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COLLEGE OF HEALTH SCIENCES

UNIVERSITY OF GHANA, LEGON.

FACTORS ASSOCIATED WITH YAWS AMONG CHILDREN IN THE UPPER WEST AKYEM AND AWUTU SENYA WEST DISTRICTS

BY

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DECLARATION

I, Rafiq Nii Attoh Okine, declare that except for other people's investigations which have been duly acknowledged, this dissertation is the result of my own original research undertaken under supervision and that it has neither in whole nor in part been presented for another degree in this university or elsewhere.

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DEDICATION

This dissertation is dedicated to my parents and siblings.

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ABSTRACT

Background: Yaws is a chronic relapsing disease caused by *Treponema pallidum pertunue*, which can result in severe disability and deformities. Children below the age of 15 years in socially disadvantaged and resource-poor communities are the most affected. Several non-specific factors have been demonstrated to facilitate the continuous transmission and resurgence of the disease in endemic communities. Rural communities in Ghana continue to report cases of yaws despite the roll out of several intervention strategies in the past years.

Objective: The objective of this study was to determine the factors associated with the transmission of yaws among children in the Upper West Akyem and Awutu Senya West districts in the Eastern and Central Regions respectively.

Methods: A community-based unmatched 1:2 case-control study was conducted among children between ages 1 – 15 years. Data on exposures (socio-demographic, environmental and behavioral factors) were collected using a structured questionnaire designed with the REDCAP software. Active case search and confirmation was done using the WHO picture guide and the Dual Path Platform (DPP) Syphilis Screen and Confirm test kit. Data were analyzed using STATA 15. Univariable and a stepwise multivariable logistic regression was done to determine the exposures that were associated with yaws infection at 0.05 significant level.

Results: One hundred and eighty-six (186) participants (62 cases and 124 controls) were recruited for the study. The median ages of cases and community controls were 11 and 10 respectively. The adjusted multivariable logistic regression model showed that yaws infection was more likely among individuals who reside in overcrowded compound houses (aOR=25.42, 95%CI=6.15 - 105.09) and with poor handwashing habits (aOR=6.46,

95%CI=1.89 - 22.04). Compared to community controls, yaws cases had a threefold increased odds of sharing bathroom with more than five persons (aOR=3.25, 95%CI=1.09 - 9.71). Male sex (aOR=4.15, 95%CI=1.29-13.36) and increasing age (aOR=5.90, 95%CI=1.97 -17.67) were also significantly associated with yaws.

Conclusion: Poor personal hygiene, overcrowding and lack of access to improved sanitary facilities are the factors that facilitate the transmission of yaws in the Awutu Senya West and Upper West Akyem districts. Yaws was also more common among males and school-aged children. Improving the living conditions, access to good sanitary facilities and encouraging good personal hygiene practices should be core features of eradication programs in endemic communities.

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LIST OF ABBREVIATIONS

CBSV	Community- based surveillance volunteers
CHPS	Community Based Health Planning and Services
DHMT	District Health Management Team
DPP	Dual Path Platform
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assay
GSS	Ghana Statistical Service
NTDs	Neglected Tropical Diseases
NYEP	National Yaws Eradication Program
PNG	Papua New Guinea
POC	Point of Care
RA	Research assistants
RPR	Rapid Plasma Reagin
TCT	Total community treatment
TDR	Tropical Disease Research
TTT	Total targeted treatment
TPHA	Treponema Pallidum Haemaglutination Assay Test
TPPA	Treponema Pallidum Particle Agglutination
UNICEF	United Nations Children's Fund
VDRL	Venereal Disease Research Laboratory
WHO	World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND

Yaws is one of the three non-venereal treponemal diseases that is considered as a neglected tropical disease (NTD) (Marks et al., 2015). The disease is transmitted by *Treponema pallidum* subspecies *pertenue*. It is a highly contagious disease which has a chronic relapsing pattern (Mitjà et al., 2015).

Yaws is transmitted through skin-to-skin contact and primarily affects children under the age of 15 years typically in areas of low socio-economic status and sanitation challenges. The disease is endemic in low-to-middle income countries and resurgence has been reported in the Pacific region, West and Central Africa and southeast Asia (Asiedu, Fitzpatrick, & Jannin, 2014) .

The disease is usually self-limiting but can lead to severe complications involving the skin and bones. Typically, this results in destructive lesions of bones and cartilages and results in severe deformities and disability. (Ayove et al., 2014).

Despite concerted efforts and strategies to eradicate yaws, the disease is still endemic in some fourteen countries (Marks et al., 2015). A systematic review published in 2015, estimated that over 80 million people were living in endemic districts (Mitjà et al., 2015).

Over 250,000 cases of yaws were reported between 2010 and 2013 to the World Health Organization (WHO) from 13 endemic countries (Ayelo et al., 2015). Eighty-four (84) percent of the cases were from Ghana, Papua New Guinea and Solomon Island (Konan et al., 2015).

The WHO launched the Morges Yaws Eradication Strategy in 2012, with a target of eradication by 2020. The major component of the new strategy was the change from the injectable benzathine penicillin to oral azithromycin. The new treatment strategy was piloted in three countries including Ghana with promising findings (Kwakye-Maclean, Agana, Gyapong, & Nortey, 2017).

The National Yaws Eradication Program (NYEP) in Ghana, which was set up in 2008 has the singular task of co-coordinating all yaws activities in the country through collaboration with international agencies. The program has set elimination targets by the end of 2017 and eradication by 2020.

The success of the eradication strategy is strongly linked to understanding the epidemiology of the disease, particularly the risk factors, since humans are the only known reservoirs.

Several districts in Ghana continue to report cases of yaws despite numerous intervention strategies (NYEP, 2016). In a survey conducted from 2010 – 2013, six regions in Ghana (Western, Central, Ashanti Volta, Eastern and Brong-Ahafo) found yaws to be highly endemic; reporting over 5000 cases over the four year study period (Mitjà, Marks, Konan, Ayelo, Gonzalez-Beiras, et al., 2015).

There is currently no vaccine for yaws and the success of the eradication strategy is largely dependent on interrupting disease transmission through identification and elimination of risk factors.

Several risk factors including climatic and geographic locations, socio-economic status, cultural beliefs and sanitation have been shown to facilitate the transmission of yaws (Kazadi et. al, 2014 & Marks et. al, 2017). Risk factors that facilitate the transmission of yaws may vary within the different endemic communities. Several studies have shown

spatial heterogeneity and clustering of the disease in endemic communities; which calls for more research in understanding the epidemiology of the disease, particularly, the transmission process (Marks et. al, 2015).

1.2 PROBLEM STATEMENT

Ghana reports high number of cases of yaws. There are case reports of yaws in all the 10 regions with 160/170 health districts reporting cases of yaws (Mitjà et al., 2015). In the last 8 years, 8000 – 36000 cases were reported in the country (NYEP, 2016).

Ghana has targeted elimination of yaws by the end of December 2017 (zero indigenous cases from a baseline of 0.7%) and total eradication by 2020 (NYEP, 2016).

Rural communities in Ghana continue to report new cases despite variety of strategies that have been implemented over the past years. A national school-based survey showed prevalence of yaws was about 20% in certain communities (Agana-nsiire et al., 2014). The Central, Eastern and Volta Regions remain endemic, reporting between 5.0 – 338 cases/100,000 population over the past 4 years. (NYEP, 2016).

Untreated yaws results in severe disfigurement and disability, which leads to school absenteeism, social stigma and loss of livelihood.

Socio-cultural beliefs, poor sanitation, poor housing, overcrowding and lack of access to prompt diagnostic tools are some of the factors that have been postulated to facilitate disease transmission (Kazadi, Asiedu, Nsiire, & Mitja, 2014). The disease transmission process is not clearly understood, with several risk factors yet to be identified. It is imperative to determine whether there are other factors that facilitate the transmission of yaws in these endemic communities.

There is no vaccine for the treatment of yaws and a key intervention in the control of the disease is the interruption of the transmission process. Humans are the only known reservoirs, thus identifying and eliminating risk factors associated with the disease transmission in endemic areas is paramount.

Failure to do this would also hamper the effective implementation of strategies towards total eradication by 2020 (Amin, Abdus, Ariful, & Faiz, 2010).

1.3 CONCEPTUAL FRAMEWORK – Factors associated with transmission of yaws

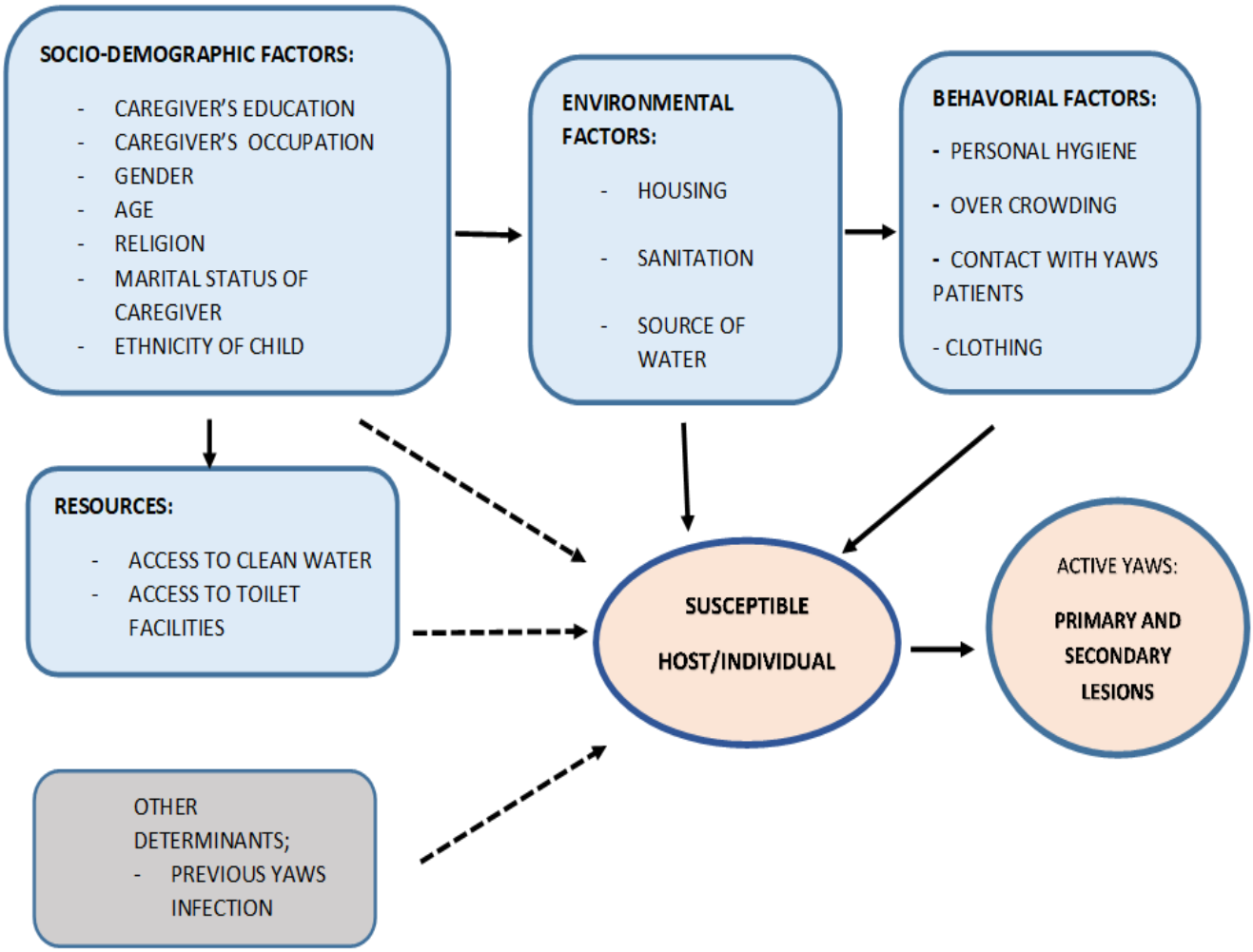

Fig. 1 Conceptual Framework

1.4 NARRATIVE SUMMARY (CONCEPTUAL FRAMEWORK)

Several non-specific factors have been shown to facilitate the transmission of yaws. The typical susceptible host or reservoir for yaws are children under fifteen years. The disease has a preponderance for males because they are more likely to engage in traumatic activities (Kazadi et al., 2014).

The level of education and occupation of the caregivers could have indirect relationships to susceptibility to yaws infection.

Yaws is also typically endemic in socially disadvantaged and resource poor communities where there is poor personal hygiene, lack of proper sanitary facilities, poor housing and lack of health care facilities.

1.5 JUSTIFICATION

Yaws predominantly affects children in socially and economically disadvantaged communities. The resulting social stigma, disfigurement and morbidity has untoward consequences (Marks, Mitjà, et al., 2015).

Ghana has been actively involved in implementing the different strategies targeted at elimination and eradication of yaws over the past years. Ghana was one of the six countries that piloted the Morges treatment strategy that was initiated in 2012 (Asiedu et al., 2014).

Yaws is however endemic in most districts in the country despite the numerous interventions. The disease has been successfully eradicated in many countries through international collaborative research and policies (Asiedu et al., 2008). Thus, achieving total eradication in Ghana is feasible.

Identification and controlling of risk factors has been a major component in the successful eradication strategies (Amin et al., 2010). Towards achieving the target of possible eradication in 2020, the data provided by this research can be incorporated into the existing strategies geared towards disease elimination and eradication.

1.6 RESEARCH QUESTION

1. What are the factors associated with the transmission of Yaws among children aged 1 – 15 years in the Upper West Akyem and Awutu Senya West districts?

1.7 STUDY OBJECTIVES

1.7.1 General Objective:

To determine the factors associated with the transmission of Yaws among children aged 1 – 15 years in the Upper West Akyem and Awutu Senya West districts.

