ANALYSIS ON THE BURDEN OF HELMINTHS-*Plasmodium falciparum* POLYPARASITISM, EFFECT ON ANAEMIA AND THE ROLE OF INTEGRATED SCHOOL BASED PARASITE CONTROL AND HEALTH EDUCATION IN ZIMBABWE.

BY

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DEDICATION

I dedicate this thesis to my dearest family, my wife and sons, who allowed me to spend time away from them whilst doing field work and come home late during the period of this thesis.

ABSTRACT

Introduction: Globally**,** 207 million; 2 billion and 243 million people are infected with schistosomiasis (SCH), soil transmitted helminths (STH) and *Plasmodium falciparum* (*P.f*) respectively. Many of the affected people are primary school age children. Clinical outcomes of these parasitic infections include anaemia, impaired cognition and malnutrition. Although these parasites have different mechanisms through which they cause anaemia, data is scarce on the extent of helminths – *Plasmodium* polyparasitism and their effect on anaemia. We determined the extent of helminths-*Plasmodium* co-infections, their effect on anaemia and the efficacy of combined school based treatment intervention on prevalence of co-infections and anaemia among primary schoolchildren in rural and farming areas in Zimbabwe.

Overall objective: To determine the prevalence of single and helminths–*Plasmodium* co-infections among primary schoolchildren living in rural and commercial farming areas, the effect of co-infections on anaemia and the efficacy of combined school based treatment intervention on prevalence of co-infections and anemia.

Settings: The study was conducted in Nyamaropa rural area, Shamva districts and Burma Valley commercial farming areas in Mutare district, Zimbabwe.

Study design: The study was a longitudinal intervention trial, which involved treatment of infected children at baseline, 6, 12 and 33 months follow up surveys.

Methodology: Enrolled participants were screened for anaemia; schistosomiasis; STHs and *P. falciparum* (P.f) using the Hemocue machine, urine filtration technique, a combination of the Kato Katz and formal ether concentration techniques and Giemsa staining respectively at each survey.

Results: Helminths- *Plasmodium* co-infections were heterogeneously distributed and were observed in the commercial farming area only. Overall, the prevalence of *Schistosoma haematobium* in the rural and farming areas was 66.8% and 52.3%, respectively, that of *S. mansoni* was 12.4% and 22.7%.. *P. f,* hookworms, *Ascaris lumbricoides* and *Trichuris trichiura* occurred only in the farming area, with a prevalence of 27.9%, 23.7%, 2.1%, 2.3%, respectively. Hookworm and *S. mansoni* infections were associated with *P. f* ($P < 0.001$, OR = 2.48, 95% CI: 1.56-3.93 and $P = 0.005$, OR = 1.85, 95% CI: 1.20-2.87). Of the 475 children screened for all parasites and anaemia, received combined treatment at baseline and successfully followed up to 33 months post treatment survey, 11.2%; 10.9%; 1.3% and 5.1% had SCH + STHs; SCH + *P. f;* STH + *P. f*; SCH+ STH + *P. f* co-infections respectively at baseline. These co-infections declined to 6.3%; 2.1%; 0.4; 1.1%, respectively at 33 months follow up survey. Overall, anaemia declined from 45.7% at baseline to 15.4% at 33 months follow up survey after treatment intervention, $p < 0.001$. School health education increased the knowledge of grade 3 children about causes of helminths and *P. falciparum*

Conclusions: There is heterogeneity in the distribution of helminths –*Plasmodium* co-infections in diverse communities. Co-infections have a multiplicative effect on anaemia. Biannual combined school based treatment intervention reduces the prevalence of helminths-*Plasmodium* co-infections and anaemia. Determination of the extent of helminths –*Plasmodium* co-infection should be prioritized in planning allocation of limited resources for control. The Government of Zimbabwe nationalized this PhD work. The work also contributed towards the national policy formulation for the control of schistosomiasis, STH and other neglected tropical diseases in Zimbabwe.

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ABREVIATIONS

ACT	Artemisinin-based combination therapy
ALB	Albendazole
AI	Ascaris lumbricoides
CCR5	Chemokine receptor 5
CDC	Centre for Disease Control
CI	Confidence Interval
CNS	Central Nervous System
CXCR4	Chemokine receptor X4
Cr	Chromium
DALY	Disability Adjusted life Years
DDT	Dichloro-diphenyl-trichloroethane
dL	decilitre
EAP	East Asia and the Pacific Islands
epg	eggs per gram stool
FGS	Female Genital Schistosomasis
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
Hw	Hookworm
KAP	Knowledge Attitudes and Practice
IL	Interleukin
IPTp	Intermittent preventive treatment
IRS	Indoor residual spraying
LAC	Latin America and the Caribbean
LLIN	Long-lasting insecticide nets
MENA	Middle East and North Africa
Morb	Morbidity
Mort	Annual mortality
NTD	Neglected tropical diseases
PI	People infected
PoR	Population at risk of infection
PPR	Percentage Prevalence Reduction
PZQ	Praziquantel
RBC	Red Blood Cell
RBM	Roll Back Malaria
RDT	Rapid diagnostic test
TNF-a	Tumor necrotic factor alpha
Tt	Trichuris trichiura
SAS	South Asia
SCI	Schistosomiasis Control Initiative
SD	Standard Deviation
SE	Standard Error
STH	Soil transmitted helminths
SSA	sub-Saharan Africa
WHA	World Health Assembly
WHO	World Health Organization

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CHAPTER 1: INTRODUCTION

The high prevalence of schistosomiasis, STH, *P. falciparum* and the striking similarity of the conditions that favour their survival, reproduction and transmission make polyparasitism common in sub Saharan Africa. The conditions include poverty, lack of preventive measures, health care, safe water, sanitary facilities and similar temperatures. These conditions overlap in certain areas in Zimbabwe.

Separate studies have shown endemicity of schistosomiasis, STHs and malaria in different and similar areas in Zimbabwe (Taylor and Makura, 1985; Taylor and Mutambu, 1986; Chandiwana, 1989; Bradley *et al.*, 1993). These studies have demonstrated high prevalence of schistosomiasis, STHs and malaria among primary schoolchildren, the majority live in rural and farming areas (Zimbabwe National Census 2002). Though only single parasites were investigated per study during the previous studies, results indicate geographic overlap of helminths and *Plasmodium.* Thus, polyparasitism could be common especially in primary school age children who are at high risk of helminths and *Plasmodium* infections, yet many of them do not have access to essential drugs.

Although schistosomes, STHs and *P. falciparum* are major contributors of anaemia (Menendez *et al.*, 2000; Hotez *et al.*, 2004; Freidman *et al.*, 2005), reports on anaemia in Zimbabwe do not make any reference to helminths and *P. falciparum* as etiological agents of the disease (ZDHS, 2005-2006). This is in spite of high prevalence of anaemia reported among Zimbabwean children aged less than 5 years (55.4% - 63.1%) and reproductive women (30.7% - 47.5%).

Data is also not available on the impact of helminths-*Plasmodium* co-infections on anaemia especially among primary school children. This age group has always been left out in national anaemia surveillance studies (ZDHS 2005-2006). Unless data on delineation of areas co-endemic for helminthiasis and malaria and the knowledge of the proportion of the population with helminths-*Plasmodium* co-infections is made available, policy markers will face challenges in allocating limited resources for control. As a result, co-morbidities including anaemia due to these communicable diseases will remain uncontrolled in Zimbabwean population and in particular among primary school children whose cognitive potential and academic performance is affected by helminthiasis and malaria (Nokes and Bundy, 1994; WHO 2005a).

1.1 LITERATURE REVIEW

1.2 Schistosomiasis

Schistosomiasis is parasitic water borne disease caused by infection with a blood borne fluke (trematode) of the genus *Schistosoma*. Schistosomiasis in man was first described by Theodor Bilharz in 1851, working at the Kasr-el-Aini hospital in Cairo (Rollingson and Southgate, 1987). Humans can be infected by five species: *S. mansoni, S. haematobium, S. japonicum, S. intercalatum* and *S. mekongi* (Rollingson and Southgate, 1987).

Of the trematodes, schistosomes are atypical in that the adult stages have two sexes and are located in blood vessels in the definitive host. The thread like female lies in a ventral longitudinal cleft in the body of the male fluke called the gynaecophoric canal (Friedberg *et al.*, 1991). *S. haematobium* adult worms live in the perivesical and other species lives in the mesenteric veins, where they feed on blood particles. The female produces eggs with a characteristic terminal or lateral spine for *S. haematobium* and *S. mansoni* respectively.

1.2.1 Schistosomiasis life cycle

The life cycle of schistosomes includes two hosts, a definitive host (e.g. man) where the parasite undergoes sexual reproduction and a single intermediate snail host (genus *Biomphalaria* for *S. mansoni*, *Bulinus* for *S. haematobium* and *S. intercalatum*, *Oncomelania* for *S. japonicum* and the genus *Tricula* for *S. mekongi*) where a number of asexual reproductive stages occur (Jourdane and Theron, 1987). Infection occurs through contact with fresh water that contains infective cercariae released from an intermediate host snail.

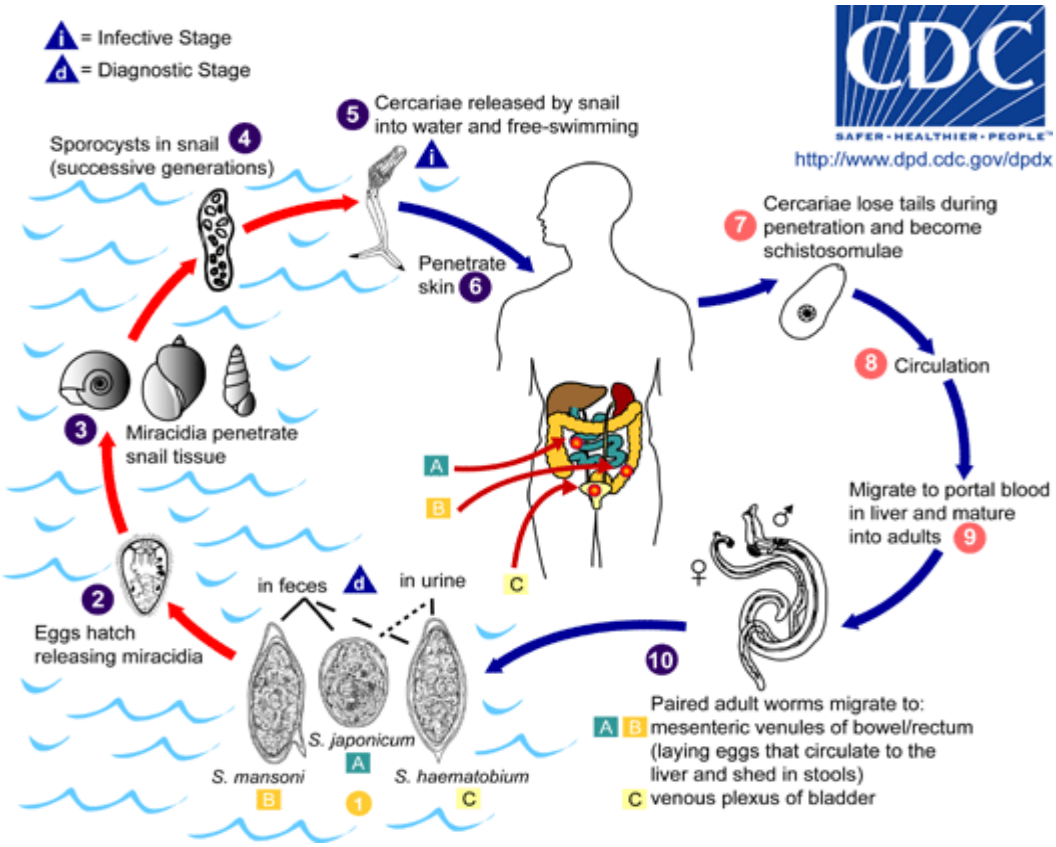

Figure 1.2.1.1: Schistosomiasis life cycle showing stages in the human host, fresh water and 3 common schistosome species (http://www.dpd.cdc.gov/dpdx/html/schistosomiasis.htm 2010)

The cercaria penetrates intact human skin and transforms into the migrating schistosomulum larva that migrates through the bloodstream to the hepatic portal system to complete the parasites lifecycle. Male and female worms differentiate, pair and migrate into the small venules draining the bladder for *S. haematobium* or the intestine for other species (Jourdane and Theron, 1987). In these sites, and fully exposed to the host immune system, adult worms live for 3 to 12 years (Friedberg *et al.*, 1991) but some can live for 30 years (Von Lichtenberg, 1987). The female worm produces several eggs each day and many eggs are deposited in the sub-mucosal layers of the bladder (Friedberg *et al.*, 1991; Jourdane and Theron, 1987).

Within the eggs, a ciliated miracidium develops in 6 days by which time it produces proteolitic enzymes which escapes through ultra-microscopic pores in the egg shells and enable many eggs to pass through the tissues and gain access to the exterior (Jourdane and Theron, 1987; Friedberg *et al.,* 1991). Eggs pass into the lumen of the intestine or bladder and if deposited in fresh water, hatch to release ciliated miracidia that infect the intermediate host snail and the life cycle continues (Jourdane and Theron, 1987).

1.2.2 Schistosomiasis pathology

Schistosomiasis is typically an immunological disease caused by granulomatous reaction to schistosome egg trapped in the tissues also referred to as delayed-type hypersensitivity human immune response (Von Lichtenberg, 1987; Friedberg *et al.,* 1991; Wyler, 1992).

The pathology associated with infection with *S. mansoni* can be divided into two main areas, acute and chronic schistosomiasis. Acute schistosomiasis is also called 'Katayama' fever in areas endemic for *S. japonicum* (Von Lichtenberg, 1987). This is associated with the onset of the female parasite laying eggs, (approximately 5 weeks after infection), and granuloma formation around eggs trapped in the liver and intestinal wall. This phase of infection is often asymptomatic, but when symptoms do occur they include fever, nausea, headache, an irritating cough. In extreme cases diarrhoea accompanied with blood, mucus and necrotic material occur. These symptoms, if present, last for 2 to 8 weeks (Friedberg *et al.,* 1991; Von Lichtenberg, 1987).

Chronic intestinal schistosomiasis and the hepatic schistosomiasis manifest a number of years after infection. The pathogenic reaction is a cellular, granulomatous inflammation around eggs trapped in the tissues, with subsequent fibrosis.

All areas of both the small and large intestine may be involved, with the large intestine showing the most severe lesions. Severe pathology in the small intestine is only rarely observed, even though large numbers of eggs may be deposited here. Colonic polyps are also sometimes seen. Chronic hepatosplenic schistosomiasis is associated with hepatosplenomegaly and portal hypertention associated with blockage of portal venules. This complication can result in death of the patient. Abdominal discomfort due to organomegally occurs. Severe endemic schistosomiasis arises from the formation of advanced fibrovascular lesions obstructing critical vessels or natural conduits rather than from scattered egg granuloma alone. These lesions form at sites of massive egg deposition (Von Lichtenberg, 1987). Thus, continuous deposition of *S. mansoni* or *S. japonicum* eggs results in diffuse portal inflammation and fibrosis with permanent vein obstruction that respond poorly to treatment.

Pathology caused by *S. haematobium*, like any other species is related to infection intensity. Adult parasites are found in small venules around the bladder and ureter, with the majority of egg deposition in the tissues of these organs as eggs pass through the bladder wall to leave the body through urine. The disease caused is chronic in nature, with the most frequently affected organ being the urinary bladder, where calcification of eggs trapped in the tissues often occurs (Von Lichtenberg, 1987)**.** The disease is characterised by blood in the urine (haematuria). Cancer of the bladder, hydronephrosis and renal failure are important complications of infection with *S. haematobium* (Von Lichtenberg, 1987).

1.2.3 Anaemia development in schistosomiasis

The mechanisms by which schistosome infection lead to anaemia, are: (i) iron deficiency due to extra-corporeal loss; (ii) splenic sequestration; (iii) autoimmune hemolysis; and (iv) anaemia of inflammation (Woodruff, 1973; Friedman *et al.*, 2005). In schistosomiasis infection, iron deficiency is caused by extra-corporeal blood loss in stools because of *S. japonicum* and *S. mansoni* infection when eggs pass through the intestinal wall into the lumen of the gut (Warren, 1982; Mahmoud, 1966; Mahmoud *et al.*, 1972). Splenomegaly, a complication that occurs in some schistosome infected individuals, causes anaemia when red blood cells are sequestered in the spleen (Mahmoud and Woodruff, 1972).

Anaemia of inflammation and chronic disease involves pro-inflammatory cytokine mediators that are produced in response to infections (Means, 2000). Tumor necrosis factor alpha (TNF-α) disrupts RBC production and longevity by decreasing the production of erythropoietin and impairing the erythropoietic response of the bone marrow. IL-6 causes up regulation of hepcidin that decreases iron absorption in the gut and alters iron metabolism by causing sequestration of iron into storage forms such as ferritin in the reticuloendothelial system resulting in the decrease in iron bioavailability (Ganz, 2003, King, 2009).

1.2.4 Epidemiology of schistosomiasis

Schistosomiasis remains one of the most prevalent parasitic diseases in the world. It is endemic in 76 countries and continues to be a public health concern in the developing world (WHO, 1999; WHO, 2002a). It is estimated that 779 million people are at risk of infection with schistosomiasis, 207 million are already infected and 120 million are experiencing severe morbidity, whilst 15-200 000 die annually due to schistosomiasis.

Recent estimates also indicate that the burden of schistosomiasis ranges from 1.7 to 4.5 million DALYs (Brooker and Utzinger, 2007). Estimates indicate that 85% of the numbers of infected people live in Africa (Chitsulo *et al.,* 2000).

The parasite *S. mansoni* is found in many countries in Africa, South America (Brazil, Surinam and Venezuela), the Caribbean and in parts of the Middle East (Rollingson and Southgate, 1987; WHO, 1999; WHO, 2002a). *S. haematobium* is found in large parts of Africa, parts of the Arabia, the Middle East, Khuzestan Province in Iran, Madagascar and Mauritius (Rollingson and Southgate, 1987; WHO, 1999; WHO, 2002a).

Schistosoma japonicum is found in the Far East, particularly China and the Philippines. In Indonesia, it is found in a few isolated valleys in Central Sulawesi (Rollingson and Southgate, 1987; WHO, 1999; WHO, 2002a). *S. intercalatum* is endemic in parts of DRC, Gabon, Cameroon, with other small foci in possibly in Central African Republic, Chad, Nigeria, Upper Volta and other parts of Central Africa (Rollingson and Southgate, 1987; WHO, 1999; WHO, 2002a). *S. mekongi* is found in Laos and Cambodia. In Laos, dogs have been demonstrated as reservoir hosts. Snails of the genus *Tricula* act as intermediate hosts (Rollingson and Southgate, 1987; WHO, 1999; WHO, 2002a).

