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Application of Area to Point Kriging to Buruli Ulcer Incidence in Ashanti and Brong Ahafo Regions of Ghana

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BY

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DECLARATION

I, LINDA OSSEI, hereby declare that this thesis submission is my own work and that neither part, nor whole of it has been presented for another degree elsewhere. Where materials have been drawn from any other sources, this has been fully acknowledged.

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ABSTRACT

Buruli ulcer (BU) is the third most common mycobacterium disease after tuberculosis and leprosy. The disease eats through the skin, muscle and bone, leaving victims with disfiguring and debilitating craters. Ghana is the second most endemic country globally, after Cote d'Ivoire with over 1,048 cases with the most endemic regions being the Ashanti, Greater Accra, Central and the Brong Ahafo. The research uses Area to Point Kriging (ATP) method to model the spatial distribution of Buruli ulcer incidence in the Ashanti and Brong Ahafo Regions of Ghana. The ATP method used consist of three steps; filtering of noise in the data based on Poisson kriging, the mapping of the corresponding risk at a fine scale and estimating geographical clustering of the disease at the administrative units. This paper focused on the spatial analysis of Buruli ulcer incidence in the Ashanti and Brong Ahafo region in terms of sex. The research revealed that there is large range of spatial autocorrelation in males than in females in the various administrative units. The administrative units in Brong Ahafo close to Ashanti region have high BU incidence than the units far away from the Ashanti. The clustering analysis revealed that only Amansie West district is statistically significant for both sexes.

Key Words: Area to point kriging, Buruli ulcer, area to area kriging, Mycobacterium ulcerans.

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DEDICATION

This Thesis is dedicated to my late uncle R.K Ossei and my children

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CHAPTER 1

Thesis Overview

This chapter provides an introduction to the research work presented in the thesis. It describes the research background and research problem that motivate the pursuance of this work. In addition it provides research questions, objectives, significant of the study as well as the structure and outline of the thesis.

1.0 Introduction

Buruli ulcer (BU) is a serious skin infection caused by Mycobacterium ulcerans (Amofa et al., 1993). BU has been described as a neglected emerging disease that affects neglected rural people in neglected areas of the world (Hayman 1991). BU is rated as the third most common mycobacterium infection after Tuberculosis and Leprosy (Portaels, 1995). Although there is a lot of literature on the possible causes of Buruli ulcer (BU), no one is sure where the bacterium lives in the environment and therefore the arguments have been purely speculative (Owusu-Sekyere, 2012). It is also a mystery how the mycobacterium enters the human body, although it is clear the bacterium is unable to do so by itself (Marsollier et al., 2004). However, current research has shown the disease is commonly associated with rapid environmental change to the landscape including deforestation, eutrophication, dam construction, irrigation, farming, mining, and habitat fragmentation (Debacker, et al. 2004). The proximity to slow moving water such as swamps, man-made lakes, dams, creaks, and living in lower elevation areas appear to have a higher risk for Buruli ulcer (Duker et al., 2004). The disease has been reported in many countries of West Africa, Indonesia, Malaysia, Maxico, France, Australia and Peru.

In most of these countries, BU is known to afflict impoverished inhabitants living in remote areas where amenities of modern medical Science are not available or expensive (Guédénon et al., 1995).

In Africa, all ages and sexes are affected, but most cases of the disease occur in children between the ages of 4– 15 years (Asiedu and Etuaful, 1998).

Ghana is the second most endemic country in the world after Cote d'Ivoire with about 1,048 Buruli Ulcer case in 2011 (WHO, 2012). Africa tops the list of most affected regions with Cote d'Ivoire leading the rate with 2,670 patients. According to recent WHO statistics, the total population of Buruli Ulcer cases recorded globally including that of Ghana is 5,076 with Africa being the worst affected (WHO, 2012). There have been a lot of studies on the disease in Ghana. However many of the studies have concentrated on small geographical areas of high prevalence. There have been several studies by Duker et al. in 2004 and 2005 on the relationship between arsenic concentrations and the mean Buruli ulcer prevalence in settlements along arsenic-enriched drainage pathways and arsenic-enriched farmland. Again, Asiedu and Etuaful, (1998) concluded that poverty was a major contributing factor to the high prevalence of the disease in the District.

1.1 Statement of Problem

The disease is known to affect impoverished inhabitants in the rural areas. Since the treatment cost of BU is high, these rural folks scarcely go to the hospitals for treatment but rather go for traditional treatment.

Following Asiedu et al., (1998), the cost of treatment of BU disease is divided into direct and indirect cost. The total direct cost of treatment for the three year period a patient is estimated to be $23,845.56 and the total indirect cost of treatment for the

same period is also $56,047.55. Apart from the direct and indirect economic cost, there are many other negative complications such as deformities, amputations, stigmatization etc. The prolonged hospitalizations also create a huge burden on the resources of the hospitals.

All these have serious implications on socioeconomic development in the Ashanti and that of Brong Ahafo Regions respectively. Bonyah et al., (2012) used Geospatial Modeling to examine Buruli Ulcer Prevalence in Amansie West District. Whereas this study is significant in expanding the knowledge towards the understanding of the causes and effects of the disease, there has not been any attempt to study the two endemic regions in the northern sector of Ghana, which are the Ashanti and Brong Ahafo Regions. It is against this background that this thesis seeks to examine area to-point kriging of Buruli ulcer disease distribution in Ashanti and Brong Ahafo region of Ghana.

1.2 Research Questions

1. What is the reliable map of the spatial distribution of Buruli ulcer mortality that accounts for small population sizes and the districts' geographies?
2. What are the estimations of the underlying risk of Buruli ulcer disease?
3. Which administrative areas which show significant higher risk of BU disease?

1.3 Objectives

The objectives of this research work are as follows:

- Create reliable map of the spatial distribution of Buruli ulcer mortality that accounts for small population sizes and the districts' geographies.
- estimations of the underlying risk of Buruli ulcer disease within the study area

- Detection of geographical clustering of the disease within the administrative units

1.4 Significant of the Study

The research would facilitate the work of various administrative units the geographical region in the distribution of social amenities especially quality water for the inhabitants. The risk map of the thesis would inform the central government to identify activities that degrade the environment and consequently become hazardous to human health in the study area. This information could help the government to develop programmes that may minimize such effect.

The result of the study would be useful in the formulation of practical policies for providing care and management practices giving to Buruli Ulcer patients. The study will share more light on the social economic effects of the disease in the District

1.5 Structure and Outline of the Thesis

Chapter 2 is devoted to the summary of the literature review on BU disease and arsenic as well as the concept of geostatistics. This chapter begins with a description of the BU history, microbiology of MU. Arsenic effect on the immune system, immune responses, treatment of BU, transmission of BU as well as social and economic impact of BU disease form of various ulcers is also presented and application of geostatistics is also described.

Chapter 3, the study area is described with regards to its geographical position, data source is explained to together with spatial data input. Geostatical approach used is presented in this chapter. Deconvolution used to fit variogram to areal data is described.

Chapter 4 discusses the results of the research. The chapter states the parameters of the various variograms, give ATA and ATP Poisson kriging estimates, as well as variance kriging. Clusters analysis are done to estimate clustering at the various districts Chapter 5 deals with the conclusions and recommendations of the research.

CHAPTER 2

LITERATURE REVIEW

2.0 History and Background of Buruli ulcer

In 1897, Sir Albert Cook, a British physician working in Uganda, described a range of skin ulcers consistent with Buruli ulcer. These cases were not published in the medical literature (Clancy et al., 1964)

In 1948, Professor Peter MacCallum and his colleagues described the disease among six patients in Australia with a detailed description of this new mycobacterial infection in man. The causative organism was subsequently named Mycobacterium ulcerans (Amofah et al., 1993).

In the 1960s through the 1970s, many cases were reported in Uganda, the Democratic Republic of the Congo, Papua New Guinea and other countries. "Buruli" is the name of a county in Uganda.

Since the 1980s, Buruli ulcer has emerged as a serious public health problem in an increasing number of countries. West Africa thus far appears to be the most affected area (Aseidu et al., 1998).

In December 1997, on the occasion of his visit to Côte d'Ivoire, Dr Hiroshi Nakajima, then Director-General of the World Health Organization (WHO), announced that

WHO would take the lead to mobilize the world's expertise and resources to fight the emergence of Buruli ulcer as a serious public health problem.

In 1998, WHO launched the Global Buruli Ulcer Initiative (GBUI) to coordinate control and research efforts, and organized the first International Conference on Buruli ulcer control and research in Yamoussoukro, Côte d'Ivoire.

The resulting Yamoussoukro Declaration on Buruli Ulcer drew attention to the severity of the disease as an emerging public health problem and expressed concern about its many poorly understood features.

In May 2004, the World Health Assembly adopted a resolution on Buruli ulcer which called for increasing surveillance and control, and for intensified research to develop tools to diagnose, treat and prevent the disease.

2.1 DEFINITION AND CAUSES OF BURULI ULCER.

Bairnsdale ulcer, Buruli ulcer and Daintree ulcer are all local names given to the same disease which is caused by Mycobacterium ulcerans (M. ulcerans). This environmental mycobacterium produces a toxin that kills fat cells, blocks capillaries and inhibits the local immune response. The disease is generally an ulcerative condition of the skin and subcutaneous fat, but can produce very extensive skin loss.

The infection occurs in humans, possums, koalas, potoroos and occasional other species, (Johnson, 1996).

Buruli Ulcer is the third mycobacterium disease after tuberculosis and leprosy. Mycobacterium ulcerans, a slow-growing acid-fast bacillus, causes widely undermined skin ulcers, subcutaneous necrosis and shiny, hyper pigmented adjacent skin known as Buruli ulcer, a term derived from the Buruli region of Uganda.

If left untreated, the initial painless nodule or papule can progress to widespread ulceration, probably due to mycolactone, a polyketide toxin from M. ulcerans which

might explain the necrosis extending beyond the colonized area. It was first observed in Bairnsdale and Victoria, Australia in 1948, cases from 30 other countries are reported, particularly from areas in Uganda and Zaire where M. ulcerans is endemic. The mode of transmission of M. ulcerans is unknown; infection might occur by pricks or bites, and is perhaps waterborne. Buruli ulcer can follow human bite, and disseminated osteomyelitis due to M. ulcerans infection after snakebite Hofer et al (1993) has reported. The differential diagnosis of pyoderma gangrenosum includes Buruli ulcer, (Atkins et al 1995). However, M. ulcerans is not involved in most cases of necrotic arachnidism (James 2003).

Buruli ulcer, named after an area of Uganda that was the site of many cases in the 1960s, (Clancey1964) is most common in West Africa.

All countries along the Gulf of Guinea are now affected. In Cote d'Ivoire, approximately 15 000 cases have been recorded since 1978, where up to 16 percent of the population in some villages are affected. In Benin, 4000 cases have been recorded since 1989 (WHO, 1998). In Ghana, 6000 cases were recorded in a national survey in 1999. There is evidence of huge under reporting of the disease (National Buruli Ulcer Control Programme1999).

Buruli ulcer, which is sweeping across Africa now, W H O (2003), is a cruel disease which silently eats through skin, muscle and bone and, in its worst form, leaves victims with disfiguring and debilitating craters. But the list of questions surrounding Buruli is daunting. No one is sure where the bacterium lives in the environment. It's also a mystery how it enters the body, although it is clear the bacterium is unable to do so by itself. It's also unclear if everyone infected with Buruli develops the disease and, if not, why some are able to fight it off. There is no diagnostic tool, other than

straight visual observation. Incubation periods are a matter of guesswork. And for unknown reasons, drugs frequently fail.

"More than 50% of the cases are in children under 15 years of age, and yet we know more about most veterinary diseases than we do about Buruli ulcer," says Kingsley Asiedu who is responsible for the World Health Organization's Buruli Ulcer Program. "At the dawn of the 21st century, when scientists have decoded the entire human genome, it is surprising to have so little knowledge about such a debilitating disease."

Finding answers to the Buruli mysteries is becoming urgent. Somehow, the bacteria pass through the protective barriers of the skin. And, in a way that is not well understood, they then disable the alarms of the immune system. Once under the skin, the bacteria release a corrosive toxin. As Buruli does its work, the normal warnings of fever and pain, which are common with other infections, rarely appear. Without these alarms to suggest a problem or an immune response to keep it in check, Buruli can eat its way through flesh for weeks or even months. Eventually, a crater, known as an ulcer, appears in the surface of the skin. A small ulcer becomes larger. So it grows until, for whatever reason, it stops. Drugs are generally ineffective in advanced cases, but can stop the disease if given early. .

But inside the body, the Buruli bacteria do not dwell inside cells which are unusual but rather live in the material surrounding cells (Ameh et at., 1997).

Some scientists strongly suspect a link between changes in the environment and the spread of the disease. Support for this belief comes from studies on a well-documented outbreak on an island resort in Australia in 1997 (Montoro et al., 1997).