1.7.2 Specific objectives:

1. To assess the social and demographic factors associated with Yaws in the districts.

2. To determine the behavioral factors that facilitate the transmission of Yaws in the districts.

3. To determine the environmental factors that are associated with Yaws in the districts.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Global Epidemiology of Yaws

Yaws is a chronic debilitating skin disease caused by *Treponema pallidum* subspecies *pertunue* that predominantly affects young children under the age of 15 years (Dzotsi et al., 2017) usually in poor and neglected rural communities. It belongs to a group of non-venereal Treponemal diseases classified as endemic treponematoses. The group also include Bejel (endemic syphilis) and Pinta caused by *Treponema pallidum endemicum* and *Treponema pallidum carateum* respectively (Asiedu et al., 2014). The disease is not fatal, but about ten percent (10%) of infected people typically experience severe complications involving bones, cartilage, skin and soft tissue (Kazadi et al., 2014).

It is estimated that up to about 42 million people live in endemic tropical areas (Kazadi et al., 2014) and close to 300,000 cases were reported to WHO from endemic countries from 2008 to 2012 (WHO, 2012). The disease is present in tropical areas in Africa, southeast Asia, and the Pacific with Papua New Guinea, Vanuatu and Solomon Islands and Ghana recording the highest number of cases. Due to underreporting of cases, the full extent of yaws in the Africa region is unknown, though evidence available indicates that the disease is present in Benin, Côte d'Ivoire, Cameroon, Sierra Leone, Central Africa Republic (CAR), Congo, the Democratic Republic of the Congo and Togo (WHO, 2012).

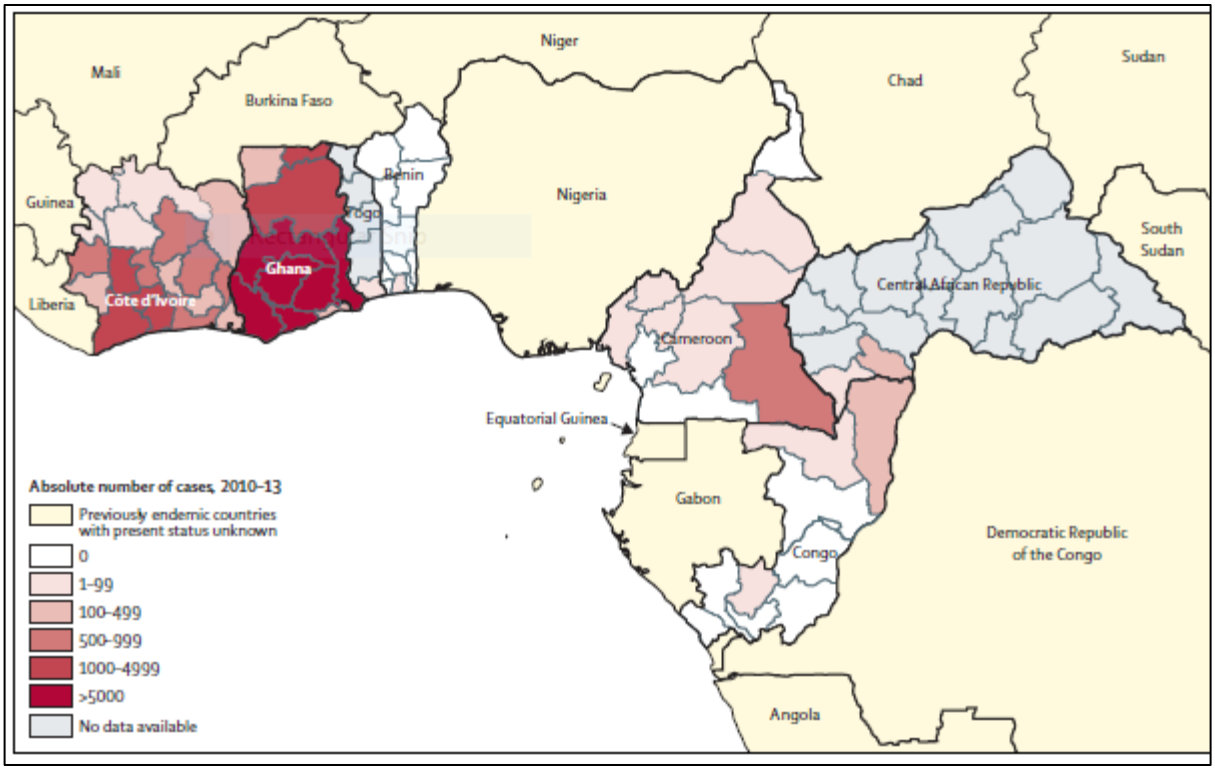

Fig. 2. Cumulative number of yaws cases reported in the WHO Africa region (2010 - 2013) (Mitjà et al., 2015).

2.2 The burden of Yaws in Ghana

There is continuous transmission of yaws in rural Ghana where living conditions are poor. Cases of yaws have been reported in all the ten regions of Ghana, typically in the remotest areas and in the WHO Africa region, Ghana is considered as the most endemic country (Kazadi et al., 2014). The country reported over 20,000 cases annually from 2007 to 2010. In a survey of clinical prevalence of yaws done in 2008 by Agana-Nsiire and colleagues, prevalence was found to be 0.68% but was as high as 20.2% in some rural communities (Agana-Nsiire et al., 2014).

There is generally low case notification and the trend of reporting has been shown to be on the decrease, that is, from 35,200 in 2009 to 9,300 in 2012. The Central, Eastern, Western,

Volta, and Ashanti regions remain the most endemic. Only 19 out of the 170 districts have not reported yaws from 2008 to 2011 (WHO, 2012).

Paucity of health facilities and personnel and weak surveillance system have been shown to facilitate the transmission of yaws in the country (Kwakye-maclean et al., 2017).

2.2.1 National Yaws Eradication Program (NYEP)

Cases of yaws have been reported in Ghana since the pre-independence era. Despite numerous interventions and eradication strategies adopted over the past years, the country remains endemic with continuous transmission and clustering of the disease in several communities in rural Ghana.

The National Yaws Eradication Program (NYEP) was established in 2008. The core mandate was to coordinate all activities geared towards elimination of yaws in Ghana by the end of 2017. The program also collaborates with international agencies and neighboring countries towards eradication of yaws, which has been tentatively set at 2020 by the WHO.

The NYEP also supervises and coordinates all the surveillance programs instituted in the country in collaboration with the various District Health Management Teams (DHMT) and community- based surveillance volunteers (CBSV) (NYEP, 2016).

2.3 Manifestations and Complications

Yaws is highly contagious and is transmitted through close skin-to-skin contact by infectious persons. The disease transmission process is facilitated by poor environmental and sanitary conditions. The clinical presentation of yaws is classified into four (4) stages (Manirakiza, Boas, Beyam, Zadanga, & Konamna, 2011). The disease has a low mortality but can lead to crippling, disfiguring and severe deformities. This is typically associated

with social stigma, school absenteeism among children and loss of livelihood (Rinaldi, 2008).

Lesions associated with yaws can broadly be grouped into early stage (primary and secondary) and late stage (tertiary lesions) (Mitjà, Asiedu, & Mabey, 2013). Early stage lesions are highly infectious and usually persists for weeks or months (Stamm, 2015).

2.3.1 Primary yaws

A lesion known as 'mother yaw' characterizes the primary stage, which is the infectious stage. This occurs as a papule, which typically develops after 2-4 weeks of incubation at the site of *Treponema* inoculation. The lesion either undergoes ulcerative changes or becomes a papilloma. The primary lesion resolves in 3 – 6 months but can result in early bone and joint disease (Manirakiza et al., 2011).

2.3.2 Secondary yaws

Secondary yaws develops after a period of latency, usually up to sixteen (16) weeks and the lesions are similar to the 'mother yaws' but the lesions are numerous and located near body orifices like the mouth and nose. The lesions may also appear near or at exactly at the same site as the primary lesion (Thami & George, 2010). The lesions involve in this stage also include nodules and plaques.

Fig. 3 Early secondary lesions of yaws appearing as eroded and crusted papules and plaques

2.3.3 'Attenuated' yaws

Fegan et al., (1990) classically described what is known as 'attenuated yaws' in their research in the Solomon Islands. This less contagious stage of the yaws infection is found in areas with low prevalence and characterized by a solitary patch or a discrete, dry and flat patches confined to intertriginous areas. Reactivation to active and infective yaws is possible.

2.3.4 Tertiary or latent yaws

The latent or tertiary stage can occur after several years and results in severe morbidity. The period of latency is variable and the characteristic lesions involve destruction of bones and cartilage (Manirakiza et al., 2011). The lesions include painful hyperkeratosis of palms and soles, skin ulceration, gumma, keratoderma, gangosa and sabre tibia.

2.4 Risk factors associated with transmission of Yaws

A key component of most strategies put in place to eradicate yaws is the identification and control of risk factors. Like most NTDs, a variety of factors; human behavior, environmental, socio-political, biological and ecological factors have been shown to facilitate disease transmission (Mackey et al., 2014).

Hill (1953), extensively describe the non-specific factors associated with the transmission of the disease. Several studies have also sought to explore other factors that affect the transmission process.

2.4.1 Geographical and ecological factors

Warm, moist and humid climates provide suitable environments for transmission and spread of yaws. Thus, the disease is most prevalent among populations living between the Tropic of Cancer and the Tropic of Capricorn. Hill (1953) reported that yaws thrives best in countries

with the mean annual isotherm of 27°C (80° F) and over. The disease is not prevalent in climates where there are extremes of temperature (Kazadi et al., 2014).

Altitude also seems to play a role in disease transmission with several studies done in the Caribbean, Central and South America reporting high number of cases at higher altitudes (Hill, 1953).

The rainfall pattern also affects the distribution of yaws, with geographical areas with an annual rainfall of greater than 50 inches (1300mm) recording high incidence of cases. Saunders et al. (1936) in their landmark study in Jamaica "reported striking differences in the lesions during the wet and dry seasons. In the rainy season a greater proportion of cases showed an open infectious type of lesion, and the papillomatous framboesides tended to be larger, more numerous, and florid".

2.4.2 Demographic factors

2.4.2.1 Age distribution

The main victims of yaws are children under the age of 15 years though the disease could also be found among the adult population. The peak incidence is between the ages of six to ten (Rinaldi, 2008). A cluster randomized survey done by Marks et al., (2015) showed that age was significantly associated with both Treponema pallidum particle agglutination (TPPA) positivity, dual seropositivity and active disease. The study also showed that prevalence of TPPA positivity increased with age within the age group examined (5 – 14 years). A clinical and serological survey conducted by Thami & George, (2010) in Vanuatu showed a higher prevalence (31.29%) among children under the age of 15 years compared to 4.04% among children above the age of 15 years. A case- control by Dzotsi et al., (2017) in

the West Akim Municipality in Ghana showed that among the cases, the most affected age group was 6-10 years (54.4%) and the least affected age group being 16-25 years (4.4%).

2.4.2.2 Sex distribution

The incidence of cases are equally distributed among males and females across the different age groups (Hill, 1953). Other studies have however shown that more males suffer from the disease compared to females. The explanation is that boys are more prone to traumas than girls and the disease most usually acquired after a cut or abrasion in the lower legs (Kazadi et al., 2014). In addition, a study by Dzotsi et al., (2017) demonstrated that "males were most affected with 71.7% (33 cases) while females represented 28.3% (13 cases). In another study conducted by Marks et. al., 2017, age adjusted analysis (<10years) showed that males were at higher risk for seropositivity and active disease compared to females.

2.4.3 Socio-economic factors, Hygiene and Sanitation

In his paper Rinaldi (2010) remarked, 'Yaws Begins Where the Road Ends''. The disease is most prevalent in highly impoverished areas and rural communities. These communities have low standard of living, lack access to facilities for sanitation and personal hygiene and overcrowding is a typical feature (Hill, 1953).

Rural and resource-poor communities typically record high number of cases with incidences of the disease falling as the economic status of the people are improved. There are extensive areas of vegetation that increases the chances of injury and thus susceptibility to infection (Kazadi et al., 2014).

The degree of village endemicity, access to hand washing facilities and number of dual seropositive household contacts were all associated with active infection (Vahi, et al., 2015).

2.4.4 Possible involvement of other reservoirs and nutritional deficiency

Currently, humans are the only known reservoirs for yaws. Some studies have however suggested the existence of non-human reservoirs particularly primates. The success of any eradication strategy will largely be hinged on elimination of such reservoirs if they exist (Berri, Souriau, Crosby, Gangl, & Randt, 2013). A survey in 2013 in Senegal, revealed *T. pallidum* antibodies in Guinea baboons with no signs of infection (Knauf et al., 2017).

Polymerase Chain Reaction (PCR) has been used to confirm infection in a variety of non-human primate species in the yaws belt of Africa (from East and West Africa) (Berri et al., 2013). This high prevalence of primate infection suggests that cross-species infection can occur.

There has been suggestions of association of nutritional deficiency with yaws infection though the relationship is not clear (Hill, 1953). A study conducted in a rural community by Findlay (1946) in colonial Ghana (Gold Coast) found that "only 3.8 % of the 233 children without signs of yaws had evidence of avitaminosis, whereas 14.8 % of the 47 children showing lesions of yaws had marked signs of food deficiency".

2.5 Diagnostic, Treatment and Eradication strategies

2.5.1 Diagnosis

Diagnosis of yaws is based on physical examination with clinical picture guides. Suspected cases are confirmed by a variety of laboratory methods with varying specificities and sensitivities. The methods used in the diagnosis of treponemal infections can be classified as treponemal specific tests and nontreponemal tests (Marks et al., 2017).

