Building an Aflatoxin Safe East African Community

Technical Policy Paper 3

Aflatoxin: Hepatitis A & B

Knowledge Platform 2015
Situational Analysis for East Africa Region

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IITA Research to Nourish Africa

JUMUIYA YA AFRIKA MASHARIKI

Aflatoxin: Hepatitis A & B

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Table of Contents

Foreword....1
Executive Summary....1
List of Abbreviations and Definitions....66
Introduction: Epidemiology of Hepatitis A and B....6
Hepatitis A....6
Virology....6
Pathophysiology....7
Age Distribution....8
Seasonality....8
Global Distribution....8
Risk Groups....8
Prevention and Treatment....9
Hepatitis B....10
Virology....10
Transmission....10
Pathophysiology....10
Disease Burden....11
Age Pattern....11
Seasonality....11
Global Distribution....11
Risk Groups....12
Prevention and Treatment....13
Knowledge Platform....13
Vaccination Protocol Against HAV and HBV Infections....13
How Aflatoxins Interact with HBV Infection....14
How Aflatoxins Interact with HAV Infection....18
Benefits of Vaccinating Against Hepatitis A and B....18

Aflatoxin and Hepatitis: Situational Analysis for the EAC 19
Population Distribution in East Africa 19
Regional Prevalence of Hepatitis A and B 20
Aflatoxin Exposure in East Africa 20
Sanitation, Cultural Practices, and Social Problems in the EAC 21
Sanitation 21
Alcohol Consumption 22
Circumcision and Scarification Practices 23
High Mother-to-Child Transmission of Hepatitis B and Aflatoxin 24
Current Immunization Policy and Schedule 24
Proposed Vaccination Protocol for EAC States 25
Challenges 26
Programmatic Challenges 26
Financial Challenges 26
Inadequate Investment into Cold Chain Equipment 28
Supply and Logistical Challenges 29
Lack of an Efficient Monitoring System 29
Ineffective Social Mobilization and Demand Generation Activities 29
Maintaining the Cold Chain 30
Inconsistent Vaccine Readiness 32
Failure to Effectively Manage Stakeholder Groups 32
Partnership Strategies for Vaccine Programs 32
Reaching All Age Groups 33
Roles of the Public and Private Sectors 33
Public Sector Roles 33
Private Sector Roles 34
Policy Recommendations 34

Appendix: Vaccine Needs Estimates 36
Introduction 36
Immunization Coverage and Supply Chain Logistics 36
Targeted Population for Each Antigen 37
Vaccine Needs Estimation 39
Hepatitis B Vaccine Needs Estimates 39
Hepatitis A Vaccine Needs Estimates 41
Cold and Dry Storage Demands for Vaccines 42
Supplies and Operations Cost Estimates 42
Vaccine Costs 43
Hepatitis B Vaccines and Supplies 43
Hepatitis A Vaccines and Supplies 44
Injection and Supplies Requirements by Country and Cohort 46
Burundi Country Calculations 46
Kenya Country Calculations 47
Rwanda Country Calculations 48
Tanzania Country Calculations 49
Uganda Country Calculations 50
EAC Summary 51
Appendix: Aflatoxin, Hepatitis, and HCC in the EAC 52
Introduction 52
The Risk Assessment Process 52
Health Impact Estimates 54
Quantitative Risk Assessment for Economic Impacts of Aflatoxin 57
Dose Response 57
Exposure Assessment 57
Tanzania 58

Burundi, Kenya, Rwanda, and Uganda 58
Risk Characterization 60
Disability Adjusted Life Years (DALYs) Lost 60
Potential Economic Value of Eliminating Excess HCC Risk 60
Health Impact Sensitivity Analysis for EAC Countries 61
References 66

Figures

Figure 1: Global endemicity of HAV. 12
Figure 2: Global epidemiology of HBV 16
Figure 3: Aflatoxin and disease pathways in humans. 17
Figure 4: Population distribution in the EAC. 19
Figure 5: East African Community population under the age of 30 years. 20
Figure 6: Rates of unimproved drinking water and sanitation facility access. 22
Figure 7: Alcohol consumption in EAC partner states. 23
Figure 8: Investment in vaccine development and cold chain equipment. 28
Figure 9: Status of cold chain capacity—EAC. 31
Figure 10: Estimating the economic impact of aflatoxin contamination. 53
Figure 11: Maize and groundnuts consumption by country. 54
Figure 12: Maize and groundnuts consumption by country. 54

Tables

Table 1: Hepatitis A and B vaccination protocol. 14
Table 2: Population estimates by cohort in East Africa. 37
Table 3: Categorized target groups for immunization. 38
Table 4: Target population and age by country. 38
Table 5: HBV vaccine needs 40
Table 6: HAV vaccine needs (above 1 year) in doses. 41
Table 7: Hepatitis B vaccine and operation costs by country and cohort.. 44

Table 8: Hepatitis A vaccine and operation costs by country and cohort. 45
Table 9: HCC incidence attributable to aflatoxin contamination. 55
Table 10: Average consumption of maize and groundnuts in EAC countries. 59
Table 11: Estimated aflatoxin-attributable HCC and DALYs for Burundi, 2012. 61
Table 12: Value of eliminating aflatoxin-related HCC mortality risk, Burundi, 2012. 62
Table 13: Aflatoxin-attributable HCC incidence and DALYs for Kenya, 2012. 62
Table 14: Value of eliminating aflatoxin-related HCC mortality risk in Kenya, 2012. 62
Table 15: Aflatoxin-attributable HCC incidence and DALYs for Rwanda, 2012.....63
Table 16: Value of eliminating aflatoxin-related HCC mortality risk, Rwanda, 2012. 63
Table 17: Aflatoxin-attributable HCC incidence and DALYs for Tanzania, 2012. 64
Table 18: Value of eliminating aflatoxin-related HCC mortality risk, Tanzania, 2012.....64
Table 19: Aflatoxin-attributable HCC incidence and DALYs for Uganda, 2012. 64
Table 20: Value of eliminating aflatoxin-related HCC mortality risk, Uganda, 2012. 65

Foreword

Viral hepatitis affects hundreds of millions of people worldwide, causing serious chronic illness from acute liver infection. This often progresses to cirrhosis and hepatocellular carcinoma (HCC). Hepatitis A virus (HAV) and hepatitis B virus (HBV) infections contribute to a large proportion of these liver conditions globally, as well as throughout the East Africa region, subsequently resulting in high morbidity and mortality rates. At this time there is no known cure for hepatitis B. Hepatitis A can be self-limiting under favorable conditions, but due to the compromised health and nutritional status of children and other vulnerable groups in the developing world, permanent damage to the liver is a frequent outcome. While it is highly likely that the burden of the hepatitis C virus (HCV) is also significant, at this time there is incomplete data to describe the prevalence of HCV within the East Africa region.

As a result of the expert working group recently brought together under a partnership led by the United States Agency for International Development (USAID), a consensus was reached to recommend the introduction of hepatitis A vaccinations. To address incomplete coverage for the hepatitis B vaccine, the expert group also recommended adolescent and adult "catch up campaigns," and ramped up efforts to improve clinic-based routine childhood immunization coverage. These landmark decisions were prompted by new information informing health professionals and policy makers about the double disease burden caused by hepatitis and high levels of dietary aflatoxin exposure for East Africans of all ages.

Aflatoxin is classified by the World Health Organization (WHO) as a Class I carcinogen, targeting the liver and exerting significant impact on the progression, severity, and prevalence of hepatocellular carcinoma (HCC) and other complications associated with liver disease. Throughout East Africa, high levels of aflatoxin in a number of widely consumed staple foods—including maize, groundnuts, cassava, rice, tree nuts, dried fruit, fish and milk—have been clearly demonstrated.

This paper describes the epidemiological landscape of hepatitis A and B across the East Africa region, provides in-depth analyses on the cost and logistics of implementing the policy and program recommendations of the expert working group for adequate immunization coverage, and presents a case study on the relationship between chronic consumption of contaminated foods and the incidence HCC in the region. This unique knowledge platform can support international donors and national governments across the East Africa region to take the necessary actions to ameliorate significant threats to the public health posed by aflatoxin.

Executive Summary

Globally, there are an estimated 1.4 million new cases of HAV infection every year. HAV is transmitted through ingestion of contaminated food and water or through direct contact with an infected person. HAV is associated with a lack of safe, potable water and poor sanitation conditions, and is one of the most frequent causes of foodborne infection. In developing countries where poor sanitation and unhygienic practices prevail, a large number of children--as high as 90 percent in the most impoverished communities--are estimated to be infected with HAV before the age of 10. However, unlike HBV and hepatitis C virus (HCV), HAV does not cause chronic liver disease and is not fatal to otherwise healthy individuals. In addition to debilitating symptoms, however, fulminant hepatitis (acute liver failure), is associated with high mortality among adults. High mortality rates have also been observed among malnourished children. Improved sanitation and the provision of the HAV vaccine are the most effective ways to combat this disease.

For all persons who are exposed to other liver toxins, such as aflatoxin, exposure to any of the hepatitis viruses can result in a significant increase in the progression and severity of the disease.

Today, more than 240 million people suffer from chronic liver infections and over 780,000 people are estimated to die every year from HBV.

HBV prevalence is highest in sub-Saharan Africa and East Asia. The virus is transmitted from person to person through contact with the blood or other body fluids of an infected person. In highly endemic areas, HBV is most commonly spread from mother to child at birth, or from person to person in early childhood. High-risk practices include illegal intravenous drug use, nonsterile traditional male circumcision practices, female genital cutting (FGC), and scarifications that involve piercing of the skin. Administration of the HBV vaccine is the mainstay of prevention, in tandem with elimination of these high-risk practices.

While studies on the burden of HAV and HBV prevalence within the East Africa region are few, there is increasing evidence to show that both of these diseases affect a large number of people. Hepatitis A and B infections remain major public health challenges within each of the partner states of the East African Community (EAC)—Kenya, Tanzania, Uganda, Rwanda, and Burundi. The cultural practices mentioned above--male circumcision, FCG, scarification--plus unattended births and lack of diagnostic tools all contribute to the high prevalence of the disease. Alcohol consumption, particularly of home brews from local grains that often contain high levels of aflatoxin, add to the challenge, especially among youth, as the combination is likely to accelerate liver damage.

The World Health Organization (WHO) has defined persons considered at the highest risk of contracting HBV as follows:

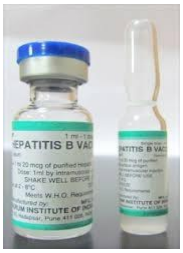
- Infants born to infected mothers
- Young children in daycare or residential settings with other children in endemic areas
- Sexual/household contacts of infected persons
- Health-care workers
- Patients and employees in dialysis centers
- Injection-drug users sharing unsterile needles
- People sharing unsterile medical or dental equipment
- People providing or receiving acupuncture and/or tattooing with unsterile medical devices
- People living in regions or traveling to regions with endemic hepatitis B50
- Sexually active heterosexuals
- Men who have sex with men.

The hepatitis B vaccine was introduced in 1982 and is 95 percent effective in preventing the disease. WHO recommends that all infants receive the HBV vaccine as soon as possible after birth, preferably within the first 24 hours. The birth dose should be subsequently followed by three additional doses, one month apart.

Current vaccination programs for the EAC do not include the HAV immunization. HBV immunizations were introduced in 2002 to the primary infant immunization program in combination with DTP and Hib vaccines (Haemophilus influenza type B vaccine), currently affording protection to children up to 12 years old, with a reported coverage rate of 70-90 percent. Hence only a small proportion of the population is protected against HAV and HBV infections in a region with a number of high risk factors.

Vaccination against HAV should be part of a comprehensive plan for the prevention and control of viral hepatitis throughout the developing world, as it is now in many developed countries. Currently Argentina, China, Israel, Turkey, the United States of America, among others, have incorporated hepatitis A vaccines in routine childhood immunization protocols.

Planning for large-scale immunization programs requires accurate cost evaluations, both initiation and recurrent, to ensure their sustainability. Such programs should operate concurrently with additional prevention methods such as improved sanitation, access to safe drinking water, adequate nutrition, improved food safety practices, and health education. In conjunction with vaccination and prevention protocols for high-risk groups, such as health workers, prevention of HBV within East Africa will require modernization to sterile procedures for male circumcision and the elimination of other harmful cultural practices that transmit infected blood and other body fluid between persons.



East Africans of all ages suffer from the double disease burden caused by hepatitis and aflatoxin exposure. Aflatoxins are a group of fungal metabolites classified by the WHO as class I carcinogens. The toxin targets the liver and has been shown to have a significant impact on the progression, severity, and prevalence of hepatocellular carcinoma (HCC) and other complications of the liver. Throughout East Africa, high levels of aflatoxin have been clearly demonstrated in a number of widely consumed staple foods—including maize, groundnuts, fish, tree nuts, dried fruit, and milk. Acute aflatoxicosis from ingesting extremely high amounts of aflatoxin, versus chronic intake of toxic but nonlethal doses over time, is characterized by liver failure, hemorrhage, and even death. Outbreaks of aflatoxicosis are episodic throughout the region.

HCC is a result of longer-term, chronic aflatoxin exposure, presenting most often in persons with chronic hepatitis B. Studies have shown that the risk of HCC increases 30-fold in individuals with HBV infection when they are also exposed to aflatoxin due to negatively synergistic interaction among the virus, the toxin, the liver, and the immune system. In the context of the high prevalence of individuals afflicted with HBV, as well as the high levels of the population who have compromised liver health due to previous HAV infection, the widespread and regular consumption of staple foods containing unsafe levels of aflatoxin presents an urgent public health challenge in the region that needs to be fully defined and addressed. In addition to measures to control aflatoxin in the food supply, the administration of HAV and HBV immunizations for all age groups of people residing in the East Africa region is a pressing health priority.

There is a growing body of evidence that aflatoxin exposure is associated with both growth impairment and suppression of the immune function in children, rendering them more susceptible to infections, including HAV and HBV. A few studies have reported a high prevalence of HepBsAg, the HBV antigen, among pregnant mothers in Kenya, Tanzania, and Uganda, suggesting that HBV vertical transmission to newborn infants and exposure levels among young adult populations are high across the region.

Given the interactions among HBV, HAV, and aflatoxin in relation to HCC, a highly effective intervention to reduce the aflatoxin related HCC would be vaccination against both HBV and HAV.

The relationship among HAV, HBV, and aflatoxin exposure has serious consequences for EAC national policy makers faced with the task of setting standards for aflatoxin contamination of foodstuffs. One study featured in this paper estimated the human health impacts if populations were exposed to aflatoxin levels at different regulated levels. The results are alarming. Levels that are accepted as safe for human consumption in the United States and European Union are often not met within the countries of the EAC,

where reliance on aflatoxin susceptible crops—maize, cassava, milk and groundnuts, for example—is very high. Study results suggest that the economic losses the residents of all EAC countries are subject to from morbidity and mortality from HCC attributable to aflatoxins is a measurable share of their countries' respective GDPs, suggesting that public funding should be invested to address this problem. Appendix Quantitative Risk Assessment for Economic Impacts of Aflatoxin, discusses at length the methodology applied to estimate the disease burden on the economics of the East Africa Community states by the double health challenges of aflatoxin contamination and the endemicity of the HBV virus.

These realities suggest that the combination of aflatoxin and hepatitis in the EAC partner states has created a public health emergency. There is an urgent need to declare the prevention of HAV and HBV infections a priority for the community. Yet this emergenc can be affordably addressed by introducing routine hepatitis A vaccination, strengthening and expanding the existing hepatitis B vaccination program, and starting the vaccination program immediately after birth. Details are provided below, in the section Vaccination Protocol Against HAV and HBV Infections.

The logistical, social, political, and cost challenges associated with such a campaign are discussed in the Challenges section. For the initial implementation phase of these programs, we recommend campaign activities as needed to reach the large "out of clinic catchment" population that is aged 30 and under. Additional priority populations for Phase I include women of childbearing age and all persons residing in the aflatoxin "hotspot" agricultural zones through the region. While cost constraints will drive the initial efforts, the EAC should open dialogue with donors providing immunizations to request an adequate and affordable supply of the vaccines and funding for the necessary training and delivery activities required for such programs.

We hypothesize that, by virtue of residing within the East Africa region, and in the context of the existing high HAV and HBV prevalence rates, coupled with an equally high prevalence of aflatoxin-contaminated staple foods, all age groups residing in the EAC fall into a high-risk category. The EAC should consider, in its policy deliberations for achieving an aflatoxin safe community over the next five years, making these immunizations available and accessible to all.

The two health impact studies appended to this document (Appendix: Vaccine Needs Estimates and Appendix: Aflatoxin, Hepatitis, and HCC in the EAC) help to quantify the significant value added to the economy derived from aggressive national campaigns for hepatitis B immunization for the largely unvaccinated 6-15 year cohort in EAC partner states. Population cancer risk was estimated by multiplying the aflatoxin exposure with the HCC

potency, defining HCC potency as an average of HBV status-specific HCC potencies weighted by HBV prevalence rates in each country. To derive the annual number of HCC cases that occur due to aflatoxin exposure, the estimated population risk was multiplied by the country populations per 1,000,000 persons.

One study estimated annual Disability Adjusted Life Years (DALYs) lost due to aflatoxin contamination-related HCC cases. DALY is an epidemiological measure of disease burden expressed in the number of healthy life years lost due to death or disability caused by disease. The second study developed country-specific costs of DALY losses for EAC partner states from the added burden of aflatoxin-related HCC cases. The cost metric used was the Value per a Statistical Life (VSL), calculated (as a range for each EAC partner state) as follows:

- Burundi—$18,000-$72,000 VSL range
- Kenya—$49,000-$207,000 VSL range
- Rwanda—$33,000-$134,000 VSL range
- Tanzania—$37,000-$161,000 VSL range
- Uganda—$31,000-$128,000 VSL range.

The study conservatively calculated the cost-benefit of hepatitis B immunization for the largely unvaccinated 6-15 year cohort using the low range of the VSL metric. Depending on the variables applied, economic savings ranged from hundreds of millions to tens of billions of dollars.

Introduction: Epidemiology of Hepatitis A and B

Hepatitis A

Hepatitis A is a liver disease caused by HAV infection, usually during community-wide outbreaks (WHO 2000).

Virology

HAV is a non-enveloped, single-stranded RNA virus, and a member of the *Hepatovirus* genus of the family *Picornaviridae*. The virus is transmitted via the fecal-oral route, either through direct contact with an infected person or when an uninfected person ingests food or water that is contaminated with the feces of an infected person. Incidence of the disease is closely associated with unsafe water, inadequate sanitation, and poor personal hygiene. Occasionally, HAV is also acquired through sexual contact (anal-oral) and blood transfusions, but these modes of transmission are rare.

Pathophysiology

HAV replicates in hepatocytes (liver cells), and interferes with liver function by initiating an immune response that results in inflammation of the liver, producing infection that is either symptomatic or asymptomatic. Symptomatic individuals typically present with abrupt onset of fever, anorexia, malaise, nausea, and abdominal discomfort, followed by jaundice and dark urine. Hepatitis A infection does not have a chronic sequela and is rarely fatal, with a case fatality rate of 0.1-0.3 percent, but it can cause debilitating symptoms and fulminant hepatitis (acute liver failure), which is associated with high mortality rates (CDC 1996). The severe form of the disease is more likely to occur in the developing countries, where co-morbidities play a role (Koff 1998).

The course of acute hepatitis A can be divided into four clinical phases:

1. Incubation period (preclinical period) that ranges from 10 to 50 days, during which the patient remains asymptomatic. In this phase, transmissibility is of greatest concern due to active replication of the virus.
2. Pre-icteric phase (Prodromal period) that ranges from several days to weeks. This period is characterized by symptoms such as loss of appetite, fatigue, abdominal pain, nausea and vomiting, fever, diarrhea, dark urine, and pale stools.
3. The icteric phase, in which jaundice develops. Although viremia ceases soon after hepatitis develops, the feces remain infectious for another one to two weeks. During this phase, most cases show low mortality rates and the disease resolves eventually. Occasionally, extensive necrosis of the liver occurs during the first six to eight weeks of illness. In these cases, mortality is highly correlated with increasing age, and survival is uncommon over 50 years of age (Lemon 1997).
4. Convalescent phase: In this stage, the disease resolves slowly. In 3-20 percent of patients, however, recovery is unsuccessful and relapsing hepatitis occurs (Lemon 1994). Another complication is cholestatichepatitis, which persists for months. Chronic sequela with persistence of HAV infection for more than 12 months is usually not observed.

