**SCHOOL OF PUBLIC HEALTH**

**COLLEGE OF HEALTH SCIENCES**

**UNIVERSITY OF GHANA**


# ADVERSE EVENTS FOLLOWING IMMUNIZATION WITH NEWLY INTRODUCED COVID-19 VACCINE FOR PERSONS WHO HAVE RECEIVED AT LEAST ONE DOSE, AWUTU SENYA EAST MUNICIPALITY, CENTRAL REGION, GHANA

**BY**

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**THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON, IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF A MASTER OF PHILOSOPHY IN APPLIED EPIDEMIOLOGY AND DISEASE CONTROL DEGREE**

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# DECLARATION

I do hereby declare that this is my own independent research and that the works of other researchers were well acknowledged. The study was undertaken under the guidance and supervision of Prof. Col. Edwin Andrews Afari (Rtd) and Dr. Samuel Sackey of the Department of Epidemiology and Disease Control, School of Public Health, University of Ghana, Legon. I declare my compliance with good conduct to the principle and guidelines of the ethical review committee. This work has not been previously submitted either in whole or in part for the award of a degree in this institution or elsewhere.

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**Supervisor (Primary)**

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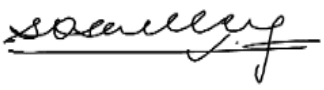
**Supervisor (Secondary)**



……. 30th September, 2022

Dr. Samuel Oko Sackey Date

# ABSTRACT

**Introduction:** Vaccines are a critical public health tool in the fight against the COVID-19 pandemic. COVISHIELD, a recombinant simian adenovirus-based COVID-19 vaccine, had been granted emergency use authorization in Ghana. Because the vaccine's early phase trials were not conducted in Ghanaians, no adverse events following immunization (AEFIs) linked to the vaccination had been identified among Ghanaians prior to the vaccine's deployment on March 2, 2021. This study aimed to assess the AEFIs of COVISHIELD in the Awutu Senya East Municipality (ASEM).

**Methods:** A prospective observational follow-up study was conducted from August to October 2021 among vaccinees aged 18 years and above. Those who consented were enrolled and subsequently followed up for adverse events within 24 hours and on days 7, 21, and 56 after the immunization. Participants were recruited from all 5 sub-municipalities in ASEM. Data was collected through face-to-face administration of questionnaires to participants at the point of enrolment. Follow-ups were done post-vaccination via telephone calls. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA 23). According to the Division of AIDS (DAIDS Version 2.1), adverse events were assessed for severity. Data was input into Excel, cleaned, and exported to STATA I/C 16 (Stata Corp LLC, Texas, USA) for analysis. Cumulative AEFI incidence was described across sociodemographic study participant variables. A 95% confidence interval was also determined for the cumulative incidence of AEFIs across participant characteristics. Pearson's chi-square test was performed to assess the relationship between AEFIs and socio-demographic factors. Approval was granted for the conduct of the study on 2nd August 2021 by the Ghana Health Service Ethics Committee.

**Results:** The overall incidence of AEFIs among the 550 vaccinees who were followed for 56 days was 16.7% (92/550). The incidence was higher in the younger age group. The AEFIs experienced were more severe among participants 60 years and older than in the younger group.

Most participants (71.7% [66/92]) who experienced AEFIs had only one event and the AEFIs experienced were mostly Grade 1 – mild (77.2% [71/92]), and Grade 2 – moderate (20.7% [19/92]) severity. No serious AEFIs were reported. More than half (52.2% [48/92]) of those who developed AEFIs observed them by the next day after the vaccination. AEFIs resolved at a median time of 2 days from onset. Asthenia (32.6% [30/92]) was the commonest AEFI, followed by headache (28.3% [26/92]), body pain (18.5% [17/92]), pyrexia (17.4% [16/92]), and injection site pain (17.4% [16/92]). The risk of AEFI incidence among the younger age group (those aged 18 to 29 years and 30 to 39 years) had 4 times increased risk of AEFI compared to older ones (those aged 70 years and over). Also, the risk of AEFI incidence was 56% higher among females than in males.

**Conclusion:** The incidence of AEFIs among the participants in the Awutu Senya East Municipal was relatively low. The events were generally mild and they disappeared quickly without hospitalization. It is, therefore, recommended that the general public get vaccinated through the national COVID-19 vaccination roll-out organized by the Expanded Program on Immunization.

## DEDICATION

This work is dedicated to all frontline health professionals who worked diligently in resource-constrained hospitals to care for COVID-19 patients when there was no vaccination and the world was only now learning about the disease.

# ACKNOWLEDGEMENT

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| | |
|---|---|
| AEFI | Adverse Events Following Immunization |
| ASEM | Awutu Senya East Municipal |
| DAIDS | Division of AIDS |
| EMA | European Medicines Agency |
| EPI | Expanded Programme on Immunization |
| FDA | Food and Drugs Authority |
| GFELTP | Ghana Field Epidemiology Laboratory Training Program |
| GHS | Ghana Health Service |
| HCW | Health Care Workers |
| ISRR | Immunization Stress Related Response |
| MenACWY | Meningococcal Vaccine |
| MHRA | Medicines and Healthcare Products Regulatory Agency |
| MOH | Ministry of Health |
| SII | Serum Institute of India |
| UNICEF | United Nations International Children Emergency Fund |
| VAERS | Vaccine Adverse Event Reporting System |
| WAHO | West African Health Organization |
| WHO | World Health Organization |

# CHAPTER ONE

# INTRODUCTION

## 1.1 Background

Vaccines serve a critical role in the prevention of infectious illnesses in all communities across the globe (Greenwood, B. 2014). However, they may have unfavourable consequences referred to as adverse events following immunization (AEFI) when administered. This is "any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine" (Mehta et al., 2000). Common adverse events to immunizations might include swelling, redness at the injection site, fever, pain, and a rash (WHO, 2010).

In December 2019, a group of individuals with unexplained pneumonia was linked to a seafood marketplace in Wuhan, China, and was later determined to be infected with 2019-nCoV, a new coronavirus (Zhu et al, 2020). Due to the virus's resemblance to the coronavirus that causes severe acute respiratory syndrome (SARS-CoV), a lineage B betacoronavirus, it was given the name SARS-CoV-2 (Lu et al., 2020). SARS-CoV-2 is the infectious virus that causes Coronavirus Disease 2019 (COVID-19), and infection with it can result in a range of clinical signs, ranging from asymptomatic infection to severe acute respiratory failure and death (Folegatti et al., 2020).

As of January 30, 2020, the World Health Organization (WHO) proclaimed the COVID-19 outbreak to be a public health emergency of international concern. On March 11, 2020, the WHO declared COVID-19 to be a global pandemic. There have been about 157.29 million confirmed cases globally with 3.28 million deaths as of May 10, 2021 (WHO, 2021a). Africa has recorded 3.32 million cases with 83,650 deaths as of May 10, 2021 (WHO, 2021b) and as of April 25, 2021, Ghana had announced a total of 93,011 confirmed cases with 783 deaths.

There was no effective antiviral therapy for COVID-19 as of January 2020, and the treatment plan was just supportive, including preventive antibiotics, steroid administration and oxygen supplementation (Yanai, H., 2020). However, vaccination remains a popular option in therapeutic alternatives and among the most profitable and safest public health measures for controlling infectious diseases (Amorij, 2012; Luyten, J., & Beutels, P., 2016). The World Health Organization (WHO) estimates that current vaccines prevent nearly two million deaths in children under the age of five per year. (Arístegui et al. 2003; Duclos et al, 2009). The Expanded Programme of Immunisation (EPI) has assisted in reducing infant mortality in Ghana. The morbidity rates of vaccine-preventable illnesses such as measles and poliomyelitis have also decreased significantly. For instance, measles has not caused any deaths since 2003, and in 2011 Ghana was recognized as having achieved eradication status for maternal and neonatal tetanus (Gyaase et al., 2021).

As of March 2, 2021, less than a year after the WHO declared COVID-19 a pandemic disease, the global research community had collaborated to develop at least 308 vaccine candidates, with 16 of them already in Phase III trials (Shrotri et al., 2021). Meanwhile, adverse events (AE) from such vaccinations are of concern. These safety issues have resulted in vaccine hesitancy with the misconception that vaccines pose a risk of infection and are not safe for use (WHO, 2014). Vaccination rates have decreased in some countries as a consequence. Among Ghanaian adults, a study was undertaken before emergency-use authorization of some COVID-19 vaccines in Ghana. When Acheampong et al., investigated the population, they discovered that 28% were "undecided" about getting the vaccine, while 21% were "somewhat unlikely or very unlikely" to get the vaccine (Acheampong et al., 2021).

In order to document the safety profile of newly introduced vaccines in the population, Ghana has a national AEFI surveillance system that is dependent on voluntary monitoring and reporting by healthcare professionals. In the last decade, improved AEFI monitoring has

increased AEFI reporting from many monitoring departments in Ghana. This surveillance system has been activated during the COVID-19 vaccination campaign. However, because of the large number of people being vaccinated, there is a risk of an apparent increase in the number of AEFIs during the vaccine campaigns (UNICEF, 2005). Recipients of the vaccines may not report mild AEFIs to the hospital, resulting in under- and biased reporting. Passive AEFI surveillance, according to studies, detects about 1 to 10 per cent of incidents. (Choe et al, 2011). Active collection of AEFI reports and assessing them is one way to preserve public trust in the COVID-19 vaccines. These findings will boost public confidence and help COVID-19 vaccines gain a greater reputation. The successful communication of the reality of the benefit-to-risk ratios for the vaccine would encourage widespread optimism as well as inform policy. As a part of the campaign to get people vaccinated, social mobilization events were held at the national, regional, and local levels. Health, education and information authorities were consulted on information management; media houses were sensitized; materials and radio jingles were made; banners and posters were printed in both official and local languages. The vaccination campaign provided an opportunity to document the safety of vaccines in the Ghanaian population by assessing adverse events related to the COVID-19 vaccine in Awutu Senya East Municipality.

### 1.2 Problem statement

In Ghana, the Ministry of Health announced the first two cases of COVID-19 in a press statement dated May 12, 2020. (MoH, 2020). Both cases were imported as a result of the persons returning from Norway and Turkey. Since then, the case count has increased, and according to statistics from the Ghana Health Service, Government of Ghana (GHS, 2021), Ghana reported a total of 93,011 confirmed cases with 783 deaths as of April 25, 2021.

The primary control method against disease transmission is vaccination, which comes with adverse events. Adverse drug events have evolved as a significant clinical and public health

concern in developed and developing nations, accounting for between 5% to 35% of hospital admissions (Howard et al., 2007). Adverse events are one of the top 10 causes of death and significantly increase the cost of treatment in the United States and Europe (Beijer et al., 2002; Kongkaew et al., 2008). In Canada, a study found the adverse event rate of occurrence to be 7.5 per 100 hospital admissions; meaning 185,000 out of 2.5 million hospital admissions annually are associated with adverse events (Baker et al., 2004). The burden of adverse events on healthcare is proportionately higher in developing nations, owing to a high disease rate, hunger, and healthcare services with insufficient resources (Bates et al., 1997). A total of 522,313 doses of the Covishield vaccine had been administered in Ghana as of April 1, 2021, with 1,733 people reporting AEFIs; this means that the reporting rate was approximately 3 reports for every 1,000 doses administered (SAFETYWATCH Update No. 04, 2021). Causality was determined for five significant AEFI reports that had investigations completed, although there were 15 serious AEFIs. The Committee found three of the serious AEFIs to be coincidental. Even though there was a clear correlation between the two remaining cases and vaccination delivery, conclusive proof of a vaccine-related incident could not be found, thus patients in those two cases were monitored indefinitely (SAFETYWATCH Update No. 04, 2021).

These adverse events may occur as a result of the vaccine's intrinsic properties such as the vaccine recipient's age, sex, race/ethnicity, weight and pre-existing medical condition (Pittman et al., 2002; Weber et al., 2014). Additionally, the vaccine's administration and composition parameters, such as the method of injection or the location where the vaccination is administered, might affect the vaccine's safety profile in a specific person (Hervé et al., 2019). The occurrence of AEFI might also be a result of coincidence, accidents or immunization-related anxiety (Siegrist et al., 2007). It is critical for both the vaccinee and the healthcare professionals who suggest and deliver vaccinations to be aware of the potential adverse effects of the vaccine. A person may refuse to get additional doses of vaccination if it is thought to be

overly reactogenic. This could result in low vaccination rates and a lack of community protection as a consequence. For effective vaccination programs to control the spread of a disease, it is crucial to maintain high vaccination rates.

The pandemic has put significant strain on healthcare services that provide care to COVID-19 patients, as well as disrupted non-COVID-19 healthcare delivery, causing detrimental economic consequences (Folegatti et al, 2020). While the majority of COVID-19 patients have a mild to moderate condition, up to 5%-10% may have a severe, possibly fatal course, necessitating the development of effective drugs (WHO, 2020). Respiratory arrest, septic shock, disseminated intravascular coagulation, and myocardial damage are also common causes of death from COVID-19 (McGonagle et al., 2020). Protecting vulnerable populations such as the elderly and those with comorbidities, particularly those with compromised immune systems, will be made easier by the introduction of a safe and efficacious vaccine for COVID-19 (Pramod et al., 2021). However, vaccinations sometimes cause adverse events (Mehta et al., 2000; WHO, 2010), which have significant financial consequences in clinical practice. Many findings have found that the morbidity and mortality caused by these AEFIs is a significant health issues for healthcare providers and the general population (Sultana, Cutroneo, & Trifir, 2013). These adverse events also lead to a misconception that vaccines pose a risk of infection and are not safe for use (WHO, 2014). These concerns contribute to widespread vaccine apprehension, resulting in decreased vaccine uptake and failure to achieve vaccination targets (herd immunity) necessary to control the COVID-19 outbreak.

On March 27, 2020, the president declared a partial lockdown of four major cities (Accra, Tema, Kasoa, and Kumasi) beginning March 30, 2020, based on recommendations from the Ministry of Health and the Ghana Health Service (Antwi-Boasiako, et al., 2021; Danquah, M., & Schotte, S., 2020). Kasoa, a peri-urban community in the Awutu Senya East Municipal (ASEM) District in Ghana's Central region, was one of the towns most hit by the COVID-19

epidemic. Additionally, ASEM was selected as the study site since it is home to various ethnic groups, cultures, and tribes from Ghana (Gbagbo, F. Y., 2020). Furthermore, since it was one of the most impacted areas in terms of COVID-19 infections, the ASEM District was among the first to get COVID-19 vaccinations throughout the roll-out. The purpose of the study was, therefore, to assess adverse events related to the COVID-19 vaccine in Awutu Senya East Municipality.

### 1.3 Conceptual Framework

Toxicity studies employing cell cultures and animal models are used to examine vaccine safety at various stages of the development process, from pre-clinical toxicology through rigorous clinical trials (Di Pasquale et al., 2016). Even after a vaccine has been licensed, it still has the potential to induce adverse reactions.

Vaccine recipients' age, sex, race/ethnicity, weight, immunity and pre-existing medical condition are all extrinsic and intrinsic variables that may contribute to the development of AEFIs (Pittman et al., 2002; Weber et al., 2014). Yamoah et al., 2019, reported that healthcare professionals need to improve their knowledge, perception and practices through more sensitization on AEFIs and vaccine safety to improve reporting of AEFIs (Yamoah et al., 2019). Additionally, the vaccine's administration and composition parameters, such as the method of injection or the location where the vaccination is administered, type of antigen, and vaccine formulation, might affect the vaccine's safety profile in a specific person (Hervé et al., 2019). The occurrence of AEFI might also be a result of coincidence, accidents or immunization-related anxiety (Siegrist et al., 2007).

Some of the factors interact with each other. For instance, the antigen dose might determine the final dose number and the appropriate dosage per age. The physiological properties of the vaccine, when altered, could affect intrinsic factors such as age, sex and medical history leading

to the occurrence of AEFI. Administration and product handling factors could also interact with vaccine product factors – inadequate storage could affect the physiological properties of the vaccine. Figure 1.1 illustrates factors that may trigger AEFIs.

The immune and neurological systems' physiological activities change throughout life. These alterations have ramifications for the body's response to vaccine-induced adverse effects. As the immune system grows throughout infancy and adolescence, AEFI reporting rates rise. Higher tolerance for pain and disease symptoms and/or a decrease in innate immune defences may explain why reporting rates of AEs decline in adulthood. Older persons tend to have lower levels of interleukin 6 & 10, and c-reactive protein in their bloodstream after immunization, which might explain why they experience fewer systemic adverse events, such as fever (El Yousfi et al., 2005).

Females have a greater prevalence of injection-site symptoms following immunization than males (Cook, I. F., 2009; Klein et al., 2010) and may have a higher risk of acute hypersensitivity responses (Griffioen et al., 2014). Possible factors include genetic or hormonal variations. For instance, a woman's body may have a higher tolerance for injection site inflammation because of differences in skin thickness, cardiac output, and neuronal structure between men and women. (McCarthy et al., 2017).

Human (or programme) errors during the process of immunization also cause AEFIs. Adverse reactions may occur when vaccination is administered by a route other than the prescribed one (Herzog, C. 2014; Dolan et al., 2017). As a general rule, most vaccinations are given via intramuscular injection, and optimum vaccination practice demands that the injection site be stretched to decrease discomfort, redness, and the danger of developing an abscess following injection (Masika et al., 2016; Zuckerman JN, 2000). The failure of various vaccination programs has been linked to healthcare professionals' lack of knowledge and perceptions concerning vaccine storage and delivery, as well as the probable AEFIs connected with vaccine

products (Netterlid et al., 2009; Gahunia et al., 2013). Temperature changes might further cause vaccine ingredients to convert to hazardous forms, which could induce AEFIs (Comes et al., 2018; WHO, 2015). If a substance is used after its expiration date, it can lose its effectiveness or become nonviable.

Local and anaphylactic reactions are all possible vaccine-induced adverse effects. Components of vaccines such as adjuvants might induce adverse events when injected. It has been noted that higher volumes of injection (0.8ml and above) might elicit more discomfort than smaller doses (Zijlstra et al., 2018). Although rare, vaccine-related adverse effects are documented at a rate of 4.8 to 83.1 per 100,000 doses of the most widely used vaccinations. Although the precise incidence of actual adverse responses to regular vaccinations is unknown, estimates for the majority of vaccines vary from 1 per 500,000 to 1 per 1,000,000 doses (Fritsche et al., 2010). Some formulations may increase the risk of life-threatening allergic responses because they include allergens such as gelatine or egg proteins. But although severe allergic responses to immunizations are very uncommon, they can occur (approximately 1 per 1,500,000 doses). There is a wide spectrum of adverse outcomes that have been linked to vaccines (Fritsche et al., 2010).

Immunization anxiety-related reactions (psychological stress) can also result in AEFIs. In anticipation of injection, some individuals become stressed and respond negatively. The substance of the vaccine has nothing to do with this reaction. Some people have a fear of needles, which makes these responses worse. Mass hysteria may occur during group immunization, especially if a vaccinee faints or exhibits other symptoms such as itching or limb weakness. The manner and type of adverse injuries recorded can also be influenced by public opinion and apprehension of safety concerns. At the time of vaccination, the vaccine can be associated with non-vaccine-related occurrences. For mass vaccination programs, such temporal correlations are inescapable due to a large number of vaccine doses being given.

Vaccine safety and public confidence in vaccinations might be improved if healthcare professionals have adequate knowledge of vaccines and their related adverse events, which they can then pass on to patients and others in their communities (Masika et al., 2016).