According to Johnson, (2000), victims with advanced disease, the only therapy is to cut away the diseased tissue. Sometimes this involves amputation. Surgery for advanced Buruli Ulcer always means a lengthy hospitalization and life-long disability. Patients are kept in hospitals for an average of three months after an operation, but in some cases rehabilitation can take as long as 18 months, (Gluckmann, 1995). Thus Buruli Ulcer is inflicting not only a harsh physical toll but a brutal economic one as well.

In Ghana, the average cost of Buruli treatment is $780, (Asiedu, 1998). This is an extraordinary amount in a country where the majority of the population lives on less than a dollar a day. Even so, surgery does not always provide a cure. In 30% of the surgery patients, Buruli returns.

With information lacking in so many key areas, WHO's strategy has been to focus on early intervention. Identification and treatment of small ulcers and nodules can be done at the local level with relatively little cost. WHO has launched an effort to raise awareness of the disease and to encourage those who even suspect they have it to seek medical treatment quickly. The goal is to prevent the widespread progression and the disabilities caused by the disease.

2.2 Epidemiology

In many areas, M. ulcerans infection has occurred only after significant environmental disturbance. In the original paper describing the disease, published in 1948, the first patient from the Bairnsdale district in Australia presented in 1938.

In December 1935, there had been the worst floods on record in the district, when all road and rail links had been cut and much property destroyed.

In Uganda, Barker (1973) examined cases of M. ukcerans in the Busoga district on the east side of the Victoria Nile, north of Lake Victoria. Although cases were known in other parts of the country, there had been no known cases in the district before 1965. Barker postulated that the outbreak was related to unprecedented flooding of the lakes of Uganda between 1962 and 1964 as a result of heavy rainfall.

In Nigeria, infections have occurred among Caucasians living on campus of the University of Ibadan after 1965, when a small stream flowing through the campus was dammed to make an artificial lake (Oluwasanmi et al., 1975). Physical contact with this lake was thought not to have occurred in the majority of cases and many patients were convinced that their lesions developed from insect bites. Examination of soil, water, and snails from the lake for M. ulcerans were negative.

The first case reported in Cote d Ivoire was a 7- year – old French boy who lived with his parents besides Lake Kossou, an artificial lake in the center of the country.

In Liberia, cases have been reported in north of the country following the introduction of a swamp rice field to replace an upland one. This agriculture change was accompanied by the construction of dams on the Major River to extend the wetlands.

In Papua New Guinea, the infection occurs mainly near the Sepik and Kumusi rivers; in the latter areas the disease is known as the ‘‘Kumusi ulcer’’ (Redford, 1974). The disease in Papua New Guinea spread after the flooding and devastation that followed the eruption of mount Lamington in 1951 (Reid, 1967) described how older people living in the villages blamed the volcano for the disease.

The recent outbreak of the disease on Philip Island, Victoria, Australia was temporally associated with the formation of a small swamp that backed up behind a newly constructed vehicle track. Improved drainage of this area was followed by a cessation of cases in the immediate vicinity of the marsh. The following years, cases continued to occur approximately one kilometer to the west of the swamp, and were centered on a golf course spray irrigation system that used a mixture of recycled sewage and groundwater. In retrospect, the two foci at Philip Island were probably interlink because some of the water that collected in the swamp the preceding year is likely to have originated on the golf course. A marked decline in cases followed modifications to this irrigation system. These observations suggested that M. ulcerans maybe present in groundwater, that a nutrient – rich environment may favour its survival and growth, that M. ulcerans is able to colonize man – made reticulation systems and that it is likely to be spread by aerosol.

The epidemiology of Buruli ulcer is poorly understood. The source(s) of M.ulcerans in nature is becoming clearer from epidemiology data and from molecular biological findings.

Because all major endemic foci are in wetlands of tropical or subtropical countries, environmental factors must play an essential role in the survival of the etiological agent.

Focal outbreaks have followed flooding, human migration and man-made topographical modifications such as dams and resorts. Deformation and increased basic agricultural activities may have significantly contributed to the recent marked increase in the incidence of M. ulcerans infections, especially in West Africa, where the disease rapidly emerging.

In Benin, for example, the disease prevalence in areas with environmental changes is about 180 per 100,000 population, where as in those without environmental changes it is about 20 per 100,000 (Portaels , 1998.).

Epidemiological evidence strongly suggests that mycobacterium ulcerans is an environmental saprophyte rather than an obligate pathogen, viz. its infection is caused by environmental contact rather than from person to person spread (Barker, 1973). However, in spite of several attempts, the causative organism has not been isolated from the environment. The largest known endemic foci are in Uganda (Barker, 1973) and Zaire (Meyers et al., 1974).

The source of mycobacterium ulcerans in nature is unknown. Infections probably begins when it is introduced into the skin by minor trauma, abrasion or possible insect bite Meyers et al. (1974) presumably from the contaminated surface of the skin.

All pervious studies have indicated that the disease occurs in riverine areas and may be associated with certain plant species notably the grass Echimochloa pyrimidalis as found in Uganda (Barker, 1973).

Thus, M. ulcerans is believed to occur in soil or vegetation infesting the dermis through thorn pricks or other penetrating injuries (Meyers et al.,1974,). However, isolation of the organization from the environment has proven difficult.

In the Agogo area Van der Warf et al., (1989) established that there is an important focus of Buruli ulcer in Afram River Valley north of Agogo.

They suggested that the disease was probably widespread in the complex of rivers and mashes around the Volta Lake. In Amansie West which is a major endemic area in

Ghana two main rivers, Offin and Oda run through the southern parts of the district. In the Ga District of Greater Accra Region the villages affected were all sited around rivers Densu and Nsaki (Addo, 1995).

Proximity to rivers or swampy areas therefore appear to be important in the ecology of the disease. However, no studies have demonstrated the existence of the organism outside the human body . As Odei and Ampofo noted there is however a strong correlation between the distribution of the disease and the surface pH (i.e. broadly the acidity or alkalinity) of the water (pH 6.2). it may also be noted that seasonal variation of the disease was observed in the Amansie West District. The peak incidence of onset of symptoms was in September and October (period of maximum rain), and a minor peak in May and June (Amofa et al., 1993).

There has been further studies and experiment to explain the link between the incidence of the disease and the environment. Before 1982, the annual number of cases diagnosed in Victoria ,Australia ranged between zero and four, all of which were associated with the eastern part of the state (Johnson 1996).

However, between 1992 and 1995 there was an outbreak of cases near the small Victoria seaside town of Cowes on Philip Island, 80km southeast of Melbourne (Flood et al 1994). Before 1992, there were no recorded cases of M.ulcerans infection on Philip Island. Between September 1992 and December 1995, there were 29 such cases, of which 28 patients either lived in or close to Cowes or were frequent visitors to the area (Johnson et al, 1996).

Almost all of these cases were confined to a sparsely populated region to the east the town center, and epidemiological investigation of this area revealed a number of

possible environmental sources of infection. These include a golf course which lay at the center of the outbreak. This golf course was irrigated with water drawn from a sewerage dam which contained a natural groundwater. A series of samples of water were collected in October, 1994 and 1995 from the irrigated golf course.

These studies have examined a large number of epidemiologically incriminated water samples collected in areas of endemicity or during epidemics (Hayman, 1991; Meyers, 1994). The results proved that M. ulcerans were responsible for the outbreak of the disease.

2.3 Aetiology of Buruli ulcer

M. ulcerans, first described by MacCullum and his colleagues in 1948, is a rod-shaped, acid-fast bacillus, 3 to 6 megrim long and 0.2 to 0.35 megrim in width, with rounded ends and parallel sides, which occurs singly or in groups in necrotic base and undermined edge of the ulcer (not in the growing, outer edge of the lesion).

Many bacilli are extra cellular; some are intra cellular in macrophages. M. ulcerans is an acid-fast slow-growing bacillus that infects the skin and the subcutaneous tissue producing indolent ulcers with undermined edges. It belongs to the same Genus as mycobacterium tuberculosis and mycobacterium leprae. The organism has the designation among the micro-bacteria group, of retarded growth at 37º C and a preference for 32 º C- 33º C. It differs from all other known bacteria causing diseases in humans, in that it produces a heat – labile toxin that has both cytotoxic and immunosuppressive properties.

This toxin is thought to be the cause of necrosis of the dermis and deep fascia, as well as pannicuitis seen in its pathology and not due to host defense. In the early stages of

infection, there is extensive fatty and subcutaneous tissues necrosis especially laterally, which may involve nerves vessels. There is characteristically inflammatory reaction at this stage. The core of the necrotic c mass may however be surrounded by epithelia cells, fibroblasts and lymphocytes. In later stages, inflammatory reactions set in and granuloma and giant cells are seen with less necrosis of the fatty tissue.

The growth of the organism on Loewenstein – Jensen medium or Petragnani at 33 º C is typically slow, taking 8 to 41 weeks or more, with growth being inhibited at 35 º C. It is not always possible to identify acids – fast bacilli from buruli specimens, especially from long standing ulcers (Ministry of Health 1999).

2.4 Mode of Transmission

Currently the mode of transmission of Buruli ulcer is not entirely known, though most epidemiological data and some hypothesis have associated the outbreak and emergence of the disease with an aquatic environment (Marsollier et al., 2002 ; Portaels et al., 1999). Most investigators have implicated insects, airborne, trauma and human to human as possible modes of transmission.

Insects are also suspected to aid the transmission of B.U. Most of the work on insects in the transmission of Buruli ulcer had tended to implicate aquatic insects as a possible mode of transmission of the etiologic agent.

Marsollier et al., (2002) experimentally infected adult water bugs of the family Naucoridae (Naucoris cimicoides) with M. ulcerans infected grubs. These insects were then made to bite the tails of mice. They found out that some of the mice tails which were bitten had developed a non-ulcerative inflammatory lesion with oedema at the site of the bite. Cultures and PCR performed on the tail lesions specimen were

positive for *M.* ulcerans. No lesions were found in mice bitten by unaffected control bugs.

They provided the strong evidence implicating insects in the transmission of Buruli ulcer. Earlier work by Portaels et al., (1999) had found out through Polymerase Chain Reaction (PCR) that, aquatic insects belonging to the Naucoridae and Family Belostomidae were M. ulcerans positive. These bugs were aggressive predators of other aquatic arthropods and molluscs and they fly from nearby ponds and streams and may bite humans. These insects which are filter feeders could concentrate *M.* ulcerans and be ingested by other aquatic organisms.

Earlier work on the role of insects was done by Lunn et al., (1965) but these turned out to be negative in all the insects samples they examined.

Hayman (1991) postulated that human infection of the disease might occur when *M. ulcerans* from lacustrine systems multiply over a period of months or years and then disseminated in aerosols to in-infect its ancestral home and incidentally to infect man. Veitch et al (1997) also hypothesized that *M.* ulcerans has an aquatic reservoir and that persons may be infected directly or indirectly by the mycobacterium when it is disseminated locally by spray irrigation. None of these postulates have however been proved. Human to human transmission of Buruli ulcer had been noted to be extremely rare (Meyers *et al.*, 1974).

The first case of human to human transmission was by (Debacker et al., 2003). This resulted after a 13 year old girl in Benin got bitten by a playmate on the forearm. Though they did not rule out the possibility of human to human transmission, they came to a conclusion that either the playmates mouth was contaminated with M. ulcerans which was considered highly unlikely or the trauma might have been

activated a latent focus of M. ulcerans at the site of the trauma. In their opinion however, the playmates might have introduced the etiological agent M. ulcerans into the patient's skin and subcutaneous tissue from an area of the skin surface that was significantly contaminated with M. ulcerans. Exner and Limperle (1987) reported the presence of M. ulcerans disease on the hand of a plastic surgeon but concluded that this may be accidental.

Eddyani et al., (2004) implicated fishes as a possible source of M. ulcerans. In their work, it was found out that all fishes that were positive for M. ulcerans DNA appear to feed on insects or planktons and they concentrate the M. ulcerans in their food source, however as to whether the M. ulcerans are transmitted directly from the fishes to man could not be proved. In Papua New Guinea, samples of fishes were investigated for the presence of M. ulcerans but all tested negative (Radford, 1974).

Marsollier et al., (2004) had reported the passive involvement of aquatic snails in harbouring M. ulcerans without offering favourable conditions for its growth and replication.

Acid fast bacilli were found in snails belonging to the family Ampulariidae and Planorbidae after they were experimentally fed with biofilm of M. ulcerans. The bacteria were detected by PCR after some period of feeding. They also found the presence of the bacteria in larvae of dragonfly (Family Gomphidae and Libellulidae) as well as in juvenile fishes of the family Cariidae. They also came to the conclusion that these aquatic organisms could concentrate the bacteria thereby helping in its dissemination in the environment.