It is important to note that the mortality rate increases considerably among patients with chronic hepatitis B, C, or underlying liver disease, who are superinfected with HAV (Hollinger and Ticehurst 1996).

Age Distribution

The course of HAV infection varies by age. Young children are easily infected with acute hepatitis A viral infection, which is usually asymptomatic, and therefore not easily diagnosed. Adults with acute infections develop mild or serious complications. The likelihood of having symptoms with HAV is directly related to age. Only 10–50 percent of infections acquired before the age of five years are symptomatic, while 70–95 percent of infected adults show clinical symptoms (Shapiro and Margolis 1993)

Seasonality

Hepatitis A has no seasonal pattern of incidence.

Global Distribution

The virus is present worldwide, and there are an estimated 1.4 million cases of hepatitis A disease every year. The risk of infection is inversely proportional to levels of sanitation and personal hygiene (Tufenkeji 2000).

In developing countries with poor environmental hygienic conditions and sanitation, there is a higher prevalence of hepatitis A infection among children. This rate, however, is largely underestimated because HAV infections in young children are mostly asymptomatic and therefore unrecognized (WHO 2000). As sanitary conditions improve, transmission shifts to older age groups and the incidence of symptomatic disease increases.

In most developed nations, hepatitis A infections are contracted by adults. Geographic areas can be characterized for high, intermediate, or low levels of endemicity patterns of HAV infection. HAV continues to spread in highly endemic regions despite the high prevalence of antibodies among the population due to its high physical stability (WHO 2000).

Risk Groups

The United Nations International Children's Emergency Fund (UNICEF) has identified groups at high risk for contracting HAV. They are:

- Children: Preschool and primary school children
- People living in areas of high endemicity with poor hygiene and sanitation
- People in household/sexual contact with infected persons
- Intravenous drug users using unsterilized injection needles
- People who practice traditional circumcision and scarification
- Health workers and medical personnel
- International travelers to HAV endemic regions

- Homosexually active men
- Persons residing in areas with extended community outbreaks
- Persons with existing chronic liver disease and exposure to aflatoxins
- Food-service establishment food handlers.

Prevention and Treatment

There are four mainstays for prevention of hepatitis A:

1. Improving clean water supply and sanitation
2. Abolishing traditional activities such as scarification and traditional circumcision
3. Mounting campaigns against drug and alcohol abuse
4. Vaccination.

Hepatitis A vaccine is available in two common forms: HAV vaccination alone, and HAV vaccination in combination with hepatitis B (HBV) vaccine. Both are safe and effective.

Currently, there are two inactivated,single-antigen virus vaccines available for protection against hepatitis A: Havrix© and Vaqta©, and the HAV/HBV combination vaccine Twinrix©.

Hepatitis A vaccine is administered as two doses six to twelve months apart.

There is currently no effective treatment for HAV infection.

Hepatitis B

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus. It is a major global health problem. It can cause chronic liver disease and chronic infection, and puts people at high risk of death from cirrhosis of the liver and HCC (Ferlay et al. 2008).

Virology

Hepatitis B infection is caused by hepatitis B virus, a double-stranded DNA virus that belongs to the *Hepadna* virus group.

Transmission

In highly endemic areas, HBV is largely spread from mother to child at birth, or from person to person through contact with bodily fluids of an infected individual. Sexual transmission and the use of contaminated needles, and injection drug use especially among injecting drug users, are also major routes of infection. Perinatal or early childhood transmission accounts for more than one third of chronic infections in areas of low endemicity. Unlike hepatitis A, HBV is not spread by contaminated food or water, and cannot be spread casually in the workplace. The hepatitis B virus can survive outside the body for at least seven days. During this time, the virus is still able to cause infection if it enters the body of a person who is non-immune.

Pathophysiology

The incubation period of the hepatitis B virus infection ranges from 30 to 180 days. The pathogenesis and clinical manifestations of hepatitis B infection result from the interaction of the virus and the host immune system. The immune system attacks HBV and causes liver injury. This results from the immunologic reaction when activated $CD4^+$ and $CD8^+$ lymphocytes recognize various HBV-derived peptides on the surface of the hepatocytes (liver cells). However, in an individual with impaired immune reactions or a relatively tolerant immune status, the infection may result in chronic hepatitis, and eventually lead to HCC. It is possible that co-morbidities, including alcohol abuse, may accelerate this disease process. (Hollinger et al. 2001). The final state of HBV disease in some people is liver cirrhosis (Robinson 1995).

With or without cirrhosis, however, patients with HBV infection are likely to develop liver cancer (Chen and Yang 2011).

Disease Burden

Hepatitis B virus infection is estimated to be the cause of 30 percent of the liver cirrhosis and 53 percent of the HCC in the world, with over 90 percent of cases occurring in the developing countries. An estimated 15-40 percent of patients with chronic HBV will develop cirrhosis, end-stage liver failure, or HCC in their lifetimes (Perz et al. 2006).

Most of the deaths (96 percent) have been attributed to complications of chronic infection, such as cirrhosis and HCC. Only 6 percent have been attributed directly to acute hepatitis B infection (Goldstein et al. 2005). According to WHO, HCC is the sixth most common cancer and the third most common cause of cancer death in the world. Chronic HBV infection is the most common cause of HCC, accounting for 50 percent of HCC cases worldwide and up to 80 percent of cases in high HBV endemic regions, as seen in the developing countries. The risk of developing HCC is greatly increased with the development of cirrhosis (Lok 2002).

Age Pattern

Infants are more likely to be infected through vertical transmission (mother-to-child) in highly endemic areas. Intravenous drug users of all ages, especially young adolescents, show high prevalence rates. The younger the patient is when the disease is acquired, the more likely it is that he or she will develop chronic liver disease or HCC. It therefore makes economic sense to focus prevention programs in these productive age groups in resource-limited settings (Lavanchy 2005).

Approximately 90 percent of infants who are infected from their mothers at birth, and between 30-50 percent of those infected before the age of five years, become chronic HBV carriers, while of the people who are newly infected as adults, only 6-10 percent have a risk of chronic infection (Goldstein et al. 2005). Hence, hepatitis B immunization is recommended for routine administration at birth.

Seasonality

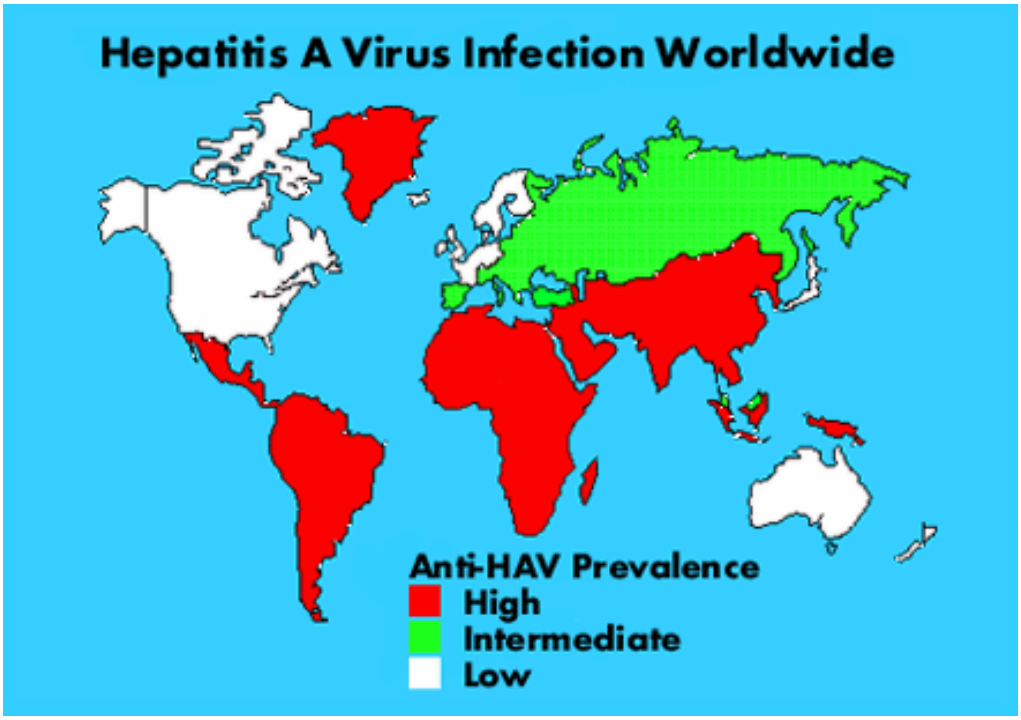
Hepatitis B shows no seasonal patterns of incidence.

Global Distribution

It is estimated that one third of the world population (more than 2 billion people) is infected with HBV. Furthermore, 360 million people out of these are chronic carriers. According to WHO July 2014 factsheets (https:/www.who.int/medicentre/factsheets), over 240 million globally have chronic liver infection due to HBV while over 780,000 people die every year due to acute or chronic consequences of hepatitis B infection. WHO also reports that the hepatitis

B vaccine, in use since 1982, is 95 percent effective in preventing the viral infection and its chronic consequences.

WHO has divided the global epidemiology of HBV into high, intermediate, and low endemic areas in the following six regions of the world: Americas, Europe, Africa, Eastern Mediterranean, Southeast Asia, and the Western Pacific. In countries of high HBV endemicity, where the prevalence of HepBsAg rate is above 8 percent, the most common modes of transmission are vertical at the time of birth from a chronically infected mother; or horizontal in early childhood from direct contact, through bites, skin lesions, or unsanitary habits (WHO 2014).



Source: WHO 2000.

Figure 1: Global endemicity of HAV.

Risk Groups

- Infants born to infected mothers
- Young children living in highly endemic regions with poor hygiene and sanitary conditions
- Sexual/household contacts of infected persons
- Health care workers
- Intravenous drug users sharing unsterile needles
- People who practice unclean circumcision and scarification
- People sharing unsterile medical or dental equipment

- Sexually active heterosexuals
- People who are exposed to aflatoxin.

Tanzanian child is immunized against hepatitis. Courtesy Merck.

Prevention and Treatment

The three mainstays of prevention are:

1. Elimination of high risk behaviors/customs
2. Improving the general hygiene of communities
3. Vaccination.

Highly effective DNA recombinant vaccines are available against HBV.
Vaccination against HBV is given routinely to newborns and infants as universal vaccination in almost all countries and can also be given to those who are at an increased risk of HBV.

The hepatitis B vaccine is available as:

1. HBV recombinant DNA vaccine (alone)
2. HBV in combination with *Heamophilus influenza* type B (Hib) vaccine
3. HBV in combination with DTap (diphtheria-tetanus-acellular pertussis) and inactivated polio vaccines
4. HBV in combination with hepatitis A (HAV) vaccine.

The vaccine is administered through intramuscular injection in three doses, usually at birth, one month and four months, but can also be given in four doses: at birth, one month, two months, and 12 months. Where vertical transmission is suspected, it is imperative to start the vaccination within 24 hours of birth. The vaccine is safe, well tolerated, and highly effective in preventing HBV disease. There is currently no effective treatment for HBV infection.

Knowledge Platform

Vaccination Protocol Against HAV and HBV Infections

Table 1 summarizes the vaccination protocol recommended by the World Health Organization (WHO) and the Advisory Committee of Immunization Practices (ACIP) for the prevention of hepatitis A and B viruses.

Table 1: Hepatitis A and B vaccination protocol.

Hepatitis A	
Infants and children under 18	**Adults over 18**
2 intramuscular injection (IM) doses given 6-12 months apart as 0.5mLs	2 IM doses, 6-12 months apart given as 1.0mLs
Hepatitis B	
Infants and children under 18	**Adults over 18**
3 IM doses given as 0.4 mLs with primary dose being given at birth 2nd dose: 1- 2 months after dose one 3rd dose: 6-18 months after dose two	3 IM doses given at 0, 1, 6 months as 1.0 mLs

Source: WHO, ACIP

How Aflatoxins Interact with HBV Infection

It has been estimated that more than 5 billion people in developing countries worldwide are at risk of chronic exposure to aflatoxins through contaminated foods. Aflatoxins are a group of fungal metabolites produced by the food-borne fungi *Aspergillus flavus* and *Aspergillus parasiticus*. These are weak and opportunistic plant pathogens which colonize commonly found agricultural crops such as maize (corn), groundnuts (peanuts), and most tropical and subtropical nuts. Wu et al. (2011), in their paper assessing the main food sources of aflatoxin consumption, reported that maize and peanuts, widely consumed in sub-Saharan Africa, are responsible for most of human exposure to aflatoxin in that region. These also happen to be the most susceptible crops to aflatoxin contamination (Wu and Khlangwiset 2010). Preharvest contamination of these crops with aflatoxins is common. *A. flavus* also causes spoilage of harvested grains during storage. Additionally, Strosnider et al. (2006) found in their studies that, when animals intended for dairy food production, such as cows, consume aflatoxins, they subsequently excrete the aflatoxins in their milk. The four major sub-groups of naturally produced aflatoxins are known as B_1, B_2, G_1 and G_2; however, other subtypes also exist. The aflatoxin in milk is the M_1 form. When dairy cows consume feeds containing aflatoxins, some of the feed aflatoxins can be converted to the M_1 form and excreted in milk. Based on this information, Chase et al. more recently were able to estimate that 1-3 percent of the aflatoxin consumed by the dairy cows is excreted in milk, a definite point of concern given the high level of milk consumption in the EAC region (Chase et al. 2013).

This study also suggested that aflatoxins may significantly harm the cattle by suppressing immunity and make them prone to other diseases--further increasing the risk of the milk being harmful to humans. Having identified that aflatoxin exposure is widespread in developing nations, the study by Wu et al. indicated that it can be difficult to understand the extent to which the specific risk of aflatoxin consumption affects society, as it can be measured only crudely in the increased death rate. This working paper looks into both the economic burden and the health risks of aflatoxin and focuses on the huge economic loss caused by aflatoxin exposure (Wu, Narrod et al. 2011). The two studies combined show that aflatoxin exposure has a large, negative impact on the heath and economic status of nations.

According to the International Agency for Research on Cancer (IARC) and WHO, aflatoxins have been classified as grade one carcinogens with some aflatoxin subtypes being highly potent carcinogens of the liver. Aflatoxin exposure in food poses a significant risk factor for HCC, especially when hepatitis B is also present. This was reported by Sylla et al. and also by Yan Liu and Felicia Wu in their paper analyzing the global burden of aflatoxin-induced HCC. This study found that 4.6 to 28.2 percent of HCC may be attributable to aflatoxin, and the negative effect of aflatoxin contamination is more significant in parts of the world with a high HBV prevalence (Sylla et al. 1999; Liu and Wu 2010). Aflatoxin B_1, the most toxic of the aflatoxins, is a potent liver carcinogen, causing HCC in humans and a variety of animal species. This disease is the third leading cause of cancer death globally, with more than half a million new cases each year (WHO 2008; Liu et al. 2010).

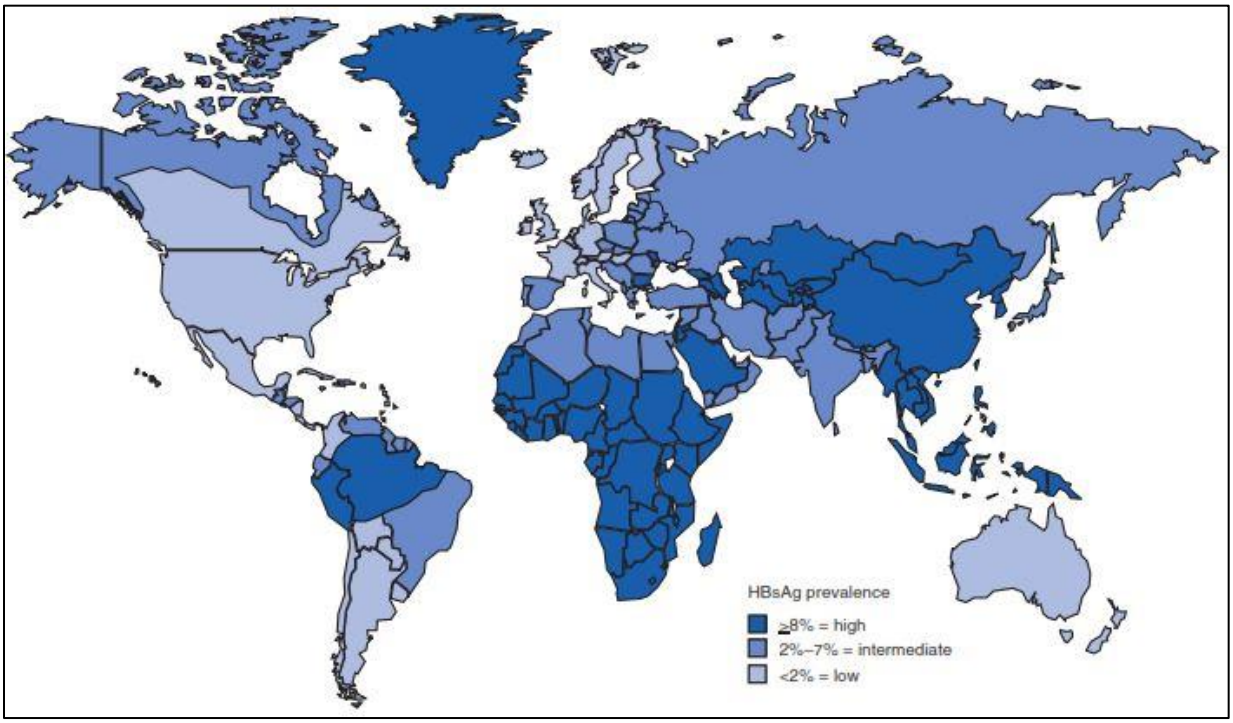
A comprehensive study by Sylla et al. 1999 and Liu et al. 2010, reiterates that aflatoxins and HBV are major risk factors for HCC, especially in high incidence areas for this cancer, namely Southeast Asia and parts of Africa. The study mentions that several epidemiological studies and animal models show the two factors can act synergistically to increase the risk of HCC. However, from the available information, it is important to note that the cellular and molecular mechanism of the interaction between these two factors is yet to be defined.

One possible mechanism observed in studies of HBV in transgenic mice is that chronic liver injury alters the expression of specific carcinogen-metabolizing enzymes, thus modulating the binding of aflatoxin to DNA in hepatocytes. An alternative hypothesis is that carcinogen exposure may alter viral infection and replication. The high levels of aflatoxin exposure that occur in many areas of the world where chronic HBV infection is endemic indicate that measures to reduce aflatoxin exposure would contribute to reducing the incidence of HCC.

This hypothesis is supported by a study by Groopman et al. (2005) that shows that in individuals exposed to both chronic HBV infection and aflatoxin, the risk of HCC jumps to about 30 times higher than the risk to individuals exposed to aflatoxin only. The same study

also discusses the synergistic relation between aflatoxin and HCC induced by the hepatitis C virus, although this quantitative relationship is not as well established as that for aflatoxin and hepatitis B virus in inducing HCC. The genetic characteristics of the virus, and the age and sex of the infected person, may play a role in increasing the risk of aflatoxin-induced HCC. But in brief, aflatoxin is probably responsible for up to 172,000 HCC cases per year, most of which would result in death within three months of diagnosis (Liu et al. 2012).

HCC as a result of chronic aflatoxin exposure has been well documented in studies, such as that of Wild and Gong (2010), presenting most often in persons with chronic hepatitis B infection. HAV infection, coupled with chronic HBV infection, appears to both accelerate liver damage and also increase the severity of the disease, leading to increased mortality. Aflatoxin liver injury exacerbates these affects. The possible mechanism could be through severe disruption of liver-cell DNA.