Certain practices by healthcare professionals have the potential to decrease vaccination efficacy. A common example is the pre- and post-vaccination usage of analgesics such as ibuprofen and paracetamol to reduce pain, fever, and inflammation related to vaccination (Manley et al., 2007). Such actions may interfere with the body's antibody response to the antigenic agent in vaccinations, limiting their capacity to inhibit the proliferation of the targeted disease-causing organisms (Prymula et al., 2009). But a systematic review found that antipyretics given after vaccination helped lower vaccine-induced fever and had no effect on the body's ability to mount an effective immune response (Das et al., 2014). It must be the practice of healthcare professionals to check vaccinations regularly to ensure that they are always maintained at temperatures that are consistent with the cold chain to avoid any contamination (Yakum et al., 2015).

Negative perceptions among healthcare providers include the belief that reporting an AEFI such as an injection abscess would make them feel guilty for causing injury and being accountable for the incident, as well as the belief that integrating primary clinical tasks with AEFI reporting is difficult (Masika et al., 2016).

Figure 1.1, as adopted and modified from Hervé et al., 2019, illustrates the factors that lead to AEFI.

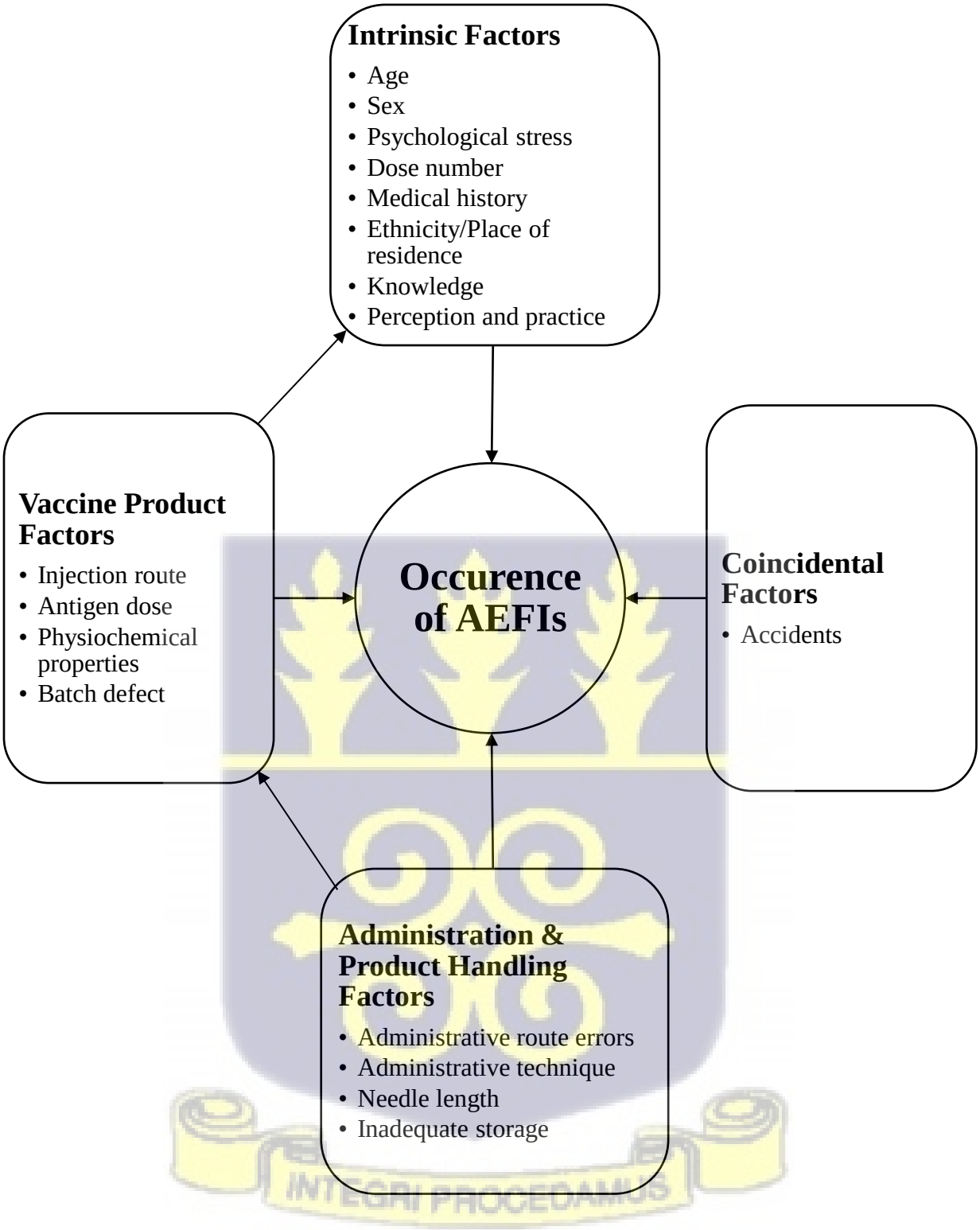


**Figure 1.1**: Conceptual Framework adopted and modified from Hervé et al., 2019 illustrating the factors that lead to Adverse Events Following Immunization.

### 1.4 Justification

Actively soliciting for AEFIs through direct patient follow-up may have provided additional information and contributed to the identification of mild AEFIs that may otherwise have gone undetected by passive surveillance systems. In Ghana, for instance, only 21% out of 59.50% of physicians who saw a patient with an adverse event reported to the National Pharmacovigilance Centre (NPC) in 2011 (Sabblah et al., 2014).

It was critical to keep a close eye on COVID-19 vaccine safety, particularly because the vaccines being used in the campaign were not just novel, but went through emergency use authorization (expedited registration). Also, none of the early phase trials of the vaccines was conducted in the Ghanaian population, so, no AEFIs related to the vaccine had been identified in Ghanaians prior to the vaccines' deployment on March 2, 2021.

In addition to existing spontaneous reporting systems and healthcare database studies (secondary data), a prospective follow-up study would be complimentary to these systems in various ways. It was more adapted to capturing the more common adverse events, such as those that were not medically attended. Extensive safety information, such as illness progression and the effect of adverse events was produced. Furthermore, unlike spontaneously provided data, the denominator of the analyzed cohort was known (in real-time), allowing AEFI frequencies to be estimated and immediately compared to data collected before licensing.

Profiling safety issues of medicines through AEFI reporting was to inform reasonable use. It was, therefore, important to actively solicit for AEFIs to provide baseline data for the COVID-19 vaccine and eventually contribute to improved signal detection and timely evaluation of safety signals. Furthermore, the findings were to help the Food and Drugs Authority (FDA) and Expanded Programme on Immunization (EPI) reliably educate the population, create public interest in the vaccine, and keep the immunization campaign going.

## 1.5 Research Questions

1. What is the incidence of AEFIs among persons living in Awutu Senya East Municipality (ASEM) who received at least one dose of the COVID-19 vaccine?
2. What are the types, severity, time-to-onset and outcome of reported AEFIs among persons living in ASEM who received at least one dose of the COVID-19 vaccine?
3. Are there possible risk factors for reported AEFIs among persons living in ASEM who received at least one dose of the COVID-19 vaccine?

## 1.6 Objectives

### General Objective

1. To assess AEFIs related to the COVID-19 vaccine among residents of ASEM who received at least one dose.

### Specific Objectives

1. To determine the incidence of AEFI among persons living in ASEM who received at least one dose of the COVID-19 vaccine.
2. To determine the type, severity, time-to-onset and outcome of AEFI among residents of ASEM who received at least one dose of the COVID-19 vaccine
3. To assess the risk of age, sex, place of residence and medical history on AEFI occurrence following COVID-19 vaccination among residents of ASEM who have received at least one dose of the COVID-19 vaccine.

# CHAPTER TWO

# LITERATURE REVIEW

## 2.1 Introduction

The globe was attacked by a significant public health danger towards the end of 2019, the COVID-19 epidemic, which has swiftly afflicted millions of individuals throughout the world. This viral infection is particularly important since it causes death in both healthy individuals and the elderly. COVID-19 mortality is greater than seasonal influenza mortality (Gates, 2020). Furthermore, COVID-19 is highly contagious, with the average infected individual infecting two or three other persons, even if they are asymptomatic (Hoehl et al., 2020). As a result, the illness has posed a global challenge to healthcare systems and services.

## 2.2 SARS-Cov-2 Disease Progression

The 2019-novel coronavirus (2019-nCoV) was first designated by the WHO (Guo et al., 2020) on January 12, 2020. The current information is that during the prodromal phase, infected individuals create a large amount of virus in the upper respiratory system, with a subsequent predilection for the lower respiratory tract (Chan et al., 2020). COVID-19 has also been linked to a variety of additional systemic symptoms (Cascella et al., 2021). Several preventative methods have been suggested to slow the virus's spread due to its unique characteristics and mechanism of transmission.

In reaction to the virus, enormous and diligent efforts have been made all across the world. Intensified disease surveillance, community spread mitigation, the creation of serological testing, as well as the start of vaccine development (Heymann et al., 2020). Ghana implemented countrywide steps including border closures, quarantine of sick individuals, contact tracing, testing, and a three-week lockdown in Accra and Kumasi, which were identified as the virus's epicentres. Immunizing the population through Emergency Use Authorization of some vaccines has been adopted by Ghana to augment the other measures to control the virus.

Vaccines today are both safe and effective. During the pre-licensure stage, they are subjected to stringent safety checks. Effective immunization campaigns include high-quality vaccines and safe immunization procedures (Joshi et al., 2018). Like most pharmaceuticals, vaccines can have adverse effects. However, vaccines seldom cause serious adverse reactions, and the most frequent reactions are mild and self-limiting. Even so, they are not fully risk-free (Mehta et al., 2000).

COVID-19 vaccines, like other vaccines, are linked with adverse events, and because of a large number of people being immunized in a campaign, the possibility of an apparent increase in AEFIs cannot be ruled out (UNICEF, 2005). Even though Ghanaian authorities licensed two vaccination brands (Sputnik V and COVISHIELD™), only COVISHIELD™ has been utilized since the country's roll-out.

### 2.3 The COVISHIELD Vaccine (ChAdOx1 nCoV-19)

COVISHIELD™ vaccine is made up of the SARS-CoV-2 Spike (S) surface glycoprotein, which is expressed by human cytomegalovirus major immediate-early promoter, which includes intron A, and a human tissue plasminogen activator leader sequence at the N terminus. Oxford University developed the COVISHIELD™ vaccine, which has a commercial production and supply arrangement with AstraZeneca. Serum Institute of India (SII) has signed a commercial-scale production and supply deal with AstraZeneca for India and global markets.

**Dosage and storage**

COVISHIELD™ is an intramuscular (IM) injection solution in a vial that is stored at 2 – 8°C. The COVISHIELD™ is available in a formulation buffer (10 mM L-Histidine and Histidine HCl, 7.5% (w/v) Sucrose, 35 mM Sodium Chloride, 1 mM, Magnesium Chloride, 0.1 % (w/v) Polysorbate 80, 0.1 mM Disodium Edetate (EDTA), 0.5% (v/v) Ethanol, pH 6.1 to 7.1 in Water for Injection).

The product is delivered as a sterile, transparent to virtually particle-free and slightly opalescent solution. An aluminium flip-off lid and a bromobutyl rubber stopper seal the transparent tubular glass vial containing COVISHIELD$^{TM}$, which is then ready for use. Vials of one, two, five, ten and twenty doses are available.

**Immunization schedule**

In a two-dose schedule, the vaccine is delivered intramuscularly in the deltoid at intervals of 8-12 weeks. For each mL of infusion, genetically modified human embryonic kidney (HEK) 293 cells are used to produce $5 \times 10^{10}$ simian adenoviral particles.

**2.4 Overall incidence of AEFI with ChAdOx1 nCoV-19 (COVISHIELD$^{TM}$ )**

In a report of a phase 1/2 trial in the UK, where 1,077 participants were assigned to the treatment (ChAdOx1 nCoV-19 (n=543) or the control (MenACWY (n=534) groups, Folegatti et al., 2020, indicated that 67% and 38% had AEFIs in both the treatment and control arms respectively. These AEFIs were typically mild to moderate in severity. The treatment group received the Covishield vaccine, and the control group received the meningococcal vaccine (MenACWY). The incidence in the control group was not a placebo, hence, cannot be reflective of the general incidence of the population without any intervention. In another clinical trial, after the first dose, 74% of persons vaccinated with the standard dose had at least one local symptom. The incidence during the second dose was 67% of persons vaccinated with the standard dose (Ramasamy et al., 2020).

Various countries have started rolling out these vaccines and real-world data are being reported. Kaur et al., 2021, reported on post-approval safety data on Covishield use in healthcare professionals in northern India. AEFIs were observed in 40% of participants after the first dose and approximately 16% of participants after the second dose. These events were much less compared to the AEFI rate seen in the UK-based population study of Oxford-AstraZeneca's ChAdOx1 vaccine. Another study among healthcare professionals in South India reported a

higher AEFI incidence of 69.7%. The AEFIs were all minor (Inbaraj et al., 2021). Jayadevan et al., 2021 also reported that 65.9% of respondents in their survey said they had had at least one post-vaccination symptom.

In the Republic of Korea, a total of 1,503 Healthcare professionals were vaccinated, with 994 (994/1,503, or 66.1%) reporting AEFIs (Jeon et al., 2021). The incidence in Korea as per this report is similar to that of India. Nepal began the first round of COVID-19 immunization with the Covishield vaccine for frontline healthcare professionals in January 2021. After the first dose of the vaccine was provided at one of the sentinel sites for immunization, active surveillance of AEFI was done. The incidence (85.04%) was higher than those seen in India (Shrestha et al., 2021).

**2.5 Common Adverse Events**

Most of the AEFIS seen with the ChAdOx1 nCoV-19 vaccine has been typically mild to moderate in severity. In the study reported by Folegatti et al., 2020, pain was reported by fewer subjects when prophylactic paracetamol was used: 50% and 32% in the treatment and control groups respectively. On the first day following immunization, the degree of local and systemic reactions was at its peak. In the first two days following vaccination with ChAdOx1 nCoV-19, an adjusted study of the impact of preventative paracetamol on adverse effects of any severity revealed substantial decreases in pain, fever, chills, muscular ache, headache, and malaise. Unsolicited adverse events in the 28 days after vaccination that were thought to be perhaps, probably, or definitely connected to treatment were mostly mild and moderate, and they went away over the follow-up period. Laboratory adverse events that were thought to be at least probably attributable to the study intervention were mostly mild or moderate in intensity and self-limiting. In the treatment group, 46% of participants had transient haematological alterations from baseline (neutropenia), compared to 7% in the control group (Folegatti et al., 2020).

Systemic AEFIs with or without local (injection site) involvement was seen in around 31% of participants, while only local site involvement was observed in 9% of people, as previously described by Kaur et al., 2021. Fever, malaise, and headache were the most frequently reported systemic AEFIs, accounting for 15.2%, 8.7%, and 5.8% of those surveyed, respectively. Only 28.7% of the AEFIs were classed as 'moderate' in severity, while 70.4% of them were categorized as mild. Based on causation assessment and the suspicion of an immunization stress response, the one serious AEFI was classed as "probable" (ISRR). It took an average of one day for AEFI victims to fully recover. Paracetamol (82), antihistamines (7), and tramadol (2) were all utilized to treat 91 patients with AEFIs.

Inbaraj et al., 2021 also indicated that, when participants were asked to rate the severity of AEFIs, 51.8% perceived it as mild, while (3.2%) rated it as severe. The most prevalent symptom was a body ache (46.8%), followed by a headache (30.3%) and a fever ((22%). Many (39% of patients) were prescribed drugs to treat their symptoms, and one patient had to be admitted to the hospital for further monitoring. 39.4% of them reported symptoms between four and twenty-four hours after receiving the vaccine, while 22.3% reported symptoms up to one day later. (Inbaraj et al., 2021).

In the Nepal study, Shrestha et al (2021) reported that 84.9% of the AEFI cases were minor. Some of the systemic AEFIs, however, were shown to be more common among people who had previously been infected with COVID-19. Those who used self-medication for symptom alleviation were 55.6%, 8.2% took time off work, and 0.76% went to the hospital for the AEFIs to be resolved. The majority of AEFIs that occurred after the first dose of vaccination were minor and went away within a few days (Shrestha et al., 2021).

In another study in India (Kataria et al., 2021), soreness and discomfort at the injection site were the most common solicited adverse events reported by daily diary cards, whereas fever, headache, myalgia, tiredness, joint pain, and nausea were the most common solicited systemic

adverse events reported on day 1. The bulk of local and systemic adverse effects occurred in the first two days following vaccination, and then disappeared. Subjects above the age of 50 had lower levels of reactogenicity. There were no adverse events that necessitated a hospital visit or the ER. When patients were divided into groups based on whether or not they had previously had COVID-19 disease, no significant differences in adverse events were found.

A study by Jayadevan et al., (2021) found that 45% of people had fatigue, 44% had myalgia, 34% had fever, 28% had headaches, 27% had pain at the injection site, and 12% had joint pain. Within the first 12 hours, 79% of those who reported symptoms noticed them. COVID-19 was reported by 8.7%. Their symptom profile was similar to that of individuals who had no prior experience.

Fatigue (92.9%) and malaise were the most often reported systemic AEFIs (83.8%) as indicated by Jeon et al., (2021). Fever (temperature 38°C) was reported by a very small number of healthcare professionals (27.6%). Two healthcare professionals (0.2%) experienced a high temperature over 40°C, and three healthcare professionals experienced severe diarrhoea (0.3%). The most prevalent local AEFIs reported by responders were grade 1 or 2 pain (87.6%) and soreness (61.2%) at the injection site. Most of the local AEFIs were grade 1 or 2. However, the number of grade 3 or higher local AEFIs was higher than the number of systemic AEFIs. It took about the same amount of time for all AEFIs for the first and most severe adverse events to start. Most of the AEFIs appeared in the first 1 to 3 days after being vaccinated and quickly went away.

**2.6 Serious Adverse Events**

A review of four studies as reported by Voysey et al., 2021, found the Covishield vaccine to be safe against the COVID-19 virus among 12, 021 (out of 23,745) participants who were in the treatment group. The vaccine had a good safety record in all four studies, with serious adverse events (SAE) and adverse events of special interest (AESI) evenly distributed across

the trial arms. SAEs occurred in 168 (0.7%) of the people who took part in the study - 79 (0.7%) of them were in the treatment group and 89 (0.8%) were in the control group. People in both treatment and control groups had 175 events. Three of them were thought to have been caused by either the experimental or control vaccination.

Even though 84.9% of the AEFI cases found in the study reported by Shrestha et al (2021) were minor, 0.05% were serious AEFIs. In the Indian study by Kataria et al., (2021), no SAEs were reported among the 1638 evaluated participants. According to Kaur et al., 2021, two AEFIs (0.62%) were of grade 3 severity, while one AEFI (0.3%) was 'serious' and required hospitalization. On the basis of causality assessment and suspicion of an immunization stress-related response, the single serious AEFI was characterized as 'possible'. In this subset of 730 patients, no significant AEFIs or deaths were observed. Shrestha et al., (2021) did not find any additional AEFI except for one incidence of anaphylaxis.

Thirteen of the respondents in the study reported on by Jeon et al., (2021) went to the emergency room or outpatient clinic. Within 10 minutes of receiving the vaccine, one patient had dyspnea, nausea, and hypotension, and was sent to the emergency room. The patient thereafter improved on his own and was discharged after getting supportive care. None of the cases required hospitalization. (Jeon et al., 2021).