1.2.5 Epidemiology of schistosomiasis in Zimbabwe

S. haematobium and *S. mansoni* are common schistosome species of medical importance in Zimbabwe (Taylor and Makura, 1985; Ndhlovu *et al.,* 1992).
S. haematobium is predominantly distributed in the country where as *S. mansoni* is discontinuously distributed. In a national survey conducted by Taylor and Makura,

(1985) among the 8-10 year old children (n = 14 619) from 157 schools, Zimbabwe was divided into three regions based on prevalence distribution of *S. haematobium*. The mean prevalence of *S. haematobium* in each zone was 63.2%, 37.1% and 14.3%. *S. mansoni* was observed in two regions with prevalence levels of 15.2% and 1.5%. The survey showed that farming areas had higher prevalence of *S. haematobium* compared to the subsistence farming areas.

In a second national survey conducted by Ndhlovu *et al.*, (1992), both schistosome species had spread to the western region of the country where they had been declared as non-existent by Taylor and Makura, (1985). This development was due to lack of comprehensive national control programmes following the first national survey. Increased dam construction, a programme implemented by the government to mitigate draught, coupled with human inter- and intra-permanent district migration could also have resulted in increased distribution of schistosomiasis in Zimbabwe.
Studies have shown existence of schistosomiasis in urban areas with prevalence of 5% in Kariba and 13.7% (341/ 2 552) of the children screened in Harare (Chimbari and Chirundu 2003a; Chimbari *et al*., 2003b; Ndamba *et al*., 1994).

1.2.6 Control of schistosomiasis

Control of schistosomiasis is achieved through various measures, which may be consolidated to improve efficacy. These options include (a) elimination of snail intermediate host; (b) elimination of the parasite from the definitive host (drug treatment); (c) prevention of infection of the definitive host; (d) prevention of infection of the intermediate host through use of toilets for human excretion and (e) health education (Montresor *et al*., 1999).

1.2.7 Schistosomiasis control in Zimbabwe

Zimbabwe has not yet implemented a comprehensive control programme for schistosomiasis. Like many other countries, this could have been due to the costs of praziquantel and the limited priority given to schistosomiasis in the wake of other highly competitive public health problems including HIV/AIDS, tuberculosis and malaria that attracted human and financial resources.

Only pilot control programmes were conducted in Zimbabwe including the use of *Phytolacca dodecandra*, a plant with berries of a known molluscicidal potency and environmental manipulation (lining of canals, flushing and drying of storage ponds) for the control of vector snails (Chandiwana *et al.,* 1988a, Ndamba *et al.,* 1989, Ndekha *et al.,* 2003). However, these pilot control programmes were not nationalised mainly due to lack of community compliance in such village self help programmes (Ndekha *et al.,* 2003).

1.2.8 Schistosomiasis treatment

The advent of safe, orally active and efficacious antischistosomal drugs, most notably, praziquantel (Groll, 1984), led in the mid 1980s to a shift in the global strategy from transmission control to morbidity control (WHO, 1985b). Today the cornerstone of schistosomiasis control is morbidity control (WHO 2002a, WHO 2002b).

The current drugs available on the market for treatment of schistosomiasis are oxamniquine and praziquantel (isoquinolin-4-one) (WHO, 1999; WHO, 2002a; WHO, 2002b). Metrifonate that was specific for the treatment of *S. haematobium* was withdrawn from the market because of its high costs, loss of patient compliance to its

long treatment dose and following the emergence of praziquantel (PZQ), a broad pectrum drug (Cioli and Mattoccia, 2002; WHO, 1999).

1.2.9 Schistosomiasis treatment in Zimbabwe

The drug of choice for schistosomiasis treatment in Zimbabwe is praziquantel. Comprehensive national surveys for schistosomiasis and intermediate host snails were conducted in 1985, 1991 resulting in production of prevalence distribution maps that defined populations infected and at risk of infection (Taylor and Makura, 1985; Makura and Kristensen, 1991, Ndhlovu *et al*., 1992). Praziquantel that could have been preferred for combined mass treatment of *S. haematobium* and *S. mansoni* co-existing in the country was still under patent and hence prohibitively expensive. Limited quantities procured were delivered through the existing drug delivery channels to the peripheral health facilities with many areas experiencing drug shortages. Praziquantel patency only expired in 2001 (WHO, 2002a).

The country has however, renewed its interest for the control schistosomiasis (National Health Strategy, 2009-2013). Plans are underway for mass praziquantel treatment of the affected individuals with the aim to achieve regular treatment of at least 75% or all primary school age children.

1.2.10 Resistance to schistosomiasis treatment

Praziquantel has been in use for a long time as the single broad-spectrum drug of choice for all schistosome species (King and Mahmoud, 1989). This has increased fears that praziquantel resistance could emerge any time especially with the onset of wide spread use of the drug as countries in sub-Saharan Africa begin national schistosomiasis control programmes (Fenwick and Webster, 2006). A European

Commission sponsored international initiative reviewed reports on praziquantel use following findings of low cure rates of PZQ to schistosomiasis in Senegal and Egypt (Picquet *et al*., 1998; Stelma *et al*., 1995). The initiative called for continuous monitoring of praziquantel resistance under the pressure of wide spread use of PZQ (Renganathan and Cioli D, 1998; WHO, 2005a).

Zimbabwe is among WHO member states that have placed control of schistosomiasis, malaria and STHs high on the agenda (National Health Strategy 2009-2013). Use of large quantities of praziquantel is therefore anticipated. However, data on efficacy of praziquantel is scarce at the time when there is increased concern that schistosomes might develop resistance to the drug (Cioli *et al.,* 2000; King *et al.,* 2000; WHO, 2005a). A single low praziquantel dose study conducted in Zimbabwe almost two decades ago (Taylor *et al.,* 1988) needs supplementation with more recent evidence regarding efficacy of praziquantel especially when recent research has shown that schistosomes from Zimbabwe are quite genetically distinct from reference strains from Egypt (Brouwer *et al.,* 2001; Shiff *et al.,* 2000).

1.3 Soil transmitted helminths

Soil transmitted helminths (STHs) include parasitic species that are widely distributed in the soil. These include hookworms, *Ascaris lumbricoides and Trichuris trichiura*. STH are not hermaphroditic and thus have separate sexes (Brown, 1975).

The adult nematode is an elongate cylindrical worm primarily bilaterally symmetrical. The anterior end may be equipped with hooks, teeth, plates, setae and papillae for purposes of abrasion, attachment and sensory response. Intestinal nematodes maintain their positions by oral attachment to the mucosa (hookworms), anchorage with their

attenuated ends (*Trichuris*), retention in the folds of the mucosa and pressure against it (*Ascaris*) (Brown, 1975). The methods of obtaining food may be classed as (1) sucking with ingestion of blood (hookworm), (2) ingestion of lysed tissues by embedded worms (*Trichuris*), feeding on intestinal contents (*Ascaris*) (Brown, 1975). Soil transmitted helminths that fall in the group of nematodes have received more global attention because of their public health significance and because of the number of people at risk and those infected is more than 2 billion (de Silva *et al.,* 2003).

1.3.1 Hookworms

Hookworm infection in humans is caused by an infection with the helminth nematode parasite *Necator americanus* and *Ancylostoma duodenale* and is transmitted through contact with contaminated soil

1.3.1.1 Hookworm life cycle

Infected people pass hookworm eggs in the stool. Under favourable conditions in the soil (moisture, warm, shade), the eggs mature rapidly and produce the rhabditiform larvae in 1 to 2 days (Mambaso *et al.,* 2003). The released rhabditiform larvae grow in the faeces and/or the soil feeding on bacteria and organic debris, and after 5 to 10 days (and two molts) they become filariform (third-stage) larvae that are infective (Fig.1.3.1.1.1**)** (Brown, 1975; Hotez *et al.,* 2004).

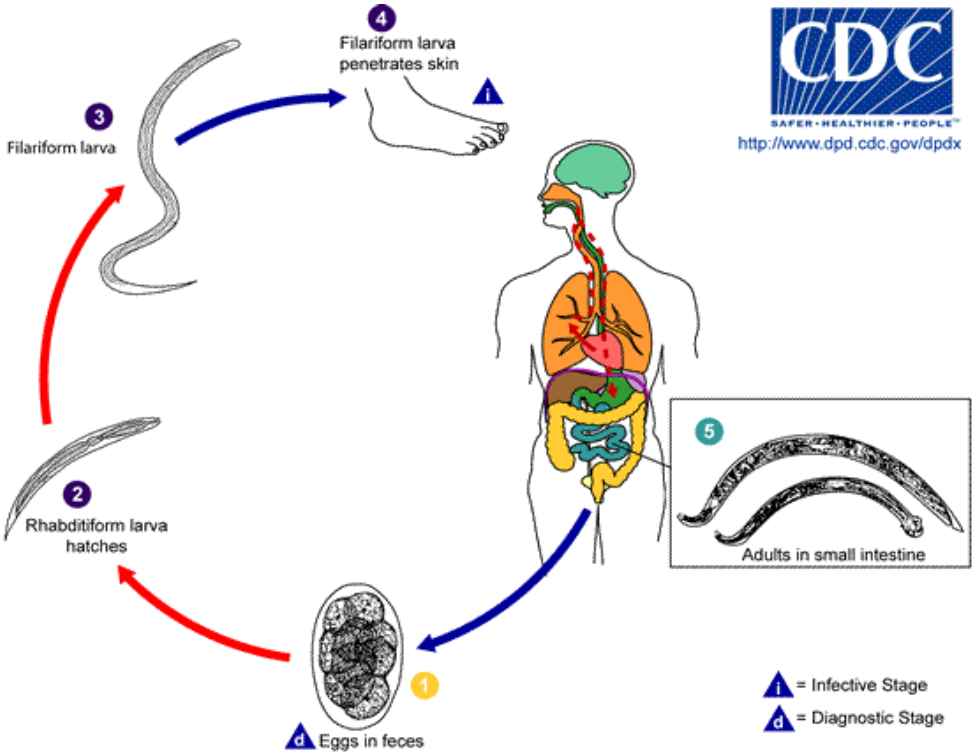

Figure 1.3.1.1.1: Hookworm life cycle showing different stage of larval developments in the environment (http://www.dpd.cdc.gov/dpdx/html/Hookworm.htm 2010)

The filariform is in the state of developmental arrest and non-feeding whilst in the soil. Development is only started on penetration of the human host (Brown, 1975; Hawdon and Hotez, 1996). On contact with human host, the larvae penetrate the skin and are carried through the blood vessels to the heart and then to the lungs. They penetrate into the pulmonary alveoli, ascend the bronchial tree to the pharynx, where they are coughed up and swallowed into the gastrointestinal canal. The larval blood and pulmonary migration takes about one week (Brown, 1975; Hotez *et al.*, 2004). The larvae reach the small intestine, where they molt twice and mature into adults. It takes 6 to 8 weeks from the time of larval penetration into human to reach sexual maturity stage (Brown, 1975). Adult worms live in the lumen of the small intestine, where they attach to the intestinal wall with resultant blood loss by the host. The

female lays thousands of eggs (10 000 for *N. americanus* and 20 000 for *A. duodenale*) daily (Brow, 1975).

1.3.1.2 Hookworms Pathology

Repeated exposure to the penetration of third stage larvae of *N. americanus* or *A. duodenale* results in a local pruritic, erythematous, papular itching rash known as ground skin (Brown, 1975; Hotez *et al.,* 2004). Within 10 days of penetration of the skin, hookworm larvae migrate to the lungs resulting in the cough and sore throat (Hotez *et al.,* 2004; Brown, 1975). Hookworm bronchitis and pneumonitis, which are usually not severe accompanies larval migration through the lungs, bronchi and trachea to the oesophagus (Brown, 1975; Ananthakrishnan *et al.,* 1997; Hotez *et al.,* 2004).

1.3.1.3 Anaemia development in hook worm infection

The term hookworm disease refers to the iron deficiency anaemia that results from moderate to heavy infection (WHO, 2002; de Silva, 2003; Hotez *et al.,* 2004). Adult hookworms attach themselves to the mucosa of the upper small intestine where they suck plugs of tissues into their buccal capsules by contraction of their muscular oesophagi to create negative pressure. This action results in rapture of the capillaries and arterioles both mechanically and chemically through the action of hydrolytic enzymes (Brown, 1975; Hotez *et al*., 2004; de Silva, 2003). Blood is lost when it passes through the hookworm's intestinal tract and is expelled during feeding. Secondary loss also occurs from bleeding of the stomach mucosa (de Silva, 2003, Brown, 1975).

Hookworm change their feeding sites every 4-6 hours leaving an anticoagulant secretion at each site that cause continual bleeding of lesions created (Brown, 1975;

de Silva, 2003). As much as 0.03ml (*N. americanus*) and up to 0.26ml (*A. duodenale*) of blood may be withdrawn by a worm in 24 hours and approximately 50% of the red blood cells are hemolysed during passage through the worm's intestine. Thus, the amount of blood loss is strongly dependent on worm load and nutritional intake of the patient (Brown, 1975; WHO, 2002; de Silva, 2003). Children and pregnant women infected with hookworms are at high risk of developing anaemia (Stoltzfus *et al.*, 1997; Brooker *et al.*, 1999; Dreyfuss *et al.*, 2000)

1.3.2 Ascaris lumbricoides

Ascaris lumbricoides is the largest and most common intestinal nematode of humans. Females are approximately 30 cm long; sexually mature males are smaller. Mated females produce fertile eggs that are oval to subspherical, 45 to 75 μm by 35 to 50 μm, and are covered by a thick shell with a light brown, mammillated, albuminous outer coat (Brown, 1975).

1.3.2. 1 *Ascaris lumbricoides* life cycle

Adult worms live in the lumen of the small intestine. A female may produce approximately 200,000 eggs per day, which are passed with the faeces (Brown, 1975). Fertile eggs embryonate and become infective after 18 days to several weeks. Mature eggs are acquired by ingestion of contaminated food, fruits, drink, water, pica and unclean personal habits such as failure to wash hands with soap after toilet (Ananthakrishnan *et al.*, 1997). After infective eggs are swallowed, the larvae hatch, invade the intestinal mucosa, and are carried via the portal vein, then systemic circulation to the lungs.

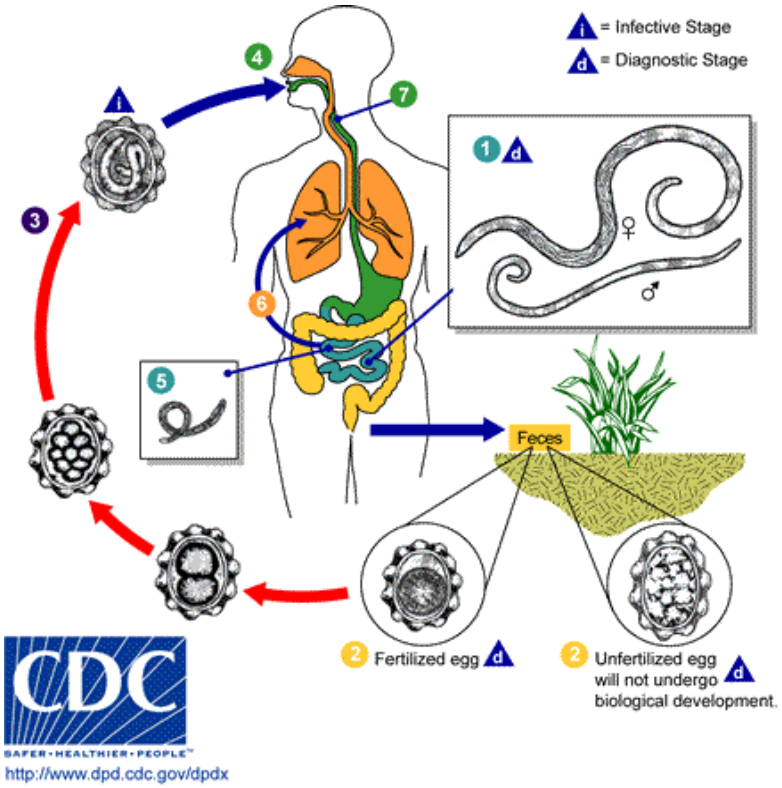

Figure 1.3.2.1.1: Life cycle for *A. lumbricoides* showing infective and diagnostic stages (http://www.dpd.cdc.gov/dpdx/html/Ascariasis.htm, 2010**)**

The larvae mature further in the lungs (10 to 14 days), penetrate the alveolar walls, ascend the bronchial tree to the throat, and are swallowed. Upon reaching the small intestine, they develop into adult worms (Fig. 1.3.2.1.1**)**. Between 2 and 3 months are required from ingestion of the infective eggs to oviposition by the adult female. Adult worms can live 1 to 2 years (Brown, 1975).

1.3.2.2 Ascariasis pathology

During the lung phase of larval migration, pulmonary symptoms can occur (cough, dyspnea, hemoptysis, eosinophilic pneumonitis - Loeffler's syndrome) (Brown, 1975; Ananthakrishnan *et al.*, 1997). The intestinal symptoms are caused by the metabolic products of the worms that irritate the sensory receptors in the intestine with resultant interference with normal peristalsis, spasmodic contractions and ishaemia of the bowel wall (Lagundoye, 1972). Migrating adult worms may cause mechanical

intestinal obstruction, symptomatic occlusion of the biliary tract and biliary lesions (Brown, 1975; Ananthakrishnan *et al.,* 1997). They can perforate the intestines; enter the peritoneal cavity and the respiratory tract (Brown, 1975). Lungs are the most severely affected by migrating larvae which may cause mild to severe cough, breathlessness, retrosternal discomfort, hemoptysis, fever and wheezing (Gelpi and Mustafa, 1967).

1.3.3 *Trichuris trichiura*

Trichuriasis is human parasitic disease that is caused by infection with *Trichuris trichiura*. It is characterized by the invasion of the colonic mucosa by the adult *Trichuris* and produces minor inflammatory changes at the site of localization (Brown, 1975).

1.3.3.1 *T. trichiura* life cycle

The life cycle of *T. trichiura* is similar to that of *A. lumbricoides* in that it is transmitted by faecal-oral route. However, there is no larval migration through the lungs. Humans become infected by ingesting contaminated soil, food or water containing infective *Trichuris* eggs previously passed in faeces (Ananthakrishnan *et al.,* 1997). Young children aged 3 to 9 years are more often infected than adults because they are likely to play with contaminated soil. Ingested eggs are activated in the stomach and they hatch in the small intestine freeing larvae. The larvae attach to and penetrate the small intestinal mucosa where they begin to mature.