The treponemal specific tests include *Treponema pallidum* particle agglutination assay (TPPA), *Treponema pallidum* hemagglutination assay (TPHA), enzyme immunoassay (EIA), enzyme-linked immunosorbent assay (ELISA) and fluorescent treponemal antibody test The nontreponemal test include the Rapid Plasma Reagin (RPR) or Venereal Disease Research Laboratory (VDRL) assays (Marks et al., 2014).

A rapid point –of- care (POC) test, the Dual Path Platform (DPP) Syphilis Screen and Confirm that can detect both antibodies to non-treponemal and treponemal antigens has been developed for screening of yaws. This test is important as it improves access to effective case detection in resource-poor communities and rural areas (Ayove et al., 2014). The device has been validated in several studies including field surveys and has demonstrated high specificity and sensitivity (Marks et al., 2017).

Figure 4. A positive Dual Path Platform (DPP) test. (NYEP, 2016)

2.5.2 Eradication Strategies and Treatment Strategies

The WHO has set a target of eradication of yaws by the year 2020. The strategies for the treatment and eradication of yaws has evolved over the past years dating back to the 1920's and 30's. The WHO and UNICEF launched mass treatment campaigns between 1952 - 1964 with intramuscular benzathine penicillin injections. There was significant success, which reduced the global burden of the disease by 95% to only 2.5 million cases (Asiedu et al., 2014).

The campaign was however not sustainable owing to weak primary health systems and weak surveillance structures in resource- poor countries. This led to a resurgence of the disease in the 1970s. Ghana launched a combined Yaws and Yellow fever campaign in 1981 in response to the resurgence of the disease (Asiedu et al., 2014).

The initial treatment strategy for yaws was based on recommendations from the Enugu conference, held in Nigeria in 1955. The treatment of cases, contacts and the community was based on disease prevalence. A groundbreaking research conducted in Papua New Guinea (PNG) showed that single oral dose of azithromycin was not inferior to benzanthine penicillin in the treatment of yaws (Mitjà et al., 2012).

Other non-inferiority clinical trials have confirmed the effectiveness of oral azithromycin (Kwakye-Maclean et al., 2017; Mitjà et al., 2012). One of the studies showed a fall in the prevalence of infectious active yaws from 2.4% at baseline to 0.3% at 6 months. The study also concluded that a single round of mass drug administration with azithromycin greatly reduced the transmission and endemicity of yaws (Hays et al., 2015).

The cure rate of oral azithromycin (>98%) has been found to be equivalent to that of a single intramuscular injection of long-acting penicillin (Kwakye-maclean et al., 2017; Mitjà et al.,

2012). The success of the initial study informed the new WHO strategy for the treatment of yaws, the Morges Strategy, in Switzerland, in 2012.

The key components of the strategy are:

1. Total community treatment (TCT): treatment of an entire endemic community, irrespective of the number of active clinical cases. For implementation purposes, in Ghana, the sub-district level is the unit of implementation.

Two or three rounds of TCT at 6–12 monthly intervals are usually required to interrupt transmission or significantly reduce prevalence of cases with a target population coverage of more than 90% (WHO, 2014).

2. Total targeted treatment (TTT): treatment of all active clinical cases and their contacts (household, school, and playmates). (Asiedu et al., 2014; WHO, 2012).

The above strategies is coupled with strengthening surveillance system for the disease, training of health care professionals and strengthening primary health care systems in endemic countries (WHO, 2012).

CHAPTER THREE

3.0 METHODS

3.1 STUDY DESIGN

The study was a community-based unmatched 1:2 case - control study conducted in the Upper West Akyem and Awutu Senya West districts. The cases and controls were selected from households and schools within the same communities.

3.2 STUDY AREAS

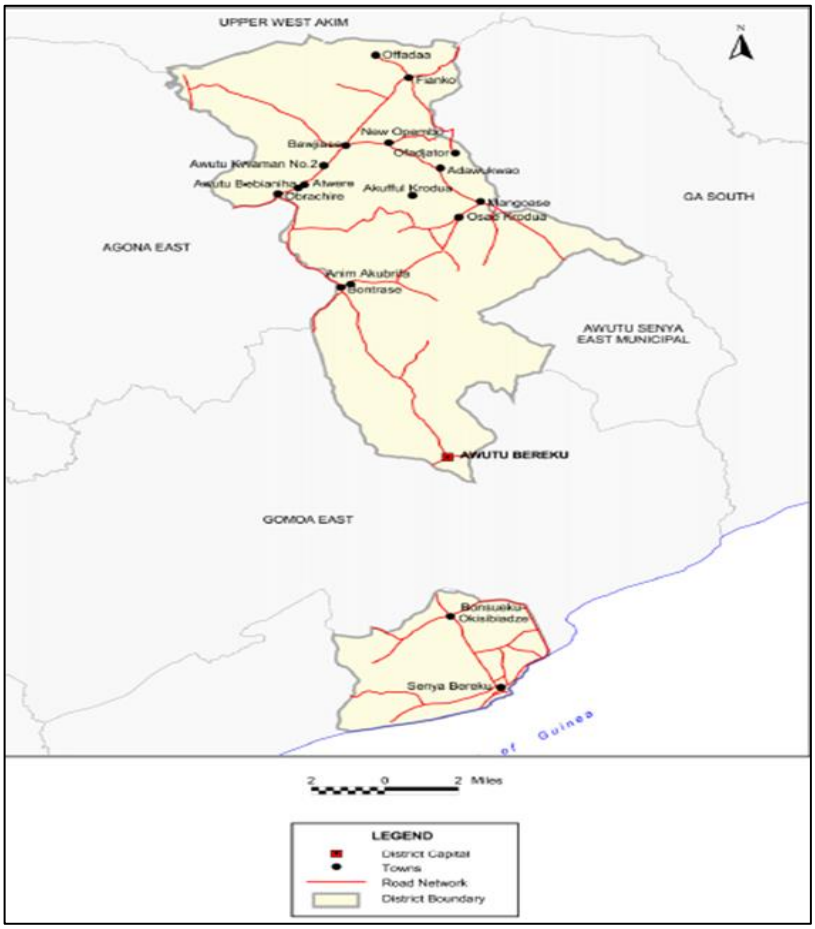

Fig. 5. District map of the Awutu Senya West (Ghana Statistical Service, 2010)

Fig. 6. District map of the Upper West Akyem (Ghana Statistical Service, 2010)

3.2.1 Geography and Socio-Demographic characteristics

The study was conducted in two districts. The two selected districts for the study continue to record high numbers of cases of yaws despite numerous interventions.

The Awutu Senya West and Upper West Akyem districts are located in the Central and Eastern Regions respectively. The two districts share a common boundary, with the Upper West Akyem district located at the northeastern border of the Awutu Senya West district. Upper West Akyem District is the only district in the Eastern Region that shares boundaries with the Central and Greater Accra Regions. The total household population of both districts

is a little over 80,000 according to the 2010 population and housing census with children under the age of 15 years constituting more than 50% of the population.

The climatic conditions; high temperatures and humidity coupled with occasional heavy rainfall facilitate the transmission of yaws and other tropical diseases.

Majority of the people live in rural areas, 52% in the Awutu Senya West district and 75% in the Upper West Akyem district.

Skilled agricultural forestry and fishery constitute the main occupations in both districts with more than half of the constituents engaging in such activities.

3.2.2 Health Facilities

The Upper West Akyem district has twenty-five facilities; four health centers and twenty-one (21) functional CHPS zones across the entire district. The Awutu Senya West district has over forty health facilities, which includes five health centers, twelve CHPS zones and over thirty private facilities.

3.2.3 Sanitation and Housing

Overcrowding is a major problem in both districts. Single room occupancy is as high as 91% in the Upper West Akyem district with more than 10% of such rooms accommodating more than 10 persons. The average number of persons per house in both districts is seven (GSS, 2010).

The most widely used method of solid waste disposal in both districts is by public dump in the open space accounting for more than 60% of waste disposal methods.

Public toilet facilities are popular in both districts and a significant number of the populace engage in open defecation. More than 40% of residents in the rural communities of both districts use open bathing cubicles.

A significant proportion of residents (about 20%) in both districts lack access to potable water and resort to rivers and streams as their main source of water for drinking and other household chores.

Mud brick/earth (32.1%) is the second most important material used for outer walls of dwelling units in Awutu Senya West district. The proportion is slightly higher in the Upper West Akyem district (52.7%) (GSS, 2010).

3.3 STUDY VARIABLES

Dependent variable: Cases or controls

Independent variables:

Socio-demographic factors: The factors examined included; age, gender, caregiver's occupation, educational level of caregivers, ethnicity and religion.

Behavioral factors: Personal hygiene practices like bathing practices, hand washing, sharing of towels, and use of soap during bathing were assessed. Other exposures examined were overcrowding, contact with yaws patients and sharing of personal items.

Environmental factors: The type of housing, the material used in the building the house and the number of people sharing a room. Other variables included availability of sanitary facilities and source of water used for domestic activities.

Resources – Access to health facilities and access to potable water.

Other factors – previous yaws infection

Table 1a. Study variables

Variable	Operational definition	Scale of Measurement	Type
Dependent variables			
Cases	Any child between the age of 1 – 15 years who is resident in the Upper West Akyem or Awutu Senya West district and meets the criteria for the case definition	Categorical	Nominal
Control	Any child between the age of 1 – 15 years who is resident in the Upper West Akyem or Awutu Senya West district without Yaws (past or present infection)	Categorical	Nominal
Independent variables			
Socio-demographic factors			
Age of participant	Age at last birthday	Continuous	Ratio
Gender	Gender of participant	Categorical	Nominal
Ethnicity	Ethnic background of child	Categorical	Nominal
Religion	Type of religion practiced by caregiver	Categorical	Nominal
Occupation	Occupation of caregiver	Categorical	Nominal
Level of education	Highest level of education attained by caregiver	Categorical	Ordinal
Schooling status of child	Whether the study participant is schooling or not	Categorical	Nominal
Level of study of study participant	The level of study of study participant if schooling	Categorical	Nominal
Marital status	Marital status of caregiver	Categorical	Nominal
Number of siblings	Number of siblings the participant has	Continuous	Ratio
Behavioral Factors			
Daily bath hygiene	Whether the participant takes a bath at least once a day	Categorical	Nominal
Bathing frequency	Number of times the study participant takes a bath in a day	Categorical	Nominal
Use of soap	Whether the study participant uses soap in taking a bath	Categorical	Nominal
Sharing of bath towels and sponge	Sharing of bath towels between study participants and other members of the household	Categorical	Nominal
Source of bath water	The regular source of bath water for the study participant	Categorical	Nominal
Sharing of bath facilities	Number of people who share bathing facility with the study participant	Categorical	Nominal
Contact with Yaws patient	Any previous close contact with persons infected with Yaws	Categorical	Nominal
Use of clothing	How frequently the study participant if fully clothed	Categorical	Nominal
Handwashing	Frequency of hand washing when required	Categorical	Nominal
Handwashing practices	The use of soap and water in hand washing	Categorical	Nominal

Table 1b. Study variables

Variable	Operational definition	Scale of Measurement	Type
Environmental factors			
Housing	Type of house the participant lives in	Categorical	Nominal
Households	Number of households on a shared compound house	Categorical	Nominal
Housing material	The material that was used in the construction of the house	Categorical	Nominal
House occupancy	Total number of people in the house	Categorical	Nominal
Room occupancy	Total number of people who share a sleeping room with the study participant	Categorical	Nominal
Source of water for the household	The regular source of water for household activities	Categorical	Nominal
Source of water within the house	Availability of source of water within the house	Categorical	Nominal
Location/Distance to water source	Time it takes to get to a preferred water source if not available within the house	Categorical	Nominal
Toilet facilities	Availability of toilet facilities with the house	Categorical	Nominal
Type of toilet facility	The type of toilet facility used by the household	Categorical	Nominal
Type of public toilet facility	The type of public toilet facility used if not available within the house	Categorical	Nominal
Previous Yaws infection	Previously confirmed and treated yaws	Categorical	Nominal

3.4 SAMPLING

3.4.1 STUDY POPULATION

Children between ages 1 – 15 years who met the criteria for cases or control and resident in the Awutu Senya West and Upper West Akyem districts.

3.4.1.1 Case definition: The cases included in the study were cases with early or active yaws. Any child between the ages of 1 – 15 years who is resident in the Upper West Akyem or Awutu Senya West district who met the following criteria:

Suspected case*:* Presence of primary and secondary lesions: papillomata, painless ulcer or hyperkeratosis. The cases were examined and selected by trained field research assistants, disease control officers, field officers and the principal investigator (PI) using the WHO picture guide.

Primary Yaws lesions: 1. Ulcers with raised edges and a crusty base or 2. Papilloma that appears as a firm yellowish skin lesion with a dark tip, on any part of the body.

Secondary Yaws lesions: Multiple ulcers or papillomata as previously defined, hyperkeratosis, macules, papules, nodules and maculopapular rash.

Probable case: A probable case was defined as any suspected case with only a positive rapid treponemal test. This test was done using the SD Bioline Syphilis 3.0® RDT.

Confirmed case: A probable case with a dually positive treponemal and non-treponemal test. Confirmation was done with rapid point of care (POC) test; The Dual Path Platform (DPP) Syphilis Screen and Confirm test kit (Chembio, Medford, NY, USA). The test kit has been shown to be highly specific and sensitive (95.2% and 92% respectively) compared to traditional *Treponemal* assays (Marks et al., 2014). Finger prick blood samples was used for the test.

3.4.1.2 Controls: Children aged between 1 - 15 years in the Awutu Senya West and Upper West Akyem districts without a history of yaws or yaws-like skin lesions and living in the same neighborhood as the cases.