Oluwasanmi et al., (1976) examined aquatic snails from shallow lake in Nigeria created by the damming of a small stream in an effort to find the cause of an outbreak

of Buruli ulcer among some residents living along the stream, all samples collected however tested negative. Most of the patients on the other hand were convinced that they developed the Buruli ulcer lesions from insects bite, also most patients were believe not have any physical contact with the lake.

Atkinson et al., (1993) investigating the implication of M. ulcerans in most cases of necrotic arachnidism could not find M. ulcerans in either the venom or the mid-gut of several Australian spiders. They deliberately infected some spiders by inoculating the fangs and digestive system but this did not yield any permanent colonization.

Buckle (1972) also in Australia, examined insectivorous bats as possible source of *M. ulcerans* in an endemic area but this all tend out to be negative.

Foci of the disease appear to develop after some form of environmental disturbance such as flooding or the formation of new dams or water storages, sand winning, where excavation have left behind large sheets of stagnant water. Veitch et al., (1997) reporting a large outbreak of the disease on Philips Island, Australia associated the source of infection to an irrigation which lay in the midst of the cluster of cases. Number of cases been reported from the community reduced after the irrigation site was modified and limited from the public

Scot et al., (2004) noted that cases of Buruli ulcer are associated with tropical wetlands of west and central Africa ,and cases have increased rapidly in theses areas since the 1980's, particularly after irrigation and dam construction.

Travis (1999) also noted that people living near slow-running waters are more likely to contract the disfiguring disease Buruli ulcer.

Portaels et al., (1989) reported that re-emergence of the disease in some developing countries may be related to environmental and socio-economic factors like deforestation leading to increased flooding, population expansion without improved agricultural techniques, thus putting more people at a risk of contracting the disease.

In assessing water-related risk factors, Aiga et al., (2004) found that the use of water from rivers and ponds for drinking, cooking, bathing and washing purposes were not significant risk factors, they however suggested that swimming or activities on river banks associated with it might be a major risk factor. Portaels, (1989) also reported the re-emergence of the disease among people who live/or work close to wetlands, especially slow-flowing (riverine) or stagnant water bodies (marshes, swamps), often created as a result of some form of human environmental disturbances.

A lot of authors have reported the association of the disease with an aquatic habitat. Asiedu et al., (1971) reported cases of the disease along the tributaries of Densu River in the Ga North District of Ghana. James et al., (2003) in Benin also identified three risk areas according to origin of patients reporting at hospitals with Buruli ulcer and noted that most of them were coming from Laguna areas of coastal Benin, marshy inland areas where market crops and rice are cultivated, and river valleys areas. All associated with aquatic environment. Carbine et al., (2003) also noted that water sources are associated with high incidence rates of the disease, Darie (2003), reported the strong association of the disease to an aquatic ecosystem. Monson et al., (1984) in Liberia described three patients with the disease establishing the Mayor River as an endemic are, they also described a patient with the disease from the St Paul river basin also in the same country.

Ravisse et al., (1975) and Boisvert (1977) in Cameroon also described cases of the disease all originating from a well circumscribed area in the Valley of Nyong River in the Central Province. They found that disease prevalence for active and/or inactive cases was higher in villages closer to the Nyong River and that frequency of identifying cases decreases with distance from the river.

In recent times, other authors have been able to use molecular biology techniques to detect the presence of M. ulcerans in environmental water suggesting that people become infected when they get into M. ulcerans infected-water. Stinear *et al*., (2000) using sequence capture Polymerase Reaction (PCR) were able to detect the presence of M. ulcerans in environmental water samples. Roberts and Hirst (1997) were also able to use immunomagnetic separation and PCR to detect the presence of M. ulcerans in water samples taken from Philip Island, Australia, which was the site of a major outbreak of the disease.

2.5 Clinical Manifestation

Once introduced into the subcutaneous tissue, the organism proliferates and elaborates a toxin that has affinity for fat cells. The resulting necrosis provides a favorable milieu for enhanced proliferation of the organism.

There is no, or very little, cellular host immune response during the necrotic phase and the buruli skin test is negative. The mechanism is unknown ; either the toxin is neutralized or the organism ceases to begin when the host develops cells – mediated immunity and buruli skin tests become positive. . The granulomas then destroy the etiological agent and the disease subsides by scarring. Bones become affected as a result of M ulcerans baceraemia. In contrast to other pathogenic mycobacterium,

which is facultative intracellular parasites of macrophages, M ulcerans occurs in lesions primarily as extra cellular micro colonies.

The clinical spectrum of the disease ranges from a nodule through an ulcer and heals with or without a sequel.

Patients in Australia initially present with a papule, where as patients in Africa present with a nodule. There are two entities of the disease: active (ongoing infection) and inactive (previous infection with characteristic depressed stellate/ star-shaped scar with or without sequelae

2.6 Treatment

Based on the characteristics and microbiology of the etiological agents, various approaches have been used in the treatment of M. ulcerans disease, though some are promising, most have been found to be ineffective. Currently the most accepted form of treatment is surgery.

Many studies have proposed the use of antibiotic therapy in the treatment of Buruli ulcer, unfortunately the results have been disappointing and there is no well defined protocol with curative activity against infection in humans (Darie et al., 1994).

Various antibiotic, either singly or in combination with others have been applied in one way or the other in the treatment of Buruli ulcer. Dega et al., (2002), in accessing the most active curative treatment of Buruli ulcer, applied two regimens, one incorporating rifampin and the other with rifampin alone in a mouse footpad model of M. ulcerans infection. In the first experiment, only rifampin was used, in the second, rifampin in combination with amikacin was applied. In a third model, rifampin was given in addition with clarithromycin and sparfloxacin. All these treatments were

begun after the footpad had swell after infection with M. ulcerans. They accessed the activity of each of the regimen in terms of reduction of the average lesion index, acid fast bacillus count and CFU count.

It was found out that all the three regimens displayed various degrees of bactericidal activity against M. ulcerans with varying degrees, with rifampin-amikacin combination the strongest, followed by rifampin-clarithromycin-sparfloxacin regimen, with rifampin alone being the least. Rifampin–amikacin was found to be able to cure established M. ulcerans infection in mice and prevent relapse 26 weeks after completion of treatment. They however could not determine the use of this regimen for treatment of M. ulcerans in humans.

In a similar report, Bentoucha et al., (2001) in determining the activity of new macrolides and fluoroquinolones against M. ulcerans infection in mice, infected the left hind foot pad with acid-fast bacilli from M. ulcerans.

These mice were then grouped and the various groups were treated by one of the following regimens for four weeks; 100mg axithromycin, 100mg clarithromycin or 50mg of azithromycin (for a duration of five days a week, three times a week or once a week). In addition, regimens of 100mg telithromycin, sparfloxacin or moxifloxacin were administered daily. 200mg of levofloxacin; 100mg of streptomycin or amikacin; 10mg of rifampin; and combination of 10mg of rifampin and 100mg of amikacin. After completion of the treatment, the mice were observed for 30 days.

The effectiveness of the regimens were accessed in terms of the delay in median time to foot pad swelling in treated mice compared with that in untreated controls. They observed clear cut bactericidal activity in streptomycin, amikacin and rifampin-amikacin treated mice. However, all the mice they treated with amikacin or

streptomycin alone had swollen foot pad before the end of the thirty week observation period, suggesting re-growth of M. ulcerans. In contrast, 50% of the mice treated with rifampin-amikacin combination exhibited no lesion even after the thirty weeks suggesting a cure. There was no bactericidal activity in those treated with 50mg azithromycin, 100mg azithromycin thrice weekly, telithromycin and levoflaxacin. Also a delay in foot pad swelling shorter than the 4 week treatment duration implying a bacteriostatic activity was found in regimen of 100mg azithromycin daily or once weekly treatment, clarithromycin thrice weekly or once weekly and moxifloxacin treatment.

Weak bactericidal activity was found in clarithromycin daily and sparfloxacin treatment. They suggested further studies on the promising results of the synergistic effect of rifampin-amikacin combination and possibly rifampin–streptomycin combination for the treatment of M. ulcerans in humans.

In an earlier report in 2000 by Dega et al., were able to determine the activities of certain antimicrobials against *M. ulcerans* infection in mice. They determine the effect of clarithromycin, minocycline, sparfloxacin, rifampin, rifabutin and amikacin on footpads of mice infected with M. ulcerans acid fast bacilli.

These mice were observed seventeen weeks after completion of the therapy. They found out that treating infected mice daily (5days/week) with 100mg of clarithromycin starting the day after infection prevented their foot pad from swelling at the tenth week. They also observed that the foot pad of the mice became swollen at week ten after infection and all controlled mice died by the fifteenth week after infection. Also all controlled mice and those treated with clarithromycin, minocycline or sparfloxacin exhibited swollen foot pads during the period of observation. In

contrast, mice treated with rifampin, rifabutin or amikacin had no foot pads welling and all inoculated cultures done after the seventeenth week were negative. Their results suggested that rifampin, rifabutin or amikacin may be effective in the treatment of human infection of M. ulcerans.

Dhople and Namba (2002) were able to determine the bactericidal activity of new fluoroquinolone sitofloxacin (DU-6859a) along with standard quinolones (oflaxacin, levoflaxacin, ciprofloxacin) either singly or in combination with rifampicin against *M. ulcerans* in vitro. They compared the effect of an individual drug by determining its inhibition of *M. ulcerans* growth in culture media as compared to control cultures without any drug. Among the fluoroquinolones, sitofloxacin was found to be the most potent in the killing of *M. ulcerans*.

The synergistic effect of sitofloxacin and rifampicin combination was found to be superior to that of oflaxacin-rifampicin combination. Effect of ciprofloxacin, levofloxacin and oflaxacin were less potent.

In the first controlled trial of a therapy for the treatment of Buruli ulcer other than surgery, Philips et al., (2004) evaluated the efficacy and safety of topical nitrogen oxide in a randomized double-blinded trail for the treatment of Buruli ulcer. They found out that treatment of patients with creams releasing nitrogen oxide increases the healing rate of ulcers caused by M. ulcerans with minimal adverse effect.

Though some antibiotic treatment are promising, there could be the development of resistant strains of M. ulcerans as reported by Marsollier et al., (2003) when they proposed the reemergence of rifampin resistant strains in experimentally infected mice treated with rifampin alone.

The most widely accepted and proven means of treating Buruli ulcer is surgery (WHO, 2001). There are several factors that affect the treatment of Buruli ulcer by surgical means; some includes inadequate health personnel and facilities in endemic areas, inaccessibility of endemic areas, risk associated with surgery. These notwithstanding, surgical excision of all the various forms of lesions is still the only effective means of treating BU and this is usually perform under general or local anaesthesia.

Excisions of lesions are made so that they include a relative amount of macroscopically healthy tissue according to the degree of in duration and also the experience of the surgeon. Pre-ulcerative lesions like papule and nodules are excised en-bloc and the wound allowed to heal be itself, if it is small or skin graft applied to aid the healing process. Non ulcerative papules are usually excised with some normal skin and skin graft applied over it.

In oedematous forms which are considered complex forms, other bacterial infections are ruled out before surgery. If diagnosis is however not certain, broad spectrum antibiotic is given for seven to ten days before surgery. If diagnosis is certain, excision is made after which the skin is grafted. In some cases, incision with irrigation of necrotic tissues is made.

Active ulcers up to 2cm in diameter are excised with its undermined edges and some healthy tissue and primarily closed. Ulcers more than 2cm diameter are excised with its undermined edges without primary closure. Skin grafting is in th2.6.3 Thermal (heat) treatment

Since the causative agent M. ulcerans is not able to grow at temperatures above 37^{o}C (Portaels et al., 1982). Some authors have tried to treat the disease with temperatures

of 40°C. Meyers et al., (1974) continuously applied local heating at 40°C through circulating water jacket to lesions caused M. ulcerans.

It was found that this type of treatment when applied constantly for four to six weeks promotes healing without excision. Heat treatment was also believed could improve blood flow, antibiotic penetration and phagocytosis. This type of treatment however was found not to be practicable in many endemic areas (Goutzamanis et al., 1995). Kreig et al., (1979) also found that heat treatment of Buruli ulcer in combination with rifampin was the most effective in various treatment regimens with mouse foot pad models en carried out after granulation has formed.

Some workers have also taken advantage of M. ulcerans ability to grow best at relatively low temperatures (28 -32°C) in devising a treatment regimen involving the application of high oxygen pressure to treat lesions of Buruli ulcer.

Kreig et al., (1979) noted that hyperbaric oxygen treatment alone was able to inhibit lesions in murine model of the disease, but this treatment was found not to be effective when used in combination with rifampicin, and heat in treating patient with Buruli ulcer lesions (Goutzamanis et al., 1995).

Unorthodox treatment such as clay and honey had also been used to treat Buruli ulcer.

Special clays which have high content of calcium and sodium) have been used for the treatment of the disease.