**2.7 Effect of Age on AEFI incidence**

The majority of COVID-19-related deaths (74%) occur in adults over the age of 65 (WHO, 2020; Mueller et al., 2020). According to several studies, age is by far the most significant risk factor for COVID-19-related mortality (Williamson et al.,2020; Santesmasses et al., 2020). COVID-19 severity, on the other hand, is highly linked to comorbidities including hypertension, diabetes, obesity, cardiovascular illness, and respiratory disorders (Mueller et al., 2020). According to the WHO, COVID-19 vaccine candidates must be aimed at the most at-risk groups, including older adults, have a favourable safety profile, be effective as measured

by prevention of virologically proven illness or transmission, or both, and provide at least 6 months of protection for people at ongoing risk of exposure to SARS-CoV-2 (Funk et al., 2021). Certain studies have established the safety data of the ChAdOx1 nCoV-19 vaccination in various age groups.

In the Ramasamy et al (2020) trial, 88 % of the 18–55-year-olds, 73% of the 56–69-year-olds, and 61% of the 70-plus-year-olds reported at least one local symptom following the main immunization with standard-dose ChAdOx1 nCoV-19. Seventy-six per cent of participants between the ages of 18 and 55, 72% of those between the ages of 56 and 69, and 55% of those over the age of 70 had at least one local symptom following the recommended dosage of ChAdOx1 nCoV-19 booster vaccine. After receiving the low-dose ChAdOx1 nCoV-19 vaccine as their primary immunization, participants in all age categories showed a similar pattern, although with fewer overall adverse reactions than those who received the standard-dose vaccine. Recipients of ChAdOx1 nCoV-19 reported no serious local effects (Ramasamy et al., 2020).

Jayadevan et al., (2021) also reported that as people became older, their chances of developing symptoms dropped. Symptoms were reported by 81% of those in the 20-29 years age group, 80% of those in the 30-39 years group, 68% of those in their 50-59 years group, 58% of those in their sixth decade, 45% of those in their seventh decade, 34% of those in their eighth decade, and 7% of those in their ninth decade (9th decade, 80-90 years). Post-vaccination AEFI symptoms were more common in women (74.7 %) than in men (58.6 %).

Individuals under the age of 35 (98.9%) were more likely to report systemic and local AEFIs than those above the age of 51. (94.6%). AEFIs were found to be more severe in younger participants (aged under 35) than older ones, according to Jeon et al, who conducted the study (2021). For the most part, the younger age group had a higher incidence and severity of local and systemic AEFIs, except for arthralgia and diarrhoea (Jeon et al., 2021).

**2.8 Time to onset of AEFI with ChAdOx1 nCoV-19 vaccine**

AEFIs were observed within 30 minutes of receiving the vaccination after the second dosage in the Kaur et al (2021) study. AEFIs were found in seven people out of a total of 802 participants (0.9%). Three recipients had systemic AEFIs, while four subjects only showed local involvement. All seven AEFIs were classified as 'mild.' The average time for complete recovery was two days. In addition, 730 people were studied for AEFIs that occurred within 24 hours, between 24 hours and 7 days after immunization, but not within 30 minutes. Among these, 93 vaccine recipients (12.73%) experienced AEFIs within 24 hours, while 22 (3%) acquired AEFIs after day 1 and until day 7 post-vaccination, respectively. AEFIs were thus detected in 115 recipients (15.7%) till day seven; 99 (13.6%) had a systemic engagement with or without local site reactivity, whereas 16 had solely local involvement (2.2%). Following the exclusion of 72 persons who were lost to follow-up, a total of 730 individuals were included for analysis of AEFIs occurring within 24 hours, between 24 hours and 7 days of vaccination, but not within 30 minutes of immunization. Among these, 93 vaccine recipients (12.73%) experienced AEFIs within 24 hours, while 22 (3%) acquired AEFIs after day 1 and until day 7 post-vaccination, respectively. AEFIs were thus detected in 115 recipients (15.7%) till day seven. 99 (13.6%) had a systemic engagement with or without local site reactivity, whereas 16 had solely local involvement (2.2%). The median time to complete recovery for AEFIs developing within 24 hours of vaccination was 2 days, as was the time to complete recovery for AEFIs occurring between 24 hours and 7 days of immunization.

Most participants (39.4%) reported symptoms between four and twenty-four hours after receiving the vaccine, whereas 22.3% reported symptoms one day later, according to the research done by Inbaraj et al (2021). Following immunization, most people experienced mild or no local or systemic side effects for 2 days or less, according to research by Kataria et al (2021). For participants who reported AEFIs in the Jayadevan et al (2021), most (79%) of them

noticed the AEFIs within the first 12 hours. Their symptom profile was similar to that of individuals who had no prior experience.

Jeon et al. (2021) in Korea similarly reported on the onset of the AEFI in their investigation in Korea. Both the earliest and most severe adverse events occurred within the same time frame following vaccination. The majority of AEFIs appeared during the first 1 to 3 days after immunization and disappeared quickly. The majority of AEFIs were recorded on the first day following immunization, and systemic AEFIs improved quicker than local AEFIs (Jeon et al., 2021).

**2.9 Rare AEFIs linked to ChAdOx1 nCoV-19 vaccine**

In Europe, the ChAdOx1 nCoV-19 vaccine was approved at the end of January 2021 and began widespread usage in February 2021. An investigation into a probable vaccine-related death was announced by Austrian authorities on March 7. A few days later, Denmark and Norway were investigating claims of blood clots and death following vaccination. After Germany's decision on March 15, many other countries followed suit. (Wise, J. (2021); Mahase, E. (2021).

According to the European Medicines Agency (EMA) and the World Health Organization (WHO), the vaccine's advantages outweigh any potential risks. It was acknowledged that there could be a "possible" link to blood clots, which could be classified as "very rare" side effects. The cause of the clots is unknown, and the investigation is still ongoing.

About 20 million doses of vaccination had been administered, resulting in 79 cases of thrombosis with low platelets, the UK medicines regulatory agency reported. Nineteen people have lost their lives as a result of the incidences that have been reported. In general, four persons out of every million who receive the vaccination are at risk of blood clots (Mahase, E., 2021).

Several factors have been related to pulmonary embolism (PE), as well as deep vein thrombosis (DVT). Cancer, advanced age, smoking, hereditary or acquired thrombophilic disorders, past thromboembolism, and hospitalization for congestive heart failure or acute exacerbation of chronic obstructive pulmonary disease are only a few instances of genetic or naturally occurring causes. PE and DVT have been related to an increased risk of death and morbidity. Their natural occurrence ranges from 56 to 182 per 100,000 persons, which should be evaluated against the three PE deaths per 20 million vaccinated people. (Tobaiqy et al., 2021; Postigo et al., 2018). According to a recent study from Croatia, the frequency of combined DVT with PE but not isolated PE or isolated DVT has increased (Mahase, 2021). As Europe is divided on vaccination safety, the WHO thinks the deployment of the AstraZeneca vaccine should continue (Mahase, 2021). In their research of non-COVID-19 patients admitted to the hospital during the pandemic, the authors observed a much older age group (60.8 17.2 years vs. 68.5 16.8 years) (Mahase, 2021).

In Europe, a rare AE occurs five out of every 10,000 people (500/million). AE that affects one in 50,000 or 20 individuals per million is considered very uncommon. Seventy-nine (79) thrombotic incidents recorded concerning the AstraZeneca vaccination would be carefully labelled as extremely uncommon occurrences based on a basic calculation of 20 million patients (approximately, 4/million) who received the immunization (Schafer, 2003).

It would be difficult to connect the AstraZeneca immunization to thrombotic events based on spontaneous reports. Because there is a lack of safety and clinical data on vaccination use in the targeted community, statistical figures may be deceiving because of the underreporting and small numbers of persons exposed to the vaccines. In addition, there are a number of other factors that contribute to the situation such as the many unknown comorbidities that individuals may have exacerbate the problem. (Tapson, 2005; Slišković et al., 2021; Sardella and Lungu, 2019).

Although the AstraZeneca vaccine has received the most attention, adverse reactions to other COVID-19 vaccinations have also been reported. Deep vein thrombosis and pulmonary embolism cases linked to the Moderna vaccine were found in the EMA database, however, no deaths were reported (Tobaiqy et al., 2021). In a similar search for Pfizer vaccination reports, 11 patients experienced pulmonary embolism as a result of the Pfizer vaccination, and two of them died (Tobaiqy et al., 2021). Folegatti et al., 2020 reported that the control group experienced one significant adverse event – a new diagnosis of haemolytic anaemia after immunization. Throughout the trial, the person was clinically healthy. The incident was described as a suspected unexpected serious adverse reaction relating to the meningococcal vaccine and not ChAdOx1 nCoV-19.

**2.10 COVID-19 vaccination-associated myelitis**

AEFI can cause neurological consequences ranging from facial palsy to stroke, which can be severe. A total of 254 (2.69%) of the 9442 AEFI associated with Pfizer-BioNTech, Moderna, and Johnson & Johnson's COVID-19 vaccines were neurological in origin, according to the CDC's Vaccine Adverse Event Reporting System (VAERS); of these, 9 instances had transverse myelitis (Goss et al., 2021). Malhotra et al., 2021, reported the first case of myelitis in India linked to ChAdOX1 nCoV-19 (Oxford/AstraZeneca, COVISHIELD$^{TM}$) vaccination.

During the trial phase, the recombinant ChAdOX1 nCoV-19 vaccination was linked to two cases of myelitis. One had multiple sclerosis in the background, while the other was referred to be a potentially connected incident (Mahase, E., 2020; Voysey et al., 2021). Even with comparable reported occurrences with the current vaccination and those recorded in the CDC's-VAERS, it's critical to keep things in perspective: India has provided a total of 50.84 million doses through March 23, 2021. (Malhotra et al., 2021). With a yearly incidence of 1–4 cases per million (Transverse Myelitis Consortium Working Group (TMCWG), 2002), a myelitis

event after more than 50 million vaccination doses seems reasonable. It is thought that the advantages of vaccination continue to exceed the hazards.

# CHAPTER THREE

# METHODS

## 3.1 Study Design

It was a prospective observational follow-up study conducted from August to October 2021 in the Awutu Senya East Municipality to assess the incidence of AEFIs. Persons who came to the vaccination centres in ASEM were approached and briefed on the study. Those who were interested and consented were recruited. Enrolment began with obtaining information on any medical incident/condition and medications within the past 4 weeks prior to being vaccinated. Information on vaccination and subsequent adverse events was collected from each participant using a questionnaire. The questionnaire was administered by Research Assistants who captured the baseline information on participants' demography, medical history and vaccination detail at enrolment. Follow-up telephone calls were made to enrolled participants 24 hours after immunization and on days 7, 21, and 56. Data on the type, severity, onset and outcome of adverse events experienced by participants were captured during the follow-up calls. In order to do the analysis, the data was uploaded to STATA I/C 16 (Stata Corporation LLC, Texas, USA).

## 3.2 Study Area and Participants

The study was conducted in the Awutu Senya East Municipal, which is one of the Central Region's twenty-two (22) districts. The Municipality of Awutu Senya East is located in the Eastern section of the Central Region, between latitudes 5°45 south and 6°00 north, and longitudes 0°20 west to 0°35 east. On the east, it is bounded by the Ga South Municipal Assembly (in the Greater Accra Region), on the north by the Awutu Senya District, and on the west and south by the Gomoa East District.

Opeikuma, Adam Nana, Kpormertey, Ofaakor, Akwelley, Walantu, and Zongo are the major settlements in the Municipality. Most of the inhabitants of the Municipality are Guans and

speak Awutu. The Gas, Akans, Ewes, Wala/Dagaba, Moshies, Basares, and countless more minor tribes are among the other settler tribes with various ethnic origins. Akan is the primary language used, while English is the official language. According to reports, Kasoa, the capital city, is one of Ghana's towns with the fastest growth rates (Ministry of Finance, 2018). The population of the Municipality is currently estimated at 131,721 *(projected with a 2.8% growth rate from the 2000 Population and Housing Census*). The municipality has a 94.1% urban population and a 5.9% rural population as well. Commerce (both official and informal), agro-processing, and wholesale and retail trade are the Municipal's primary economic drivers. About 35.7% of the working population in the Municipality is employed by trading and associated businesses, according to the 2010 Population and Housing Census. There are many additional sectors of the economy, such as production, wholesale/retail trade, and transportation services (Ghana, G. S. S., 2010).

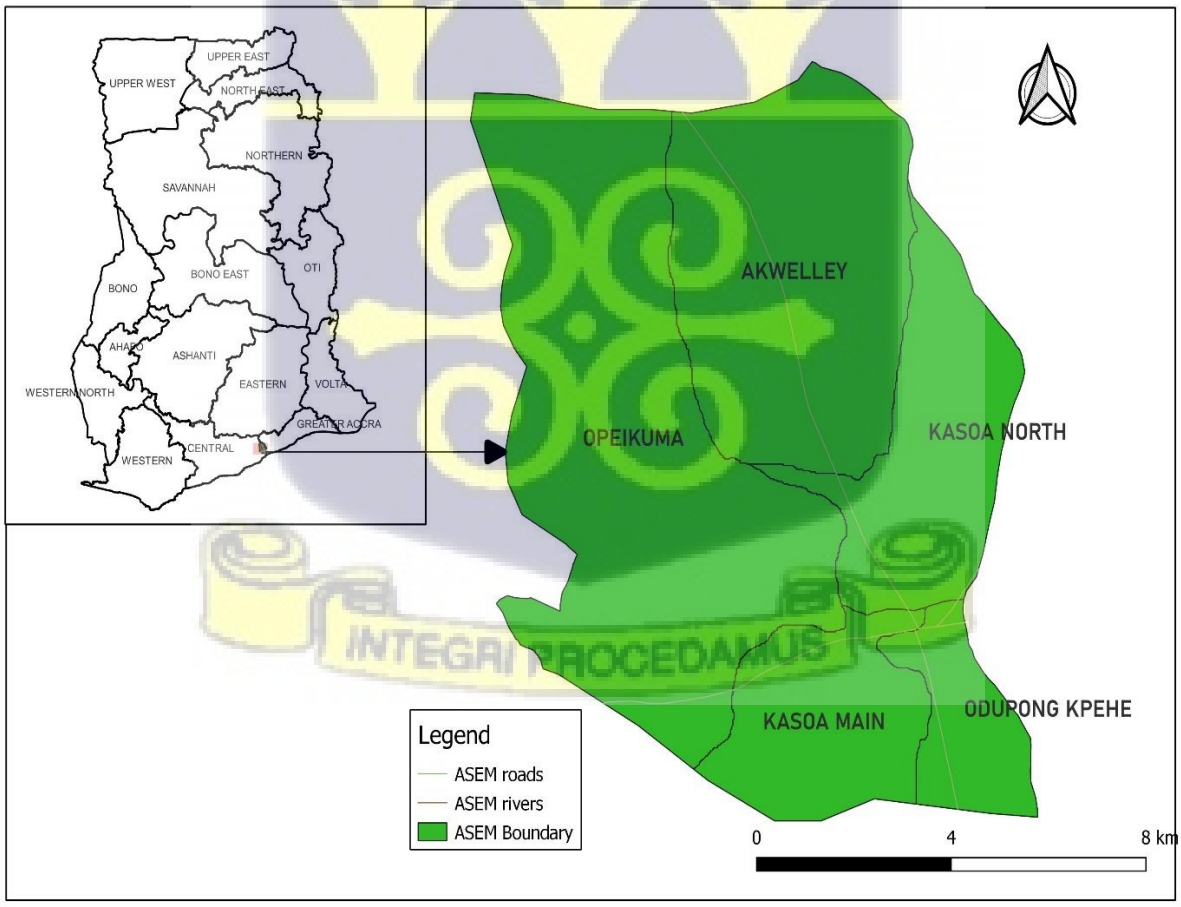


**Figure 3. 1 Map of Awutu Senya East Municipal (ASEM)**

The municipality's health services are delivered by several sectors, including the government (about 60%) and private health establishments. For efficient health administration, the municipality is split into five (5) sub-municipalities – Akwelley, Kasoa North, Kasoa Main, Odupong Kpehe, and Opeikuma. There were five vaccination centres in the municipality – one at each sub-municipality, and these centres participated in a 2-week long vaccination campaign.

**Table 3. 1: Summary of Sub-Municipal Profile**

| Sub-Municipals | Population | Communities | Outreach points | CHPS Zones |
|---|---|---|---|---|
| **Akwelley** | 26344 | 24 | 14 | 6 |
| **Kasoa North** | 25027 | 10 | 10 | 6 |
| **Kasoa Main** | 34247 | 14 | 8 | 6 |
| **Odupong Kpehe** | 23710 | 7 | 5 | 3 |
| **Opeikuma** | 22393 | 12 | 5 | 3 |
| **Municipal Total** | 131721 | **67** | **42** | **24** |

Source: Awutu Senya Municipal Health Directorate, 2020

The proportion of the estimated population who qualify for the COVID-19 vaccination was 60.1% (79,113/131,721). This proportion is made up of adults aged 18 years and above.

All persons aged 18 years and above who received the COVID-19 vaccine at the Awutu Senya East Municipality's vaccination clinics and were willing to participate in the study were enrolled.

### 3.3 Study Variables

#### 3.3.1 Dependent Variable

In this study, the dependent variable was adverse events following immunization with the COVID-19 vaccine. Regarding the AEFIs, participants were asked about local site symptoms such as pain, erythema, swelling, tenderness, and the degree of physical activity limitation. They were also questioned about systemic symptoms such as fever, fatigability, myalgia,

arthralgia, headache, nausea, vomiting, diarrhoea, rash, chest tightness and dyspnoea. Information on the onset of AEFIs, the severity of AEFIs, the treatments needed to manage AEFIs, the outcomes of AEFIs, the time it took to fully recover, and the causality of AEFIs were documented.

### 3.3.2 Independent Variables

Individual parameters such as age and sex were used as independent variables in this study. Participants' medical history, including existing co-morbidities, any presenting symptoms at the time of vaccination or sickness (medical event) within the past 7 days, concurrent medication history, and history of allergy to any known stimuli were also used as independent variables. Dose number and place of residence were also captured.

## 3.4 Sample Size Determination

This was a longitudinal study of people who had received the COVID-19 vaccine and were followed up for 8 weeks. There was no control group; hence, the sample size estimation for independent cohort studies was used to calculate the minimum sample size:

$$n = \frac{\left[z_{1-\alpha/2}\sqrt{\left(\frac{1+1}{m}\right)\bar{p}(1-\bar{p})} + z_{1-\beta}\sqrt{\frac{p_0(1-p_0)}{m} + p_1(1-p_1)}\right]^2}{(p_0 - p_1)^2}$$

Where:

- n represents the minimum sample size of desired participants to identify true relative risk with a 2-sided Type-I error
- m represents the number of participants (control) per experimental participant
- $Z_{1-\beta}$ represents the desired power
- $Z_{1-\alpha/2}$ represents a standard value for the corresponding level of confidence.
- $p_0$ represents the incidence of events in controls

- $p_1$ represents the estimated incidence or proportion with any incident of adverse event following COVID-19 immunization with COVISHIELD
- $\bar{p} = \frac{p_1 + m p_0}{m+1}$

Studies that had examined the safety and reactogenicity of COVISHIELD vaccines had yielded ambiguous results on the incidence of adverse events: 74% by Ramasamy et al., 2020, 40% after the first dose and 16% after the second dose by Kaur et al., 2021, 69.7% by Inbaraj et al., 2021, 85% by Jayadevan et al., 2021, and 66.1% by Jeon et al., 2021. Studies other than the clinical trials did not include controls. Folegatti et al., 2020, reported 67% AEFI incidence among the COVISHIELD group and 38% among the controls, however, this was not a placebo but an active control (Meningococcal A vaccine). None of the incidences of AEFI had been identified with the Ghanaian population. Because there were no Ghanaian-specific data, the incidence of variables with the minimum sample size was used, which is the 40% reported by Kaur et al., 2021 and assumed 30% AEFI incidence in control.

