

The background of the cover is a vibrant green. In the upper half, a silver stethoscope is positioned horizontally, with its chest piece on the left and the earpieces extending to the right. Below the stethoscope, a portion of a globe is visible, showing the continents of North and South America. The globe is slightly out of focus compared to the stethoscope.

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## Full Length Research Paper

# Occurrence of verocytotoxigenic *Escherichia coli* (VTEC) in processed chicken from retail chicken markets in FCT, Abuja, Nigeria

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Chicken meat is one of the predominantly consumed foods of animal origin in Nigeria with constant increase in demand normally met by local retail market. Processed chicken at the retail chicken meat markets in Abuja were screened for the presence of verocytotoxigenic *Escherichia coli* (VTEC) strains. A total of 273 faecal samples were collected using moistened sterile swabs and processed for *E. coli* isolation following standard cultural and biochemical procedures. Isolated *E. coli* samples were cultured on sorbitol McConkey (SMAC) and cefiximetellurite sorbitol McConkey (CT-SMAC) agar to assess their ability to ferment sorbitol. Samples were further characterized using commercially procured dry spot polyvalent serocheck and specific seroscreen agglutination test kits. Two (0.73%) of the samples tested positive to O157VTEC, while 5 (1.83%) tested positive to non-O157VTEC. There was no significant association ( $p>0.05$ ) between VTEC infection and season. The study indicated that processed chicken meat sold at the retail chicken market may serve as a potential vehicle for the spread of VTEC infection and other food borne pathogens. Consumer food safety education is important in control programmes.

**Key words:** Occurrence, verocytotoxigenic *Escherichia coli* (VTEC), processed chicken, retail market, strain.

## INTRODUCTION

Since the first isolation of *E. coli* O157:H7 from an outbreak of human bloody diarrhea in 1982, it has been reported from hundreds of sporadic cases and outbreaks in more than thirty countries of the world (Carter et al., 1987). In addition to *E. coli* O157, many other serogroups of VTEC cause disease and are called non O157 VTEC [Centre for Disease Control (CDC), 2005]. Most attempts

to isolate VTEC have been done in dairy and beef cattle because they are most often associated with human disease episode (Dorn, 1995). Cattle are believed to be the principal reservoir for the organisms (Borczyk et al., 1987). Other animal species including birds sometimes pick up VTEC from the environment and may spread it.

VTEC comprise a diverse group that elaborate one or

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both shiga toxins (stx1 and stx2) and can cause diarrhea, haemorrhagic colitis and haemolyticuraemic syndrome (HUS) in human beings (Grant et al., 2011; Gyles, 2007). Meat obtained from farmed and wild game animals contaminated with VTEC has the potential to cause infections in humans, while most of these *E. coli* infections are caused by *E. coli* O157:H7, 20 – 70% of VTEC infections throughout the world are attributed to non-O157 VTEC (Brooks et al., 2005). Of the 81 serotypes identified worldwide, 71% of the isolates recovered from human beings belonged to the “top 6” ‘O’-groups (O26, O45, O111, O103, O121 and O145) (Brooks et al., 2005). In 2012, these 6 non – O157 VTEC O-groups in addition to O157 earlier considered were included as adulterants in beef produced in the United States [United States Department of Agriculture-Food Safety Inspection Services (USDA-FSIS), 2012].

Production of safe poultry meat requires systematic and continuous control of the carcasses during all the production steps including slaughterhouses and retail shops (Daci et al., 2016). Microbiological risk from poultry meat is due to contamination during rearing, slaughtering process, and the marketing conditions at the retail shops. Contamination with specific pathogens is common and one of the main concerns of the public Health authorities worldwide (Mead et al., 1994). The importance of this study is linked to the role of poultry meat as one of the main sources of food borne diseases (Fitzgerald et al., 2000).

There has been an increased participation in poultry production in the country in recent time. Live chicks and chicken including their products have been imported and distributed among poultry farmers in all parts of the country. This may lead to introduction of the organism into the environment and then to the food chain hence the need to investigate the organism in processed chicken.

The study is aimed at investigating the occurrence of VTEC O157 and non O157 in processed chicken from retail chicken market in Abuja, FCT, Nigeria in order to evaluate their zoonotic potentials.

## MATERIALS AND METHODS

The study was carried out in the Federal Capital Territory (FCT), Abuja located between 8° and 9°25' North of the equator and longitude 6°45' and 7°45' East of the Greenwich meridian (Dawan, 2000). Selected processed chickens through cluster sampling method from retail markets and outlets were studied in 3 out of the 6 Area Councils, selected by simple random sampling. The study design was cross sectional.

Faecal samples from 273 processed chickens were collected using moistened sterile swab immediately after de-feathering and before the chicken was opened in the retail market. Precautionary measures were taken to prevent cross-contamination of samples in transit and at the laboratory. An enriched medium of buffered peptone water (BPW) supplemented with 8 mg/l vancomycin, 10 mg/l cef sulodin and 0.05 mg/l cefixime (BPW-VCC) was prepared to suppress the growth of Gram positive organisms, *Aeromonas*

**Table 1.** Prevalence of O157 and non-O157 VTEC in processed chicken.

Serogroup	No. tested	No. positive	Positive (%)
O157	273	2	0.73
Non O157	273	5	1.83

**Table 2.** Distribution of the 5 non-O157 detected in processed chicken.

Serotype	No. positive	Positive (%)
O26	1	0.37
O103	-	-
O111	1	0.37
O145	1	0.37
O91	1	0.37
Untyped	1	0.37

and *Proteus* spp. (Pritchard, 2000). Approximately, 0.5 g of the faecal sample was inoculated into 5 ml of the prepared BPW-VCC and incubated at 37°C for 6-8 h (Pritchard, 2000). Samples were first cultured on McConkey agar (MCA) then those lactose fermenting organisms (pinkish colonies on MCA) were streaked on eosine methylene blue (EMB) agar and incubated at 37°C for 24 h. The cultured isolates exhibited the typical greenish sheen colouration characteristic of *E. coli* on EMB agar. Biochemical tests were carried out to confirm the isolates as typical *E. coli* and they exhibited similar IMViC pattern of + + - - and showed negative to both urease and hydrogen sulphide production.

*E. coli* isolates ex-EMB were sub-cultured into plates of Sorbitol McConkey agar (SMAC) and Cefixime-Tellurite Sorbitol McConkey agar (CT-SMAC) and incubated at 37°C for 18 to 24 h (March and Rotnam, 1986). Non sorbitol fermenting (NSF) isolates that appear as colourless or neutral gray with smokey center and 1-2 mm in diameter on the two plates were presumptive of *Escherichia coli* O157, while sorbitol fermenting (SF) isolates that appear pinkish in colour were presumptive of *E. coli* non-O157 (Zadik et al., 1993).

Both the NSF and the SF stored in nutrient agar slants were further characterized using latex agglutination test kits called dry spot *E. coli* seroscreen and polyvalent serocheck which were commercially procured from Oxoid™ England. The kit contained seroscreen for O157 and serocheck for O26, O103, O111, O91 and O145.

## RESULTS

The prevalence of VTEC O157 in processed chicken was 0.73% (2) while the prevalence for non-O157 VTEC was 1.83% (5) (Table 1). The distribution of the 5 non-O157 detected were also determined. VTEC O26, O111, O145 and O91 and the untyped were 1 each, while VTEC O103 was 0 (Table 2).

The seasonal distribution of VTEC O157 and non-O157 VTEC was studied. Of the 273 samples collected, 145 were during the dry season, while 128 were during the wet season. The number of isolates for VTEC O157 was

**Table 3.** Seasonal distribution of VTEC O157 and non-O157 in processed chicken.

Season	No collected	No positive for O157	No positive for Non-O157
Dry	145	2	4
Wet	128	-	1
Total	273	2	5

$p > 0.05$ .

2 in the dry season and none in the wet season, while for non-O157 VTEC, 4 was positive in the dry season and 1 positive in the wet season. There was no significant difference between infection and season ( $p > 0.05$ ) (Table 3).

## DISCUSSION

This work detected the presence of O157, O26, O111, O145 and O91 in processed chicken. The results carried out elsewhere on processed chicken agreed with the result of this study. Doyle and Schoeni (1997) assayed 263 fresh, uncooked chicken samples and isolated the organisms from 1.5% (4) of the samples. In Thailand, Suthienkul et al. (1990) found 1% (9) out of 107 chicken carcasses contaminated with *E. coli* that did not produce shiga like toxin. In another study performed in UK, 1 to 2% of chicken lamb and pork meat samples were found to be contaminated by *E. coli* O157:H7 (Adams and Moss, 1995). Vemozy-Rozand et al. (1997) analyzed 250 samples of meat and meat products in France and found 4 chicken meat samples (1.6%) to be positive to non verotoxin producing *E. coli*. El-Jakere et al. (2012) collected 12 VTEC isolates from chicken to study their diversity and O2, O6, O8, O26, O27, O78, O86, O111, O128, O136 and O157 were typed from the chicken. Although, genetically diverse, avian *E. coli* isolates share several genes or traits associated with virulence in chicken (Ngeleka, 1996). *E. coli* isolates were recovered by Cook et al. (2012) from the skin-off chicken breasts, 33% (33) of 99, than from the skin-on chicken breasts, 41% (77) of 187 ( $p = 0.204$ ) and VTEC was detected on a single skin-off chicken breast. Verocytotoxigenic *E. coli* are a specialized group of *E. coli* that can cause severe colonic disease and renal failure.

Although, Heuvalink et al. (1998) could not find any VTEC O157 in chicken faeces, 1.3% of 459 pooled samples from turkeys were positive and one isolate contained genes for type 2 verotoxin, attaching-and-effacing capability and the relevant haemolysin. Akkaya et al. (2006) isolated *E. coli* O157:H7 from 2 (1.0%) of the 190 samples of poultry meat examined with all the strains producing both VT1 and VT2 verotoxin indicating that poultry meat can also be a source of VTEC infection to humans.

In Egypt, Abdul-Raouf et al. (1996) examined 50

boneless chicken meat samples and were able to detect *E. coli* O157:H7 in 2 samples. Zhao et al. (2001) reported 38.7% prevalence of *E. coli* in chicken meat in a study in Washington D.C, USA. Chapman et al. (1997) recorded no positive result from 1000 chicken tested for O157 VTEC.

The isolation of VTEC strains from processed chicken may be due to cross-contamination during slaughter, processing or transportation. The contamination might occur in the chicken slaughter house at various stages such as during evisceration, scalding, plucking and or cutting processes. The presence of *E. coli* O157:H7 on chicken carcasses suggests that chickens may be natural carriers of the microorganisms (Akkaya et al., 2006).

The result of this research showed low prevalence in processed chicken suggesting that the organism is rare in these products in the study area. Published research findings show that VTEC O157 is rare in poultry whether in live birds or on processed products and when it was found, tests for the necessary virulence factors was not carried out (Schmidt et al., 1990). Read et al. (1990) recorded zero isolation in chicken in South Western Ontario indicating that the organism is actually rare in chicken and chicken products. VTEC O157:H7 has been documented to colonize the gastrointestinal tract of chickens under experimental conditions (Barry et al., 1985; Stavric et al., (1993).

There was no significant difference between season and infection with VTEC in processed chicken. No available records showed that research has been done on seasonal distribution of VTEC in processed chicken.

## Conclusion

The isolation of VTEC organisms in processed chicken meat as determined in this study is indicative that processed chicken meat may serve as a source of infection to humans. Control strategies aimed at protecting public health should be adopted to eliminate contamination of any sort with the pathogen. Consumer food safety education is important as prevention and control measures.

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*Full Length Research Paper*

# Modeling the risks of Ebola reemergence in Nigeria: Any lessons from outbreaks in Africa?

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**Ebola virus Disease EVD is deleterious to the health system, food security and social activities. However, here we highlight the risk and fiscal impact an outbreak can exert - economic cost (direct cost of clinical treatment, contact tracing and surveillance system) and repugnant cost on the citizens and foreign business partners. This paper reviews the indicator parameters (risk factors) that can lead to an EVD index case in Nigeria using probabilistic risk model, exponential and Beta-Poisson distribution model. It examines the negative impact of EVD in hardest hit countries during the 2014 West African outbreak, and the need for preemptive attention in Nigeria. Although this risk assessment process has limitation of exposure data with many assumptions, precautionary lessons are drawn from ecological, sociological and environmental drivers that lead to Ebola virus spill over and/or emergence in previously known outbreaks since 1976.**

**Key words:** Ebola virus, risk, probability, infection.

## INTRODUCTION

Once an epidemic is over, it is important to reassess the risk of reoccurrence. Risk assessment systematically determines the likelihood of negative consequences resulting from exposure to biological hazards. In epidemiology, risk assessment is used for disease surveillance and a basis for evaluating the potential future consequences of exposure to any hazardous biological agent. Comprehensively assessing the risk factors of Ebola re-emergence and the sustained human-to-human transmission is important as precautionary measures for importation or emergence of the disease. Three components in risk assessment are hazard assessment (identification of the etiology-Ebola virus), exposure

assessment (evaluation of the population exposed to the etiology, that is dose-response), and context assessments (evaluation of the physical and socio-economic environment the event is taking place) (WHO, 2012).

Several studies have determined the risks of EVD outbreak based on these components. United Nation Development Group (UNDG) simulated the probability of Ebola prevalence in 15 West African countries, and grouped countries into high or low Ebola scenario. From the model, the probability of having Ebola index in Nigeria is between 0.1 and 0.2 which places the country in the medium-risk group (UNDG, 2015). Another study uses

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the Susceptible-Exposed-Infectious-Removed model (SEIR) and estimated the reproductive number of EVD and risk of an outbreak from an undetected case at 9.0 and 89% respectively (Althaus et al., 2014). Although these estimates provide an immediate insight into the likelihood of outbreak in Nigeria, they do not elucidate several specific risk factors capable of driving Ebola epidemic in the country. What are these risk factors in Nigeria that leads to EVD index and sustained human transmission, and what impact can an outbreak wield on the Economy?