Source: U.S. Centers for Disease Control and Prevention

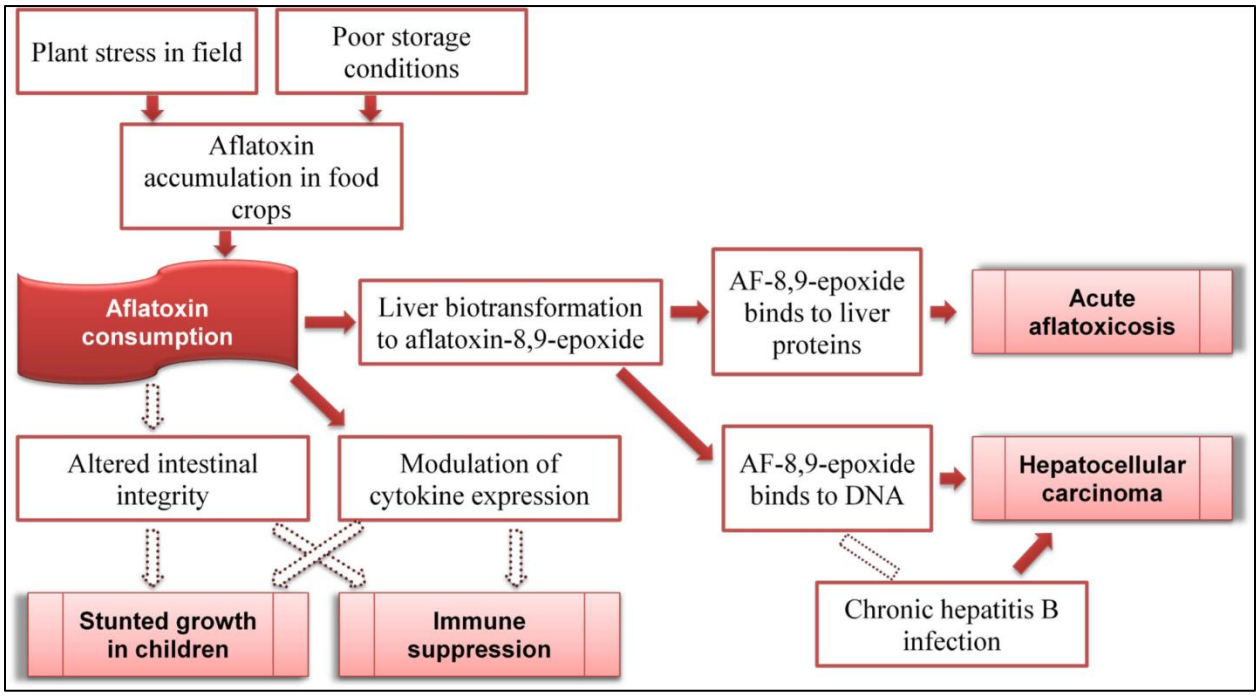
Figure 2: Global epidemiology of HBV

Wild and Gong (2010) documented a pathway to show how aflatoxins accumulate in food crops to cause adverse health effects. In this pathway, many factors affect the growth of *Aspergillus* fungi and the level of aflatoxin contamination in food. Contamination can occur at any stage of food production, from preharvest to storage. Factors that affect aflatoxin contamination include the climate of the region, the genotype of the crop planted, soil type, minimum and maximum daily temperatures, and daily net evaporation. Aflatoxin

contamination is also promoted by stress or damage to the crop due to drought prior to harvest, insect activity, heavy rains at harvest and postharvest, and inadequate drying of the crop before storage. Humidity, temperature, and aeration during drying and storage are also important factors.

Figure 3 depicts the pathway by which aflatoxin accumulates in food crops and contributes to health effects. The main predisposing factor in preharvest aflatoxin contamination is stress of the host plant, such as maize or peanuts. Stress can be caused by multiple factors, including the use of the wrong hybrid type of crops (that is, those that are unsuitable for the local geography), drought stress, high temperatures, and insect damage. All these increase the risk of crop plants being infected by *A. flavus* or *A. parasaticus*. The main predisposing factors in postharvest aflatoxin accumulations in food are poor storage conditions, namely, excessive heat and moisture, pest-related crop damage, and more than several months spent in storage.

Specific P450 enzymes in the liver metabolize aflatoxin into a reactive oxygen species (aflatoxin-8, 9-epoxide), which may then bind to proteins, causing acute toxicity (aflatoxicosis)--or to DNA and induce HCC (Wild and Gong 2010; Wu and Khlangwiset 2010).



Source: Wu 2010. *Figure 3: Aflatoxin and disease pathways in humans.*

Acute aflatoxicosis in humans is associated with extremely high levels of aflatoxin, and is characterized by hemorrhage, acute liver damage, edema, and even death.

children, as reported by three studies (Gong et al. 2002, 2004; Khlangwiset et al. 2011).

The study by Williams et al. (2004) showed that aflatoxin exposure is associated with immune system disorders and diminished weight and height in children. More than three decades of animal studies have found that aflatoxin may have an immunosuppressive effect on individuals. In addition, although aflatoxin and immunosuppression in humans has been relatively less well-documented, it is reported to have enormous significance from a global health perspective.

Jiang et al. (2005) report that several recent human studies have shown evidence of immunomodulation, though the actual outcomes of such immunomodulation have yet to be characterized. Gong et al. (2004) propose another explanation in their study, namely that aflatoxins alter the intestinal integrity and hence diminishing nutrient uptake and eventually causing deficiencies that lead to stunting and wasting.

Most developed nations, as a consequence of successfully regulated aflatoxin exposure, do not consider it a high risk substance. Unfortunately, this is not the case for many developing nations. Many developing nations are affected by this highly carcinogenic metabolite, and there are very few epidemiological studies in these countries to actually prove that aflatoxin exposure is a direct major public health concern especially with the added burden of hepatitis A and B infections (Williams et al. 2004).

Existing chronic damage to the liver as a result of hepatitis B or A superimposed on aflatoxin exposure or vice versa can mean that there are large populations being affected. More awareness of the synergistic effects of these factors is required.

How Aflatoxins Interact with HAV

The liver is the primary target of aflatoxins in people of all ages. When the integrity of liver functions is impaired by HAV, additional and persistent bombardment of this organ due to chronic intake of dietary aflatoxin is likely to impair the recovery process. This will be further exacerbated as the immune system is simultaneously depressed by HAV and aflatoxins, accelerating the pathological changes driven by the usual immune response of the liver caused by HAV. Malnutrition among infants and young children becomes another antagonist in this process. While the literature has not explored the direct relationship between aflatoxin and HAV, we do know that both contribute to chronic inflammation of the liver, which has been associated with cellular mutation.

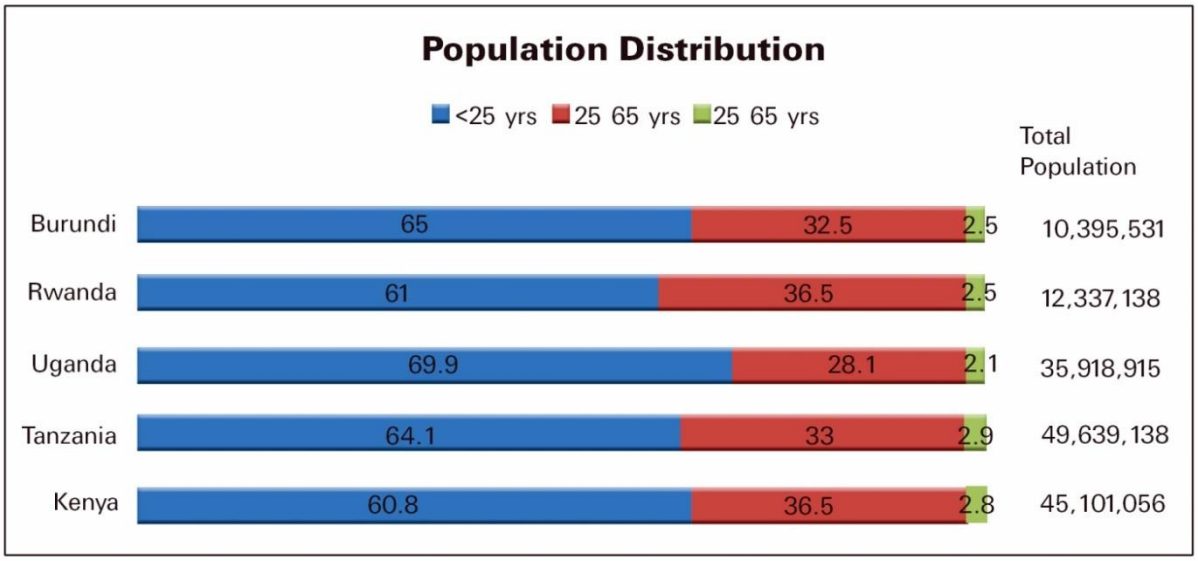
Benefits of Vaccinating Against Hepatitis A and B

According to two studies by Bonanni et al. (2003) and Williams et al. (2004), vaccination against HBV is a highly effective clinical intervention to reduce aflatoxin-related HCC. Health is fundamental to economic growth for developing countries and vaccinations form the bedrock of their public health programs. The benefits of vaccination extend beyond prevention of specific diseases in individuals. Vaccination makes good economic sense, and meets the need to care for the weakest members of societies.

Reducing global child mortality by facilitating universal access to safe vaccines of proven efficacy is a moral obligation for the international community. It is a human right for every individual to have the opportunity to live a full and healthy life.

Aflatoxin and Hepatitis in the EAC: Situational Analysis

The EAC is an intergovernmental organization with five partner states: Burundi, Kenya, Rwanda, Tanzania, and Uganda. According to the Central Intelligence Agency World Fact Book (https:/www.cia.gov/publication/the-world-factbook pdf July 2014), the combined population of all the five EAC partner states was estimated to be 153.3 million as of July 2014, with about 70 percent under 30 years of age. This is similar to the figure given by the WHO country statistics website (https:/www.who-int/gho/countries/cn/..pdf) of 153,126,000 with the same age distribution.



Source: UN population statistics and country specific demographic profiles

Figure 4: Population distribution in the EAC

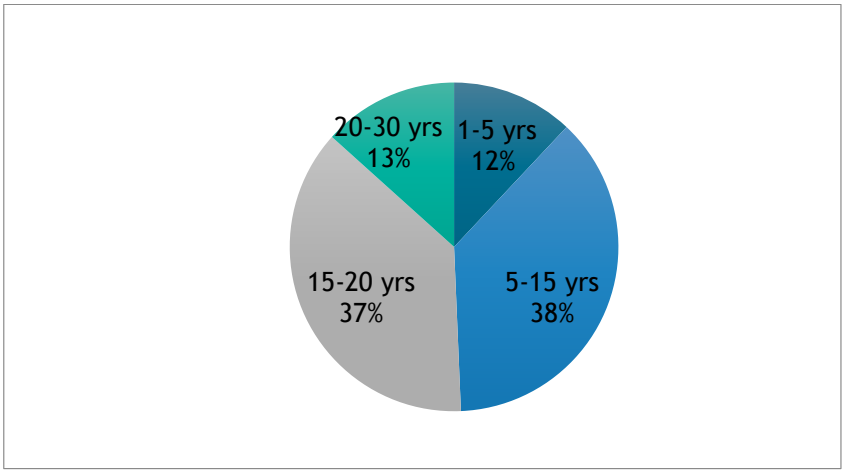
Population Distribution in East Africa

A large percentage of the population (60-70 percent) is below 25 years in all five countries, followed by those between 25-65 years of age, and a very small proportion

older than 65. This skews the population demographics toward the young in all five countries. Out of the combined population of people under 30, 38 percent are 5-15 years old, followed by 37 percent falling into the age bracket of 15-20 years of age. Infants and adolescents make up a lower percentage-- 12 and 13 percent respectively. It can be assumed from this that those aged below 5 years have a high mortality rate and require more attention regarding preventive measures to reduce it.

Regional Prevalence of Hepatitis A and B

Although there is significant information regarding the global distribution of HAV and HBV, there are very few studies on the prevalence of hepatitis A and B infections in these five states. The burden of disease due to these viruses can only be approximated from the global distribution while considering factors such as socio-cultural practices that increase the risk of infection. All five EAC states show a high degree of risk for HAV infection (CIA World Fact Book).



Source: UN population statistics and country specific demographic profiles

Figure 5: East African Community population under the age of 30 years.

Aflatoxin Exposure in East Africa

Aflatoxin is a common contaminant of foods, particularly in the staple diets of many developing countries (Williams et al. 2004). Various studies by the International Institute of Tropical Agriculture (IITA) report that staple foods consumed in the EAC partner states are contaminated with aflatoxins. There have been several reported cases of acute aflatoxicosis in Africa, associated with consumption of contaminated home-grown maize, including the outbreaks in Kenya in 1982, in which 12 people died, and more recently in 2004, during which 317 people were severely ill and 125 people died in the eastern and parts of the central counties. The use of biomarkers of exposure has enabled more studies of aflatoxin exposure

in the region, revealing high exposure in Tanzania, Kenya, and Uganda. A recent study in Tanzania found a significant association between aflatoxin M_1 exposure and impaired growth in infants under six months (Magoha 2014).

Common foods found with high levels of aflatoxin, including maize flour, animal milk, peanuts, farmed fish, and poultry, are widely consumed in the EAC partner states, further emphasizing the point that a large population in these nations is exposed to aflatoxins (Van Egmond et al. 2005).

Furthermore, in developing nations, aflatoxin contamination in food is a serious health problem because of the already existing exposure of a large population to hepatitis A and B viruses (Wild and Hall 2000).

Studies by Bonanni et al. (2003) and Williams et al. (2004) conclude that a highly effective clinical intervention to reduce aflatoxin related HCC is vaccination against HBV. It is postulated that vaccinating target populations will, over time, lessen the global carcinogenic impact of aflatoxin, because eliminating the synergistic impact between HBV and aflatoxin exposure would significantly reduce HCC risk (Liu and Wu 2010). This underscores the importance of vaccinating against hepatitis B and A.

Our hypothesis is that a pressing public health threat exists across the East African region due to the pervasive and high levels of consumption of aflatoxin-contaminated staple foods across the general population. Based on the current knowledge that there is a negative and synergistic impact on morbidity and mortality among aflatoxin consumption, HBV infection, HAV infection, and liver disease, we are recommending that all East African nations be classified as “at high risk” and that heir citizens receive the full series of hepatitis A and B immunizations.

Sanitation, Cultural Practices, and Social Problems in the EAC

Sanitation

Poor hygienic practices and inadequate sanitary conditions play a major role in the transmission of many communicable diseases, including hepatitis A (Stapleton and Lemon 1994).

A significant proportion of the population in the EAC partner states still does not have access to adequate and safe water supplies and sanitation facilities. In addition, knowledge of good hygiene behaviors and practices remains very low in rural regions and informal settlements of most EAC countries (UNICEF 2014).

A study by WaterAid (2006) reported that in Uganda, 80 percent of incidences of disease, including from HAV and HBV infections, are linked to poor sanitation. Despite its

importance in achieving better health, water and sanitation coverage has been low in East Africa, especially in rural areas. Major efforts have focused more on urban slum dwellers than on informal rural settlements.

Statistics show that all five EAC partner states show poor rates of sanitation facility access and high rates of unimproved drinking water sources, particulary in informal urban, and rural areas, of these countries (Figure 6).

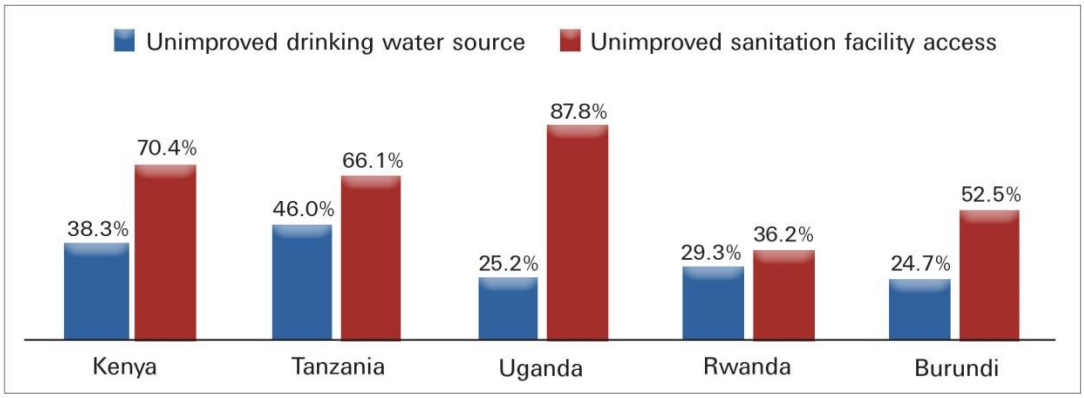


Figure 6: Rates of unimproved drinking water and sanitation facility access.

Alcohol Consumption

Some risky behaviors, such as heavy drinking by young people, increase the risk of developing chronic liver damage. Heavy alcohol use also dramatically increases the chances of alcohol-induced hepatitis, making full recovery a difficult process (Chevilotte et al. 1983). Alcohol abuse is a common social behavior in the young adolescent populations of these countries; however, its actual burden is underestimated due to lack of formal data.

The Global Status on Alcohol and Health report (2014) indicates that 23.7 liters of pure alcohol are consumed per capita per year by drinkers in Uganda annually (Figure 7). Rwanda and Burundi follow, each registering 22.0 liters per capita per year. Kenyans follow with a registered 18.9 liters of alcohol consumed per capita per year, while Tanzanians on average consume 18.4 liters per capita per year (*East African magazine* 2014). It is important to note that most of this is locally brewed from barley, wheat, and other grains--all of which are contaminated with aflatoxins, providing another route of exposure to the fungal toxins.

Figure 7: Alcohol consumption in EAC partner states.

Alcohol consumption in EAC partner states (liters per capita per year)	
Uganda	23.7
Burundi	22.0
Rwanda	22.0
Kenya	18.9
Tanzania	18.4

Source: East African magazine, July 2014.

Circumcision and Scarification Practices

Although horizontal spread is the primary mode of transmission of hepatitis B in developing nations, local and cultural practices that cause bleeding and ulceration increase the risk of percutaneous transmission. These practices include circumcision, body scarification, unsafe deliveries, and even ear piercing, which are often performed in unsterile environments with unsterile tools, by traditional healers and birth attendants rather than trained medical personnel (Chukwuka et al. 2003).

In the EAC partner states, several ethnic groups practice traditional circumcision and scarification with prevalence rates of male circumcision estimated to be as high over 80 percent in Kenya (Williams et al. 2006). It is not yet documented what proportion is performed in unsterile environments and/or using unsafe procedures. Nevertheless, it is probable that large populations living in the rural areas still use traditional methods Uganda, Tanzania, and Burundi are thought to have an intermediate prevalence rate of circumcision, ranging from 40-60 percent, while Rwanda has a prevalence rate of less than 20 percent. Most of these practices are not well documented or reported, however: actual rates could be much higher.

FGC is undoubtedly a significant source of transmission of hepatitis B. Most East African countries still practice female genital cutting. The 2009 Female Genital Mutilation survey in Kenya indicates that 27 percent of women aged 15-49 have undergone cutting, with the vast majority (83 percent) undergoing Type II excision. Prevalence varies by religion in Kenya; FGC affects 50 percent of Muslim women, 33 percent of Catholics, and 30 percent of Protestant women. A 2005 survey in Tanzania reported the FGC prevalence rate as 14.6 percent of all women aged 15-49, with Type II and Type III being the more common

type. Uganda, Rwanda, and Burundi show lower rates-- less than 5 percent.

With these high-risk practices targeting mainly the younger population bracket, this age group is at a much higher risk for HBV infection and therefore need urgent programs for the prevention of infection.