After approximately one week, the immature worms move passively to the large intestines and proximal colon. The worms' anterior portions penetrate the mucosal epithelium, half of its length embedded in the mucosal surface. The adult worms live in the cecum and ascending colon. The females lay eggs 30 to 90 days after infection

(Brown, 1975). They lay between 3,000 and 20,000 eggs per day. Unembryonated eggs are passed with the stool. In the soil they embryonate and become infective in 15 to 30 days (Brown, 1975).

1.3.3.2 Trichuriasis pathology

Light infections with *T. trichiura* are usually asymptomatic (Ananthakrishnan *et al.*, 1997; WHO, 2002). However, massive *T. trichiura* infection causes severe anaemia because of blood loss due to the sucking of blood by the worms (Layrisse *et al.*, 1967) and exudation from the damaged epithelium, dysentery or rectal prolapse (Bundy and Cooper, 1989). Abdominal pain and tenderness, nausea and vomiting, constipation and chronic appendiceal syndrome are also clinical manifestations of heavy *T. trichiura* infection (Sun, 1999; Ananthakrishnan *et al.*, 1997; Bundy and Cooper, 1989). Tumor necrotic factor alpha produced in response to *trichuris* infection causes chronic anorexia leading to reduced food intake and anaemia (de Silva, 2003). Severe chronic diarrhoea or dysentery lasts 6 months to 3 years with blood and excess mucus in the stools. *T. trichiura* dysentery syndrome produces gastrointestinal problems.

1.3.4. Impact of STHs on Education

Infection with STHs and especially the intensity of *T. trichiura* and *A. lumbricoides* are associated with reduction in school performance among primary school children (Nokes *et al.*, 1991, Nokes *et al.*, 1993, Nokes and Bundy, 1994).

1.3.5 Global epidemiology of STHs

Helminths are widely distributed in the warm and moist tropical and sub- tropical regions of the world. In these areas malnutrition, low standard of living, crowding, poor sanitation, lack of water, personal hygiene and lack of access to health care favour the survival, multiplication and transmission of these parasites among poor

people (Ananthakrishnan *et al.*, 1997; de Silva *et al.*, 2003). Global estimates indicate that ascariasis is the most prevalent STHs with 1.2 billion infections; trichuriasis and hookworm amount to 700–800 million infections each. Hookworms infect 400 million people in China and sub- Saharan Africa (de Silva *et al.*, 2003).

Ascaris infection is predominantly found in China and Southeast Asia, in the coastal regions of West Africa, and in Central Africa. *Trichuris trichiura* is most common in Central Africa, southern India and Southeast Asia (de Silva *et al.*, 2003). Hookworm infections are common throughout much of sub-Saharan Africa, in addition to South China and Southeast Asia (de Silva *et al.*, 2003).

Overall, STHs are among the most prevalent infections of school-age children and they tend to occur at highest intensity in this age group (Brooker *et al.*, 2006a; Brooker *et al.*, 2007a). More recent estimates made by Brooker *et al.*, (2006b) indicate that 35.4 million, 40.1 million and over 41.1 million African primary school aged children are infected with *A. lumbricoides, T. trichiura* and hookworms, respectively.

Table 1.3.5.1 shows the current global estimates of populations at risk, infected, experiencing morbidity, mortality and the burden of disease due to STHs infections (Brooker and Utzinger, 2007)

Table 1.3.5.1: Current global estimates of populations at risk, number of people infected, suffering from morbidity, annual mortality rates and burden estimates.

Disease	PoR ($X10^6$)	PI ($X10^6$)	Morb ($X10^6$)	Mort ($X10^6$)	DALYs ($X10^6$)
Ascariasis	4 211	807-1 221	350	3-60	1.82-10.5
Hookworm	3 195	576-740	150	3-65	0.06-22.1
Trichuriasis	3 312	604-795	220	3-10	1.01-6.4

Source: Brooker and Utzinger, (2007)

Key: PoR = Population at risk of infection, PI= People infected, Morb = Morbidity
Mort = Annual mortality, DALY = Disability adjusted life years (disease burden),

1.3.6 The epidemiological distribution of STH in Zimbabwe

There has not been a comprehensive survey at national level to determine the prevalence distribution of STHs in Zimbabwe. However, during the national survey conducted by Taylor and Makura between 1981 and 1982, some stool samples were collected from 14 619 children (age range 8-10) from 157 primary schools aimed at screening children for *S. mansoni* infection. In addition to *S. mansoni* screening STHs were also investigated (Chandiwana *et al.,* 1989). Data from the survey indicate prevalence rates of 1.6% for hookworms and 0.5% for *A. lumbricoides*. *Trichuris trichiura* was not reported (Chandiwana *et al.,* 1989). It was observed that the majority of infected children were found in the North - East, the Zambezi Valley, the central and South - Eastern low-veld areas. There was negligible prevalence of STHs in the dry region (western region). However, Chandiwana indicated that results from the 1985 national schistosomiasis survey needed to be considered with caution since the original aim for stool collection from schoolchildren was for the diagnosis of

S. mansoni, the methodology may not have been suitable for the diagnosis of STHs (Chandiwana, 1989).

Some small-scale studies were conducted mainly in the Burma Valley commercial farming areas and Kariba eastern basin region of Zimbabwe. The results show that hookworm is the predominant STHs occurring in Zimbabwe (Goldsmid, 1968; Goldsmid, 1976; Chandiwana *et al.*, 1989, Chandiwana and Makaza, 1983; Bradley *et al.*, 1992). There is no published data on the distribution of STHs in urban areas in Zimbabwe.

1.3.7 Control of STHs

In response to the public health impact of STHs and schistosomiasis especially on school age children, the 54th World Health Assembly, (2001) declared a minimum pragmatic target stipulating that regular treatment should be given to at least 75% or all primary school children at risk of morbidity due to schistosomiasis and STHs infection. This is because regular anthelminthic treatment will reduce worm burden and, thus, morbidity even in populations where STHs transmission force leading to re-infection is high. The drugs of choice are mebendazole and albendazole (WHO, 2006a).

Improved sanitation and health education to improve hygienic practices, limit the rate of STHs transmission. Use of protective clothing such as wearing shoes prevents contact with contaminated soil and hookworm penetration during farming and when walking about in areas where the use of bush toilets is practiced (WHO, 2002).

Whilst there is a renewed global interest to control morbidity due to STHs (54th WHA, 2001), surprisingly there is still a paucity of data regarding the national distribution of STHs across sub Saharan Africa and their underlying environmental determinants (Brooker *et al.*, 2006b). Understanding where at-risk populations live is fundamental for appropriate resource allocation and cost-effective disease control. Mapping the distribution of STHs, therefore, remains a priority if control strategies are to be planned at country level throughout sub Saharan Africa.

1.3.8 Control of STHs in Zimbabwe

There has virtually been no comprehensive large-scale control programme for STHs in Zimbabwe. However, the country has an annual budget to procure imported antihelminthic drugs that are distributed throughout the country's rural and urban health centres (Chandiwana, 1989).

1.4 Malaria

The malarial parasites of man are species of the genus *Plasmodium* of the class sporozoa in which the asexual cycle (*schizogony* takes place in the red blood cells of vertebrates and the sexual cycle (*sporogony*) in mosquitoes (Brown, 1975).

1.4.1 Malaria life cycle

Malaria is caused by blood parasites of the genus *Plasmodium*. Four species are considered true parasites of humans, as they utilize humans almost exclusively as a natural intermediate host: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.

Malaria parasite life cycle involves two hosts. During a blood meal, a malaria-infected female *Anopheles* mosquito inoculates sporozoites into the human host. Sporozoites traverse to the liver in about 20 to 30 minutes and infect liver cells (Sinnis and Sim,

1997). A small number of sporozoites (2-10) can initiate infection. Following development in the hepatocytes for 7-10 days, 10 000 to 30 000 merozites are produced and released into the blood stream to establish the intra-erythrocyte cycle (Ponnudurai *et al.*, 1991; Khusmith *et al.*, 1994). Merozoites released from infected hepatocytes infect red blood cells and develop asexually from ring forms to trophozoites.

Trophozoites undergo multiple rounds of mitosis to form multinucleated schizonts that develop into the blood stream after lysis of an infected red blood cell. These merozoites go on to initiate a new erythrocytic cycle. Some merozoites differentiate into sexual erythrocytic stages (gametocytes).

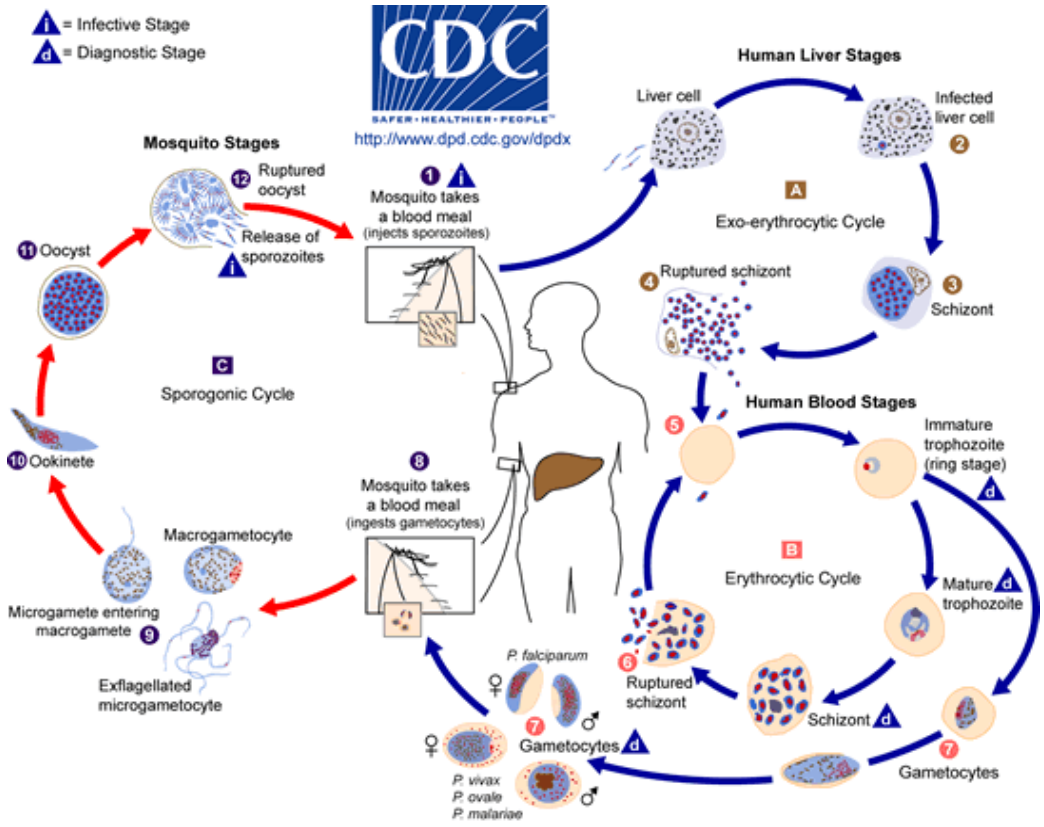

Figure 1.4.1.1: Malaria life cycle showing stages in the vertebrate and human host (http://www.cdc.gov/malaria/about/distribution.html, 2010)

An Anopheles mosquito ingests the male (microgametocytes) and female (macrogametocytes) during a blood meal. Parasite multiplication in the mosquito is known as sporogonic cycle. Once gametocytes gain access to the mosquito's mid gut, the female and male gametocytes undergo gametogenesis and develop into extracellular female and male gametes. A drop in temperature of about 5^{o}C, an increase in pH to between 8.0 and 8.2 and the presence of xanthurenic acid trigger male gametocyte exflagellation (Paul *et al.*, 2002; Biliker *et al.*, 1998; Bhattacharyya and Kumar, 2001). The exflagellated microgametes penetrate the macrogametes generating zygotes. The zygotes in turn become motile and elongated (ookinetes) which invade the mid gut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the

mosquito's salivary glands. Inoculation of the sporozoites into a new human host perpetuates malaria life cycle.

1.4.2 Malaria pathology

Clinical symptoms of malaria begin when the asexual parasite invades and multiplies in the red blood cells. However, the clinical presentation depends on the biology of the parasite, the level of parasitaemia and patient immune status (Miller *et al.*, 2002). The most frequent symptoms include fever and chills, which can be accompanied by headache, myalgias, arthralgias, weakness, vomiting, and diarrhoea. Other clinical features include splenomegaly, anaemia, thrombocytopenia, hypoglycemia, pulmonary or renal dysfunction, and neurologic changes. Infections caused by *P. falciparum* can progress to severe, potentially fatal forms with central nervous system involvement (cerebral malaria), acute renal failure, severe anaemia, or adult respiratory distress syndrome.

Adherence of parasites to the endothelial cells in the brain mediated mainly by intracellular adhesion molecule 1 (ICAM-1) is important in understanding cerebral malaria (Newbold *et al.*, 1999). Sequestration of parasites explains cerebral malaria in adults than in children where hypoglycaemia, sub-clinical convulsions and bacteremia seem to be more involved in the clinical presentation of cerebral malaria (Silamut *et al.*, 1999; Suh *et al.*, 2004).

1.4.3 Anaemia in malaria

Anaemia is an important cause of morbidity and mortality in *P. falciparum* malaria (WHO, 1990). It results from a combination of parasitized erythrocyte destruction

when matured schizont rupture, accelerated removal of both parasitized and unparasitized red blood cells, and decreased erythropoiesis (Weatherall and Abdalla, 1982; Looareesuwan *et al.,* 1987; Phillips and Pasvol, 1992; Menendez *et al.,* 2000). Reduced red blood cell (RBC) deformability is thought to play an important role in the removal of senescent red blood cells from the circulation by the spleen contributing to anaemia of malaria (Lee *at al.,* 1989).

The characteristic pathological feature of *falciparum* malaria is the adherence of erythrocytes containing mature forms of the parasite to venous and capillary endothelium in organs such as brain, heart, and kidney. Such deep vascular sequestration is thought to be a major factor in the genesis of vital organ dysfunction (White, 1986). While non-adherent *P. falciparum* parasite infected RBC are rapidly cleared by the spleen (Looareesuwan, 1987), some parasites express intracellular adhesion molecule1 (ICAM-1) and *P. falciparum* erythrocyte membrane protein-1 (PfEMP-1) that mediate adherence of erythrocytes containing mature forms of the parasite to the endothelial cells (Kyes *et al.,* 2001; Chen *et al.,* 2000). This contributes to the rapid development of anaemia in severe infections through clumping of uninfected cells and rosetting of infected red blood cells (Davis *et al.,* 1990). Immune system destroys clumped RBCs (Chang and Stevenson, 2004).

Severe forms of malaria cause rigidification of RBCs resulting in reduced deformability of RBCs that are rapidly cleared by the spleen causing anaemia of severe *Plasmodium* malaria (Dondorp *et al.,* 1999). In response to acute malaria, there is proliferation and hyperactivity of macrophages in the reticuloendothelial system (RES), with phagocytosis of both parasitized and unparasitized RBC, which have

abnormally rigid membranes. Removal of unparasitized RBC is the most important mechanism leading to the persisting or worsening anaemia in the weeks following clearance of parasitaemia (Menendez *et al.,* 2000).

1.4.4 Impact of malaria on school attendance

Brooker *et al*., (2000a) estimated that malaria is responsible for 4–10 million schooldays (1% of all days) lost in Kenya per year. This has a negative impact on children's school performance.

1.4.5 Global Malaria epidemiology

Of the four known malaria parasites, *P. falciparum* is responsible for severe clinical malaria. It is widely distributed in the tropics and sub-tropics. *P. vivax* has the broadest distribution in temperate climates as well as tropical and sub-tropical climates. *P. ovale* is less common than *P. vivax* and *P. falciparum*. Itis found in tropical Africa while *P. malariae* is sporadic and overlaps with *P. falciparum* in its distribution (Gilles, 1993). There is no animal reservoir for the four species and because of this the natural transmission of the disease is determined by the human host, the mosquito vector and environmental factors, (Gilles, 1993).

Currently malaria is endemic in 108 countries (WHO malaria report, 2009). Global estimates indicate 243 million cases of malaria worldwide of which (85%) were reported in the African region only, followed by the South-East Asia (10%) and Eastern Mediterranean regions (4%) (WHO malaria report, 2009). Malaria accounted for an estimated 863 000 deaths in 2008, of which 89% occurred in the African region, followed by the Eastern Mediterranean (6%) and the South- East Asian regions (5%) (WHO malaria report, 2009). Brooker and Utzinger, (2007) estimated

the global annual mortality and the burden of malaria expressed as DALY to be 1.272 million and 46.49 million respectively.

1.4.6 The burden of *Anophelene gambiae* in sub-Saharan Africa

Anopheles gambiae mosquitoes are present throughout tropical Africa and its offshore islands. The complex comprise of some two important species largely responsible for transmission of malaria (*An. gabiae* and *An. arabiensis*). Some studies have shown that at least 6 cryptic or "sibling" species are involved (Coetzee *et al.,* 2000). The six species have the following scientific names: species A: *An. gambiae*; species B: *An. arabiensis*; species C: *An. quadriannulatus*; species D: *An. bwambae*; East African salt-water breeder: *An. merus*; and West African salt-water breeder: *An. melas* (Coetzee *et al.,* 2000). Apart from *An. quadriannulatus,* all *species* are malaria vectors (White, GB 1974).

Species A and B occur together in most areas, extending southwards to sub-tropical latitudes and eastward to Mauritius. Proportions of mixed A-B populations may depend directly or indirectly on relative humidity, with A favoured when humidity approach saturation (White GB, 1974). Species B is often absent from areas of highest humidity, but thrives in relatively arid savannas and steppes. Species C and D have relict distributions. Both saltwater species are coastal: *melas* in West Africa and *merus* in East Africa and larger islands except Zanzibar; *merus* also spreads inland (White GB, 1774; Coetzee *et al*., 2000).

1.4.7 Epidemiological distribution of malaria in Zimbabwe

Malaria remains a serious public health challenge causing immense mortality and morbidity in Zimbabwe. Transmission of the disease is largely unstable. All age

groups are at risk of malaria. About 50% of the country's population is at risk of contracting malaria each year (National Malaria Control Programme, 2008). The high-risk population includes pregnant mothers and children less than 5 years of age because of their susceptibility to malarial anaemia. On average 2 198 deaths occur annually due to malaria (National Health Report, 2001-2008). Table 1.4.7.1 describes the reported malaria hospital admissions and malaria related deaths in Zimbabwe from 2001 to 2008.