### Brief overview and epidemiology of ebola virus

Ebola virus disease EVD or “Ebola” is a severe human and non-human primate disease caused by Ebola viruses. These viruses belongs to the family Filoviridae, Genus Ebola virus, which include the species *Tai forest ebolavirus* (TAFV), *Reston ebolavirus* (RESTV), *Sudan ebolavirus* (SUDV), *Zaire ebolavirus* (EBOV) and *Bundibugyo ebolavirus* (BOBV) (Bukreyev et al, 2014). *Zaire ebolavirus* (ZEBOV) is the most virulent of the genus and accounts for the highest numbers of outbreaks. The virus spreads by direct contact with body fluids or secretions of infected animals. Although the natural reservoir of the virus is yet to be ascertained, several scientific studies has proven that fruit bats is the natural host (Olival et al., 2013; Calisher et al., 2006; Swanepoel et al., 1996; Biek et al., 2006). Humans get infected through direct physical contact with infected bats or other animals (duikers and non-human primates) that serve as intermediate hosts. Ebola virus then spreads among humans through contact with symptomatic person or contaminated fomite. There have been various speculations with regards to the pathogenesis of EBOV. Generally, studies have shown that on a successful entry into body tissues, the virus invade the immune system suppressing the production and response of interferon proteins using its VP24 and VP35 (Hoenen et al., 2006). It infects monocytes, macrophages and dendritic cells resulting in rapid viral replication, hemorrhage and hypovolemic shock and edema, fever and gastrointestinal dysfunction (Lai et al., 2014). The incubation period is usually 2 to 21 days, as disease symptoms is usually characterize by fever, pains in joints and muscles, headache, bloody vomit and diarrhea, abdominal pains and internal or external bleeding. Diagnostic technique include detecting viral RNA, antigen or protein using Polymerase Chain Reaction (PCR), viral particle isolation using cell culture and detecting viral antibodies using Enzyme Link Immunosorbent Assay (ELISA). Currently, there are no effective drugs or vaccines against Ebola virus.<sup>1</sup> Treatment is achieved through oral or intravenous

rehydration to replace lost body fluid and electrolytes and treating clinical symptoms (Spickler, 2004).

The first outbreaks of EVD occurred on August 1976 in Nzara, South Sudan and Yambuko, Zaire (Democratic Republic of Congo, DRC). Prior to the 2014 West Africa outbreak, about 24 episodes of EVD have been reported in 7 African countries-Sudan, DRC, Uganda, Gabon, Congo republic of, Ivory Coast and South Africa- with 2387 reported cases, (case fatality rate 50-90%)<sup>2</sup> (WHO, 2015). The West African ZEBOV epidemic began in December 2013 in Guinea and had spread to other West African countries- Liberia, Sierra Leone, Nigeria, Senegal and Mali, and outside West Africa- Spain and USA. As of August 2015, World Health Organization (WHO) has reported 28639 cases including 11316 deaths have been reported worldwide, the most occurred in Liberia, Guinea and Sierra Leone (WHO, 2016). The index case for the 2013 outbreak which began in Guèckedou region of Guinea is believed to be through contact with infected bat (Saéz et al., 2015). The index case in Nigeria was imported by a Liberian-American, resulting in 20 confirmed cases with 8 deaths. On 20<sup>th</sup> October 2014, Nigeria was declared Ebola free by WHO after successfully containing the virus.

### Probability of EVD emergence in Nigeria

Understanding the trend that leads to outbreak of EVD throughout history will aid clarify risk factors in Nigeria. Although identifying the main reservoirs of Ebola virus and their geographic boundaries still remain limited. Human EVD cases prospectively resulted from contact with infected bats, duikers and non-human primates. (Swanepoel et al) demonstrated in laboratory conditions that bats might be the natural reservoir of Ebola virus. They are very common in sub-Saharan Africa and can migrate up to 2500 kilometers (McGuire, 2012). The 2007 outbreak in DRC is evidently linked to the annual massive migration and hunting of fruit bats in the region (Leroy et al., 2009). In 2008, Ebola virus antibodies were detected in 32 of 88 bats screened in Ghana, of these, 9 were ZEBOV positive (Hayman et al., 2012). The existence of 9 bats in Ghana infected with ZEBOV suggest that they may have migrated from Central Africa, since this viral species is believed to originate from Central Africa (Sylla et al., 2015). ZEBOV did not spillover into human population in Ghana, probably no susceptible person had contact the infected bats. Evidently, prior to any outbreak, the virus may have being in the reservoirs host or intermediate host for unascertained period of time, for conditions for spillover (hunting) to presented itself.

Several outbreaks of EVD are associated with hunting and physical contact with zoonotic non-human primates.

<sup>1</sup> Few pharmaceutical companies are making progress in vaccine and drug development with phase 1 safety trial now underway.

<sup>2</sup> This report is exclusive of asymptomatic Reston virus Ebola virus cases in USA, Philippine and Italy and the laboratory contamination of ZEV cases in Russia, 1996 and 2004 respectively.

Most times, the reservoir host (bats) sheds the virus to its recipient host (non-human primates and duikers) which in turn serves as intermediate host for humans (Plowright et al 2015).

The 1976 index case in DRC was thought to handle carcasses of Antelope and Monkey on his way back to Yambuko (Muyembe-Tamfum et al., 2012). A female etiologist in Cote d'Ivoire tested positive to EVD after performing necropsy on chimpanzees (Formenty et al., 1999). 1996/1997 and 2001-2003 outbreaks in Gabon and DR Congo respectively, were associated with butchering and consumption of infected non-human primates (Rouquet et al., 2005).

In Nigeria, there have been no study investigating the population of bats and its consumption rate, despite the fact that this animal is highly used for food, cultural and ritual purposes by some ethnic groups, nor it is certain whether or not there are EBOV infected Bats. However, other virulent viruses have been isolated from bats in Nigeria and studies showed that an infected Bat can circulate the viral particle among other congeners in the roost (Kia, 2014). The 2008 Bat's screening in Ghana, the 1994 Ebola infected chimpanzees and the 2014 outbreak in Guinea strikingly demonstrate the feasibility of EBOV infected bats migrating into Nigeria. The dissemination of EBOV among bat and close human contact with this animal show the potential of spill over into human population. A survey among 50 hunters in Idanre, south west Nigeria showed an average hunts of 11.20 Bats (*Eidolon helvum*) per hunter, within five months (Bifarin et al., 2008), excluding hunting by other residents of the region.

In another survey, bush meat trading in Oban Hill region, South East Nigeria shows the consumption rate of Primates in this area- 35 chimpanzees, 2937 African monkeys within December and October (Eniang et al., 2008). Bush meat buyers travel thousands of kilometers to this region to purchase various species of animals. Apparently continuous consumption of Bats and non-human primates posts a public health risk of EVD index.

### Cross boarder risk

The index case of Ebola in Senegal was a young man in incubation period, travelled by road to Dakar, from Guinea. Mali had the first case from migration of a two-year-old child from Guinea. The disease was introduced into Sierra Leone when EVD patients from Guinea illegally cross boarder to seek for cure from a traditional healer in Kenema (WHO, 2015). A symptomatic air traveler from Liberia introduced the virus in Nigeria. Although this index in Nigeria was through an approved terminal, it is pertinent to consider the risk of illegal borders. Comptroller General of Nigeria Immigration Service revealed that there are well over 1,400 illegal unmanned routes, with only 84 approved border control posts across 4,000 sq. km (Ogundele, 2014). This

creates a fertile ground to smuggle the particle into Nigeria. Illegal Importation of EVD index may likely have its first contact in Nigerian rural communities with poor health facilities.

Thus, the initiation of EVD in Nigeria can be from physical contact with an infected animal and/or initiated by infected emigrant (imported human-to-human transmission).

### Risk analysis

Studies by (UNDG, 2015) estimated that the probability of EVD prevalence in Nigeria ranges between 0.1 and 0.2. The above discussed risk factors are systematically evaluated using probabilistic risk assessment (PRA) model. This method uses several specific models like Boolean Logic method or models, which includes deductive method like Fault Tree Analysis (FTA) and inductive method like Event Tree Analysis (ETA) (Stamatelatos, 2000). FTA (Figure 1) identifies single or combination of faults - (risk factors) that can leads to undesirable consequence of having EBOV infected person in Nigeria.

The above Fault Tree Analysis shows the possibility of human contact with Ebola zoonotic and/or the possibility of human importation from other infected country. Spillover of the virus depends on the distribution and population of infected Bats, shedding and viability of the virus and the immunity of recipient host. Consider human contact with EBOV zoonotic as shown in Figure 1. Though EBOV is highly virulent, many in the exposed group do not develop clinical symptoms of infection or disease. This may be rightly attributed to variations in infective dose (ID) present in the inoculum and the host immune response (Schmid-Hempel and Frank, 2007), thus the need to model the probability of infection using disease exponential model and beta-Poisson model. Now, consider a successful entry of the virus into a human host, from single-hit hypothesis, the likelihood of a single viral particle survive all immunological barriers has a non-zero value of  $P_m$ , then the probability of effecting the host is  $(1 - P_m)$ , and the probability for the second viral particle in the same inoculum to cause infection is  $(1 - P_m)^2$ , and for  $n$  numbers of particles, the probability is  $(1 - P_m)^n$ . Thus the probability of infection ( $P_{inf}$ ) in individual who had zoonotic contact can be expressed as:

$$P_{inf}(n, P_m) = 1 - (1 - P_m)^n \quad (1)$$

Where the viral particles in the inoculum are assumed to be at random, then using exponential model,

$$P_{inf}(n, P_m) = 1 - e^{(-P_m n)} \quad (2)$$

$P_m$  = the dose of Ebola viral particles that survives the host immune system to cause

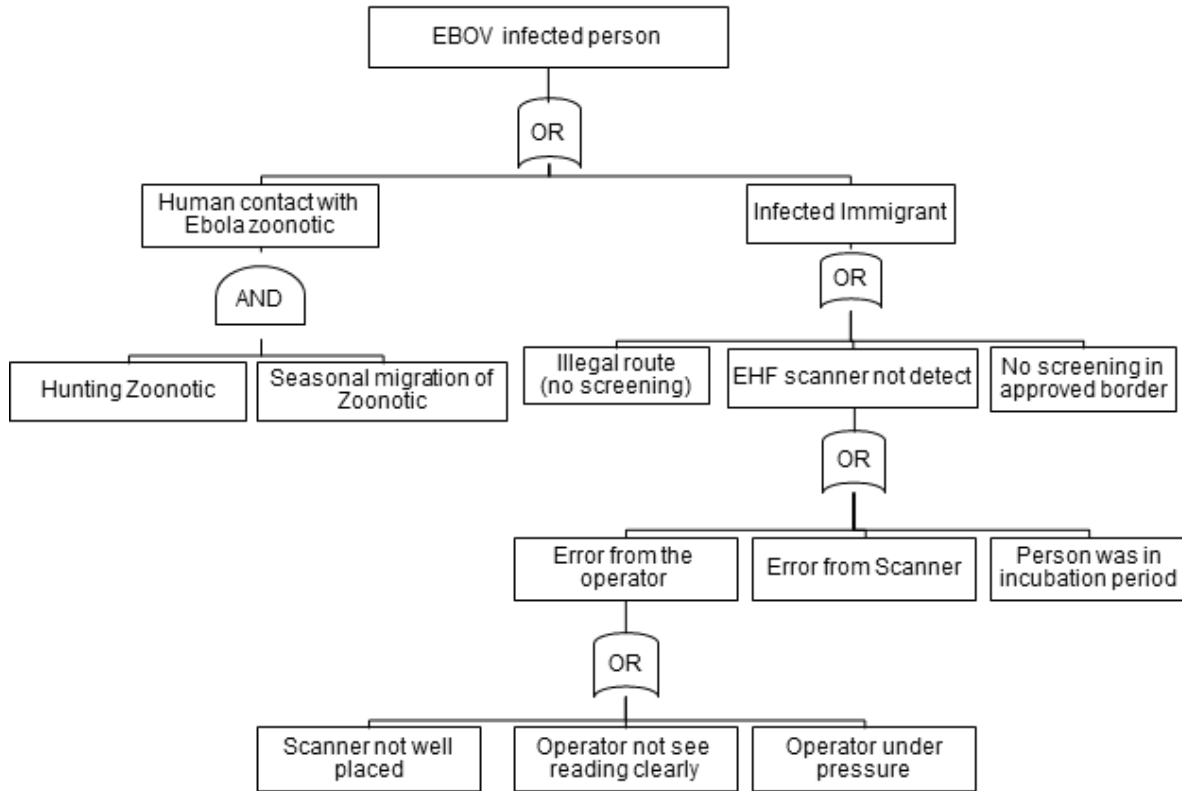


Figure 1. Fault tree analysis.

$P_m$  infection.  $n$  = the mean numbers of particles that had a successful entry, then

The probability of starting an infection varies with the host, following beta-Poisson distribution:

$$P_{inf}(n; \alpha, \beta) = 1 - \left(1 + \frac{n}{\beta}\right)^{-\alpha} \tag{3}$$

Where  $\alpha$  and  $\beta$  are the parameters of beta distribution.

### Transmission

With the initiation of EVD index, transmission from human-to-human could easily spread the virus away from the source. The transmission of the disease depends on an infectious individual, a susceptible individual and an effective contact<sup>3</sup>. Effective contact  $E_c$  is expressed as:

$$E_c = T \times P_{inf} \tag{4}$$

Where:  $T$  is the total contact rate (the total number of contacts, effective or not per unit time),  $P_{inf}$  is the probability of infection.

For EVD outbreak, Nigeria has an estimated Basic Reproductive Number<sup>4</sup>  $R_0$  of 9.01. From the estimated  $R_0$ , the risk of an epidemic from an undetected case is 89% (Althaus et al., 2014). The 2014 EVD cases in Nigeria were in urban areas with relatively good health infrastructure and quick, effective intervention measures. However, most outbreaks of EVD among humans are often initiated in rural communities, and in most case, goes undetected for a while. From the Nigerian health care system, Primary Health Care (PHC) is responsible for disease prevention and promoting good health at the community level, however it receives the least resources. Generally, infrastructures in many Nigerian PHCs are in poor, decaying condition (WorldBank, 2010), with no source of electricity, clean water onsite, frequently run out of supply of drugs and stock and low skilled personals (FMoH, 2014). In addition, referral mechanism is not effective (Abdulraheem et al., 2012). Thus on emergence of EVD, PHCs likely the first point of contact, cannot provide appropriate containment measures. Poor health system creates viable conditions for infected persons having contact with susceptible individuals. Event tree analysis inductively describes a series of possible paths (failures) that can lead to high reproductive number

<sup>3</sup> An effective contact is any kind of contact between an infectious individual and a susceptible individual, such that the infectious can infect the susceptible

<sup>4</sup> Reproductive Number is the number of susceptible persons that can be infected by an infectious individual over the course of his/her illness.