High Mother-to-Child Transmission of Hepatitis B and Aflatoxin

In addition, a study conducted on over 2,000 pregnant mothers in Kenya showed the prevalence of HepBsAg (marker for Hep B infection) to be as high as 9.3 percent with a sero-conversion rate of 30.2 percent (Okoth et al. 2006). These data indicate that a large adult population carries the hepatitis B antigen. Considering that this population had not been vaccinated against hepatitis B in infancy, the data suggest existence of a large pool of carrier adults as well as an increasing risk of mother-to-child transmission. Although no follow up was carried out to establish the mother-to-child transmission rate, it is reasonable to assume that this would be high. This, in part, has informed the practice of vaccinating newborn infants against HBV infection in some private institutions in Kenya. This HBV epidemiology can be extrapolated to the other four East African nations.

In addition to HBV, it is evident that aflatoxin exposure in humans occurs throughout life, including during gestation (Wild and Gong 2010). Aflatoxin exposure in utero not only reduces the neonatal birth weight but may also play a role in stunted growth in early childhood (up 24 months).

This brings out the urgent question of whether infancy HBV vaccination should not start at birth in the EAC. The current protocol that starts at six weeks in the form of the pentavalent vaccine means that from birth to six weeks, newborns are exposed to both hepatitis infections and aflatoxins.

The bottom line is that the current vaccination programs available in the EAC partner states cover a very small proportion of the population at risk.

Current Immunization Policy and Schedule

The national immunization programs of all EAC partner states introduced the hepatitis B vaccine in combination with the DPT (Diphtheria, Pertussis, Tetanus) and Hib (*Haemophilus Influenza* type B) vaccines (Pentavalent Vaccine) in 2002 (EAC Immunization and Vaccines Partners' Meeting 2013). This means that most of the children immunized in infancy in the last 14 years have had the hepatitis B vaccine. However, populations older than 14 have not been immunized against hepatitis B.

Pentavalent vaccine is currently being given to infants as a routine vaccination in three doses of 0.5mLs per dose at 6, 10, and 14 weeks. This gives a window period for a large population to be exposed to perinatal infection.

Some countries do immunize selected populations such as health workers, but this is negligible.

DPT3-Hib-Hep B coverage in the EAC region is estimated to be approximately 90 percent, as established in the East African Regional Technical experts meeting 2013-2014. WHO and UNICEF (2014) suggest that coverage may be as low as 80 percent. In any case, total immunization coverage is a goal still unmet, especially among rural populations.

As opposed to hepatits B, none of the EAC partner states have policies or programs on vaccination against HAV infection. There is negligible private sector vaccination offered in one or two of the states (mainly in Kenyan urban areas).

The situation outlined above makes it urgent to declare prevention of HAV and HBV infections a public health necesazsity throughout the EAC.

Proposed Vaccination Protocol for EAC States

A prudent proposal is that each of the targeted populations for hepatitis B receive three doses of the vaccine; those targeted for hepatitis A will receive two doses of vaccine. The specifications of the protocol follow. National campaigns for vaccination are noted.

Hepatitis A vaccination

0-12 months	To commence routine childhood vaccination: Two doses of 0.5 mL six months apart, from age one year
1-18 years	Two doses six to 12 months apart given as 0.5mL (national campaign initially)
19 years and older	Two doses, six to 12 months apart, given as 1.0mL (national campaign)

Hepatitis B vaccination

0-12 months	Introduce the birth dose Three doses given with the scheduled DTPs as combined vaccine; 0.5mLs every four weeks as currently
13 months -10 years	Three doses given as 0.5mLs per dose four weeks apart at 0, one month followed by a third dose after six months (national campaign)
11 years and older	Three doses given as 1.0mLs per dose in the same format as above (national campaign)

Challenges

There will be various challenges anticipated in reaching the populations with the vaccine.

- Programmatic
- Financial
- Logistics and supply management
- Other challenges.

Programmatic Challenges

A national vaccination campaign faces human-resources challenges at all levels, including weak governance at national level, and limited availability of skilled health-care workers at vaccine delivery points. A review of the training of health workers in Uganda prior to introduction of pneumococcal vaccine showed that only five districts supported by an EPI partner (Maternal Child Health Immunization Program [MCHIP]) had training completed at the time of the launch. Uganda has 112 districts. In Tanzania, an EPI situational analysis done in 2010 showed similar trends, with human resource constraints resulting in inadequate time allocated for EPI at regional and district levels.

The quality of training was affected by:

- Time lag between training of trainers and health workers' training
- Lack of demonstration vaccines for practice
- Low satisfaction with quality of training
- Training rushed to meet the launch date
- Lack of post-training supervision
- Having wrong staff attending the training.

Other constraints include:

- Lack of human resources at national, subnational, district, and service delivery points
- Cost of vaccines and related supplies
- Cold chain equipment costs and overhead (installation, energy, maintenance, and repair)
- Data collection
- Social mobilization, communication, and advocacy
- Disease surveillance, particularly on adverse events following immunization (AEFI).

Financial Challenges

Financial challenges incude above all inadequate and delayed release of funds. The introduction of pneumococcal vaccine in African countries confronted significant

challenges in ensuring timely release of funds at all levels. This resulted in less than optimal support for preparatory tasks for vaccine introduction. Such delays were noted in obtaining Global Alliance for Vaccines and Immunizations (GAVI) Vaccine Introduction Grant (VIG) by country (GAVI 2014). The delays were also noted in in-country disbursement of funds.

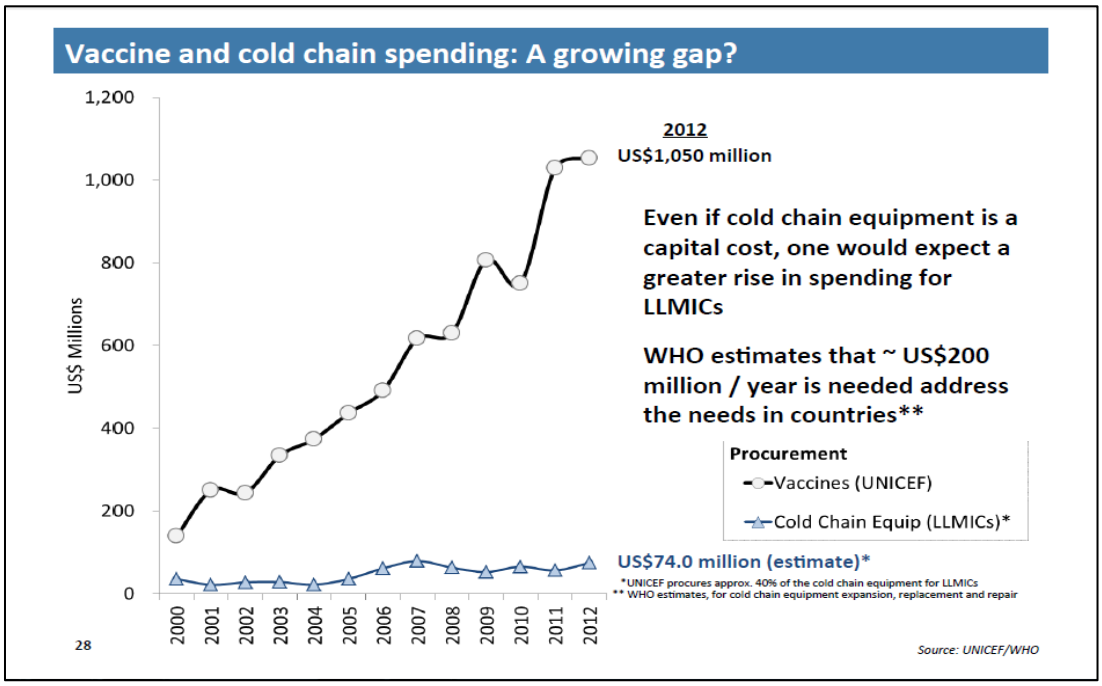
Uncertainties in the timing of GAVI VIG disbursement is usually for supporting operational activities. Delays in this area result in overall delay in implementing the entire national program (GAVI 2014).

In addition to general delays in receiving funding for new vaccines, countries are already incurring a high burden of costs to procure vaccines, for example, the Reproductive, Maternal, Neonatal, Child and Adolescent Health (RMNCH) costed plan for Uganda requires the country to procure vaccines worth USD 160 million over a period of five years, taking 25.7 percent of the total RMNCH total budget. The new vaccines (rotavirus and pneumococcus) are projected to cost 43 percent of the total five year vaccine requirements. This will stretch the country budget at a time when it is already coping to introduce additional vaccines within the projected period. The funding gap for the entire RMNCH budget is estimated to be about USD 600 million. The costs of new vaccines will eventually be far above the cost of traditional vaccines currently in use in the country, and there is therefore a strong need for external support.[1]

In Burundi, a decade of armed conflict provoked a series of negative consequences that undermined the economy.[2] This led to deep economic imbalances such as a negative balance of payment with an accompanying high inflation rate. The country has insufficient national resources in the face of growing needs seen in the public sectors, especially the health sector. These economic challenges may significantly compromise the ability of the country to carry out new vaccine campaigns.

[1] MoH, Uganda 2013. A promise Renewed: Reproductive maternal, Newborn and Child Health Sharpened Plan for Uganda. 2013, Ministry of Health: Kampala, Uganda.

[2] MoH, Burundi 2010. Burundi situation analysis, multi year plan 2010-2014.



Source: UNICEF/World Health Organization

Figure 8: Investment in vaccine development and cold chain equipment.

Inadequate Investment in Cold Chain Equipment

Figure 8 shows a clear discrepancy between expenditure on vaccines and the cold chain equipment needed to maintain their potency. This discrepancy, calculated by WHO, will increasingly affect the ability of countries to maintain the cold chain as new vaccines come on board.

Experience in introducing new vaccines in Tanzania revealed that a new vaccine's introduction always challenges the nation's cold storage capacity, particularly at national and regional vaccine stores. Due to inadequate capacity, there was no space for buffer stock at all stores; consequently the number of vaccine shipments at the national level increased from three to eight shipments a year.

Other under-used vaccines currently provided in the country outside of WHO's Expanded Program on Immunization (EPI) schedule are Yellow Fever and meningococcal vaccines to international travelers, anti-rabies and tetanus toxoid (TT) to injured persons. These vaccines also occupy the cold chain storage space.

In Burundi, inventory data (2010) showed that most of the cold chain equipment needed to be replaced, and country-wide power outages posed problems for the cold chain and vaccine storage. Other issues raised included lack of resources to obtain cold chain

maintenance supplies.[3] Limited prioritization of EPI activities at district level translates into limited funds allocation for EPI activities.

Supply and Logistical Challenges

Supply and logistical challenges include:

- Low levels of vaccine stocks at district levels due to inaccurate quantification
- Weak program data management, creating unreliable data
- Inadequate monitoring tools, such as Child Health Cards, TT cards, Child Registers, vaccine and injection materials, control books, and tally sheets
- Lack of transport, e.g., vehicles and motorcycles for EPI activities at all levels, which affected integrated outreaches
- Inadequate program logistical equipment, mainly in the cold chain system.

Lack of an Efficient Monitoring System

Countries in East Africa are challenged by the lack of an efficient monitoring and evaluation system. For example, EPI data collection tools (cards and registers, monthly summary forms, registers), need to be updated and distributed regularly to service delivery points as new vaccines come on board; this is usually not done in a timely manner. In addition, post-launch monitoring and supervision is typically lax, usually due to competing priorities. The EPI situation analysis done in 2010 in Tanzania confirmed a similar scenario: the main factors affecting performance of the program were inadequately focused supportive supervision, particularly from national, zonal, and regional levels, and less than optimal surveillance due to lack of transport and funding.[4]

Ineffective Social Mobilization and Demand Generation Activities

Activities designed for public awareness are often uncoordinated and poorly thought out. For example, misalignment between social-mobilization activities and actual implementation of the vaccine launch was reported in Uganda. The launch took place in only one district--while the campaign was countrywide. Caretakers in districts that did not participate in the launch ended up demanding the vaccine. Rushed implementation also led to inaccurate messages. For example, the wrong age groups were informed of the opportunity to receive the vaccine. In addition, rushed mobilization leads to shortage of materials at the health-facility level.

[3] MoH, Burundi 2013. Burundi situation analysis, multi year plan 2010-2014. 2013.

[4] MoH, Tanzania 2010. Expanded Program on Immunization 2010-2015. Comprehensive Multi Year Plan.

Maintaining the Cold Chain

The introduction of the new and/or expanded hepatitis A&B program presents a great opportunity to control diseases of public health importance. But it also comes with increased cold chain needs. For vaccines that are not combined with other traditional vaccines, these will definitely require additional space at each level of distribution. Many countries in the region lack or have not effectively implemented a cold chain maintenance policy. This gap in national policy could be responsible for the high percentage of cold chain equipment left in disrepair.

The Twinrix vaccination for hepatitis A and B. Courtesy SmithGlaxoKline.

It is important to keep the cold chain at e recommended temperatures to maintain the viability of vaccines. Vaccines should be stored at 2-8°C but not frozen, because freezing destroys the potency of the vaccine. This calls for continuous monitoring to:

- Ensure product efficacy and minimize vaccine failures
- Ensure proper resource management to reduce vaccine wastage
- Avoid lost opportunities to immunize especially in hard-to-reach areas
- Maintain confidence in public health by avoiding re-immunization of those who received ineffective vaccines.

Currently, the monitoring system using the vaccine vial monitor (VVM), informs health workers by color changes when vaccines are exposed to heat. But no equivalent detection method exists for damages caused by freezing exposure. A systematic literature review (Matthias et al. 2007) found that 34 out of 35 temperature studies cited freezing temperatures in the cold chain, and 14 of those found more than 50 percent occurrence of

freezing among recorded temperatures. Monitoring of fridge temperatures is expected to be done at least daily, but in most cases the temperature monitoring charts are updated weekly or monthly, depending on when the busy health workers are expecting support supervision. This lack of regular monitoring greatly affects the viability of vaccines.

Storage Capacity

Most countries in East-Africa have inadequate cold storage capacity at varying levels. Cold chain assessment in Rwanda in 2013 revealed that the national vaccine cold store did not have enough capacity to store its existing antigens and would require an additional 10.72 m3 capacity of storage space to take on new vaccines.[5] In addition, the majority of the health facilities did not have adequate storage to take on new vaccines. In Kenya, at central and regional levels, the situational analysis documented that there is adequate storage space at central vaccine storage facilities, but regional stores, district stores, and district facilities had inadequate space.[6] For more information, see Figure 9: Status of cold chain capacity—EAC.

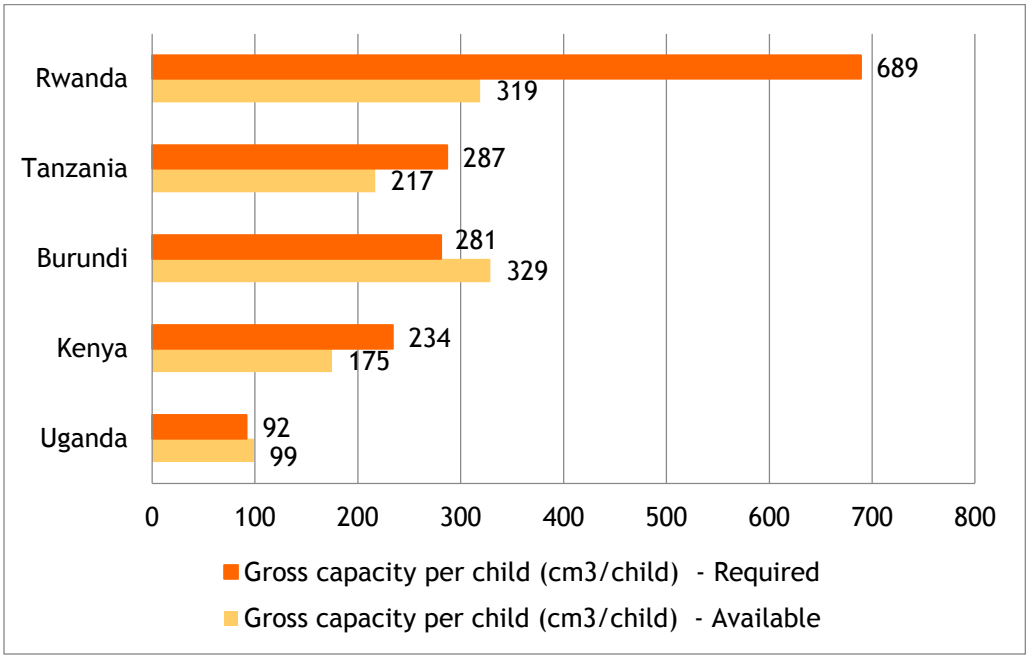


Figure 9: Status of cold chain capacity—EAC.

[5]Final Cold Chain Assessment Report, 2013, Rwanda.

[6]Ministry of Public Health and Sanitation, Kenya. Division of vaccine and immunization comprehensive multiyear plan 2013-2017. 2013.

Distribution of Cold Chain Equipment

In some countries, there is irrational distribution of the cold chain equipment not proportional to demographic data. This leads to underutilization of the equipment in the sparsely populated areas.

Inconsistent Vaccine Readiness

Previous experience in East Africa shows that there is lack of clear understanding of program-wide readiness for new vaccines. For example, countries were required to verify their readiness by confirming whether health workers were well trained and fridges labeled with stickers. Most of the countries, however focused on making cold chain space available, thereby failing the readiness assessment/test.

Failure to Effectively Manage Stakeholder Groups

Setting an unrealistic launch date during the application process because of inadequate planning or lack of understanding of the requirements can make it difficult to coordinate stakeholders effectively. Frequent adjustment of launch dates without clear proactive communication and lack of coordination of preparatory activities after the postponement decision weaken coordination efforts. Inability to adjust the launch date when postponement was desirable or necessary can negate earlier efforts at carrying out a successful launch.

Partnership Strategies for Vaccine Programs

Ineffective partnerships have shown:

- Lack of clear communication and assistance to countries to navigate GAVI's policies, processes, and procedures, especially with less experienced government managers
- Inadequate proactive communication among global and in-country levels
- Failure to explicitly define roles and responsibilities of partners
- Failure to provide broad perspective and coordination of inter-related processes for new vaccine introduction
- Emerging anti-immunization resistance groups, e.g. Triple 6 (Gospel Church) in Eastern Uganda and the polio boycott in northern Uganda
- Inadequate social mobilization activities for uptake of routine immunization services
- Failure to provide pre-emptive assistance to prevent crises and emergencies.

Reaching All Age Groups

Different age groups require different communications modalities. For example:

- 0-5 age group: Can be approached through the routine immunization schedule or at birth. All pregnant women should be tested for hepatitis B (HBsAg blood test); infants born to HBV-infected mothers should be given HBIG (hepatitis B immune globulin) and vaccine within 12 hours of birth.
- Older children: Can be reached through school programs
- Adolescents: Those in school can be reached through clinic visits and school health programs, though most of the school health programs require revitalization in East Africa. The program can piggyback on existing immunization programs such as human papilloma virus and TT vaccination for adolescents in schools. Adolescents out of school can be accessed through youth-friendly centers/corners and religious gatherings.
- Adults: Can be accessed through the existing community posts and outreach posts using a mass campaign approach.

Roles of the Public and Private Sectors

Public-private partnerships in their various forms are increasingly seen as playing a critical role in improving the performance of health systems worldwide, by bringing together the best characteristics of the public and private sectors to improve efficiency, quality, innovation, and health impact of both private and public systems.

Public Sector Roles

- Advocate for allocation of adequate resources for an expanded hepatitis A&B immunization program. For example, the health sectors should partner with a parliamentarian committee on social services to advocate for increased resource allocation. In addition, parliamentarians can be good advocates for the program within their constituencies
- Training of health workers and revising and updating guidelines as appropriate as well as disseminating guidelines
- Coordination of partnership among key partners
- Counteracting rumors and myths about immunization
- Establishing a robust M&E system to capture data, as well as conducting supervision and monitoring
- Setting standards for quality assurance
- Providing immunization services, including extending services in hard to reach areas.