Table 1.4.7.1: Reported malaria hospital admissions in Zimbabwe (2001-2008)

Year	Cases	Deaths	Case Fatality Ratio
2001	45 643	1 512	3.3
2002	36 013	1 844	5.1
2003	23 805	1 044	4.4
2004	44 111	1 809	4.1
2005	22 262	895	4.0
2006	23 343	802	3.4
2007	7 901	446	5.6
2008	11350	232	2.0

Source: National Health Report, 2001-2008

1.4.8 Stratification of malaria by transmission levels in Zimbabwe

New malaria stratification was formulated in 2001 using expert opinion, epidemiological and entomological data. Out of the 59 rural districts, malaria occurs in 54 districts whose levels of transmission vary from very high and seasonal to sporadic (National Malaria Control Programme, 2008). The districts are classified as

follows: six with high and seasonal transmission; twelve with moderate and seasonal transmission; fifteen with low and short seasonal transmission; twenty with one sporadic transmission and five are free of malaria (National Malaria Control Programme, 2008). Figure 1.4.9.1 describes this stratification. Thirty-three (33) districts have high malaria transmission warranting some interventions.

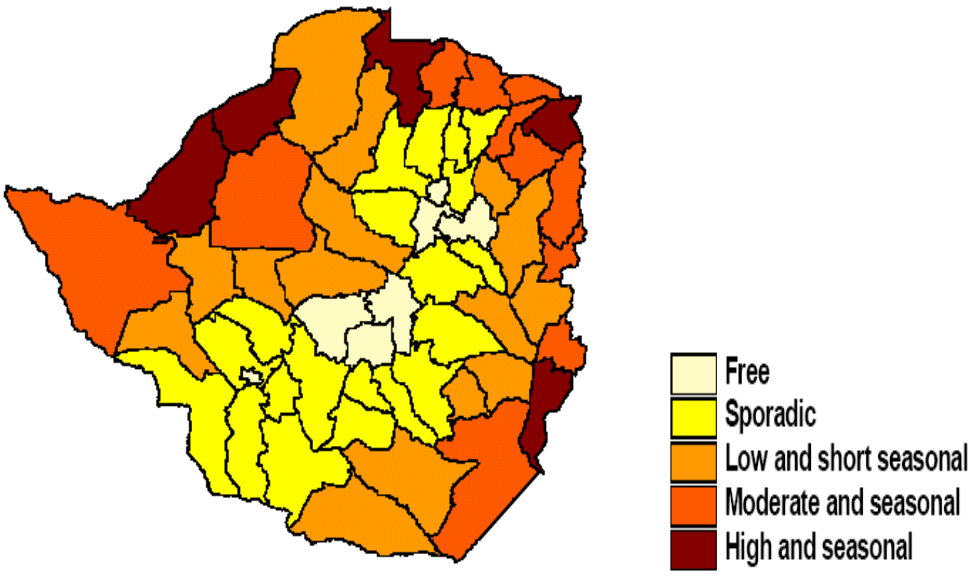

Figure 1.4.8.1: Malaria stratification by transmission levels in Zimbabwe (Adapted from National Malaria Control Programme, 2008)

Plasmodium falciparum is responsible for 97.8% of all malaria cases, followed by *P. malariae* and *P. ovale* with prevalence of 1.8% and 0.3% respectively (Taylor and Mutambu, 1986; National Malaria control programme, 2008). The major mosquito vector for malaria transmission is the female *Anopheles arabiensis* (Taylor and Mutambu, 1986). Peak transmission of malaria occurs between February and May with little or no transmission in winter and dry seasons, from July to October (Taylor and Mutambu, 1986).

Malaria prevalence in Zimbabwe is dependent on altitude with the highest cases 30.5% occurring in altitude less than 600 m above sea level to the north of the country (Taylor and Mutambu, 1986). In these areas, malaria is stable and hyperendemic. Areas of similar altitude to the south east of the country are mesoendemic comprising of 10% of the total malaria prevalence. At altitudes of about 900 to 1200 m above sea level, malaria is hypoendemic and absent in areas above 1200 m (Taylor and Mutambu, 1986). Table 1.4.9.1 describes the distribution of *P. falciparum* by age group and altitude.

Table 1.4.8.1: Age prevalence of *P. falciparum* by altitude zones

Altitude	n (% + vet)				
	<1 yr	1-4 yrs	5-9 yrs	10-14 yrs	≥15yrs
< 600mN	69(8.7)	317(25.2)	711(29.3)	870(21.1)	1192(15.3)
< 600mS	15(0)	112(10.7)	2460(15.8)	659(11.1)	417(7.4)
> 600nN	758(2.9)	3958(4.7)	1865(5.5)	671(8.5)	1129(9.8)
> 600mS	366(0.8)	1821(3.4)	2462(2.4)	2330(1.0)	3169(2.3)

Source: Taylor and Mutambu, (1986)
Key: mS = metres above sea level to the south of the country
mN = metres above sea level to the north of the country

1.4.9 Malaria vectors in Zimbabwe

The major mosquito vector for malaria in Zimbabwe is the female *Anopheles arabiensis. Anopheles gambiae, An. fenestus, An. quadranulatus* and *An. merus* are also potential vectors (Taylor and Mutambu, 1986, Masendu *et al*., 2004). The following species: *An. arabiensis* (90%), *An. gambiae* (4%) and *An. quadriannulatus* (6%) occur in Kanyembe in Zimbabwe (Masendu *et al*., 2004).

1.4.10 Global Malaria control strategies

The current global malaria control strategies are based on: (i) prompt treatment with an artemisinin-based combination therapy (ACT) . This is based on parasitological confirmation of malaria cases by microscopy or with a rapid diagnostic test (RDT) (WHO malaria report, 2009), (ii) in-door residual spraying (IRS) with WHO-approved chemicals including dichloro-diphenyl-trichloroethane (DDT), (iii) universal provision of long-lasting insecticide nets (LLINs) to people at high risk of infection, (iv) intermittent preventive treatment of pregnant women (IPTp). The 2005 World Health Assembly advanced Roll Back Malaria (RBM) targets defined in 2000 by African heads of state and set coverage of 80% or more for the four key interventions (WHO malaria report, 2009). The goals postulated by the Global Malaria Action Plan (World Health Organization, 2008) were that the interventions should reduce the numbers of malaria cases and deaths per capita by 50% or more between 2000 and 2010 and by 75% or more between 2000 and 2015. Currently there are 5 ACTs recommended for use: artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine, artesunate-sulfadoxine pyrimethamine and dihydro-artemisinin-piperaquin.

1.4.11 Control of malaria in Zimbabwe

Zimbabwe is implementing the four key strategies for malaria control although universal coverage of LLINs to people at high risk of malaria is still to be scaled up. Following emergence of resistance to a combination of chloroquine and sulfadoxine pyrimethamine therapy in Zimbabwe, the country switched to artemether-lumefantrine (Coartem) as the first line malaria treatment ACT combination therapy for uncomplicated malaria in 2008. According to policy guidelines, malaria suspected cases are confirmed using the rapid diagnostic kits (RTD), and microscopic

examination of thick and thin blood smears to confirm malaria infection. Confirmed cases are treated with the first line ACT (Coartem) according to treatment guidelines.

Complicated cases or cases failing to respond to first line drugs are administered quinine either orally or intravenously. Pregnant women are given sulfadoxine pyrimethamine (Fansidar) as IPTp two times during pregnancy. Intermittent preventive treatment (IPTp) is restricted to pregnant women in malarious areas or districts.

1.4.12 Malaria vector control

Malaria vector control is protects individuals against infective mosquito bites and, at the community level, to reduce the intensity of local malaria transmission. The current interventions include provision of insecticide-treated nets (ITN) and indoor residual spraying (IRS) using dichloro-diphenyl-trichloroethane (DDT) and pyrethroids. Larval control or environmental management complement these core interventions in some specific settings and circumstances if the breeding sites are few, fixed and easy to identify (National Malaria control programme, 2008).

1. 5 Helminths-*Plasmodium* co-infections (polyparasitism)

Co-infection is the existence of two or more diseases in the same individual. Recent studies based on geographical information systems (GIS) have helped in the production of risk maps for schistosomiasis, malaria and STHs distribution in different geographical areas and in particular in sub-Saharan Africa (Brooker *et al.,* 2000b; Brooker *et al*., 2006a; Raso *et al.,* 2006a**;** Raso *et al.,* 2007a; Raso *et al.,* 2007b). Using such maps, the overlap in geographical and spatial distribution of parasitic infections with schistosomiasis and STHs; helminths and HIV; TB and

malaria can be deduced (Bundy *et al.,* 2000a; Brooker *et al.*, 2000b; Raso *et al.,* 2007a). This is despite the fact that GIS maps still need an update with comprehensive parasitological data collected systematically from the field (Brooker *et al.,* 2000b).

The high prevalence of schistosomiasis, STHs and *P. falciparum* infections in tropical and sub-tropical areas make co-infections with these parasites a norm rather than an exception (Keiser *et al*., 2002; Raso *et al*., 2004a; Brooker *et al.,* 2006a; Brooker *et al.,* 2007a; Mazigo *et al.,* 2010; Mwangi *et al.,* 2006; Hotez *et al.,* 2006; Raso *et al.,* 2006b). The similarities between schistosomiasis, STHs and malaria are that the diseases are linked to agricultural and water development schemes (Bradley *et al.,* 1993; Chandiwana *et al*., 1983; Chandiwana *et al*., 1989). Schistosomes and STHs are transmitted through contamination of the environment with faecal matter or urine and poor sanitary facility (WHO, 2002; de Silva *et al.,* 2003). They also share relatively similar temperature conditions 23^{o}c to 33^{o}C, humid climate and both exist in poor communities (Brooker *et al.,* 2007b; Mehanna *et al.,* 1994; Raso *et al.,* 2006b).

The high- risk group for schistosomiasis and STH is the same; children aged 5-15 years (Brooker *et al.,* 2007a; Taylor and Makura, 1985; WHO, 2002; Salvioli *et al.,* 2002; Montresor *et al.,* 2002; Raso *et al.,* 2007b). Morbidity due to schistosomiasis and STHs is directly related to worm burden (Olsen *et al.,* 1998; Brooker *et al.,* 2007a). Persons of the same age range experience frequent malaria attacks if they live in stable malaria transmission areas (Taylor and Mutambu, 1986; Brooker *et al.,* 2006a; Brooker *et al.,* 2007a). Thus, primary schoolchildren are at high risk of co-infection with schistosomiasis, malaria and STHs. In spite of their exposure to the devastating consequences of helminths–*Plasmodium* co-infection, data is scarce on

the extent of polyparasitism and the consequences of helminths–*Plasmodium* co-infections among primary school children and the general population (Keiser *et al*., 2002; Raso *et al.*, 2004a; Brooker *et al*., 2007a).

Using mathematical models Brooker *et al.*, (2006a) estimated that of the 179.3 million school-aged children 5–14 years living in sub-Saharan Africa, 50 million are infected with hookworm, 90.8 million (50.7%) are exposed to stable endemic malaria transmission and 45.1 million (25%) are at coincidental risk of hookworm and malaria infection. As a result, several reports have shown global interest in investigating occurrence of polyparasitism with neglected tropical diseases (including schistosomiasis and STHs) and *Plasmodium.* This is because the world is shifting onto cost effective integrated control strategies in areas where there is evidence of co-existence of multiple parasitic infections (Hotez *et al.,* 2006; Mwangi *et al.,* 2006; WHO, 2006a).

1.5.1 Helminths–*Plasmodium* co-infection in Zimbabwe

Several epidemiological studies conducted in Zimbabwe over the past decades were vertical in nature. They described age specific prevalence distribution of single parasitic diseases even in areas where geographic and socio-economic conditions clearly show that schistosomiasis, STHs and *Plasmodium* coexist in the same settings. For example Taylor and Makura, (1985) described the national distribution of schistosomiasis, indicating high prevalence in primary school age children (8-15) living in rural and farming areas in Zimbabwe. They showed predominant distribution of *S. haematobium* in the rest of the country with low to zero prevalence in the western region of the country. Taylor and Mutambu, (1986) described the national distribution of *Plasmodium* malaria in Zimbabwe. They demonstrated that

Plasmodium falciparum malaria was highly prevalent among children aged 5-15 years especially in low-lying areas (≤ 600m above sea level) compared to other age profiles.

Although results from these major national surveys show overlap of helminths and malaria in some areas, there has not been any study conducted to describe the epidemiological existence of helminths-*Plasmodium* polyparasitism in the country. Furthermore, there is growing evidence that helminths impair immune response of the host to *Plasmodium* infection adversely affecting the clinical outcome of malaria. This is because helminth infections are known to drive immune responses towards the production of the non-cytophilic subclasses (IgG2, IgG4 and IgM), whereas protection against malaria is associated with the presence of the IgG1 and IgG3 cytophilic subclasses (Druilhe, 2005).

The paucity of data on the extent to which polyparasitism occur has resulted in little effort being given to the exploration of the feasibility of integrated helminths-*Plasmodium* control strategies (Hotez *et al.,* 2006; Mwangi *et al.,* 2006; Brooker *et al.,* 2007a). Therefore, understanding of polyparasitism is not only relevant from a fundamental point of view, but also to harness programmatic similarities for integrated, cost-effective and sustainable control.

1.5.2 Anaemia in helminths-*Plasmodium* co-infections

Anaemia is a global public health problem affecting both developing and developed countries with major consequences for human health, social and economic development. Although it occurs among all age ranges, global estimates demonstrate that it is more prevalent in pregnant women and young children (Tatala *et al.,* 1998; WHO, 2008c). It affects 1.62 billion people worldwide with the highest prevalence

occurring in pre-school children (47.4%) and the least in men (12.7%). World Health Organization regional estimates generated for preschool-age children, pregnant and non-pregnant women indicate that the highest proportion of individuals affected are in Africa (47.5-67.6%), while the greatest number affected are in South-East Asia where 315 million individuals in these three population groups are affected (WHO, 2008c).

Childhood iron-deficiency anaemia has a strong link with impaired cognitive functioning, reduced school performance, reduced physical performance, growth and particularly work productivity in adults (Nokes and Bundy, 1994; Grantham-McGregor, 2001, Halterman *et al.,* 2001; WHO, 2008c). The etiology of anaemia is multi-factorial. A variety of isolated causes of anaemia can be synergistic if they co-exist, a condition that is most often (Tatala *et al*., 1998; WHO, 2008c).

However, the global most significant contributor to the onset of anaemia is iron deficiency (IDA). The main risk factors for IDA include a low intake of iron (Tatala *et al.,* 1998), poor absorption of iron from diets high in phytate or phenolic compounds, and period of life when iron requirements are high especially during childhood growth and pregnancy (WHO, 2008c). The presence of other micronutrient deficiencies, including vitamins A and B12, folate, riboflavin, and copper can increase the risk of anaemia (WHO, 2008c).

Whilst the etiology of anaemia is multi-factorial, heavy blood loss due to parasitic diseases including schistosomiasis, STHs and *Plasmodium* malaria infection also contribute to anaemia. Surprisingly, although distinct mechanisms through which helminths and *Plasmodium* malaria cause anaemia exist, there is a paucity of data on

the effect of their coincidental infection on the level and severity of anaemia (Hotez *et al.,* 2006; Broker *et al.,* 2007a). Several studies have only explored the effect of single parasitic infections (Flemming *et al.,* 2006; Koukounari *et al.,* 2006). Studies on the impact of schistosomes, STHs and *P. falciparum* co-infection on anaemia particularly in primary schoolchildren are relevant for the design and implementation of integrated control programmes aimed at reducing anaemia and other associated morbidities.

1.5.3 Integrated control of polyparasitism

Basing on the overlap of conditions that favour polyparasitism with schistosomes, STHs and *P. falciparum* and the devastating morbidities associated with these communicable diseases, the global interest to explore the feasibility of integrated control strategies has grown (Hotez *et al.,* 2006; Mwangi *et al.,* 2006; Brooker *et al.,* 2007, 54thWHA, 2001). In 2006, WHO introduced preventive chemotherapy strategy that encourages integrated control of neglected tropical disease in co-endemic communities (WHO, 2006a). This strategy shows the global interest for cost effective integrated control of NTDs STHs, schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma and Human African trypanosomiasis (WHO, 2006a). However, the success of this initiative is premised on the knowledge of the extent of co-infection with NTDs in endemic countries (Hall and Horton, 2009; WHO, 2002; WHO, 2006a). Thus, baseline studies that identify the number of people with single, co-infections, and those at risk of co-infection with NTDs have a potential to promote evidence-based priority setting. It also enables careful targeting of limited financial resources, resulting in enhancement of sustained integrated control of co-infections.

Other proponents of integrated control strategies have seen greater opportunities for control of neglected tropical diseases (NTDs) if they are integrated with control of malaria, tuberculosis or HIV/AIDS referred to as "the big three diseases." This is due to the high international attention given to HIV/AIDS, malaria and TB leading to major funding for their control (Hotez *et al.,* 2006; Mwangi *et al.,* 2006). The arguments in favour of these proposals are that the big 3 diseases are geographically overlapping with NTDs in the developing world and that the combined impact of NTDs on DALYs is equivalent to any one of the big 3 diseases (Hotez *et al*., 2006).

Lack of evidence has created a need to investigate the extent to which co-infections with NTDs and malaria, tuberculosis or HIV occurs in various settings (Brooker *et al.,* 2007a; Hotez *et al.,* 2006; Mwangi *et al.,* 2006). That the primary school age children (5-15 years) who are at high risk of parasitic diseases' co-infections have been neglected in prominent disease control strategies, is shown by the scarcity of data on anaemia of this age group at country and global level (WHO, 2008c). It is also shown by the conspicuous bias towards effective malaria control in children less than five years and pregnant women through provision of LLN as well as IPTp (WHO malaria report, 2009).

1.5.4 Knowledge attitudes and practices in relation to parasitic diseases

As part of a strategy to monitor and evaluate large-scale anthelminthic control programmes, the World Health Organization recommends baseline epidemiological survey to be conducted among specifically grade 3 children (age range 8-10 years). This age group has a high prevalence of helminthic infection in any endemic community (Montresor *et al.,* 1999). Thus, the prevalence of helminths in this age group can be used as a proxy for assessing community prevalence (Montresor *et al.,*

1999; Guyatt *et al.*, 1999). Surprisingly, little attention has been given to investigate knowledge, attitudes and practices of grade 3 children in relation to schistosomiasis, STHs and malaria in Zimbabwean and elsewhere.

The impact of school based health education on knowledge and extent of behaviour modification among this target population is scarce, yet modification of human practice, a product of health promotion is among the mainstays of schistosomiasis, STHs and malaria control (Montresor *et al*., 1999; Montresor *et al*., 2002; WHO, 2006a). Health promotion in schools also helps to improve students' health, knowledge and practices required to combat the challenge of communicable diseases (Lee *et al*., 2008).