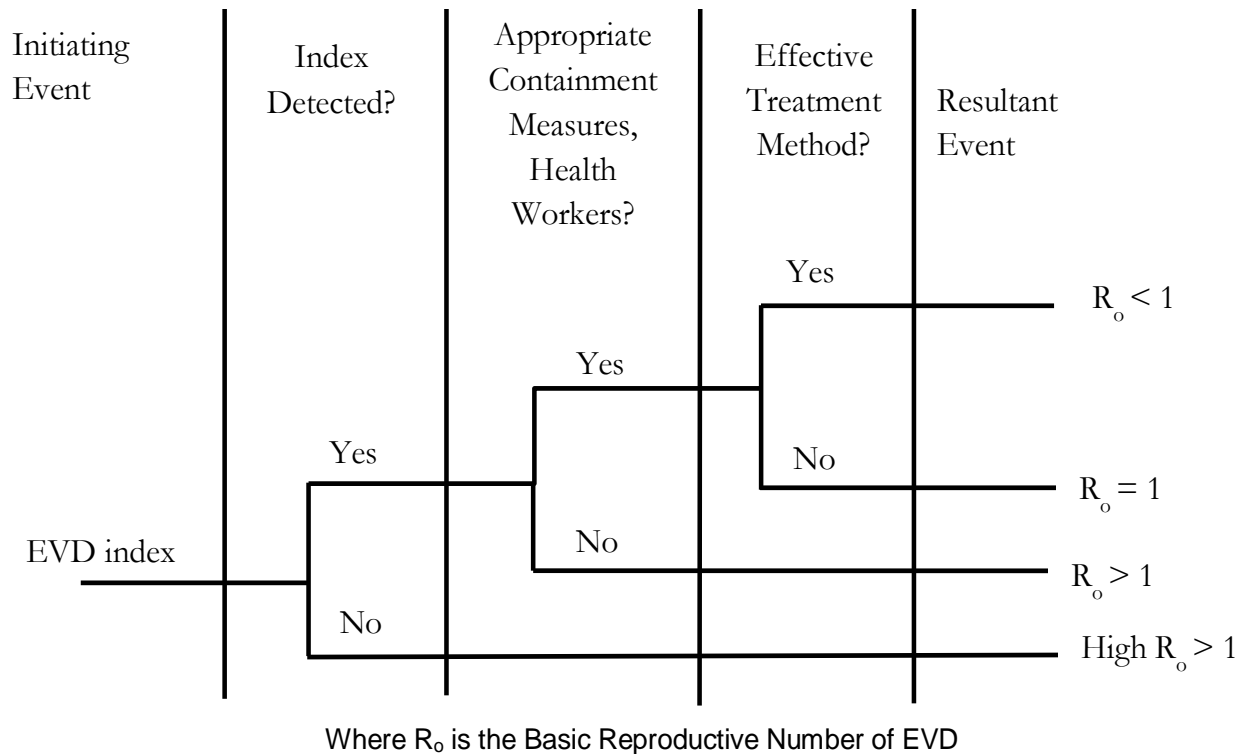


Figure 2. Event tree analysis.

of EVD (Figure 2) (Clemens, 2002).

**What is the cost to the economy?**

The 2014 outbreak in the epicenter countries has enormous fiscal effect, ranging from reduction in revenue, human capital investment to increase in expenditures on treatment, contact tracing and quarantine, and community outreach. The economic impact is also measurable in terms of direct cost of behavioral change that results in restricted mobility, lower supply of labor and income, heightened poverty rate and amplified food insecurity. This behavioral effect has negatively influenced sector of the economy- Mining, Agriculture, Manufacturing and Services. Consequently, World Bank report (WorldBank, 2014) show a significant reduction in Gross Domestic Product (GDP) GDP? in the hard-hit countries. GDP growth in Liberia reduced from 5.9 to 2.2%, Sierra Leone shrink in GDP growth from 11.3 to 4.0% while Guinea had a decrease from 4.5 to 0.5%. With a reduction in revenues, Liberia, Sierra Leone and Guinea have made direct public cost of containing Ebola of US\$62 million, US\$43 million and US\$106 million respectively. This can be compared to their 2013 health expenditure of US\$191 million, US\$584 million and US\$291 million for Liberia, Sierra Leone and Guinea respectively (WHO, 2015). This truly damaged the future growth process. As of July 2015, World Bank has

mobilized US\$1.62 billion to support containment measures- US\$385 million for Liberia, US\$318 million for Sierra Leone and US\$260 million for Guinea (UNDG, 2015).

Thus, at the macroeconomic level, the friable economies of this countries now meets fiscal shortfall as a result of reduction in fiscal revenue and economic activities, and increase in health expenditure. The outbreak exerts damages to the health sector, reducing other healthcare services and depleting trained healthcare work force. In addition, it lessened the feeble minimum health care packages, education and other service sectors, resulting in low human capital development. Post-Ebola recovery plan to re-commence the economy costs US\$1.3 billion for Liberia, US\$1,063 million for Sierra Leone and US\$2.9 billion for Guinea (WorldBank, 2015).

United Nation Development Group (UNDG, 2015) modified Bloom and Mahal's HIV/AIDS economic model to express the economic consequences of EVD (in terms of GDP) as:

$$GDP_t = \alpha + \gamma_1 GDP_{(t-1)} + \gamma_2 GDP_{(t-2)} + \beta X_t + \delta Z_t^j + \varepsilon_t \tag{5}$$

Where:

$GDP$  is the Gross Domestic product per capita;  $\alpha$  is a constant;  $\gamma$  &  $\beta$  are vector of parameters;  $\varepsilon$  is the error each with zero mean;  $\delta$  is the coefficient of  $Z_t^j$ ;  $Z_t^j$  is the

probability of having EVD case;  $J$  is Ebola scenario;  $X$  are variables that determines GDP and  $T$  is the time.

Although there was no significant reduction in GDP growth, Nigerian government spent about US\$13 million for direct cost of containing EVD (WorldBank, 2014). The health sector also had a prick as 4 health workers died from the disease. In addition, behavioral change in the two affected cities led to slight reduction in local business activities.

## CONCLUSION AND RECOMMENDATION

Should Nigeria close its border with affected and high prone countries? On one hand, this might help to protect its citizens from exposure; on the other hand, closing approved borders can result in increased illegal emigrants with less supervision and negative impact on trade-flow. Besides, border closure does not prevent animal migration from highly prone countries. Rather, strengthening the health system to a responsive and efficient healthcare delivery system will contain Ebola spread lest an outbreak. The health system in the epicenter was not prepared for highly virulent viral disease, resulting in average reproductive number of 2.5 (UNDG, 2015).

Nigerian health system indicators are almost similar to Liberia, Sierra Leone, and Guinea (WHO, 2015). An outstanding factor resulting in Nigeria's success in containing EVD is that the index was detected in good secondary health facility in developed urban centers. It is important to consider having and index in rural communities, utilizing PHC facilities. The economic consequence of such outweighs the direct cost of prevention. "The cost of [2014/2015] Ebola response is estimated to be at least US\$4.3 billion.

This is nearly three times the funding gap of US\$1.58 billion needed to provide the minimum package of essential health service for all in Sierra Leone, Guinea and Liberia" and 15 times their annual health budget (STCF, 2015). This demonstrates that investment in health is a direct function of economic growth, "health is wealth", it is substantial to poverty reduction. Strengthening prevention and preparedness plan involves improving epidemiological surveillance, effective alert and referral system in rural PHCs and convalescing supply chain system. Integrating EVD prevention and preparedness courses in the training curricula during capacity building of public health workers will improve standard medical practice during care giving, regardless of patient's presumed diagnosis. Nigeria being in medium risk of EVD outbreak indicates that proper attention should be given to this, for the economic consequences outweighs the direct cost of prevention.

## Conflict of Interests

The authors have not declared any conflict of interests.

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*Full Length Research Paper*

## Engaging currently available tested and proven strategies to tackle Hepatitis B viral epidemic: The HBV-4-Pronged Approach (HBV4PA)

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**Globally, Hepatitis B viral infection is a major epidemic and responsible for one of the commonest cancers in males reference needed because the HBsAg seroprevalence in males slightly higher than females, especially in sub-Saharan Africa. However, although its treatment is available and effective, it is out of the reach of the common person. Many have, because of cost of treatment, succumbed to the chronic effects of HBV infection, such as liver cirrhosis and primary liver cell carcinoma. In this article, we make a case for the provision of free antiviral drugs to all HBV patients by expanding the current HIV services to HBV-infected individuals using the PMTCT model. This, when implemented, will save lives, prevent unnecessary and escalating health expenditure and ensure sustainable development.**

**Key words:** Hepatitis B viral infection, HIV PMTCT, Nigeria, expanding HIV services

### INTRODUCTION

Globally, chronic hepatitis B virus (HBV) infection is a common public health problem and a major risk factor for cirrhosis and liver cancer affecting over two billion people and leading to chronic infection in about 250 to 350 million people worldwide (Ott et al., 2012; Uneke et al., 2005; Utoo, 2014; World Health Organization [WHO], 2015). Age at infection is important in determining the risk of chronic infection as chronicity follows acute infection in over 90% of neonates (particularly babies born to HBV e

antigen-positive mothers not only HBV e antigen-positive mothers but mothers with active infection), 20-60% of children under the age of 5 years, but less than 2-6% when infection occurs in adulthood (Centers for Disease Control and Prevention [CDC], 2015; WHO, 2015).

HBV is the second most frequent known carcinogen after tobacco and in sub-Saharan Africa, HBV-associated liver cancer is the most common cause of death amongst young men and the second most prevalent cancer

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worldwide (Harry et al., 1994; Uneke et al., 2005). In Nigeria, the global burden of cancer in 2013 shows liver cancer to be the commonest cause of cancer death (Naghavi, 2015). HBV infection is also highly endemic in Nigeria as about 75% of the Nigerian population may have been exposed to HBV at one time or the other in their life and an estimated 12% of the total population have chronic carriage of HBV (Owolabi et al., 2014; Sirisena et al., 2002) and is reported to be the most common cause of liver disease (Musa et al., 2015). With high rates of blood transfusion following road traffic accidents, pregnancy and its complications, malaria and sickle cell diseases (in addition to more recognized risk factors, such as intravenous drug usage, unprotected sexual intercourse and poor sterilization of surgical or dental equipment), it is not surprising to see the prevalence of HBV infection over 30% in some regions of the country (Luka et al., 2008; Mbaawuaga et al., 2008).

The epidemic of HBV spares no population, as a study among clergymen who presented themselves for blood donation revealed a positivity rate of 15.1% for HBV and 4.3% for HCV. HIV was found only in 2.7% of the clergy, making it a less important issue of public health concern (Egah, et al., 2007) even this low percentage (2.7%) among a non-risky group should be considered as important issue of public health. Among doctors and dentists, the prevalence was high as active infection was detected in 10/22 (45%) dentists and 19/53 (35.8%) doctors against 5/25 (20%) of local blood donors (Olubuyide et al., 1997). There are also data to suggest that HBV infection is more common in the rural than urban areas (Amazigo and Chime, 1990; Jombo et al., 2004); and also seen among adolescents (Eke et al., 2015).

As HBV is a blood-borne disease, the common drivers of this epidemic are traditional practices like tattooing, vertical transmission from mother to child, sexual practices (both heterosexual and homosexual), occupational exposures, clustering of carriers in families and institutions, behavioral factors, marital status it is not precise that marital status is a common drivers of the disease, and exposure amongst prisoners (Amazigo and Chime, 1990; Ansa et al., 2002; Jombo et al., 2004; Luka et al., 2008). However, studies have shown that HBV transmission in sub-Saharan Africa is mainly through the horizontal route in childhood rather than the perinatal route (Kiire, 1996).

For those millions of people who are chronically infected with a viral load over 2000 IU/mL and/or the presence of hepatic fibrosis, it is also treatable with current pharmaceuticals, such as Tenofovir, a drug that is familiar to many as a treatment for HIV. Although Tenofovir rarely leads to surface antigen seroconversion and virological cure, the viral suppression that it provides may lead to a reduced incidence of complications, such as cirrhosis or liver cancer (Lemoine et al., 2016).

## HIV and HBV infections

Studies have shown that HBV infection commonly co-exist with HIV (Hamza et al., 2013; Uneke et al., 2005). For instance, studies by Uneke and colleagues in Jos Plateau revealed a higher incidence of HBV infection among HIV positive individuals when compared with the general population and blood donors (Uneke et al., 2005). This was collaborated by another study in Kano (Mustapha and Jibrin, 2004). In Uneke et al. (2005). This was corroborated by another study in Kano (Mustapha and Jibrin, 2004). In the study by Uneke and colleagues, although males had a slightly higher sero-prevalence than females (14.6% vs 12.9%), among the HIV subpopulation, males had a significantly higher sero-prevalence (31.8% vs. 22.1% (Uneke et al., 2005)). Apart from HBV, some individuals with HIV also had HCV infection as was demonstrated in North-Central Nigeria (Forbi et al., 2007). Taking a closer look at this, co-infection is critical as HBV negatively affects the ability of antiretroviral drugs to improve CD4 counts in patients (Idoko et al., 2009). Immunization against HBV can improve the prognosis of HIV as well as the efficacy of antiretroviral drugs (Hamza et al., 2013). Left unmanaged, HBV infection impacts negatively on disease progression in HIV-infected children, increasing morbidity and mortality (Nwolisa et al., 2013).