3.4.2 Procedure for the Standard SD Bioline Syphilis Rapid Diagnostic Test (RDT)

1. Finger prick blood was used for test. About 20 µl of capillary blood was used.
2. Blood samples were added to the sample wells.
3. Four drops of the assay diluent was then added to the sample well.
4. The test result was read after five to fifteen minutes.
5. The appearance of both the control and test lines in the results window confirmed a reactive test (NPHL/HIV/STI Programme, 2014).

3.4.3 Procedure for the Dual Path Platform (DPP) Syphilis Screen and Confirm test kit

1. Finger prick blood sample was collected (about 20µl) from study participants with a positive treponemal RDT.
2. The sample collected was placed into the first well on the test plate and the buffer was added (2-3 drops).
3. The test was allowed to run for five minutes before additional buffer (2 drops) was added to the second well.
4. Test results were read after ten to fifteen minutes.
5. A positive confirmation is the appearance of two test lines (T1 and T2) in addition to the control lines on the test kit (Marks et al., 2014).

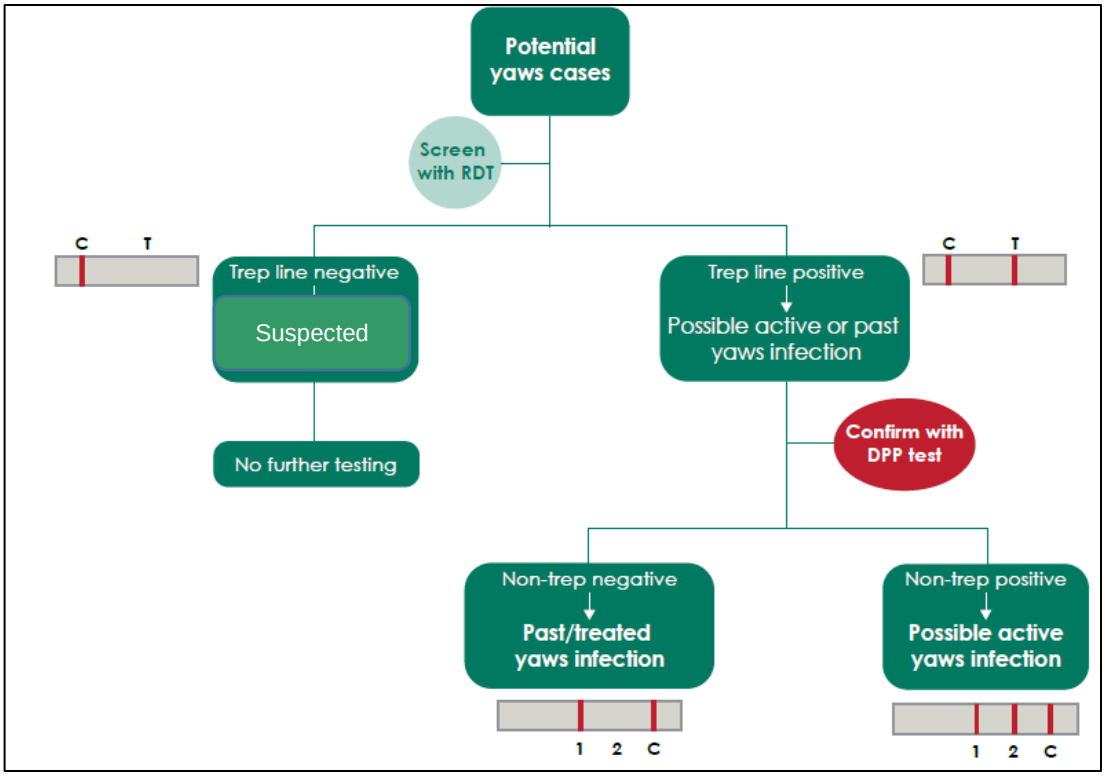

Figure 7. Algorithm for selection of cases (Adapted from WHO)

3.4.4 SAMPLE SIZE

The sample size for the study was calculated assuming a power of 80% to detect an odds ratio of 3.0 with 18% exposure among controls (Dzotsi et al., 2017; Kwakye-maclean, 2015) at an alpha level of 0.05. OpenEpi Version 3 was used in the sample size determination using the formula below (Kelsey et al., 1996).

$$N_{1=}(r+1)/r * \bar{p}(1-\bar{p})(Z_{\beta}-Z_{\alpha/2})^2 / (p_1-p_2)^2 \qquad N_{2=} rN_1$$

Where $N_{1=}$ number of cases
N_2= number of controls
$Z_{\beta=}$ desired power, 0.84 for a power of 80% $Z_{\alpha/2}$= confidence level (95%)= 1.96
p_1= proportion of cases with exposure
p_2 = proportion of controls with exposure= 18%
r = ratio of controls to cases
and $\bar{p} = (p_1+rp_2)/(r+1)$

Minimum sample size calculated from the above N_1 (cases) = 56 N_2 (controls) = 112;

Total = **168**

To account for a 10% non-response rate; total minimum sample size = 168+16.8 = 185

This was adjusted to **186** to give a total of 62 cases: 124 controls.

3.4.5 SAMPLING METHOD/TECHNIQUE

Case selection: Trained research assistants, field officers and the PI identified cases from communities and schools in the district through active search using the criteria above.

Controls: Controls were selected from the same communities as cases. Two controls were selected for each case. A cardinal point, that is, east, west, north or south was selected through balloting in the house of an identified case. Two houses were then selected in the balloted direction. A control was then selected in each house. Numbers were assigned to all children who met the criteria for controls in the house. A number was selected through balloting and the participant was included in the study. If no eligible controls were found in a selected house, the next house in the same direction was selected and the process repeated. Controls were also selected in schools in instances where cases were identified in schools. The controls were selected from the same class where the cases were found. The selection was done through balloting, all eligible controls in the identified class were included in the balloting process. The number of controls subsequently selected was based on the number of cases identified in the class using a case to control ratio of 1:2.

3.5 DATA COLLECTION TECHNIQUE AND TOOLS

Data on exposures among cases and controls were collected using pre-coded structured interviewer-administered questionnaire designed using the Research Electronic Data Capture (REDCAP®) software. Field and research assistants were trained on using a mobile phone based application version of the software for the collection of data. The questionnaire assessed the socio-demographic, environmental and behavioral factors associated with the transmission of yaws, which was captured under different sections. Skin lesions among cases were identified using the WHO picture guide and documented after obtaining permission from the study participants.

3.6 DATA PROCESSING AND ANALYSIS

All data captured on the field were extracted to a central database using the REDCAP® software and then Microsoft Excel 2016. The data was cleaned before the analysis with Stata 15 statistical software.

Descriptive statistics was performed for all variables and expressed as means and standard deviation for continuous variables such as age. Categorical variables including educational status, caregiver's occupation and gender were expressed as proportions and presented as graphs or charts where appropriate.

The Chi-square test and Student t-test was used to test the association of categorical and continuous exposure variables and yaws infection, respectively.

Univariable analysis (logistic regression) was done to test the association between socio-demographic factors, behavioral factors and yaws infection. This was presented as crude odds ratios on a 95% confidence interval. The final age and sex-adjusted multivariable

logistic regression model fitted to determine the factors associated with yaws was done using backward stepwise approach (exposure variables with p values ≤ 0.1 were added and those with p values ≥ 0.2 were removed).

All statistical analysis was done at a 95% significance level with p values < 0.05 considered as statistically significant.

3.7 QUALITY CONTROL

Experienced field technicians and disease control officers from the district health directorate trained field and research assistants on case identification using the WHO picture guide. To avoid discrepancies with case selection, disease control officers supervised the research assistants. The research assistants were also given extensive training on the use of the REDCAP® software for the collection of data using their mobile phones. Laboratory field staff from the health directorate assisted with use of the Syphilis and DPP point of care (POC) test kit for case confirmation.

The pre-testing of the study questionnaire involving forty-five children between ages 1-15 years was done in a selected community at the Hohoe Municipality with similar characteristics as the study areas.

3.8 ETHICAL CLEARANCE

Ethical approval was obtained from the Ghana Health Service Ethics Review Committee (GHS-ERC: 034/12/18) and permission was sought from the District Health and Educational directorates respectively.

The study was explained to the participants and caregivers in clear and unambiguous language. Written informed consent and assent were obtained before inclusion in the study.

Participation in the study was strictly voluntary with no consequences for withdrawal or refusal to participate. The process of obtaining finger pricked blood samples from identified cases was explained to caregivers and documented on the consent and assent forms.

All data that were collected were kept confidential by assigning codes to replace personal information gathered to make it untraceable to study participants. Access to the final password-protected database was restricted to only the PI.

All identified cases and their contacts were treated using the current WHO treatment guidelines for yaws. Though the project specifically screened the participants for yaws, other detected skin conditions among the cases and controls were referred appropriately (*Clinical assessment and referral form attached, Appendix C*).

There is no conflict of interest to declare and the WHO/TDR program funded the study.

CHAPTER FOUR

4.0 RESULTS

The research was a community-based unmatched 1:2 case control study conducted between June 2, 2018 – June 20, 2018 in the Upper West Akyem and Awutu Senya West districts.

One hundred and eighty-six (186) participants were recruited in the two districts, comprising of sixty-two (62) cases and one hundred and twenty-four (124) controls. The distribution of cases in communities in the two study districts is shown in Table 2.

In the Upper West Akyem district, more than half of the cases (51.6%, 16/31) were recorded in the Kwasi Nyarko, Ndoda and Okurase communities. The Fianko and Topiase communities in the Awutu Senya West districts recorded the most cases, 25.8%, (8/31) and 22.6%, (7/31) respectively.

Table 2. Distribution of yaws cases in the Upper West Akyem and Awutu Senya West districts

Upper West Akyem			Awutu Senya West		
Community	Number of cases	%	Community	Number of cases	%
Kwasi Nyarko	6	19.4	Fianko	8	25.8
Ndoda	5	16.1	Topiase	7	22.6
Okurase	5	16.1	Okwabena	5	16.1
Gamali	3	9.7	Ayensuako	4	12.9
Asikasu	2	6.5	Ofadaa	4	12.9
Ntekyerekye	2	6.5	Mayenda	3	9.7
Adeiso	1	3.2	Total	31	100.0
Sukrong Canaan	1	3.2			
Alhaji Akura	1	3.2			
Tiokrom	1	3.2			
Danso	1	3.2			
Alafia	1	3.2			
Singer	1	3.2			
Dzakpatra	1	3.2			
Total	31	100.0			

Over hundred and fifty children with skin lesions were examined in communities and schools in the two districts. The classification of cases after the screening process is as shown below (Figure 8).

Half of the cases 50.0%, (31/62) were classified as suspected cases using the WHO picture guide, four cases (6.5%) were classified as probable cases and twenty-seven (43.6%) were confirmed using the DPP rapid test kit.

Thirty-one cases were selected from each district. The classification and distribution of cases for each district is as shown in Table 3 below.

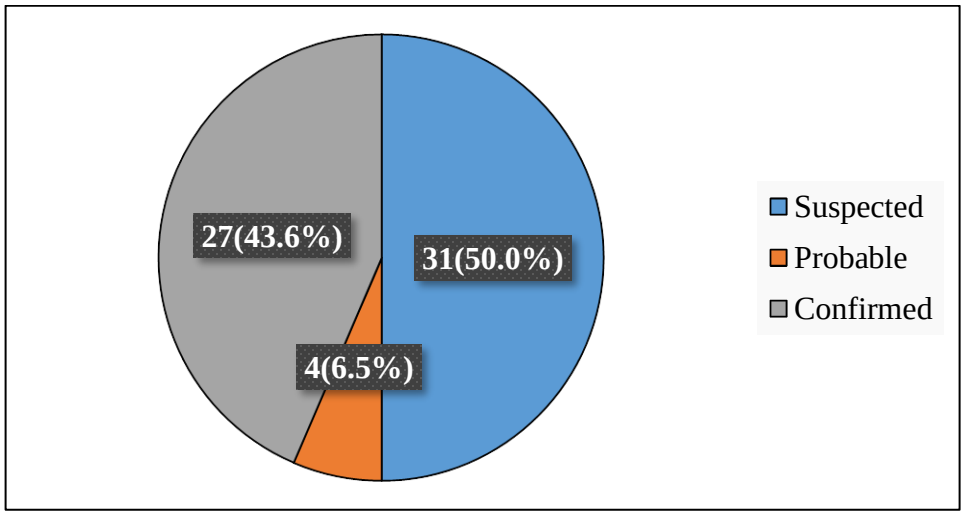

Figure 8. Classification of cases

Table 3. Yaws case classification and distribution in Upper West Akyem and Awutu Senya West districts

	Case category N (%)			
Name of district	**Suspected**	**Probable**	**Confirmed**	**Total**
Awutu Senya West	15 (48.4)	4 (100)	12 (44.4)	31
Upper West Akyem	16 (51.6)	0(0)	15 (55.6)	31

4.1 Type and distribution of yaws lesions

Primary yaws lesions were the most common (73%, 45/62) (Figure 9). Majority of the lesions were ulcers (67%, 42/62), the second most frequent lesion was papilloma (19.4%, 12/62). The other types of lesions; papules, macules, hyperkeratosis and maculopapular rash were less frequent contributing to less than 5% of the total number of cases seen (Figure 10).

