, close personal contact, or direct contact with infected nasal or throat secretions. It has a basic reproductive rate of 17-20, which means one case of measles in a susceptible community spawns 17-20 new cases [15]. The virus remains contagious and active in the air or on infected surfaces for up to 2 hours [19]. Measles patients are usually infectious from just before the symptoms begin until 4 days after the appearance of the rash [16].

#### **Treatment of Measles**

There is no specific antiviral drug available for fighting the measles virus. Measles patients usually undergo symptomatic treatment in addition to resting and drinking enough fluids to avoid dehydration. According to WHO recommendations, all measles patients, especially children, should receive two doses of vitamin A supplements given 24 hours apart. This approach restores low vitamin A levels, an issue affecting even well-nourished children. Vitamin A supplements help prevent eye damage and blindness and have been shown to reduce the number of deaths from measles by 50% [19].

### **Measles Prevention**

The key public health strategies to reduce global measles deaths are routine measles immunizations for all children combined with mass immunization campaigns in the countries with high case and death rates. The measles vaccine was introduced to the public in the late 1960s. It is safe, effective and inexpensive. Measles vaccine costs less than one U.S. dollar and is often incorporated with rubella and mumps vaccines in countries where these illnesses are common. It is equally effective in the single or combined form [19].

Measles patients should stay at home until they are no longer infectious (which is 4 days after the rash starts). The best protection against measles is vaccination, specifically the use of two doses of the MMR vaccine. This vaccine provides protection against infection with measles, mumps and rubella. The first dose is given to children at the age of 12 months, and the second dose is given at age 4. It is safe for the vaccine to be administered more than twice. The MMR vaccine can sometimes prevent measles infections from developing in people who have had contact with a person with measles if given within 3 days of exposure, or if immunoglobulin is given within 7 days of exposure [19].

There are three phases for measles immunization programs. The Control Phase is defined as the aim for a significant reduction in measles incidence and mortality rates. When high levels of vaccine coverage rate are sustained (above 80%), measles incidence decreases and the intervals between outbreaks are lengthened. When these levels of vaccine coverage are sustained, an increasing proportion of cases will occur among older age groups. As vaccine coverage expands, the proportion of cases with a vaccination history increases [15].

The Outbreak Prevention Phase occurs after achieving the measles control goal in the community; future outbreaks can be prevented by the timely administration of vaccination to susceptible individuals who are at higher risk and by improving the overall levels of vaccine coverage in the community [15]. The term outbreak means the number of cases detected is greater than the number normally expected in the same geographic area for the same period of time.

The Measles Elimination Phase involves the effort to fully eliminate the indigenous transmission of measles virus by the worldwide implementation of pioneering measles vaccination and surveillance strategies. Measles elimination is defined as the absence of endemic measles transmission in a defined geographic area (e.g., region or country) for  $\geq 12$  months in the presence of a well-performing surveillance system [20].

The elaboration of these strategies has been inspired by the persistence of low-level transmission and intermittent outbreaks in the world. Measles elimination strategies, according to WHO/UNICEF, 2012-2020 Global Measles & Rubella Strategic Plan, are summarized in five points below:

 Accomplish and maintain high levels of community immunity by providing high immunization coverage with two doses of measles- and rubella-containing vaccines [12].

- Screen for the disease using effective surveillance and evaluate efforts to ensure progress [12].
- 3. Improve and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases [12].
- 4. Communicate with and involve the community to build public confidence and demand for vaccination [12].
- 5. Implement the research and improvement needed to support cost-effective operations and improve immunization and diagnostic tools [12].

### **Global Measles Elimination Efforts**

The extensive use of measles vaccine since 1980 has led to a significant decrease in global measles morbidity and mortality. The Measles and Rubella Initiative (MR) was launched in 2001 and led by the Centers for Disease Control and Prevention (CDC), American Red Cross (ARC), United Nations Foundation (UNF), United Nations Children's Fund (UNICEF), and World Health Organization (WHO) to support financially and technically enhanced measles control activities [12].

As a result of MR Initiative efforts, measles deaths dropped from 535,000 in 2000 to 139,000 in 2010 (74% decrease); in addition, there was a 23% drop in < 5 year old deaths worldwide between 1990 and 2008 [21]. The World Health Assembly is dedicated to reducing measles deaths by 95% from the 2000 levels by 2015 [12].

In 2012, the MR Initiative and its partners endorsed the Global Measles and Rubella Strategic Plan 2012-2020 [12]. It reveals regional and national experiences and alterations in disease epidemiology, and integrates insights from research findings, guidance and recommendations available since the last Measles Strategic Plan published in 2005. By 2011, all 194 WHO Member States had begun the process of introducing a twodose measles vaccination strategy provided through routine immunization services and/ or supplementary immunization activities (SIAs) [12].

All six WHO regions are devoted to measles elimination and five regions have set target dates. The WHO Region of the Americas (AMR) achieved the goal in 2002 [20]; the Western Pacific Region (WPR) aimed to eliminate measles by end of 2012; and the Eastern Mediterranean (EMR) and European (EUR) Regions are enhancing their measles control activities in order to eliminate measles by 2015. In 2011, countries in the African Region (AFR) were assigned the goal of eliminating measles by 2020, and in 2010 the South-East Asia Region (SEAR) implemented a resolution urging countries to assemble resources to support their measles elimination goals [12].