## Current control and prevention strategies in Nigeria

HBV vaccination has recently been added to the routine vaccinations for newborn babies. Although this vaccine is effective, its effectiveness is time-bound as only children vaccinated within the first 24 hours of birth reliably develop an adequate immune response and are able to generate sufficient antibodies (WHO, 2015). But as few pregnant women deliver within the health facilities and majority of the health facilities may not even have the vaccine at the time of delivery, very few children actually have the vaccination during the correct window at birth.

Vaccination against HBV is low in many sub-Saharan African countries (Musa et al., 2015). For instance, the 2013 National Demographic Health Survey reveals that only 19.9% of infants received the HBV vaccine at birth (National Population Commission [NPC] and ICF International, 2013). Similarly, the same study revealed that only 17.3% and 14.7% received the second and third doses respectively. This is similar to the Nigerian national immunization coverage rate for the period, which was less than 25%. It therefore shows that relying on childhood vaccination for HBV infection control and prevention may be beneficial, but definitely not a sufficient approach to eliminating this virus from the population.

Unlike HBV, HIV prevention, care and treatment is well

funded. Patients with HIV have access to free testing, free counselling and free medication. In addition, they are supported to access these services. When HIV-positive individuals cannot access care and treatment due to economic difficulties, they are given financial assistance to help them live a healthier life. However, like HIV, HBV results in debilitating disease and significant end stage problems, such as liver cancer, which is a common cause of cancer deaths in young males in the sub-region (Harry et al., 1994; Yang et al., 2015).

Also HBV is known to be 50-100 times more infectious than the HIV virus (CDC, 2015). Despite the public health hazard of HBV, there is no active drive to ensure either the prevention of HBV infection, as is seen in HIV. With HIV, there are various prevention messages, behavioral change communications, and provision of condoms and other protective equipment to prevent transmission of HIV. Furthermore, while individuals infected with HIV are begged, cajoled and even supported to access care, the majorities of people with HBV infection die in ignorance of what their disease is, or discover the infection very late, or are accidentally informed of their infection during blood drives or premarital screening. There is therefore the need to adopt a new approach to curtail the menace of HBV control or eliminate HBV-associated chronic liver disease. To achieve this, we propose the HBV-4-Pronged Approach (HBV4PA), which is adapted from the PMTCT program.

#### **HBV-4-Pronged Approach (HBV4PA): Adopting the HIV control strategies for HBV infection prevention and control**

HBV affects all age groups, and can be transmitted through sexual contact and by vertical transmission, similar to HIV. Thus, HIV prevention strategies should be up-scaled to prevent HBV infection. Like PMTCT in HIV program, HBV can benefit from the four prongs of PMTCT as defined by the World Health organization:

##### **Primary prevention of HBV infection**

Keeping a woman HBV infection-free before, during and after delivery keeps the infant free of HBV infection. Like HIV, a HBV-negative individual living in a discordant relationship has a risk of becoming HBV-infected unlike a person living in a concordant HBV negative relationship. Detecting discordant couples through couples counselling and testing will help deliver targeted intervention to spouses whose partners are infected. This will reduce the risk of cross infection. Treating discordant couples also reduced the possibility of transmission to the uninfected child.

To prevent primary infection of HBV, counselling and

testing (including couples counselling), disclosure, condom distribution, and also targeted prevention programs for high risk populations, such as female sex workers, injection drug users and male who have sex with men is critical. Women who tested negative in the early part of their pregnancies can also be re-tested later, in the third trimester. These measures are in line with calls for improved efforts to promote routine screening of pregnant women and other subpopulations due to rising HBV prevalence in Nigeria (Hamza et al., 2013). Retesting allows identification of women who seroconvert during pregnancy, delivery, or even in the breastfeeding period. For those pregnant women who do test negative, then the HBV vaccine can be offered as a further primary prevention measure. The availability of rapid diagnostic testing for HBV infection makes testing easier with minimal barriers and delays. Implementing of HBV testing within the health institutions should be encouraged.

Secondly, alcohol risk reduction and biomedical interventions involving the use of routine use of HBV antivirals, such as Tenofovir for infected partners are possible avenues for disease control. This will be most easily up-scaled as the drug and associated services are distributed free to all exposed or infected individuals who HIV and therefore, the infrastructure to extend this to HBV exists. It is worthy of note that Tenofovir is currently free in sub-Saharan Africa for HIV, but not for HBV, costing patients about \$US 8000 per year. Furthermore, treating sexually transmitted infections are essential for primary prevention. Use of male circumcision may also reduce the rate of new infection as is seen in HIV and other sexually transmitted infections – but this need to be further studied and validated (Weiss et al., 2000, 2006).

The risk of perinatal HBV infection among infants born to mothers already infected with HBV ranges from 10%-85%, depending on the mother's hepatitis B e antigen (HBeAg) status. If the mother is positive for both hepatitis B surface antigen (HBsAg) and HBeAg, the risk of perinatal transmission is 70%-90%. By contrast, if the mother is HBsAg-positive, but HBeAg-negative, the risk of perinatal transmission is <10%. A proper birth dose vaccine with full implementation of the three vaccine doses in the first year of life can reduce neonatal infection and the potential sequelae by 95%. So, the use of routine use of HBV antivirals, such as Tenofovir (the drug that cannot cause cure and is costly) for infected partners will not add the needed value.

Thirdly, to prevent primary HBV infection, structural factors that hinder people's access to HBV testing, counselling (testing and counseling should be the first part of the primary prevention or even after the vaccine usage strategy) and drugs should be removed. This can be achieved by making testing and vaccination for negative mothers for HBV infection free, and creating relevant awareness through HBV prevention messages in social and mass media across the nations of the world.

Testing and counselling can be fully integrated into the current HIV testing and counselling drive in line with the UNAIDS 90-90-90 agenda. Drugs for HBV (Tenofovir) could be provided with ARTs in supported service delivery points. Integrating HBV services in HIV programs will be most appropriate as both diseases have a lot in common, including common treatments. An additional benefit is that it is cost effective, will not require new human resources for health, will utilize already existing structures, and if well managed, be quickly taken over by national health leaders.

### ***Preventing unintended pregnancies among HBV infected women***

To further prevent the impact, incidence and prevalence of HBV infection, there is the need to reduce unintended pregnancies among women infected with HBV. This will lead to a reduction in the number of infants born to HBV-infected mothers, and thus reduce the number of HBV-exposed infants. As family planning is critical towards the achievement of this goal, and family planning is a severely unmet need in Africa, coupling HBV with HIV will give the world another vital reason to drive improvement in access, availability and even affordability of family planning services and consumables across Africa and beyond. The use of protective equipment such as condoms for family planning will serve dual purposes – preventing pregnancies with a collateral advantage of preventing new infections in discordant couples.

To address this unmet need for family planning, governments should implement the modified United Nations Population Fund (UNFPA) recommendations of linking sexual and reproductive health with HBV interventions at the policy, systems and service-delivery levels; engaging communities, getting more men involved, engaging organizations of people living with HBV (where they exist), and ensuring the provision of nondiscriminatory services in stigma-free settings (UNFPA, 2012). Applying these steps will result in commonization of HBV services and its full integration into the healthcare delivery model in any country.

### ***Preventing HBV Infection from HB- infected pregnant women to their children***

To ensure a HBV-free generation, all pregnant women should be granted access to HBV testing and counseling (HbTC) during antenatal services; and all those that have HBV infection granted access to anti-HBV medications and supportive care. During labour, every effort should be made to prevent transmission of the virus to the newborn baby. This could be achieved through safe obstetric practices, judicious use of cesarean sections when appropriate and provision of intra- and immediate

postpartum HBV medication (which medication could be used to prevent the postpartum transmission of the virus), and hyper-immune globulin/vaccines to the newborns. Vigilance in preventing HBV infection from HBV-infected pregnant women to their children should continue for at least the first year. Infected mothers should be followed-up and supported, counselled on child nutrition and care, and encouraged to use appropriate anti-HBV medications, while their babies receive all three vaccine doses in the first year of life. Also, early infant diagnosis for exposed babies should be developed and implemented. Breastfeeding mothers (Examination of relevant studies indicates that there is no evidence that breastfeeding poses any additional risk to infants of HBV carrier mothers) should be provided with appropriate HBV antivirals, and infants with confirmed HBV-infection should be given appropriate medications as 90% of them will go on to develop chronic infection. Even after breastfeeding, infected mothers should continue their medication until such times as they seroconvert, but being mindful of the fact that treatment for many is life-long.

In this prong, the strategy for use HBIG and the vaccination for the infant should be added and explained.

### ***Care, treatment, and support to women living with HBV, their children and families***

This is the fourth prong and it is designed to provide adequate care, treatment and support services for people living with HBV, their children and families. This will result in lower morbidity and mortality, improved overall health and quality of life of HBV positive individuals, and reduced rate of transmission. Furthermore, starting HBV antivirals early will result in better outcomes and lower risk of chronic liver diseases. Hepatitis B immunoglobulins (HBIG) will also be helpful in the management of infected patients with high viral loads. Exposed but uninfected infants should be vaccinated.

This HBV4PA plan provides a comprehensive approach to HBV prevention, treatment and control. HBV service provision can make use of the already existing HIV structures to reach millions of people who need services within a short time.

For instance, the ongoing HTC saturation drive could be up-scaled to include Rapid Diagnostic Test (RDT) for HBV. It would use the same healthcare workers, facilities, non-governmental associations and community contacts as HIV with little impact for further resource allocation.

As most studies referenced in this report are facility-based figures, testing both males and women within their communities will help document community prevalence rate of HBV. This would be compared with HIV prevalence within the same communities. Also, the prevalence of co-infection (HIV and HBV) should be

documented. Infected persons would then be linked to care, treatment and support; while the pregnant women would be provided with relevant services to ensure that the unborn child is adequately protected.

Children born to HBV-infected women with high viral loads should receive the same attention given to HIV-exposed babies and their HBV vaccine and HBIG should be given on the same day of birth. EID using DBS could be used to make early diagnosis. Thus samples collected for HIV-exposed babies should also be tested for HBV if parents were co-infected. Samples from exposed infants should also be collected for analysis at 18 months when maternal antigens capacity to produce false positive results has significantly reduced.

Riding on the success of HIV, services can be provided that covers all aspects of HBV infection at very minimal extra cost to the system.

## Conclusion

Although there is a global decline in HBV infection prevalence which may be related to expanded immunization, this is not the case in Nigeria where there is an increasing overall number of individuals chronically infected with HBV (Amazigo and Chime, 1990). This widespread global difference in HBV prevalence calls for targeted approaches to tackle HBV-related mortality and morbidity (Finlayson et al., 1999).

While, HBV infection prevalence data are needed at country and sub-national level to estimate disease burden and guide health and vaccine policy, upscaling current HIV programs to include HBV is possible and making the anti-retroviral drug, Tenofovir, which is already in free circulation for HIV, free for the treatment of HBV will drastically reduce both mortality and morbidity of this disease. Governments, the WHO and the World Bank would however, have to ask the manufacturers to expand their coverage beyond HIV.

This strategy to be successful, it should be implemented in all health care institutions and even governmental or non-governmental organizations.

Furthermore, HBV services – testing, care and treatment could be integrated into hospital services. There is no moral justification for free HIV services while HBV services remain fully-paid and unsubsidised. We believe that the time to change all this is now. Let the change begin with provision of free Tenofovir for all HBV patients who require it. This strategy has been shown in recent studies to be an effective HBV control intervention (Lemoine et al, 2016)..

## Conflict of Interests

The authors have not declared any conflict of interests.

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## Full Length Research Paper

## Prevalence of intestinal parasites of the human population in the City of Pombal-PB, Brazil

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The intestinal parasitic diseases caused by protozoa and helminths are infestations that may trigger changes in the physical, psychosomatic and social state of patients, directly interfering with their quality of life. The aim of this study is to determine the major intestinal parasites causing diseases that are distributed in the City of Pombal-PB, either in endemic or epidemic form, and to observe the incidence/prevalence and factors that favor the proliferation of these parasites so that they can be diagnosed, controlled or treated. The study was developed by quantitative method. The data were collected from sample collection made in the Diagnosis Health Unit Laboratory of Dr. Avelino Elias Queiroga in the City of Pombal-PB. They were stored in medical records used in internal control from January 2012 to December 2013. From a total of 3,144 surveys analyzed, 29% had parasites (*Endolimax nana* the most common protozoan with 35.72% and *Hymenolepis nana* with 0.29% among helminthes). Among the results of positive tests for parasites, 8% had poliparasitose frame, 53% had monoparasitose and 39% had biparasitose. The results of this study demonstrate the need for the population to be aware of the importance of diagnosis, treatment and follow-up of positive cases.

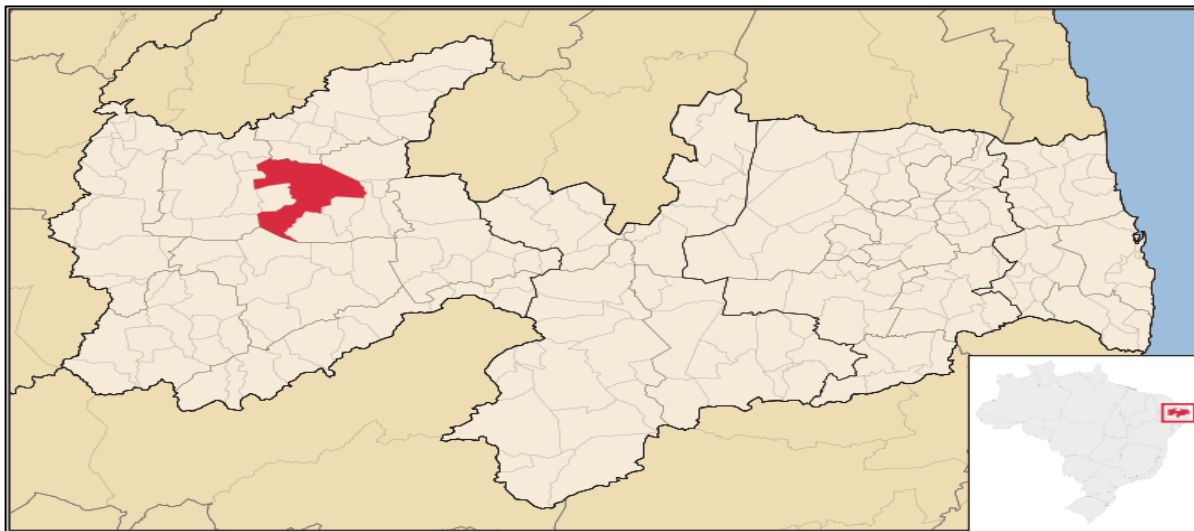
**Key words:** Intestinal parasitosis, prevalence, helminths, protozoa.