Clay first absorbs the toxins (heavy metals, free radicals etc) attracting them to its extensive surface area where they adhere and are absorbed. Healing clays do not only draws toxic materials from the body, but also reduces pain and infection on wounds.

Some authors have also tried to treat Buruli ulcers with unprocessed honey, but the results have not been encouraging. Efem (1988), treated patients with wounds and ulcers with honey, most of them responded well to the honey, but one case later diagnosed to be Buruli ulcer failed to respond. Honey had been found to debrids wounds rapidly, replacing sloughs with granulation tissues. It also promotes rapid epithelialization and absorption of oedema from around the ulcer margins. Honey had been known to have both bactericidal and bacteriostatic activity, as well as been anti-fungal, (Molan 1998).

He also noted that various antimicrobial activities in honey are achieved through its osmotic effect, its characteristic high acidity of pH between 3.2 and 4.5, which is low enough to inhibit many pathogenic growths. The major anti-microbial activity in honey was found to be due to the presence hydrogen peroxide produced enzymatically in honey.

2.7 Prevention

At the moment there are no preventive strategies for Buruli ulcer. BCG vaccination appeared to offer protection in two control clinical trials in Uganda but the protective effect lasted for 6 months.

Based on these findings, it may be possible to increase thee protection through repeated BCG vaccination in the endemic countries. This may be a feasible approach until a specific vaccine is developed for the disease. (Asiedu,1998)

2.8 Socio economic Cost of Buruli Ulcer

A study was conducted by Asiedu and Etuaful in 1998 to examine some of the socioeconomic cost of treating 102 cases of Buruli ulcer between 1994 and 1996 at St.

Martin's Catholic Hospital at Agroyesum in the Amansie West district of the Ashanti Region of Ghana. In their study, seventy percent (70%) of the cases were children (up to 15 years of age).

There was no sex difference in the distribution of cases. Hospitalization was prolonged (average = 186days in 1994, 103 days in 1995, and 102 days in 1996) with no significant age and sex differences. There were 10 limbs amputations, 12 patients were left with contracture deformities, one patient lost sight in one eye, and two died of sepsis and tetanus. The average total treatment cost per patient was $966.85 (62% indirect) in 1994, $706.08 (79% indirect) in 1996. with increasing number of cases high treatment costs and serious complications, urgent attention should be given to disease in terms of control and research efforts aimed at early detection and treatment. (Asiedu and Etuaful 1998).

2.9 Estimation of Direct Cost.

The direct cost is the expenditure on the treatment of the disease that could be quantified in monetary terms. They included the in-patient charge pay day multiplied by the number of days of hospitalization, surgery, laboratory test, dressing of wounds and drugs. However, because of the difficulty in measuring the staff time used on patients with Buruli Ulcer, labour cost was excluded, though it must be stated that the time and energy spent on surgery (skin grafting) and wound dressing could be considerable and well acknowledged (Asiedu et al,1998).

2.10 Estimation of Indirect Cost

This is the daily loss of productivity by the patient and the attending relative multiplied by the number of days of hospitalization.

The loss of productivity was calculated based on the average of two options as follows: Option 1: by assuming that 30% of patients who are adults work in addition to the attending relatives for seven days a week; Option 2: by assuming that 30% of the patients who are adults work in addition to the attending relatives for five days a week. The results of the survey indicated that out of 102 patients with Buruli ulcer, 36 were treated in 1994, 34 in 1995, and 32 in 1996. There were 46 males (45%), 56 females (55%), 71 children (70%), and 31 adults (30%). The average duration of hospitalization was 186 days in 1994, 103 days in1995 and 102 days in 1996. There was no substantial difference by age or sex in the duration of hospitalization.

There were 10 amputations of limbs, 12 patients had contracture of a joint, one person lost sight in one eye, and there were two deaths due to tetanus and sepsis, respectively (complication rate 24.5%). The average number of operations per patient was 1.45. Apart from the 10 amputations, 65 cases had wound excision(s) with a skin graft, 25 had only wound excision, and two patients had bone involvement as a result of Buruli ulcer requiring wound excision and sequestectomy.

The direct treatment cost shows a downward trend over the three year period. The total direct treatment cost was $13,377.18 in 1994, $6000.23 in 1995, and $4,468.15 in 1996. Therefore the total direct cost of treating Buruli ulcer for the period was $23,845.56.

The total indirect cost in 1994 was $ 21,429.59, $18006.53 in 1995, and $16,611.43 in 1996.The total indirect cost was thus $56,047.55. The total treatment cost for the period, that is direct and indirect put together was $79,893.11. The distribution of the total cost showed that indirect costs constitute 70% and direct cost constitutes 30%.

The district health budget excluding salaries for the three year was $58,835.00 (Amofa, et al., 1993).- This means that the district health budget cannot even treat Buruli ulcer let alone the treatment of other diseases.

Drummond and James (1997) have written on the socioeconomic implications Buruli ulcer in Australia to access the cost of diagnose treatment and lost of income. A survey of 26 confirmed cases of the disease in Victoria was under taken. Data were collected on demographic details, diagnostic tests, treatment, time off work, and travel to obtain treatment. All cost are reported in Austriallian dollars in 1997 – 1998 prices.

The cost varies considerably with disease severity. For mild cases the average cost was $6803 and for severe cases the cost was $27681. Hospitalization accounted for 61 – 90% of the cost and indirect cost was about 24%.

Buruli ulcer can be expensive disease to diagnose and to treatment (Ross et al 1997). These therefore means that cost be reduced by early diagnose and a definitive treatment. It is better to always seek preventive measures than curative measures.

Mycobacterium is costly to treat. This study found that the average cost of diagnosing and treating a case was $14,608. This figure is approximately seven times the average health expenditure per person in Australia in 1997-98 of $2,557 .

Hospitalization costs form most of the overall cots, accounting for 90% of the total cost for severe cases and 79% for all cases. Indirect cots accounted for 25% of the overall (direct, indirect, and transportation) cost but considerably more for individual patients. For those with mild disease, income losses accounted for 47% of the overall cost.

These cost assessments are conservative for several reasons. First, most patients were treated in public hospitals as public patients; in Australia, such treatment is usually less costly than treating a private patient.

Thus these costs could have been substantially higher if more cases were treated privately in Australia and could vary substantially in other populations. Second, income losses would have been much grater if more patients had been in the income-generating age group. Third, the cost of impaired productivity of parents caring for their children and accompanying them for appointments and hospitalizations was not included in this study, but this cost is likely to have been considerable.

The patients who had one skin graft incurred the highest cost for medications because they were treated with longer courses of drugs specific for mycobacterium. Three of these patients were treated for / 6 months. These patients were given a trial of medication in an attempt to avert the need for surgery or as an adjunct to surgery in an attempt to prevent recurrence of the disease.

The marked decrease in general practitioner costs in severe cases reflects the referral pattern for this disease. Some patients with severe disease had previous contact with a specialist (usually a surgeon) as a result of treatment for a previous lesion, or they required more extensive surgery and skin grafting, which general practitioners would not normally perform. As patients with severe cases received more treatment as inpatients, and the cost of surgeon visits while in the hospital were included in the hospital charges, the cost of specialist treatment incurred by the patient does not clearly reflect the amount of care they received.

Variation around the mean cost within each category of disease severity was marked. Some of this variation was due to the lack of standardized, accepted treatment

regimes. In addition, delays until definitive treatment varied greatly between patients, sometimes because of difficulties in making the correct diagnosis. This wide range probably accounted for the failure of indirect costs to increase in direct proportion to disease severity. A limitation of this study was its reliance upon a patient questionnaire to collect data on diagnosis, treatment services received, and time off work.

Because of the considerable amount of time that had lapsed since their illness, some patients had difficulty accurately recalling details of the events in their disease history. The number of visits to physicians and the duration of particular events such as hospitalization or time missed from work were most difficult to recall precisely.

Some patients provided very accurate information because of diaries or prescriptions that they had kept during their illness or because of records from hospitals and the physicians who treated them.

Another limitation to this study was the validation of some of the information provided by patients, for example, the date of onset, time before seeking medical help, and date of cure were frequently not documented. A prospective study, performed at the time of an outbreak of this disease, would be useful to more accurately determine the cost of treatment.

The early diagnosis and implementation of effective, definitive treatment would greatly reduce both the illness and economic impact from Mycobacterium ulcerans infection. Education of medical practitioners and the public is required

The role of medication directed against mycobacteria, heat therapy, and other therapies reported as helpful by individual patients requires investigation. An

alternative to the extensive surgery currently required by most patients would greatly reduce the illness and cost of this disease. Recently, much progress has been made in detecting these bacteria in the environment and in rapidly diagnosing lesions.

Mycobacterium ulcerans is of increasing public health concern worldwide. In African countries, treatment costs for one case far exceed the governmental health spending per capita. The increasing number of case in many countries, the increasing number of countries affected and the substantial disability and loss of income that result from this disease underscore the need for continuing research into rapid diagnosis methods and cost-effective treatments.

TABLE 2.1: TYPES OF BURULI ULCER CASES REPORTED 2007-2010

YEAR	2007	2008	2009	2010	TOTAL
NODULE	31	22	26	39	118
PLAGUE	13	20	20	28	81
OEDEMA	6	13	4	14	37
ULCER	82	55	62	101	300
TOTAL	132	110	112	182	536

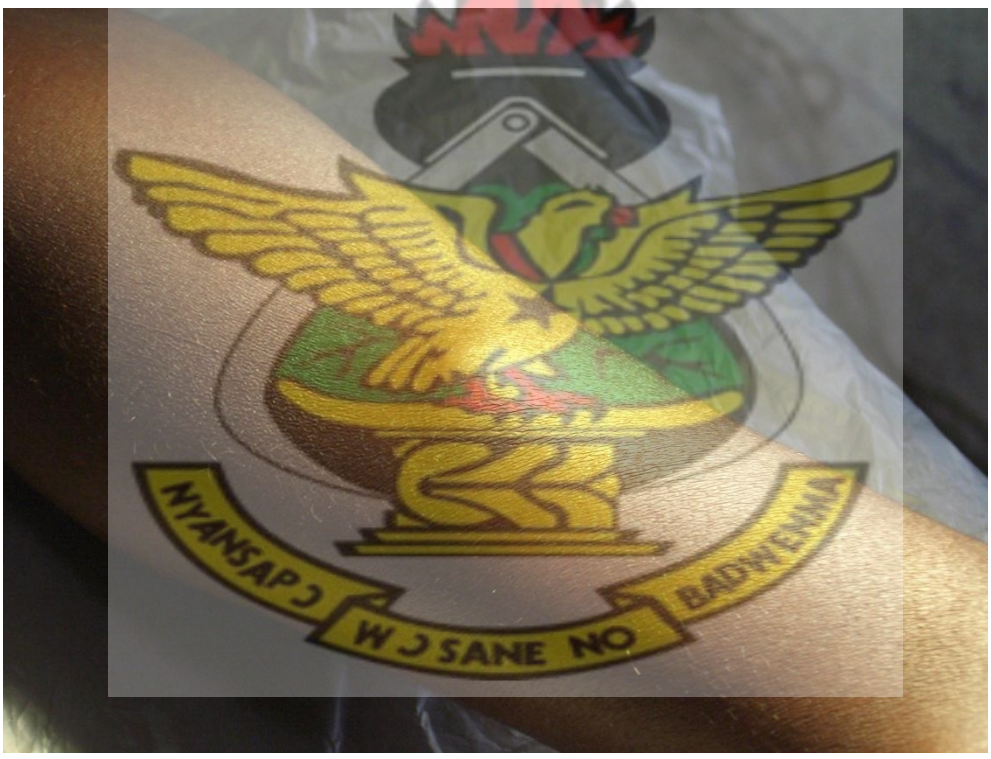
Source: St Martins Hospital, Agroyesum, 2011

NODULE: A nodule is a lesion that extends from the skin into subcutaneous tissue.

It looks like a small pimple and is 1 – 2cm in diameter. It is usually painless but may itch and the surrounding skin may be discolored compared to adjacent areas.

Available records show that the number of cases at the nodule stage is high, (Table 3.3). One hundred and eighteen nodule cases were recorded from 2001 to 2004. At this stage the disease has not fully developed. It looks like a small pimple and requires early minor surgical operation called nodulectomy to have it removed. Records from the St Martins Hospital indicate that year- to- year recorded cases of the nodule stage of the disease is on the increase. It increased from twenty two (22) cases in 2003 to thirty-nine (39) in 2004. If the nodule is not removed, it develops into a plague.