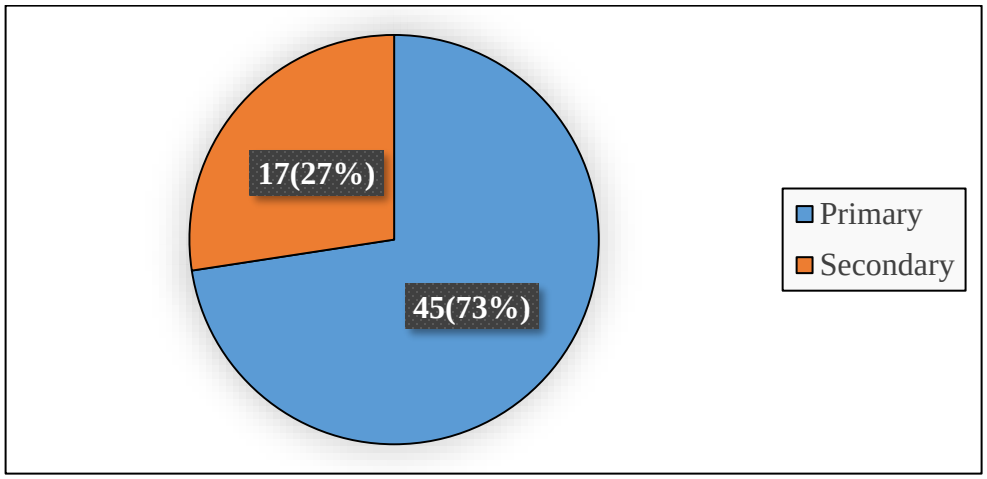

Figure 9. Clinical staging of yaws

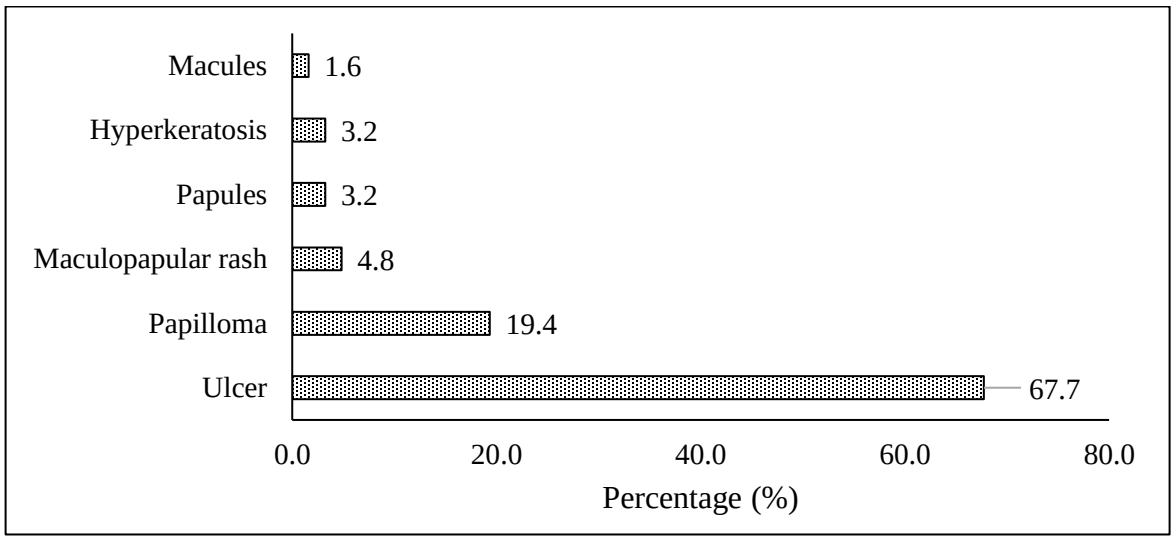

Figure 10. Distribution of yaws lesions among study participants

More than half (67.7%, 42/62) of the lesions were found on the lower limbs of the study participants. The other frequently affected site was either the head, neck or face. Lesions on the upper limbs and trunk were infrequent (13% and 1.6% respectively) (Table.4)

Table 4. Location of yaws lesions

Location of lesion	Frequency (%)
Lower limbs	42 (67.7)
Head/neck/face	11 (17.7)
Upper limbs	8 (13.0)
Trunk	1 (1.6)

4.2 Socio-demographic characteristics of study participants

The age range of the study participants was between 3 – 15 years. Cases were older than controls. The median age of cases was 11 years and the median age of controls was 10 years. There was however no statistical significant difference between the ages ($p > 0.05$). There was no significant statistical difference between the ages of males and females.

Majority of the study participants in both districts were between the ages of 10 – 15 years, constituting more than half of participants in each district (Table 5). The age and sex distribution of study participants are shown in Table 5.

Table 5. Age and sex distribution of study participants

	Age (years)			
	Minimum	**Maximum**	**Median(IQR)**	**p**
Controls	3	15	10 (8,13)	0.076
Cases	3	15	11 (9,13)	
Male	4	15	11 (9,13)	0.611
Female	3	15	11 (8,13)	
	Awutu Senya West	**Upper West Akyem**		
Age group	**N (%)**	**N (%)**	**Total**	**p**
< 5 years	3 (50)	3 (50)	6	0.646
5-9 years	29 (45.3)	35 (54.7)	64	
10-15 years	61 (52.6)	55 (47.4)	116	
	Males	**Females**		
Age group	**N (%)**	**N (%)**	**Total**	**p**
< 5 years	2 (33.3)	4 (66.7)	6	0.222
5-9 years	42 (65.6)	22 (34.4)	64	
10-15 years	66 (56.9)	50 (43.1)	116	

Majority (59.1%, 110/186) of the study participants were males. The different ethnic groups were almost equally represented with people of northern descent being the least represented (12.4%, 23/186). The most predominant ethnic group was Akan, (35.5%, 66/186).

Most of the study participants were Christians (80.1%, 149/186) and primary education (96/185) was the highest level of education among the caregivers.

More than eighty percent (143/186) of the study participants were currently in school. The distribution of other socio-demographic characteristics is as shown in Table 6.

Table 6. Socio-demographic characteristics of study participants

Socio-demographic characteristics	Frequency (%)
Sex(n=186)	
Male	110 (59.1)
Female	76 (40.9)
Ethnic background (n=186)	
Akan	66 (35.5)
Ga/Adangme	43 (23.1)
Ewe	54 (29.3)
Northerner	23 (12.4)
Religion (n=186)	
Christian	149 (80.1)
Muslim	20 (10.8)
Traditional	17 (9.1)
Educational level of caregiver (n=185)	
None	34 (18.3)
Primary	96 (51.9)
JHS	49 (26.5)
SHS and above	6 (3.2)
Marital status of care giver (n=186)	
Single	65 (35.0)
Married	95 (51.0)
Divorced	8 (4.3)
Widowed	11 (5.9)
Co-habiting	7 (3.8)
Educational level of study participants (n=143)	
Pre-school	6 (4.2)
Lower Primary (1 -3)	55 (38.4)
Upper Primary (4 -6)	54 (37.8)
JHS	28 (19.6)

JHS- Junior High School SHS- Senior High School

4.3 Assessment of factors associated with yaws

4.3.1 Socio-demographic factors

There was a significant association between sex and yaws infection. A greater proportion of cases were males compared to community controls (cOR= 2.7, 95% CI= 1.38 - 5.26).

Yaws was less frequent among the northern ethnic group compared to the Ga /Adangme (cOR= 4.80, 95% CI= 1.23 – 18.63) and Ewe (cOR= 4.95, 95% CI= 1.31 - 18.66) ethnic groups.

There was no significant association between religion, level of education and schooling status (of study participant) with yaws, however, cases had a higher odds (cOR= 2.7, 95% CI= 1.13 – 6.47) of being previously treated for yaws compared to community controls.

The univariable analysis of socio-demographic factors and yaws infection is shown in Table 7.

Table 7. Univariate analysis of socio-demographic factors and all cases of yaws in the Upper West Akyem and Awutu Senya West districts

Socio-demographic characteristics	All Cases (n=62) N (%)	Controls(n=124) N (%)	cOR (95% CI)	p
Sex				
Female[1]	16 (40.9)	60 (48.4)		
Male	46 (74.1)	64 (51.6)	2.7 (1.38 – 5.26)	**0.004***
Age(years)				
< 5[1]	2 (3.2)	4 (3.2)		
5 – 9	15 (24.2)	49 (39.5)	0.61 (0.10 – 3.68)	0.592
10 - 15	45 (72.6)	71 (57.3)	1.27 (0.22 – 7.21)	0.789
Ethnic background				
Northerner[1]	3 (4.8)	20 (16.1)		
Akan	18 (29.0)	48 (38.7)	2.5 (0.66 – 9.44)	0.177
Ga/Adangme	18 (29.0)	25 (20.2)	4.8 (1.23 – 18.63)	**0.023***
Ewe	23 (37.2)	31 (25)	4.95 (1.31 – 18.66)	**0.018***
Religion				
Traditional[1]	4 (6.5)	13 (10.5)		
Christian	55 (88.7)	94 (75.8)	1.9 (0.59 – 6.12)	0.281
Muslim	3 (4.8)	17 (13.7)	0.57 (0.11 – 3.02)	0.512
Is study participant in school?				
No[1]	11 (17.7)	32 (25.8)		
Yes	51 (82.3)	92 (74.1)	1.61 (0.75 – 3.47)	0.221
Level of education of caregiver				
None[1]	11 (18.0)	23 (18.6)		
Primary	33 (54.1)	63 (50.8)	1.1 (0.48 – 2.50)	0.83
JHS	15 (24.6)	34 (27.4)	0.92 (0.36 – 2.36)	0.866
SHS	2 (3.3)	4 (3.2)	1.05 (0.17 – 6.60)	0.962
Past treatment for Yaws				
No[1]	48 (78.7)	110 (90.9)		
Yes	13 (13.2)	11 (9.1)	2.7 (1.13 - 6.47)	**0.025***

**- p < 0.05 – statistically significant* [1] *– reference group* *cOR-crude odds ratio*

4.3.2 Behavioral factors

A significantly greater proportion of cases compared to controls (30.6% vs. 14.5%) did not have their bath every day (cOR= 2.76, 95% CI= 1.31 - 5.80) (Table 8). The frequency of bathing was also associated with yaws infection. Cases had increased odds of having their bath once daily compared to community controls (cOR= 1.98, 95% CI= 1.07 – 3.68).

Sharing of personal items such as towels and sponge (cOR= 3.1, 95% CI= 1.40 – 6.97) and sharing a bathroom with more than five persons (cOR= 2.57, 95% CI= 1.36 – 4.80) were associated with active yaws infection.

A previous contact with someone who had yaws was associated with yaws infection. Compared to community controls, yaws cases had an increased odds of previous exposure to the disease (cOR= 2.7, 95% CI= 1.42 - 5.11).

Comparatively, cases were less likely to be fully clothed or dressed regularly (cOR= 2.76, 95% CI= 1.15 – 6.59).

The source of water for bathing and the use of soap in bathing were not associated with yaws.

Table 8. Univariate analysis of behavioral factors and all cases of yaws in the Upper West Akyem and Awutu Senya West districts

Behavioral factors	All Cases (n=62) N (%)	Controls (n=124) N (%)	cOR (95% CI)	p
Bath every day				
Yes[1]	43 (69.4)	106 (86.2)		
No	19 (19.5)	17 (30.7)	2.76 (1.31 - 5.80)	**0.008***
How many times do you take your bath in a day?				
Twice[1]	26 (41.9)	73 (58.9)		
Once	36 (46.8)	51 (58.06)	1.98 (1.07 - 3.68)	**0.03***
Do you bathe with soap?				
Yes[1]	58 (95.1)	115 (95)		
No	3 (4.9)	6 (5.0)	0.99 (0.23 - 4.11)	0.99
Sharing of towels or sponge				
No[1]	9 (14.5)	42 (34.7)		
Yes	53 (85.5)	79 (65.3)	3.1 (1.40 - 6.97)	**0.005***
Number of persons that share a bathroom				
3 – 5[1]	22 (32.3)	72 (58.5)		
More than 5	40 (64.5)	51 (41.5)	2.57 (1.36 – 4.80)	**0.003***
Source of water for bathing				
Pipe borne water[1]	7 (11.3)	7 (5.7)		
Borehole	3 (4.8)	15 (12.2)	0.2 (0.04 - 1.01)	0.052**
Well	12 (19.4)	27 (22)	0.44 (0.13 - 1.55)	0.203
Steams/rivers/ponds	40 (64.5)	74 (60.1)	0.54 (0.18 - 1.05)	0.28
Previous contact with yaws				
No[1]	32 (66.7)	92 (74.2)		
Yes	30 (33.3)	32 (48.4)	2.7 (1.42 - 5.11)	**0.002***
Use of clothing/dressing				
All the time[1]	10 (16.1)	35 (28.2)		
Most often	26 (41.9)	56 (45.2)	1.6 (0.69 - 3.78)	0.259
Not regularly	26 (41.9)	33 (26.6)	2.76 (1.15 - 6.59)	**0.022***

**- p < 0.05 – statistically significant ** - variable included in multivariate analysis [1] –reference group cOR-crude odds ratio*

4.3.3 Environmental factors

4.3.3.1 Housing

Yaws cases had an increased odds of staying in a compound house compared to controls (cOR= 2.91, 95% CI= 1.53 - 5.50) (Table 9). The number of households on a compound was not significantly associated with yaws though a greater proportion of cases (23.8%, 10/42) had more than seven households on the compound compared to controls (18.9%, 10/53).

Yaws cases were more likely to share overcrowded sleeping rooms and homes. Compared to community controls, cases had an increased odds of sharing a sleeping room with more than four persons (cOR= 3.31, 95% CI= 1.71 – 6.41) or sharing a house with 5 – 8 persons (cOR= 4.65, 95% CI= 1.68 – 12.86) or more than eight persons (cOR= 6.78, 95% CI= 2.24 – 20.50).

The type of building material used was not associated with yaws infection.