#### **Measles Elimination Efforts in KSA**

The effort to fight measles in KSA is divided into the control and elimination phases [9]. The control phase was started in 1974 with the introduction of a single measles vaccine dose (Schwarts) targeted at children aged 1-9 years old [10]. Before the introduction of the control phase, all children in KSA usually become immune to measles by the age of 5 years. At the beginning of control phase the vaccination was not mandatory. Then, in order to increase the vaccination coverage rate, a royal decree was issued in 1982 that made the measles vaccine a mandatory requirement for all infants in order to obtain the national birth certificate [10].

As a result, the measles vaccine coverage rate increased from 8% in 1980 to 80% in 1984 and exceeded 90% in 1990 [9]. In the early 1990s, the Edmonston-Zagreb Measles

Vaccine and the two- dose strategy were implemented in Saudi Arabia to reduce primary measles vaccine failure due to persistent maternal antibodies after the administration of the Schwarts vaccine [9]. The main goal of this phase was to reduce measles mortality and morbidity among KSA's population. The elimination phase started in 1998 and has continued until the present. In 2001, the introduction of lab confirmation strengthened the measles surveillance system [9].

# **Chapter 3: Manuscript**

# Measles Trends in the Kingdom of Saudi Arabia, 2002 – 2012

Fawaz S. Alrasheedi<sup>1</sup>; Scott J.N. McNabb<sup>2</sup>

<sup>1</sup> Ministry of Health, Kingdom of Saudi Arabia

<sup>2</sup> Emory University, Rollins School of Public Health, 1518 Clifton Rd, Atlanta GA, USA

Contact Emails:

- 1- drfawaz2009@hotmail.com
- 2- scottjnmcnabb@emory.edu

### Abstract

**Purpose**: The Kingdom of Saudi Arabia (KSA) aims to achieve measles elimination by 2015. Since the beginning of elimination efforts in early 2000, there has not been a study tracking the national incidence over time. Thus, we described the distribution and incidence rates (IR) of measles in all 13 provinces of KSA from 2002 - 2012. This should give policymakers a clear picture about how to improve measles surveillance and accelerate elimination efforts.

**Methods**: Using the national measles notification data reported to the Ministry of Health from 2002 through 2012 from all 13 provinces of KSA, trends in annual measles IR in KSA were determined and described by age, gender, nationality, province, month, and immunization status.

**Results**: There were 9,643 confirmed cases of measles reported in KSA from 2002 - 2012. Most were reported from Makkah (21.9%) and were among the age group 0 - 14 years of age. Madinah province showed a continuous IR increase from 2009. Baha province has been measles free since 2008.

**Conclusion:** KSA could eliminate measles by 2015 by maintaining high vaccination coverage in the population and improving public health surveillance.

#### Keywords

Measles, Elimination, KSA, Vaccination, Immunizable diseases

#### Introduction

Measles is a highly viral infectious diseases that can cause severe illness, permanent complications and death [12, 16]. It has a basic reproductive rate of 17-20, which means one case of measles in a susceptible community spawns 17-20 new cases [15]. The virus remains contagious and active in the air or on infected surfaces for up to 2 hours [19]. Measles symptoms clinically begin with a prodromal illness characterized by fever, tiredness, coryza, cough, runny nose, and painful red eyes. This is followed a few days later by the appearance of maculopapular rash, which starts on the face and behind the ears, spreads down to the body and lasts for 4-7 days [16, 19]. One third of those with measles develop complications due to secondary infections, which can lead to ear infections, diarrhea, dehydration and pneumonia, and may require hospitalization [16].

Complications are common in children < five years of age or adults > the age of 20 [17]. The most dangerous complication is encephalitis (brain infection), which occurs in 1 out of 1000 patient and death was reported in 0.3% of the cases [18]. Unvaccinated children and pregnant women are at highest risk of measles and its complications, including death [19]. Before the introduction of measles vaccines, measles was one of the most overwhelming infectious diseases and caused millions of deaths and disabilities worldwide each year [13].

The key public health strategies to reduce global measles deaths are routine measles immunizations for all children combined with mass immunization campaigns in countries with high case and death rates [19]. The extensive use of measles vaccine since 1980 has led to a significant decrease in global measles morbidity and mortality. The Measles and Rubella Initiative (MR) was launched in 2001 and led by the Centers for Disease Control and Prevention (CDC), American Red Cross (ARC), United Nations Foundation (UNF), United Nations Children's Fund (UNICEF), and World Health Organization (WHO) to support financially and technically enhanced measles control activities [12, 21]. All six WHO regions are devoted to measles elimination and five regions have set target dates. The WHO Region of the Americas (AMR) achieved the goal in 2002 [20]; the Western Pacific Region (WPR) aimed to eliminate measles by end of 2012; and the Eastern Mediterranean (EMR) and European (EUR) Regions are enhancing their measles control activities in order to eliminate measles by 2015. In 2011, countries in the African Region (AFR) were assigned the goal of eliminating measles by 2020, and in 2010 the South-East Asia Region (SEAR) implemented a resolution urging countries to assemble resources to support their measles elimination goals [12].