- Establishing and operationalizing a robust surveillance system, including surveillance for adverse events following immunization
- Establishing a robust cold chain system and regularly providing cold chain maintenance services to ensure potency of vaccines at all levels
- Quantification and forecasting of needs for vaccine and related materials
- Creating awareness among communities on the benefits of immunization
- Developing a communications strategy to guide stakeholders
- Training health workers in immunization during pre-service training.

Private Sector Roles

- Participate in policy formulation
- Training health workers in vaccination policies and procedures, especially during pre-service training
- Providing immunization services to communities
- Community mobilization and education on benefits of immunization
- Carrying out program communication activities
- Maintaining cold chain facilities at their premises
- Resource mobilization to support underfunded program areas
- Distribution of vaccines
- Participating in collecting and submitting immunization data
- Conducting research and sharing lessons learned.

Policy Recommendations

1. Currently, 20 percent of children and adolescents ages 0–15 years, who should have been immunized for hepatitis B under a current Ministry of Health approved immunization protocol, have not been vaccinated. We recommend a clinic-based effort to reach this group.
2. All persons 16 years and older fell outside of the revised hepatitis B immunization programs for the region. For this subpopulation, we also recommend an adult immunization catch-up campaign against the hepatitis B virus.
3. In accordance with new WHO recommendations, the hepatitis B "birth dose" should be adopted as part of the routine immunization program.
4. Given the high percentage of births occurring outside of the clinical setting across the East Africa region, special programs should be designed and implemented to reach these infants with the hepatitis B birth dose.
5. Social marketing for the proposed catch up campaigns should also be a key component of the EAC's Five Year Communications Strategy for an Aflatoxin Safe East Africa Region.
6. Regional and national cancer registries should be strengthened to more accurately capture the actual incidence and prevalence of HCC.
7 Partner states and the EAC should seek funding for further research to better understand the relationships between the consumption of aflatoxin-contaminated commodities and its impact on the incidence of HCC, and interactions with the hepatitis A, B, and C viruses.
8. Information on aflatoxin, liver disease, preventive care, and diagnostics should be integrated into the curricula of medical and nursing schools, schools of public health, and training programs for community nutritionist and other health workers regionwide.
9. To further reduce high-risk practices for the transmission of HBV, efforts should be made to accelerate elimination of FGC.
10. To encourage infection control against HBV and HCV, male circumcision practices should conform with WHO guidelines.
11. BCC programs should be conducted to reach practitioners of scarification, tattooing, and other body piercing, to reduce the spread of HBV and HCV, especially among youth.

Appendix: Vaccine Needs Estimates

Introduction

This appendix provides a country-by-country vaccine needs estimation for hepatitis A and hepatitis B by age cohort, and the best available estimate of vaccine costs by EAC partner state. It also elaborates on the challenges of storing and transporting the vaccines, which require dry cold chain coverage, and the need for auxiliary supplies for vaccination delivery, administration, and reporting.

Immunization Coverage and Supply Chain Logistics

To reduce the risks of HCC associated with aflatoxins and viral hepatitis, it is recommended that populations at risk be immunized against hepatitis A and B viruses, which are associated with inflammation of the liver. There are safe and effective vaccines that can prevent hepatitis A and hepatitis B infections. Active immunization is recommended and consists of three injection vaccines of hepatitis B intramuscularly in the arm and two injections of hepatitis A.

Introducing these vaccines into the existing programs within the EAC partner states requires proper planning, which includes logistical support to ensure the availability of appropriate equipment and an adequate supply of high-quality vaccines and immunization-related materials to all levels of the program. It is also important to ensure correct implementation of relevant strategies to help save on program costs in ensuring program implementation efficiently without sacrificing the quality of service delivery.

The target populations for the introduction of hepatitis A and strengthening of hepatitis B vaccination have been computed using 2015 projected populations and specific risk target age groups, taking into consideration existing immunization coverage for hepatitis B. The target populations are the basis of the estimation of vaccines and related materials.

The UN Population Division's projected figures for the partner states for 2015 are: Burundi: 10.8 millon; Kenya: 47 million; Rwanda: 12 million; Tanzania: 48 million; and Uganda: 40 mllion.

Various age categories per country have been used to compute the needs. Age categories of under 1, 1 – 5 years, 6 – 15 years, 16 – 20 years, 21 – 30 years, 31 – 50 years and 51+ years have been considered for estimating needs. Following country-specific age distribution percentages of the total population, the computation for each country age category populations has been established.

The projected population for EAC partner countries for 2015 including those of the proposed target populations is summarized in Table 2.

The population in the East African countries is young, with over 70 percent below 30 years of age. The table below summarizes the population for each of the five countries by age cohort. The highest risk populations are prioritized for vaccination against hepatitis A and B.

Table 2: Population estimates by cohort in East Africa.

2015 Projected populations by age category-EAC					
Age Category	**Burundi**	**Kenya**	**Rwanda**	**Tanzania**	**Uganda**
Live births	432,520	1,596,266	347,984	1,592,644	1,685,926
1-5 years	1,524,633	6,572,860	1,615,640	7,239,291	6,623,282
6 -15 years	3,038,453	12,676,230	3,330,704	12,741,153	11,359,931
16-20 years	1,167,804	5,164,390	1,416,792	5,260,552	4,616,227
21-30 years	1,794,958	7,981,330	2,174,900	8,204,530	6,221,871
31-50 years	1,838,210	8,450,820	2,299,180	8,638,888	6,422,576
51 + years	1,016,422	4,507,104	1,242,800	4,584,884	3,211,288
Total	10,813,000	46,949,000	12,428,000	48,261,942	40,141,100

Source: Projected UN populations and country specific demographic profiles

Targeted Population for Each Antigen

There are four target groups categorized by antigen. Three target groups will be reached with HBV and one target group with HAV. Table 3 summarizes each category and the antigen planned for each group.

Table 3: Categorized target groups for immunization.

	Target group	Remarks
1	Target Group 1 (HBV) = 20 percent of each age category - Unvaccinated	The group includes a proportion of the population aged 1-15 years, which will be targeted for **hepatitis B vaccination**. The assumption is that 80 percent have been covered through routine immunization with pentavalent vaccine. Some 20 percent of the population aged between 1-15 years will therefore be targeted (unvaccinated).
2	Target Group 2 (HBV) = 95 percent of the age category - unvaccinated	The 95 percent of the population 16 years and above will be targeted for **hepatitis B vaccination.** The remaining 5 percent is estimated to have been covered by the private sector and the ongoing health workers' HBV vaccination.
3	Target Group 3 (HBV) = 100 percent of the live births	All live births will be targeted for **hepatitis B vaccination.**
4	Target Group 4 (HAV) = 100 percent of the age category	The entire population above one year will be targeted for **hepatitis A vaccination.**

Table 4 summarizes the target population and age categories in each partner state.

Table 4: Target population and age by country.

	Age	Burundi	Kenya	Rwanda	Tanzania	Uganda
Target Group 1 (HBV) 20 percent of each age category - unvaccinated	1 - 5 years	304,927	1,314,572	323,128	1,447,858	1,324,656
	6 - 15 years	607,691	2,535,246	666,141	2,548,231	2,271,986
	Total group 1	**912,617**	**3,849,818**	**989,269**	**3,996,089**	**3,596,643**
Target Group 2 (HBV) 95 percent of the age category - unvaccinated	16 - 20 years	1,109,414	4,906,171	1,345,952	4,997,524	4,385,416
	21 - 30 years	1,705,210	7,582,264	2,066,155	7,794,304	5,910,777
	31 - 50 years	1,746,300	8,028,279	2,184,221	8,206,944	6,101,447
	51 + years	965,601	4,281,749	1,180,660	4,355,640	3,050,724
	Total group 2	**5,526,524**	**24,798,462**	**6,776,988**	**25,354,411**	**19,448,364**
Target Group 3 (HBV) 100 percent of the live births	Live births	432,520	1,596,266	347,984	1,592,644	1,685,926
	Total group 3	**432,520**	**1,596,266**	**347,984**	**1,592,644**	**1,685,926**
Target Group 4 (HAV) 100 percent of the age category	1 - 5 years	1,524,633	6,572,860	1,615,640	7,239,291	6,623,282
	6 - 15 years	3,038,453	12,676,230	3,330,704	12,741,153	11,359,931
	16 - 20 years	1,167,804	5,164,390	1,416,792	5,260,552	4,616,227
	21 - 30 years	1,794,958	7,981,330	2,174,900	8,204,530	6,221,871
	31 - 50 years	1,838,210	8,450,820	2,299,180	8,638,888	6,422,576
	51 + years	1,016,422	4,507,104	1,242,800	4,584,884	3,211,288
	Total group	**10,380,480**	**45,352,734**	**12,080,016**	**46,669,298**	**38,455,175**

Vaccine Needs Estimation

The estimation of the planned introduction and strengthening of HAV and HBV vaccination programs is based upon target population and the expected immunization coverages per age categories. The vaccines and logistic estimates required for the implementation are computed by partner state by antigen.

Each of the targeted populations for hepatitis B vaccine will receive three doses of the vaccine while those targeted for hepatitis A will receive two doses of vaccine. This is adopted from the dose schedules from the Advisory Committee on Immunization Practices (ACIP) of the USA and the existing WHO recommended vaccination schedule for developing countries.

Estimations for the four categories have been considered.

- Hepatitis B vaccine for the populations with some coverage from DPT-HepB-Hib (pentavalent) vaccination coverage (1–15 years)
- Hepatitis B with no coverage history (16 years and above)
- Hepatitis B for live births to prevent mother-to-child transmission
- Hepatitis A for all above 1 year.

Hepatitis B Vaccine Needs Estimates

The hepatitis B vaccine is the mainstay of hepatitis B prevention. WHO recommends that all infants receive the hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. The birth dose should be followed by two or three doses to complete the primary series. The vaccine has an excellent record of safety and effectiveness.

The vaccine needs are guided by the statistics for the targeted population. The population estimates are as computed in Table 2 above. Table 3 shows the number of unvaccinated children with the pentavalent vaccine. As explained in part A of Table 5, 80 percent of the children reached is subtracted from the group that ought to have been reached with the routine pentavalent dose since the introduction of the vaccine in these countries in the year 2002. Part A thus summarizes the vaccine required to reach 20 percent of the population below the age of 15 years.

Part B of Table 5 indicates the HBV vaccine needs for population aged up to 16 years and above 16 years.

Table 5: HBV vaccine needs.

Part A: HBV vaccine needs for population aged 1 - 15 years (doses)					
Age Category	Burundi	Kenya	Rwanda	Tanzania	Uganda
1 - 5 years	114,347	492,965	121,173	542,947	496,746
6 - 15 years	227,884	950,717	249,803	955,586	851,995
Total	**342,231**	**1,443,682**	**370,976**	**1,498,533**	**1,348,741**
Part B: HBV vaccine needs for population aged 16 years and older (doses)					
Age Category	Burundi	Kenya	Rwanda	Tanzania	Uganda
16 - 20 years	4,160,302	18,398,139	5,047,322	18,740,715	16,445,307
21 - 30 years	6,394,538	28,433,488	7,748,081	29,228,639	22,165,414
31 - 50 years	6,548,623	30,106,046	8,190,829	30,776,037	22,880,427
51 + years	3,621,003	16,056,558	4,427,475	16,333,651	11,440,214
Total	**20,724,466**	**92,994,232**	**25,413,707**	**95,079,042**	**72,931,361**
Part C: HBV vaccine needs for live births (doses)					
Age Category	Burundi	Kenya	Rwanda	Tanzania	Uganda
Under 1 year	540,650	1,995,333	434,980	1,990,805	2,107,408
Total	**540,650**	**1,995,333**	**434,980**	**1,990,805**	**2,107,408**
Grand total	**21,607,348**	**96,433,246**	**26,219,662**	**98,568,381**	**76,387,510**

Table 5 Part A shows the vaccine needs for population aged 1-15 years of age. Most of this population has received at least 3 doses of HBV through the ongoing routine immunization programs for DPT+hepB+Hib (pentavalent). Based on routine administrative data reported from the countries in the year 2013, 80 percent of these populations have been covered. This leaves 20 percent of the population unimmunized. The vaccine and supplies required for this population to ensure that they are vaccinated remain to be computed.

For 16 years and above: 95 percent of this age category is believed to have not received HBV and will require vaccination. The group has been split into categories of 16-20, 21-30, 31-50, and 51+. Some 5 percent is assumed to have been covered by private clinics or during the health worker immunization programs.

Live births: 100 percent of this population will receive 1onedose at birth to prevent mother-to-child transmission of hepatitis B virus. This birth dose vaccine will become part of the routine immunization antigen to be annually planned for.[7]

Hepatitis A Vaccine Needs Estimates

Hepatitis A vaccination provides pre-exposure protection from HAV infection. It is recommended for persons who are at increased risk for infection and for any person wishing to obtain immunity. There are two types of hepatitis A vaccines currently in use worldwide: 1) formaldehyde inactivated vaccines, and 2) live attenuated vaccines. At least two doses of inactivated hepatitis A vaccine are needed to induce protective efficacies of 90-95 percent, or more. Inactivated hepatitis A vaccines both alone or in fixed combinations are widely used and licensed for use in children ≥12 months of age. The recommended dosage is a two-dose schedule with 6–12 (up to 18-36) months interval between doses.

At least four inactivated vaccines (Havrix®, Vaqta®, Epaxal®, and Avaxim®) are commercially available in some parts of the world. They all have excellent safety profiles and are highly immunogenic in humans. Nearly 100 percent of vaccines will develop protective levels of antibody within a month of the first dose of vaccine. Two doses of hepatitis A vaccine given six months apart ensure protection. We have estimated the needs for hepatitis A vaccination doses and equipment for all age categories in the EAC partner states, except for individuals who are not eligible for the vaccination. Table 6 shows these calculations.

Table 6: HAV vaccine needs, above 1 year (doses).

Age	Burundi	Kenya	Rwanda	Tanzania	Uganda
1 - 5 years	3,201,729	13,803,006	3,392,844	15,202,512	13,908,891
6 - 15 years	6,380,751	26,620,083	6,994,478	26,756,421	23,855,856
16 - 20 years	2,452,388	10,845,219	2,975,263	11,047,159	9,694,076
21 - 30 years	3,769,412	16,760,793	4,567,290	17,229,513	13,065,928
31 - 50 years	3,860,241	17,746,722	4,828,278	18,141,664	13,487,410
51 + years	2,134,486	9,464,918	2,609,880	9,628,257	6,743,705
Total	**21,799,008**	**95,240,741**	**25,368,034**	**98,005,526**	**80,755,865**

[7]The EAC partner states have set tentative introduction dates of birth dose HBV in their routine programs as follows: Burundi – 2017, Kenya –2017, Rwanda – 2018, Tanzania – 2018, and Uganda – 2017.

Cold and Dry Storage Demands for Vaccines

Ideal vaccine management principles are at the heart of delivering a high quality, safe, and effective immunization program in which patients and the public at large have confidence.

Exposing vaccines to freezing temperatures can result in irreversible damage that reduces vaccine efficacy. The extent of damage depends on vaccine type, the temperature the vaccine was exposed to, and exposure time. Live attenuated vaccines are more sensitive to heat than inactivated vaccines. However, every vaccine has different heat sensitivity and degradation rate, with the level of degradation accelerating as the temperature increases.

The delivery of vaccines must be subject to a rigorous cold chain maintenance procedure in which vaccines are stored, as per the manufacturer's recommendations, between +2°C and +8°C. Since national campaigns deal with huge numbers of vaccines, there are requirements for additional cold storage needs, including refrigerators, cold boxes, vaccine carriers, and ice packs. The volume of vaccines also requires dry storage needs for associated supplies.

The temporary expansion of the cold chain, dry storage, and vaccine transport systems must be considered. There will be extra fuel to operate additional cold chain equipment and vehicles required to accommodate the transportation of the vaccine (especially for vaccines with large storage requirements like HAV). In addition, there will be possible additional personnel costs from the usual routine with more frequent vaccine deliveries (e.g., drivers).

Supplies and Operations Cost Estimates

At its initial stage and during planning, there should be maintenance and repair of the existing equipment and vehicles needed to accommodate the vaccine. Similarly, there will be repairs, or sourcing for addition of, waste-management facilities to handle the additional medical waste generated by the new vaccine.

Additional costs include training of health workers at all levels, including refresher training. There will also be an adjustment increase in personnel, such as central staff from the WHO EPI and trained health workers to handle the additional workload and hence an increase in incentives and other personnel costs. The delivery of this vaccine will also require an increase in the number of EPI sessions due to the extra time needed to administer HBV and HAV vaccine and/or to an increase in demand for immunization services that it may generate.

The costs include vaccine costs, auto-disable syringes, safety boxes, operational costs ($1 per dose given), training, vaccine and supplies distribution, data collection tools and process monitoring and communication and social mobilization.[8]

Vaccine Costs

Hepatitis B Vaccines and Supplies

The costs for our estimates are in U.S. dollars (USD).

The UNICEF cost per dose for HBV vaccine including shipping procured through UNICEF will be USD 0.5 per dose. The costing is based on 10 dose vials with a wastage rate of 20 percent (wastage multiplier of 1.25).

The auto-disable syringes and needles of 0.5mL will cost approximately USD 0.06 per piece and the safety boxes are priced at USD 1 per 5 liter piece. These supplies have been estimated with wastage of 5 percent for both the syringes and needles.

The additional cold storage requirements have been estimated at USD 10 per liter. This may require local hiring for extra storage and freezing for ice packs for use during the campaigns. These costs are already included, as shown in the section titled Injection and Supplies Requirements by Country and Cohort. Operational costs include those required for training, transportation for vaccine and dry supplies, data collection tools, process monitoring, and communication and social mobilization activities. The unit cost for operations is estimated at USD 1 per dose given.

Table 7 summarizes the total cost (vaccines and operations) required to implement HBV vaccination in each country by targeted cohort.

[8]The procurement for the vaccine and associated supplies will be done in consultation and support from UNICEF Supply Division procurement procedures. The prices reflected are UNICEF subsidized costs.

Table 7: Hepatitis B vaccine and operation costs by country and cohort.

Hepatitis B vaccines supplies and operation costs for group 15 years and below						
Age	Burundi	Kenya	Rwanda	Tanzania	Uganda	Total cost (USD)
1 - 5 years	160,455	691,738	170,032	761,874	697,044	2,481,143
6 - 15 years	319,771	1,334,065	350,528	1,340,898	1,195,536	4,540,799
Total	480,226	2,025,803	520,561	2,102,772	1,892,580	7,021,942
Hepatitis B vaccines supplies and operation costs for target group 16 years+						
Age	Burundi	Kenya	Rwanda	Tanzania	Uganda	Total cost (USD)
16 - 20 years	5,837,819	11,098,126	7,082,502	26,297,347	23,076,384	73,392,177
21 - 30 years	8,972,943	17,151,649	10,872,263	41,014,210	31,102,952	109,114,017
31 - 50 years	9,189,159	18,160,569	11,493,535	43,185,551	32,106,273	114,135,086
51 + years	5,081,064	9,685,637	6,212,721	22,919,706	16,053,136	59,952,265
Total	29,080,985	56,095,980	35,661,021	133,416,813	102,338,744	356,593,545
Age	Burundi	Kenya	Rwanda	Tanzania	Uganda	Total cost (USD)
Total for live births	758,651	1,596,266	610,373	2,793,538	2,957,157	8,715,984
Grand total	30,319,862	59,718,050	36,791,955	138,313,123	107,188,481	372,331,471

Hepatitis A Vaccines and Supplies

Hepatitis A vaccine is available in single dose vials only. The cost is estimated at USD 15.6 per dose. The recommended dosage is a 2-dose schedule with 6-12 (up to 18-36) months interval between the two doses. Once it is introduced for massive use by programs, the cost is likely to drop. Another drop in price in the future is anticipated once the vaccine becomes available in multidose vials.

Table 8: Hepatitis A vaccine and operation costs by country and cohort.