### INTRODUCTION

The incidence of intestinal parasites is a serious public health problem worldwide (Mamus et al., 2008). In Brazil, these diseases occur in different regions of the country, whether in rural or urban areas and in different age groups (Monteiro et al., 2009; Fonseca et al., 2010). These conditions correlate with lower socioeconomic

status and poor sanitation conditions, representing a scourge, particularly for the poorest populations (Grillo et al., 2000). The parasite (an aggressive agent) and the host (shelter and food source) establish an association where only the first one benefits while the other is always impaired (Neves, 2000). Parasitism is a reflection of the

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**Figure 1.** Location of the city of Pombal in the state of Paraíba.

host-parasite fight, which depends on the result of forces at work, the parasite mechanisms of aggression and host defense (Cimerman, and Cimerman, 2001). These parasites are part of life and thus need to be known vastly, not only in terms of environmental and socially (Neves, 2011). The intestinal parasitic diseases caused by protozoa and helminths affect children from lower social classes, and those with poor sanitary conditions and malnutrition; they also affect kindergartens, schools, nursing homes and orphanages, with ease of contamination and dissemination (Zaiden et al., 2008).

The transmission of parasitic diseases is generally oro-fecal, that is, by ingestion of helminth eggs and cysts of protozoa present in food, water or even in some contaminated object with feces, or ingestion of these forms through dirty hands or fecal waste. Asymptomatic individuals, who are in direct contact with food, may become potential source of contamination of various pathogens, especially enteroparasites (Roberts, 2005). Intestinal parasites can cause a lot of harm to their sufferers. The most common clinical manifestations caused by intestinal parasites in the host, are diarrhea, gastrointestinal bleeding, anemia, weight loss, abdominal pain, anxiety, nervousness, restlessness and, in critical situations, death (de Souza Abraham et al., 2007). Although intestinal parasites are ignored, it is necessary to implement measures to reduce the number of infected individuals, measures that are able to stop the transmission mechanisms. For this to occur, it is crucial to know the prevalent species of each site. The combination of these measures enables a possible improvement of the population's living conditions, thus reducing the progression to more severe disease (Goia, 2007). Thus, the present study aims to determine the main intestinal parasites causing diseases that are

distributed in the City of Pombal-PB, either in endemic or epidemic form, and to observe the incidence/prevalence and factors that favor the proliferation of these parasites so that they can be diagnosed, controlled or treated.

## MATERIALS AND METHODS

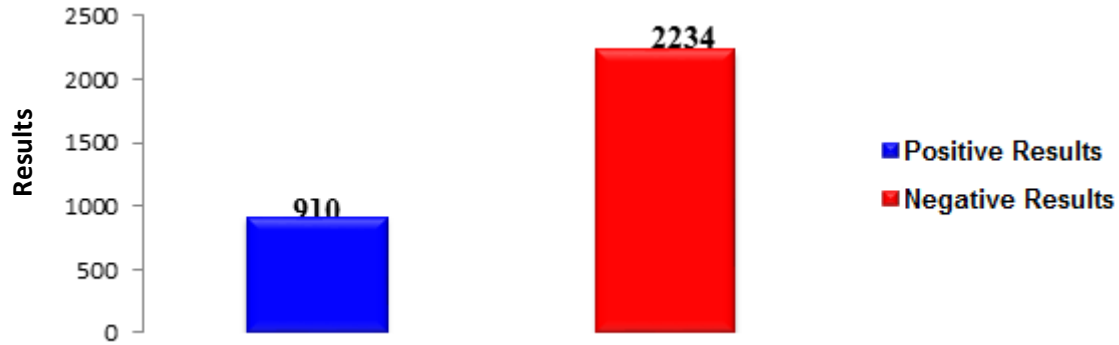
### Study area

The study was conducted in the City of Pombal, Paraíba (Figure 1), located in the Western region of the state of Paraíba, mesoregion Hinterland and Microregion Sousa; it is about 371 km from the capital, João Pessoa. The annual average temperature is 27°C, with monthly averages varying from each other a bit. It is one of the oldest and second largest in the state with 889 km<sup>2</sup>. It has an annual growth rate of 1.86%, has the 15th highest HDI of Paraíba, and life expectancy in the city is on average 66.2 years. Its population is over 33,000 inhabitants (IBGE, 2010). The health facilities in the City of Pombal-PB are 90% municipal, 10% private and there is no presence of state and federal health agencies. It has a regional hospital, Polyclinic Dr. Avelino Elias Queiroga and Emergency Unit that work for 24 h (UPA). Sanitary sewage project of Pombal is composed of several stages, due to the volume of service and high cost of the work, because the proposal is to meet the entire urban area. Running the first and second stages of the sewage entails the following: household connections: 6.775 m; catch network: 11.305, 26 m; collection station and discharge outfall network: 3.850 m; treatment station and final emissary: 1.864 m.

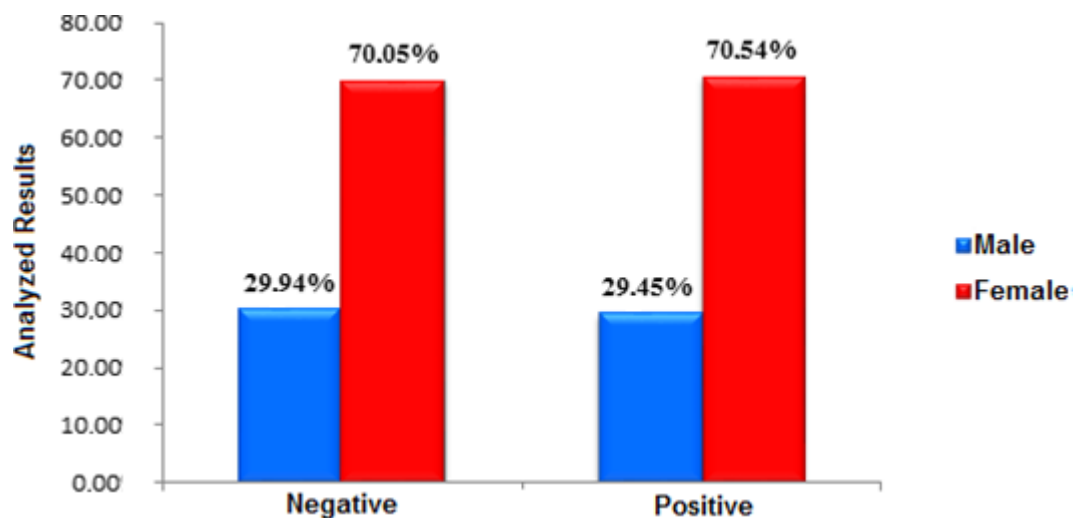
### Data collection

This study was developed by quantitative method. Data were collected from sample collection in the Health Unit of Laboratory Diagnosis, Dr. Avelino Queiroga of the City of Pombal-PB. They were stored in medical records used in internal control from January 2012 to December 2013. The method used for diagnosis of the samples was Hoffman; it was used for the detection of cysts, oocysts, eggs and larvae. It is a spontaneous sedimentation in





**Figure 2.** Results of the examinations of intestinal parasites in the period 2012-2013, in Pombal-PB.



**Figure 3.** Percentual of intestinal parasites in relation to the sex of the host, from January 2012 to December 2013.

water and is suitable for the recovery of heavy eggs considered as *Taenia* species, *Schistosoma mansoni* and eggs of *Ascaris lumbricoides* (Neves, 2011).

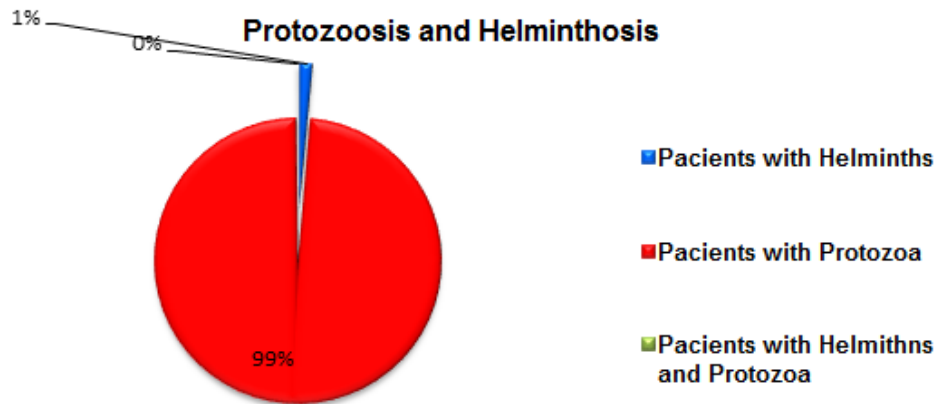
The data were separated into positive and negative, and then the parasites and their frequency were analyzed in the results. They were separated based on the gender of the patient. Microsoft Excel for database assembly was used, and the data collected were analyzed. Statistical analysis was done quantitatively and qualitatively, which led to the justifications of the data obtained. The project was submitted to Brazil Platform, where the development of the research did not go against Article 196/96 on research ethics code with humans.

## RESULTS

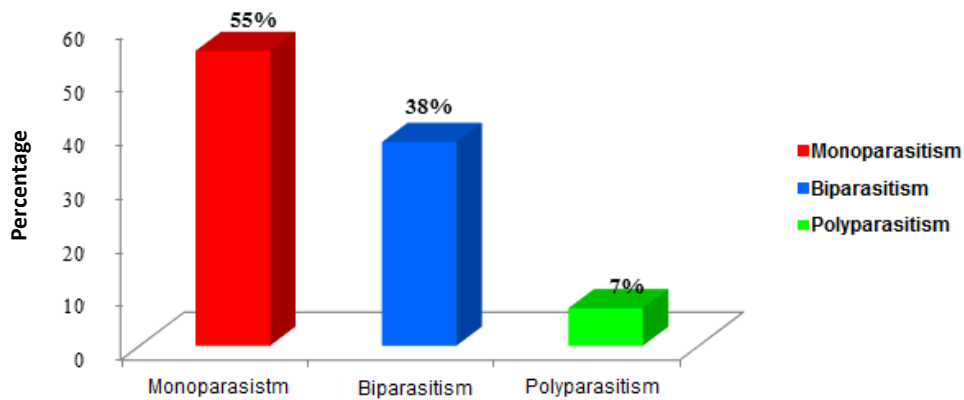
Three thousand one hundred and forty-four (3,144) results of parasitological examinations of stools (EPF) were analyzed from January 2012 to December 2013 in the City of Pombal-PB. Of the 3,144 results analyzed, 29% was positive for intestinal parasites and 71% was

negative (Figure 2). The data (Figure 3) show that the prevalence of intestinal parasites in the blood tests based on gender was predominant for females, both negative (70.05%) and positive (70.54%). Then, it appears that there is a real difference between the genders of the patients seen at Polyclinic Dr. Avelino de Queiroga in the City of Pombal-PB. According to the 910 positive results (Figure 4), 1% of patients had intestinal helminth infections; 99% showed only the presence of protozoa. Regarding infections, the data show that monoparasitose prevailed in the cases of patients studied (55%) compared to the others. While biparasitose and polyparasitose had 38 and 7% of parasites present in the tests studied (Figure 5).

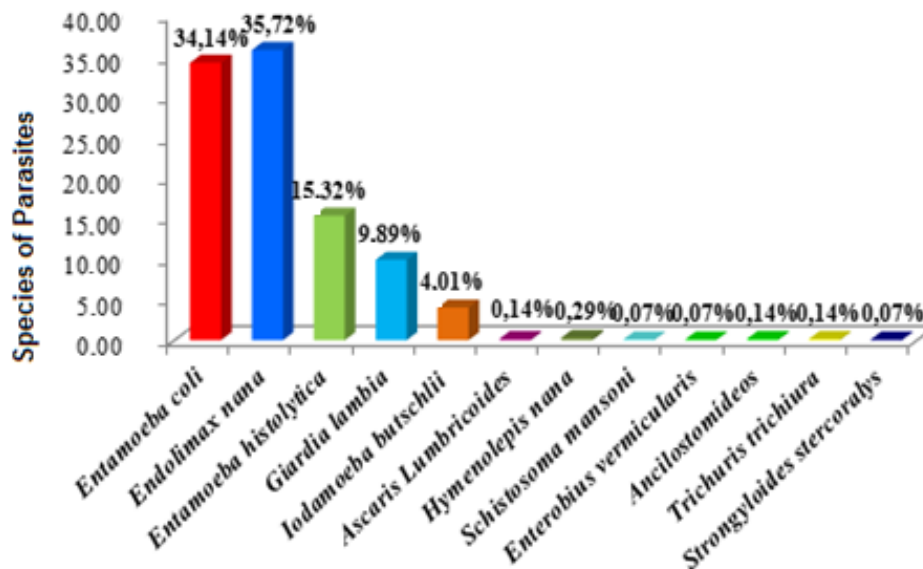
Figure 6 shows the frequencies of each species found. One can analyze the images of the types of parasites found in the studied population; they are in the form of eggs for helminth and protozoan cysts (Figure 7). The sum of the frequencies was 100% due to cases of multiple



**Figure 4.** Distribution of protozoa and helminths found in infected patients and parasitic association in the same individuals, performed between January 2012 to December