PLATE 3.1: A BURULI ULCER NODULE



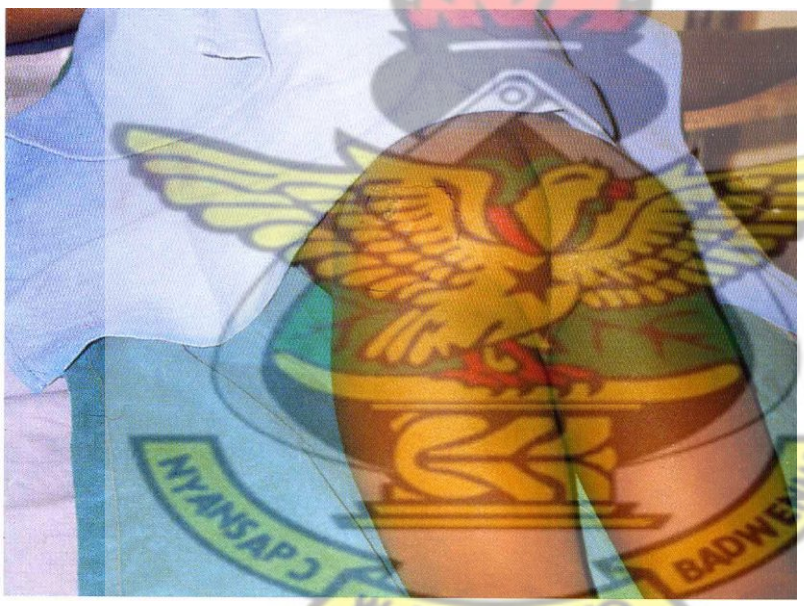
Source: St Martins Hospital, Agroyesum, 2011

PLAGUE: This is the second stage of the disease where the affected part of the skin is reddened and well demarcated.

The reported cases of the plague are not as many as the nodule stage. "Many of the nodules that are bought to this hospital are removed and therefore do not proceed to the plague" (Mr. Asamoah St Martins Hospital Agroyesum). The number of plague cases reported to the Hospital increased for thirteen (13) in 2007 to Twenty-eight (28) in 2010.

The total plague case recorded for 2007 to 2010 is eighty one (81). A comparative analysis of the reported cases shows a drastic difference between the nodule and plague cases.

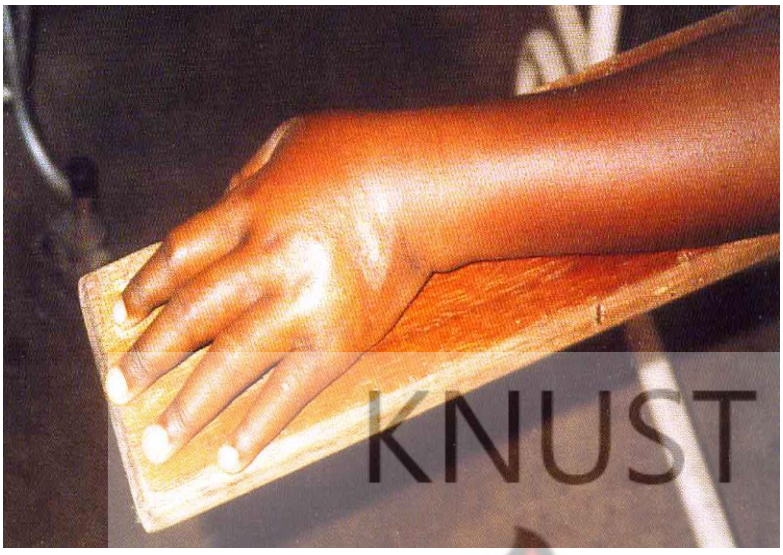
PLATE 3.2: A BURULI ULCER PLAGUE WITH WELL DEMARCATED



Source: St Martins Hospital, Agroyesum, 2011

OEDEMA: At this stage, the swelling becomes longer and is painful. There is a well defined edge for the swelling. It is the period when the swelling is about to break down to ulcer.

PLATE 3.3: OEDEMATOUS FORM OF BURULI ULCER

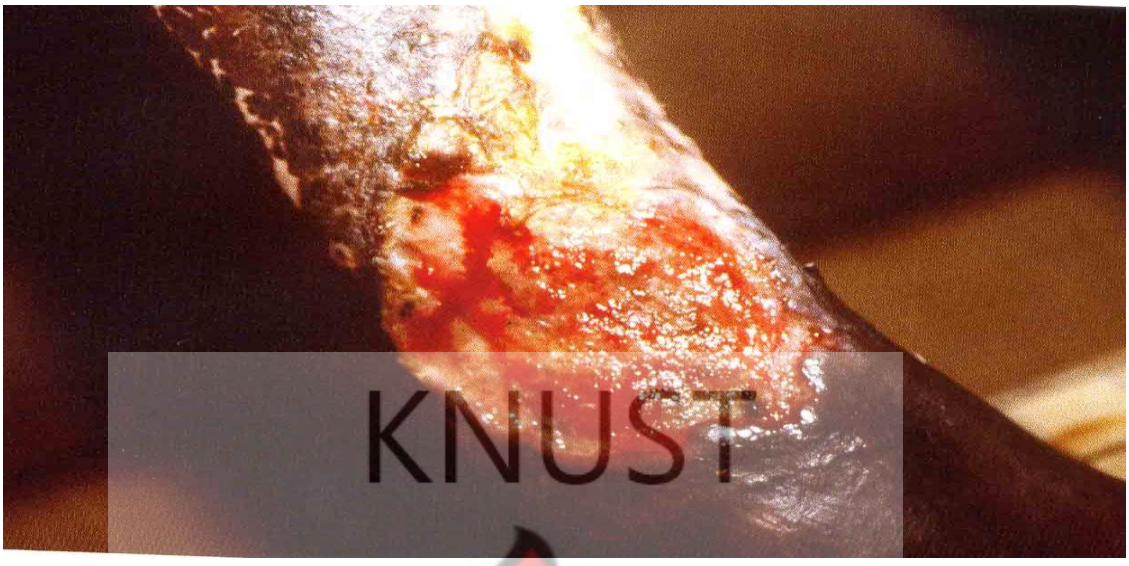


Source: St Martins Hospital Agroyesum, 2011

The number of reported cases of the Oedema stage of the disease is not high as compared to the nodule and plague stage. A total of 37 cases were recorded for the four (4) year period under review. This is because at the Oedema stage the swellen.is about to break down to ulcer. In fact it must be stated here that the ulcerative stage starts at the Oedemaneous stage. Therefore the Oedema stage is considered as the early ulcer stage.

ULCER: At this stage, the swelling eventually breaks down and a larger skin ulcer develops. It is normally painful.

PLATE 3.4: BURULI ULCER DISEASE AT THE ULCERATIVE STAGE



Source: St Martins Hospital, Agroyesum, 2011

This is where the swelling eventually breaks into larger skin ulcer. The affected part of the skin tissue is completely destroyed and if immediate action is not taken, it may affect the bone. Cases of the ulcerative stage of the disease are high. Eighty-two (82) cases were recorded in 2007 and this increased to one hundred and one (101) in 2010.

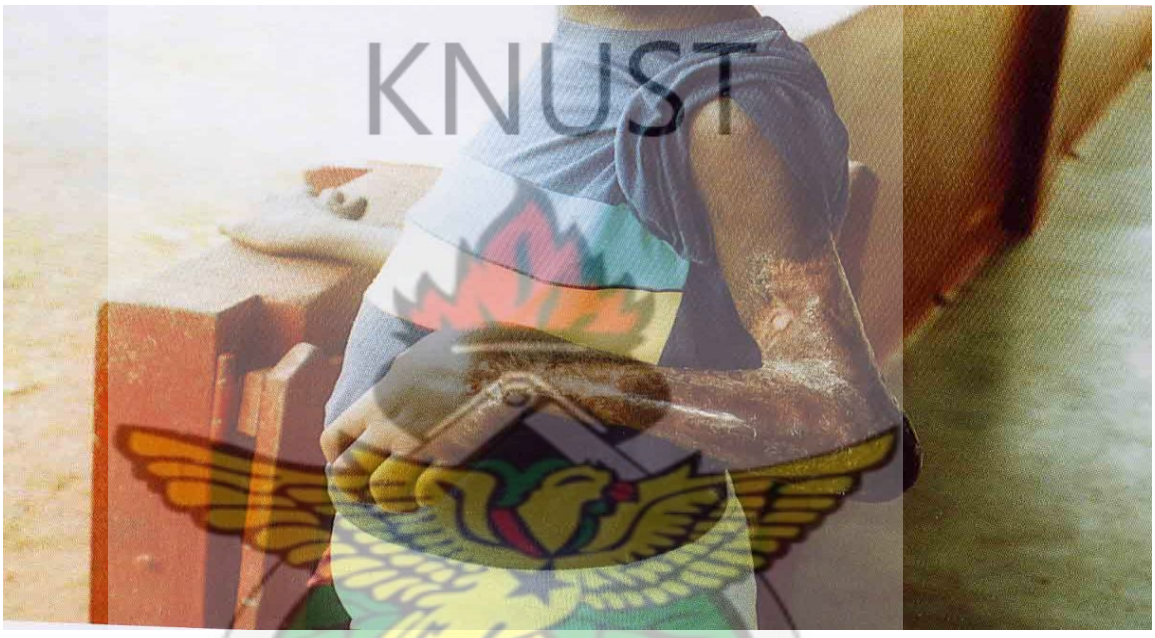
The total ulcerative case recorded for the four years under review was three hundred. (300), table 3.3. The high cases of the ulcer are because most of the patients do not report for treatment at the unset of the disease. This is because they do not realize that the nodule is Buruli ulcer until it develops into an ulcer.

Socio cultural beliefs and practices strongly influence the health-seeking behaviors of people affected by BU. The first recourse is often traditional treatment. In addition to the high cost of surgical treatment, fear of surgery and concerns about the resulting scars and possible amputations may also prevail. Due to the disfiguration, stigma is a

problem that also prevents people from seeking treatment. As a consequence, most patients seek treatment too late.

Another form of active ulcerative Buruli ulcer involving infection of the bone is osteomyelitis and reactive osteitis.

PLATE 2.5: OSTEOMYELITIS BURU ULCER



Source: field work 2011

Reactive or contagious osteitis occurs as a consequence of deep destruction of overlying soft tissue. Occasionally, the bone is exposed to the point of devascularization, necrosis of cortical bone, sequestration and osteomyelitis

Osteomyelitis Buruli ulcer infection may be focal or multifocal. The overlying skin is often intact with no obvious lesion. *M. ulcerans* osteomyelitis may occur as a primary condition or as a metastatic condition, sometimes at a distance from a cutanous lesion(s) or after the cutanous lesion has healed. It is initially painless, but with time

2.11 Geostatistics Application to Disease Modeling

Since its early development for the assessment of mineral deposits, geostatistics have been applied in a growing number of disciplines dealing with the analysis of data distributed in space and/or time.

One field that has given little attention in the geostatistical literature is medical geography or spatial epidemiology, which has to deal with the study of spatial patterns of disease incidence and mortality, and the identification of potential "causes" such as environmental exposure or socio-demographic factors (Waller and Gotway 2004). This lack of attention draw back against the increasing need for methods to analyze health data following the emergence of new infectious diseases (e.g.,West Nile Virus, bird flu), the higher occurrence of cancer mortality associated with longer life expectancy, and the burden of a widely polluted environment on human health.

The first attempt to tailor geostatistical tools to the analysis of disease rates must be credited to Christian Lajaunie (1991) from the Center of geostatistics in Fontainebleau, France.

He came out with an approach that accounts for spatial heterogeneity in the population of children to estimate the semivariogram of the "risk of developing cancer" from the semivariogram of observed mortality rates. Binomial cokriging was then used to produce a map of the risk of childhood cancer in theWest Midlands of England (Oliver et al. 1993, 1998; Webster et al. 1994).

Later, the same methodology was employed in mapping lung cancer mortality across USA (Goovaerts 2005a). In his book, Cressie (1993,pp. 385–402) analyzed the spatial distribution of the counts of sudden-infant-death-syndromes (SID) for 100 counties of North Carolina.

He proposed a two-step transform of the data to remove first the mean–variance dependence of the data and next the heteroscedasticity. Traditional variography was then applied to the transformed residuals. In contrast, Christakos and Lai (1997) incorporated the fuzziness or softness of the data into the computation of the sample semivariogram and into the kriging equations using the BME (Bayesian Maximum Entropy) formalism directly. More recently, geostatistics was applied for mapping the number of low birth weight (LBW) babies at the Census tract level, accounting for county-level LBW data and covariates measured over different spatial supports, such as a fine grid of ground-level particulate matter concentrations or tract population (Gotway and Young 2007).

Goovaerts (2005b, 2006a, 2006b) introduced a geostatistical approach to solve all three issues and compared its performances to empirical and Bayesian methods which have been traditionally used in health science. The filtering method is based on Poisson kriging and semivariogram estimators developed by Monestiez et al., (2006) for mapping the relative abundance of species in the presence of spatially heterogeneous observation efforts and sparse animal sightings.