1.5.5 Study rationale

Sixty percent (60%) of 3 million primary school children live in farming, peri-urban or rural areas in Zimbabwe. Many children in these communities still lack access to anti-helminthic drugs and do not have access to LLNs as these are directed towards protection of pregnant women and children less than 5 years old. Earlier studies conducted separately in Zimbabwe have shown occurrence of high prevalence of schistosomiasis, STHs and malaria among primary school aged children (Taylor and Makura, 1985; Taylor and Mutambu, 1986; Bradley *et al.*, 1992). Surprisingly data is scarce on extent of polyparasitism with schistosomiasis, STHs and malaria in primary school children in Zimbabwe and elsewhere (Brooker *et al.*, 2007b). There is also a paucity of data on the effect of helminths-*Plasmodium* co-infections on anaemia although these communicable diseases are etiological agents of anaemia. Little is known on feasibility of integrating helminths and malaria control and the effect that it

would have on polyparasitism and anaemia. This data is important for formulating pragmatic and sustainable integrated control strategies targeting schoolchildren. This study was conducted to determine the prevalence of polyparasitism among primary school children living in rural and commercial farming areas in Zimbabwe. The effect of polyparasitism on anaemia, the effect of combined school based treatment of co-infections on anaemia and prevalence of polyparasitism in primary school children were determined. Efficacy of praziquantel against *S. haematobium* treatment and the effectiveness of school based health education on the knowledge, attitudes and practice of grade 3 primary school children were also determined.

1.5.6 Overall hypothesis

Co-infections with schistosomes, STH and *Plasmodium falciparum* are common in different communities in Zimbabwe and combined treatment of co-infections has no effect on anaemia among primary school children.

1.5.7 Main objective

To determine the prevalence of single and helminths – *Plasmodium* co-infections among primary school children living in rural and commercial farming areas in Zimbabwe, the effect of co-infections on anaemia and efficacy of combined treatment intervention on prevalence of co-infections and anemia.

1.5.7.1 Specific objectives 1

To determine the prevalence distribution of single and co- infection with schistosomes, STHs and *P. falciparum* among primary schoolchildren living in rural and commercial farming areas in Zimbabwe.

1.5.7.1.1 Null hypothesis 1

Single and co-infections with schistosomes, STH and *P. falciparum* are common in diverse communities in Zimbabwe.

1.5.7.1.2 Overview 1

Previous studies on infections with schistosomiasis, STH and *P. falciparum* provided data only on single infections in Zimbabwe and elsewhere (Taylor and Makura, 1985; Taylor and Mutambu, 1986; Chandiwana, 1989; Bradley *et al*., 1993). This study was aimed at determining the extent of single and co-infections with schistosomes, STH and *P. falciparum* in rural and commercial farming areas in Zimbabwe. Stool, urine and venous blood were collected from primary schoolchildren and analysed parasitologically in order to determine the occurrence of parasites.

1.5.7.2 Specific Objective 2

To determine the consequence of polyparasitism on anaemia among primary school-children living in co-endemic areas for schistosomiasis, STH and *P. falciparum*.

1.5.7.2.1 Null hypothesis 2

Polyparasitism with schistosomes, soil transmitted helminths and *P. falciparum* has no effect on prevalence of anaemia.

1.5.7.2.2 Overview 2

Schistosomes, STH and *P. falciparum* are etiologic factors of anaemia (Hotez *et al*; 2004; Freidman *et al*., 2005; Menendez *et al.*, 2000). Surprisingly, several studies on the impact of these parasites on anaemia in populations living in co-endemic areas have always focused on single infections (Koukounari *et al*., 2006; Stoltzfus *et al*., 1997; Geerligs *et al*., 2003). However, polyparasitism with helminths-*Plasmodium* co-infections is common in tropical and sub-tropical countries (Keiser *et al.*, 2002;

Hotez *et al.*, 2006; Mazigo *et al*., 2010). Data on the effect of co-infections on the prevalence and severity of anaemia is scarce. This study provided data on the combined effect of polyparasitism with schistosomes, STH and *P. falciparum* on anaemia. Venous blood samples were collected from primary school children living in the commercial farming area in Zimbabwe and anaemia was assessed using the portable Hemocue machine. Stool and urine samples were also taken and screened for intestinal helminths and *S. haematobium* respectively. *Plasmodium falciparum* was determined from venous blood.

1.5.7.3 Specific Objective 3

To determine efficacy and side effects of praziquantel treatment against *Schistosoma haematobium* infection among primary school children in Zimbabwe.

1.5.7.3.1 Null hypothesis 3

Praziquantel treatment against *S. haematobium* is not efficacious among Zimbabwean primary school age children**.**

1.5.7.3.2 Overview 3

S. haematobium is predominantly distributed in the Zimbabwe (Taylor and Makura, 1985; Chandiwana *et al*., 1988b). Zimbabwe has drafted a plan of action for the control of schistosomiasis adopting a school based mass drug administration approach (MOHCW, 2006). However, there in no current data on efficacy of praziquantel treatment against schistosomiasis treatment. Praziquantel treatment efficacy against *S. haematobium* infection ahead of its anticipated wide-spread use was assessed. Children found infected with *S. haematobium* at baseline, received praziquantel treatment and successfully followed up at six weeks post treatment survey. A quantitative urine filtration technique was used to determine *S. haematobium* infection

status at baseline and 6 weeks post treatment surveys. Parasitological cure and egg reduction rates were calculated as determinants of treatment efficacy.

1.5.7.4 Specific objective 4

To determine and describe changes in prevalence of helminths-*Plasmodium* co-infections, anaemia and intensity of helminths at 6, 12 and 33 months following introduction of combined school based praziquantel, albendazole and prompt malaria treatment at baseline and at any follow up survey when infection was detected.

1.5.7.4.1 Null hypothesis 4

Combined school based de-worming and prompt malaria treatment will not results in prevalence reduction of anaemia, single parasitic infections and polyparasitism among primary school children.

1.5.7.4.2 Overview 4

The efficacy of combined treatment for schistosomiasis, STHs and *P. falciparum* on prevalence of helminths-*Plasmodium* co-infections and anaemia is not known (Brooker *et al*., 2007a; Hotez *et al*., 2006; Mwangi *et al*., 2006). This study provides data on the effect of combined school based treatment of schistosomiasis, STHs and malaria treatment over 33 months on prevalence of co-infection and anaemia. Of the 1 303 primary school children enrolled into the study, 475 participants were diagnosed for all parasites, screened for anaemia and were stratified into co-infection combinations at baseline. They received the corresponding combined treatment at baseline, and were successfully followed up being diagnosed for all parasites and anaemia at all follow up surveys. They also received treatment at any other follow up survey if found infected. The follow up data from these participants was used to

determine the effect of combined treatment intervention on prevalence of co-infections, helminths infection intensities and anaemia.

1.5.7.5 Specific objective 5

To assess grade three children's knowledge, attitudes and practices regarding schistosomiasis, STHs and malaria before and after school health promotion campaigns.

1.5.7.5.1 Null hypothesis 5

School based health education in relation to causes and prevention measures of schistosomiasis, STH and malaria does not improve knowledge and behaviour of primary school children towards the prevention of these diseases.

1.5.7.5.2 Overview 5

Grade three children are known to harbour high prevalence and intensities of schistosomes, STH and malaria in endemic communities (Montresor *et al*., 1999). It is for this epidemiological reason that the prevalence of helminths in grade 3 children is used as a proxy of the prevalence of helminthiasis in the community in which they live (Montresor *et al.,* 2002; Guyatt *et al.,* 1999). They are also at high risk of *P. falciparum* infection (Taylor and Mutambu, 1986). However, grade three children's knowledge, attitude and practices (KAP) in relation to these parasitic diseases are not known. The role of school based health education about schistosomiasis, STHs and malaria on the KAP of these children is also not known. A KAP questionnaire was administered to grade 3 children before school health education intervention and at 6 months after intervention in order to assesses the effectiveness of intervention on children's KAP in relation to these communicable diseases.

CHAPTER 2: MATERIALS AND METHODS

2.1 Study design

This study was a longitudinal intervention trial that involved screening of participants for anaemia, diagnosis of schistosomes; STHs, *P. falciparum* and treatment of infected individuals at baseline, 6, 12 and 33 months follow up surveys.

2.2 Study setting, sampling of wards and schools

Manicaland province was conveniently chosen for the study due to its geographical location (Eastern Highlands) characterised by high annual rainfalls, wet soils and malaria endemicity (Zimbabwe National Health Profile, 2002; Mutapi *et al*., 2000). These conditions are conducive for survival of schistosome species, STHs and malaria vector mosquitoes. Mashonaland central was also conveniently chosen due to the known high schistosomiasis endemicity in the province (Taylor and Makura, 1985; Chandiwana *et al.*, 1988b). Multistage sampling technique was used to select the districts, wards and schools in which the study was conducted. Mutare district was randomly selected from 7 districts in Manicaland province. Ward 7 was randomly selected from 36 wards in Mutare district and three of the 5 primary schools in ward 7 were randomly selected. Shamva district was also randomly selected in Mashonaland Central province and Ward 10 was selected from the 29 wards in the district. Since only Nyamaropa primary school is situated in Ward 10 and the school enrolment of over 700 pupils exceeded the calculated sample size, the school was included in the study without further selection. Every child at each school was eligible except for grade 7 children and those who were not willing to participate in the study.

Figure 2.2.1 show the map of Zimbabwe with the location of sites selected for the study. The provinces from which the sites were selected are also highlighted.

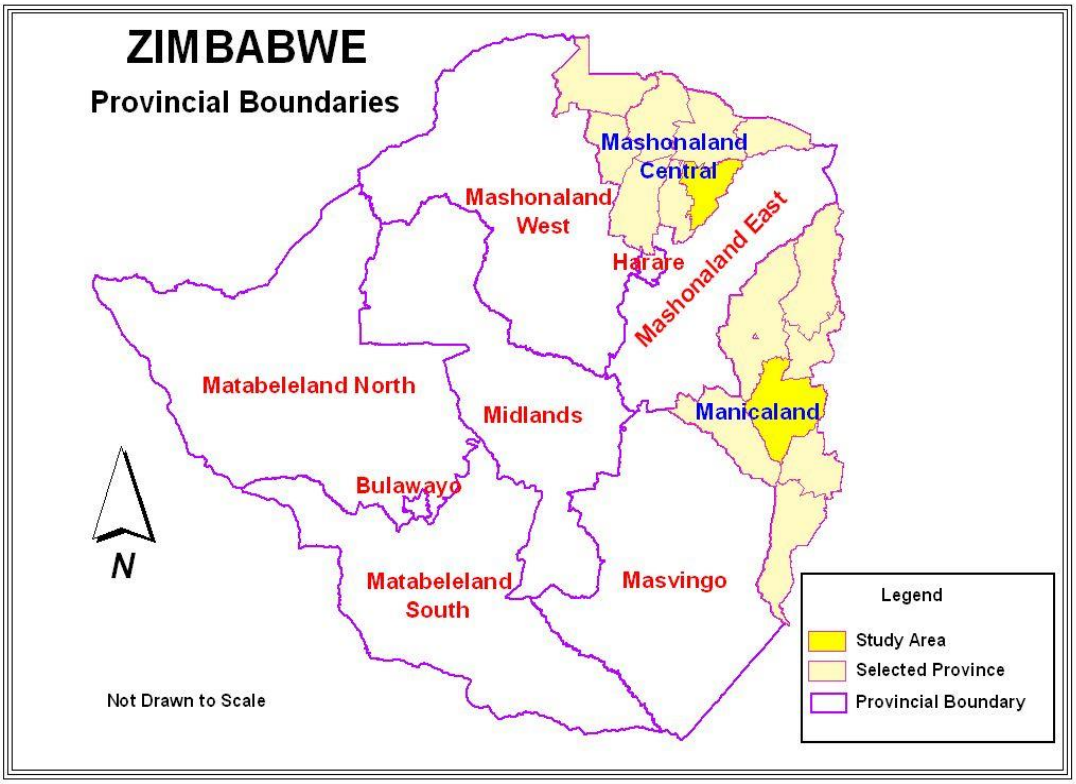

Figure 2.2.1: Map of Zimbabwe showing the location of the study sites.

Burma Valley, which borders with Mozambique, is located in Mutare district, Manicaland province, about 300 km east of Harare. It receives heavy rainfall, which averages 202 mm/month in summer (November-March) and is warm to hot throughout the year. Perennial rivers and streams drain from the mountain ranges to the south. The area is divided into 12 commercial farms and two new resettlement areas. Each farm has a compound where farm labourers live. The communities living in the farm compounds use communal piped water located at strategic points. They also use communal toilets and bathrooms distributed around the compounds. The predominant commercial crops grown in the area include bananas, flowers, butternut squash and tobacco. Abundant irrigation activities keep the soil wet all year round.

Three primary schools (Valhalla, Msapa and Kaswa) drawing children from the farming communities were included in our study. The schools are served with Burma Valley (Mazonwe) clinic that is located at the centre of Burma Valley and provides health services to the population. Msapa Primary school is about 500 m away from the clinic whilst Kaswa and Valhalla are about 10 km away to the west respectively. Figure 2.2.2 shows the map of Mutare district with the wards numbered 1-36. Ward 7 was randomly selected for the study.

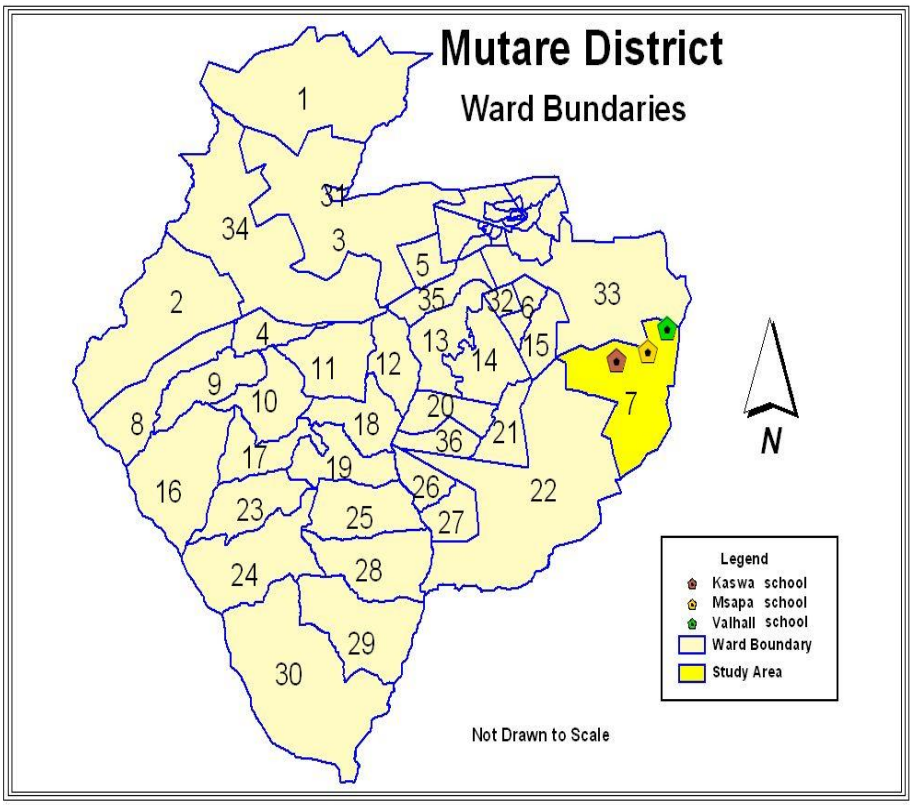

Figure 2.2.2: Wards in Mutare district, Manicaland province, Zimbabwe

Nyamaropa is a typical rural area located in Shamva district, 160 km north east of the capital city, Harare. The area receives high rainfall, which averages 175 mm/month during the rainy season (November-March), but is dry between May and October. The inhabitants practice subsistence farming. The major source of water is Eben dam on

the perennial Mupfurudzi River. The community has no access to tape water. It draws water for domestic purposes from open wells and a few boreholes distributed in the area. During the dry season, the community is heavily involved in vegetable gardening along the rivers and near the dam. Children from this area included in the study attended Nyamaropa primary school and were drawn from 19 villages that surround the school.

Figure 2.2.3 shows the map of Shamva district with the wards numbered 1-29. Ward 10 was randomly selected for the study.

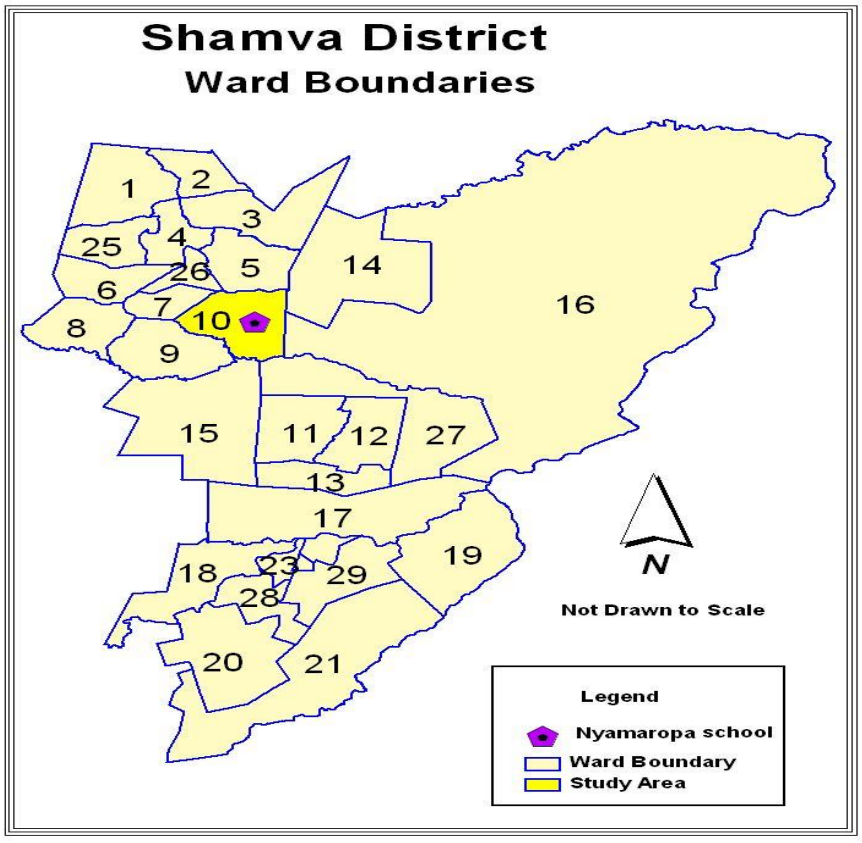

Figure 2.2.3: Wards in Shamva district, Mashonaland Central province, Zimbabwe

2.3 Sample size determination

The sample size was calculated on the basis of specific objective 1.5.7.1: To determine and describe prevalence of co- infection with schistosomes, STHs and *P. falciparum* among primary school children living in Nyamaropa rural and Burma Valley commercial farming areas in Zimbabwe. The sample size was calculated using the prevalence of hookworm, 61.7%, *S. haematobium,* 58.7% and malaria, 23.5% observed in the Burma Valley commercial farming area from previous studies (Chandiwana *et al.,* 1989; Mutapi *et al.,* 2000). The prevalence of *S. haematobium* (53.1%) observed by Chandiwana *et al.,* (1988b) in Chiweshe and Bushu communal areas, was used to calculate the sample size in Nyamaropa rural area. Chiweshe and Bushu are located in the same province with Shamva district and are also close to Nyamaropa rural area. The following formula was used to calculate the sample size: $\mathbf{n = (z/delta)^2 P(1-P),}$ where n = the sample size required, Z = 1.96, delta (margin of error) = 0.05 and P = proportion or prevalence of the disease (61.7%, 58.7%, 23.5% and 53.1% respectively). The optimum sample size (n = 373) was estimated for each site. This was adjusted by 30% to n = 485 considering possible loss due to follow up.