KSA is the largest country in the Arabian Peninsula. The birthplace of Islam, the country is home to the two holiest Islamic cities of Makkah and Madinah [1]. Measles prevention efforts are divided into two main phases: the control and elimination phases [9]. The control phase was started in 1974 [22] with the introduction of a single measles vaccine dose (Schwarts) that targeted children from 1-9 years old [10]. Before the introduction of the control phase, children in KSA usually become immune to measles by the age of 5 years. At the beginning of control phase the vaccination was not mandatory. Then, in order to increase the vaccination coverage rate, a royal decree was issued in 1982 that made the measles vaccine a mandatory requirement for all infants in order to obtain the national birth certificate [10].

As a result, the measles vaccine coverage rate increased from 8 % in 1980 to 80% in 1984 and exceeded 90 % in 1990 [9]. In the early 1990s, the Edmonston-Zagreb Measles Vaccine and the two- dose strategy were implemented in Saudi Arabia to reduce primary measles vaccine failure due to persistent maternal antibodies after the administration of the Schwarts vaccine [9]. The main goal of this phase was to reduce measles mortality and

morbidity among KSA's population. The elimination phase started in 1998 and has continued until the present. In 2001, the introduction of lab confirmation strengthened the measles surveillance system [9].

The goal of this study is to provide information to KSA policymakers about measles trends from 2002 through 2012, and to track the progress towards the goal of elimination and guide policy development.

### Methods

#### **Data Source**

This study uses the national measles notification system's data reported to the MOH from 2002 through 2012 from all 13 provinces of KSA. The data were first translated from Arabic to English using Google doc. The translation process was then evaluated for its accuracy by the first author (a native Arabic speaker). The data were de-identified.

#### **Data Analysis**

We calculated only laboratory-confirmed measles cases and cleaned, organized and removed inaccurate data. Then age groups were recorded according to the total population. A dataset was created in SAS and queried to produce frequencies tables, which were outputted into Excel. Incidence rate and confidence intervals were calculated in Excel with these tables. The annual incidence rate of measles per 100,000 populations was described by nationality, gender, age group, region, month, and immunization status.

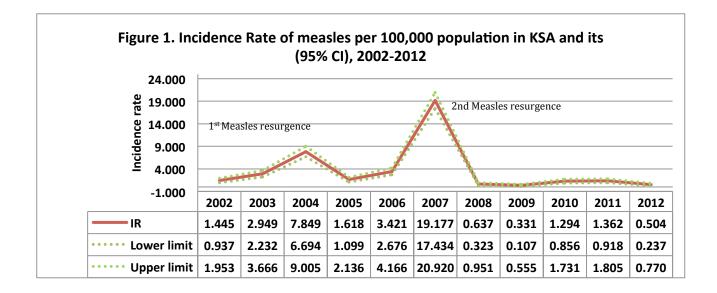
Population data was obtained from the Ministry of Economy and Planning, Central Department of Statistics and Information in KSA and included data for the entire nation by age, gender, nationality, and province for the years 2002 – 2012. The data includes only the first four months of the year of 2012.

#### **Ethics**

This study is a descriptive study using secondary data analysis of de-identified preexisted data, which was not considered as human subject research and did not require Emory or KSA IRB approval.

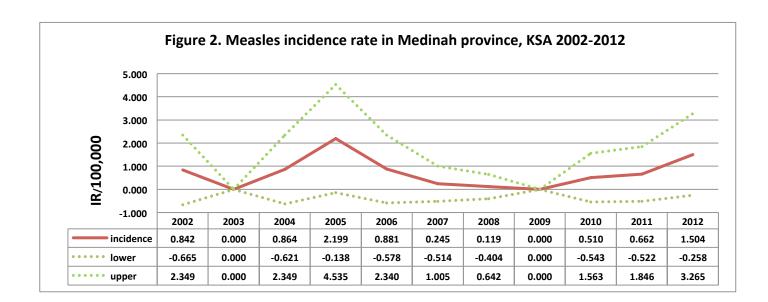
#### Results

There were 9,643 confirmed measles cases reported in KSA from 2002 - 2012. In 2007, 4,649 (48.2%) cases occurred; there were 1,772 (18.4%) in 2004. The national measles incidence rate (IR) shows a slight decline during the past 11 years with two epidemic spikes in 2004 and 2007 (Fig. 1).



Almost all provinces show decrease in measles incidence rate except for Madinah

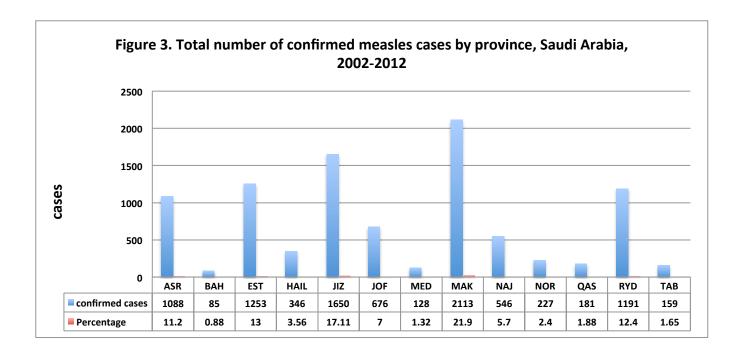
province that experience continuous increase of IR since 2010 (Figure. 2).



The lowest IR reached was 0.33/100,000 of population in 2009, and the highest was 19.2/100,000 of population in 2007. In general, Saudi nationals are more affected than non-Saudis except in 2005 (Table. 1).