Table 9. Univariate analysis of housing factors and all cases of yaws in the Upper West Akyem and Awutu Senya West districts

Housing factors	All Cases (n=62) N (%)	Controls (n=124) N (%)	cOR (95% CI)	p
Type of housing				
Single unit[1]	20 (32.3)	72 (58.1)		
Compound	42 (67.7)	52 (41.9)	2.91 (1.53 - 5.50)	**0.001***
Number of households on the compound				
2 - 4[1]	14 (33.3)	22 (41.5)		
5 – 7	18 (42.9)	21 (39.6)	1.34 (0.54 - 3.38)	0.525
> 7	10 (23.8)	10 (18.9)	1.57 (0.52 - 4.73)	0.422
Building material				
Cement block[1]	24 (38.7)	50 (40.3)		
Mud	38 (61.3)	74 (59.7)	1.06 (0.51 – 2.0)	0.832
Number of persons sharing a sleeping room				
2 – 4[1]	33 (53.2)	98 (79.0)		
> 4	29 (46.8)	26 (21.0)	3.31 (1.71 – 6.41)	**< 0.0001***
Number of persons staying in the house				
< 5[1]	5 (8.1)	39 (31.5)		
5 – 8	37 (59.7)	62 (50)	4.65 (1.68 - 12.86)	**0.003***
> 8	20 (32.3)	23 (18.6)	6.78 (2.24 - 20.50)	**0.001***

**- p < 0.05 – statistically significant* [1] *– reference group* *cOR-crude odds ratio*

4.3.3.2 Sanitation

The source of water for household activities, distance and location of the water source were not associated with yaws infection (Table 10). Similarly, access to a toilet facility at home was also not associated with yaws (cOR=1.07, 95%CI=0.56 - 2.06) though the type of toilet facility used was associated with risk of yaws infection. Compared to community controls, yaws cases had increased odds of practicing open defecation (cOR=2.7, 95%CI=1.25 – 6.16).

Good hand washing practices was less frequent among cases compared to community controls. A greater proportion of cases compared to controls (cOR=4.98, 95% CI= 2.42 – 10.27) reported that they did not wash their hands regularly when required.

Table 10. Univariate analysis of sanitary factors and all cases of yaws in the Upper West Akyem and Awutu Senya West districts

	All Cases (n=62)	Controls (n=124)		
Sanitary factors	**N (%)**		**cOR (95% CI)**	**p**
Water source in the house				
Yes[1]	4 (6.5)	13 (10.5)		
No	58 (93.5)	111 (89.5)	1.7 (0.53 - 5.44)	0.373
Source of water for household activities				
Pipe borne water[1]	8 (7.5)	6 (4.8)		
Bore hole	4 (6.5)	16 (12.9)	0.58 (0.12 - 2.66)	0.484
Well	16 (25.8)	24 (19.4)	1.63 (0.55 - 4.78)	0.375
Streams/rivers/ponds	34 (54.8)	78 (62.9)	1.52 (0.59 - 3.96)	0.389
Distance from water source				
less than 5 minutes[1]	7 (12.1)	21 (18.9)		
5 - 10 minutes	25 (43.1)	47 (42.3)	1.69 (0.60 - 4.27)	0.352
more than 10 minutes	26 (44.9)	43 (38.7)	1.81 (0.68 - 4.85)	0.236
Toilet facility at home				
Yes[1]	20 (32.3)	42 (33.9)		
No	42 (67.7)	82 (66.1)	1.07 (0.56 - 2.06)	0.826
Type of toilet facility used				
Improved latrine[1]	23 (54.8)	64 (77.1)		
Open defecation	19 (45.2)	19 (22.9)	2.7 (1.25 – 6.16)	**0.012***
Handwashing(1)				
Most often[1]	12 (17.7)	67 (47.2)		
Not regularly	50 (80.7)	56 (45.5)	4.98 (2.42 – 10.27)	**<0.0001***
Handwashing (2)				
Soap and water[1]	32 (51.6)	80 (64.5)		
Water	30 (39.8)	44 (35.5)	1.7 (0.91 - 3.17)	0.091**

**- p < 0.05 – statistically significant ** - variable included in multivariate analysis [1] – reference*

cOR- crude odds ratio

4.4 Summary of univariate analysis

Simple logistic regression was used to determine the exposure variables that were independently associated with all cases of yaws (suspected, probable and confirmed) as previously described.

Table 11 summarizes the crude odds ratios of exposures using all the different case categories of yaws compared to only confirmed cases of yaws. The analysis showed that nearly all the variables that were associated with yaws (using all case categories) were also significantly associated with only confirmed cases of yaws.

The results also showed a general increase in odds for majority of the exposure variables when only confirmed cases was used in the analysis. For instance, yaws cases (all case categories) had almost three times increased odds of not having a bath every day (cOR=2.76 95% CI=1.31 - 5.80), however confirmed cases had almost a fivefold increased odds of not having a bath everyday compared to community controls (cOR=4.5, 95%CI=1.87 - 10.84).

Similarly, compared to all case categories of yaws (cOR=2.7, 95% CI=1.13 - 6.47), confirmed cases had an increased odds of previous treatment for yaws (cOR=3.48, 95%CI=1.26 - 9.60) compared to controls.

The summary of the analysis is shown in Table 11.

Table 11. Summary of univariate analysis- Factors significantly associated with yaws (All cases and confirmed cases).

Variables	All Cases		Confirmed Cases	
Socio-demographic factors	**cOR (95% CI)**	**p value**	**cOR (95% CI)**	**p value**
Sex **(Male)**	2.7 (1.38 - 5.26)	0.004	2.70 (1.12 - 6.49)	0.027
Ethnicity **(Ga/Adangme)**	4.8 (1.23 - 18.63)	0.023	NS	
Ethnicity **(Ewes)**	4.95 (1.31 - 18.66)	0.018	9.68 (1.18 - 79.09)	0.034
Past treatment for yaws **(Yes)**	2.7 (1.13 - 6.47)	0.025	3.48 (1.26 - 9.60)	0.016
Behavioral factors				
Bath every day **(No)**	2.76 (1.31 - 5.80)	0.008	4.5 (1.87 - 10.84)	0.001
Frequency of bathing/day **(Once)**	1.98 (1.07 - 3.68)	0.03	3.5 (1.49 - 8.21)	0.004
Sharing of towels/sponge **(Yes)**	3.1 (1.40 - 6.97)	0.005	3.5 (1.17 - 10.94)	0.025
Bathroom **(used by > 5 persons)**	2.57 (1.36 – 4.80)	0.003	NS	
Contact with yaws **(Yes)**	2.7 (1.42 - 5.11)	0.002	5.23 (2.26 - 12.09)	< 0.0001
Use of clothing **(Not regularly)**	2.76 (1.15 - 6.59)	0.022	NS	
Handwashing **(Not regularly)**	4.98 (2.42 – 10.27)	<0.0001	4.10 (1.65 - 10.22)	0.002
Environmental factors				
Type of housing **(Compound)**	2.91 (1.53 - 5.50)	0.001	4.74 (1.90 - 11.84)	0.001
Sleeping room occupancy **(> 4 persons)**	3.31 (1.71 - 6.41)	< 0.001	4.5 (1.20 - 10.49)	< 0.0001
House occupancy **(> 8 persons)**	6.78 (2.24 - 20.50)	0.001	6.22 (1.57 - 24.63)	0.009
Toilet facility **(open defecation)**	2.7 (1.25 – 6.16)	0.012	3.70 (1.37 - 10.04)	0.01

cOR- crude odds ratio *NS- No statistical significance*

4.5. Multivariate analysis

The multivariable logistic regression model (Table 12) was fitted using a backwards stepwise approach whilst controlling for age and sex.

The factors associated with yaws from the adjusted analysis were the type of housing, age, male sex and number of persons sharing a bathroom.

Increasing age was associated with an increased odds of infection (aOR=5.90, 95% CI=1.97 – 17.67).

Yaws cases were more frequent among males (aOR=4.15, 95% CI=1.29 – 13.36).

Compared to community controls, yaws cases were more likely to reside in compound houses (aOR=25.42, 95% CI=6.15 – 105.09). Yaws cases had a threefold increased odds of sharing a bathroom with more than five persons (aOR=3.25, 95%CI= 1.09 – 9.71).

Poor handwashing practices was more frequent among cases compared to community controls (aOR=6.46, 95%CI= 1.89 – 22.04).

The number of persons that share a sleeping room and the type of toilet facility used were not associated with yaws infection in the multivariable analysis (Table 12).

Table 12. Multivariate analysis of factors associated with yaws in the Upper West Akyem and Awutu Senya West districts.

Variables	aOR	95% CI	p
Age (**years**)	5.90	1.97 - 17.67	0.002*
Sex ***(Male)***	4.15	1.29 - 13.36	0.039*
Handwashing ***(Not regularly)***	6.46	1.89 - 22.04	0.003*
Number of persons sharing a bathroom ***(More than 5 persons)***	3.25	1.09 - 9.71	0.035*
Type of toilet facility ***(open defecation)***	3.59	0.99 - 12.99	0.052
Type of housing ***(Compound house)***	25.42	6.15 - 105.09	< 0.0001*
Sleeping room occupancy ***(More than 4 persons)***	2.60	0.79 - 8.58	0.117

**- $p < 0.05$ – statistically significant aOR-adjusted odds ratio*

4.6 Yaws lesions

Figure 11. Multiple papillomas on the neck and lower limbs of two study participants

Figure 12. Yaws ulcers showing the pathognomonic "punched out" edges

CHAPTER FIVE

5.0 DISCUSSION

Poor personal hygiene, overcrowding and lack of access to improved sanitary facilities are the major factors that facilitate the transmission of yaws in the Awutu Senya West and Upper West Akyem districts. This is partly enhanced by the poor living standards in endemic communities in both districts.

5.1 Type and distribution of yaws lesions

Ulcers (67.7%) and papilloma (19.4%) which are the most infectious lesions were the commonest lesions found during the research. This is similar to research findings by Boock at. al., (2017). Their observational study carried out in rural communities in Cameroon showed that the most common lesions were ulcers (69%) and papillomas (19%). Similarly, in a study conducted by Kwakye-Maclean et. al., (2017) in three yaws endemic districts in Ghana, the most frequent yaws lesion was ulcer (47.3%).

Majority of the lesions were found on the lower limbs. Yaws lesions are typically found on the lower limbs as also demonstrated by Fegan and colleagues (2010) because the lower limbs are more susceptible to trauma and cuts.

5.2 Socio-demographic characteristics

The predominant age group in this study was the 10-15 years (116/186). There was no statistical significant association between age and yaws in the univariable analysis, though previous studies have shown that the highest burden of the disease is seen between the ages of 6 – 10 years (Marks, Vahi, et al., 2015; Rinaldi, 2008).

Case – control studies conducted in Ghana by Dzotsi et al., (2017) and Kwakye-maclean, (2017) showed no significant association between age and yaws. In this study however, the adjusted analysis showed that increasing age was associated with an increased odds of infection. This is similar to findings by Marks et al., (2015). Their sero-prevalence study demonstrated that increasing age was significantly associated with active disease. Exposure to activities that can lead to trauma and abrasions tend to increase with age more especially among males. This increases the risk of infection with the bacterium.

Yaws is common among males because males are more adventurous and participate in activities that result in injuries. The injury sites serve as conducive environments and portals that facilitate the transmission of yaws. The adjusted analysis showed that yaws infection was more likely (about fourfold) among males. Similar findings of increased risk of yaws among males has been reported by several studies (Capuano & Ozaki, 2011; Dzotsi et al., 2017; Marks, Vahi, et al., 2015)

The univariable analysis showed that yaws was significantly present among the Ewe and Ga/Adangme ethnic groups compared to the other ethnic groups. Though studies (Boock, Awah, Mou, & Nichter, 2017; Marks, Vahi, et al., 2015) have shown that the disease tends to cluster in specific geographical areas, no association was seen in previous studies with

regards to tribe or ethnic background. The finding from the research could be because Ewes and Ga Adangmes are part of the predominant ethnic groups in the study area.

A previous infection with yaws does not result in long lasting immunity and individuals previously infected carry a significant risk of reinfection. This could possibly be as a result of reactivation of latent yaws in a previously untreated patient (Agana-nsiire et al., 2014). This study showed that yaws cases had a threefold increased odds of being previously infected which is similar to previous findings, which indicated that the incidence of yaws was two times higher in study participants who had a previous infection. (Arisanti, Hutapea, Maladan, Wahyuni, & Rokmad, 2017).

This confirms the fact that relapses of asymptomatic, infected individuals is a major factor that drives the reemergence of yaws particularly in communities that have benefited from control efforts (Mitjà et al., 2013). Several communities in the two study areas were involved in the non-inferiority clinical trial that ushered in the Morges strategy.

The occupation of caregivers was not significantly associated with yaws although children whose parents are farmers and tend to work on farms were susceptible to trauma and abrasions, hence yaws infection. It has also been reported that communities that often rely on outdoor activity for labour and income, such as agricultural or sustenance farming, are more likely to encounter NTDs (Mackey et al., 2014).

Caregiver's educational level and religion were not significantly associated with yaws as demonstrated by Dzotsi et al., (2017) and Tettey (2009).

The schooling status of study participants did not carry a significant risk for infection, though studies have shown that yaws is predominant in schools in endemic areas because of

the increased probability of contact and overcrowding (Agana-nsiire et al., 2014; Kwakye-maclean, 2017).

5.3 Behavioral Factors

Poor personal hygiene is a significant independent risk factor for yaws infection. This study showed that yaws cases were less likely to have their bath every day or bathe more than once every day compared to community controls. Dirty and unclean sores facilitate infection and transmission of yaws.

Bathing with soap was not significantly associated with risk of infection though (Arisanti et al., 2017; Kwakye-maclean, 2015; Tettey, 2009) identified it as a significant independent risk factor.

Transmission of yaws occurs through contact with infected fluid from lesions. The univariable analysis showed that the risk of infection was higher among study participants who share personal items like towels and sponge or use bathrooms shared by more than four persons. Arisanti et. al., (2017) reported similar findings in their sero-prevalence study. They reported that sharing of towels and other personal items carried a three- fold increased risk of yaws infection.