Hepatitis A vaccines supplies and operation costs						
Age	Burundi	Kenya	Rwanda	Tanzania	Uganda	Total cost USD
1 - 5 years	53,362,841	216,907,338	56,548,127	238,899,871	231,817,833	797,536,009
6 - 15 years	106,347,222	418,321,294	116,576,139	420,463,772	397,602,707	1,459,311,135
16 - 20 years	40,873,666	170,427,194	49,588,358	173,600,573	161,570,005	596,059,794
21 - 30 years	62,824,338	263,387,482	76,122,479	270,753,187	217,768,267	890,855,752
31 - 50 years	64,338,177	278,880,863	80,472,335	285,087,179	224,793,050	933,571,604
51+ years	35,575,227	148,736,460	43,498,559	151,303,251	112,396,525	491,510,023
Total	200,583,729	1,496,660,631	422,805,996	832,964,215	790,990,545	3,744,005,116

Injection and Supplies Requirements by Country and Cohort

Burundi Country Calculations

1.BURUNDI : country calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
Burundi	10,813,000	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	#NAME?												
1 - 5 yrs	30,493	10	3	114,347	57,174	96,052	5,763	1,009	1,009	503	5,031	91,478	**160,455**
6 - 15yrs	60,769	10	3	227,884	113,942	191,423	11,485	2,010	2,010	1,003	10,027	182,307	**319,771**
Total	**91,262**			**342,231**	**171,116**	**287,474**	**17,248**	**3,018**	**3,018**	**1,506**	**15,058**	273,785	**480,226**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

2.BURUNDI : country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
Burundi	10,813,000	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
16 - 20 yrs	1,109,414	10	3	4,160,302	2,080,151	3,494,653	209,679	36,694	36,694	18,305	183,053	3,328,241	5,837,819
21 - 30 yrs	1,705,210	10	3	6,394,538	3,197,269	5,371,412	322,285	56,400	56,400	28,136	281,360	5,115,630	8,972,943
31 - 50 yrs	1,746,300	10	3	6,548,623	3,274,312	5,500,843	330,051	57,759	57,759	28,814	288,139	5,238,899	9,189,159
51 + yrs	965,601	10	3	3,621,003	1,810,502	3,041,643	182,499	31,937	31,937	15,932	159,324	2,896,803	5,081,064
Total	**5,526,524**			**20,724,466**	**10,362,233**	**17,408,552**	**1,044,513**	**182,790**	**182,790**	**91,188**	**911,877**	**16,579,573**	**29,080,985**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

3. BURUNDI : country calculations for HepB birth dose													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational	
Burundi	10,813,000	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
Live births	432,520	10	1	540,650	270,325	454,146	27,249	4,769	4,769	2,379	23,789	432,520	**758,651**
Total				**540,650**	**270,325**	**454,146**	**27,249**	**4,769**	**4,769**	**2,379**	**23,789**	**432,520**	**758,651**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

BURUNDI : country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
Burundi	10,813,000	**HepA Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	1,524,633	1	2	3,201,729	49,946,977	3,201,729	192,104	33,618	33,618	14,088	140,876	3,049,266	53,362,841
6 - 15yrs	3,038,453	1	2	6,380,751	99,539,720	6,380,751	382,845	66,998	66,998	28,075	280,753	6,076,906	106,347,222
16 - 20 yrs	1,167,804	1	2	2,452,388	38,257,259	2,452,388	147,143	25,750	25,750	10,791	107,905	2,335,608	40,873,666
21 - 30 yrs	1,794,958	1	2	3,769,412	58,802,824	3,769,412	226,165	39,579	39,579	16,585	165,854	3,589,916	62,824,338
31 - 50 yrs	1,838,210	1	2	3,860,241	60,219,760	3,860,241	231,614	40,533	40,533	16,985	169,851	3,676,420	64,338,177
51 + yrs	1,016,422	1	2	2,134,486	33,297,985	2,134,486	128,069	22,412	22,412	9,392	93,917	2,032,844	35,575,227
Total	**10,380,480**			**12,034,869**	**187,743,956**	**12,034,869**	**722,092**	**126,366**	**126,366**	**52,953**	**529,534**	**11,461,780**	**200,583,729**
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

Kenya Country Calculations

1.KENYA : country calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
KENYA	46,949,000	HepB Vial size	Doses per client	Total Doses required	Cost of vaccine	0.5 ml Ad syringes required	Cost of Ad syeinges	Safety Boxes required	Total cost of Safety Boxes	Extra cold chain net storage capacity(litres)	Cost of cold chain upgrade		Total Cost us$
category	population												
1 - 5 yrs	131,457	10	3	492,965	246,482	414,090	24,845	4,348	4,348	2,169	21,690	394,372	691,738
6 - 15yrs	253,525	10	3	950,717	475,359	798,602	47,916	8,385	8,385	4,183	41,832	760,574	1,334,065
Total				1,443,682	721,841	1,212,693	72,762	12,733	12,733	6,352	63,522	1,154,945	2,025,803
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

2.KENYA : country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs			
KENYA	46,949,000	HepB Vial size	Doses per client	Total Doses required	Cost of vaccine	0.5 ml Ad syringes required	Cost of Ad syeinges	Safety Boxes required	Total cost of Safety Boxes	Extra cold chain net storage capacity(litres)	Cost of cold chain upgrade	Operational Cost	Total Cost us$
category	population												
16 - 20 yrs	4,906,171	10	3	18,398,139	9,199,070	15,454,437	927,266	162,272	162,272	80,952	809,518	14,718,512	11,098,126
21 - 30 yrs	7,582,264	10	3	28,433,488	14,216,744	23,884,130	1,433,048	250,783	250,783	125,107	1,251,073	22,746,791	17,151,649
31 - 50 yrs	8,028,279	10	3	30,106,046	15,053,023	25,289,079	1,517,345	265,535	265,535	132,467	1,324,666	24,084,837	18,160,569
51 + yrs	4,281,749	10	3	16,056,558	8,028,279	13,487,509	809,251	141,619	141,619	70,649	706,489	12,845,246	9,685,637
Total	44,601,550			92,994,232	46,497,116	78,115,155	4,686,909	820,209	820,209	409,175	4,091,746	74,395,385	56,095,980
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

3. KENYA : country calculations for HepB (birth dose)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational	
KENYA	46,949,000	HepB Vial size	Doses per client	Total Doses required	Cost of vaccine	0.5 ml Ad syringes required	Cost of Ad syringes	Safety Boxes required	Total cost of Safety Boxes	Extra cold chain net storage capacity(litres)	Cost of cold chain upgrade		Total Cost us$
category	population												
live births	1,596,266	10	1	1,995,333	997,666	1,676,079	100,565	17,599	17,599	8,779	87,795	1,596,266	1,596,266
Total				1,995,333	997,666	1,676,079	100,565	17,599	17,599	8,779	87,795	1,596,266	1,596,266
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

KENYA: country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
KENYA: cou	46,949,000	HepA Vial size	Doses per client	Total Doses required	Cost of vaccine	0.5 ml Ad syringes required	Cost of Ad syringes	Safety Boxes required	Total cost of Safety Boxes	Extra cold chain net storage capacity(litres)	Cost of cold chain upgrade		Total Cost us$
category	population												
1 - 5 yrs	6,572,860	1	2	13,803,006	215,326,894	13,803,006	828,180	144,932	144,932	60,733	607,332	13,145,720	216,907,338
6 - 15yrs	12,676,230	1	2	26,620,083	415,273,295	26,620,083	1,597,205	279,511	279,511	117,128	1,171,284	25,352,460	418,321,294
16 - 20 yrs	5,164,390	1	2	10,845,219	169,185,416	10,845,219	650,713	113,875	113,875	47,719	477,190	10,328,780	170,427,194
21 - 30 yrs	7,981,330	1	2	16,760,793	261,468,371	16,760,793	1,005,648	175,988	175,988	73,747	737,475	15,962,660	263,387,482
31 - 50 yrs	8,450,820	1	2	17,746,722	276,848,863	17,746,722	1,064,803	186,341	186,341	78,086	780,856	16,901,640	278,880,863
51 + yrs	4,507,104	1	2	9,464,918	147,652,727	9,464,918	567,895	99,382	99,382	41,646	416,456	9,014,208	148,736,460
Total	45,352,734			95,240,741	1,485,755,566	95,240,741	5,714,444	1,000,028	1,000,028	419,059	4,190,593	90,705,468	1,496,660,631
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the above one population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

Rwanda Country Calculations

1.RWANDA: country calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational	
RWANDA	12,428,000	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	32,313	10	3	121,173	60,587	101,785	6,107	1,069	1,069	533	5,332	96,938	170,032
6 - 15yrs	66,614	10	3	249,803	124,901	209,834	12,590	2,203	2,203	1,099	10,991	199,842	350,528
Total	**98,927**			**370,976**	**185,488**	**311,620**	**18,697**	**3,272**	**3,272**	**1,632**	**16,323**	**296,781**	**520,561**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

2.RWANDA : country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Cost	
RWANDA	12,428,000	**HepB Vial**	**Doses per**	**Total Doses**	**Cost of**	**0.5 ml Ad**	**Cost of Ad**	**Safety Boxes**	**Total cost**	**Extra cold chain**	**Cost of cold**		**Total Cost us$**
category	population												
16 - 20 yrs	1,345,952	10	3	5,047,322	2,523,661	4,239,750	254,385	44,517	44,517	22,208	222,082	4,037,857	7,082,502
21 - 30 yrs	2,066,155	10	3	7,748,081	3,874,041	6,508,388	390,503	68,338	68,338	34,092	340,916	6,198,465	10,872,263
31 - 50 yrs	2,184,221	10	3	8,190,829	4,095,414	6,880,296	412,818	72,243	72,243	36,040	360,396	6,552,663	11,493,535
51 + yrs	1,180,660	10	3	4,427,475	2,213,738	3,719,079	223,145	39,050	39,050	19,481	194,809	3,541,980	6,212,721
Total	**6,776,988**			**25,413,707**	**12,706,853**	**21,347,513**	**1,280,851**	**224,149**	**224,149**	**111,820**	**1,118,203**	**20,330,965**	**35,661,021**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

3. RWANDA : country calculations for HepB (birth dose)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
RWANDA	12,428,000	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
Live births	347,984	10	1	434,980	217,490	365,383	21,923	3,837	3,837	1,914	19,139	347,984	610,373
Total				**434,980**	**217,490**	**365,383**	**21,923**	**3,837**	**3,837**	**1,914**	**19,139**	**347,984**	**610,373**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

RWANDA: country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
RWANDA: c	12,428,000	**HepA Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	1,615,640	1	2	3,392,844	52,928,366	3,392,844	203,571	35,625	35,625	14,929	149,285	3,231,280	56,548,127
6 - 15yrs	3,330,704	1	2	6,994,478	109,113,863	6,994,478	419,669	73,442	73,442	30,776	307,757	6,661,408	116,576,139
16 - 20 yrs	1,416,792	1	2	2,975,263	46,414,106	2,975,263	178,516	31,240	31,240	13,091	130,912	2,833,584	49,588,358
21 - 30 yrs	2,174,900	1	2	4,567,290	71,249,724	4,567,290	274,037	47,957	47,957	20,096	200,961	4,349,800	76,122,479
31 - 50 yrs	2,299,180	1	2	4,828,278	75,321,137	4,828,278	289,697	50,697	50,697	21,244	212,444	4,598,360	80,472,335
51 + yrs	1,242,800	1	2	2,609,880	40,714,128	2,609,880	156,593	27,404	27,404	11,483	114,835	2,485,600	43,498,559
Total	**12,080,016**			**25,368,034**	**395,741,324**	**25,368,034**	**1,522,082**	**266,364**	**266,364**	**111,619**	**1,116,193**	**24,160,032**	**422,805,996**
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

Tanzania Country Calculations

1.TANZANIA: country calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
TANZANIA	48,261,942	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	144,786	10	3	542,947	271,473	456,075	27,365	4,789	4,789	2,389	23,890	434,357	761,874
6 - 15yrs	254,823	10	3	955,586	477,793	802,693	48,162	8,428	8,428	4,205	42,046	764,469	1,340,898
Total	**399,609**			**1,498,533**	**749,267**	**1,258,768**	**75,526**	**13,217**	**13,217**	**6,594**	**65,935**	**1,198,827**	**2,102,772**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

2.TANZANIA : country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
TANZANIA	48,261,942	**HepB Vial**	**Doses per**	**Total Doses**	**Cost of**	**0.5 ml Ad**	**Cost of Ad**	**Safety Boxes**	**Total cost**	**Extra cold chain**	**Cost of cold**		**Total Cost us$**
category	population												
16 - 20 yrs	4,997,524	10	3	18,740,715	9,370,358	15,742,201	944,532	165,293	165,293	82,459	824,591	14,992,572	26,297,347
21 - 30 yrs	7,794,304	10	3	29,228,639	14,614,319	24,552,056	1,473,123	257,797	257,797	128,606	1,286,060	23,382,911	41,014,210
31 - 50 yrs	8,206,943	10	3	30,776,037	15,388,019	25,851,871	1,551,112	271,445	271,445	135,415	1,354,146	24,620,830	43,185,551
51 + yrs	4,355,640	10	3	16,333,651	8,166,825	13,720,267	823,216	144,063	144,063	71,868	718,681	13,066,921	22,919,706
Total	**25,354,411**			**95,079,042**	**47,539,521**	**79,866,395**	**4,791,984**	**838,597**	**838,597**	**418,348**	**4,183,478**	**76,063,234**	**133,416,813**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

3. TANZANIA : country calculations for HepB (birth dose)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
TANZANIA	48,261,942	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
live births	1,592,644	10	1	1,990,805	995,403	1,672,276	100,337	17,559	17,559	8,760	87,595	1,592,644	2,793,538
Total				**1,990,805**	**995,403**	**1,672,276**	**100,337**	**17,559**	**17,559**	**8,760**	**87,595**	**1,592,644**	**2,793,538**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

TANZANIA: country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Costs	
TANZANIA:	48,261,942	**HepA Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	7,239,291	1	2	15,202,512	237,159,183	15,202,512	912,151	159,626	159,626	66,891	668,911		238,899,871
6 - 15yrs	12,741,153	1	2	26,756,421	417,400,162	26,756,421	1,605,385	280,942	280,942	117,728	1,177,283		420,463,772
16 - 20 yrs	5,260,552	1	2	11,047,159	172,335,673	11,047,159	662,830	115,995	115,995	48,607	486,075		173,600,573
21 - 30 yrs	8,204,530	1	2	17,229,513	268,780,407	17,229,513	1,033,771	180,910	180,910	75,810	758,099		270,753,187
31 - 50 yrs	8,638,888	1	2	18,141,664	283,009,958	18,141,664	1,088,500	190,487	190,487	79,823	798,233		285,087,179
51 + yrs	4,584,884	1	2	9,628,257	150,200,816	9,628,257	577,695	101,097	101,097	42,364	423,643		151,303,251
Total	**46,669,298**			**53,006,091**	**826,895,018**	**53,006,091**	**3,180,365**	**556,564**	**556,564**	**233,227**	**2,332,268**		**832,964,215**
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

Uganda Country Calculations

1.UGANDA: country calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational	
UGANDA	40,141,100	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	132,466	10	3	496,746	248,373	417,267	25,036	4,381	4,381	2,186	21,857	397,397	697,044
6 - 15yrs	227,199	10	3	851,995	425,997	715,676	42,941	7,515	7,515	3,749	37,488	681,596	1,195,536
Total	**359,664**			**1,348,741**	**674,370**	**1,132,942**	**67,977**	**11,896**	**11,896**	**5,934**	**59,345**	**1,078,993**	**1,892,580**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

2.UGANDA : country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Cost	
UGANDA	40,141,100	**HepB Vial**	**Doses per**	**Total Doses**	**Cost of**	**0.5 ml Ad**	**Cost of Ad**	**Safety Boxes**	**Total cost**	**Extra cold chain**	**Cost of cold**		**Total Cost us$**
category	population												
16 - 20 yrs	4,385,415	10	3	16,445,307	8,222,653	13,814,058	828,843	145,048	145,048	72,359	723,594	13,156,246	23,076,384
21 - 30 yrs	5,910,777	10	3	22,165,414	11,082,707	18,618,947	1,117,137	195,499	195,499	97,528	975,278	17,732,331	31,102,952
31 - 50 yrs	6,101,447	10	3	22,880,427	11,440,214	19,219,559	1,153,174	201,805	201,805	100,674	1,006,739	18,304,342	32,106,273
51 + yrs	3,050,724	10	3	11,440,214	5,720,107	9,609,779	576,587	100,903	100,903	50,337	503,369	9,152,171	16,053,136
Total	**19,448,363**			**72,931,361**	**36,465,681**	**61,262,343**	**3,675,741**	**643,255**	**643,255**	**320,898**	**3,208,980**	**58,345,089**	**102,338,744**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

3. UGANDA : country calculations for HepB (birth dose)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
UGANDA	40,141,100	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes us$**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade us$**		**Total Cost us$**
category	population												
Live birhs	1,685,926	10	1	2,107,408	1,053,704	1,770,223	106,213	18,587	18,587	9,273	92,726	1,685,926	2,957,157
Total				**2,107,408**	**1,053,704**	**1,770,223**	**106,213**	**18,587**	**18,587**	**9,273**	**92,726**	**1,685,926**	**2,957,157**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

UGANDA: country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
UGANDA	40,141,100	**HepA Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	6,623,282	1	2	13,908,891	216,978,702	13,908,891	834,533	146,043	146,043	61,199	611,991	13,246,563	231,817,833
6 - 15yrs	11,359,931	1	2	23,855,856	372,151,349	23,855,856	1,431,351	250,486	250,486	104,966	1,049,658	22,719,863	397,602,707
16 - 20 yrs	4,616,227	1	2	9,694,076	151,227,580	9,694,076	581,645	101,788	101,788	42,654	426,539	9,232,453	161,570,005
21 - 30 yrs	6,221,871	1	2	13,065,928	203,828,478	13,065,928	783,956	137,192	137,192	57,490	574,901	12,443,741	217,768,267
31 - 50 yrs	6,422,576	1	2	13,487,410	210,403,590	13,487,410	809,245	141,618	141,618	59,345	593,446	12,845,152	224,793,050
51 + yrs	3,211,288	1	2	6,743,705	105,201,795	6,743,705	404,622	70,809	70,809	29,672	296,723	6,422,576	112,396,525
Total	**38,455,174**			**47,458,823**	**740,357,631**	**47,458,823**	**2,847,529**	**498,318**	**498,318**	**208,819**	**2,088,188**	**45,198,879**	**790,990,545**
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

EAC Summary

SUMMARY: calculations for HepB with coverage(15 and below)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
EA	158,593,042	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	Population												
1 - 5 yrs	471,514	10	3	1,768,178	884,089	1,485,269	89,116	15,595	15,595	7,780	77,800	1,414,542	2,481,143
6 - 15yrs	862,929	10	3	3,235,985	1,617,993	2,718,228	163,094	28,541	28,541	14,238	142,383	2,588,788	4,540,799
Total	1,334,444			5,004,163	**2,502,082**	**4,203,497**	**252,210**	**44,137**	**44,137**	**22,018**	**220,183**	**4,003,331**	**7,021,942**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

20% of age category populations are planned for catch up campaign. 80 % 0f these populations have been immunized during routine immunization.