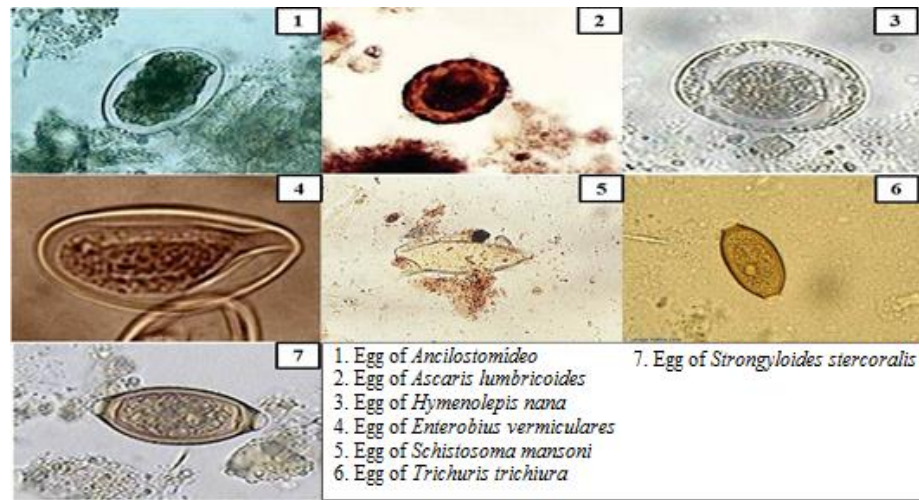


**Figure 5.** Characterization of helminths and protozoa of individuals in the study.

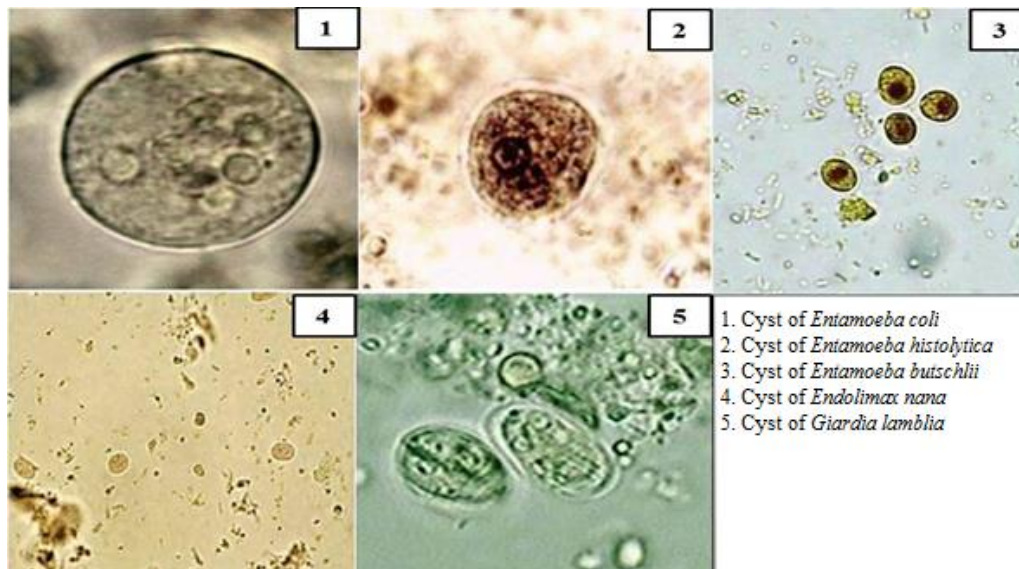


**Figure 6.** Distribution of species of parasites, from January 2012 to December 2013.

### HELMINTHS



### PROTOZOA



**Figure 7.** Images of helminth eggs and protozoan cysts found in the population studied.

parasitic infections. Among the species of intestinal parasites found in the examination of fecal samples of surveyed individuals, protozoa (*Endolimax nana* (35.72%) and *Entamoeba coli* (34.14%)) were more frequent than helminths. Among the helminths, *Hymenolepis nana* was the most frequent (0.29%). Comparing the years, it appears that 2012 was predominantly used for test than 2013 (Figure 8). The data showed that in 2012, the results of the positive and negative tests were higher compared to that of year 2013. In Figure 9, we can see that when comparing 2012 and 2013 years studied, monoparasitose had higher percentage in 2013 than in 2012, with a value of 57%. Both biparasitose (39%) and poliparasitose (8%) had higher percentages in 2012.

Figure 10 shows the comparison of sex of individuals in 2012 and 2013. In 2012, males (58%) had higher percentage than females, while in 2013, females (44%) had higher one than males. Figure 11 shows the comparison of intestinal parasites separated by year, noting that all parasitic species were higher in 2012.

### DISCUSSION

In the development of this work, it was found that these parasites over the years continue to be an important disease in the country, affecting individuals of all genders and ages. The highest percentages of prevalence of

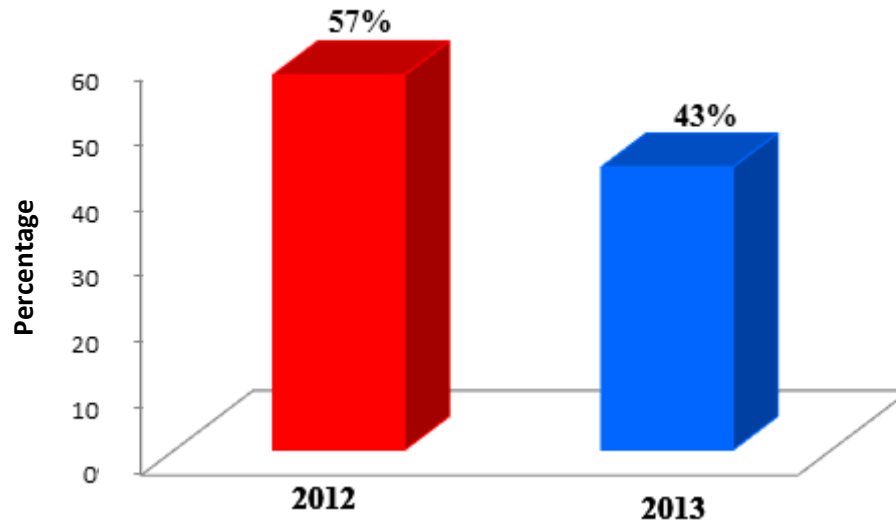


Figure 8. Comparison tests performed annually.

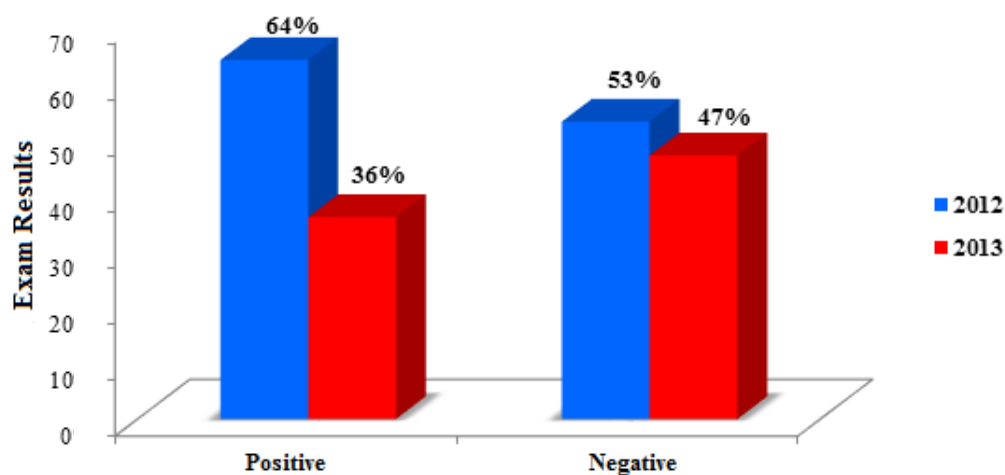


Figure 9. Comparison of test results analyzed positive and negative per year.

intestinal parasites were observed in female individuals (70%), thereby detecting differences between the genders of individuals treated at Polyclinic Dr. Avelino Elias Queiroga in the City of Pombal-PB. According to Gomes et al. (2007), the discrepancy in demand for health services related to gender shows that women seek access to basic care more than men. Thus, this high prevalence is evident among women, observing that men use primary health care services less. This seems to occur because the culture of the society reaffirms the belief that man does not need prophylaxis and care (Costa et al., 2012). Gomes et al. (2007) showed that men are more affected by chronic diseases and often severe compared to women. The mortality rate for the same situations is greater. Even with these significant data, it is observed that men attend less of primary health

care services, this seems to occur because the culture of the society reaffirms the belief that man does not need prophylaxis and care (Menezes, 2013).

From the data analyzed in this study, the prevalence of protozoal infections (99%) was higher than that of helminths (1%) in infected individuals; and the same prevalence of parasites was found in the study of Amorim et al. (2013), where protozoan infections were more frequent (32.7%) than helminths (5.4%). The prevalence rates found for protozoa are as follows: *Endolimax nana* (35.72%), *Entamoeba coli* (34.14%), *Entamoeba histolytica* (15.32%), *Giardia lamblia* (9.89%), *Iodamoeba butschlii* (4.01%). For intestinal helminths, the following prevalence was found: *Hymenolepis nana* (0.29%), *Ascaris lumbricoides* (0.14%), *Trichuris trichiura* (0.14%), *Enterobius vermicularis* (0.07%), *Schistosoma mansoni*

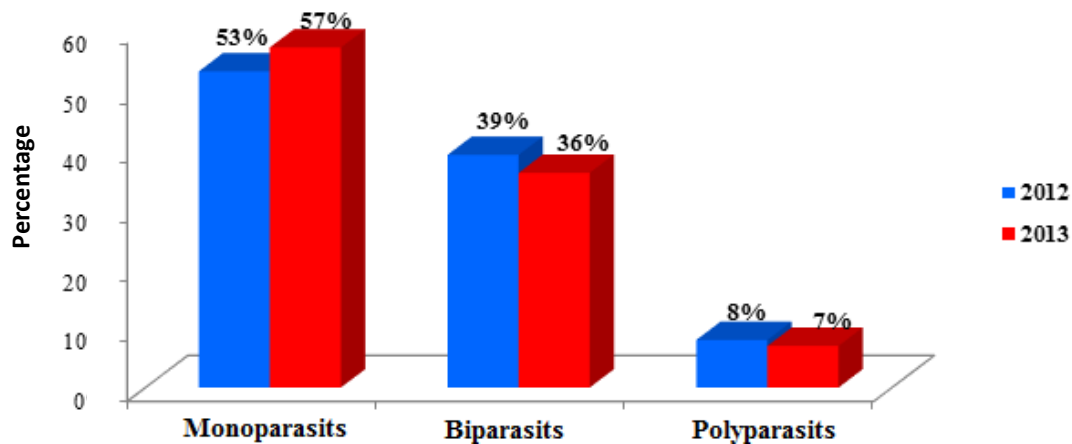


Figure 10. Comparison of test results analyzed positive and negative per year.

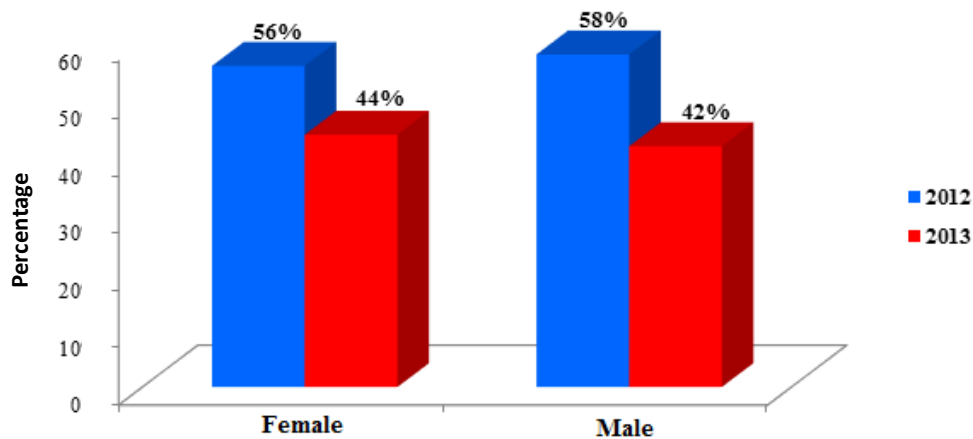


Figure 11. Comparison of gender over the years.

(0.07%) and *Ancilostomídeos* (0.07%), *Ancylostoma duodenale* (0.07%) and *Strongyloides stercoralis* (0.07%). Regarding the characterization of intestinal parasites, the data analyzed show that monoparasitose prevails in the cases of patients studied (Figure 5). The occurrence of individuals presenting monoparasitose, biparasitose and polyparasitose in epidemiological studies is common because of the spread of these intestinal parasites and the ease with which they are transmitted (Armengol et al., 1997). Considering that the forms of transmission of these parasites occur particularly through contaminated water and food, it is fundamental to do a reassessment of the current frame of parasitosis, seeking to identify the causes and sources of contamination (Armengol et al., 1997). In 2012, there was a higher prevalence of positive tests for some kinds of parasites (Figure 10). This is due to greater realization of tests in this year; in 2013, there was a reduction in these examinations due to demand from individuals. It can also be included in this study, that

2012 was where all the parasitic species were higher than the year 2013 (Figure 12).

## Conclusion

Despite the fact that the prevalence values are lower than those of other studies, these data are worrying. It is noticed that the positivity of the tests are due to lack of personal hygiene, sanitation and not knowing clearly the vermin that causes contamination. Given the results, it is clear that there is the need to implement public policies for sanitation, education and health of the population to control the intestinal parasites.

## Conflict of interests

The authors have not declared any conflict of interests.

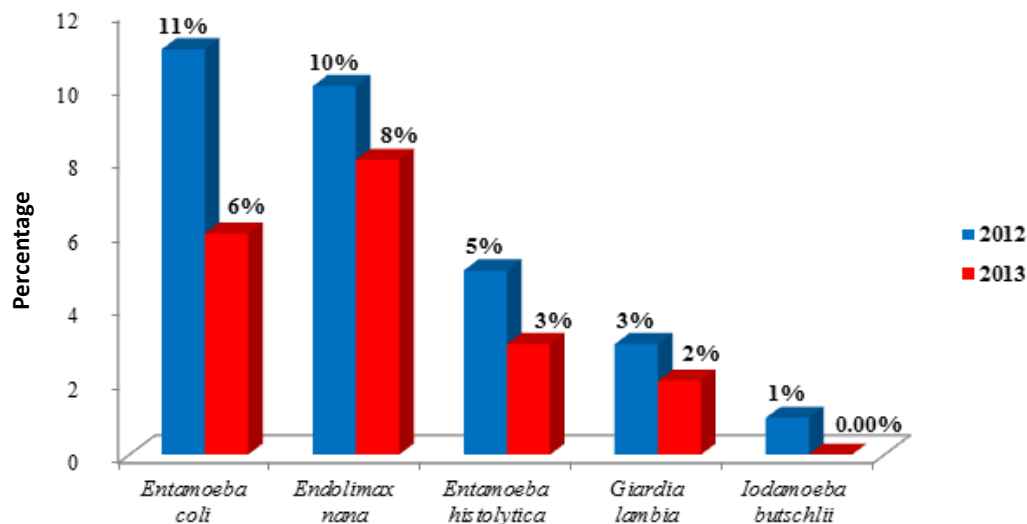


Figure 12. Comparison of the parasitic species separated by year.