2.3 Inclusion and exclusion criteria

All children attending each primary school, except those attending grade seven were eligible for the stury. Grade seven children could not be included in the 33 months longitudinal study since would leave primary school the following year. However, they received treatment for helminths and malaria if they sought. Children severely affected with other diseases and those not willing to give samples were not included in the study. In order to determine efficacy of praziquantel treatment against *S. haematobium* infection, only those children diagnosed *S. haematobium* positive

parasitologically, received treatment at baseline and were successfully diagnosed for *S. haematobium* again at six weeks follow up survey, were included. Children diagnosed *S. haematobium* negative and those who failed to submit urine samples at baseline for urinary schistosomiasis diagnosis were excluded from the praziquantel efficacy study. Only grade 3 children willing to respond to the knowledge attitudes (KAP) and practice questionnaire were included in the KAP study.

2.4 Socio-demographic data collection

Demographic data that includes age, gender, were recorded onto a questionnaire. Ages of participants were also obtained from the class registers provided by teachers when available.

2.5 Parasitological techniques

Parasitological techniques used during the study included the urine filtration technique for the diagnosis of urinary schistosomiasis, the Kato Katz technique and the formal ether concentration for the diagnosis of intestinal helminths (*S. mansoni*, hookworm, *T. trichiura* and *A. lumbricoides*) and the Giemsa staining technique for the diagnosis of malaria. These techniques were performed at each follow up survey as at baseline.

Urine and faecal samples were collected between 10:00 am and 2:00 pm in separate wide mouth plastic specimen bottles (100 ml in size) correspondingly labelled with the laboratory identification numbers assigned to each individual. The samples were processed within two hours of collection. Diagnosis of *S. haematobium* and intestinal helminths (*S. mansoni*, hookworms, *T. trichiura* and *A. lumbricoides*) was based on the detection of worm eggs in urine and faeces, respectively.

2.5.1 Detection of urinary schistosomiasis

Infection with *S. haematobium* was diagnosed using the urine filtration technique as described by Mott *et al*., (1982). In brief; 10 ml of urine was filtered through the Nytrile filter membrane. The filter was stained with Lugol's iodine and examined with an x10 light microscope objective. *S. haematobium* egg intensity was expressed as the number of eggs detected per 10milliliters (egp10ml) of urine. The same procedure was repeated on three consecutive days in order to prevent misdiagnosis due to day-to-day variation of egg excretion (Doehring *et al*., 1983; Engels *et al.,* 1996).

2.5.2 Detection of intestinal helminths (*S. mansoni* and STHs)

The overall intestinal helminths infection status of participants was decided based on the combination of results from the formal ether concentration (Cheesbrough, 1998) and Kato Katz (Katz *et al.,* 1972) techniques in order to improve sensitivity of diagnosis (Goodman *et al.,* 2007). Table 2.5.2.1 describes how the combined results were interpreted from the two techniques. Diagnosis of helminths infection by the two techniques is dependent on microscopic visualisation of helminths eggs on the slide preparation. The difference is that in the formal ether concentration technique about a gram stool is subjected to centrifugal force in order to concentrate the eggs after which the slide is prepared from the sediment. This technique is qualitative. The Kato Katz is quantitative since the number of eggs counted on a faecal thick smear prepared from the strained fine stool (41.7 mg) is converted to number of eggs per gram stool.

Firstly about 1 gram portion of each stool specimen collected on the first day was preserved in a tube containing 10% formalin. The preserved specimens were processed using the formal ether concentration technique without modification.

Secondly, a stool specimen was collected per study participant on 2 successive days and a single faecal thick smear was prepared from each specimen using a 41.7 mg template (Katz *et al.,* 1972). Faecal smears prepared were examined within 30 - 60 minutes using a light microscope in order to detect and quantify hookworm and other STHs eggs. Smears were left to clear for at least 24 hours and were re- examined to detect *S. mansoni* eggs. The Kato-Katz technique was performed on stool specimens collected on two consecutive days. The templates used to prepare the thick smear hold 41.7 mg of strained stool. This quantity of stool is 1/24 of a gram. Therefore, the number of eggs detected from each Kato Katz thick smear was multiplied by 24 in order to express infection intensities as number of eggs per gram stool (epg).

Table 2.5.2.1 Interpretation of parasitological results of intestinal helminths

Interpretation (Combined result)	Results from individual techniques	
	Kato Katz	Formal Ether concentration
Negative	no eggs observed	no eggs observed
Positive	eggs observed	no eggs observed
Positive	no eggs observed	eggs observed
Positive	eggs observed	eggs observed

2.5.3 Infection combination

In order to determine parasite infection combinations at baseline, participants were stratified into the following groups: (i) those participants that were diagnosed for all parasites and (ii) those not diagnosed for all parasites. The later group also included those participants that were not diagnosed for any parasite because like those not

diagnosed for all parasites they would not be given a specific parasite combination in the absence of parasitological results. Table 2.5.3.1 describe the different combinations. Classification of participants into infection combinations was done at baseline, 6, 12 and 33 months follow up surveys.

Table 2.5.3.1: Stratification of participants into co- infection combinations

Group code	Diagnosis compliance	Infection combination
0	Diagnosed for all parasites	Not infect by all parasites
1	Diagnosed for all parasites	SCH only
2	Diagnosed for all parasites	STH only
3	Diagnosed for all parasites	*P. f* only
4	Diagnosed for all parasites	SCH + STH
5	Diagnosed for all parasites	SCH + *P. f*
6	Diagnosed for all parasites	STH + *P. f*
7	Diagnosed for all parasites	SCH + STH+ *P. f*
8	Not diagnose for all parasites	No infection combination

Key:

SCH = schistosomiasis

STH = soil transmitted helminths

2.5.4 Intestinal helminths egg intensities

Egg intensities for intestinal helminths were determined based on the number of eggs detected from each Kato Katz thick smear. Intestinal helminths egg intensities were

classified according to the World Health Organization guidelines at each survey (WHO 2002). Table 2.5.4.1 describes the different categories of intestinal helminths infection intensities and urinary schistosomiasis.

Table 2.5.4.1: Classification of intestinal helminths egg intensities (WHO 202)

Parasite	epg stool or 10 ml urine in each infection intensity category		
	Light	Moderate	Heavy
S. haematobium	1-49 egp10ml	-	≥ 50
S. mansoni	1-99 epg	100-399 epg	≥ 400 epg
Hookworm	1-1 999 epg	2000-3 999 epg	≥ 4000 epg
A. lumbricoides	1-4 999 epg	5000- 49 999 epg	≥ 50 000 epg
T. trichiura	1-999 epg	1000- 9 999 epg	≥ 10 000 epg

2.6 Blood collection and processing

Approximately 5 ml of venous blood was drawn from each willing participant in blood collection tubes containing ethylene diamine tetra acetic acid (EDTA) as anticoagulant. Thick blood smears for malaria diagnosis were prepared from anticoagulated blood. Haemoglobin determination was performed on anticoagulated blood as well. The remaining blood was stored overnight at 4^0C, centrifuged at 3000 rpm for one minute. The plasma separated was aliquoted into 2 ml screw cap storage vials and stored at -70 ^{0}C. Another 5ml of venous blood was drawn in 5 ml plain blood collection tubes, stored at 4^0C overnight after which the blood tubes were centrifuged at 3000 rpm for one minutes. Serum was separated and stored at -70 ^{0}C for later determination of serum ferritin.

2.7 Detection of *P. falciparum*

Thick malaria blood smears were prepared, air dried, Giemsa-stained and observed under the microscope for the identification and quantification of malaria parasites. Malaria parasites were counted against 200 leukocytes (Cheesbrough, 1998). The presence of either ring forms or gametocytes was a conclusive diagnosis of *P. falciparum* infection. *P. falciparum* parasitaemia was estimated by the number of asexual parasites against 200 white blood cell count (WBC) and then multiplying by 40 assuming 8000 WBCs/ul. In this study *P. falciparum* parasitaemia was classified as follows: uninfected, light infection for 1-1000 parasites/µl of blood, moderate infection for 1001-5000 parasites/µl of blood and heavy infection for >5000 parasites/µl.

2.8 Determination of haemoglobin concentrations

Haemoglobin (Hb) concentration was measured using the HemoCue photometer (HemoCue AB, Angelhome, Sweden). In brief, anticoagulated venous blood from each participant was mixed gently. A drop of blood was placed onto a plastic film using a pipette. The HemoCue microcuvette was filled with a drop of blood, placed in the HemoCue cuvette holder and the displayed haemoglobin value of blood was taken within 60 seconds. The Hb values were used to determine if participants were anaemic or non-anaemic.

Anaemia was defined according to WHO guidelines on age and gender cut off thresholds. It was difined as a dichotomous variable taking the value of 1 for children from 5 to 11 years with Hb < 11.5 g/dL, children aged 12 to 14 years with Hb < 12 g/dL, females ≥ 15 years with Hb < 12.0 g/dL and males ≥ 15 years with Hb < 13

g/dL (WHO 2008c). Anaemia was classified into mild (Hb >10.0 < 11.5 g/dL), moderate (Hb >7.1-10.0 g/dL) and severe (Hb ≤ 7.0 g/dL).

2.9 Determination of serum ferritin concentration

Serum ferritin concentration was determined using the Enzyme Linked Immunoassay kit (Spectro Ferritin, Ramco Laboratories. Inc. Stafford. Texas, USA) following manufacturer's instructions.

According to the manufacturer's protocol, iron stores were considered depleted if serum ferritin concentration was < 20 ng/ml, IDA was defined as serum ferritin < 20 ng/ml among anaemic individuals. Serum ferritin values between 20 and 100 ng/ml in anaemic patients were suggestive of a combination of iron deficiency with some cause of anaemia. Overall, IDA was considered as a combination of IDA and iron deficiency with some cause of anaemia. Serum ferritin concentration > 300 ng/ml indicated increased iron stores. Serum ferritin iron was only determined at baseline among participants living in Burma Valley farming area that gave blood for anaemia screening.

2.10 Treatment intervention

Due to ethical reasons, our study design did not follow an orthodox dose dependant treatment in which mass treatment would be administered to the study population regardless of infection status. The study also involved treatment of malaria with a combination of chloroquine, sulphudoxine/pyrimethamine (EDLIZ 2004), which could not be administered indiscriminately and regularly to children but only to infected individuals. Thus, in our study design only children found infected with any specific parasite under investigation using parasitological methods at baseline

received treatment. All study participants were followed up at 6, 12 and 33 months follow up surveys and treatment was given only to those individuals with either single infections, schistosome-STHs co- infection or helminths-*Plasmodium* co-infection at each survey. The exception was treatment of malaria that was given based on parasitological results when the research team was in the field and based on signs and symptoms when the team was not in the field.

Children infected with any of the schistosome species and STHs received a single dose of praziquantel at 40 mg/kg body weight and a single dose of 400 mg albendazole respectively. Bread and orange juice (500 ml/child) were given as supplementary food following swallowing of tablets in order to enhance absorption and reduce the nauseating effect of PZQ.

2.10.1 Prompt malaria treatment

After administration of the baseline knowledge, attitudes and practices questionnaire to grade 3 children, all primary school children were given leaflets indicating that: malaria is caused by a bite from mosquito, malaria causes anaemia and kills, malaria is prevented by early identification of signs and symptoms and seeking early treatment. Signs and symptoms of malaria include fever, headache, vomiting, general body weakness and joint pains. If one experiences any of such symptoms, one should immediately tell the class teacher or parent and seek prompt malaria treatment at the nearest clinic.

2.10.2 Combined treatment intervention

Combined treatment was defined as complete treatment for any two or three parasitic co-infection combinations: schistosomiasis + STH; schistosomiasis + *P. falciparum*; STH + *P. falciparum* or schistosomiasis + STH + *P. falciparum*. If a participant was

infected with schistosomiasis + STH and received albendazole treatment for STHs only, the participant was considered untreated for co-infections. The same explanation applied for other co-infection combinations. Those participants infected with single parasites received specific treatment for the particular parasites. Children who had helminths-*Plasmodium* co-infection received treatment for helminths on day one and for malaria 24 hours later (day 2).

2.10.3 Treatment compliance at baseline and action taken

During baseline, it was expected that children diagnosed would automatically line up for treatment on treatment days as explained. However, due to the bitterness of praziquantel, some participants (n = 92) did not comply even though they were diagnosed positive for schistosomiasis. At six weeks follow up survey, the research team mobilized parents and teachers to encourage their children to receive treatment at each follow up survey if they had parasitic infections under investigation.

The research team explained to parents and teachers that it would be unethical for children to be excluded from treatment when diagnosed positive for any of the diseases under investigation. However, it was also explained that as participants were voluntarily participating, their failure to submit specimen would mean their unwillingness to participate or receive treatment which would not be given to them unless they personally requested for it. Children who missed praziquantel treatment at baseline received treatment at six weeks follow up survey. Thereafter treatment was closely monitored at each follow up survey for those who voluntarily submitted specimens for diagnosis.

2.11 Investigation for side effects

A side effects questionnaire containing closed and open ended questions was administered to children who received praziquantel treatment for *S. haematobium* based on parasitological finding of eggs in urine**.** The questionnaire was administered 24hours after treatment.

2.12 Knowledge, attitudes and practices (KAP) studies

Knowledge, attitudes and practice studies were conducted on grade 3 children. A questionnaire that contained questions on demographic data, sources of water, presence of sanitary facilities at home, knowledge of participants about causes and preventive measures for schistosomiasis, STHs and malaria, attitudes and practice of children in relation to the diseases under investigation was administerd the research team at the beginning of the main study (June 2004). Results of the baseline KAP study were used to design health education material that was administered in schools beginning at 6 months follow up survey. The same KAP questionnaire was administered again at 12 months follow up survey..

2.13 School heath education intervention

Health education was conducted in two ways. (1) The research team introduced health education material to the school authorities before introducing it to school children. Teachers were taught how to use the flip chart that contained health education material about schistosomiasis. A single flip chart designed by the Japanese International Cooperation Agency (JICA), (appendix C) was given to each school. Teachers were asked to circulate the chart in turns on weekly bases so that each class would have a chance to learn from the teacher about schistosomiasis. The lessons would be done during free periods as this intervention had not been formally fitted

into the school syllabus. (2) The research team provided health education to school children each time they visited schools using the same material prepared after baseline KAP survey. Focus group discussions were conducted by the research team with school children all assembled out side their classes (appendix C).

Health education leaflets about malaria, schistosomiasis and STHs written in local language were distributed to all school children regardless of their participation in the KAP study (appendix C). Children were asked to read the leaflets and share the health information with their friends and families. As part of health education, children were taught about the signs and symptoms of malaria. They were asked to seek prompt malaria treatment from the nearest clinic if they experience malaria symptoms.

2.14 Ethical consideration

The Medical Research Council of Zimbabwe approved the study. In addition, Provincial and District Medical and Education Directors, chiefs, councillors and village head-men granted permission for the study to be conducted in the selected study sites. General information regarding the nature of study and objectives was explained to the community and study participants. Feed back and consent was sought at schools, farms and village meetings. Inclusion of children into the study took place after free individual, parental and school authority informed consent. Children joined the study voluntarily and were free to drop out at any time they wished without any prejudice. Due to ethical issues we could not include the control group that did not receive treatment or received placebo during the course of the study. Uniform treatment intervention was given to all participants with helminths and *P. falciparum* infection. In this study the subject was used as his/her own control and paired data analysis was used.

CHAPTER 3: DATA PROCESSING AND ANALYSIS METHODS

3.1 Data quality control

Parasitological data was collected on designed parasitological data collection forms. The forms were checked for completeness whilst in the field. All questionnaires were pre-tested before application. Data on questionnaires was quality controlled in the field for completeness and consistency.

3.2 Data entry

Database for baseline, 6 weeks, 6, 12 and 33 months was created in SPSS version 8.0 and checked for any data entry errors.

3.3 Data analysis

Data was analyzed using Statistical Package for Social Scientists (SPSS) version 8.0 for Windows, SPSS inc. Chicago, USA. It was analysed to determine baseline burden of polyparasitism with helminths and plasmodium by site and consequences of co-infections on anaemia in the farming area. Efficacy of praziquantel treatment against *S. haematobium* infection and efficacy of combined treatment of co-infections on prevalence of polyparasitism, helminths infection intensities and anaemia were assed. Effectiveness of school based health education intervention on grade 3 primary school children's KAP in relation to schistosomiasis, STHs and malaria was assessed. The five studies are numbered I, II, III, IV, V.

3.4 Baseline burden of helminths-*Plasmodium* polyparasitism (I)

Description of the study population was done by area of residence. Prevalence of *P. falciparum,* schistosomes and STHs among primary school children was compared for those living in rural and commercial farming areas using the Pearson Chi-Square test or Fisher's Exact test where appropriate.

Odds ratios were calculated for risk estimation. Mixed parasitic infections were compared for those living in rural and farming areas. Association of helminths infection with *P. falciparum* infection outcome was done using Pearson Chi-Square test. In our study, double infection was defined as co-infection with any two parasite species. Triple infection was defined as infection with three-parasite species. The significance level of this analysis was set at 5%.

3.5 Consequences of co-infections on anaemia (II)

Associations of helminths and *P. falciparum* infection with anaemia were determined using the Pearson Chi-Square test. Analysis of variance was used to determine any significant difference in haemoglobin levels between different infection intensity categories of helminths. Independent sample t-test was used to determine differences in Hb levels by gender and between individuals infected with parasites and those not infected. A multivariate regression analysis was performed using Hb concentration as the dependent variable in order to determine the possible predictors of low Hb levels in the study population. Age group, sex, presence of *P. falciparum*, mean egg intensities of *S. haematobium, S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* stratified according to the World Health Organisation guidelines (Goodman, 2007) were independent variables. Multivariate logistic regression was performed to calculate odds ratios for the association between parasitic infections and anaemia. The relationship between co-infection and haematological characteristics (Hb and anaemia) was determined. Statistical significance for all analyses was determined at $p < 0.05$.