Hence, m = 1, $Z_{1-\beta}$ = 1.282 (90% power), $Z_{1-\alpha/2}$ = 1.96 (at 95% CI), $p_0$ = 0.3, $p_1$ = 0.4

$$\bar{p} = \frac{0.4+1*0.3}{1+1} = 0.35$$

$$n = \frac{\left[1.96\sqrt{\left(\frac{1+1}{1}\right)*0.35(1-0.35)} + 1.282\sqrt{\frac{0.3(1-0.3)}{1}+0.4(1-0.4)}\right]^2}{(0.3-0.4)^2}$$

$$n = \frac{[1.96 * 0.675 + 1.282 * 0.671]^2}{(-0.1)^2}$$

$$n = \frac{[1.323 + 0.86]^2}{0.01}$$

$n = 476.55 \approx 477$

A 15% loss to follow-up was considered based on the Kaur et al., 2021 study; which was additional 72 vaccinees. Therefore, the minimum sample size for the study was calculated to be 549 vaccinees. However, the estimated minimum sample size was rounded up to 550.

### 3.5 Sampling technique

Participants were sampled from five vaccination centres in the Municipality – one Vaccination Centre randomly selected from each sub-municipality. The sample size for each vaccination centre was calculated proportionately to the sub-municipality's population size. The average vaccine uptake per the vaccination centres was 55 persons per day for the 2-week long COVID-19 vaccination campaign.

Members of the public who came to the vaccination centres to receive the COVID-19 vaccine were approached and spoken to by trained Research Assistants. They explained the study's aim to the potential participants and those who consented were recruited into the study. The selection of individuals was based on inclusion criteria and the individual's willingness to provide information during the follow-up period. As part of the routine vaccination process, all vaccine recipients were observed at vaccination centres for 30 minutes after receiving the vaccine. Enrolled individuals were contacted by phone 24 hours after immunization and on days 7, 21, and 56.

### 3.6 Vaccination Process

The vaccine used for the campaign was COVISHIELD. The vaccination was given in two doses of 0.5 mL each, separated by 8-12 weeks, and administered intramuscularly in the deltoid. Each dosage of 1ml comprises $5 \times 10^{10}$ simian adenoviral particles generated in the genetically engineered human embryonic kidney (HEK) 293 cells. Healthcare professionals at the vaccination centres took turns sensitizing the public on the COVID-19 vaccine and other vaccination-related issues. This included common AEFIs associated with the vaccines and how to report them.

### 3.7 Inclusion Criteria

Anyone aged 18 years and above who resided in the Awutu Senya East Municipality and visited one of the selected COVID-19 immunization locations.

### 3.8 Exclusion Criteria

Anyone eligible per the inclusion criteria (3.7) but would not be available for the follow-up calls was excluded from the study.

### 3.9 Data Collection techniques and tools

Data was collected through a face-to-face administration of a questionnaire to participants at the point of enrolment. Follow-ups were done post-vaccination via telephone calls. Participants' demographic data – enrolment and follow-ups, as well as their medical histories, were captured using a data collection tool (checklist). To gather information on adverse events, an updated national AEFI checklist was used. Information was captured on Google Forms. Participants were followed-up within 24 hours after immunization and on days 7, 21, and 56 (window period +/-2 days). To ensure minimal or no loss to follow-up, a second telephone contact of someone living in the same house as the participant was obtained at the time of enrolment to ensure that participants were reached on follow-up days. The Research Assistants called those who had missed their specified follow-up dates and kept trying until they were reached within the window period.

### 3.10 Data Storage and Processing

Data collected was stored on a computer and protected with a password. Codes were used to identify participants. Data would be made available on a need-to-know basis. The adverse events data gathered was coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.

There are five levels to the MedDRA hierarchy, arranged from very specific to very general. At the most specific level, called “Lowest Level Terms” (LLTs), there are more than 80,000

terms that parallel how information is communicated. These LLTs reflect how an observation might be reported in practice. This level directly supports assigning MedDRA terms within a user database. Each member of the next level, "Preferred Terms" (PTs), is a distinct descriptor (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic. Related PTs are grouped into "High Level Terms" (HLTs) based upon anatomy, pathology, physiology, aetiology or function. HLTs, related to each other by anatomy, pathology, physiology, aetiology or function, are in turn linked to "High Level Group Terms" (HLGTs). Finally, HLGTs are grouped into "System Organ Classes" (SOCs) which are groupings by aetiology (e.g., *Infections and infestations*), manifestation site (e.g., *Gastrointestinal disorders*) or purpose (e.g., *Surgical and medical procedures*). For this study, the AEFIs were grouped into 3 - System Organ Class, High Level Term and Preferred Term.

The severity of adverse events was assessed according to the *Division of AIDS* (*DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1*. The DAIDS grading table provides an AE severity grading scale ranging from grades 1 to 5 with descriptions for each AE based on the following general guidelines: Grade 1 indicates a mild event; Grade 2 indicates a moderate event; Grade 3 indicates a severe event; Grade 4 indicates a potentially life-threatening event or death. Those graded "Mild" are symptoms causing no or minimal interference with usual social and functional activities with intervention not indicated. AEs graded "Moderate" are symptoms causing greater than minimal interference with usual social and functional activities with intervention indicated. AEs graded as "Severe" are symptoms causing the inability to perform usual social and functional activities with intervention or hospitalization indicated. The most severe are those graded as "Potentially Life-threatening" and they are symptoms causing the inability to perform basic self-care functions with intervention indicated to prevent permanent impairment, persistent disability, or death.

The data collected on the sheets were checked for errors and missing values. Data were then entered into Google Form (Microsoft Excel), checked for errors, and exported to STATA I/C 16 (Stata Corp LLC, Texas, USA) for analysis.

### 3.11 Statistical Data Analysis

For categorical variables, frequency and percentage were used, and for continuous variables, median and interquartile ranges were used to describe the characteristics of study participants. Pre-existing medical conditions among study participants were described using the bar chart. The AEFIs among study participants were described using bar charts in three different systems of description namely, high level term description, preferred term definition and system organ class for AEFIs.

The cumulative incidence of AEFIs was described across the various socio-demographic characteristics of study participants. A 95% confidence interval of the cumulative incidence of AEFIs was also estimated across the various characteristics of the study participants. The association between the cumulative incidence of AEFIs and socio-demographic factors was assessed using Pearson's chi-square test. Using the number of days to experience AEFIs in the first two months after vaccination as a time variable, the incidence rate and the corresponding 95% confidence were also estimated across the various demographic characteristics.

The number of different AEFIs was further described across the demographic characteristics of the study participants and Fischer's exact chi-square test was used to assess the significance of the association. The association between demographic characteristics and severity of AEFIs among those who experience AEFIs were also assessed using Fischer's exact chi-square test. Further analysis was performed to assess the relationship between the various AEFIs experienced and the severity of AEFIs using Fischer's exact test.

The multivariable analysis was performed using the Poisson regression model to estimate the crude and adjusted incidence rate ratio and identify the factors independently associated with

the incidence of AEFIs. First, the crude risk ratio of AEFIs was estimated across the various characteristic of study participants without controlling for any other variable and time using the Poisson regression model. In the second model, the time to experience AEFIs or exit the study was adjusted for each variable in estimating the incidence rate ratios using the Poisson model. Lastly, together with time to experience AEFIs or exit the study at two months, the age group, sex, sub-district, presentation of symptoms at the time of vaccination, known allergies, medical event in the last 7 days, pre-existing medical condition, medication at the time of vaccination and medication in the past 7 days were all run together in a multiple Poisson regression model to estimate the adjusted incidence rate ratio of AEFIs among the participants. Corresponding 95% confidence intervals of all rate ratios were estimated.

The predictive power of the final Poisson regression model was assessed using the Area Under the Receiver Operating Characteristic Curve (AUROCC). This indicates the model's ability to differentiate between two diagnostic groupings (in this case, those with AEFI and those without AEFI). The higher the AUROCC, the more accurately the Poisson regression model predicts those with AEFIs and those without AEFIs. A good model has an AUROCC close to 100%, indicating a high degree of separability. A model with an AUROCC close to 0 has the poorest possible metric of separability. In actuality, it implies that it is reciprocating the effect. And when AUROCC reaches 50%, the model has absolutely no class separation capability. The fitness of the model was assessed using the Deviance goodness of fit test. Finally, multicollinearity between the independent variables was evaluated in the final model using the variance inflation factor (VIF) below the threshold of 10. When there is a correlation between the predictors (i.e. the independent variables), we get multicollinearity, which might skew the findings of the regression analysis. In the presence of multicollinearity, the variances of the estimated coefficients tend to be overstated. Increases in R-squared, a measure of multicollinearity's effect on model fit, are another negative consequence. The VIF calculates an estimate for the degree to which multicollinearity in the model inflates the variance of a

regression coefficient. VIFs greater than 10 indicate severe multicollinearity that has to be corrected for, whereas VIFs of 1 indicate that there is no association between the specific predictor and the other predictor variables. All statistical significance in this study was considered at an alpha level of 0.05. STATA IC version 16 was used to perform all analyses in this study.

### 3.12 Quality control

Healthcare staff were recruited and qualified as Research Assistants to ensure high-quality data. During data gathering, the Research Assistants were monitored by frequent site visits. Data was captured on a paper form and later transferred onto the Google Form. Data input fields were designed to have built-in consistency and range checks. Five per cent (5%) of the completed forms were sampled and double followed up by the principal investigator.

COVD-19 were remedied with appropriate precautions. The use of a nose mask, social distancing, hand washing, and the use of hand sanitisers were among these strategies. Participants who did not have were given a nose mask and instructions on how to follow COVID-19 safety measures. To minimize congestion, study participants were approached and talked to individually and not put into groups.

### 3.13 Ethical clearance

The Ethical Review Committee of the Ghana Health Service approved the protocol for this study. The approval was granted for the conduct of the study on 2nd August 2021 with ethics approval number **GHS-ERC 024/06/21** (Appendix I). Permission was sought from the Awutu Senya East Municipal Health Directorate to conduct this study (Appendix II).

The participants were adequately informed about the study's goal. Although there was no direct risk or advantage to participating in this research, participants were informed that they would be required to answer a few questions from Research Assistants who would contact them often during the study period. They were advised that they could drop out of the research at any time.

If they had further questions about the study, they could contact the principal investigator (PI) and Academic Supervisor.

Participants were also informed that any information they provided would be kept completely confidential and utilized strictly for the study's purposes. Access to data collected was limited to the PI and supervisors on a password-protected computer. They were told that the collected data would be devoid of their names and other personal identifiers. Those who accepted to participate in the study were asked to sign or thumbprint a consent form before any information was gathered from them.

Participants who experienced AEFIs were advised to follow the Ghana Health Service protocols by visiting a nearby government facility for treatment.

**3.14 Sponsorship**

This study was supported by the Ghana Field Epidemiology Laboratory Training Program (GFELTP) in collaboration with the West African Health Organization (WAHO).

# CHAPTER FOUR

# RESULTS

## 4.1 Demographic Characteristics of the Study Population

Five hundred and fifty (550) adults between the ages of 18 years and 90 years who consented to be part of the study were recruited from five sub-districts in the Awutu Senya East Districts and followed for 8 weeks. The median age was 60 years (IQR = 44, 66). Table 4.1 shows the distribution of age groups with ages between 60 – 69 years with the highest number of participants of 35.1% (193/550) and 18 – 29 years being the lowest at 7.5% (41/550). Two hundred and eighty-eight (52.4%) were males and 262 (47.6%) were females. Participants were recruited from each of the 5 sub-municipals proportionate to the population size as shown in Table 4.1 with the majority of participants recruited from Kasoa North, 26% (143/550), followed by Akwelley with 20% (110/550), and the lowest of participants from Odupongkpehe with 16.9% (93/550). Each sub-district had a vaccination centre.

Table 4. 1: Demographic characteristics of study participants

| Variables | Frequency (N=550) | Percentage Frequency |
|---|---|---|
| **Age (years), median (IQR)** | 60.0 (44.0, 66.0) | |
| **Age group** | | |
| 18-29 years | 41 | 7.5 |
| 30-39 years | 67 | 12.2 |
| 40-49 years | 72 | 13.1 |
| 50-59 years | 93 | 16.9 |
| 60-69 years | 193 | 35.1 |
| 70+ years | 84 | 15.3 |
| **Sex** | | |
| Female | 262 | 47.6 |
| Male | 288 | 52.4 |
| **Sub-Districts** | | |
| Akwelley | 110 | 20 |
| Kasoa main | 105 | 19.1 |
| Kasoa north | 143 | 26 |
| Odupongkpehe | 93 | 16.9 |
| Opeikuma | 99 | 18 |

### 4.2 Medical History of participants

Six participants (1.1%) presented symptoms at the time of vaccination with symptoms ranging from headache, body pains, shivering and whitlow. Participants with known allergies were 12 (2.2%) and those who had had any medical event in the last 7 days before the vaccination were 13 (2.4%). Two hundred and twenty-nine (41.6%) participants had pre-existing conditions and two hundred and twelve (38.5%) of the participants were on medication at the time of vaccination. Table 4.2 shows the medical history of the study participants.

Table 4. 2: Medical History of Study Participants

| Variables | Frequency (N=550) | Percentage Frequency |
|---|---|---|
| **Presenting Symptoms at the Time of Vaccination** | | |
| No symptoms at the time of vaccination | 544 | 98.9 |
| Any symptoms at the time of vaccination | 6 | 1.1 |
| **Presenting Symptoms at the Time of Vaccination** | | |
| Body Pains | 1 | 16.7 |
| Headache | 3 | 50.0 |
| Shivering | 1 | 16.7 |
| Whitlow | 1 | 16.7 |
| **Known Allergies** | | |
| Allergies absent | 538 | 97.8 |
| Allergies present | 12 | 2.2 |
| **Medical Events (sickness) in the Last 7 days** | | |
| No Medical event | 537 | 97.6 |
| Presence of Medical event | 13 | 2.4 |
| **Pre-existing Conditions (e.g., diabetes, hypertension, etc)** | | |
| No medical condition | 321 | 58.4 |
| Presence of a medical condition | 229 | 41.6 |
| **Medication(s) at the time of Vaccination** | | |
| None taken | 338 | 61.5 |
| On medication at the time | 212 | 38.5 |
| **Medication(s) in the past 7 days** | | |
| No medication | 331 | 60.2 |
| On medication | 219 | 39.8 |

Hypertension accounted for the highest pre-existing condition, 80.3% (184/229); followed by diabetes, 30.1% (69/229). Figure 4.1 shows the relative frequency of pre-existing medical conditions among study participants prior to vaccination.

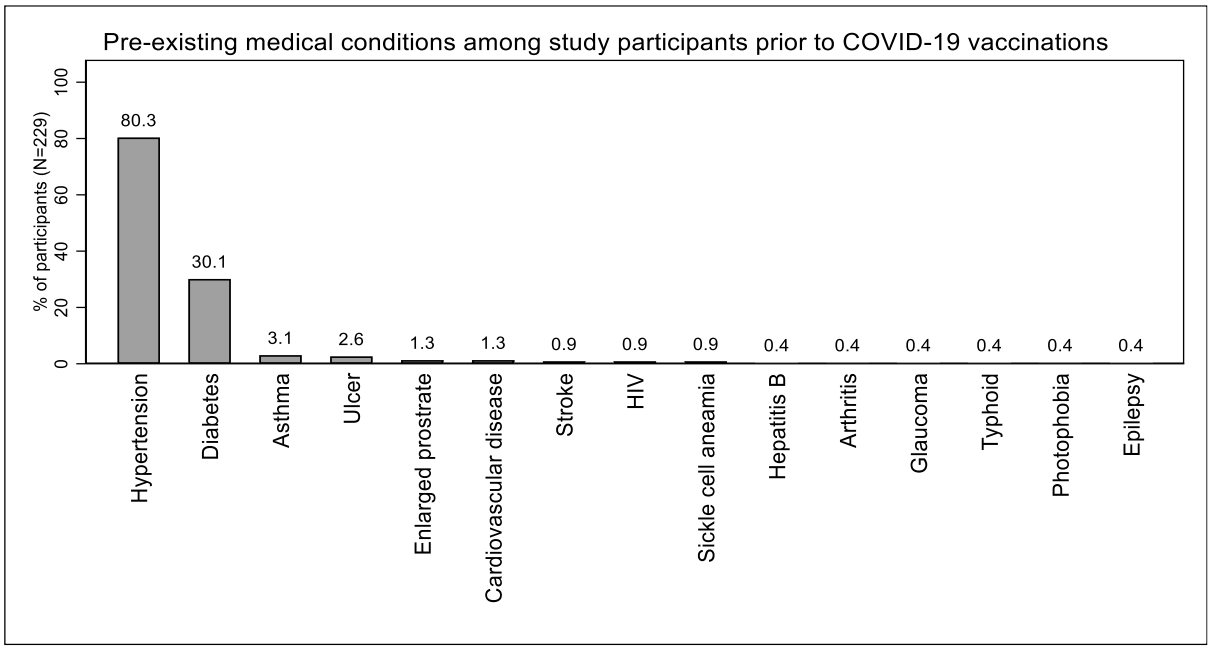


**Figure 4. 1: Pre-existing Medical Conditions among Participants**

### 4.3 Cumulative Incidence of AEFI

The overall cumulative incidence of AEFI among the participants was 16.7% (92/550) (95% CI: 13.8, 20.1). Among the age groups, those who were between the ages of 18 years and 29 years had the highest incidence of AEFI, 26.8% (11/41) (95% CI: 15.5, 42.3). The age group with the lowest incidence of AEFI was those aged 70 years and above, 10.7% (9/92) (95% CI: 5.7, 19.4). Table 4.3 shows that the cumulative incidence of AEFI increased with decreasing age group, thus, the younger the age group, the higher the AEFI incidence and this was statistically significant (p=0.048).

The incidence of AEFI among females was 20.6% (54/262) (95% CI: 16.1, 26.0) and among males was 13.2% (38/250) (95% CI: 9.7, 17.6). The incidence among females and males was statistically significant (p=0.02). The sub-district with the highest incidence was Odupongkpehe, 19.4% (18/93) and Opeikuma had the lowest incidence of 13.1% (13/99). However, the incidence among the sub-districts was not statistically significant (p=0.732).

Table 4. 3: Cumulative Incidence of AEFI among study participants by Age, Sex and Place of Residence

| Variables | Total N | Experienced any AEFI | | | Chi-square | P-value |
|---|---|---|---|---|---|---|
| | | No AEFI n (%) | AEFI n (%) | 95% CI of AEFI | | |
| Total sample size | 550 | 458 (83.3) | 92 (16.7) | (13.8, 20.1) | | |
| **Age group** | | | | | 11.1 | **0.048** |
| 18-29 years | 41 | 30 (73.2) | 11 (26.8) | (15.5, 42.3) | | |
| 30-39 years | 67 | 50 (74.6) | 17 (25.4) | (16.4, 37.1) | | |
| 40-49 years | 72 | 58 (80.6) | 14 (19.4) | (11.9, 30.2) | | |
| 50-59 years | 93 | 77 (82.8) | 16 (17.2) | (10.8, 26.3) | | |
| 60-69 years | 193 | 168 (87.0) | 25 (13.0) | (8.9, 18.5) | | |
| 70+ years | 84 | 75 (89.3) | 9 (10.7) | (5.7, 19.4) | | |
| **Sex** | | | | | 5.4 | **0.020** |
| Female | 262 | 208 (79.4) | 54 (20.6) | (16.1, 26.0) | | |
| Male | 288 | 250 (86.8) | 38 (13.2) | (9.7, 17.6) | | |
| **Sub-Districts** | | | | | 2.0 | 0.732 |
| Akwelley | 110 | 89 (80.9) | 21 (19.1) | (12.8, 27.5) | | |
| Kasoa main | 105 | 87 (82.9) | 18 (17.1) | (11.1, 25.6) | | |
| Kasoa north | 143 | 121 (84.6) | 22 (15.4) | (10.3, 22.3) | | |
| Odupongkpehe | 93 | 75 (80.6) | 18 (19.4) | (12.5, 28.7) | | |
| Opeikuma | 99 | 86 (86.9) | 13 (13.1) | (7.8, 21.3) | | |

All tests are Pearson's chi-square test. CI: confidence interval

The incidence among those who presented symptoms or those without symptoms at the time of vaccination was 16.7%. The incidence among those who presented symptoms at the time of vaccination and those who did not was not statistically significant (p=1.0). Participants with known allergies also had the same incidence of 16.7% as those with unknown allergies. Among them, the incidence was not statistically significant (p=1.0).