Table 1.	Measles incidence rate per 100,000 population by nationality and year in KSA									
Year		Saudi	Non-Saudi							
	IR	95% CI	95% CI							
2002	1.97	(1.27, 2.66)	0.05	(-0.13, 0.23)						
2003	3.73	(2.79, 4.68)	0.85	(0.11, 1.59)						
2004	9.87	(8.35, 11.39)	2.43	(1.2, 3.67)						
2005	1.57	(0.97, 2.17)	1.74	(0.71, 2.77)						
2006	4.23	(3.26, 5.20)	1.23	(0.37, 2.09)						
2007	25.03	(22.7, 27.36)	3.37	(1.97, 4.78)						
2008	0.83	(0.41, 1.25)	0.11	(-0.14, 0.35)						
2009	0.39	(0.11, 0.68)	0.16	(-0.14, 0.46)						
2010	1.42	(0.89, 1.96)	0.95	(0.22, 1.67)						
2011	0.53	(1.16, 2.33)	0.32	(-0.09, 0.74)						
2012	0.53	(0.21, 0.85)	0.44	(-0.04, 0.92)						

Most of the measles cases occurred in Makkah (21.9%), Jizan (17.1%), Eastern region (13%), Riyadh (12.4), and Aseer (11.2%) (Figure 3).



Most occurred among the very young; 73% of cases were among those in the age group of 0-14 years of age; 13.4% of reported cases were among those between 15-24 years; and 9.7% were within the 25-34 year age group (Table 2).

Table 2.	Total confirmed measles cases by age group and year in KSA, 2002-2012											
Age groups in Years	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
0 - 14	231 2.40 3.28 74.28	529 5.49 7.52 81.51	1404 14.58 19.95 79.23	303 3.15 4.31 81.02	616 6.40 8.75 76.05	3251 33.75 46.21 69.93	89 0.92 1.26 56.33	48 0.50 0.68 57.14	228 2.37 3.24 67.86	262 2.72 3.72 72.38	75 0.78 1.07 59.06	7036 73.05
15 - 24	47 0.49 3.63 15.11	58 0.60 4.48 8.94	189 1.96 14.61 10.67	33 0.34 2.55 8.82	79 0.82 6.11 9.75	749 7.78 57.88 16.11	34 0.35 2.63 21.52	14 0.15 1.08 16.67	41 0.43 3.17 12.20	41 0.43 3.17 11.33	9 0.09 0.70 7.09	1294 13.43
25 - 34	27 0.28 2.89 8.68	47 0.49 5.03 7.24	134 1.39 14.33 7.56	23 0.24 2.46 6.15	87 0.90 9.30 10.74	467 4.85 49.95 10.05	24 0.25 2.57 15.19	20 0.21 2.14 23.81	40 0.42 4.28 11.90	35 0.36 3.74 9.67	31 0.32 3.32 24.41	935 9.71
35 - 44	6 0.06 1.96 1.93	14 0.15 4.58 2.16	38 0.39 12.42 2.14	13 0.13 4.25 3.48	25 0.26 8.17 3.09	150 1.56 49.02 3.23	8 0.08 2.61 5.06	2 0.02 0.65 2.38	19 0.20 6.21 5.65	20 0.21 6.54 5.52	11 0.11 3.59 8.66	306 3.18
45 - 54	0 0.00 0.00 0.00	1 0.01 2.44 0.15	6 0.06 14.63 0.34	1 0.01 2.44 0.27	2 0.02 4.88 0.25	20 0.21 48.78 0.43	2 0.02 4.88 1.27	0 0.00 0.00 0.00	5 0.05 12.20 1.49	4 0.04 9.76 1.10	0 0.00 0.00 0.00	41 0.43
55 - 64	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	7 0.07 63.64 0.15	1 0.01 9.09 0.63	0 0.00 0.00 0.00	3 0.03 27.27 0.89	0 0.00 0.00 0.00	0 0.00 0.00 0.00	11 0.11
≥ 65	0 0.00 0.00 0.00	0 0.00 0.00 0.00	1 0.01 11.11 0.06	1 0.01 11.11 0.27	1 0.01 11.11 0.12	5 0.05 55.56 0.11	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	1 0.01 11.11 0.79	9 0.09
Total	311 3.23	649 6.74	1772 18.40	374 3.88	810 8.41	4649 48.27	158 1.64	84 0.87	336 3.49	362 3.76	127 1.32	9632 100.00

Frequency Missing = 11

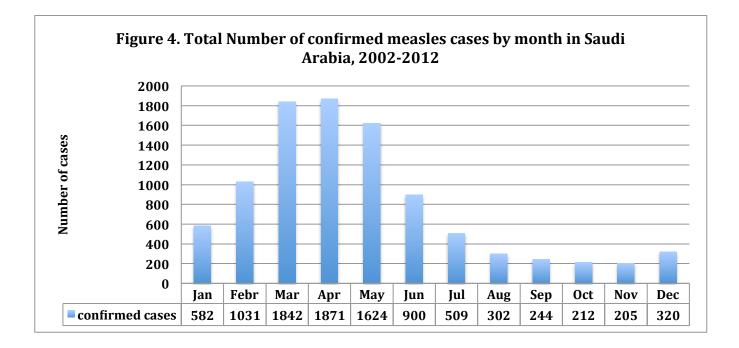
Numbers are arranged longitudinally as below:

Frequency

Percent

Row percent

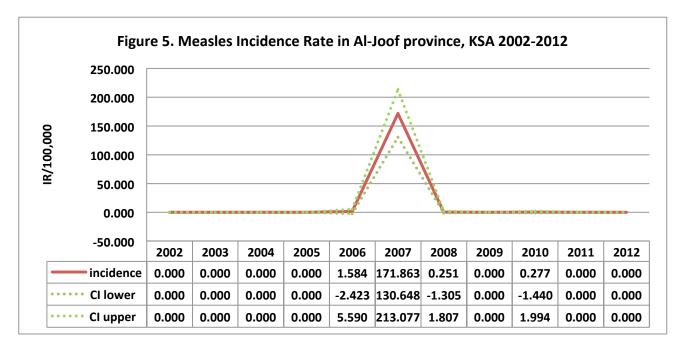
Column percent



The bulk of cases (66%) were reported between February and May (Figure 4).

On the level of provinces the highest IR rate was found in Al-Joof, 2007 (171.9 per

100,000) as shown in (Figure 5).



IR was higher among non-Saudis in Madinah and Riyadh provinces only. Females had a higher IR than males in KSA (Figure 6).

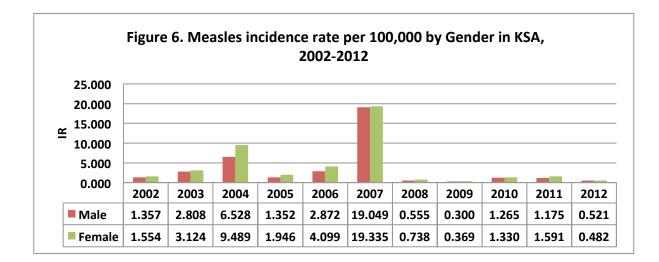


Table 3 shows 4742 (54%) of measles cases among Saudis were among a nonvaccinated group; 1018 (21.5%) were in Jizan; 854 (18%) in the Eastern province; 851 (17.95%) in Makkah; 669 (14.1%) in Aseer; and 411 (8.7%) in Riyadh.

	Tab	ole 3. Me	easles ca	ases cou	nt by In	nmuniza	tion sta	tus and	provinc	e in KSA	A, 2002-	2012		
					Contro	lling for N	lationality	y = Saudi						
Immunization Status	Province													
	ASR	BAH	EST	HAIL	JIZ	JOF	MED	МАК	NAJ	NOR	QAS	RYD	ТАВ	Total
Not Vaccinated	669 7.61 14.11 62.52	31 0.35 0.65 36.90	854 9.72 18.01 72.25	153 1.74 3.23 44.35	1018 11.59 21.47 67.82	286 3.25 6.03 42.56	56 0.64 1.18 70.00	851 9.68 17.95 51.51	203 2.31 4.28 39.42	92 1.05 1.94 41.63	41 0.47 0.86 24.40	411 4.68 8.67 35.99	77 0.88 1.62 49.68	4742 53.97
Unknown	90 1.02 7.26 8.41	6 0.07 0.48 7.14	119 1.35 9.60 10.07	45 0.51 3.63 13.04	231 2.63 18.64 15.39	214 2.44 17.27 31.85	7 0.08 0.56 8.75	202 2.30 16.30 12.23	117 1.33 9.44 22.72	15 0.17 1.21 6.79	45 0.51 3.63 26.79	131 1.49 10.57 11.47	17 0.19 1.37 10.97	1239 14.10
Vaccinated	311 3.54 11.08 29.07	47 0.53 1.67 55.95	209 2.38 7.45 17.68	147 1.67 5.24 42.61	252 2.87 8.98 16.79	172 1.96 6.13 25.60	17 0.19 0.61 21.25	599 6.82 21.35 36.26	195 2.22 6.95 37.86	114 1.30 4.06 51.58	82 0.93 2.92 48.81	600 6.83 21.38 52.54	61 0.69 2.17 39.35	2806 31.93
Total	1070 12.18	84 0.96	1182 13.45	345 3.93	1501 17.08	672 7.65	80 0.91	1652 18.80	515 5.86	221 2.52	168 1.91	1142 13.00	155 1.76	8787 100.00
Frequency						Missing =	105							

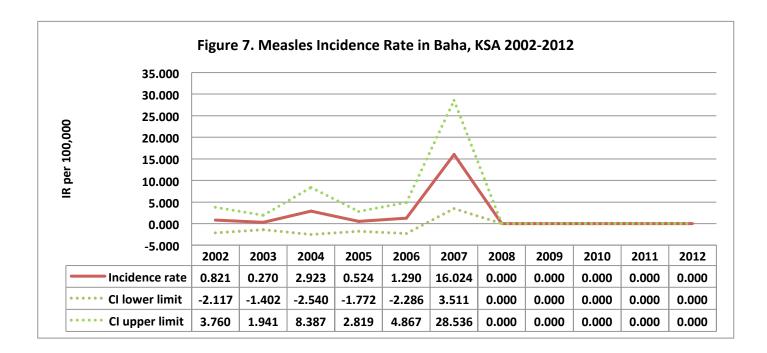
Among non-Saudis who had measles, 432 (60%) of 719 were not vaccinated; 241

(55.8%) were located in Makkah; 93 (21.5%) in Jizan and 40 (9.3%) in the Eastern province

(Table 4).