3.6 Efficacy of praziquantel treatment against *S. haematobium* infection (III)

The arithmetic S. haematobium mean egg count, based on three urine samples taken on three successive days, was calculated for each child at baseline and six weeks post treatment surveys. This was subdivided into three infection intensities: (i) no infection, (ii) light infection and (iii) heavy infection. The cure rate was calculated as the number of children who had S. haematobium eggs in their urine before praziquantel treatment at baseline but excreted no eggs at six week after treatment divided by the number of children examined at both baseline and six weeks psot treatment surveys. Association of side effects with egg intensities and the association of cure rate with gender and age strata were determined using the Pearson Chi-Square test. Paired t-test was used to determine any significant reduction in geometric egg counts following treatment.

3.7 Efficacy of combined treatment on co-infections and anaemia (IV)

Arithmetic mean egg counts and mean *P. falciparum* parasitaemia (parasites/µl) were used in the analysis in order to assess the impact of intervention. Paired t-test was used to determine the significant difference in Hb levels between baseline, 6, 12 and 33 months post treatment survey.

Independent t-test was used to test for any significant difference in mean Hb levels between children living in the farming area and those living in rural area at different treatment points. McNemar's test was used to test for significant difference in proportions of parasite infections and anaemia at each follow up point from baseline. The χ^2 –test was used to test for any significant difference in proportions of children infected with schistosomiasis in the farming area and rural area and the difference in proportion of anaemic children between rural and farming area at baseline and each follow up survey.

3.7.1 Treatment effect

The effect of treatment intervention was determined by calculating:

(i) the percentage reduction in prevalence of single parasitic infection and co-infections among participants who received treatment at baseline and followed up successfully.

(ii) the percentage reduction in helminths infection intensities as measured by urine filtration and the Kato Katz techniques and stratified according to WHO guidelines among those participants who received treatment at baseline and were followed up successfully.

(iii) the percentage reduction in proportion of anaemia among children stratified into different co-infection combination, received treatment at baseline and successfully followed up.

3.8 Effectiveness of school based health education intervention (V).

Chi-square and McNemar's test were used where appropriate. The percentage reduction in prevalence and infection intensities of parasites was calculated.
Also 95% confidence intervals were calculated to compare different proportions of response regarding the KAP between children living in rural and farming areas and also between pre- and post intervention surveys.

CHAPTER 4: RESULTS

4.1 Burden of helminths -*Plasmodium* polyparasitism (I)

4.1.1 Demographic characteristics of the study population

Overall, 1303 children were enrolled from a rural area (53.3%) and commercial farming area (46.7%). Age of participants ranged from 5-17 years. Children were enrolled from three primary schools in a commercial farming area (Valhalla, Msapa and Kaswa) and one primary school (Nyamaropa) in a rural area. This criterion was based on the enrolment of children in both areas. Characteristics of the study population are shown in Table 4.1.1.1. Overall, 677 (52%) males and 626 (48%) females were enrolled. Nine hundred and ninety four (994) children voluntarily gave blood. Among these, malaria testing was performed on 945 (95.1%).

Table 4.1.1.1: Description of the study population according to gender, age group and sites

Parameter	**Overall**	**Farming**	**Rural**
Study participants	1303	609 (46.7)	694 (53.3)
Gender			
Male **(%)**	677	307 (45.3)	370 (54.7)
Female**(%)**	626	302 (48.2)	324 (51.8)
Age group (year)			
5-7 (%)	186	71 (38.2)	115 (61.8)
8-10 (%)	579	271 (46.8)	308 (53.2)
11-13 (%)	461	221 (47.9)	240 (52.1)
14-17 (%)	77	46 (59.7)	31 (40.3)

4.1.2 Distribution of schistosomes, STHs and *P. falciparum*

The distribution of schistosomiasis among primary school children living in rural and commercial farming areas is shown in Table 4.1.2.1a. *S. haematobium* was the predominant parasite in both rural and commercial farming areas. Children living in the rural areas were more likely to be infected with *S. haematobium* compared to those living in the farming area.

Table 4.1.2.1 (a): Prevalence of *S. haematobium* and *S. mansoni* among primary school children living in commercial farming and rural areas in Zimbabwe

Parasite	Overall (%)	Farming n (%)	Rural n (%)	Fisher's Exact (p – value)	Odds Ratio (95 % CI)
S. haematobium					
Number examined	1279 (100)	599 (100)	680 (100)		
Number infected	767 (60.0)	313 (52.3)	454 (66.8)	28.48 (<0.001)*	0.54 (0.43-0.68)
S. mansoni					
Number examined	1249 (100)	577 (100)	672 (100)		
Number infected	214 (17.1)	131 (22.7)	83 (12.4)	23.43 (<0.001)*	2.08 (1.54-2.82)

*Chi square test used

The distribution of STH and *Plasmodium falciparum* is shown in table 4.1.2.1b. *P. falciparum* and STHs were common in the farming area and did not exist in the rural area. Only one individual in the rural area had hookworm infection.

Table 4.1.2.1(b): Prevalence of STH and *P. falciparum* among primary school children living in commercial farming and rural areas in Zimbabwe

Parasite	**Overall (%)**	**Farming**	**Rural**	**Fisher's Exact**	**Odds Ratio**
		n (%)	**n (%)**	**(p – value)**	**(95 % CI)**
Hookworm					
Number examined	1249 (100)	575 (100)	674 (100)		
Number infected	137 (11.0)	136 (23.7)	1 (0.1)	(<0.001)	208.49 (29.05-1496.27)
A. lumbricoides					
Number examined	1249 (100)	575 (100)	674 (100)		
Number infected	12 (1.0)	12 (2.1)	0	(<0.001)	Indeterminable
T. trichiura					
Number examined	1249 (100)	575 (100)	674 (100)		
Number infected	13 (1.0)	13 (2.3)	0	(<0.001)	Indeterminable
P. falciparum					
Number examined	935 (100)	512 (100)	423 (100)		
Number infected	143 (15.3)	143 (27.9)	0	(<0.001)	Indeterminable

*Chi square test used

4.1.3 Distribution of polyparasitism

The distribution of polyparasitism among primary school children living in rural and commercial farming areas is described in Table 4.1.3.1a and b. Co-infection with Schistosomes and STHs was observed in the commercial farming area. A similar observation was made for schistosomes and *P. falciparum*, STHs and *P. falciparum* and triple infection with schistosomes, STH and *P. falciparum*. Except for a single person who had schistosomes + STH co-infection, there were no helminths-*Plasmodium* co-infections in the rural area. Single infection from schistosomes was predominant in the rural area.

Table 4.1.3.1(a): Distribution of polyparasitism among primary school children living in farming and rural areas in Zimbabwe

Parasite combination	Overall (%)	Farming (%)	Rural (%)	Fischer's Exact (p – value)	Odds Ratio (95 % CI)
Schistosomes					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	444 (48.5)	157 (31.8)	289 (68.5)	124.91 (<0.001)*	0.21 (0.16-0.28)
STH					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	29 (3.2)	29 (5.9)	0	(<0.001)	Indeterminable
SCH + STH					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	67 (7.3)	66 (13.0)	1 (0.2)	(<0.001)	62.81 (8.67-454.80)

* Chi square test used

Table 4.1.3.1(b): Distribution of polyparasitism among primary school children living in farming and rural areas in Zimbabwe

Parasite combination	**Overall (%) (%)**	**Farming (%)**	**Rural (p – value)**	**Fischer's Exact (95 % CI)**	**Odds Ratio**
SCH + *P. f*					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	58 (6.6)	58 (11.8)	0	(<0.001)	Indeterminable
STH + *P. f*					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	7 (0.8)	7 (1.4)	0	(0.017)	Indeterminable
SCH + STH + *P. f*					
Number examined	915 (100)	493 (100)	422 (100)		
Number infected	26 (2.8)	26 (5.3)	0	(<0.001)	Indeterminable

* Chi square test used

4.1.4 Association of helminths with *P. falciparum* malaria

The association of helminths with *P. falciparum* is displayed in Table 4.1.4.1a and b. Children who had hookworm infection were more likely to be infected with *P. falciparum* malaria, $\chi^2 = 15.68$, p = 0.001, OR = 2.48, 95 % CI: 1.56 - 3.93. There was also a significant association between *S. mansoni* with *P. falciparum* infection, $\chi^2 = 7.90$; p = 0.005, OR = 1.85, 95% CI: 1.20-2.87. There was no relationship between *S. haematobium*, *A. lumbricoides* or *T. trichiura* with *P. falciparum* malaria infection.

Table 4.1.4.1 (a): Association of helminths with *P. falciparum* infection among primary school children living in farming and rural areas in Zimbabwe

Parasite combination	Overall	Malaria positive (%)	Malaria negative (%)	Chi square (p – value)	Odds Ratio (95 % CI)
S. haematobium					
Number examined	920 (100)	140 (100)	780 (100)		
Number infected	546 (59.3)	85 (60.7)	461 (59.1)	0.13 (0.72)	1.07(0.74-1.55)
S. mansoni					
Number examined	906 (100)	132 (100)	774 (100)		
Number infected	156 (17.2)	34 (25.8)	122 (15.8)	7.90 (0.005)	1.85(1.20-2.87)

*P value based on Fisher's exact test

Table 4.1.4.1(b): Association of helminths with *P. falciparum* infection among primary school children living in farming and rural areas in Zimbabwe

Parasite combination	Overall	Malaria positive (%)	Malaria negative (%)	Chi square (p – value)	Odds Ratio (95 % CI)
Hookworm					
Number examined	905 (100)	131 (100)	774 (100)		
Number infected	117 (12.9)	31 (23.7)	86 (11.1)	15.68 (<0.001)	2.48 (1.56-3.93)
T. trichiura					
Number examined	905 (100)	131 (100)	774 (100)		
Number infected	11 (1.2)	3 (2.3)	8 (1.0)	(0.205*)	2.24 (0.59-8.57)
A. lumbricoides					
Number examined	905 (100)	131 (100)	774 (100)		
Number infected	8 (0.9)	1 (0.8)	7 (0.9)	(1.000*)	0.81 (0.10-6.91)

*P value based on Fisher's exact test

4.2 Consequences of polyparasitism on anaemia (II)

This study was carried out among primary school children living in Burma Valley commercial farming area using baseline data.

4.2.1 Description of participants' compliance

Six hundred and nine (609) children were recruited into the study and 50.4% of these were males. The overall mean (SD) age for the study population was 10.3 (2.3) years age range (6-17 years). Figure 4.2.1.1 describes compliance of the study population.

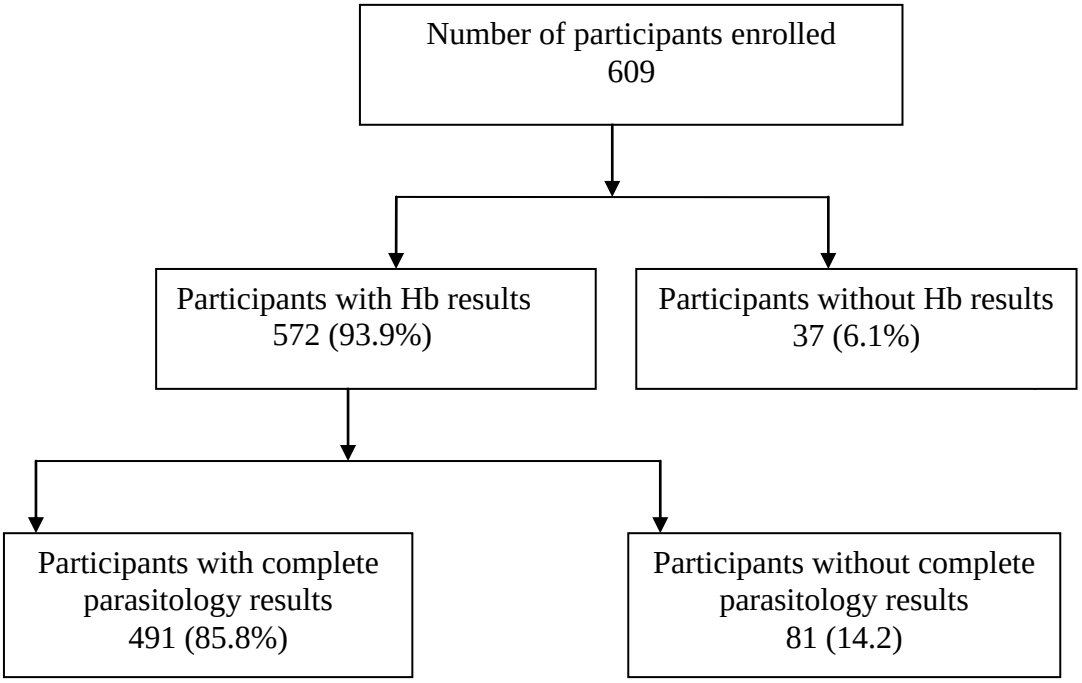

Figure 4.2.1.1: Study population compliance stratified according to haemoglobin and parasitological results

4.2.2 Distribution of parasites in Burma Valley farming area

The distribution of parasites and their egg intensities categorised according to WHO guidelines are shown in Table 4.2.2.1. *S. haematobium* was the most prevalent of all parasites investigated. Overall, 74.1% of children were infected with at least one of the parasites (*P. falciparum*, schistosomes or STHs). Among children with complete parasitological and Hb results 31.4% (154/491) had co-infections. Of the 154 children with co-infections the prevalence of malaria, STHs and schistosomiasis were 59.1% (91/154), 61.5% (96/156) and 95.5% (149/154) respectively.

Table 4.2.2.1: Baseline prevalence of parasitic infection among 609 primary schoolchildren living in Burma Valley farming area

Parameter	Parasites					
	S. haematobium	*S. Mansoni*	Hookworm	*A. Lumbricoides*	*T. trichiura*	*P. falciparum*
Number examined (%)	599 (98.4)	577 (94.7)	575 (94.4)	575 (94.4)	575 (94.4)	512 (84.1)
% infected*	52.3	22.7	23.7	2.1	2.3	27.9
% infected using Kato** Katz technique only	N/A	14.0	16.7	1.6	1.4	N/A
Parasitic infection intensity According WHO guidelines***						
% light infection	67.7	44.4	84.4	66.7	100	N/A
% moderate infection	N/A	39.5	12.5	33.3	0.0	N/A
% heavy infection	32.3	16.0	3.1	0.0	0.0	N/A

*Prevalence of *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* was based on the combination of results from the Kato Katz and formal ether concentration techniques.
** Prevalence of *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* was based on the Kato Katz technique only.
*** Infection intensities were categorised for those participants diagnosed positive by the urine filtration technique for *S. haematobium* and the Kato Katz technique only for *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura*.

4.2.3 Overall haematological results

Among children who were screened for anaemia (n = 572), 51.4% were females. The mean Hb level was 11.6 g/dl (95%CI: 11.5-11.8). Males had significantly higher mean Hb level than females (11.8 g/dL vs 11.3 g/dL, t = 2.868, p = 0.004).

Overall, the prevalence of anaemia was 48.4% (277/572). Of the anaemic children 79.1% (219/277), 19.5% (54/277) and 1.4% (4/277) had mild, moderate and severe anaemia, respectively. Females were significantly more anaemic than males (χ^2 = 4.29, p = 0.038). The overall prevalence of IDA was 38.1%. After stratifying children into different age groups: 5 -7, 8 -10, 11-13 and ≥ 14 years (n = 69, 248, 209, 46 respectively), the youngest age group had the highest prevalence of severe anaemia (1.4%). The prevalence of anaemia and IDA were highest in the age group ≥14 years (60.9% and 69.7% respectively). There was a significant difference in IDA between different age groups (χ^2= 16.54, p = 0.001). However, there was no significant difference observed in the distribution of anaemia cases between age groups (χ^2 = 3.16, p = 0.367).

4.2.4 Parasitic infection and anaemia

Tables 4.2.4.1a and b. describe the distribution of Hb levels and anaemia in single parasite infections. The mean Hb levels were significantly lower among children who had *P. falciparum, S. haematobium* and hookworm infection compared to the mean Hb levels among corresponding negative individuals (11.0 g/dL vs11.9 g/dL, t = -6.556, p < 0.001), (11.4 g/dL vs 11.9 g/dL), t = -3.973, p < 0.001) and (11.3 g/dL vs 11.8 g/dL, t = -2.986, p = 0.003) respectively.

Analysis of variance showed a significant decrease in Hb levels with increasing egg intensities for *S. haematobium* categorised according to WHO guidelines, $F_{S.haematobium} = 8.824$, $p < 0.001$. Bonferroni multiple analysis revealed that the group of participants that was uninfected had significantly higher mean Hb levels compared to those with light infection (mean Hb difference = 0.4 g/dL, 95%CI = 0.087-0.721, p = 0.007). Also non infected participants had higher mean Hb levels than those with heavy infection (mean Hb difference = 0.6 g/dL, 95%CI = 0.227-1.028, p = 0.001). The same analysis showed no significant difference in Hb levels between children with *S. haematobium* light infection and those with heavy infection (mean Hb difference = 0.2 g/dL, 95%CI = -0.192- 0.639, p = 0.592). Although there was an apparent decrease in Hb levels with increasing hookworm egg intensities (Table 4.2.4.1b), ANOVA showed no significant difference in Hb levels between different intensity categories ($F_{hookworm} = 1.737$, $p = 0.158$). The same trend was observed for the relationship between *S. mansoni* infection intensity categories ($F_{S.mansoni} = 1.201$, $p = 0.309$).