SUMMARY: country calculations for HepB with coverage(16 and above)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
EA	158,593,042	**HepB Vial**	**Doses per**	**Total Doses**	**Cost of vaccine**	**0.5 ml Ad syringes**	**Cost of Ad syeinges**	**Safety Boxes**	**Total cost of Safety**	**Extra cold chain net**	**Cost of cold chain**		**Total Cost us$**
category	population												
16 - 20 yrs	16,744,476	10	3	62,791,785	31,395,892	52,745,099	3,164,706	553,824	553,824	276,284	2,762,839	50,233,428	88,110,688
21 - 30 yrs	25,058,709	10	3	93,970,160	46,985,080	78,934,934	4,736,096	828,817	828,817	413,469	4,134,687	75,176,128	131,860,807
31 - 50 yrs	26,267,190	10	3	98,501,962	49,250,981	82,741,648	4,964,499	868,787	868,787	433,409	4,334,086	78,801,570	138,219,923
51 + yrs	13,834,374	10	3	51,878,901	25,939,450	43,578,277	2,614,697	457,572	457,572	228,267	2,282,672	41,503,121	72,797,511
Total	**81,904,749**			**307,142,808**	**153,571,404**	**257,999,958**	**15,479,998**	**2,709,000**	**2,709,000**	**1,351,428**	**13,514,284**	**245,714,246**	**430,988,930**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

5% of the populations are assumed to have gotten HepB Vaccinations from the private sector and/or the health worker immunization programs

Wastege multiplier is 1,25 fo 10 dose vials

SUMMARY : country calculations for HepB (birth dose)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
EA	158,593,042	**HepB Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syringes**	**Safety Boxes required**	**Total cost of Safety Boxes us$**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade us$**		**Total Cost us$**
category	population												
Live birhs	5,655,340	10	1	7,069,175	3,534,588	5,938,107	356,286	62,350	62,350	31,104	311,044	5,655,340	9,919,608
Total	**5,655,340**			**7,069,175**	**3,534,588**	**5,938,107**	**356,286**	**62,350**	**62,350**	**31,104**	**311,044**	**5,655,340**	**9,919,608**
Costs; vaccine- 0.5 US$ per dose (10 dose vials UNICEF),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre.													

Wastage multplier is 1.25 for 10 dose vials

SUMMARY: country calculations for HepA (Above 1 year)													
2015 Projected Populations		Vaccines				Injection Materials				Cold chain Needs		Operational Cost	
EA	158,593,042	**HepA Vial size**	**Doses per client**	**Total Doses required**	**Cost of vaccine**	**0.5 ml Ad syringes required**	**Cost of Ad syeinges**	**Safety Boxes required**	**Total cost of Safety Boxes**	**Extra cold chain net storage capacity(litres)**	**Cost of cold chain upgrade**		**Total Cost us$**
category	population												
1 - 5 yrs	23,575,706	1	2	49,508,982	772,340,122	49,508,982	2,970,539	519,844	519,844	217,840	2,178,395	32,672,829	797,536,009
6 - 15yrs	43,146,471	1	2	90,607,589	1,413,478,390	90,607,589	5,436,455	951,380	951,380	398,673	3,986,734	60,810,637	1,459,311,135
16 - 20 yrs	17,625,764	1	2	37,014,105	577,420,034	37,014,105	2,220,846	388,648	388,648	162,862	1,628,621	24,730,425	596,059,794
21 - 30 yrs	26,377,589	1	2	55,392,936	864,129,804	55,392,936	3,323,576	581,626	581,626	243,729	2,437,289	36,346,117	890,855,752
31 - 50 yrs	27,649,674	1	2	58,064,315	905,803,308	58,064,315	3,483,859	609,675	609,675	255,483	2,554,830	38,021,572	933,571,604
51 + yrs	14,562,498	1	2	30,581,247	477,067,451	30,581,247	1,834,875	321,103	321,103	134,557	1,345,575	19,955,228	491,510,023
Total	**152,937,702**			**321,169,174**	**5,010,239,108**	**321,169,174**	**19,270,150**	**3,372,276**	**3,372,276**	**1,413,144**	**14,131,444**	**212,536,808**	**5,168,844,318**
Costs; vaccine- 15.6 US$ per dose (1 dose vials CDC Source),Ads 0.5ml= 0.06 US$, Safety boxes 5l = 1 us$ per piece,cold space = 10 us$ per litre of net storage capacity.													

100 % of the population to be vaccinated against hepatitis A vaccine.

The cost of HAV per dose is very high @15.6 US$ per dose. This si because the vaccine is available in single dose vials only. Once it is introduced for massive use by programs, ans it becomes available in multidose vials, the cost will drastically reduce to the level of the current cost of HBV.

Appendix: Aflatoxin, Hepatitis, and HCC in the EAC

Introduction

This appendix provides a case study of the relationship between aflatoxin contamination of food supplies in the EAC and the increased risk of hepatocellular carcinoma (HCC) in humans who consume the contaminated food.

This appendix also presents a quantitative risk assessment for the impacts of aflatoxin exposure, measured in estimated annual Disability Adjusted Life Years (DALYs) lost due to aflatoxin contamination-related HCC cases. Our methodology for the risk assessment and impact drills down to the national level for each EAC partner state, using data from national governments as available, the FAO, and the World Health Organization. We monetized DALY data with the measurement of VSL, value per statistical life, to calculate the economic benefits of addressing the issue of aflatoxin contamination and HCC. This assessment provides a starting point for measuring the positive economic impact of ameliorating HCC cases related to aflatoxin exposure.

The references section provides a extensive bibliography on the relationship between aflatoxin and hepatitis.

The Risk Assessment Process

Consumption of aflatoxin-contaminated food by humans has serious adverse health impacts on the populations in the EAC region. These health impacts, in turn, have serious economic consequences.

In this appendix, we consider one of the most serious health impacts of aflatoxin-contaminated food: the increased risk of hepatocellular carcinoma (HCC). We report on the results of a quantitative assessment of aflatoxin burden in 2012, measured by HCC risk, and the economic value of eliminating this risk.

To further study this causal relationship, we followed the four-step risk assessment process: hazard identification, dose-response assessment, exposure assessment, and risk characterization. To estimate this relationship, we relied on the cancer potencies developed by the Joint FAO/WHO Expert Committee on Food Additives to allow for a more consistent methodology across the EAC countries (World Health Organization, 1998).[9] Other health hazards do not have a well-established causal relationship (e.g.,

[9] Local studies are preferable for quantitative risk assessment, but they were not available for all countries in the analysis. Therefore we opted for a consistent dose-response specification for the EAC partner countries. This approach has been used by other supra-regional risk assessments (e.g., Liu and Wu 2010).

aflatoxin's impacts on stunting). Based on this finding, we conducted the quantitative analysis for only HCC and performed the remaining steps of the risk assessment. We then combined the results of the risk characterization with information on the potential economic value of reducing aflatoxin exposure risks. Figure 10 illustrates this methodology.

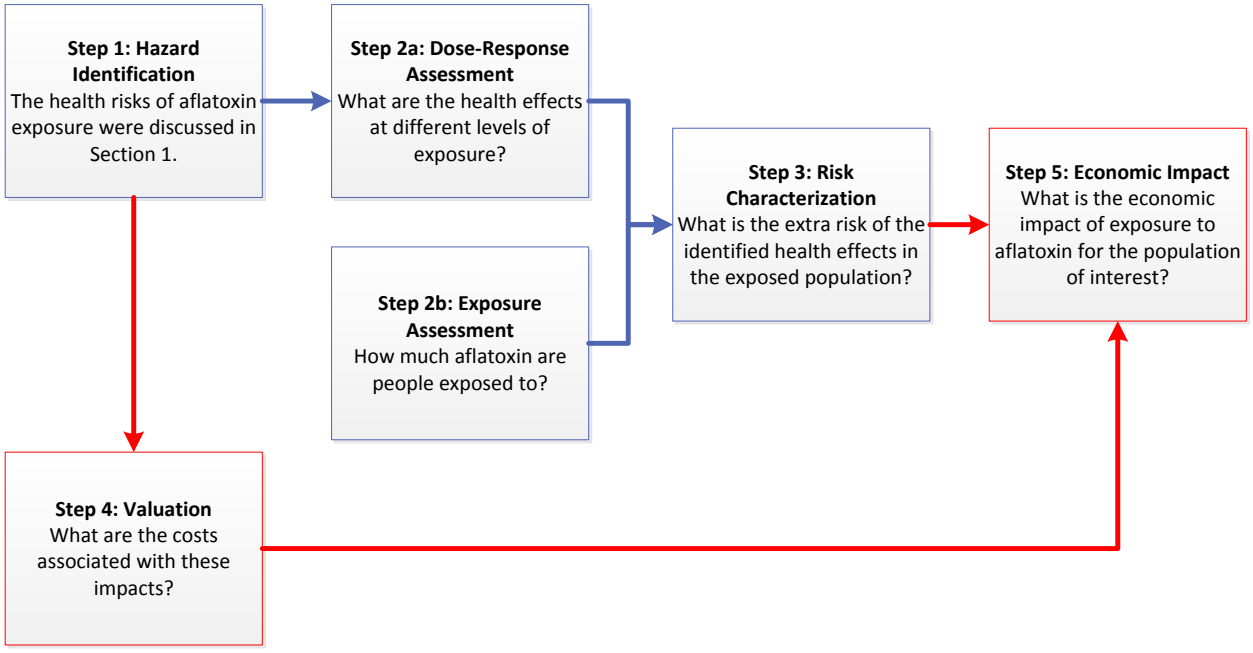


Figure 10: Estimating the economic impact of aflatoxin contamination.

Section Quantitative Risk Assessment for Economic Impacts of Aflatoxin, provides an extensive discussion of aflatoxin health hazards (hazard identification), and concludes that a causal relationship—that is, a dose/response relationship—exists between HCC and aflatoxin exposure.

The exposure assessment depends on both the levels of aflatoxin contamination in crops and the consumption levels of the crops. Figure 11 summarizes consumption information for maize and groundnuts, the staple crops of concern for the EAC region.[10] Data on daily consumption of maize and groundnuts was derived from the 2008-2009 World Bank Living Standards Measurement Study (LSMS) survey for Tanzania, while for the other four EAC countries, estimates of individual consumption are based on FAO Food Balance Sheets (FAO 2014). We converted these into consumption estimates per kilogram body weight using estimates of average body weight.[11]

Overall, the potential for exposure is high in Tanzania, Kenya, Burundi, and Uganda, in that order, because of high consumption of maize and peanuts (Figure 11).

10 Since our estimates are for maize and groundnuts only, the total impact of aflatoxin in food is likely to be underestimated.
11 For the four EAC countries lacking LSMS data, we may be overestimating average body weight and, thus, underestimating contaminated food consumption per kilogram body weight.

In Rwanda, the consumption of these two aflatoxin susceptible crops is low.
Since recent data on occurrence of aflatoxin B1 in maize and groundnuts is not consistently

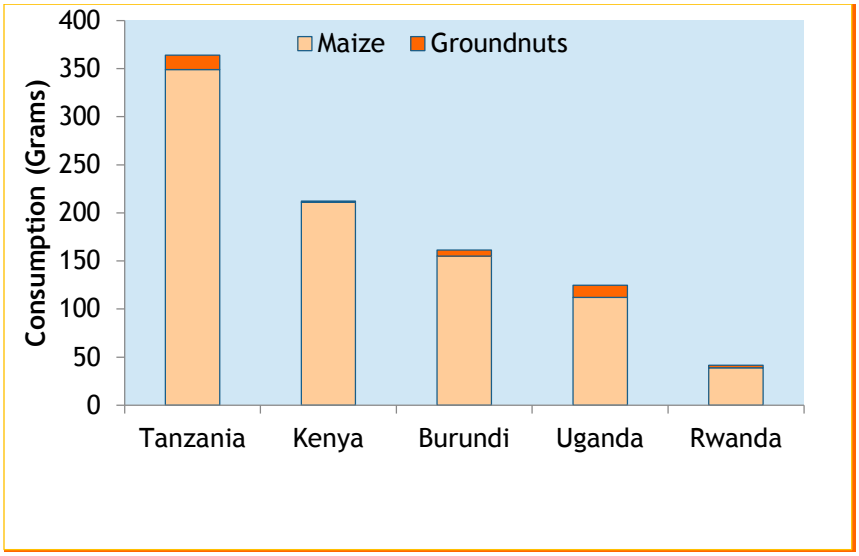


Figure 11: Maize and groundnuts consumption by country.

available for EAC countries, we conduct sensitivity analyses of income impact at different contamination levels: 4, 20, and 100 ppb, where 4 ppb and 20 ppb are the European Union (EU) and U.S. regulated levels.

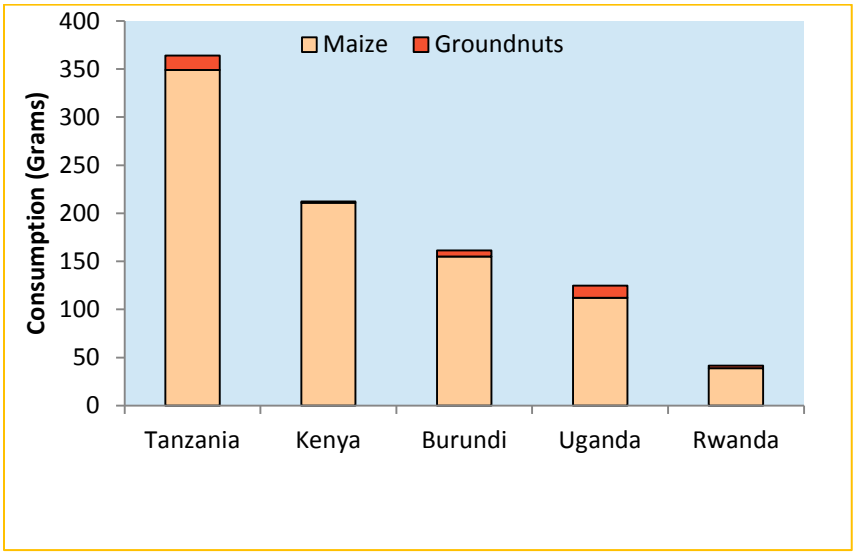


Figure 12: Maize and groundnuts consumption by country.

Health Impact Estimates

Our results are presented in Table 9.

Table 9: HCC incidence attributable to aflatoxin contamination.

		Aflatoxin Levels (ppb)		
Country	**Result Type[a]**	**4**	**20**	**100**
Burundi	Incidence	50	230	1,150
	DALY	1,800	8,800	44,000
	Value (Mill. 2012$)	2-10	*11-48*	56-238
	percent 2012 HCC incidence	9 percent	42 percent	209 percent
	percent 2012 GDP	0.4 percent	1.9 percent	9.6 percent
Kenya	Incidence	240	1,180	5,900
	DALY	9,000	45,200	226,100
	Value (Mill. 2012$)	12-49	58-244	289-1,221
	percent 2012 HCC incidence	10 percent	49 percent	245 percent
	percent 2012 GDP	0.1 percent	0.6 percent	3.0 percent
Rwanda	Incidence	10	60	320
	DALY	500	2,400	12,100
	Value (Mill. 2012$)	1-3	3-13	16-66
	percent 2012 HCC incidence	2 percent	9 percent	49 percent
	percent 2012 GDP	0.0 percent	0.2 percent	0.9 percent
Tanzania	Incidence	460	2,310	11,550
	DALY	17,700	88,700	443,500
	Value (Mill. 2012$)	17-74	85-372	427-1,860
	percent 2012 HCC incidence	18 percent	90 percent	451 percent
	percent 2012 GDP	0.3 percent	1.3 percent	6.6 percent
Uganda	Incidence	120	580	2,880
	DALY	4,400	22,100	110,400
	Value (Mill. 2012$)	6-24	*28-119*	141-596
	percent 2012 HCC incidence	6 percent	31 percent	153 percent
	percent 2012 GDP	0.1 percent	0.6 percent	3.0 percent

At the U.S.-regulated level for total aflatoxins (20 ppb), high reliance on maize and groundnuts in daily diets in all EAC countries except Rwanda implies that HCC incidence due to aflatoxin contamination could explain a very large percentage of overall 2012 HCC incidence in each country except Rwanda, accounting for 90 percent of cases in Tanzania and 49 percent in Kenya.[12]

[12] Note that the estimates for all countries except for Rwanda are implausible at 100 ppb (i.e., the incidence estimate is greater than overall HCC incidence).

For these countries, economic value estimates for an aflatoxin level at 20 ppb come close to 1 percent of the countries' GDP. These results indicate that public health damages from aflatoxin contamination in maize and groundnuts are significant relative to the size of the overall economy in all but one of the EAC countries. Even at the EU regulated levels, (4 ppb) high consumption of maize and groundnuts in the EAC countries means that HCC incidence due to aflatoxin contamination could explain as many as 18 percent of 2012 HCC incidence in Tanzania, 10 percent in Kenya, 9 percent in Burundi, and 6 percent in Uganda—which is not insignificant by any measure.

Sources for the consumption levels are: LSMS for Tanzania; EAC regional data from FAO for Burundi; and country-specific data for all other countries from FAO. Sources for body weights are: LSMS and WHO reference weights for Tanzania; and USAID Demographic and Health Surveys for the other countries. 2012 HCC incidence is based on the 2011 WHO rate of HCC deaths for each country. 2012 GDP is from the World Bank's World Development Indicators. The percentage of GDP is based on the high-end estimate. Italicized economic values indicate those where part of the range comes close to 1 percent of GDP and where the incidence estimate is plausible.[13]

In the face of uncertainty about aflatoxin occurrence, we estimate what the human health impacts would be if the population were exposed to aflatoxin levels at the different regulated levels. The results are alarming. Levels that are accepted as protective in the United States and EU may not be appropriate for EAC countries, where the reliance on aflatoxin susceptible crops—maize and groundnuts—is very high. This is notable, given that we may be underestimating overall health impacts because we do not account for the exposure resulting from other aflatoxin-susceptible crops.

Lack of household expenditure surveys from all partner states but Tanzania leads to further downward bias in our estimates. Furthermore, we do not account for all the health endpoints. Our results suggest that the value the residents of all EAC countries (except Rwanda) might be willing to pay to eliminate the risk of death from HCC attributable to aflatoxins is a measurable share of their countries' respective GDPs, suggesting that taxpayers' money can be invested to address this problem with public support. However, better surveillance of aflatoxin occurrence is needed to better address the problem.

[13]The estimates in Table 9 are based on current consumption levels. As discussed in detail Appendix 1, these consumption levels are uncertain, particularly for countries other than Tanzania, since household budget survey data were not used. Appendix 2 presents country-specific health impact estimates using a range of possible consumption levels.

Quantitative Risk Assessment for Economic Impacts of Aflatoxin

Dose Response

Although there are a number of regional and local studies estimating the relationship between HCC and aflatoxin exposure (Wogan 1975; Gong et al. 2012), we relied on the cancer potencies developed by the Joint FAO/WHO Expert Committee on Food Additives (World Health Organization 1998).[14] It is important to note that, in the case of HCC, the dose-response relationship is defined for aflatoxin B_1. This dose-response relationship between aflatoxin exposure, measured in nanograms (ng) of aflatoxin per kilogram (kg) of body weight (bw) per day, and HCC incidence per 100,000 population is linear. Further, consistent with other carcinogens, *it is assumed that the dose-response relationship does not have a threshold, meaning that any aflatoxin exposure level can cause a risk*.

Cancer potency (i.e., an increase in annual HCC incidence rate per unit change in aflatoxin exposure) varies across populations by HBV status: There is a 30-fold higher HCC risk for HBV-positive individuals. Specifically, in HBV-positive populations, aflatoxin HCC potency is 0.3 cancers/year per 100,000 population per one ng/kg-bw/day, while in HBV-negative populations, aflatoxin HCC potency is 0.01 cancers/year per 100,000 population per one ng/kg-bw/day (World Health Organization 1998). Therefore, we explicitly model this HBV status-related variability in our assessment.

Exposure Assessment

Dietary-based exposure assessment requires information on the amount of aflatoxin-contaminated food consumed by individuals, and the concentration of aflatoxin in the food. In addition, the body weight of the individual affects health impacts.

Exposure assessment establishes the total exposure to aflatoxins, which is estimated by multiplying the amount of food consumed (in grams per day) and aflatoxin concentration in the consumed food (measured in nanograms of aflatoxin per gram of food) divided by the total body weight of the person (measured in kilograms).

$$\text{Exposure (ng/kg-bw/day)} = \frac{\text{AmountConsumed}(\frac{g}{day})\text{X Aflatoxin Concentration (ng/g)}}{\text{Body Weight (kg)}}$$

In our assessment, we focused on consumption of maize and groundnuts, the crops of concern for the EAC region. Since our estimates are for maize and groundnuts only, the total impact of

[14] Local studies are preferable for quantitative risk assessment, but they were not available for all countries in the analysis. Therefore we opted for a consistent dose-response specification for the EAC partner countries. This approach has been used by other supra-regional risk assessments (Liu and Wu 2010).

aflatoxin in food is likely to be underestimated. Since recent data on occurrence of aflatoxin B_1 in maize and groundnuts are not consistently available for EAC countries, we conducted sensitivity analyses at different contamination levels: 4, 20, and 100 ppb. In addition, due to differences in data availability across the EAC countries, we took different approaches to estimating the ratio of daily consumption amounts to body weight.