Infected persons serve as important reservoirs for continuous transmission of yaws. Thus, contact with an infected person significantly increases the risk of infection. Asymptomatic individuals with latent yaws infection also serve as potential sources of reintroduction of infection into the community (Mitjà et al., 2013). In this study, yaws patients had almost fivefold-increased odds of previous contact or exposure to yaws. Dzotsi et. al. (2017) also demonstrated in their case control study that playing or sharing a room with a yaws case was associated with a markedly increased risk of infection.

The source of water used in bathing and for other household activities did not significantly increase the risk of infection, though majority of the study participants (controls and cases) used water from streams, rivers or ponds as their main source of water. This is consistent with reports from case-control studies conducted in other yaws endemic communities in Ghana (Dzotsi et al., 2017; Kwakye-maclean, 2015).

Conversely, other reports demonstrated increased cases of yaws along the Mbam River and Mape dam in a cross sectional study carried out in Cameroon (Boock et al., 2017). Tettey, (2009) also demonstrated in a study conducted in the Ga West Municipality that using water from dams for household activities was associated with increased risk of yaws infection.

Thus, the source of water used for household activities could possibly be a potential source for yaws transmission, though this was not evident in this research.

Frequently exposed skin carries a significant risk for yaws infection. Individuals in endemic areas who are seldom clothed or wear footwear have increased risk of contracting the disease.

In this research, infrequent use of clothing was an independent risk factor for yaws. In his landmark study that outlined the non-specific factors associated with yaws, Hill (1953) noted that prevalence of yaws dropped when clothing and footwear were provided to socially disadvantaged communities. In recent efforts aimed at eradicating yaws in endemic countries, supply of clothing to remote areas is a key component of the strategy.

5.4 Environmental Factors

5.4.1 Housing

Overcrowding which is a feature of sub-standard housing conditions is one of the most important factors that facilitates the transmission of yaws (Mackey et al., 2014). Yaws thrives in socio-economically disadvantaged communities where overcrowding is common. Significant factors associated with yaws in both the unadjusted analysis were staying in a compound house, sharing a sleeping room with more than four persons or staying in an overcrowded house.

Overcrowding increases the risk of transmission of yaws typically in households where individuals with active yaws lesions share close contact with other people. In a cluster randomized study by Marks et al., (2015) in the Solomon Islands, TPPA positivity and dual sero-positivity were associated with increased number of dual positive household contacts.

Similar findings regarding the significant association of yaws and overcrowding has been reported by Dzotsi et al., (2017), Kwakye-maclean (2015) and Tettey (2009).

The research showed that the type of building material used was not associated with yaws though the predominant material used for housing in both districts was mud. Low quality housing could however facilitate the transmission of yaws as was demonstrated in studies by Tettey (2009) and Kwakye-maclean (2015). In both studies, unadjusted analysis showed that yaws cases were more likely to stay in mud houses.

5.4.2 Water and sanitation

Lack of access to proper sanitation such as potable drinking water, appropriate waste disposal facilities and toilet facilities facilitate the transmission of NTDs particularly, yaws (Mackey et al., 2014). In this study however, neither the source of water nor distance from a water source was significantly associated with yaws. Similar findings was reported in a community based case-control study by Dzotsi et al., (2017).

Access to a toilet facility at home was not significantly associated with yaws though the unadjusted analysis showed that the risk of infection was higher among persons who practice open defecation. A study conducted in yaws and trachoma co-endemic provinces in Vanuatu showed that there was increased risk of TF positivity among households who used unimproved latrines (Taleo et al., 2017).

Good handwashing practices was associated with reduced odds of yaws infection. Yaws cases were eight times more likely to wash their hands infrequently compared to community controls. Marks and colleagues (2015) also showed that access to handwashing facilities was protective against TPPA positivity and dual sero-positivity.

The spread of yaws is facilitated by the entry of the bacteria through breached skin (Wicher et. al., 2000). Handwashing improves skin health and reduces the number of small abrasions and lesions, which serve as portals of entry for the bacteria (Marks, Vahi, et al., 2015).

5.5 Limitations of study

The exposure profile in case control studies is obtained through recall. Thus, recall bias is common in case control studies. Typically, cases because of the disease experience are more likely to recollect exposures compared to controls.

Swabs from yaws-like ulcers in some endemic areas have shown a co-infection with *Haemophilus ducreyi* (Marks et al., 2018)**.** Thus, it is possible some of the suspected cases (ulcers) could be due to *H. ducreyi* infections.

Prevalence-incidence bias is encountered in case control studies where exposures may rather tend to be protective typically when the disease involved is chronic. To reduce this, incident cases (active disease) were included in the study.

Research assistants used in this study were all experienced field officers who knew about yaws, thus interviewer bias was an area of concern for the study. To minimize this, research assistants were encouraged to avoid probing questions and coercion during the interviews.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

In this study, the factors associated with yaws in the Awutu Senya West and Upper West Akyem districts were age, male sex, sharing of overcrowded bathrooms or homes and poor hand hygiene practices.

The continuous transmission and resurgence of yaws especially in communities that have benefited from MDAs or TCTs reemphasizes the importance of multi-sectorial collaboration in the eradication efforts. Improving the socio-economic well-being and improving access to improved sanitary facilities in endemic communities should be a cardinal focus in eradication programs.

6.2 Recommendations

- **National Yaws Eradication Program**
  - Eradication strategy should involve inter sectorial collaboration; ministries of local government, water and sanitation, environment and finance.
  - Mapping out of yaws endemic communities using GIS technology to enable targeted interventions.
- **District Assembly and District Health Directorate**
  - Yaws screening should be an important component of the school health program especially in endemic communities.
  - Active surveillance and contact tracing must be intensified at the district level.

- Community outreaches in affected communities to educate them on early recognition of yaws to avoid complications and education on personal hygiene.
- The district assemblies must improve access to improved sanitary facilities and improve the living conditions in remote and hard to reach areas.

- **District Education Service**
- Students must be taught personal hygiene and recognition of yaws can be incorporated in lessons in schools in endemic communities.

- **Opportunities for further research**
- To explore the involvement of other factors associated with yaws, longitudinal data may produce more accurate findings that would help in eradication efforts.

7.0 REFERENCES

Agana-nsiire, P., Kaitoo, E., Erasmus, E., Agongo, A., Bonsu, G., Kyei-faried, S.,& Bonsu, F. A. (2014). Yaws Prevalence , Lessons from the Field and the Way Forward towards Yaws Eradication in Ghana. *International Scholarly Research Notices*, *2014*, 1–17. https://doi.org/10.1155/2014/910937

Amin, R., Abdus, S., Ariful, B., & Faiz. (2010). *Eradication of Yaws*. *Journal of Clinical Medicine and Research* (Vol. 2). https://doi.org/10.1371/journal.pntd.0000275.g001(20).long

Arisanti, Y., Hutapea, H., Maladan, Y., Wahyuni, T., & Rokmad, M. F. (2017). Serologic observation and risk factor of yaws in Hamadi Public Health Center , Jayapura. *Health Science Journal of Indonesia Research*, *8*(1), 25–29. https://doi.org/10.22435/hsji.v8i1.6387.Yuli

Asiedu, K., Amouzou, B., Dhariwal, A., Karam, M., Lobo, D., & Meheus, A. (2008). Yaws eradication : past efforts and future perspectives. *Bulletin of the World Health Organization*, *86*(July), 10–11. https://doi.org/10.2471/BLT.08.055608

Asiedu, K., Fitzpatrick, C., & Jannin, J. (2014). Eradication of Yaws : Historical Efforts and Achieving WHO ' s 2020 Target. *PLoS Neglected Tropical Diseases*, *8*(9). https://doi.org/10.1371/journal.pntd.0003016

Ayove, T., Houniei, W., Wangnapi, R., Bieb, S. V, Kazadi, W., Luke, L., & Paru, R. (2014). Sensitivity and specifi city of a rapid point-of-care test for active yaws : a comparative study. *Lancet Global Health*, *2*, 415–421. https://doi.org/10.1016/S2214-109X(14)70231-1

Berri, M., Souriau, A., Crosby, M., Gangl, A., & Randt, A. (2013). Treponemal Infection in Nonhuman Primates as Possible Reservoir for Human Yaws. *Emerging Infectious Diseases*, *19*(12), 2058–2060.

Boock, A. U., Awah, P. K., Mou, F., & Nichter, M. (2017). Yaws resurgence in Bankim, Cameroon: The relative effectiveness of different means of detection in rural communities. *PLoS Neglected Tropical Diseases*, *11*(5), 1–14. https://doi.org/10.1371/journal.pntd.0005557

Capuano, C., & Ozaki, M. (2011). Yaws in the western pacific region: A review of the literature. *Journal of Tropical Medicine*, *2011*, 1–15. https://doi.org/10.1155/2011/642832

Dzotsi, E., Agana, N., Ohene, S., Adjabeng, M., Aziz, A., & Odoom, J. K. (2017). Factors Associated with Yaws Infections in the West Akim Municipality, Ghana. *International Journal of Tropical Diseases & Health*, *22*(3), 1–9. https://doi.org/10.9734/IJTDH/2017/32425

Findlay, G. M .& Ampofo, O. (1951). Terramycin in the treatment of yaws and tropical ulcer. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *45*(2), 261-3.

Hays, R., Lukehart, S., Ph, D., Godornes, C., Sc, B.,….& Bieb, S. V. (2015). Mass Treatment with Single-Dose Azithromycin for Yaws. *The New England Journal of Medicine*, *372*(8), 703–710. https://doi.org/10.1056/NEJMoa1408586

Hill, K. R. (1953). Non-specific factors in the epidemiology of Yaws. *Bulletin of the World Health Organization*, *8*, 17–47.

Kazadi, W., Asiedu, K., Nsiire, A., & Mitja, O. (2014). Epidemiology of yaws : an update. *Clinical Epidemiology*, *6*, 119–128. https://doi.org/http://dx.doi.org/10.2147/CLEP.S44553

Kelsey, J.L, Whittemore, A.S, Evans, A.S, & Thompson WD. Methods in Observational Epidemiology. Oxford University Press, 1996.

Knauf, S., Gogarten, J., Schuenemann, V. J., Nys, H. M. De, Duex, A., Strouhal, M.,& Calvignac-Spencer, S. (2017). African Nonhuman Primates Are Infected With The Yaws Bacterium Treponema pallidum subsp. pertenue. *Research Gate*, (May), 1–9. https://doi.org/10.1101/135491

Kwakye-maclean, C. (2015). School of Public Health , College of Health Sciences , University of Ghana , Legon. A single dose oral azithromycin versus intramuscular benzathine benzylpenicillin for the treatment of yaws- a randomised non inferiority trial in Ghana .

Kwakye-maclean, C., Agana, N., Gyapong, J., & Nortey, P. (2017). A Single Dose Oral Azithromycin versus Intramuscular Benzathine Penicillin for the Treatment of Yaws-A Randomized Non Inferiority Trial in Ghana. *PLoS Neglected Tropical Diseases*, *11*(1), 1–13. https://doi.org/10.1371/journal.pntd.0005154

Mackey, T. K., Liang, B. A., Cuomo, R., Hafen, R., Brouwer, K. C., & Lee, D. E. (2014). Emerging and Reemerging Neglected Tropical Diseases : a Review of Key Characteristics , Risk Factors , and the Policy and Innovation Environment. *Clinical Microbiology Reviews*, *27*(4), 949–979. https://doi.org/10.1128/CMR.00045-14

Manirakiza, A., Boas, S. V., Beyam, N., Zadanga, G., & Konamna, F. X. (2011). Clinical outcome of skin yaws lesions after treatment with benzathinebenzylpenicillin in a pygmy population in Lobaye , Central African Republic. *BMC Research Notes*, *543*(4), 2–7. Retrieved from http://www.biomedcentral.com/1756-0500/4/543

Marks, M., Fookes, M., Wagner, J., Butcher, R., Ghinai, R., Sokana, O.,& Thomson, N. (2018). Diagnostics for Yaws Eradication: Insights from Direct Next-Generation Sequencing of Cutaneous Strains of Treponema pallidum. *Clinical Infectious Diseases*, *66*(6), 818–824. https://doi.org/10.1093/cid/cix892

Marks, M., Goncalves, A., Vahi, V., Sokana, O., Puiahi, E., Zhang, Z., & Solomon, A. W. (2014). Evaluation of a Rapid Diagnostic Test for Yaws Infection in a Community Surveillance Setting. *PLoS Neglected Tropical Diseases*, *8*(9), 1–5. https://doi.org/10.1371/journal.pntd.0003156

Marks, M., Mitjà, O., Vestergaard, L. S., Pillay, A., Knauf, S., Chen, C.,& Mabey, D. C. W. (2015). Challenges and key research questions for yaws eradication. *Lancet*, *15*(October), 1220–1225. https://doi.org/10.1016/S1473-3099(15)00136-X

Marks, M., Vahi, V., Sokana, O., Puiahi, E., Pavluck, A., Zhang, Z., & Solomon, A. W. (2015). Mapping the Epidemiology of Yaws in the Solomon Islands : A Cluster Randomized Survey. *American Journal of Tropical Medicine and Hygiene*, *92*(1), 129–133. https://doi.org/10.4269/ajtmh.14-0438

Marks, M., Yin, Y., Chen, X., Castro, A., Causer, L., Guy, R., & Aziz, A. (2017). Metaanalysis of the Performance of a Combined Treponemal and Nontreponemal Rapid Diagnostic Test for Syphilis and Yaws. *Clinical Infectious Diseases*, *63*(September), 627–633. https://doi.org/10.1093/cid/ciw348

Mitjà, O., Asiedu, K., & Mabey, D. (2013). Yaws. *The Lancet*, *381*(9868), 763–773. https://doi.org/10.1016/S0140-6736(12)62130-8

Mitjà, O., Hays, R., Ipai, A., Penias, M., Paru, R., Fagaho, D., & Bassat, Q. (2012). Single-dose azithromycin versus benzathine benzylpenicillin for treatment of yaws in children in Papua New Guinea : an open-label , non-inferiority , randomised trial. *Lancet*, *6736*(11), 61624–3. https://doi.org/10.1016/S0140-6736(11)61624-3

Mitjà, O., Marks, M., Konan, D. J. P., Ayelo, G., Gonzalez-Beiras, C., Boua, B., &Asiedu, K. (2015). Global epidemiology of yaws: a systematic review. *The Lancet Global Health*, *3*(6), e324–e331. https://doi.org/10.1016/S2214-109X(15)00011-X

Mitjà, O., Marks, M., Konan, D. J. P., Ayelo, G., Gonzalez-beiras, C., Boua, B., & Tabah, E. N. (2015). Global epidemiology of yaws : a systematic review. *The Lancet Global Health*, *3*, 324–331. https://doi.org/10.1016/S2214-109X(15)00011-X

NPHL/HIV/STI Programme. (2014). *HIV and Syphilis Testing in Non-Clinical*.