Those with pre-existing conditions such as hypertension and diabetes had an AEFI incidence of 17% (39/229) and those without any pre-existing condition had an AEFI incidence of 16.5% (53/321). The incidence among those with or without pre-existing conditions was not statistically significant (p=0.872).

Some participants were taking medications (mostly antihypertensives and antidiabetics) at the time of the vaccination and they had an AEFI incidence of 17.5% (37/212). Those who were

not on any medication at the time of vaccination had an incidence of 16.3% (55/283). The incidence among those taking medication at the time of vaccination and those who were not taking any medication was not statistically significant (p=0.718).

Table 4. 4: Cumulative Incidence of AEFI among Study Participants by Medical History

| | | Experienced any AEFI | | | | |
|---|---|---|---|---|---|---|
| **Variables** | **Total N** | **No AEFI n (%)** | **AEFI n (%)** | **95% CI of AEFI** | **Chi-square** | **P-value** |
| Total sample size | 550 | 458 (83.3) | 92 (16.7) | (13.8, 20.1) | | |
| **Presenting Symptoms at the Time of Vaccination** | | | | | # | 1.000 |
| No symptoms at the time of vaccination | 544 | 453 (83.3) | 91 (16.7) | (13.8, 20.1) | | |
| Any symptoms at the time of vaccination | 6 | 5 (83.3) | 1 (16.7) | (2.3, 63.2) | | |
| **Known Allergies** | | | | | # | 1.000 |
| Allergies absent | 538 | 448 (83.3) | 90 (16.7) | (13.8, 20.1) | | |
| Allergies present | 12 | 10 (83.3) | 2 (16.7) | (4.2, 47.8) | | |
| **Medical Events in the Last 7 days** | | | | | # | 0.247 |
| No Medical event | 537 | 449 (83.6) | 88 (16.4) | (13.5, 19.8) | | |
| Presence of Medical event | 13 | 9 (69.2) | 4 (30.8) | (12.0, 59.1) | | |
| **Pre-existing Conditions (e.g., diabetes, hypertension, etc)** | | | | | 0.0 | 0.872 |
| No medical condition | 321 | 268 (83.5) | 53 (16.5) | (12.8, 21.0) | | |
| Presence of medical condition | 229 | 190 (83.0) | 39 (17.0) | (12.7, 22.5) | | |
| **Medication(s) at the time of Vaccination** | | | | | 0.1 | 0.718 |
| None taken | 338 | 283 (83.7) | 55 (16.3) | (12.7, 20.6) | | |
| On medication at the time | 212 | 175 (82.5) | 37 (17.5) | (12.9, 23.2) | | |
| **Medication(s) in the past 7 days** | | | | | 0.1 | 0.750 |
| No medication | 331 | 277 (83.7) | 54 (16.3) | (12.7, 20.7) | | |
| On medication | 219 | 181 (82.6) | 38 (17.4) | (12.9, 23.0) | | |

#: Fisher's exact chi-square test. All other tests are Pearson's chi-square test. CI: confidence interval

### 4.4 Frequency of AEFI experienced among study participants

The total number of individual AEFIs experienced was 124 and this was among 92 study participants. This is because some participants had more than 1 AEFI. Participants who experienced only 1 AEFI constituted 71.7% (66/92) of all those who had AEFIs and with an AEFI incidence of 12% (66/550). Those who had exactly 2 AEFIs constituted 21.7% (20/92) of all who had AEFIs with an incidence of 3.6% (20/550). The highest number of AEFIs experienced by an individual was 3 and they constituted 6.5% (6/92) of all those who had AEFIs, with an AEFI incidence of 1.1% (6/550).

Among the age groups, 18 to 29 years had the highest AEFI incidence for those who experienced only 1 AEFI (17.1% (7/41)) and those who experienced 2 AEFIs (7.3% (3/41)). For those who experienced 3 AEFIs, the 30 to 39 years group had the highest incidence of 3% (2/67). The age group, 70 years and above, had the lowest AEFI incidence for all the categories – only 1 AEFI (8.3% (7/84)); exactly 2 AEFIs (1.2% (1/84)) and for 3 AEFIs, 1.2% (1/84)). The incidence among the age groups for the number of individual AEFIs was not statistically significant (p=0.38) as shown in Table 4.5.

The incidence of 1 AEFI occurring among females was 13.7% (36/262) and in males was 10.4% (30/288). For 2 AEFIs, the incidence among females was 4.6% (12/262) and males accounted for 2.8% (8/288). No male experienced 3 AEFIs, however, there was a 1.1% (6/262) incidence among females. The incidence of AEFI among sex with respect to the number of individual AEFIs was statistically significant (p=0.015) as shown in Table 4.5.

The Odupongkpehe sub-district had the highest incidence of 14% (13/93) for those who experienced 1 AEFI. For 2 AEFIs, the Kasoa Main sub-district had the highest incidence of 5.7% (6/105). The Akwelley sub-district had the highest incidence of 1.8% (2/110) for participants who experienced 3 AEFIs. The incidence among the groups was not statistically significant (p=0.85).

For participants who had medical events in the last 7 days before receiving the vaccine, there was a 30.8% (4/13) incidence for those who experienced 1 AEFI and none of them experienced more than 2 AEFIs. The incidence among the two groups was not statistically significant (p=0.22).

The incidence in those with pre-existing conditions was 10.9% (25/229) for those who experienced 1 AEFI. Those who experienced 2 and 3 AEFIs had 4.4% (10/229) and 1.7% (4/229) as their cumulative incidences respectively. The incidence among the two groups was not statistically significant (p=0.47).

Participants who were on medications in the past 7 days prior to vaccination had the following incidences: 11.9% (26/219) for 1 AEFI, 4.1% (9/219) for 2 AEFIs and 1.4% (3/219) for 3 AEFIs. Some participants were not on any medication in the past 7 days prior to vaccination and their incidences are as follows: 12.1% (40/331) for 1 AEFI, 3.3% (11/331) for 2 AEFIs and 0.9% (3/331) for 3 AEFIs. The incidence among the two groups was not statistically significant (p=0.89).

Table 4. 5: Number of AEFI experienced among Study Participants

| | | Number of AEFI conditions | | | | |
|---|---|---|---|---|---|---|
| **Variables** | Total N | None n (%) | 1 AEFI n (%) | 2 AEFIs n (%) | 3 AEFIs n (%) | P-value |
| Total sample size | 550 | 458 (83.3) | 66 (12.0) | 20 (3.6) | 6 (1.1) | |
| **Age (years), median (IQR)** | | 60.0 (46.0, 66.0) | 51.0 (38.0, 63.0) | 49.5 (34.5, 63.0) | 47.5 (34.0, 65.0) | 0.005 K |
| **Age group** | | | | | | 0.380 |
| 18-29 years | 41 | 30 (73.2) | 7 (17.1) | 3 (7.3) | 1 (2.4) | |
| 30-39 years | 67 | 50 (74.6) | 11 (16.4) | 4 (6.0) | 2 (3.0) | |
| 40-49 years | 72 | 58 (80.6) | 11 (15.3) | 3 (4.2) | 0 (0.0) | |
| 50-59 years | 93 | 77 (82.8) | 12 (12.9) | 4 (4.3) | 0 (0.0) | |
| 60-69 years | 193 | 168 (87.0) | 18 (9.3) | 5 (2.6) | 2 (1.0) | |
| 70+ years | 84 | 75 (89.3) | 7 (8.3) | 1 (1.2) | 1 (1.2) | |
| **Sex** | | | | | | 0.015 |
| Female | 262 | 208 (79.4) | 36 (13.7) | 12 (4.6) | 6 (2.3) | |
| Male | 288 | 250 (86.8) | 30 (10.4) | 8 (2.8) | 0 (0.0) | |
| **Sub-Districts** | | | | | | 0.850 |
| Akwelley | 110 | 89 (80.9) | 14 (12.7) | 5 (4.5) | 2 (1.8) | |
| Kasoa main | 105 | 87 (82.9) | 11 (10.5) | 6 (5.7) | 1 (1.0) | |
| Kasoa north | 143 | 121 (84.6) | 18 (12.6) | 2 (1.4) | 2 (1.4) | |

| Variables | Total N | Number of AEFI conditions: None n (%) | 1 AEFI n (%) | 2 AEFIs n (%) | 3 AEFIs n (%) | P-value |
|---|---|---|---|---|---|---|
| Odupongkpehe | 93 | 75 (80.6) | 13 (14.0) | 4 (4.3) | 1 (1.1) | |
| Opeikuma | 99 | 86 (86.9) | 10 (10.1) | 3 (3.0) | 0 (0.0) | |
| **Presenting Symptoms at the Time of Vaccination** | | | | | | 0.670 |
| No symptoms at the time of vaccination | 544 | 453 (83.3) | 65 (11.9) | 20 (3.7) | 6 (1.1) | |
| Any symptoms at the time of vaccination | 6 | 5 (83.3) | 1 (16.7) | 0 (0.0) | 0 (0.0) | |
| **Known Allergies** | | | | | | 0.810 |
| Allergies absent | 538 | 448 (83.3) | 64 (11.9) | 20 (3.7) | 6 (1.1) | |
| Allergies present | 12 | 10 (83.3) | 2 (16.7) | 0 (0.0) | 0 (0.0) | |
| **Medical Events in the Last 7 days** | | | | | | 0.220 |
| No Medical event | 537 | 449 (83.6) | 62 (11.5) | 20 (3.7) | 6 (1.1) | |
| Presence of Medical event | 13 | 9 (69.2) | 4 (30.8) | 0 (0.0) | 0 (0.0) | |
| **Pre-existing Conditions (e.g., diabetes, hypertension, etc)** | | | | | | 0.470 |
| No medical condition | 321 | 268 (83.5) | 41 (12.8) | 10 (3.1) | 2 (0.6) | |
| Presence of medical condition | 229 | 190 (83.0) | 25 (10.9) | 10 (4.4) | 4 (1.7) | |
| **Medication(s) at the time of Vaccination** | | | | | | 0.850 |
| None taken | 338 | 283 (83.7) | 41 (12.1) | 11 (3.3) | 3 (0.9) | |
| On medication at the time | 212 | 175 (82.5) | 25 (11.8) | 9 (4.3) | 3 (1.4) | |
| **Medication(s) in the past 7 days** | | | | | | 0.890 |
| No medication | 331 | 277 (83.7) | 40 (12.1) | 11 (3.3) | 3 (0.9) | |
| On medication | 219 | 181 (82.6) | 26 (11.9) | 9 (4.1) | 3 (1.4) | |

[K]: P-value from the Kruskal Wallis test. All other p-values are from Fisher's exact chi-square test

### 4.5 Time to Onset of AEFI

The median time to onset for AEFI occurrence was 1 day (IQR=1, 1). Within 24 hours of immunization, three participants (3.26%) had AEFI, and by the next day, 92.39% (85/92) had developed 1 or more AEFIs. The maximum number of days it took for one to experience AEFI was seven.

### 4.6 Severity of AEFI conditions among participants who experienced any AEFI

The severity of the AEFIs experienced by the participants was categorized into mild (grade 1), moderate (grade 2), severe (grade 3), potentially life-threatening (grade 4) and death (grade 5)

using the DAIDS grading system. None of the AEFIs had a grading above grade 3 as shown in Table 4.6. Out of the total number of persons who experienced AEFIs (92), 77.2% (71/92) were graded as Mild, 20.7% (19/92) as Moderate and 2.2% (2/92) graded as severe. The incidence of Mild AEFIs was 12.91% (71/550), those graded Moderate was 3.45% (19/550) and the severe AEFIs had an incidence of 0.36% (2/550) as indicated in Table 4.6.

Of all the AEFIs for participants aged 18 to 29 years, 100% (11/11) were graded as Mild. For those in the 30 to 39 years group, 94.1% (16/17) were graded as Mild and 5.9% (1/17) as Moderate. AEFIs graded as Mild for the 40 to 49 years group constituted 78.6% (11/14) whiles 21.4% (3/14) were graded as Moderate. The AEFIs recorded by those aged 50 to 59 years had 87.5% (14/16) graded as Mild and 12.5% (2/16) as Moderate. There were 2 cases graded as severe with 1 occurring among the 60 to 69 years old and the other experienced among those in the 70-year plus group. The severity of AEFI among the age groups was statistically significant (p=0.049).

Most of the AEFIs in both sexes were graded as Mild – male (86.8% (33/38)) and female (70.4% (38/54)). Both sexes had a case each of Severe AEFI, however, 27.8% of the AEFIs experienced by females were graded as Moderate as indicated in Table 4.6.

All the severe AEFIs were recorded by participants from the Akwelley sub-district. For AEFIs graded Moderate, the Akwelley sub-district had the most occurrences of 23.8% (5/21). Table 4.6 shows the severity of AEFI per sub-district.

Only 1 participant among those who presented symptoms at the time of vaccination had AEFI and was graded as Mild. Also, 2 participants with known allergies and 4 participants with medical events in the last 7 days had AEFIs but they were all graded as Mild.

All (5.1%) severe AEFIs occurred among those with a pre-existing condition. Those who had Mild AEFIs were 61.5% (24/39) and those with Moderate AEFIs were 33.3% (13/39). The

AEFIs were more severe in those with pre-existing conditions than those who were not and the severity among these groups was statistically significant (p=0.006).

Participants who were on medications at the time of vaccination and in the past 7 days had a similar pattern in terms of severity of the AEFIs. The severe cases were found among those who were on medications whether at the time of vaccination (5.4% (2/37)) or the past 7 days (5.3% (2/38)). The severity among these groups was statistically significant (p=0.002).

Table 4. 6: Severity of AEFI conditions among Participants who experienced any AEFI

| | | Severity of AEFI experienced | | | |
|---|---|---|---|---|---|
| **Variables** | Total N | Mild n (%) | Moderate n (%) | Severe n (%) | P-value |
| Total sample size | 550 | 71 (12.9) | 19 (3.5) | 2 (0.4) | |
| Total AEFIs | 92 | 71 (77.2) | 19 (20.7) | 2 (2.2) | |
| **Age (years), median (IQR)** | | 48.0 (34.0, 60.0) | 63.0 (53.0, 66.0) | 65.0 (60.0, 70.0) | <0.001 K |
| **Age group** | | | | | 0.049 |
| 18-29 years | 11 | 11 (100.0) | 0 (0.0) | 0 (0.0) | |
| 30-39 years | 17 | 16 (94.1) | 1 (5.9) | 0 (0.0) | |
| 40-49 years | 14 | 11 (78.6) | 3 (21.4) | 0 (0.0) | |
| 50-59 years | 16 | 14 (87.5) | 2 (12.5) | 0 (0.0) | |
| 60-69 years | 25 | 14 (56.0) | 10 (40.0) | 1 (4.0) | |
| 70+ years | 9 | 5 (55.6) | 3 (33.3) | 1 (11.1) | |
| **Sex** | | | | | 0.073 |
| Female | 54 | 38 (70.4) | 15 (27.8) | 1 (1.9) | |
| Male | 38 | 33 (86.8) | 4 (10.5) | 1 (2.6) | |
| **Sub-Districts** | | | | | 0.820 |
| Akwelley | 21 | 14 (66.7) | 5 (23.8) | 2 (9.5) | |
| Kasoa main | 18 | 14 (77.8) | 4 (22.2) | 0 (0.0) | |
| Kasoa north | 22 | 18 (81.8) | 4 (18.2) | 0 (0.0) | |
| Odupongkpehe | 18 | 15 (83.3) | 3 (16.7) | 0 (0.0) | |
| Opeikuma | 13 | 10 (76.9) | 3 (23.1) | 0 (0.0) | |
| **Presenting Symptoms at the Time of Vaccination** | | | | | 1.000 |
| No symptoms at the time of vaccination | 91 | 70 (76.9) | 19 (20.9) | 2 (2.2) | |
| Symptoms at the time of vaccination | 1 | 1 (100.0) | 0 (0.0) | 0 (0.0) | |
| **Known Allergies** | | | | | 1.000 |
| Allergies absent | 90 | 69 (76.7) | 19 (21.1) | 2 (2.2) | |
| Allergies present | 2 | 2 (100.0) | 0 (0.0) | 0 (0.0) | |
| **Medical Events in the Last 7 days** | | | | | 0.610 |
| No Medical event | 88 | 67 (76.1) | 19 (21.6) | 2 (2.3) | |
| Presence of Medical event | 4 | 4 (100.0) | 0 (0.0) | 0 (0.0) | |

| Variables | Total N | Severity of AEFI experienced | | | P-value |
|---|---|---|---|---|---|
| | | Mild n (%) | Moderate n (%) | Severe n (%) | |
| **Pre-existing Conditions (e.g., diabetes, hypertension, etc)** | | | | | 0.006 |
| No medical condition | 53 | 47 (88.7) | 6 (11.3) | 0 (0.0) | |
| Presence of medical condition | 39 | 24 (61.5) | 13 (33.3) | 2 (5.1) | |
| **Medication(s) at the time of Vaccination** | | | | | 0.002 |
| None taken | 55 | 49 (89.1) | 6 (10.9) | 0 (0.0) | |
| On medication at the time | 37 | 22 (59.5) | 13 (35.1) | 2 (5.4) | |
| **Medication(s) in the past 7 days** | | | | | 0.003 |
| No medication | 54 | 48 (88.9) | 6 (11.1) | 0 (0.0) | |
| On medication | 38 | 23 (60.5) | 13 (34.2) | 2 (5.3) | |

$^{K}$: P-value from the Kruskal Wallis test. All other p-values are from Fisher's exact chi-square test

### 4.7 AEFI Classification

Each AEFI was grouped based on the MedDRA classification – "System Organ Class (SOC), High Level Term (HLT) and Preferred Term (PT)". For SOC, the proportion of persons who experienced General disorders and administration site conditions accounted for 85.9% (79/92) of the total AEFIs; followed by Nervous System Disorders also accounted for 28.3% (26/92) as shown in Figure 4.2.