Tanzania

For Tanzania, information on consumption was derived from the 2008-2009 World Bank *Living Standards Measurement Study* survey for Tanzania that provides household-level weekly consumption of various food items and several individual characteristics (age, sex, height, and/or weight).To allocate household consumption to individuals and obtain estimates of individuals' daily consumption of maize and groundnuts, we used the Adult Male Equivalent approach that has been applied to develop inputs for food fortification and other nutrition program evaluations (Neufeld et al. 2012). This approach uses individuals' age and sex, reference body weights from WHO, basal metabolic rate (BMR) based on body weight, and physical activity levels (PAL) to calculate total daily energy requirements (TEE).[15] Once age- and sex-specific estimates of daily consumption-to-body weight ratios were estimated, we used sex-specific life expectancies to compute the corresponding lifetime average ratios. These ratios were used to characterize risk.

Burundi, Kenya, Rwanda, and Uganda

For these countries, estimates of individual consumption are based on FAO Food Balance Sheets (FAO 2014). The balance sheets are calculated at the national level and provide estimates of per capita supply of specific food items, including maize and groundnuts.[16] FAO uses production and trade data to calculate national-level food supply, which is then divided by the relevant population. FAO (2001) notes that per capita supply is sometimes used as an approximation of individual consumption, but this measure may overestimate the amount of food actually consumed, due to losses in the household (during storage, preparation, and cooking, etc.). However, the production statistics available for each country are often based on commercialized crops only, and do not include households' production for their own consumption.

[15]WHO reference weights: We use the weights provided by Weisell and Dop (2012) for adult men and women and WHO weight-for-age tables for children aged 0-9 years. For children aged 10-17 years, weight-for-age tables are not available. Therefore, we estimate body weight based on body mass index (BMI) and height at each age, using WHO reference tables. Note that the estimated weights (based on BMI) for age 17 would be higher than the adult weights given by Weisell and Dop (2012). Therefore, we truncate weights at 64 kg for males and 55 kg for females. BMR equations: BMR equations are provided in Schofield (1985) for adults and Table 5.2 of FAO (2004) for children. PAL: We assume a PAL value of 1.75 based on Weisell and Dop (2012). TEE equations: The equations for TEE are from Section 4.2 of FAO (2004) for children and from Section 5.3 of FAO (2004) for adults.

[16] Note that country-specific data were not available for Burundi, so we used data for East Africa in general.

Given that a large portion of the maize and groundnut harvest is used for producers' at-home consumption, the food balance sheets may underestimate individual consumption.

To obtain consumption estimates per kilogram of body weight for these four EAC countries, we relied on multiple data sources. We used the latest available USAID Demographic and Health Surveys (DHS) to get average country-specific body weights for adult females (aged 15 or older).[17] Available DHSs did not collect anthropometric data for adult males (ages 15 or older). Therefore, we estimated average adult male body weights by adjusting DHS-based anthropometric data for adult females using information on country-specific: (i) age-standardized male-to-female BMI ratio based on WHO; and (ii) male-to-female height ratio based on Gustafsson and Lindenfors (2008).

For children aged one to four years, we derived sex-specific average body weights using DHS data on sex- and country-specific shares of children below -3 standard deviation (SD) and -2SD of WHO 2007 weight reference curves. The average sex-specific weights for children aged 5–14 years were computed using linear interpolation between estimated weight at age four and estimated weight in adulthood. Finally, we calculated average country-specific body weight (individuals aged one year and older) using age- and sex-specific population shares based on 2012 data from the international census. We note, however, that for Tanzania this estimation procedure generated an average body weight estimate that was higher than the LSMS-based body weight estimate (43 kg vs. 39 kg). Therefore, for the four EAC countries lacking LSMS data, we may be overestimating average body weight and, thus, underestimating contaminated food consumption per kilogram body weight. Table 10 presents the estimated average consumption of maize and groundnuts in grams per person, as well as per person per kilogram of body weight.

Table 10: Average consumption of maize and groundnuts in EAC countries.

	Grams per day		Grams per day per kg body weight	
Country	**Maize**	**Groundnuts**	**Maize**	**Groundnuts**
Burundi	211	6.3	3.9	0.20
Kenya	39	1.1	4.7	0.02
Rwanda	349	2.5	0.9	0.06
Tanzania	112	15	8.9	0.40
Uganda		12.6	2.6	0.30

Sources: Tanzania LSMS (2009); FAO Food Balance Sheets (2014)

[17] The latest available DHSs for each country are: 2008-09 for Kenya, 2010 for Burundi and Rwanda, and 2011 for Uganda.

Risk Characterization

The population cancer risk is estimated by multiplying the aflatoxin exposure with the HCC potency, which is an average of HBV status-specific HCC potencies (Bowers et al. 1993), weighted by HBV prevalence in each country (based on Ott et al. 2012):

Population Risk (cancers/year/100,000) = Exposure ×

(Share of HBV-positive × HBV-positive HCC Potency +

Share of HBV-negative × HBV-negative HCC Potency)

To derive the annual number of HCC cases that occur due to aflatoxin exposure, we multiplied the estimated population risk by the country populations (expressed in 100,000's).[18]

Disability Adjusted Life Years (DALYs) Lost

Using the assumption that all estimated HCC cases result in death within the same year, we estimated annual Disability Adjusted Life Years (DALYs) lost due to aflatoxin contamination-related HCC cases. DALY is an epidemiological measure of disease burden expressed in the number of healthy life years lost due to death or disability caused by disease. We used estimates of total HCC deaths and total HCC DALYs from WHO Global Health Estimates for 2011 (WHO 2013) to derive a DALY value for an HCC case in eastern Africa.[19]

Potential Economic Value of Eliminating Excess HCC Risk

Assuming that all estimated HCC cases result in death within the same year, we estimated the economic value that residents of the respective EAC countries might place on elimination of the aflatoxin-related HCC death risk in 2012. We used a value transfer approach proposed by Hammitt and Robinson (2011). Specifically, we started with an estimate of willingness to pay for small changes in mortality risk—i.e., the value per a statistical life (VSL)—developed for the OECD.[20] This value was adjusted for differences in income per capita between OECD countries and each EAC country.[21] Following recommendations in Hammitt and Robinson (2011), we assumed that mortality risk reductions were a luxury good and used income elasticity values of one and two for the transfer. We bound the derived VSL estimate from below using the present value of future consumption (at a 3 percent discount rate).[22]

[18] Note that for Tanzania, population risk was characterized separately in each region for males and females by estimating sex-specific maize and groundnut consumption, HBV prevalence, and population.

[19] We derived sex-specific HCC DALY estimates using WHO's AFR region data. The estimated value for males was 40.7 DALYs per HCC case and the estimated value for females was 36.1 DALYs per HCC case.

[20] This OECD VSL is $2.9 million in 2005 USD at 2005 income levels (OECD 2011). It was adjusted for inflation and income growth between 2005 and 2010. The updated VSL value used in our calculations was USD $3.4 million in 2012 U.S. dollars.

[21] The Purchasing Power Parity (PPP) based GNI per capita for 2012 (from the World Development Indicators Database, http://data.worldbank.org/indicator) were used in all calculations.

[22] We derived country-specific VSL estimates (upper and lower bounds) in 2012 USD dollars: $18,000-$72,000 for Burundi; $49,000-$207,000 for Kenya; $33,000-$134,000 for Rwanda; $37,000-$161,000 for Tanzania; and $31,000-$128,000 for Uganda.

Health Impact Sensitivity Analysis for EAC Countries

The tables below show the health impact results for each country, using a range of consumption levels. For each country, we estimated overall HCC mortality incidence, based on WHO HCC mortality rates (WHO 2013) and 2012 population estimates from the U.S. Census Bureau's International Data Base (U.S. Census 2013).

Table 11 reports our estimates of aflatoxin-attributable HCC incidence and DALYs for 2012.

Table 12 reports the corresponding valuation estimates for Burundi. In 2012, we estimated an overall HCC mortality incidence of 550. Therefore, some of the aflatoxin-attributable HCC incidence estimates in Table 11 are implausible (see values in italics), since they correspond to over 100 percent of the current HCC incidence.

Table 12 shows that, for the plausible estimates of attributable HCC incidence, the economic value of eliminating the aflatoxin-related HCC death risk (at high VSL estimate) is greater than 0.5 percent of GDP in 2012 for the following combinations of aflatoxin contamination and consumption levels: 100 ppb aflatoxin and 50 g/person (60kg)/day; 20 ppb aflatoxin and 200 g/person (60kg)/day; and 4 ppb aflatoxin and 500 g/person (60kg)/day. Economic values based on implausible incidence estimates are italicized.

Table 11: Estimated aflatoxin-attributable HCC and DALYs for Burundi, 2012.

Aflatoxin Level (ppb)	Incidence			DALY		
	50	**200**	**500**	**50**	**200**	**500**
4	10	40	90	400	1,400	3,600
20	50	190	*470*	1,800	7,200	18,100
100	240	*940*	*2,360*	9,000	*36,200*	*90,400*

Notes: DALY estimates are based on sex-specific HCC DALY estimates using WHO's AFR region data: 40.7 DALYs per HCC case for males, and 36.1 DALYs per HCC case for females. Total annual HCC incidence in Burundi was 550 in 2012. Italicized values for incidence are implausible (i.e., they are greater than overall HCC mortality incidence). Italicized values for DALYs are based on implausible incidence estimates.

Table 12: Value of eliminating aflatoxin-related HCC mortality risk, Burundi, 2012.

Aflatoxin Level (ppb)	Low Value (mill. 2012$)			High Value (mill. 2012$)		
	50	200	500	50	200	500
4	0.5	2	5	2	8	20
20	2	9	23	10	39	98
100	12	*46*	*116*	49	*195*	*488*

Notes: We derived a VSL estimate for Burundi of $18,000-$72,000, in U.S. 2012 dollars. 0.5 percent of GDP in Burundi was $1.2 million in 2012. Italicized values are based on implausible incidence estimates.

Table 13 shows our estimates of aflatoxin-attributable HCC incidence and DALYs for 2012 in Kenya; Table 14 reports the corresponding valuation estimates. Given an overall HCC mortality incidence of 2,410 in Kenya, some of the aflatoxin-attributable HCC incidence estimates in Table 13 are implausible (in italics), since they correspond to over 100 percent of the current HCC incidence. Table 14 shows that, for the plausible estimates of attributable HCC incidence, the economic value of eliminating the aflatoxin-related HCC mortality risk (at high VSL estimate) is greater than 0.5 percent of GDP in 2012 for one combination of aflatoxin contamination and consumption level: 100 ppb aflatoxin and 50 g/person (60kg)/day.

Table 13: Aflatoxin-attributable HCC incidence and DALYs for Kenya, 2012.

Aflatoxin Level (ppb)	Incidence			DALY		
	50	200	500	50	200	500
4	40	170	420	1,600	6,400	15,900
20	210	830	2,070	7,900	31,800	79,500
100	1,040	*4,150*	*10,370*	39,700	*159,000*	*397,400*

Notes: DALY estimates are based on sex-specific HCC DALY estimates using WHO's AFR region data: 40.7 DALYs per HCC case for males, and 36.1 DALYs per HCC case for females. Total annual HCC incidence in Kenya was 2,410 in 2012. Italicized values for incidence are implausible (i.e., they are greater than overall HCC mortality incidence). Italicized values for DALYs are based on implausible incidence estimates.

Table 14: Value of eliminating aflatoxin-related HCC mortality risk Kenya, 2012.

Aflatoxin Level (ppb)	Low Value (mill. 2012$)			High Value (mill. 2012$)		
	50	200	500	50	200	500
4	2	8	20	9	34	86
20	10	41	102	43	172	429
100	51	*203*	*508*	215	*859*	*2,147*

Notes: We derived a VSL estimate for Kenya of USD $49,000-$207,000, in. 2012 dollars .0.5 percent of GDP in Kenya was USD $20.1 million in 2012. Italicized values are based on implausible incidence estimates.

Table 15 reports our estimates of aflatoxin-attributable HCC incidence and DALYs for 2012 in Rwanda; Table 16 reports the corresponding valuation estimates. Given an overall HCC mortality incidence of 650 in Rwanda, some of the aflatoxin-attributable HCC incidence estimates in Table 15 are implausible (values in italics), corresponding to over 100 percent of the current HCC incidence. Table 16 shows that, for the plausible estimates of attributable HCC incidence, the economic value of eliminating the aflatoxin-related HCC mortality risk (at high VSL estimate) is greater than 0.5 percent of GDP in 2012 for the following combinations of aflatoxin contamination and consumption levels: 100 ppb aflatoxin and 50 g/person (60kg)/day; and 20 ppb aflatoxin and 200 g/person (60kg)/day.

Table 15: Aflatoxin-attributable HCC incidence and DALYs for Rwanda, 2012.

Aflatoxin Level (ppb)	Incidence			DALY		
	50	200	500	50	200	500
4	10	50	110	400	1,700	4,300
20	60	230	560	2,200	8,600	21,600
100	280	*1,130*	*2,820*	10,800	*43,200*	*108,100*

Notes: DALY estimates are based on sex-specific HCC DALY estimates using WHO's AFR region data: 40.7 DALYs per HCC case for males, and 36.1 DALYs per HCC case for females. Total annual HCC incidence in Rwanda was 650 in 2012. Italicized values for incidence are implausible (i.e., they are greater than overall HCC mortality incidence). Italicized values for DALYs are based on implausible incidence estimates.

Table 16: Value of eliminating aflatoxin-related HCC mortality risk, Rwanda, 2012.

Aflatoxin Level (ppb)	Low Value (mill. 2012$)			High Value (mill. 2012$)		
	50	**200**	**500**	**50**	**200**	**500**
4	0.6	2	6	2	9	23
20	3	11	28	12	47	117
100	14	*55*	*138*	58	*233*	*584*

Notes: We derived a VSL estimate for Rwanda of USD $33,000-$134,000, in 2012 dollars. 0.5 percent of GDP in Rwanda was USD $3.6 million in 2012. Italicized values are based on implausible incidence estimates.

Table 17 reports our estimates of aflatoxin-attributable HCC incidence and DALYs for 2012 in Tanzania, while Table 18 reports the corresponding valuation estimates. Given an overall HCC mortality incidence of 650 in Tanzania, some of the aflatoxin-attributable HCC incidence estimates in Table 17 are implausible (see values in italics), since they correspond to over 100 percent of the current HCC incidence. Table 18 shows that, for the plausible estimates of attributable HCC incidence, the economic value of eliminating the

aflatoxin-related HCC mortality risk (at high VSL estimate) is greater than 0.5 percent of GDP in 2012 for the following combinations of aflatoxin contamination and consumption levels: 100 ppb aflatoxin and 50 g/person (60kg)/day; and 20 ppb aflatoxin and 200 g/person (60kg)/day.

Table 17: Aflatoxin-attributable HCC incidence and DALYs for Tanzania, 2012.

Aflatoxin Level (ppb)	Incidence			DALY		
	50	200	500	50	200	500
4	40	180	440	1,700	6,800	17,000
20	220	890	2,220	8,500	34,000	85,000
100	1,110	*4,430*	*11,070*	42,500	*170,000*	*424,900*

Notes: DALY estimates are based on sex-specific HCC DALY estimates using WHO's AFR region data: 40.7 DALYs per HCC case for males, and 36.1 DALYs per HCC case for females. Total annual HCC incidence in Tanzania was 2,560 in 2012.Italicized values for incidence are implausible (i.e., they are greater than overall HCC mortality incidence). Italicized values for DALYs are based on implausible incidence estimates.

Table 18: Value of eliminating aflatoxin-related HCC mortality risk, Tanzania, 2012.

Aflatoxin Level (ppb)	Low Value (mill. 2012$)			High Value (mill. 2012$)		
	50	200	500	50	200	500
4	2	7	16	7	29	71
20	8	33	82	36	143	357
100	41	*164*	*410*	178	*713*	*1,783*

Notes: We derived a VSL estimate for Tanzania of $37,000-$161,000, in U.S. 2012 dollars.0.5 percent of GDP in Tanzania was $14.1 million in 2012. Italicized values are based on implausible incidence estimates.

Table 19 reports our estimates of aflatoxin-attributable HCC incidence and DALYs for 2012 in Uganda, while Table 20 reports the corresponding valuation estimates. Given an overall HCC mortality incidence of 1880 in Uganda, some of the aflatoxin-attributable HCC incidence estimates in Table 19 are implausible (see values in italics), since they correspond to over 100 percent of the current HCC incidence. Table 20 shows that, for the plausible estimates of attributable HCC incidence, the economic value of eliminating the aflatoxin-related HCC mortality risk (at high VSL estimate) is greater than 0.5 percent of GDP in 2012 for the following combinations of aflatoxin contamination and consumption levels: 100 ppb aflatoxin and 50 g/person (60kg)/day; and 20 ppb aflatoxin and 200 g/person (60kg)/day.

Table 19: Aflatoxin-attributable HCC incidence and DALYs for Uganda, 2012.

Aflatoxin Level (ppb)	Incidence			DALY		
	50	200	500	50	200	500
4	30	130	330	1,300	5,000	12,600
20	170	660	1,650	6,300	25,200	63,100

100	820	*3,290*	*8,230*	31,500	*126,100*	*315,400*

Notes: DALY estimates are based on sex-specific HCC DALY estimates using WHO's AFR region data: 40.7 DALYs per HCC case for males, and 36.1 DALYs per HCC case for females. Total annual HCC incidence in Uganda was 1,880 in 2012. Italicized values for incidence are implausible (i.e., they are greater than overall HCC mortality incidence). Italicized values for DALYs are based on implausible incidence estimates.

Table 20: Value of eliminating aflatoxin-related HCC mortality risk, Uganda, 2012.

Aflatoxin Level (ppb)	Low Value (mill. 2012$)			High Value (mill. 2012$)		
	50	**200**	**500**	**50**	**200**	**500**
4	2	6	16	7	27	68
20	8	32	81	34	136	341
100	40	*161*	*403*	170	*681*	*1,703*

Notes: We derived a VSL estimate for Uganda of USD $31,000-$128,000, in U.S. 2012 dollars. 0.5 percent of GDP in Uganda was $10.0 million in 2012. Italicized values are based on implausible incidence estimates.

List of Abbreviations and Definitions

Term	Definition
ACIP	Advisory Committee on Immunization Practices
AEFI	adverse events following immunization
AID	U.S. Agency for International Development
BCC	Behavior change and communication
BMI	Body Mass Index
BMR	Basal metabolic rate
CDC	U.S. Centers for Disease Control and Prevention
DALY	Disability Adjusted Life Year
DHS	Demographic and Health Survey
DNA	deoxyribonucleic Acid
DPT	(Diphtheria, Pertussis, Tetanus vaccine
EAC	East African Community
EPI	Expanded Program on Immunization
EU	European Union
FAO	UN Food and Agriculture Organization
FGC	female genital cutting
GAVI	Global Alliance for Vaccines and Immunization
HAV	hepatitis A virus
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
IARC	International Agency for Research on Cancer
IITA	International Institute of Tropical Agriculture
PAL	physical activity level
LSMS	Living Standards Measurement Study
M&E	Monitoring and Evaluation

MCHIP	Maternal Child Health Immunization Program
ppb	parts per billion
ppm	parts per million
PPP	Purchasing Power Party
RMNCH	Reproductive, Maternal, Neonatal, Child and Adolescent Health
SD	standard deviation
TT	Tetanus Toxoid
UN	United Nations
UNICEF	United Nations International Children's Emergency Fund
USD	U.S. dollar
VIG	Vaccine Introduction Grant
VVM	Vaccine Vial Monitor
VSL	Value per statistical life
WHO	World Health Organization

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