				Cont	rolling for	Nationali	ty = Non-	Saudi					
Immunization Status	Province												
	ASR	BAH	EST	HAIL	JIZ	JOF	MED	МАК	NAJ	QAS	RYD	ТАВ	Total
Not Vaccinated	2 0.28 0.46 50.00	1 0.14 0.23 100.00	40 5.56 9.26 60.61	1 0.14 0.23 100.00	93 12.93 21.53 65.96	1 0.14 0.23 25.00	11 1.53 2.55 55.00	241 33.52 55.79 61.79	17 2.36 3.94 54.84	7 0.97 1.62 53.85	15 2.09 3.47 38.46	2 0.28 0.46 66.67	432 60.08
Unknown	1 0.14 0.99 25.00	0 0.00 0.00 0.00	13 1.81 12.87 19.70	0 0.00 0.00 0.00	28 3.89 27.72 19.86	3 0.42 2.97 75.00	6 0.83 5.94 30.00	41 5.70 40.59 10.51	4 0.56 3.96 12.90	0 0.00 0.00 0.00	2 0.28 1.98 5.13	0 0.00 0.00 0.00	101 14.05
Vaccinated	1 0.14 0.54 25.00	0 0.00 0.00 0.00	13 1.81 6.99 19.70	0 0.00 0.00 0.00	20 2.78 10.75 14.18	0 0.00 0.00 0.00	3 0.42 1.61 15.00	108 15.02 58.06 27.69	10 1.39 5.38 32.26	6 0.83 3.23 46.15	22 3.06 11.83 56.41	1 0.14 0.54 33.33	186 25.87
Total	4 0.56	1 0.14	66 9.18	1 0.14	141 19.61	4 0.56	20 2.78	390 54.24	31 4.31	13 1.81	39 5.42	3 0.42	719 100.00

Baha province reported no measles cases since 2008, and Joof province reported none since 2011 (Figures 5, 7). Madinah was completely free of measles in the year 2009 (Figure 2), and Hail and Qassim had no cases in the first four months of 2012.



### Discussion

Measles rates from 2002 – 2012 showed a slight decrease, but epidemics still occur approximately every 3 years. KSA has maintained a measles vaccination coverage rate of above 95% since 2001 [23]; over half of the cases (54%) occurred among non-vaccinated Saudis and non-Saudis (non-vaccinated people are defined here as those who have not had any previous doses of MCV).

The resurgence of measles could be due to an accumulation of susceptible cases among those in the vulnerable age group of 0-14 years in highly populated provinces like Makkah, Riyadh, Eastern Province, Aseer and Jizan.

Most of the non-vaccinated cases among both Saudis and non- Saudis were located in Makkah, Jizan, Eastern and Riyadh provinces. Makkah is a challenge because of the Hajj, the biggest mass gathering in the world, with an estimated 2-3 million pilgrims traveling there each year [24]. The immunization process and PHS must be reevaluated in these provinces. Yemanis accounted for 280 (35%) of the total non-Saudi cases; 75% of those cases were distributed in Jizan and Jeddah, a city in Makkah province.

Measles infections usually occur during late winter and early summer (Figure 5). Saudis may have a higher measles incidence rate than non-Saudis because infections occur and spread mainly among preschool and school-age children, and the majority of the non-Saudis are adults coming to KSA for Hajj, Umrah, or to stay illegally looking for a job or working.

Al-Madinah province should pay close attention to its trends because it is the only province with a continuous increase of measles incidence among both Saudis and non-Saudis since 2009.

Sustainable elimination has been achieved in Baha province; it is the only province that has been free of measles since 2008. Joof province has also sustained elimination since 2011. This achievement is also possible in the Qassim and Hail provinces, as they showed no measles cases for the first 4 months of 2012.

#### Limitations

This study only included confirmed measles cases; susceptible measles and rubella cases were out of scope. We didn't have complete Saudi census data for all of the different age groups from 2002 - 2012; we calculated the census population data by computing the annual population growth rate from data on the Saudi and non-Saudi population census from 2005 - 2009.

#### Recommendations

Because the measles vaccine is safe, effective, and inexpensive (costing less than one U.S. dollar [19]), we recommend adding the measles vaccination to the list of required vaccinations before issuing Hajj or work visas. We recommend data registry training sessions for those who are working on the measles PHS so that the data would be clearer, more readable, and more complete. Also, we recommend paying more attention to the vaccination process in Makkah, Riyadh, Jizan, Eastern Province, and Aseer because these provinces have the greatest number of cases. We recommend targeting preschool and school-age groups and all of those from 0-14 years every 3 years to reduce the chance of measles resurgence due to the accumulation of non-vaccinated groups. Finally, KSA is moving with continuous steps toward measles elimination by 2015, but we need greater political and public health commitment.

# **Competing interests**

No competing interests.

#### **Chapter 4: Conclusions and Recommendations**

The measles elimination goal is a challenge for KSA's healthcare system. This program, as well as other vaccination programs, is implemented and monitored by the MOH. The MOH's unilateral role doesn't seem to be effective in bringing about the complete elimination of measles, which they began in 1998. Measles elimination efforts should be distributed throughout the whole healthcare system through the implementation of specific strategies that target the most vulnerable groups, increasing national awareness about these efforts, engaging the community in these activities and maintaining open communication and collaboration with various healthcare providers like military hospitals, medical cities, medical schools and universities.