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*Full Length Research Paper*

# Sensitivity analysis of the economic burden using social insurance claim data

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The study is aimed at examining changes in economic burden in comparison with figures cited in previous studies. Data from South Korea's National Health Insurance claims database are used to measure the economic burden of chronic disease. Both direct and indirect costs are considered. Direct costs are those associated directly with treatment, medication, and transportation, and indirect costs are assessed in terms of the loss of productivity and their caregivers and consist of morbidity and mortality costs. We also undertake sensitivity analysis, wherein we extract incidence cases and categorize them in terms of their frequency of hospital visits (from one time to five times). The total economic burden posed by chronic disease in South Korea in 2010 was found to be approximately 3.7 million USD; indirect costs and direct medical costs accounted for most of the economic burden, although the rates of these varied from disease to disease. In a comparison of disability-adjusted life years values and the economic burden of diseases, diseases varied widely in terms of their burden. The findings of this study can be used to inform policymakers as they establish public health policies that address various disease burden indexes.

**Key words:** Chronic illness, economic analysis, measurement.

## INTRODUCTION

As of 2010, worldwide, chronic diseases such as cardiovascular disease, cancer, chronic respiratory disease, and diabetes accounted for 60% of all deaths worldwide (35 million), and 80% or more of all deaths in developing and underdeveloped countries (WHO, 2005). It is also estimated that in 2015, 41 million people will die of chronic disease without having received preventive care or treatment (Strong et al., 2005). For this reason, the management of chronic diseases is important to maintaining stability and solidarity within the whole of society, in addition to improving personal health

conditions. With the general increase in life expectancy and aging in society, the presence of chronic disease may indeed extend the period of medical service and create quality-of-life problems.

In terms of worldwide research activities, in line with the "Global Burden of Disease" (GBD) of 1990, the use of the disability-adjusted life years (DALY) metric to assess quantitatively the risk inherent in chronic diseases and thus better understand the severity of various chronic diseases, has proliferated. The World Health Organization (WHO) developed a GBD research

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methodology and proposed its use to measure disease burden. The ensuing indexes include DALY, health-adjusted life years (HeaLY), disability-free life expectancy (DFLE), health-adjusted life expectancy (HALE), and disability-adjusted life expectancy (DALE) (Murray et al., 2000).

These indexes are used in the literature to assess in a country-specific manner the burdens related to all chronic diseases (Strong et al., 2005), as well as income-specific disease burdens (Abegunde et al., 2007). However, these studies feature low levels of precision, since they undertake DALY assessments while using data from unidentifiable sources; as a result, the estimated values are not based on accurate epidemiological data of the country in question.

In South Korea, DALY measurements have been undertaken of single diseases, such as dementia (Park et al., 2013), cancers (Cho et al., 2013), and stroke (Hong et al., 2011); disease burden has also been assessed in terms of risk factors, such as high levels of alcohol consumption (Lee et al., 2005). The majority of the studies had reliable results, because they actively excluded estimated values on the basis of insurance claim data, used domestic data, and worked to reflect actual health conditions; nonetheless, they failed to grasp the severity of chronic disease in terms of the burden it poses.

With an eye to mitigating the aforementioned limitations, the present study measures disease burden in terms of demographic characteristics; it also assesses the severity of various diseases, in consideration of the number of deaths caused by chronic disease over a certain period. This study also considers the periods of struggle against disease, by determining the average morbidity periods. This study examines results vis-à-vis the disease burden that South Koreans faced in 2010 on account of chronic disease, and compares its results to those of previous studies.

## METHODS

### Definition of "chronic disease"

The WHO defines "chronic disease" as a disease of a long duration, where impairment is permanent and irreversible, and where special training for rehabilitation is required; additionally, there is a need for long-term investigation or care. Here, we additionally describe a chronic disease as a "non communicable disease"; this is in line with the WHO's GBD project definition (WHO, 2005).

### Data source

This study estimates the economic burden of chronic disease, using a prevalence-based approach that features a societal perspective. Claim data for in and outpatients, as drawn from the database of the National Health Insurance Corporation (NHIC) of South Korea, were used to collect information about chronic disease cases. Under the operational definition of "chronic disease" were cases who claimed from the NHIC for having a non-communicable

disease, in line with the GBD projects in the International Classification of Disease (10<sup>th</sup> version), as a primary or secondary diagnosis in 2010, either more than three times on an outpatient basis or once as an admission case.

### Prevalence

This study measures the economic burden of chronic disease by using a prevalence approach. The proposed prices were estimated in U.S. dollars (USD) (with USD1 = 1,104.76 South Korean won [KRW]) by applying the average 2010 exchange rate of the Korea Exchange Bank. For outpatient visiting frequency, given concerns regarding code validity (e.g., the sometimes-incorrect recording of disease codes), we considered the test unreliable. We therefore calculated how many of the same subjects used medical institutions on account of having a given disease over 2010; the economic burden of that chronic disease was calculated by adding together the medical costs during that year for outpatient cases with more than three clinic visits and for inpatients admitted once.

### Cost

South Korea has a single-insurer system, and 97% of its population is enrolled with the NHIC. Thus, it is rational to assume that data about spending and medical expenses that were derived from the NHIC database would be representative of the country's population. Since claim data from the NHIC do not consider non-covered service costs, transportation expenses, guardian expenses, and the like, but rather include only insurance-covered costs, it was difficult to estimate the total costs. This study uses South Korean health panel data to compensate for this limitation.

To calculate the socioeconomic burden of chronic disease, we classified costs as direct or indirect costs. Direct costs relate to treating disease; furthermore, they include direct medical care costs and direct nonmedical care costs. Direct medical care costs are covered by a variety of payers, including insurers and patients, and include non-covered care costs and pharmaceutical costs. To estimate non-covered care costs, we consulted the results of the NHIC's "Out of pocket expenses research"-data about the ratio of non-covered care costs to all costs. Pharmaceutical costs were estimated on the basis of the outpatient pharmaceutical cost rate of 56.13%, which is drawn from the annual statistics of the NHIC (HIRI, 2013). For sensitivity analysis, we adjusted the pharmaceutical cost rate by 80 to 120%.

The annual direct health care cost can be calculated as follows:

$$\text{Annual direct health care cost} = \sum_{m=1}^{12} DHC_m$$

$$DHC = \left[ IC_m + \frac{(IC_m \times NBR_i)}{(1 - NBR_i)} + IPC_m \right] + \left[ OC_m + \frac{(OC_m \times NBR_o)}{(1 - NBR_o)} + OPC_m \right] + RC_m$$

Where, DHC = direct health care cost; IC = inpatient cost; NBR<sub>i</sub> = non-covered rate of inpatients; IPC = inpatient pharmaceutical cost; OC = outpatient cost; NBR<sub>o</sub> = non-covered rate of outpatients; OPC = outpatient pharmaceutical cost, and RC = rehabilitation aid cost

Direct nonmedical costs comprise transportation costs incurred while visiting hospitals; they also include those incurred by guardians. We calculated the transportation cost by determining the number of hospitalizations and the days of visiting outpatient clinics, both of which were drawn from 2010 NHIC data, and multiplying it by per-trip transportation cost. South Korea health panel data from



2010 were used to determine the cost of round-trip transportation, as follows.

To calculate an outpatient's transportation cost, we used USD0.70, the cost of a one-way fare to visit a clinic. The transportation cost for an inpatient was therefore USD6.90 (including guardian) multiplied by 2 (that is, a round trip). We defined all patients aged 0 to 19 years, or 60 years or over, as requiring the assistance of a caregiver, and so for these individuals, transportations costs for two people were calculated.

South Korea has a culture where, rather than use the services of paid health care assistants, patients tend to be nursed by 20 to 60-year-old women within their family; alternatively, patients have relatives who act as guardians. The guardian costs were therefore

calculated by multiplying the total number of days of hospitalization by USD 51.40, the average daily wage among 20 to 50-year-old women in South Korea in 2009. However, since this caregiver cost was calculated for use with 2010 data, we needed to adjust the wage through the use of a price index. The caregiver expense was in this way found to be USD104.60, in 2010 dollars. For outpatients, we assumed that those aged 0 to 19 years or 60 years or older would be accompanied by a caregiver, and as with inpatients, we calculated the average caregiver wage per day in 2010 dollars. We assumed that the time taken to visit a clinic constituted one-third of the working hours in a day.

The annual direct non health care cost can be calculated as follows:

$$\text{Annual direct non - healthcare cost} = \sum_{m=1}^{12} NHC_m$$

$$NHC = \sum_{ag=0}^9 TFi \times Fi, ag \times 2 \times 2 + \sum_{ag=0}^1 TFo \times Fo, ag \times 2 \times 2 + \sum_{ag=6}^9 TFo \times Fo, ag \times 2 \times 2 + \sum_{ag=2}^5 TFo \times Fo, ag \times 2$$

$$+ \sum_{ag=0}^9 WC \times Fi, ag \times \frac{I_{2010}}{2009} + \sum_{ag=0}^1 WC \times Fo, ag \times \frac{I_{2010}}{2009} \times \frac{1}{3} + \sum_{ag=6}^9 WC \times Fo, ag \times \frac{I_{2010}}{2009} \times \frac{1}{3}$$

Where, NHC = direct non health care cost; TFi = one-way transportation fee for inpatient; Fi, ag = frequency of inpatients per age group; TFo = one-way transportation fee for outpatient, Fo, ag = frequency of outpatients per age group; WC = wage of caregivers and  $I_{2010/2009}$  = price index for 2010, as per 2009 values. The indirect cost consisted of the cost of lost productivity and the cost of premature death; it was calculated through the use of the human resource approach( Kim et al., 2013). To calculate the cost of lost productivity, in the case of inpatients, we multiplied the number of days of hospitalization by the average wage per day.

Since we assumed that patients aged 0 to 19 years or 70 years or older do not participate in financially productivity activities, the cost due to lost productivity was calculated only for those aged 20 to 69 years. Statistics from the Ministry of Labor were used to estimate the average wage per day and the average working hours by age group. The opportunity cost related to visiting a clinic was estimated by multiplying the average number of visiting hours by the number of days visited. The average number of hours per outpatient was calculated as one-third of the working hours per day, including both transportation and actual visit time.

$$\text{Annual indirect Cost} = \sum_{m=1}^{12} IDC_m$$

$$IDC = \sum_{ag=2}^6 (AWag \times Fi, ag) + \sum_{ag=2}^6 (AWag \times Fo, ag \times \frac{1}{3}) + \sum_{ag=0}^6 (PAWag \times Fd, ag)$$

Where IDC = indirect cost; AWag = average wage of a certain age group; Fi, ag = frequency of inpatients per age group; Fo, ag = frequency of outpatients per age group; PAWag = present value of averaged wage on a certain age group and Fd, ag = frequency of deceased people per age group

Table 1 provides detailed information regarding the variables used in the current study.

The cost of premature death was estimated by cause of death, as reported by the National Statistical Office. Future incomes were discounted by 0.05 per year, to create a present value; these values were calculated until the age of 65 years. The annual indirect cost can be calculated as follows:

**RESULTS**

Figure 1 lists our findings vis-à-vis disease-specific economic burden, in terms of item-specific expenses. The total economic burden generated by chronic disease in

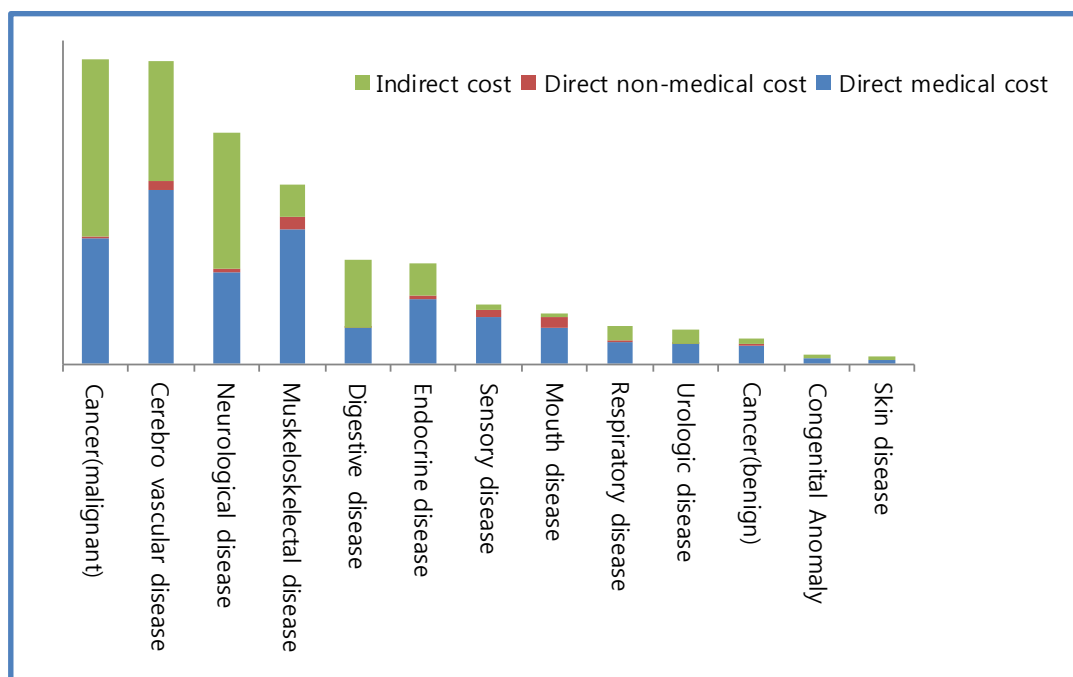
South Korea in 2010 was found to be approximately 3.7 million USD.