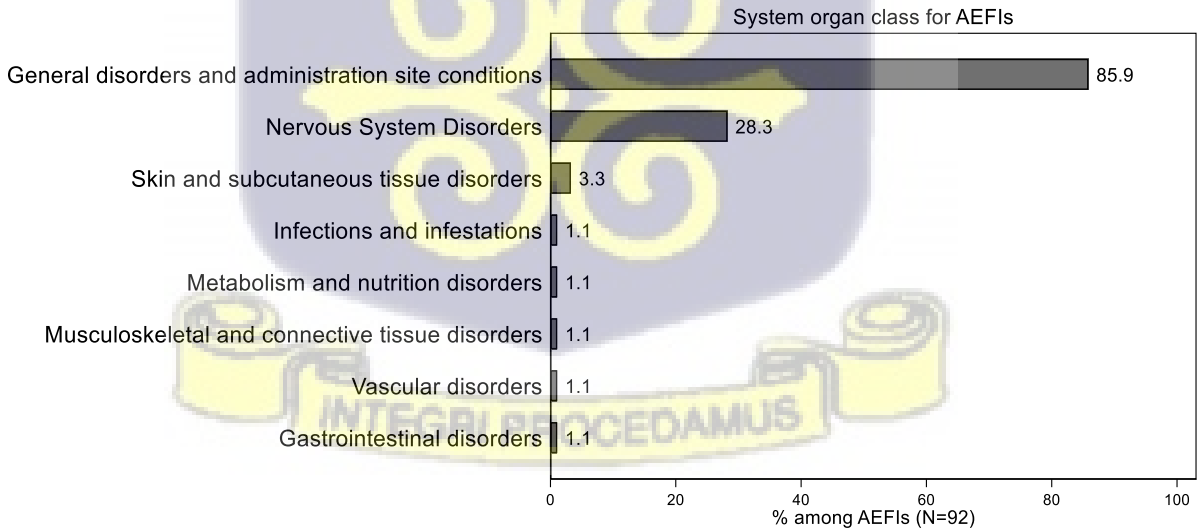


**Figure 4. 2: AEFI classified by *System Organ Class* among Participants**

For HLT classification, the proportion of persons who experienced Asthenic conditions accounted for the highest AEFIs (32.6% (30/92)); followed by Headaches NEC (28.3% (26/92)), Body Pain and Discomfort NEC (18.5% (17/92)). There were Injection site reactions and Febrile disorders that each also accounted for 17.4% (16/92)) as indicated in figure 4.3.

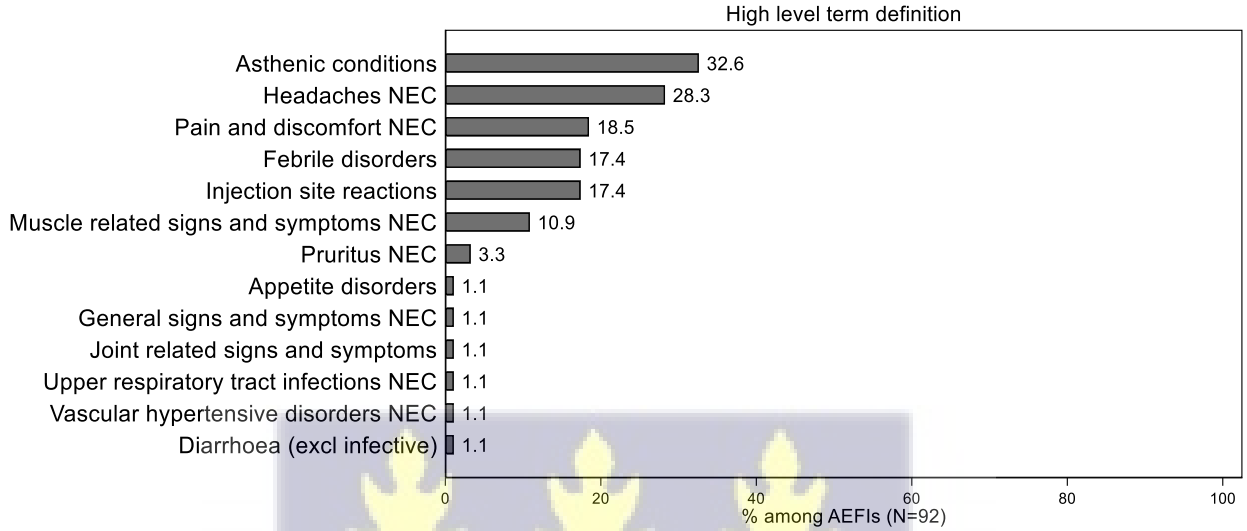


**Figure 4. 3: AEFI classified by *High Level Term* among Participants**

The AEFIs were also classified based on Preferred Term with persons who experienced Asthenia being the highest (32.6% (30/92)); followed by Headache (28.3% (26/92)), and Body Pain (18.5% (17/92)). Among AEFI descriptions depicted in Figure 4.4 include Pyrexia, injection site pain and swelling.

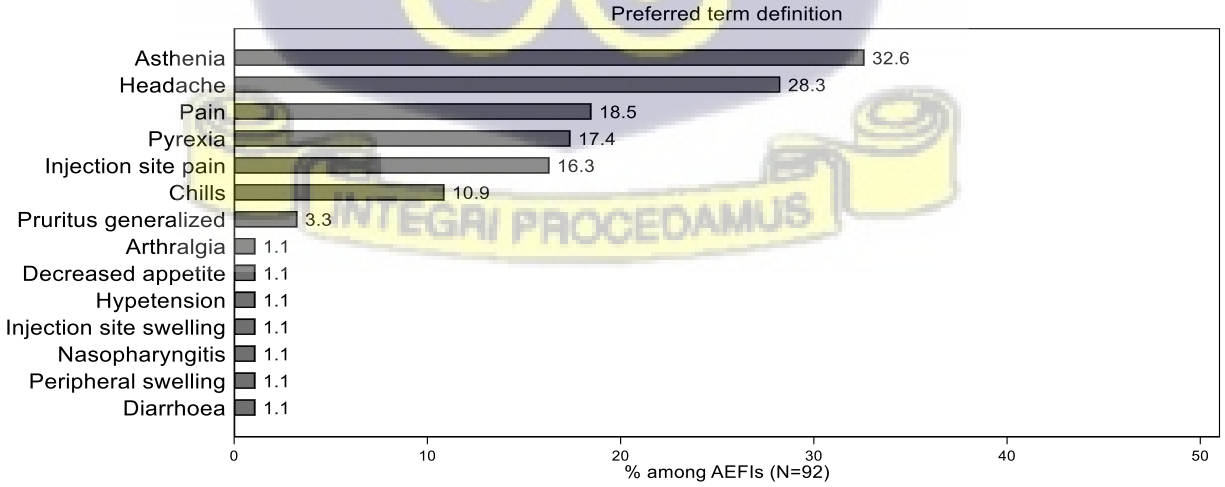


**Figure 4. 4: AEFI classified by *Preferred Term* among Participants**

### 4.8 Association between AEFI Severity and Number of AEFI per Participant

Figure 4.5 shows that 74.6% (53/71) of the Mild AEFIs were participants who had only 1 AEFI; 21.1% (15/71) of the Mild AEFIs were participants who had 2 AEFIs and those who had 3 AEFIs constituted 4.2% (3/71) of the Mild AEFIs. For AEFIs graded Moderate, 68.4% (13/19) were participants who had only 1 AEFI; 21.1% (4/19) were those who had 2 AEFIs and 10.5% (2/19) had 3 AEFIs. There were 2 severe AEFIs; 50% (1/2) each in those who had 2 AEFIs and 3 AEFIs. There was no association between the severity of AEFIs and the number of AEFIs experienced by a participant (p= 0.578).

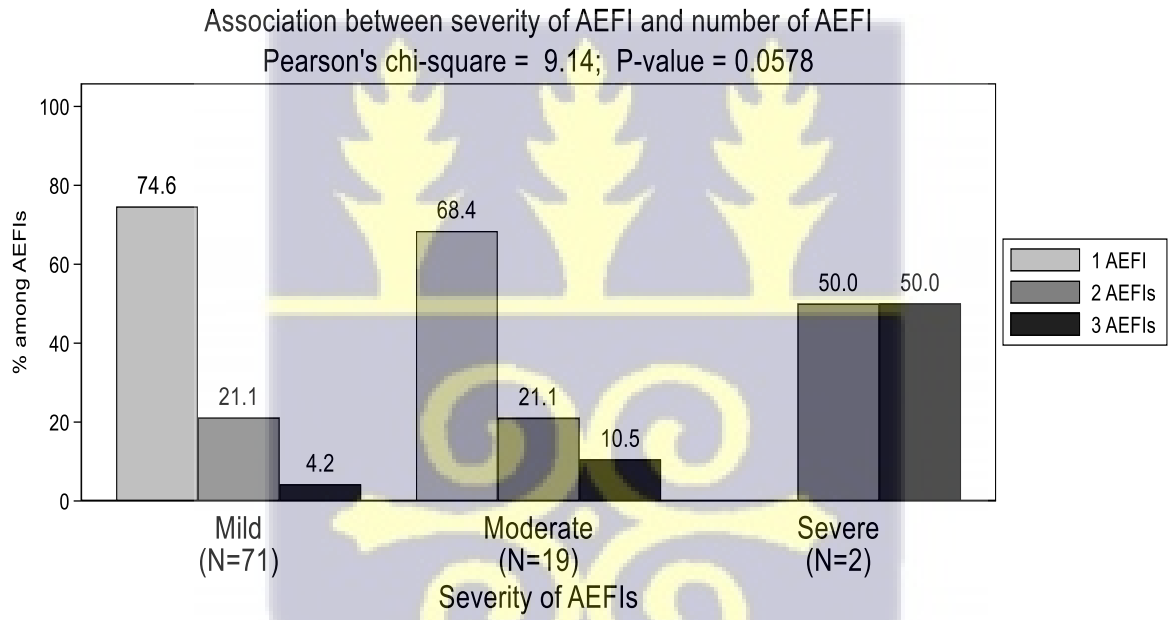


**Figure 4. 5: Association between Severity of AEFI and Number of AEFI**

### 4.9: Outcome of AEFI

All the participants recovered fully within a minimum of 1 day to 7 days maximum of experiencing AEFI as indicated in Figure 4.6. The median time from onset of AEFI to recovery was 2 days (2, 3). More than half of the participants (52.2% (48/92)) had recovered by the end of the 2nd day of experiencing AEFI. By the end of the 4th day, 94.6% (87/92). No one had serious AEFI that was life-threatening, resulting in hospitalization or death.

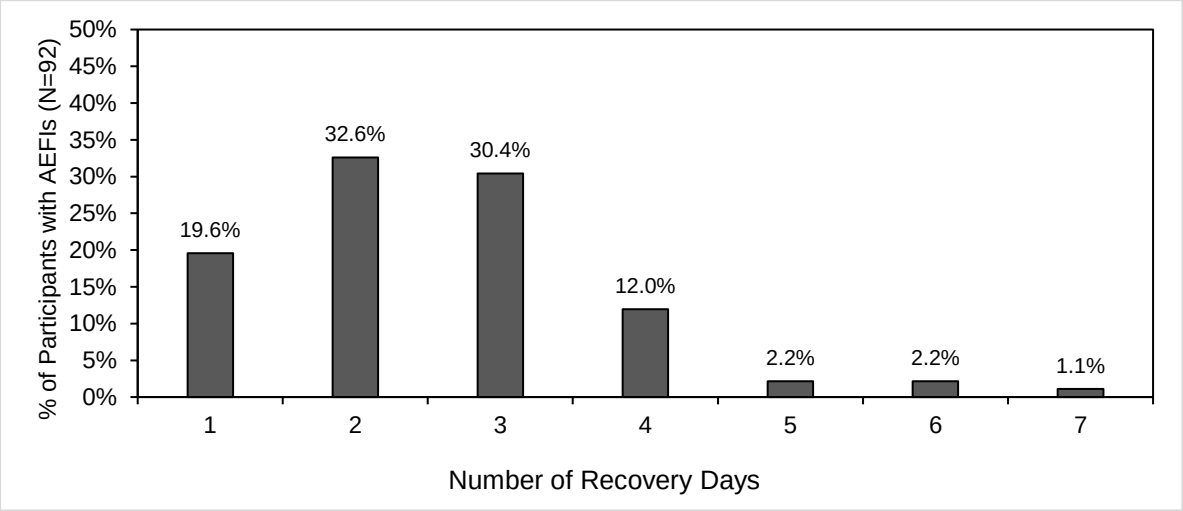


**Figure 4. 6: Maximum Recovery Days among Participants with AEFIs**

The association between the number of recovery days and the severity of AEFI was analyzed. All those who recovered a day after experiencing AEFI were Mild (18/18); this was similar for those who recovered by the end of the second day (30/30). None of the AEFIs graded moderate and severe recovered by the end of the first or second days. For the third day of recovery, 75% (21/28) of the recoveries were mild while 25% (7/28) were moderate. The majority (81.8% (9/11)) of recoveries on the fourth day were moderate AEFIs, with the rest being Mild. Those who had severe AEFIs recovered on the sixth (50% (1/2)) and seventh (100% (1/1)) days as shown in figure 4.7. The data shows that increased AEFI severity means longer recovery days and this was statistically significant (p=0.0000).

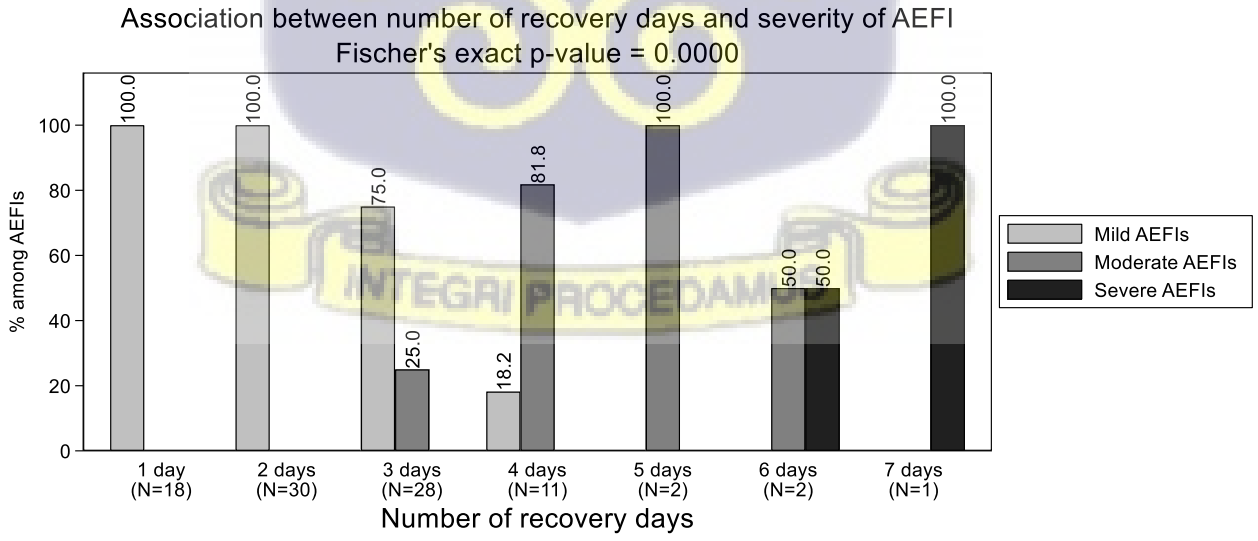


**Figure 4. 7: Association between Number of Recovery Days and Severity of AEFIs**

Also, the association between the number of recovery days and the number of AEFIs experienced per participant was assessed. Figure 4.8 shows the distribution of AEFIs per participant and their recovery days. A participant who had 2 AEFIs was the only one to recover on the seventh day. Two people recovered on the sixth day and they all had 3 AEFIs. The two participants who recovered on the fifth day had only 1 AEFI. Among those who recovered by the second day, 7.1% (2/28) were in the 3 AEFIs category. There was no association between the number of recovery days and the number of AEFIs experienced per participant (P = 0.134).

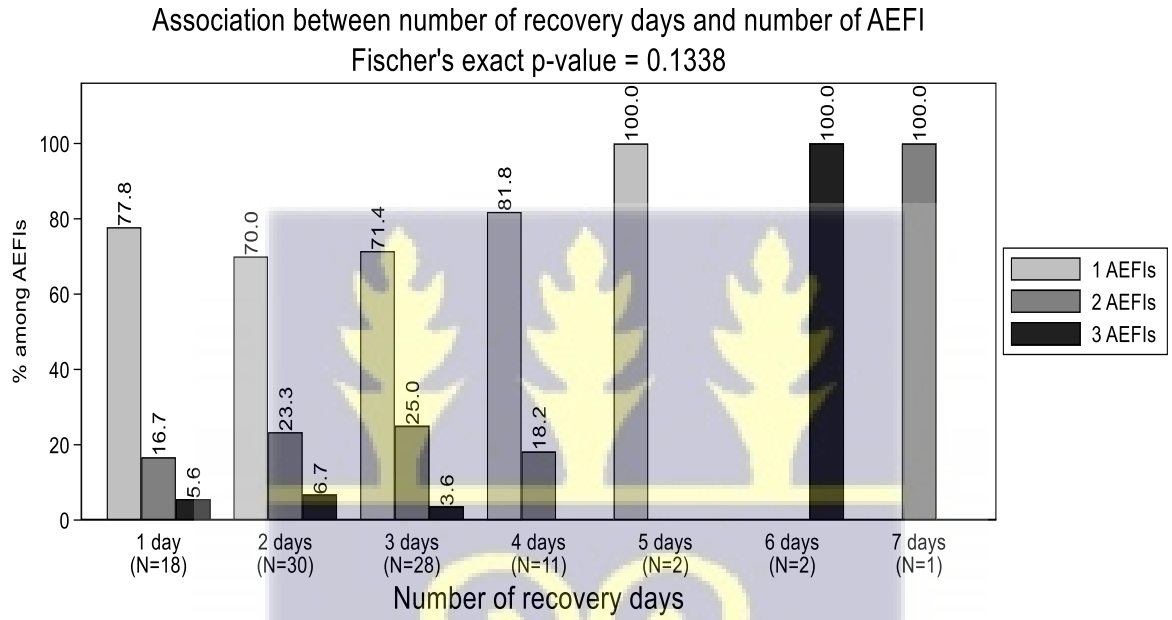


**Figure 4. 8: Association between Number of Recovery Days and Number of AEFIs**

### 4.10 Risk of AEFI Incidence among Study Participants

Table 4.7 shows the risk of AEFI incidence among study participants. The various age groups were compared to those aged 70 years and above which had the lowest AEFI incidence. For the unadjusted model, the risk of AEFI incidence among those aged 18 to 29 years was 2.5 times as high as the risk of AEFI in those aged 70 years and over. This was statistically significant (uRR = 2.50, 95% CI: 1.04, 6.04; P =0.041). When only time was adjusted, the risk increased to 3 times as high in those aged 18 to 29 years as compared to those aged 70 years and above (aRR1 =3.03, 95% CI: 1.26, 7.31; P = 0.014). The risk further increased to about 4

times as high in the 18-to-29-age group compared to the 70 years and above age group when all parameters were adjusted (Table 4.7). This was also statistically significant (aRR2 =3.93, 95% CI: 1.52, 10.17; P = 0.005). The 30 to 39 years group also had 2.37 times as high risk of AEFI incidence compared to those aged 70 years and over in the unadjusted model (uRR =2.37, 95% CI: 1.06, 5.31; P = 0.036). There was a steady increase of the risk in the 30 to 39 years group to 2.77 times as high compared to those aged 70 and above when only time was adjusted (aRR1 =2.77, 95% CI: 1.23, 6.21; P = 0.014). When all other variables were adjusted, the risk of AEFI incidence in the 30 to 39 years group increased to 4 times as high compared to those aged 70 years and over (aRR2 =4.11, 95% CI: 1.68, 10.08; P = 0.002) as indicated in Table 4.7.

From Table 4.7, the risk of AEFI incidence was 56% higher in females than in males and this was statistically significant (uRR =1.56, 95% CI: 1.03, 2.37; P = 0.035). When only time was adjusted, the risk increased to 71% in females compared to males (aRR1 =1.71, 95% CI: 1.13, 2.59; P = 0.011). When all parameters were adjusted, the risk of AEFI incidence was 65% higher in females than in males and this was also statistically significant (aRR2 =1.65, 95% CI: 1.08, 2.52; P = 0.021).