The MOH strategies for measles elimination were adopted in 1997 for all WHO Eastern Mediterranean Region (EMR) country members [25] to eliminate measles by 2010 (then extended to 2015). The WHO declaration recommended the following four strategies to achieve this goal: reaching and maintaining 95% routine measles vaccination coverage among children aged  $\geq$ 1 year; conducting a one-time, nationwide, mass immunization campaign or catch-up campaign targeting all children of preschool and school ages (usually 9 months–15 years) without regard to their measles or vaccination history; conducting episodic national follow-up campaigns every 3–5 years that target all children born since the last campaign (usually those aged 9 months–4 years) or achieving 95% routine coverage with a second routine dose of measles vaccine; and strengthening measles surveillance and laboratory confirmation of cases [26].

These strategies need to be modified slightly to accommodate the persistent case occurrences within population-dense provinces (e.g., Makkah, Riyadh, Jizan, Aseer and Eastern Province) and to reduce and prevent imported cases from other countries during the Hajj and Umrah seasons. The four strategies mainly focus on increasing the immunization coverage and improving public health surveillance, so we will discuss our recommendations according to these two categories.

#### **Immunization Coverage**

Measles immunization coverage rates have been maintained above 95% since 2001, according to the *Health Statistical Year Book* published by the MOH in 2011 [23]. The immunization programs must be evaluated because we found that approximately 50% of the total number of confirmed measles cases from 2002 – 2012 occurred in 2007, and non-vaccinated populations accounted for almost 50% of the 2007 epidemic.

This pattern could be an indicator for a vaccine failure and/or failure to vaccinate, which may have led to an accumulation of susceptible cases which were not tracked and followed up on. Inappropriate vaccine handling, defective administrative procedures, breaks in the cold-chain, and factors related to the environment and host could all be potential reasons for a vaccine failure [27].

So, the evaluation process of vaccination coverage must be considered in every province to make sure that at least 95% of infants have gotten the first dose of MCV1 and that the older children at school have successfully been administered the second dose. In this situation, we need to collaborate with the Ministry of Education to provide us full information about the exact number of children that should be targeted for the immunization campaigns. If there is a province that shows less than a 95% immunization coverage rate, we recommend reaching those children through Supplemental Immunization Activities (SIAs).

A full 60% of measles cases among the non-Saudi population occurred among the nonvaccinated group, most of whom came for Hajj or to look for a job in KSA. Because the previous groups are usually not targeted by immunization program or catch-up and follow up campaigns, we recommend adding the measles vaccination as a compulsory requirement for Hajj and work Visas. This action may needs more communication and collaboration with other authorities (e.g., Ministry of Hajj, Ministry of Labor, and Ministry of Interior). The hardest goal in KSA is not achieving zero cases of measles but sustaining elimination status for long time. A good example of this obstacle is the epidemic of measles in USA, 2011 [28], 95% of epidemic were among imported cases through travellers from affected countries.

#### **Public Health Surveillance (PHS)**

PHS for measles in KSA is case-based surveillance because measles is included in the notification system of infectious diseases as a Class-I Notifiable Disease; any suspected measles case requires compulsory immediate notification (within 24 hours) by phone or fax from hospitals, health centers and clinics to the Regional Directorate of Health Affairs in each province. The PHS data line list includes patient's age, sex, nationality, measles vaccination status, household location, history of contact with other measles cases, date of visit at health setting, date of specimen collection, date of rash appearance, date of specimen sent to the laboratory, and date of investigation at patient's house [29].

Looking at the main dataset, we immediately noticed that a lot of information was missing and that the information was written in two languages (Arabic and English). Recorders used both Islamic and Georgian calendars, and one nationality might be spelled 10 different ways in the main dataset. This is clear evidence that the registration process of these data was poor, and I highly recommend taking urgent action to resolve this. It would be helpful if the data registration processes were reviewed on a regular basis to make sure that they were complete, clear, organized, and valid.

In 2007, there were two studies conducted in Qassim [22] and in Tabuk [29]. Both failed to find the cause of the epidemic that year, but both had the same conclusion on the performance of the PHS. Out of five performance indicators recommended by WHO for measles surveillance, two were not satisfactory. First, a large proportion (76.5%) of the

suspected cases were reported to the Tabuk Directorate at least 48 hours after the onset of the rash. In the Qassim outbreak, 33% of suspected cases were reported after the WHO's standard time limit. Second, despite collecting and sending all blood samples on time, laboratory results for 21.5% of the suspected measles cases were received at least 7 days afterward. This kind of delay indicates a crucial need for a change in the surveillance staff's attitude toward their work. The staff should take more responsibility in case detection and investigation procedures in order to detect the epidemic source and work on interrupting the infection from the beginning through the adoption of a rapid notification system. Furthermore, the reporting process should be reevaluated and monitored because a number of notifications were late due to the lack of outbreak awareness among the staff in the healthcare settings.

For these reasons, it is time to take more aggressive steps to enhance the case detection and reporting process. I recommend opening new laboratories for measles confirmation tests to reduce the work overload in the MOH laboratories. These labs could help a great deal if they are located in provinces with high-density populations. The MOH should plan to engage multiple players to handle and share the responsibilities of the prevention programs. Community participation should be facilitated to increase awareness of these goals and to help in effective case detection, especially during epidemics. Eliminating measles within the non-Saudi population is a difficult task. So, the MOH must find a way to reach illegal immigrants and gain their cooperation. The MOH should plan specific supplementary immunization activities that target these foreign populations.