In addition, Poisson kriging can be combined with stochastic simulation to generate multiple realizations of the spatial distribution of disease risk, which allows one to quantify numerically how the uncertainty about the spatial distribution of health

outcomes translates into uncertainty about the location of disease clusters (Goovaerts 2006a), the presence of significant boundaries (Goovaerts 2008b), or the relationship between health outcomes and putative risk factors.

The last change of support issue was solved recently in the geostatistical literature (Gotway and Young 2002, 2005; Kyriakidis 2004; Goovaerts 2008a). In its general form, kriging can accommodate different spatial supports for the data and the prediction, while ensuring the coherence of the predictions so that disaggregated estimates of count data are non-negative (Yoo and Kyriakidis 2006) and their sum is equal to the original areal count. However, the coherence property needs to be tailored to the current situation where areal rate data have various degrees of reliability depending on the size of the population at risk (Goovaerts 2006b).

Geostatistics represents an attractive alternative to increasingly popular Bayesian spatial models in that it is easier to implement and less CPU-intensive, since it does not require lengthy and potentially non-converging iterative estimation procedures, and it accounts for the size and shape of geographical units, avoiding the limitations of conditional auto-regressive (CAR) models commonly used in Bayesian algorithms, while allowing for risk prediction over any spatial support. Goovaerts and Gebreab (2008) conducted a simulation-based evaluation of performance of geostatistical and full Bayesian disease-mapping models, using the BYM model (Besag et al. 1991) as a benchmark for Bayesian methods. They found that the geostatistical approach yields smaller prediction errors, more precise and accurate probability intervals, and allows a better discrimination between counties with high and low mortality risks.

The BYM model also produces smoother risk surfaces, leading to a much larger proportion of false negatives than the geostatistical model in particular as the risk

threshold rises. The benefit of Poisson kriging increases as the county geography becomes more heterogeneous and when

CHAPTER 3

METHODOLOGY

3.1 Study area

For the purpose of this study, the Ashanti and Brong Ahafo regions were compacted together as one geographical unit for easy analysis and interpretation. The study area is drained by rivers such as Tano and Oda. The area is home to the Kintampo waterfalls and the Bui Dam. Lake Volta flows along the eastern edge of Brong-Ahafo and the port of Yeji. The area has moist-semi deciduous forest, mostly in the southern and south eastern parts and a guinea savannah, which is pre-dominant in the North-eastern portion. The area has a tropical climate, with high temperatures averaging 23.9^{o}C (750F) and a double maxima rainfall pattern. Rainfall ranges, from an average of 1000 millimeters in the northern parts to 1400 millimeters in the southern parts. Agriculture is the Dominant economic activity because of the rich agricultural lands. There is also small scale mining, timber and logging and petty trading. The study area has a population of about 7,007,174 million made up of 3,449,862 males and 3,557,312 females (GSS,2010). There are two referral hospitals, the Komfo Anokye teaching hospital located in Kumasi in the Ashanti Region and the Sunyani government hospital located in sunyani in the Brong Ahafo Region. With the exception of the two referral hospitals, the rest of the districts lack access to quality health care thus aggravating the disease situation in the area.

- Create reliable map of the spatial distribution of Buruli ulcer mortality that accounts for small population sizes and the districts' geographies.
- estimations of the underlying risk of Buruli ulcer disease within the study area
- Detection of geographical clustering of the disease within the administrative units

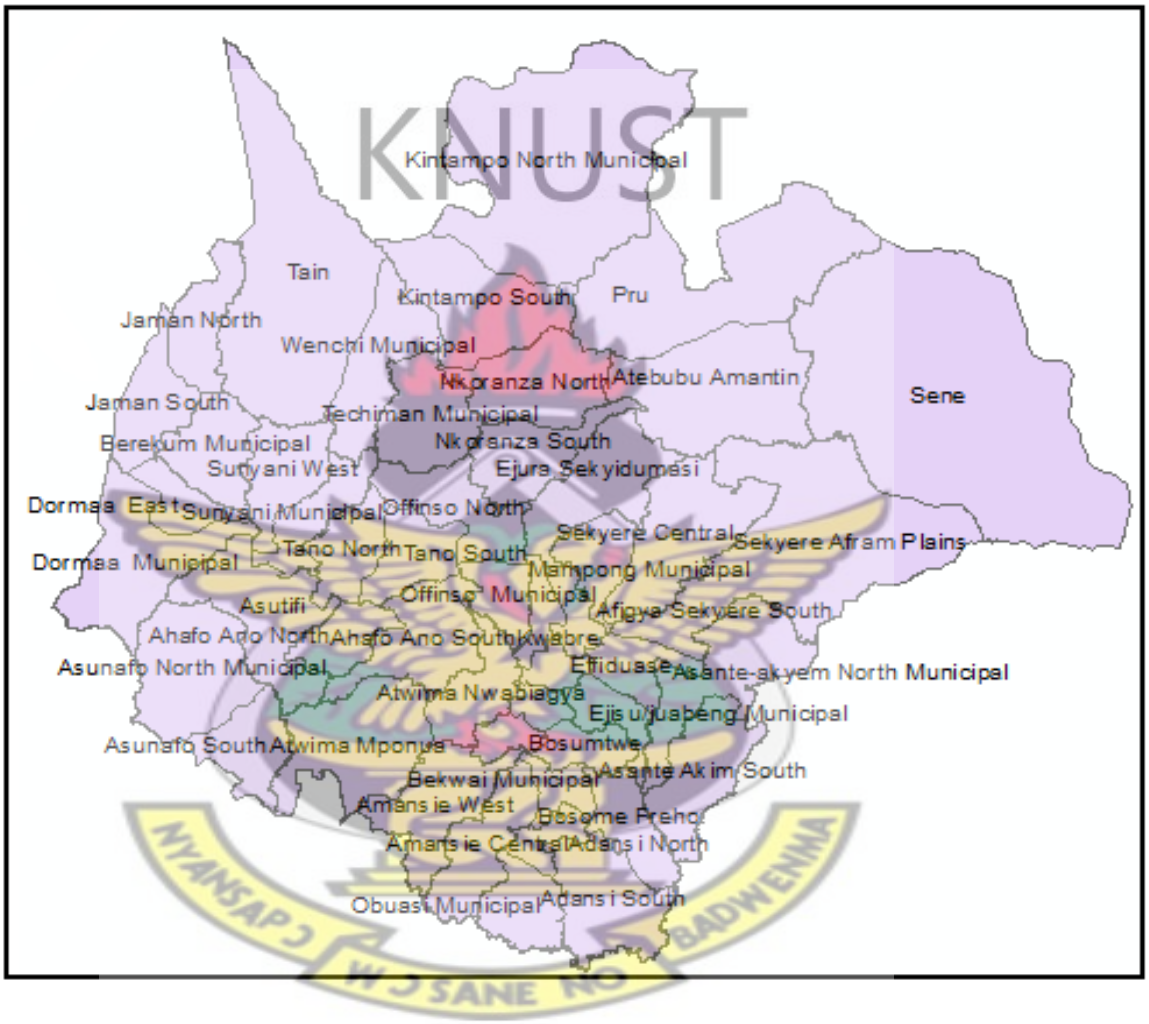


Figure 3.1 Map of the Study area with District capitals

3.2 Data Sources

Data for the study was obtained from Disease Control Units (DCU) of the two regions. The confirmed cases of Buruli ulcer disease as of the time of the study were 1590 for males and 1356 for Females. The data classification on the basis of sex was

to find out the incidence rates between the two sex groups at the various administrative units.

Population data obtained from Ghana Statistical Service was used in computing the raw rates of Buruli ulcer disease. Raw rates were calculated as the number of BU cases in each district divided by the estimated Population in 2010. In order to better, appreciate the risk of the disease; the raw rates were rescaled by multiplying it by a factor of 100,000. This expresses the raw rates as per 100,000 people.

3.3 Geostatistical Approach

3.3.1 Area to- Area Poisson Kriging

For a given number N of geographical units v_α (e.g., counties), denote the observed mortality rates (areal data) as $z(v_\alpha) = d(v_\alpha)/n(v_\alpha)$, where $d(v_\alpha)$ is the number of recorded mortality Buruli ulcer cases and $n(v_\alpha)$ is the size of the population at risk. The disease count $d(v_\alpha)$ is construed as a realization of a random variable $D(v_\alpha)$ that adopts a Poisson distribution with one parameter (expected number of counts) that is the product of the population size $n(v_\alpha)$ by the local risk $R(v_\alpha)$. The noise-filtered mortality rate for a given area v_α, called mortality risk, is forecasted as a linear combination of the kernel rate $z(v_\alpha)$ and the rates observed in (K −1) neighboring entities

$$\hat{r}(v_\alpha) = \sum_{i=1}^{K} \lambda_i z(v_i) \qquad (1)$$

The weights λi given to the K rates are worked out by solving the following system of linear equations, known as the "Poisson kriging" system

$$\sum_{j=1}^{k} \lambda_j [\overline{C}_R(v_i, v_j) + \delta_{ij} \frac{m^*}{n(v_i)}] + \mu(v_\alpha) = \overline{C}_R(v_i, v_\alpha) \qquad \text{i=1,…, K} \qquad (2)$$

$$\sum_{j=1}^{k} \lambda_j = 1$$

where δij = 1 if i = j and 0 otherwise. $m*$ is the population-weighted mean of the N rates. The "error variance" term, $m*/n(v_i)$, leads to smaller weights for less reliable data (e.g., rates measured over smaller populations). In addition to the population size, the kriging system accounts for the spatial correlation among geographical units through the area-to-area covariance terms $\overline{C}R(vi, vj) = \text{Cov}\{R(vi), R(vj)\}$ and $\overline{C}$ R(vi, vα).

Those covariances are numerically approximated by averaging the point-support covariance $CR(\mathbf{h})$, computed between any two locations discretizing the areas *vi* and *vj*

$$\overline{C}_R(v_i, v_j) = \frac{1}{\sum_{s=1}^{P_i}\sum_{s'=1}^{P_j} wss'} \sum_{s'=1}^{P_j} wss' C_R(u_s - u_{s'}) \qquad (3)$$

where P_i and P_j are the number of points used to discretize the two areas *vi* and v_j, respectively.

The weights wss' are computed as the product of population sizes assigned to each discretizing point **u***s* and $\mathbf{u}\,s'$

$$w_{ss'} = n(u_s) \times n(u_{s'}) \text{ with } \sum_{s=1}^{P_i} n(u_s) = n(v_i) \text{ and } \sum_{s=1}^{P_i} n(u_{s'}) = n(v_j)$$

The uncertainty of the Buruli ulcer mortality risk persisting within the geographical unit v_α can be modeled using the conditional cumulative distribution function (ccdf) of the risk variable $R(v_\alpha)$. Under the assumption of normality of the prediction errors, that ccdf is defined as

$$F(v_\alpha; r|(K)) = \Pr ob\{R(v_\alpha) \le r|(K)) = G\left(\frac{r - \hat{r}(v_\alpha)}{\hat{\sigma}(v_\alpha)}\right) \quad (4)$$

G(.) is the cumulative distribution function of the standard normal random variable, and $\hat{\sigma}(v_\alpha)$ is the square root of the kriging variance estimated as

$$\sigma^2(v_\alpha) = \overline{C}_R(v_\alpha, v_\alpha) - \sum_{i=1}^{K} \lambda_i \overline{C}_R(v_i, v_\alpha) - \mu(v_\alpha) \quad (5)$$

where $\overline{C}R(v_\alpha, v_\alpha)$ is the within-area covariance that is computed according to (3) with $v_i = v_j = v_\alpha$. The notation "|(K)" expresses conditioning to the local information, say, *K* neighboring observed rates. The function (4) gives the probability that the unknown risk is no greater than any given threshold *r*. It is modeled as a Gaussian distribution with the mean and the variance corresponding to the Poisson kriging estimate and variance.

3.3.2 Area-to-Point (ATP) Poisson Kriging

A particular case of ATA kriging is when the prediction support is so small that it can be assimilated to a point $\mathbf{u}_s$, leading to the following area-to-point Poisson kriging estimator and kriging variance

$$\hat{r}_{PK}(u_s) = \sum_{i=1}^{K} \lambda_i(u_s) z(v_i) \quad (6)$$

$$\hat{\sigma}^2_{PK}(u_s) = C_R(0) - \sum_{i=1}^{K} (u_s) \overline{C}_R(v_i, u_s) - \mu(u_s) \quad (7)$$

The kriging weights and the Lagrange parameter $\mu(\mathbf{u}_s)$ are computed by solving the following system of linear equations

$$\sum_{j=1}^{K}\lambda_j(u_s)\left[\overline{C}_R(v_i,v_j)+\delta ij\frac{m*}{n(v_i)}\right]+\mu(u_s)=\overline{C}_R(v_i,u_s), i=1,...,K \quad (8)$$

$$\sum_{j=1}^{K}\lambda_j(u_s)=1$$

The ATP kriging system is similar to the ATA kriging system (2), except for the right-hand-side term where the area-to-area covariances $\overline{C}R(v_i, v_\alpha)$ are replaced by area-to-point covariances $\overline{C}$

$R(v_i, \mathbf{u}_s)$ that are approximated as

$$\overline{C}_R(v_i,u_s)=\frac{1}{\sum_{s'=1}^{P_i}ws's}\sum_{s'=1}^{P_i}ws'sC_R(u_{s'},u_s) \quad (9)$$

where P_i is the number of points used to discretize the area *vi* and the weights *ws's* are computed as for expression (3). ATP kriging can be conducted at each node of a grid covering the study area, resulting in a continuous (isopleth) map of mortality risk and reducing the visual bias that is typically associated with the interpretation of choropleth maps.