Rinaldi, A. (2008). Yaws : A Second (and Maybe Last ?) Chance for Eradication. *PLoS Neglected Tropical Diseases*, *2*(8), 1–6. https://doi.org/10.1371/journal.pntd.0000275

Stamm, L. V. (2015). Yaws: 110 Years after Castellani's discovery of Treponema pallidum subspecies pertenue. *American Journal of Tropical Medicine and Hygiene*, *93*(1), 4–6. https://doi.org/10.4269/ajtmh.15-0147

Taleo, F., Macleod, C. K., Marks, M., Sokana, O., Last, A., Willis, R., & Solomon, A. W. (2017). Integrated Mapping of Yaws and Trachoma in the Five Northern-Most Provinces of Vanuatu. *PLoS Neglected Tropical Diseases*, *11*(1), 1–11. https://doi.org/10.1371/journal.pntd.0005267

Tettey, A. (2009). School of Public Health, College of Health sciences, University of Ghana-Legon. Factors associated with yaws in the Ga West district of Ghana (A Case-control study at Obom).

Thami, Y., & George, M. P. H. (2010). Resurgence of yaws in Tanna,Vanuatu: time for a newapproach? *Tropical Doctor*, *40*(April), 68–69. https://doi.org/10.1258/td.2009.090249

WHO. (2012). *Summary report of a consultation on the eradication of yaws*.

WHO. (2014). *Yaws strategy development*.

8. 0 APPENDICES

8.1 APPENDIX A (CONSENT FORM).

Consent Form (To be translated into an appropriate local language) for guardians/caregivers of study participants (1 – 9 years).

FACTORS ASSOCIATED WITH YAWS AMONG CHILDREN IN THE UPPER WEST AKYEM AND AWUTU SENYA WEST DISTRICTS

Name of Participant: Study ID:

Yaws is a bacterial infection that usually affects children under 15 years. The disease can result in severe disability and deformity, which leads to school absenteeism, social stigma and loss of livelihood. The disease has been successfully eradicated in most countries. Your community has been reporting cases of yaws despite the strategies put in place to eliminate and possibly eradicate the disease.

The aim of this research is to find out the factors that are possibly responsible for the continuous transmission of yaws in the community. With the knowledge of these factors, the appropriate measures can be put in place to control the disease.

The research will include both children between the ages of 1- 15 years with yaws and those without yaws. A small blood sample will be taken from the finger of children suspected to have yaws to confirm the disease. All the children who are confirmed to have yaws will be appropriately referred to the health facility for treatment. The treatment will be at no cost to the participant.

All the information collected from the study participants will be kept confidential and will not be traceable to the participants. The study participants will be given a unique code and

access to the final password-protected database will be restricted to only the principal investigator.

There will be possible discomfort because of pain from the samples taken from the finger to confirm yaws.

The study will be conducted in accordance with guidelines stipulated by the Ethics Review Committee (ERC). Participation in this study is voluntary and decision to participate, stay or withdraw from study is at the discretion of participant and parent/guardian and will be of no consequence.

Additional Information:

Any questions or additional information should be directed to the Principal Investigator (PI)

Rafiq Nii Attoh Okine

Department of Epidemiology and Disease Control, School of Public Health, University of Ghana

0244- 094-752 or Miss Hannah Frimpong, of the Ethics Review Committee (ERC) of the Ghana Health Service (GHS), Phone Contact: 0507041223

Email: hannah.frimpong@ghsmail.org or ghserc@gmail.com

Consent (Guardians/caregivers of study participants (1 – 9 years)

I have read or have had someone read to me, the entire explanation of this study. I have also been given the opportunity to discuss any questions. I understand the nature, risk and benefits of this study and that I may withdraw my ward at any time from the study without any consequence. I have also received a copy of this informed consent document. I hereby consent to include my child/ward to participate in study.

…….. …….....

Date Signature / Right Thumbprint

(parent/guardian)

If a caregiver cannot read the form themselves, a witness reads and sign below:

I was present while the nature, benefits, risks and procedures were read to the participant. All questions were answered and the parent/guardian has agreed for their child/ward to take part in the research.

…….....

……

Date Signature / Right Thumbprint

(Witness)

…… ……..

Date Name and Signature of the person who obtained the consent

8.2 APPENDIX B (ASSENT FORM)

Assent Form (To be translated into an appropriate local language) for Adolescent study participants (10 – 15 years).

FACTORS ASSOCIATED WITH YAWS AMONG CHILDREN IN THE UPPER WEST AKYEM AND AWUTU SENYA WEST DISTRICTS

Name of Participant: Study ID:

Yaws is a bacterial infection that usually affects children under 15 years. The disease can result in severe disability and deformity, which leads to school absenteeism, social stigma and loss of livelihood. The disease has been successfully eradicated in most countries. Your community has been reporting cases of yaws despite the strategies put in place to eliminate and possibly eradicate the disease.

The aim of this research is to find out the factors that are possibly responsible for the continuous transmission of yaws in the community. With the knowledge of these factors, the appropriate measures can be put in place to control the disease.

The research will include both children between the ages of 1- 15 years with yaws and those without yaws. A small blood sample will be taken from your finger if you are suspected to have yaws to confirm the disease. Anyone who is confirmed to have yaws will be appropriately referred to the health facility for treatment. The treatment will be at no cost to the participant.

All the information collected from you and other the study participants will be kept confidential and will not be traceable to the participants. The study participants will be given a unique code and access to the final password-protected database will be restricted to only the principal investigator.

There will be possible discomfort because of pain from the samples taken from the finger to confirm yaws.

The study will be conducted in accordance with guidelines stipulated by the Ethics Review Committee (ERC). Participation in this study is voluntary and decision to participate, stay or withdraw from study is at your discretion and will be of no consequence.

Additional Information:

Any questions or additional information should be directed to the Principal Investigator (PI)

Rafiq Nii Attoh Okine

Department of Epidemiology and Disease Control, School of Public Health, University of Ghana

0244- 094-752 or Miss Hannah Frimpong, of the Ethics Review Committee (ERC) of the Ghana Health Service (GHS), Phone Contact: 0507041223,

Email: hannah.frimpong@ghsmail.org or ghserc@gmail.com

Assent: Adolescent study participants (10 – 15 years)

I have read or have had someone read to me, the entire explanation of this study. I have also been given the opportunity to discuss any questions. I understand the nature, risk and benefits of this study and that I may withdraw my ward at any time from the study without any consequence. I have also received a copy of this informed consent document. I hereby consent to to participate in study.

…….. …….....

Date Signature / Right Thumbprint

(Parent/guardian/school teacher)

If a caregiver cannot read the form themselves, a witness reads and sign below:

I was present while the nature, benefits, risks and procedures were read to the participant. All questions were answered and the parent/guardian has agreed for their child/ward to take part in the research.

…….....

……

Date Signature / Right Thumbprint

(Witness)

…… ……..

Date Name and Signature of the person who obtained the consent

8.3 APPENDIX C (QUESTIONNAIRE)

FACTORS ASSOCIATED WITH YAWS AMONG CHILDREN IN THE UPPER WEST AKYEM AND AWUTU SENYA WEST DISTRICTS

Instruction: Tick the relevant option and write in the space provided on the right

Introduction

I am…… of the School of Public Health, University of Ghana with a team of researchers. We are conducting a study in your community to determine the possible factors that are associated with yaws in your community. You will be required to answer a few questions about yourself and your child/ward.

The data collected will be kept confidential. The findings will be helpful in putting measures in place to control the disease in the community. The interview will last about 10 – 15 minutes.

……..

Date of Interview

SOCIO-DEMOGRAHPIC BACKGROUND

Record ID	_____
Study Participant ID	_____
Name of community or school	_____
Name of research assistant	_____
Name of district	◯ Awutu Senya West ◯ Upper West Akyem
Status	◯ Control ◯ Case
Name or initial of participant	_____
Name or initial of caregiver	_____
Age at last birthday	_____ (age at last birthday in years)
Sex	◯ Male ◯ Female
Ethnic background	◯ Akan ◯ Ga/Adangme ◯ Ewe ◯ Northerner ◯ other
Other, please specify	_____ (specify other ethnicity)
Religion	◯ Christian ◯ Muslim ◯ Traditional ◯ Other
Other, please specify	_____ (specify other religion)

Level of education of caregiver	◯ Primary ◯ JHS ◯ SHS ◯ Tertiary ◯ Vocational ◯ None
Is study participant in school?	◯ No ◯ Yes
Level of study	◯ Pre-school ◯ Lower Primary (1 -3) ◯ Upper Primary (4 -6) ◯ JHS
Marital status of caregiver	◯ Single ◯ Married ◯ Divorced ◯ Widowed ◯ Co-habiting
Number of siblings	_____
Have you ever been treated for Yaws?	◯ No ◯ Yes

BEHAVIORAL FACTORS

Record ID	_____
Do you take your bath everyday?	◯ No ◯ Yes
How many times do you take your bath?	◯ Once ◯ Twice
Do you bathe with soap?	◯ No ◯ Yes
Do you share bathing towels or sponge?	◯ No ◯ Yes
Source of water for bathing?	◯ Pipe borne water ◯ Borehole ◯ Well ◯ Steams/rivers/ponds
How many people do you share a bathroom with?	◯ 3 - 5 ◯ More than 5
Have you had any contact with anyone with Yaws in the past?	◯ No ◯ Yes
How often are you fully clothed or dressed?	◯ All the time ◯ Most often ◯ Not regularly ◯ Never

HOUSING

Record ID	_____
Type of housing	◯ Single unit ◯ Compound
How many households are on the compound?	◯ 2 - 4 ◯ 5 - 7 ◯ More than 7
What material is your house made of ?	◯ Wood ◯ Cement block ◯ Mud ◯ Other
Other, specify	_____ (specify other housing material)
How many people do you share a sleeping room with?	◯ 2 - 4 ◯ More than 4
How many people stay in the house?	_____
How many people stay in the house? (categorical)	◯ Less than 5 ◯ 5 - 8 ◯ More than 8 (fill based on previous question)

SANITATION

Record ID	_____
Is the source of water for household activities located in the house?	◯ No ◯ Yes
Source of water for household activities	◯ Pipe borne water ◯ Bore hole ◯ Well ◯ Streams/rivers/ponds
How far is the water source from the house?	◯ less than 5 minutes ◯ 5 - 10 minutes ◯ more than 10 minutes (if water source is not in the house)
Do you have any toilet facility in the house?	◯ No ◯ Yes
Type of toilet facility at home?	◯ Water closet ◯ Pit Latrine ◯ K(VIP) ◯ Other (if yes to previous question)
Type of public toilet facility used	◯ Improved latrines ◯ Open defecation (if public facility is used)
How often do you wash your hands after visiting the toilet, eating or any activity you deem fit?	◯ Most often ◯ Not regularly
What do you wash your hands with?	◯ Soap and water ◯ Water

CLINICAL ASSESSMENT FORM

Record ID	_____
Name or Initials of Study Participant	_____
Status of patient	◯ Control ◯ Case
District	◯ Awutu Senya West ◯ Upper West Akyem
Name of community or school	_____
Age at last birthday	_____
Sex	◯ Male ◯ Female
Yaws-like skin lesion present?	◯ No ◯ Yes
Type of Yaws-like lesion	◯ Ulcer ◯ Papilloma ◯ Macules ◯ Papules ◯ Maculopapular rash ◯ Hyperkeratosis ◯ Early sabre tibia
Location of lesion	◯ Head/neck/face ◯ Upper limbs ◯ Lower limbs ◯ Trunk
Clinical Stage of Yaws	◯ Primary ◯ Secondary
Other suspected skin lesions apart from Yaws	_____ (Please specify other skin lesions noted)
Rapid POC Syphilis test	◯ Negative ◯ Positive
Rapid POC DPP test	◯ Negative ◯ Positive
Case category	◯ Suspected ◯ Probable ◯ Confirmed

Letter should be quoted.

P. O. Box MB 190
Accra
Tel: +233-302-681109
Fax + 233-302-685424
Email: ghserc@gmail.com

MyRef. GHS/RDD/ERC/Admin/App 118/019
Your Ref. No.

8th April, 2018

Rafiq Nii Attoh Okine
University of Ghana
School of Public Health
Legon, Accra

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

GHS-ERC Number	**GHS-ERC: 034/12/18**
Project Title	Factors Associated with Yaws in the Upper West Akyem and Awutu Senya West Districts - A Case- Control Study
Approval Date	8th April, 2018
Expiry Date	7th April, 2019
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. CYNTHIA BANNERMAN
(GHS-ERC CHAIRPERSON)

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