I believe measles elimination is an opportunity for the MOH to generate and test new approaches in the prevention field. InshaAllah, one day we will celebrate achieving this target.

# References

- 1. The World Factbook, C.I.A. 2013; Available from: https://<u>http://www.cia.gov/library/publications/the-world-factbook/geos/sa.html</u>.
- 2. Royal Embassy of Saudi Arabia, W., D.C. *About Saudi Arabia.* 2012; Available from: <u>http://www.saudiembassy.net/about/country-information/history</u>.
- 3. The Saudi Network, S.A.G.I. and Available from: <u>http://www.the-saudi.net/saudi-arabia/saudi-informations.htm</u>.
- 4. Central Department of Statistics & Information, S.A. *Statistical Yearbook*. 2010; Available from: <u>http://www.cdsi.gov.sa/english/index.php</u>
- 5. Almalki, M., G. Fitzgerald, and M. Clark, *Health care system in Saudi Arabia: an overview.* East Mediterr Health J, 2011. **17**(10): p. 784-93.
- 6. The Ministry of Health, S.A. *About the Ministry*. 2012; Available from: http://www.moh.gov.sa/en/Ministry/About/Pages/default.aspx.
- 7. Al-Rabeeah, A., *The history of health care in the Kingdom of Saudi Arabia with emphasis on pediatric surgery.* Saudi Med J, 2003. **24 Suppl**: p. S9-10.
- 8. Al-Sharqi, O.Z. and M.T. Abdullah, "*Diagnosing*" Saudi health reforms: is NHIS the right "prescription"? Int J Health Plann Manage, 2012.
- 9. Khalil, M.K., et al., *Measles in Saudi Arabia: from control to elimination.* Ann Saudi Med, 2005. **25**(4): p. 324-8.
- 10. Khalil, M.K., et al., *Measles immunization in Saudi Arabia: the need for change.* East Mediterr Health J, 2001. **7**(4-5): p. 829-34.
- 11. Morley, D., *Severe measles in the tropics. I.* Br Med J, 1969. **1**(5639): p. 297-300 contd.
- 12. PLAN, S., Global Measles and Rubella. 2012.
- 13. Moss, W.J. and D.E. Griffin, *Measles*. Lancet, 2012. **379**(9811): p. 153-64.
- 14. Omer, M.I., *Measles: a disease that has to be eradicated*. Ann Trop Paediatr, 1999. **19**(2): p. 125-34.
- 15. Cluster, W.H.O.C.D., W.H.O.H. Technology, and Pharmaceuticals, *WHO Guidelines* for Epidemic Preparedness and Response of Measles Outbreaks. 1999: World Health Organization, Expanded Programme on Immunization, Vaccines and other Biologicals [and] Department of Communicable Disease Surveillance and Response.
- 16. *Factsheet: measles.* N S W Public Health Bull, 2012. **23**(9-10): p. 209.
- 17. Perry, R.T. and N.A. Halsey, *The clinical significance of measles: a review.* J Infect Dis, 2004. **189 Suppl 1**: p. S4-16.
- 18. Preeta Kutty MD; Jennifer Rota MPH, W.B.P., Susan B. Redd, *Measles*, 2012, Centers for Disease Control and Prevention.
- 19. World Health Organization. *Measles*. 2013 [cited 2013; Available from: http://www.who.int/mediacentre/factsheets/fs286/en/.
- 20. *Global control and regional elimination of measles, 2000-2011.* MMWR Morb Mortal Wkly Rep, 2013. **62**(2): p. 27-31.
- 21. van den Ent, M.M., et al., *Measles mortality reduction contributes substantially to reduction of all cause mortality among children less than five years of age, 1990–2008.* Journal of Infectious Diseases, 2011. **204**(suppl 1): p. S18-S23.
- 22. Jahan, S., et al., *Measles outbreak in Qassim, Saudi Arabia 2007: epidemiology and evaluation of outbreak response.* J Public Health (Oxf), 2008. **30**(4): p. 384-90.

- 23. Ministry of Health, S.A., *Health Statistical Year Book*, 2011. p. 44.
- 24. Memish, Z.A., *Infection control in Saudi Arabia: meeting the challenge.* Am J Infect Control, 2002. **30**(1): p. 57-65.
- Gaafar, T., E. Moshni, and F. Lievano, *The challenge of achieving measles elimination in the eastern Mediterranean region by 2010.* J Infect Dis, 2003. 187
   Suppl 1: p. S164-71.
- 26. De Quadros, C.A., et al., *Measles elimination in the Americas.* JAMA: the journal of the American Medical Association, 1996. **275**(3): p. 224-229.
- 27. Fine, P.E. and E.R. Zell, *Outbreaks in highly vaccinated populations: implications for studies of vaccine performance.* American journal of epidemiology, 1994.
  139(1): p. 77-90.
- 28. Control, C.f.D. and Prevention, *Measles-United States, January-May 20, 2011.* MMWR Morb Mortal Wkly Rep, 2011. **60**: p. 666-668.
- 29. Al-Arabi Al-Ghamdi, A.M., et al., *Epidemiological analysis of notified measles cases and review of surveillance system during an outbreak in Tabuk, Saudi Arabia.* Ann Epidemiol, 2011. **21**(4): p. 262-71.