Another interesting property of the ATP kriging estimator is its coherence. The population-weighted average of the risk values estimated at the P_α points $\mathbf{u}_s$ discretizing a given entity *vα* yields the ATA risk estimate for this entity

$$\hat{r}_{PK}(v_\alpha)=\frac{1}{n(v_\alpha)}\sum_{s=1}^{P_\alpha}n(u_s)\hat{r}_{PK}(u_s) \quad (10)$$

Constraint (10) is satisfied if the same *K* areal data are used for the ATP kriging of the P_α risk values

3.3.3 Deconvolution of the Semivariogram of the Risk

Both ATA and ATP kriging require knowledge of the point support covariance of the risk CR(**h**), or equivalently the semivariogram γR(**h**). This function cannot be estimated directly from the observed rates, since only areal data is available. Thus, only the regularized semivariogram of the risk can be estimated as

$$\hat{r}\gamma_R(h) = \frac{1}{2\sum_{\alpha,\beta}^{N(h)} \frac{n(v_\alpha)n(v_\beta)}{n(v_\alpha)+n(v_\beta)}} \sum_{\alpha,\beta}^{N(h)} \left\{ \frac{n(v_\alpha)n(v_\beta)}{n(v_\alpha)+n(v_\beta)} [z(v_\alpha) - z(v_\beta)]^2 - m* \right\} \qquad (11)$$

where N(**h**) is the number of pairs of areas (v_α, v_β) whose population-weighted centriods are separated by the vector h. The different spatial increments $[z(v_\alpha) - z(v_\beta)]^2$ are weighted by a function of their respective population sizes, $n(v_\alpha)n(v_\beta)/[n(v_\alpha)+n(v_\beta)]$, which is term that is inversely proportional to their standard deviations Monestieze et. al. (2006)

Derivation of a point-support variogram $\gamma(h)$ from the variogram $\gamma_R(h)$ fitted to areal data is called the deconvolution.

Derivation of a point-support semivariogram from the experimental semivariogram γˆRv(h) computed from areal data is called "deconvolution", an operation that has been the topic of much research (Gotway and Young 2007; Kyriakidis 2004). In this paper, we adopted the iterative procedure introduced for rate data measured over

irregular geographical units (Goovaerts 2006b), whereby one seeks the point-support model that, once regularized, is the closest to the model fitted to areal data.

This innovative algorithm starts with the derivation of an initial deconvolved model γ (0)(**h**); for example, the model *γ*Rv*(***h***)* fitted to the areal data. This initial model is then regularized using the following expression

$$\gamma_{regul}(h) = \bar{\gamma}_{h}^{(0)}(v, v_h) - \bar{\gamma}^{(0)}(v, v) \quad (12)$$

where $\bar{\gamma}^{(0)}(v, v_h)$ is the area-to-area semivariogram value for any two counties separated by a distance *h*. It is approximated by the population-weighted average (3), using $\gamma^{(0)}(\mathbf{h})$ instead of $C(\mathbf{h})$. The second term, $\bar{\gamma}_{h}^{(0)}(v, v)$, is the within-area semivariogram value. Unlike the expression commonly found in the literature, this term varies as a function of the separation distance since smaller areas tend to be paired at shorter distances.

To account for heterogeneous population density, the distance between any two counties is estimated as a population-weighted average of distances between locations discretizing the pair of counties

$$Dist(v_i, v_j) = \frac{1}{\sum_{s=1}^{P_i}\sum_{s'=1}^{P_j} n(u_s)n(u_{s'})} \sum_{s=1}^{P_i}\sum_{s'=1}^{P_j} n(u_s)n(u_{s'}) \left\| u_s - u_{s'} \right\| \quad (13)$$

where n($\mathbf{u}_s$) is the population size assigned to the discretizing point $\mathbf{u}_s$. In other words, what matters is the distance between individuals living in these counties, not the distance between the centroids of these geographical units. Note that the blockto-block distances (13) are numerically very close to the Euclidean distances computed between population-weighted centroids (Goovaerts 2006b).

The theoretically regularized model, γregul(**h**), is compared to the model fitted to experimental values, γRv(**h**), and the relative difference between the two curves, denoted D, is used as an optimization criterion. A new candidate point-support semivariogram $\gamma^{(1)}$ (**h**) is derived by rescaling the initial point-support model $\gamma^{(0)}$(**h**), and then regularizing it according to expression (12). Model $\gamma^{(1)}$(**h**) becomes the new optimum if the theoretically regularized semivariogram model $\gamma^{(1)}$ regul(**h**) gets closer to the model fitted to areal data, that is if D(1) <D(0). Rescaling coefficients are then updated to account for the difference between $\gamma^{(1)}$ regul(**h**) and γRv(**h**), leading to a new candidate model $\gamma^{(2)}$(**h**) for the next iteration

3.4 Cluster analysis

A common task in disease analysis is to examine administrative units in adjacent geographical locations that are significantly similar or different. Similarity between the Buruli ulcer incidence rate observed within area v_β and those recorded in the $j(v_\alpha)$ neighboring areas v_α can be computed by the local *Moran statistic* Anselin (2000) as:

$$l(v_\alpha) = \left[\frac{z(v_\alpha) - m}{s}\right] \times \left(\sum_{j=1}^{j(v_\alpha)} \frac{1}{j(v_\alpha)} \times \left[\frac{z(v_j) - m}{s}\right]\right) \quad (14)$$

where m and s are the mean and standard deviation of the set of N area incident rates respectively. This local indicator of spatial association (LISA) is simply the product of the kernel rate and the average of the neighboring rates.

The distribution of the local *Moran statistic* under the null hypothesis of complete spatial randomness is usually obtained through a random of shuffling all the count(s) except at v_α each time calculating (14) to get the distribution of simulated LISA values.

CHAPTER 4

RESULTS AND DISCUSSIONS

The figures 4.1 and 4.2 indicate the omnidirectional variogram of Buruli ulcer for females and males using the risk computed from district- level rates, using estimator (11). The experimental variogram was fitted using a Cubic model with a range of 37.5km for females and 41.5km for males. However, BU incidence for males has better range of spatial autocorrelation than incidence for females in each administrative unit. Each model was deconvoluted using the iterative procedure.

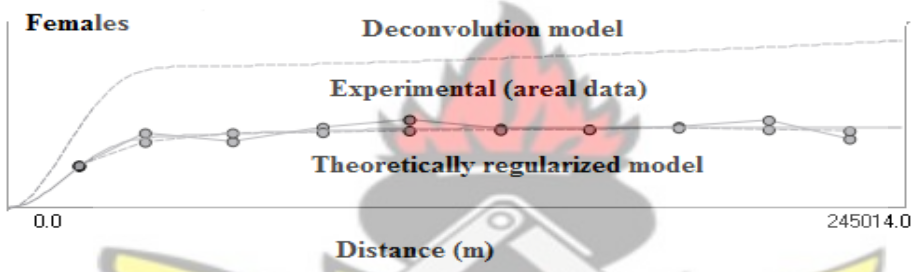


Figure 4.1 Experimental variogram and model from areal data; theoretically regularized variogram and deconvoluted model for females with Buruli ulcer disease at administrative units

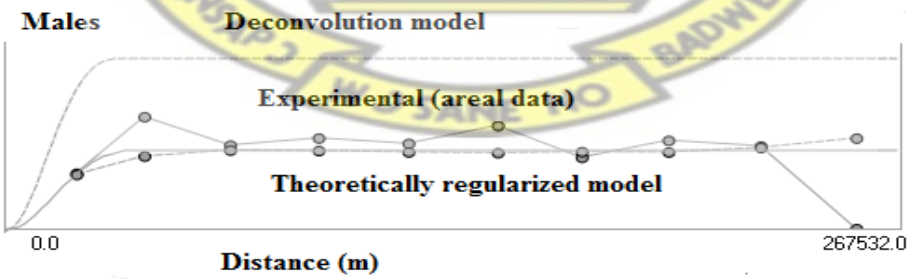


Figure 4.2 Experimental variogram and model from areal data; theoretically regularized variogram and deconvoluted model for males with Buruli ulcer disease at administrative units.

The deconvoluted variogram model was then used to compute aggregated risk values at the district level in both regions using ATA and ATP kriging, see figure 4.3. In all cases, the estimation was based on the K=32 closest observations, which were selected according to the population- weighted districts, for ATA kriging. All the kriging maps of Buruli ulcer incidence for females were smoother than the map for the raw rates because the noise, due to the population size was filtered

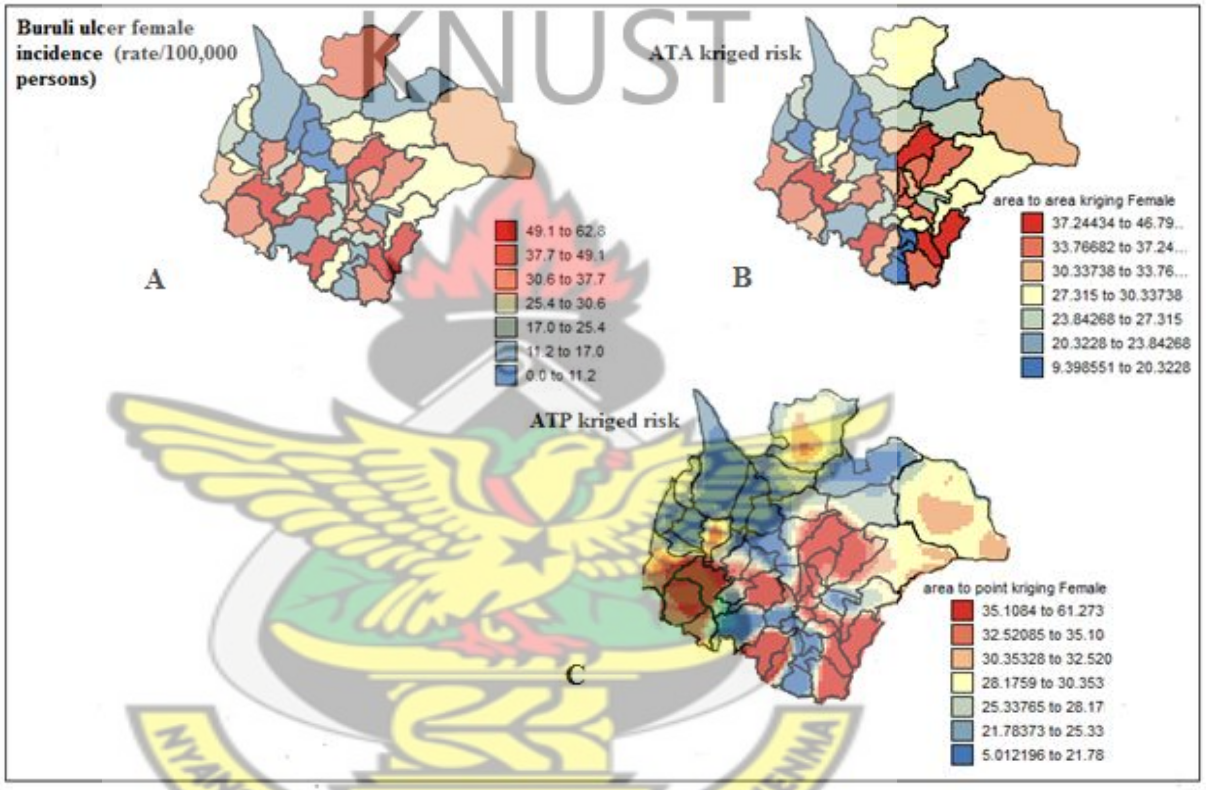


Figure 4.3: Females' kriging maps of Buruli ulcer incidence at various administrative units estimated by Buruli ulcer rate per 10, 000 people.