The cost of hospitalization and outpatient treatment accounted for the greatest proportion of direct medical costs, followed by pharmaceutical costs; rankings, however, differed from disease to disease. Premature death costs accounted for the greatest proportion of indirect costs among malignant tumors, cardio-cerebrovascular diseases, and digestive diseases, while among neurological diseases, nursing costs exceeded premature death costs (Figure 2).

When we compared the socioeconomic disease burden values to DALY values (Kim et al., 2013), we found that gastric and liver cancers, both of which had low DALY values, had relatively low socioeconomic disease burdens, while stroke and osteoarthritis had relatively larger socioeconomic disease burdens (Figure 3).

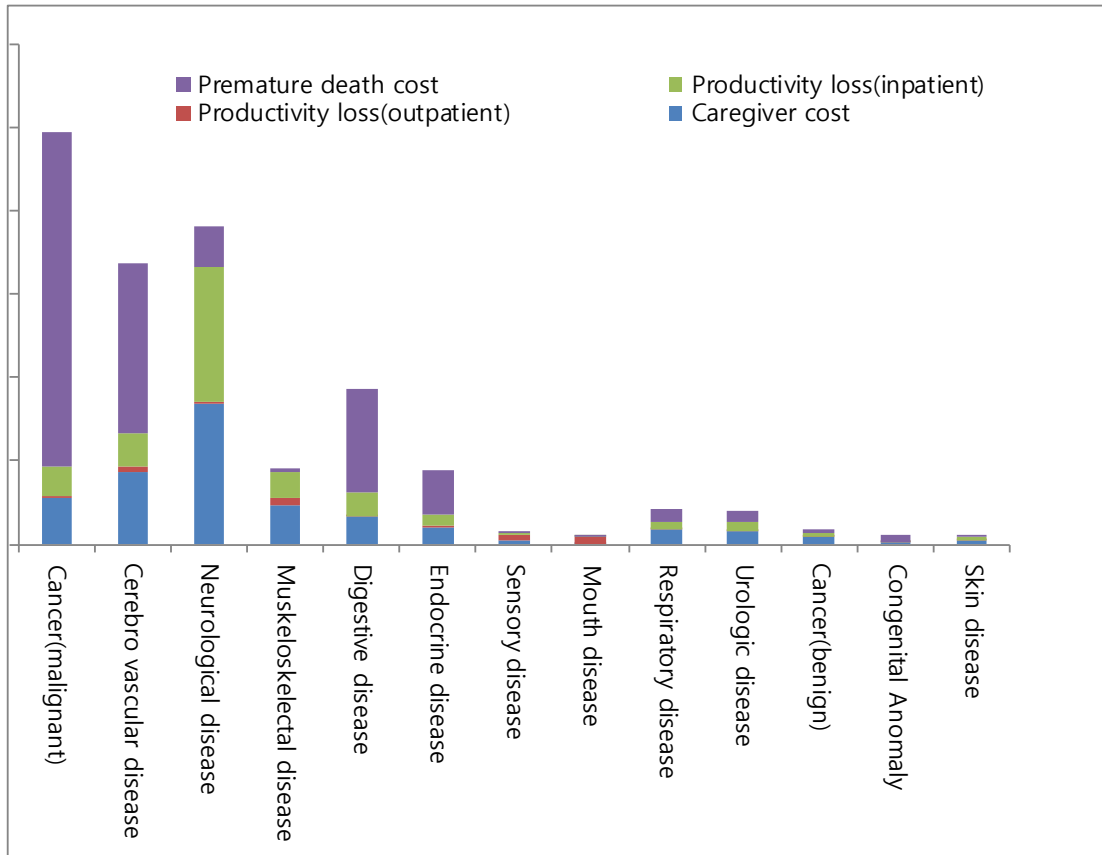
**Table 1.** Detailed variables and data sources per cost item.

Cost items	Detailed variables	Data sources	
Health cost	Direct medical cost	Inpatient costs: Average inpatient health care costs; average admission rate; non benefit rate: inpatients Outpatient costs: Average outpatient health care costs; average outpatient visit rate; non benefit rate: inpatients; pharmaceutical costs	NHIC claim data; data from 2011 survey regarding out-of-pocket payments made by patients otherwise covered by the NHIC NHIC claim data; data from 2011 survey regarding out-of-pocket payments made by patients otherwise covered by the NHIC; 2011 National Insurance Statistical Yearbook
	Direct non-fee medical cost	Transportation costs: Average admission rate; average number of admissions; one-way transportation fees for inpatients; average outpatient visit rate; average number of outpatient visits; one-way transportation fees for outpatients Caregiver costs: Average days of admission; average number of outpatient visits; average wage per day Productivity loss: average days of admission; average number of outpatient visits; average wage per day; average employment rate	NHIC claim data; the Third Korea National Health and Nutrition Examination Survey (KNHANES III), 2010: Health Service Utilization; 2009 national statistics: consumer price index NHIC claim data; 2009 national statistics: South Korean income data 2009 national statistics: South Korean income data; 2009 national employment and labor statistics
Indirect cost	Premature death cost	Average wage in per year, by age group; average retirement age; number of deaths per age group; interest rate	2009 national statistics: South Korean income data; 2009 annual report on cause-of-death statistics

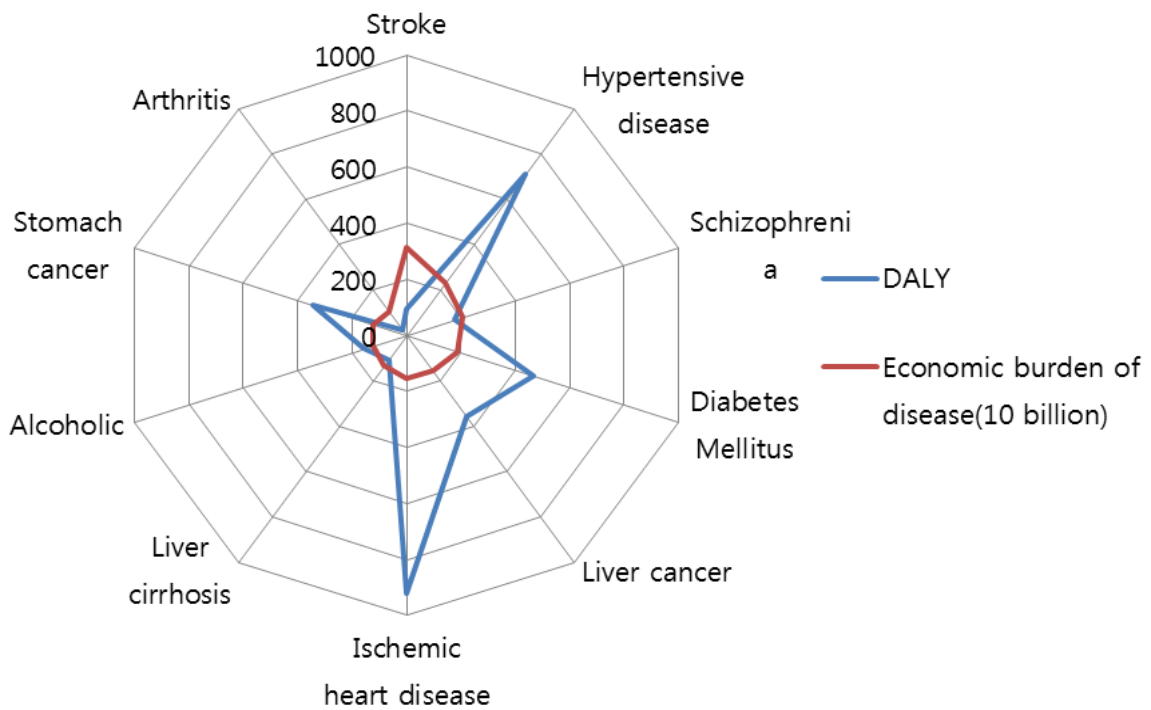
**Figure 1.** Socioeconomic burden of chronic disease in South Korea (2010), per disease .

According to the results of sensitivity analysis with the estimated values, the economic burden values were found not to be greatly affected by a loss of productivity

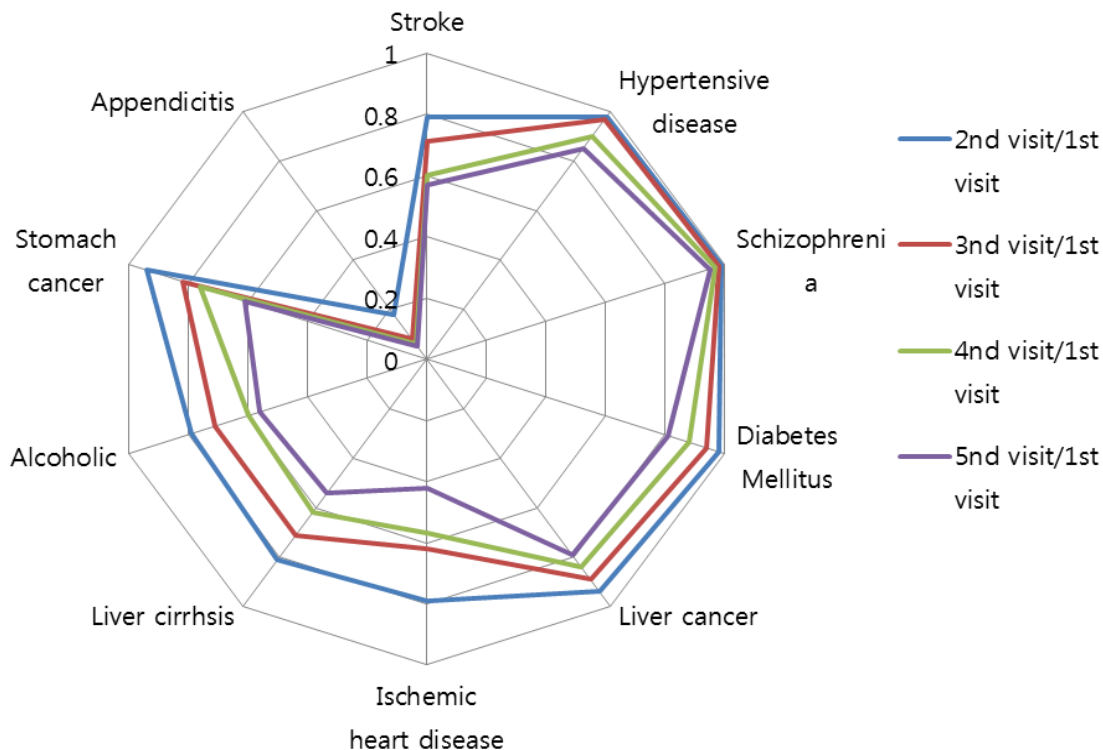
on account of the nonpayment rate of health insurance, wages, and the like; they were, however, greatly affected by a broad range of discount rates. In excluding cases



**Figure 2.** Indirect cost of chronic disease in South Korea (2010), per disease.



**Figure 3.** Comparisons of DALY and economic burden of disease values.



**Figure 4.** Sensitivity analysis of frequency of outpatient visits, per disease.

involving fewer than five visits, we found there to be no difference among the values among liver cancers, diabetes mellitus, schizophrenia, and hypertensive diseases, among others, all of which require continuous visits and involve detailed clinical pathological data and expert findings. However, other diseases showed values that differed from those of the others, among 50% or more of the cases (Figure 4).

## DISCUSSION

This study compared social expenses incurred in 2010 on account of WHO-defined chronic disease; its main data source was South Korea's National Health Insurance Corporation (NHIC) database for the year 2010. We found the total economic burden incurred in that year by the presence of chronic disease to be approximately 3.7 million USD indirect and direct medical costs accounted for the greatest proportion of the overall economic burden, although these values varied from disease to disease.

Within the study year, an approximately USD8.2-billion economic burden was associated with malignant cancer, a disease that accounted for the greatest proportion of economic burden; this was followed closely by the USD 7.88 billion burden associated with cardio-cerebrovascular diseases. In the United States, as a point of comparison, approximately USD209.9 billion of economic burden was associated with cancers in 2005, while USD10.88 billion and USD14.9 billion was

associated with hypertension in 1998 and 2007, respectively (Hodgson and Cai, 2011). According to the 2008 GBD study, the economic burden associated with cardio-cerebrovascular diseases and cancers has increased among economically advanced countries. In this sense, the disease burden associated with chronic disease has increased sharply in South Korea, a country whose disease distribution has gradually changed to more closely resemble that seen in advanced countries (WHO, 2008).

In the current study, the medical cost for hospitalization and outpatient treatment accounted for the highest rate of direct medical costs, followed by pharmaceutical costs, although the ranking of these did vary from disease to disease. The death cost accounted for the highest proportion of indirect costs in malignant tumors, cardio-cerebrovascular diseases and digestive diseases, while among neurogenic diseases; nursing costs exceeded the death cost. This indicates that a disease with a high rate of fatality tends to incur a high productivity loss by causing early death, and that health problems stemming from a chronic disease may threaten the quality of life among the patient and his or her family members alike.

Especially after undertaking a comparison of DALY and economic burden of disease values, we found there to be great variance in the magnitude of disease burden among the diseases studied. These findings indicate that it is necessary to establish a method by which to measure economic disease burden in consideration of sensitivity to certain disease characteristics. This finding suggests that

policy should be established to address the various disease burden index values.

This study has some limitations. Its main data source is the database of South Korea's NHIC, and we were often compelled to exclude duplicate records, so as to prevent overestimation; there were also problems within the database with respect to erroneous classification information, possibly stemming from data entry error. In addition, this study does not take into consideration social costs related to folk remedies, nor cost increases that stem from comorbidity or complications.

In any case, the results of this study suggest the import of generating data that will inform various health policies.

These data can be generated by carrying out various follow-up studies and by continuously monitoring disease burden by using high-quality information culled from examinations of medical records and patients.

### Conflicts of Interests

The authors have not declared any conflict of interests.

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