The risk of AEFI incidences for various sub-districts was compared to AEFI incidence in the Opeikuma sub-district. The highest risk of AEFI incidence among the sub-districts compared to Opeikuma was Odupongkpehe with a 47% higher risk in the unadjusted model (uRR =1.47, 95% CI: 0.72, 3.01; P = 0.286) and 58% higher risk in the time-only adjusted model (uRR =1.58, 95% CI: 0.77, 3.22; P = 0.210). From Table 4.7, the adjusted model, the risk of AEFI incidence was 92% higher in Odupongkpehe than Opeikuma and was not statistically significant (aRR =1.92, 95% CI: 0.92, 4.01; P = 0.083). The rest of the sub-districts compared to Opeikuma for all models have been indicated in Table 4.7. None of the relative risks was statistically significant.

There was no difference in the risk of AEFI incidence among those who presented symptoms at the time of vaccination and those who did not present symptoms at the time of vaccination for both unadjusted and time-only adjusted models. This was not statistically significant for the unadjusted (uRR =1.00, 95% CI: 0.14, 7.15; P = 0.997) and the time-only adjusted (aRR1 =1.00, 95% CI: 0.14, 7.17; P = 0.999). There was, however, a 41% reduced risk of AEFI incidence among those who presented symptoms at the time of vaccination compared to those who did not present symptoms at the time of vaccination when all parameters were adjusted but were not statistically significant (aRR2 = 0.59, 95% CI: 0.08, 4.48; P = 0.614).

There was no difference in the risk of AEFI incidence among those with known allergies and those without known allergies for both unadjusted and time-only adjusted models. This was not statistically significant for the unadjusted (uRR =1.00, 95% CI: 0.25, 4.05; P = 0.996) and the time-only adjusted (aRR1 =1.00, 95% CI: 0.25, 4.05; P = 0.996). There was, however, a 22% reduced risk of AEFI incidence among those with known allergies compared to those without known allergies when all parameters were adjusted but was not statistically significant (aRR2 = 0.78, 95% CI: 0.18, 3.29; P = 0.731).

From table 4.7, those who had medical events in the past 7 days before receiving the vaccine had an increased risk of 88% in the unadjusted model (uRR =1.88, 95% CI: 0.69, 5.11; P = 0.218) and 2.26 times as higher risk in the time-only model (aRR1 =1.00, 95% CI: 0.83, 6.17; P = 0.110) compared to those who did not have any medical events in the past 7 days prior to vaccination. When all parameters were adjusted, the risk of AEFI incidence among those who had medical events in the past 7 days prior to receiving the vaccine was 2.46 times higher compared to those who had no medical events in the past 7 days prior to receiving the vaccine (aRR2 = 2.46, 95% CI: 0.83, 7.22; P = 0.103).

There was a slightly increased risk of AEFI incidence among those with pre-existing conditions compared to those without pre-existing conditions. There was 3% increased risk in the

unadjusted model (uRR =1.03, 95% CI: 0.68, 1.56; P = 0.883), 4% in the time-only adjusted model (aRR1 =1.04, 95% CI: 0.69, 1.57; P = 0.848) and 22% increased risk when all parameters were adjusted (aRR2 =1.22, 95% CI: 0.50, 3.02; P = 0.664).

The risk of AEFI incidence among those who had been on medications in the past 7 days prior to taking the vaccination was 6% as high compared to those who were not on any medication in the unadjusted model (uRR =1.06, 95% CI: 0.70, 1.61; P = 0.771) and 8% as high in the time-only adjusted model (aRR1 =1.08, 95% CI: 0.71, 1.64; P = 0.716). There was, however, a 31% reduced risk of AEFI incidence among participants who were on medication in the past 7 days prior to vaccination compared to those who were not on any medications in the past 7 days when all parameters were adjusted (aRR2 = 0.69, 95% CI: 0.08, 5.77; P = 0.731). This was not statistically significant.

**Table 4. 7: Poisson regression model of the Incidence of AEFI among Study Participants**



| | | | Poisson regression model of the incidence of AEFI among study participants | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | AEFI | unadjusted model | | Time adjusted model 1 | | Time Adjusted model 2 | |
| **Variables** | **N** | **n (%)** | **uRR (95% CI)** | **P-value** | **aRR1 (95% CI)** | **P-value** | **aRR2 (95% CI)** | **P-value** |
| **Total sample size** | 550 | 92 (16.7) | | | | | | |
| **Age group** | | | | | | | | |
| 18-29 years | 41 | 11 (26.8) | 2.50 (1.04, 6.04) | **0.041** | 3.03 (1.26, 7.31) | **0.014** | 3.93 (1.52, 10.17) | **0.005** |
| 30-39 years | 67 | 17 (25.4) | 2.37 (1.06, 5.31) | **0.036** | 2.77 (1.23, 6.21) | **0.014** | 4.11 (1.68, 10.08) | **0.002** |
| 40-49 years | 72 | 14 (19.4) | 1.81 (0.79, 4.19) | 0.163 | 2.00 (0.87, 4.62) | 0.105 | 2.65 (1.10, 6.37) | **0.029** |
| 50-59 years | 93 | 16 (17.2) | 1.61 (0.71, 3.63) | 0.256 | 1.73 (0.76, 3.91) | 0.189 | 1.71 (0.74, 3.95) | 0.211 |
| 60-69 years | 193 | 25 (13.0) | 1.21 (0.56, 2.59) | 0.625 | 1.24 (0.58, 2.65) | 0.582 | 1.26 (0.58, 2.70) | 0.561 |
| 70+ years | 84 | 9 (10.7) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| **Sex** | | | | | | | | |
| Female | 262 | 54 (20.6) | 1.56 (1.03, 2.37) | **0.035** | 1.71 (1.13, 2.59) | **0.011** | 1.65 (1.08, 2.52) | **0.021** |
| Male | 288 | 38 (13.2) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| **Sub-Districts** | | | | | | | | |
| Akwelley | 110 | 21 (19.1) | 1.45 (0.73, 2.90) | 0.289 | 1.54 (0.77, 3.08) | 0.220 | 1.91 (0.94, 3.88) | 0.074 |
| Kasoa main | 105 | 18 (17.1) | 1.31 (0.64, 2.66) | 0.464 | 1.37 (0.67, 2.79) | 0.390 | 1.71 (0.82, 3.57) | 0.150 |
| Kasoa north | 143 | 22 (15.4) | 1.17 (0.59, 2.33) | 0.651 | 1.20 (0.61, 2.38) | 0.601 | 1.50 (0.74, 3.03) | 0.262 |
| Odupongkpehe | 93 | 18 (19.4) | 1.47 (0.72, 3.01) | 0.286 | 1.58 (0.77, 3.22) | 0.210 | 1.92 (0.92, 4.01) | 0.083 |
| Opeikuma | 99 | 13 (13.1) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| **Presenting Symptoms at the Time of Vaccination** | | | | | | | | |
| No symptoms at the time of vaccination | 544 | 91 (16.7) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| Any symptoms at the time of vaccination | 6 | 1 (16.7) | 1.00 (0.14, 7.15) | 0.997 | 1.00 (0.14, 7.17) | 0.999 | 0.59 (0.08, 4.48) | 0.614 |
| **Known Allergies** | | | | | | | | |
| Allergies absent | 538 | 90 (16.7) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| Allergies present | 12 | 2 (16.7) | 1.00 (0.25, 4.05) | 0.996 | 1.00 (0.25, 4.05) | 0.999 | 0.78 (0.18, 3.29) | 0.731 |
| **Medical Events (sickness) in the Last 7 days** | | | | | | | | |
| No Medical event | 537 | 88 (16.4) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| Presence of Medical event | 13 | 4 (30.8) | 1.88 (0.69, 5.11) | 0.218 | 2.26 (0.83, 6.17) | 0.110 | 2.46 (0.83, 7.22) | 0.103 |
| **Pre-existing Conditions (e.g., diabetes, hypertension, etc)** | | | | | | | | |
| No medical condition | 321 | 53 (16.5) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| Presence of medical condition | 229 | 39 (17.0) | 1.03 (0.68, 1.56) | 0.883 | 1.04 (0.69, 1.57) | 0.848 | 1.22 (0.50, 3.02) | 0.664 |
| **Medication(s) at the time of Vaccination** | | | | | | | | |
| None taken | 338 | 55 (16.3) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| On medication at the time | 212 | 37 (17.5) | 1.07 (0.71, 1.63) | 0.742 | 1.09 (0.72, 1.65) | 0.683 | 2.21 (0.26, 18.76) | 0.467 |
| **Medication(s) in the past 7 days** | | | | | | | | |
| No medication | 331 | 54 (16.3) | 1.00 reference | | 1.00 (reference) | | 1.00 (reference) | |
| On medication | 219 | 38 (17.4) | 1.06 (0.70, 1.61) | 0.771 | 1.08 (0.71, 1.64) | 0.716 | 0.69 (0.08, 5.77) | 0.731 |

AEFI: adverse event following immunization. uRR: unadjusted risk ratio. aRR: adjusted risk ratio. CI: confidence interval
Time adjusted model 1: Time to experience of AEFI was only controlled for.
Time adjusted model 2: Time to experience AEFI, age group, sex, sub-districts, symptoms at time of vaccination, known allergies, medical event in last 7 days, pre-existing conditions, medication at time of vaccination and medication in the past 7 days were adjusted.

The predictive strength of the final Poisson regression model using AUROCC showed a predictiveness of 65.4% (95% CI: 59.1% to 71.7%). This was above 50% and closer to 100% than 0. Hence, the predictive strength of the Poisson regression model was indicative of a good measure of separability – in this case, between those who had AEFIs and those who did not after receiving the COVID-19 vaccine. The Deviance goodness of fit test yielded a non-significant p-value of 0.9881, suggesting that the final model was properly fit. The multicollinearity between the independent variables in the final model had a mean estimate of 2.45 (minimum= 1.04 and maximum = 8.57), all below the threshold of 10. This indicated acceptable levels of multicollinearity in the final model.

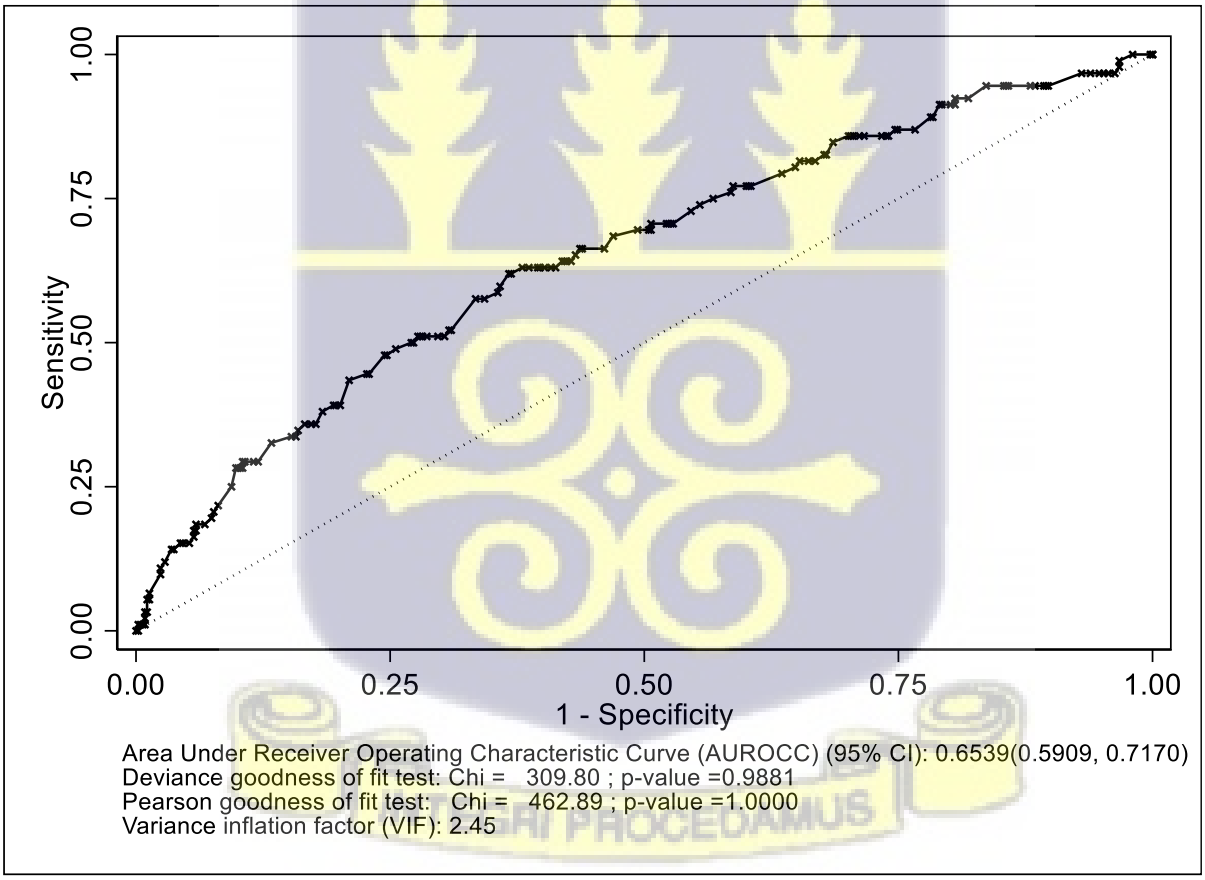


**Figure 4. 9: Model assessment of the multivariable Poisson regression model**

# CHAPTER FIVE

# DISCUSSION

## 5.1 Cumulative Incidence of AEFI

The overall cumulative incidence of AEFI among the participants in Awutu Senya East Municipality was lower, compared to incidences of AEFIs associated with the COVISHIELD vaccine found in other studies.

According to Folegatti et al., 2020, the treatment group had a greater incidence of AEFI. Ramasamy et al., 2020, also found an increased AEFI incidence following the first dose in another clinical trial conducted in the United Kingdom. When the vaccine was used in the real world, Kaur et al., 2021, observed a greater AEFI incidence following the first dose in a study in north India; and Kamal et al., 2021, reported a similar increase in AEFI incidence following the first dose in south India. Additionally, Shrestha et al., 2021, observed a greater incidence of AEFI in Nepal. COVISHIELD AEFI incidence varies by population. The AEFI incidence for COVISHIELD varies with different populations. These differences in incidences with varying geographical populations were also observed among the sub-districts where participants were selected. For instance, Odupongkpehe had a higher AEFI incidence than Opeikuma. Different administrative techniques used by healthcare experts in charge of the various immunization centres might have accounted for the variations in incidences at the various geographical locations (Masika et al., 2016; Zuckerman JN, 2000). Different sensitization approaches used before vaccination may have influenced the public's varying ability to detect adverse events after immunization.

The younger age groups had higher AEFI incidences compared to the older age groups with the highest incidence in those aged 18 years to 29 years and the lowest incidence in those aged 70 years and above. The cumulative incidence of AEFI increased with decreasing age group and this

is similar to what Ramasamy et al., 2020, found after participants had received the standard dose. Jayadevan et al., (2021) also reported a similar trend among the age groups, that as people became older, their chances of developing AEFIs decreased. In the study conducted by Kataria et al., 2021, participants aged >50 years had lower reactogenicity. Although the incidence of AEFI decreased with increasing age, the AEFIs experienced were more severe in those aged 60 years and above. This might be because old age brings its own set of health issues; as a result, mild occurrences associated with the vaccine were not even identified for reporting – only severe ones were noted.

The incidence of AEFI among females was higher than among males in this study. Studies by Hervé et al. (2019), Beyer et al. (1996), and Potluri et al. (2019) found that the incidence of adverse events after vaccination was greater in females than in males. Hormonal differences are known to affect cytokine levels and the immunological response to vaccination; thus, this might be a contributing factor. After immunisation, females are said to generate more neutralising titres than males (Potluri et al., 2019). In a recent study, the same research has also shown that younger persons had a greater immunological response, making them more prone to report AEFI (Jayadevan et al., 2021). Low levels of CRP, IL-10, and IL-6 following immunisation have been linked to a reduced risk of systemic adverse events in the elderly as reported by Hervé et al., 2019.

### 5.2 Type, Severity, Time-to-Onset and Outcome of AEFI

Even though there was no significant difference in incidence among participants with pre-existing conditions such as hypertension and diabetes and those without, AEFIs were significantly more severe in those with pre-existing conditions than those who were not. None of the other medical histories assessed was statistically significant in terms of AEFI incidence. Most participants who experienced AEFIs had only one event and the AEFIs experienced were mostly grade 1 – mild,

and grade 2 – moderate in terms of severity. A few were graded severe and none was graded as serious (grades 4 and 5). Based on their results, Kaur et al., 2021 concluded that the majority of AEFIs were classified as "mild," followed by "moderate," and just a handful was classified as "severe." The findings of this study are comparable to those of Inbaraj et al., 2021, in which the majority of AEFIs were classified as 'mild,' although the proportion of mild AEFIs in this study was higher. For this study and Inbaraj et al., 2021, severe AEFI findings (percentage) were in the minority. Inbaraj et al., 2021, however, found a slightly higher incidence of severe AEFI. The statistical disparity could be explained by differences in how the AEFI was rated — this study used established DAIDs criteria, whereas participants in the Inbaraj trial were required to self-evaluate their feelings. Additionally, Shrestha et al., 2021, observed that the majority of AEFIs observed were minor. The AEFIs were shown to be more severe in individuals who had taken medication within the previous seven days or at the time of immunization, compared to those who had not. The severity was comparable between those using medication and those with pre-existing conditions, which could be explained by the fact that almost everyone taking medication had pre-existing conditions. This investigation identified no serious AEFI, and Kataria et al., 2021 reported similar findings. This contrasted with the findings of Voysey et al., 2021, Kaur et al., 2021, and Shrestha et al., 2021, all of which found serious adverse events in their respective studies. Low incidence and severity of AEFIs mean the populace could have confidence in the prophylactic therapy to arrest the COVID-19 pandemic using the available vaccines, even though no early clinical trials were performed in Ghana.

The median time to onset for most AEFI occurrences was found to be in line with several previous studies. Inbaraj et al., 2021, indicated that most of the participants experienced symptoms within 4 hours to a day after taking the vaccine. Kataria et al., 2021, reported that the majority of AEFIs

were seen in the first 2 days post-vaccination and thereafter they resolved. For participants who reported AEFIs in Jayadevan et al., 2021, most of them noticed the AEFIs within the first 12 hours. The pattern is similar to what was reported by Jeon et al., 2021, in that majority of AEFIs appeared during the first 1 to 3 days after immunization and disappeared quickly. Even though there are racial differences between this study and what had been reported in literature, the pattern of recovery for those who had AEFIs was similar. This consistency is also a good assurance of the safety of the vaccines in the local population.

It was also found that the AEFIs resolved quickly. This was consistent with several studies such as Shrestha et al., 2021, who found that majority of AEFIs that occurred after the first dose of vaccination were minor and went away within a few days. The latest was resolved by day 7 from the onset of AEFI. The study demonstrated that the more severe the AEFI, the longer the recovery days.

Symptoms like fever, muscular soreness, and inflammation at the injection site are all common side effects of injecting a foreign chemical into the body. Innate immunological mechanisms are responsible for mediating these responses. An immunological reaction shown as fever, chills, nausea, and muscular discomfort is triggered when neutrophils or macrophages in the body recognize vaccine components and release cytokines. This cytokine response is typical after the introduction of a foreign substance into the circulatory system (Vogel, W. H., 2010). AEFIs classified as *general disorders and administrative site conditions* (per SOC) were in the majority of the study. Asthenia (body weakness) was found to be the most common followed by headache which is classified under *nervous system disorders*. Pain and discomfort as well as pyrexia (fever) were also recorded. This finding agrees with Kaur et al., 2021, and Jeon et al., 2021, whose studies reported fever, malaise and headache as the commonly reported AEFIs. The frequencies were

however not the same as found in this study. Inbaraj et al., 2021, found body aches to be the most common symptom followed by headache and fever in their study. Body pain, fever and headache were also among the most common AEFIs found by Kataria et al., 2021.