The BU incidence rate for females at the various administrative units (Fig.4.3C) shows that the disease is more endemic in the southern districts of the study area than the other districts. Incidentally, the southern portions represent the Ashanti region. It can therefore be implied from the results that the Ashanti region has more endemic districts than the Brong Ahafo region as evidenced in figure 4.3C which represents the

ATP risk map of Buruli ulcer for females in the study area. Within the ATP risk map for females (fig 4.3C) some isolated districts in Brong Ahafo region which shares border with the Ashanti region such as Tano North and South, Asunafo North and South also have high risk of BU. The same situation is observed in figure (4.3B) the choropleth map which is based on the size of polygon. It also showed that areas close to Ashanti are more endemic. The incidence map figure 4.3A which is the raw data depict similar patterns in the spread of BU within the study area. This revelation by this paper is not to say that the other districts are free from the disease incidence. It is not surprising that the southern districts of the ATP risk map shows high incidence of the disease because these areas are characterized by massive agricultural and artisanal mining activities that disturb the environment and contributes to the spread of the disease. These findings are consistent with a study conducted by the Ministry of Health in 2010 which concluded that for the past five years, the incidence of the disease in the two regions have been very high due to artisanal mining activities which have destroyed most of the water bodies in the area. This is the condition for which mycobacterium ulcerans (MU) thrive well. Again, these communities lack access to proper health care and therefore, majority of the women with the disease do not report for medical attention.

The unreported cases are also fueled by the high cost of treatment and the level of stigmatization, (Owusu-Sekyere, 2012). The northern part of Brong Ahafo such as Kintampo, Jaman North and South are less endemic, probably because these are dry areas with less stagnant waters, pounds, rivers and streams. The mycobacterium does not do well in such environment.

Contrary to the studies by Amofa et al. (2002) in the Amansie West that females were more infected than their male counterparts, this study found the opposite. This

research revealed that more males suffered the disease in the study area than their female counterparts, fig 4.4F. Again, figure 4.4F further suggests that the incidence of Buruli ulcer for males is quite wide spread unlike their female counterparts that tended to concentrate only on the southern portion of the study area. There are majority of cases among males in the Northern districts of the study area which happens to be districts in the Brong Ahafo region.

The high prevalence of the disease among males could be attributed to the changing nature of livelihood activities which is more male oriented such as the mining activities.

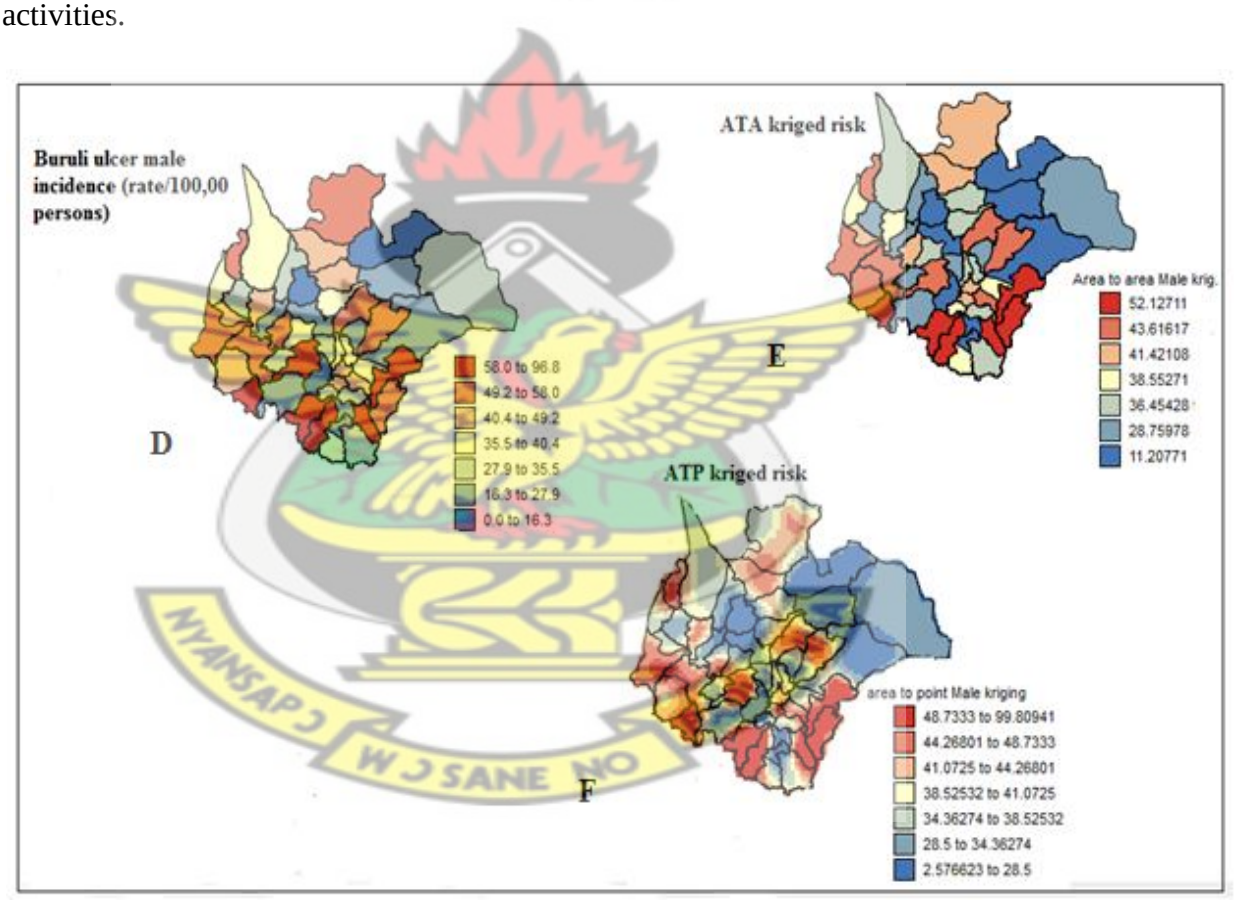


Figure 4.4: Maps of BU incidence rate estimated by BU rate per10,000 person, ATA Poisson kriging and ATP kriging on males at various administrative units (D,E and F).

Similarly, districts that did not report of female case now reports high males Buruli ulcer incidence, one of such districts is Kintampo North, see figure 4.4F. This situation could be attributed to the mobility of men in search of greener pastures.

As was the case with the female sexes, there were more males with the Buruli ulcer disease in the southern districts of the study area. These areas represent the southern part of the Brong Ahafo region and the Ashanti region.

The endemic districts are the Amansie West-most endemic in Ghana, Tano North and South. These districts have had the worst environmental degradation for the past five years (EPA, 2010). This is also evidenced in figure 4.4 A and D where southern part of Brong Ahafo exhibits high incident rates and few isolated places within the middle portion of the region. Even though figure 3.4 A and D do not explain the viability within each administrative unit.

Finally, the estimated geographical clustering of the disease at the administrative units showed that only two administrative units, the Amansie West District and the Bekwai Municpal were significant, figure 4.5K.

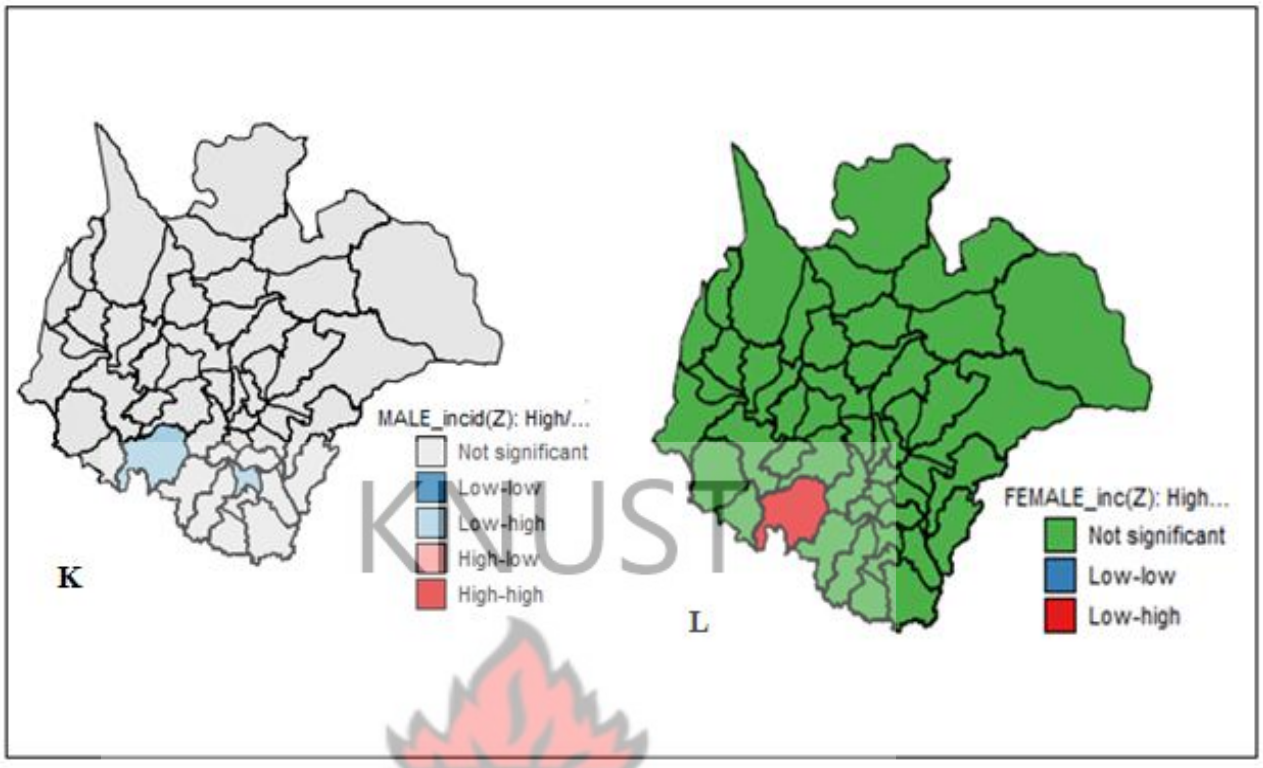


Figure 4.5: Results of the local cluster analysis conducted by Buruli ulcer incidence rate for females and males (K and L).

The Local Moran statistic (Fig. 4.5L) shows that only Amansie West District is significant. This administrative unit by implication has the highest Buruli ulcer incidence in the area under study. The disease is clustered around the major rivers which are Offin, Punpuni, and Oda and the most affected communities are Tontokrom, Edubea and Kaniago which are all found around the major rivers (Bonya and Sekyere 2012). The fact that the other administrative units are not significant (p-value > 0.05), does not imply they are free from the incidence of the Buruli ulcer disease. The high incidence of the disease for males in the District has been blamed on the activities of artisanal mining (MOH 2010). The mining activities have led to the contamination all the water bodies with arsenic. The high levels of Arsenic (As) concentrations could cause BU occurrence to increase. This is supported by Duker et al., (2006) that the influence of arsenic on gold activities enhances the bacteria called

water bug which is believed to host Mycobacterium ulreans and when bitten by these insects may contribute to the spread of BU. According to Duker et al, (2006) arsenic may play a vital role in the spatial distribution of BU.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 CONCLUSION

This study has demonstrated how geostatical method can be used to modell Buruli ulcer incidence by sex distribution. Geostatistical modeling using Area to Point Kriging (ATP) method used in this study has revealed an insight into more localized potential ‘‘hot spots’’ for the Buruli ulcer disease that may not be evident when non geostatiscal methods are employed. ATP kriging is used to create a continuous risk surface that reduces the visual bias associated with large administrative units. The research showed a large range of spatial autocorrelation in males than that of females in the distribution of BU disease. The research further showed that the risk associated with Buruli ulcer was centered in the southern districts of the study area which co-incidentally, represents the Ashanti region and few districts in the Brong Ahafo region.

The research revealed that the worst endemic areas had suffered massive environmental degradation through agricultural and artisanal mining activities. The artisanal mining for example had elevated arsenic content in soils and water bodies thus exposing the population to the disease causing organisms. The Moran scan cluster analysis was performed and that Amansie West district was identified to be significance for the spread of the disease. It has also been observed that geographical boundaries close to Ashanti region to Brong Ahafo have strong relation in terms of

the spread of the disease. There was no significant clustering of the disease in any district in the Brong Ahafo Region.

5.2 RECOMMENDATION

We state that in future, space and time dimension of the disease should be studied. In addition to this, other regions where the disease is endemic have to be included in future studies to obtain national perspectives of the spread of the disease.

Area to point kriging should be used in the analysis of the spread of diseases such a Buruli ulcer as against traditional descriptive statistics. Since this will give more viability of the spread of the disease.

The various districts that have been seen in this study which have high risk of spreading the disease should be encouraged to be active partner in the crusade of fighting the disease. Part of the revenue that comes to the district assembly must therefore, be channeled into improving the socio economic well being of the people specially provision of quality pipe borne water.

The government on his part should make resources available through its agencies especially the Environmental Protection Agency (EPA) to monitor the environment and provide the necessary advice to the various district assemblies in order to reduce the spread

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