### 5.3 Risk of Age, Sex, Place of Residence and Medical History on AEFI Occurrence

There was a significant difference in the risk of AEFI incidence between the younger and the older age groups. The younger age group had a higher risk of AEFI incidence. AEFIs were found to be more severe in younger participants (aged under 35) than older ones, according to Jeon et al, who conducted the study (2021). Gianfredi et al., (2021), also analyzed the risk of AEFI in their study and found it to be lower in older people, and this was consistent with the results of this study. There was a greater risk of AEFI in females compared to men. Females are more prone than men to develop post-vaccination symptoms according to Jayadevan et al., 2021. This finding was similar to a study done by Menni et al., 2021 in the United Kingdom.

### 5.4 Strengths and Limitations

The longitudinal research design enabled the assessment of the AEFI incidence among vaccinees residing in Awutu Senya East Municipality, which was a strength of the study. To the best of my knowledge, this study was among the first few safety studies to be conducted on COVID-19 vaccines in Ghana. AEFI data was obtained through phone conversations rather than in-person interaction to reduce the risk of Data Collectors contracting COVID-19. One limitation was that a few of the phone numbers provided by the participants during enrolment were for other family members; hence, they could not be reached at all times during the follow-up. However, efforts were made to reach all participants within the follow-up window period.

# CHAPTER SIX

# CONCLUSIONS AND RECOMMENDATIONS

## 6.1 Conclusions

The incidence of adverse events following COVISHIELD immunization among the participants in the Awutu Senya East Municipal was low. The events were generally mild and they disappeared quickly with none serious enough to require hospitalization. The incidence of AEFI increased with decreasing age group, however, the AEFIs experienced were more severe in those aged 60 years and above. AEFIs occurred more frequently among females than males. Asthenia (body weakness) was found to be the most common event associated with COVISHIELD among the participants. Age and sex were factors found to modify the risk of adverse events following COVISHIELD immunization.

It could also be inferred that the incidence of adverse events following COVISHIELD vaccination was low and that the vaccine was considered safe. The overall risk of serious adverse events is still very low, and the advantages of using the COVISHIELD vaccination to protect against the broad COVID-19 threat continue to exceed the risks of adverse reactions.

## 6.2 Recommendations

The following recommendations are being made for consideration:

**Awutu Senya East Municipal Health Directorate**

1. The Municipal Health Directorate (MHD) could also conduct similar studies on other brands of COVID-19 vaccines to determine incidences of AEFIs among their population.

**Food and Drugs Authority (FDA)**

2. Similar studies could be conducted in selected areas in Ghana to determine the average incidence of AEFIs for all COVID-19 vaccines.

**Expanded Programme on Immunization (EPI)**

3. The EPI could use the findings from this study as a basis to continue engaging all stakeholders on the safety of the vaccines to foster trust in the vaccine and the immunization programme.

**Participants & General Population**

4. Due to the low rate of AEFI, participants are urged to go through with their second vaccination dose and any subsequent booster vaccinations that may be necessary. It is recommended that the general public be vaccinated as well since the vaccinations have been shown to be safe for the Ghanaian population.

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# APPENDICES

## APPENDIX I: ETHICS APPROVAL

**GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE**

*In case of reply the number and date of this Letter should be quoted.*

*My Ref. GHS/RDD/ERC/Admin/App* 21\307
*Your Ref. No.*

Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
Digital Address: GA-050-3303
Mob: +233-50-3539896
Tel: +233-302-681109
Fax + 233-302-685424
Email: ethics.research@ghsmail.org
2nd August, 2021

Richard Osei Buabeng
School of Public Health,
P. O. Box LG 571,
University Of Ghana, Legon-Accra, Ghana

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

| | |
|---|---|
| GHS-ERC Number | **GHS-ERC 024/06/21** |
| Project Title | Adverse Events Following Immunization with Newly Introduced COVID-19 Vaccine for Persons Who Have Received at Least One Dose in Awutu Senya East Municipality, Central Region, Ghana |
| Approval Date | 2nd August, 2021 |
| Expiry Date | 1st August, 2022 |
| GHS-ERC Decision | **Approved** |

**This approval requires the following from the Principal Investigator**

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.
- Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....
Dr. James Akazili
(Head, Ethics & Research Management Department)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

## APPENDIX II: PARTICIPANT'S INFORMATION SHEET

**Project Title:** Adverse Events following Immunization with Newly Introduced Covid-19 Vaccine for Persons who have Received at Least One Dose in Awutu Senya East Municipality

**Principal Investigator (PI):** Richard Osei Buabeng (0243312687; nanaseibuabeng@gmail.com)

**Name of Supervisor:** Prof. Col. Edwin Andrews Afari (Rtd) (0208131828**,** afariea@yahoo.co.uk)

**Address:** Department of Epidemiology and Disease Control, School of Public Health, College of Health Sciences, University of Ghana, Legon, Accra

**Introduction:** I am a student of the School of Public Health, University of Ghana. I am conducting a study to assess the adverse events following immunization with newly introduced COVID-19 vaccine in the Awutu Senya East Municipality, Ghana. This is in partial fulfillment of the requirement of a Master of Philosophy Degree in Applied Epidemiology and Disease Control. Your participation and honest information in this study will be most appreciated.

**Background and Purpose:** Vaccines are a critical public health tool in the fight against the COVID-19 pandemic. COVISHIELD has been certified for emergency usage in Ghana and is now being rolled-out in a few areas, including Awutu Senya East Municipality. COVID-19 vaccine pre-approval trials have primarily been conducted in healthy people in controlled settings, with little representation of people of other races. As a result, such trials may not catch all of the safety risks that appear when vaccines are marketed to the broader public. The goal of this study is to identify and evaluate adverse events following COVISHIELD vaccination. The findings of this study will be submitted to the University of Ghana as a part of the thesis and also published in a peer-reviewed journal to inform and implement policies that will reduce the burden of AEFIs in Ghana.

**Procedure:** You will be admitted into the study after taking the COVID-19 vaccine and followed-up for eight weeks. During the period, you will be observed for any untoward medical occurrence which follows the immunization.

**Potential risk:** There is no direct risk in participating in this study. You may, however, be required to answer few questions from research assistants that will frequently call you during the study period.

**Benefits:** There are no direct benefits from this study. However, findings from this study will be used to inform policy formulation and improve immunization activities in the municipality and the country as whole**.**

**Cost:** There will be no financial costs for participating in this study. About 10 minutes of your time will be spent during enrolment and 5 minutes for each subsequent follow-up calls.

**Compensation:** Participants will not be compensated for participating in this research.

**Confidentiality:** Any information you will provide will be treated with strict confidentiality and will be used solely for the purpose of which it is has been collected - academic work. Thus, your responses will not be shared with anyone who is not part of the team involved in the study. To ensure anonymity, data will be analyzed at the aggregate level and your responses will not be traced to you.

**Voluntary participation and withdrawal:** Participation is voluntary and you may withdraw from the study at any point without any consequences.

**Outcome and feedback:** The outcome of the study will be shared with the School of Public Health, the University of Ghana, the Tamale Metropolitan Assembly, the division of Non-Communicable Diseases in the Ghana Health Service, and the general public through publication in a journal.

**Funding Information:** This study is funded by the Principal Investigator and the West Africa Health Organization (WAHO) through the Ghana Field Epidemiology and Laboratory Training Programme (GFELTP)

**Sharing of participants information/data:** The data generated from this study will be solely for the principal investigator and will only be shared with other individuals and organizations such as Food and Drugs Authority, Expanded Programme on Immunization, Ghana Health Services on a need-to-know basis.

**Further clarification/questions:** If you have further questions on the study you can contact; Richard Osei Buabeng (Principal Investigator, 0243312687, **nanabuabeng@yahoo.com),** Prof. Col. Edwin Andrews Afari (Rtd) (Academic Supervisor, 0208131828**, afariea@yahoo.co.uk**)

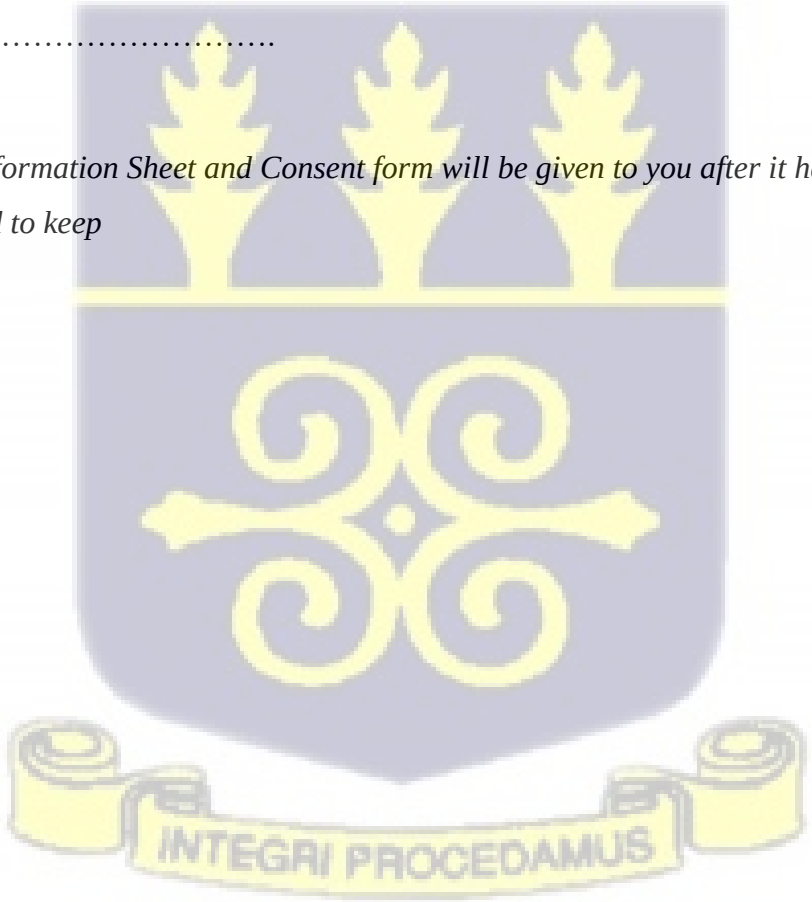
**Ethical concerns:** In case of ethical concerns, kindly contact: Nana Abena Apatu (Administrator, Ghana Health Service Review Committee, 0503539896, ethics.research@ghsmail.org).

Name or Initials of Participant……ID code /__/__/__/__/

Participants' signature……..OR Thumbprint……..

Date …….

*A copy of this Information Sheet and Consent form will be given to you after it has been signed or thumb-printed to keep*



**APPENDIX III: CONSENT FORM**

**Study Title:** Adverse Events following Immunization with Newly Introduced Covid-19 Vaccine for Persons who have Received at Least One Dose in Awutu Senya East Municipality

**PARTICIPANT'S STATEMENT**

I acknowledge that I have read or have had the purpose and contents of the participants' Information Sheet read and satisfactorily explained to me in a language I understand (English, Twi, Ga). I have had the opportunity to ask questions, and any question I have asked has been answered to my satisfaction. I fully understand the contents and any potential implications as well as my right to change my mind (i.e. withdraw from the research) even after I have signed this form. I voluntarily agree to be part of this research.

Name or Initials of Participant……..ID Code……..

Participants' signature……OR Thumbprint……..

Date……

**INTERPRETER'S STATEMENT**

I interpreted the purpose and contents of the Participants' Information Sheet to the aforenamed participant to the best of my ability in the language (English, Twi, Ga) to his proper understanding.

All questions, appropriate clarifications sort by the participant, and answers were also duly interpreted to his/her satisfaction.

Name of Interpreter……

Signature of Interpreter……

Contact Details /__/__/__/__/__/__/__/__/__/__/

Date……

**STATEMENT OF WITNESS**

I was present when the purpose and contents of the Participant Information Sheet was read and explained satisfactorily to the participant in the language he/she understood (English, Twi, Ga). I confirm that he/she was given the opportunity to ask questions/seek clarifications and same were duly answered to his/her satisfaction before voluntarily agreeing to be part of the research.

Name…….

Signature…….OR Thumb Print……

Date ……..

**INVESTIGATOR'S STATEMENT AND SIGNATURE**

I declare that I have given enough information to the participant to make an informed decision about participating in the study.

I certify that the participant has been given ample time to read and learn about the study. All questions and clarifications raised by the participant have been addressed.

Researcher's name: ……

Signature: …….

Date: ……

**APPENDIX IV: RESEARCH QUESTIONNAIRE**

**SCHOOL OF PUBLIC HEALTH**
**UNIVERSITY OF GHANA**
**RESEARCH QUESTIONNAIRE (ENROLMENT FORM)**
**ADVERSE EVENT FOLLOWING IMMUNIZATION WITH COVID-19 VACCINE**

1. Demographic Details of Participant:

| | |
|---|---|
| Participant ID: | Sex: |
| First Name: | Tel No. (Participant): |
| Surname: | Tel No. (Relative): |
| Date of Birth (dd/mm/yyyy): | Email Address: |
| Age (years) | House No./Landmark: |

2. Medical History of Participant:
   a. Are there any presenting symptoms at the time of being vaccinated? (If any, list them)
   b. Are there any known allergies? (If any, list them)
   c. Have there been any medical events in the last 7 days? (If any, list them)
   d. Does the participant have any pre-existing medical conditions (e.g. diabetes, hypertension, asthma)? (If any, list them)
   e. Is the participant taking any medication(s) at the time of vaccination? ((If any, list them)
   f. Has the participant taken any medication(s) in the past 7 days prior to the day of vaccination? (If any, list name of the medicine and its indication)

3. Details of Vaccine Administered – Dose: 1 ☐ 2 ☐

| | |
|---|---|
| a. Name (Brand name): | d. Expiry Date (dd/mm/yyyy): |
| b. Manufacturer: | e. Date Vaccine was given (dd/mm/yyyy) |
| c. Batch/Lot Number: | f. Vaccination Centre: |

4. Planned Follow-up Dates

| | |
|---|---|
| a. FU1 (dd/mm/yyyy) | c. FU3 (dd/mm/yyyy) |
| b. FU2 (dd/mm/yyyy) | d. FU4 (dd/mm/yyyy) |

5. Details of Research Assistants:
   a. Name: …… b. Telephone Number: …… c. Email: ……

**SCHOOL OF PUBLIC HEALTH**

**UNIVERSITY OF GHANA**

**RESEARCH QUESTIONNAIRE (FOLLOW-UP (FU) FORM)**

**ADVERSE EVENT FOLLOWING IMMUNIZATION WITH COVID-19 VACCINE**

Demographic Details of Participant:

| | |
|---|---|
| Participant ID: | Sex: |
| First Name: | Tel No. (Participant): |
| Surname: | Tel No. (Relative): |
| Date of Birth (dd/mm/yyyy): | Email Address: |
| Age (years) | House No./Landmark: |

Follow-up 1:

| | |
|---|---|
| Date of Follow-up: (dd/mm/yyyy)<br>Dose: 1 ☐ 2 ☐<br>Participant reached on FU: Yes ☐ No ☐ | Did the Participant have an AEFI: Yes ☐ No ☐<br>If Yes (d), AEFI form completed? Yes ☐ No ☐<br>Next FU date: (dd/mm/yyyy) |

Follow-up 2:

| | |
|---|---|
| Date of Follow-up: (dd/mm/yyyy)<br>Dose: 1 ☐ 2 ☐<br>Participant reached on FU: Yes ☐ No ☐ | Did the Participant have an AEFI: Yes ☐ No ☐<br>If Yes (d), AEFI form completed? Yes ☐ No ☐<br>Next FU date: (dd/mm/yyyy) |

Follow-up 3:

| | |
|---|---|
| Date of Follow-up: (dd/mm/yyyy)<br>Dose: 1 ☐ 2 ☐<br>Participant reached on FU: Yes ☐ No ☐ | Did the Participant have an AEFI: Yes ☐ No ☐<br>If Yes (d), AEFI form completed? Yes ☐ No ☐<br>Next FU date: (dd/mm/yyyy) |

Follow-up 4:

| | |
|---|---|
| Date of Follow-up: (dd/mm/yyyy)<br>Dose: 1 ☐ 2 ☐<br>Participant reached on FU: Yes ☐ No ☐ | Did the Participant have an AEFI: Yes ☐ No ☐<br>If Yes (d), AEFI form completed? Yes ☐ No ☐<br>Next FU date: (dd/mm/yyyy) |

# REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNISATION (AEFI)-GHANA

Reporting ➔ Sub-District: District: Region:

**AEFI Reporting ID Number**
Region Code ☐☐☐ District Code ☐☐☐ Year ☐☐ Serial Number ☐☐☐

Vaccination Card/Booklet ☐ Yes ☐ No

If no, state other source of information:

## A. PATIENT DETAILS

*Name:

Sex: ☐ M ☐ F

If Female: Pregnant: ☐ Lactating: ☐

Contact Phone No:

Vaccination centre:

Community:

*Date of birth (DD/MM/YYYY): __/__/____

OR Age at onset: ☐☐ Years ☐☐ Months ☐☐☐ Days

OR Age Group: ☐ < 1 Year ☐ 1 to 5 Years ☐ > 5-18 Years ☐ >18-60 Years ☐ > 60 Years

*Address (landmarks and other contact information):

## *B. DESCRIPTION OF AEFI

☐ Severe local reaction ☐ >3 days ☐ beyond nearest joint
☐ Seizures febrile afebrile
☐ Abscess
☐ Sepsis
☐ Encephalopathy
☐ Toxic shock syndrome
☐ Thrombocytopenia
☐ Anaphylaxis
☐ Fever≥38°C
Other (specify).....

Date AEFI started (DD/MM/YYYY): ☐☐/☐☐/____

Time AEFI started Hr Min

AEFI (Signs and symptoms- please give a summary of the case):

Indicate treatment given for the AEFI:

Past medical history (including history of similar reaction or other allergies), concomitant medication and dates of administration (exclude those used to treat reaction) other relevant information (e. g. other cases). Use additional sheet if needed: ……

……

## *C. OUTCOME OF AEFI

*Serious¶: ☐ Yes ☐ No; ➔ If Yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly

Other important medical event (Specify)_____)

*Outcome: ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown

Died If died, date of death (DD/MM/YYYY): __/__/____ Autopsy done: ☐ Yes ☐ No ☐ Unknown

## D. DETAILS OF ALL VACCINE (S) ADMINISTERED

| VACCINE(S) | | | | | | | DILUENT (if applicable) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Name of Vaccine (Generic/Brand) | *Date and time of Vaccination | | *Route (if injection indicate L/R site) | *Lot / Batch No. | Dose (e.g. 1st, 2nd, etc.) | Expiry Date | Manufacturer | *Lot / Batch No. | Expiry Date | Date and time of reconstitution | |
| | Date | Time | | | | | | | | Date | Time |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |

## E. REPORTER DETAILS

*Name: Profession/Designation: Tel No.:

Name of Institution: Today's Date: __/__/____ Signature:

**For District Level Office**

| Date Report Received: __/__/____ | Checked by: | Designation: |
|---|---|---|
| Investigation needed ☐ Y ☐ F | If yes, date started: __/__/____ | |

**For National/Central Level Office**

| Date Report Received: ___/___/_____ | Checked by: | Designation: |
|---|---|---|
| Comments (include results of Causality Assessment): | | |

¶All serious AEFIs & AEFI clusters (two or more cases of the same adverse event related in time, place or vaccine administered) should be investigated.

*Mandatory fields