Table 4.2.4.1 (a): Overall, anaemia and IDA by parasitic infection status among children living in Burma Valley farming area in Zimbabwe in 2004

Parasite	n	Hb ± S.E	Anaemia (%)	χ^2 p – value	n	IDA (%)	χ^2 p - value
P. falciparum							
Negative	369	11.9 ± 0.07[a]	38.8		313	32.0	
Positive	143	11.0 ± 0.11	76.9	< 0.001	127	49.6	<0.001
S. haematobium							
0 egp10ml	262	11.9 ± 0.08[b]	36.0		197	26.4	
1- 49 egp10ml	204	11.5 ± 0.11	54.4		178	42.7	
≥ 50 egp10ml	99	11.3 ± 0.14	67.7	<0.001	94	55.3	<0.001
*S. mansoni**							
0 epg	470	11.7 ± 0.06	47.2		390	36.2	
1-99 epg	35	11.5 ± 0.26	60.0		27	51.9	
100-399 epg	31	11.3 ± 0.33	51.6		26	53.8	
≥ 400 epg	12	12.1 ± 0.38	33.3	0.344	10	40.0	0.137

Only children who gave blood were considered in this analysis hence variation in sample sizes for each parasite
*Kato Katz results used to stratify egg intensities according to (WHO 2002) guidelines.
[a]Student's t-test of significant difference, p < 0.001; [b]ANOVA test of significant difference, p = < 0.001

Table 4.2.4.1 (b): Overall, anaemia and IDA by parasitic infection status among children living in Burma Valley farming area in Zimbabwe in 2004

Parasite	n	Hb ± S.E	Anaemia (%)	χ^2 p – value	n	IDA (%)	χ^2 p - value
*Hookworm**							
0 epg	455	11.8 ± 0.07	44.8		372	35.5	
1-1 999 epg	78	11.4 ± 0.18	60.3		68	45.6	
2 000-3 999 epg	12	11.3 ± 0.28	66.7		11	63.6	
≥ 4000 epg	2	10.7 ± 2.15	50.0	0.043	5	50.0	0.119
*T. trichiura**							
0 epg	539	11.7 ± 0.06	47.9		448	37.9	
1-999 epg	8	12.2 ± 0.28	25.0	0.199	5	20.0	0.410
A. lumbricoides							
Negative	536	11.7 ± 0.06	47.4		447	37.4	
Positive	11	11.8 ± 0.22	54.5	0.638	6	66.7	0.141

Only children who gave blood were considered in this analysis hence variation in sample sizes for each parasite
*Kato Katz results used to stratify egg intensities according to (WHO 2002) guidelines.
[a]Student's t-test of significant difference, $p < 0.001$; [b]ANOVA test of significant difference, $p = < 0.001$

4.2.5 Haematological characteristics in co-infection combinations

The relationship between indicators of iron status and different parasitic co-infection combinations among children who had haematological results are presented in Table 4.2.5.1. Among 491 children who had haematological and complete parasitological results, 22.6% (111), 46.0% (226) and 31.4% (154) had no parasitic infection at all, had single parasitic infection and co-infections respectively. Of those with co-infections (n = 154), 83.1% (128) had double infections and 16.9% (26) had triple infections. There was a significant difference in mean Hb levels between groups of individuals that were uninfected and those infected with single or multiple parasitic infections (F_{ANOVA} = 6.927, 8- 563 d.f, $p < 0.001$).

The mean Hb for individuals with single infection from schistosomiasis was significantly higher than mean Hb for those with other co- infections. . Although there were apparent differences in Hb levels between different co-infection combinations, these were not significant.

The prevalence of anaemia and IDA increased from individuals who did not have any parasitic infection through children who had single infections with schistosomes, STHs and *P. falciparum* to children with polyparasitism respectively. Anaemia, iron deficiency and IDA prevalence were highest in helminths-*Plasmodium* co-infections. Co-infections had almost a doubling effect on the corresponding prevalence of anaemia and IDA in non–infected and single infected individuals. The highest IDA occurred in schistosomiasis + *P. falciparum* and schistosomiasis + STHs + *P. falciparum* co-infections (Table 4.2.5.1).

Prevalence of anaemia among children who did not have complete parasitological results (n = 81) was 46.9% and the mean haemoglobin level ± standard error was 11.8 ± 0.2 g/dl.

Table 4.2.5.1: Relationships between parasitic co-infections with haematological characteristics among 491 children living in Burma Valley farming area in Zimbabwe

Parasite	Haemoglobin				Iron		
	n	Hb ± S.E	Anaemia (%)	χ^2 p-value	n	IDA (%)	χ^2 p-value
No parasitic infection	111	12.1 ± 0.1	28.6		88	20.5	
SCH positive only	157	11.9 ± 0.1	37.6		139	30.2	
STH positive only	29	11.8 ± 0.2	37.9		24	29.2	
SCH + STH	63	11.2 ± 0.2	58.7		54	53.7	
STH + *P. f*	7	11.2 ± 0.4	71.4		7	28.6	
P. f positive only	40	11.1 ± 0.2	72.5		30	40.0	
Schisto + *P. f*	58	10.9 ± 0.2	77.7		54	57.4	
Schisto + STHs + *P. f*	26	11.0 ± 0.3	80.8	< 0.001	25	56.0	< 0.001

4.2.5.1 Bonferroni analysis of differences in mean Hb between co-infection combinations

Bonferroni multiple analyses showed significant differences in mean Hb levels between groups of individuals that had no infection with those that had *P. falciparum* infection only and the groups of individuals with different parasite co-infections (Table 4.2.5.1.1a and b).

Table 4.2.5.1.1 (a): Post Hoc test with Bonferroni multiple analysis test for significant difference between groups of individuals with different parasitic infection combinations.

Mean Hb			
Combination 1- Combination 2	Mean difference (g/dl)	S.E	p-value
No parasitic infection – SCH only	0.20	0.17	1.000
No parasitic infection - STH only	0.29	0.29	1.000
No parasitic infection – *P. f* only	1.06	0.25	0.001
No parasitic infection – SCH + STHs	0.88	0.22	0.002
No parasitic infection – SCH + *P. f*	1.18	0.22	<0.001
No parasitic infection – STH + *P. f*	0.88	0.54	1.000
No parasitic infection – SCH + STH + *P. f*	1.16	0.30	0.004
SCH only – STHs only	0.01	0.28	1.000
SCH only – *P. f* only	0.86	0.24	0.016
SCH only – SCH+ STH	0.68	0.21	0.035

Table 4.2.5.1.1 (b): Post Hoc test with Bonferroni multiple analysis test for significant difference between groups of individuals with different parasitic infection combinations.

Mean Hb

Combination 1- Combination 2	Mean difference (g/dl)	S.E	p-value
SCH only – SCH + *P. f*	0.98	0.21	< 0.001
SCH only – STH + *P. f*	0.68	0.53	1.000
SCH only – SCH + STH + *P. f*	0.97	0.29	0.036
SCH + *P. f* - *P. f*	-0.12	0.28	1.000
SCH + *P. f* – SCH + STH	-0.30	0.25	1.000
SCH+ *P. f* – *P. f* + STH	-0.30	0.55	1.000
SCH + *P. f* – *P. f* + SCH + STH	-0.01	0.33	1.000

4.2.6 Predictors of Hb levels and anaemia

4.2.6.1 Multivariate regression analysis

Multivariate regression analysis using Hb level as the dependent variable where as age categories, sex, presence of *P. falciparum* and helminths infection intensities categorised according to WHO guidelines were explanatory variables showed that age groups 11-13 years, sex and *P. falciparum* were significantly associated with Hb levels (Table 4.2.6.1 a and b). Heavy *S. haematobium* infection was a predictor of low Hb level. Multiple logistic regression analysis showed that children aged ≥ 14 years, presence of *P. falciparum*, light and heavy *S. haematobium* infection intensities, moderate and heavy *S. mansoni* and light hookworm infection intensities were predictors of anaemia. Sex, *A. lumbricoides*, *T. trichiura* infection intensities, light *S. mansoni* infection and the other age groups were not associated with anaemia.

Table 4.2.6.1.1(a): Multivariate regression analysis exploring the relationship between Hb with age, sex, presence of *P. falciparum*, intensities of *S. haematobium*, *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* infections

Independent variable	Coefficient	S.E	t-value	p-value
Age-group (years)				
5-7	Reference			
8-10	0.271	0.203	1.34	0.182
11-13	0.440	0.210	2.09	0.037
≥ 14	0.404	0.305	1.33	0.185
Sex	-.251	0.129	-1.95	0.051
P. falciparum	0773	0.144	5.36	<0.001
S. haematobium intensity (WHO categories)				
Uninfected	Reference			
Light: 1-49 egp10ml urine	-0.257	0.141	-1.82	0.070
Heavy: ≥ 50 egp10ml urine	-0.473	0.181	2.61	0.009
Hookworm intensity				
Uninfected	Reference			
Light: 1-1999 epg	-0.389	0.188	-2.07	0.039
Moderate: 2000-3999 epg	-0.241	0.473	-0.51	0.611
Heavy: ≥ 4 000 epg	-2.576	1.415	-1.82	0.069

* Only light and moderate infection intensities were observed for *A. lumbricoides*
** Only light infection intensity was observed for *T. trichiura*.

Table 4.2.6.1.1(b): Multivariate regression analysis exploring the relationship between Hb with age, sex, presence of *P. falciparum*, intensities of *S. haematobium*, *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* infections

Independent variable	**Coefficient**	**S.E**	**t-value**	**p-value**
S. mansoni intensity				
Uninfected	Reference			
Light: 1-99 epg	0.020	0.280	0.07	0.942
Moderate: 100-399 epg	-0.037	0.293	-0.13	0.899
Heavy: ≥ 400 epg	0.776	0.448	1.71	0.088
A. lumbricoides intensity *				
Uninfected	Reference			
Light: 1-4999 epg	-0.119	0.629	-0.19	0.850
Moderate: 5000-49 999 epg	-0.277	1.014	-0.27	0.785
T. trichiura intensity **				
Light: 1-999 epg	0.459	0.524	0.88	0.381

* Only light and moderate infection intensities were observed for *A. lumbricoides*
** Only light infection intensity was observed for *T. trichiura*.

4.2.6.2 Multiple logistic regression analysis

Multiple logistic regression analysis showed that children aged ≥ 14 years, presence of *P. falciparum*, light and heavy *S. haematobium* infection intensities, moderate and heavy *S. mansoni* and light hookworm infection intensities were predictors of anaemia. Sex, *A. lumbricoides*, *T. trichiura* infection intensities, light *S. mansoni* infection and the other age groups were not associated with anaemia (Table 4.2.6.2.1a and b).

Table 4.2.6.2.1(a): Multivariate logistic regression analysis exploring the relationship between anaemia with age, sex, presence of *P. falciparum*, intensities of *S. haematobium*, *S. mansoni*, hookworm, *A. lumbricoides*, *T. trichiura* infections.

Independent variable	Odds ratio	95%CI	z	p-value
Age-group (years)				
5-7	Reference			
8-10	0.837	0.442-1.582	-0.55	0.583
11-13	1.049	0.542-2.030	0.14	0.887
≥ 14	3.150	1.161-8.545	2.25	0.024
Sex	1.336	0.887-2.013	1.39	0.166
P. falciparum	5.347	2.269-8.744	6.68	<0.001
S. haematobium intensity (WHO categories)				
Uninfected	Reference			
Light: 1-49 egp10ml urine	1.660	1.062-2.595	2.22	0.026
Heavy: ≥ 50egp10ml urine	3.737	2.059-6.782	4.34	<0.001
S. mansoni intensity				
Uninfected	Reference			
Light: 1-99 epg	1.045	0.416-2.626	0.09	0.925
Moderate: 100-399 epg	0.364	0.137-0.967	-2.03	0.043
Heavy: ≥ 400 epg	0.141	0.025-0.786	-2.23	0.025

* Only two cases had hookworm heavy infection and they were left out in this analysis
** Due low numbers and lack of moderate to heavy infection for *A. lumbricoides* and only light infection intensity was observed for *T. trichiura*

Table 4.2.6.2.1(b): Multivariate logistic regression analysis exploring the relationship between anaemia with age, sex, presence of *P. falciparum*, intensities of *S. haematobium*, *S. mansoni*, hookworm, *A. lumbricoides*, *T. trichiura* infections.

Independent variable	Odds ratio	95%CI	z	p-value
*Hookworm intensity**				
Uninfected	Reference			
Light: 1-1999 epg	2.238	1.207-4.148	2.56	0.011
Moderate: 2000-3999 epg	3.215	0.539-19.189	1.28	0.200
*A. lumbricoides intensity***				
Uninfected	Reference			
Light: 1-4999 epg	4.067	0.506-32.717	1.32	0.187
*T. trichiura intensity***				
Uninfected	Reference			
Light: 1-999 epg	0.247	0.259-2.359	-1.21	0.225

* Only two cases had hookworm heavy infection and they were left out in this analysis

** Due low numbers and lack of moderate to heavy infection for *A. lumbricoides* and only light infection intensity was observed for *T. trichiura*

4.3 Efficacy of praziquantel treatment against *S. haematobium* infection (III)

4.3.1 Operational results and study compliance

Out of 1 303 children (age range 5-17 years) enrolled into the study, 1 279 (98%) individuals were diagnosed for *S. haematobium* using the urine filtration technique. Among these children, 767 (60%) were infected and 675 (88%) of the infected individuals received a single oral dose of PZQ at 40 mg/kg under supervision from the state registered nurse.

The remaining 92 (12%) children did not receive treatment either because of religious reasons or they absconded. Figure 4.3.1.1 describes the operational results and study compliance. The mean age (standard deviation) of children infected with *S. haematobium* was 10.2 (2.30) years, age range (5-17 years). There were slightly more boys (51.4%) than girls (48.6%). In the analysis of PZQ efficacy and side effects, only those participants who received treatment at baseline (n = 675) were considered.

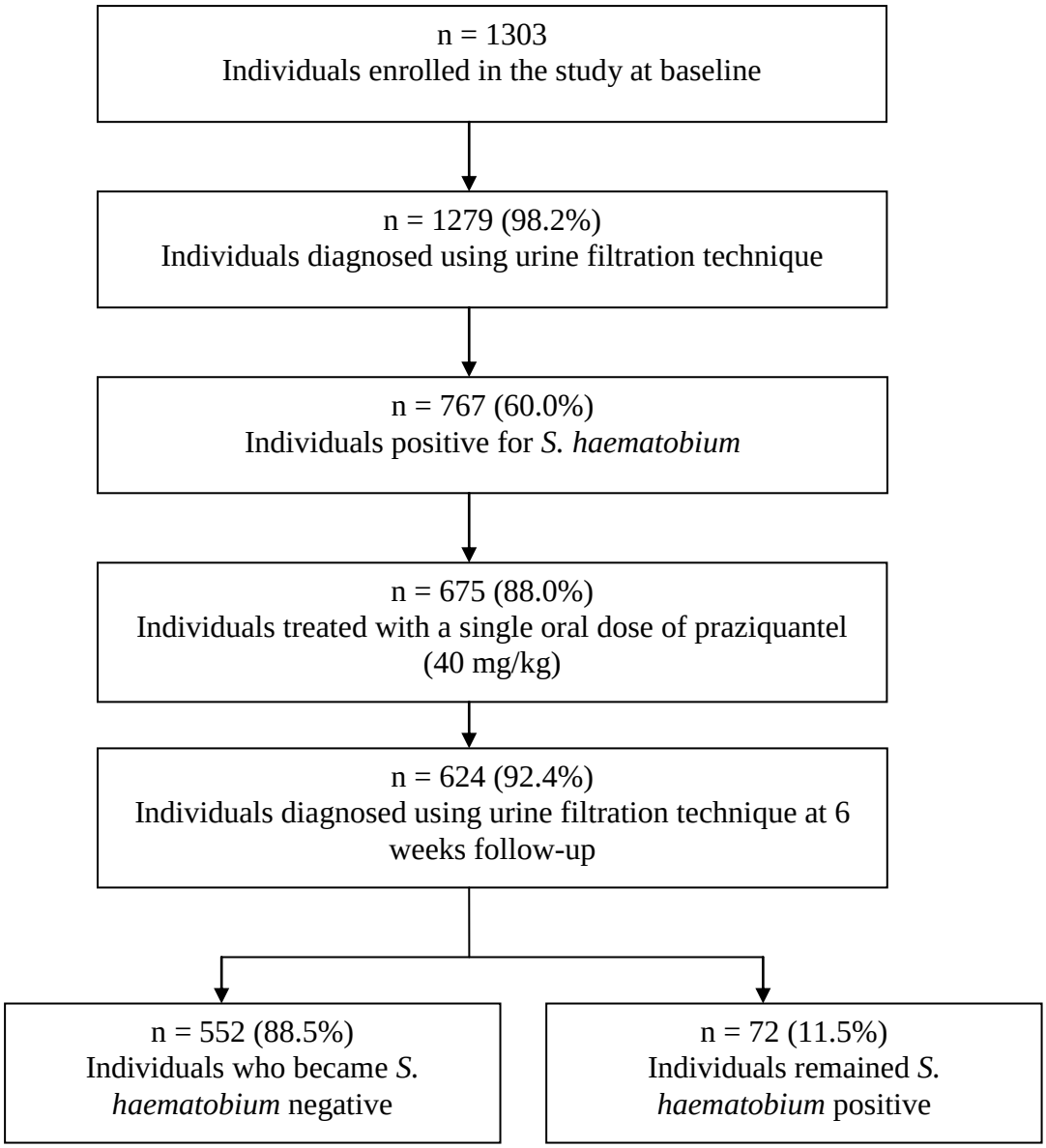

Figure 4.3.1.1: Operational results and study compliance for the assessment of efficacy and side effects of PZQ against *S. haematobium* in rural and farming areas of Zimbabwe

As this is a flow chart showing compliance of participants, the percentage in each cell is calculated from the number in the immediate preceding cell.

4.3.2 *S. haematobium* infection before treatment

Table 4.3.2.1 describes infection intensities of *S. haematobium* before administration of praziquantel. At day one 170 participants were falsely classified as negative. This figure declined to zero after examination of the third urine specimen on day 3. Thus, a considerable number of light infections had been missed by a single urine examination.

Table 4.3.2.1: Number of study participants with *S. haematobium* infection and their arithmetic mean egg intensity based on 3 consecutive urine samples acquired before treatment.

***S haematobium* infection level (egp 10 ml urine)**	**Cumulative results: number of individuals before treatment (%)**		
	After first sample	**After second sample**	**After third sample**
No infection (0 egp10 ml urine)	170 (25.4)	49 (7.3)	0
Light infection (< 50 egp10 ml urine)	295 (44.1)	391 (58.2)	447 (66.2)
Heavy infection (≥ 50 egp10 ml urine)	204 (30.5)	232 (34.5)	228 (33.8)
Total	669	672	675 (100)

Table 4.3.2.2 shows the distribution of infection intensities by gender and age. There were significant associations between the level of infection intensity and gender with the percentage of heavy infection being higher in males than females. Compared to females, the odds ratios of heavy infection among males was 1.52 (95 % CI = 1.1-2.1). Heavy and light infection intensities were predominant among the age groups 8-10 and 11-13 years although there was no statistical significant association between infection intensity and age.

Table 4.3.2.2: Baseline characteristics of *S. haematobium* infections among 675 study participants with regard to sex and age group mean egg intensity before and after treatment

Indicator	**Infection Intensity (WHO Classification)**			χ^2	**P-value**
	Heavy (%)	Light (%)	Total		
Gender					
Male	133 (38.3)	214 (61.7)	347		
Female	95 (29.0)	233 (71.0)	328		
Total	228 (33.8)	447 (66.2)	675	6.61	0.010
Age group (years)					
5-7	23 (26.4)	64 (73.6)	87		
8-10	95 (32.9)	194 (67.1)	289		
11-13	92 (36.2)	162 (63.8)	254		
14-17	18 (40.0)	27 (60.0)	45		
Total	228 (33.8)	447 (66.2)	675	3.73	0.292

4.3.3 Parasitological cure rate

The cure rate of *S. haematobium* at six weeks following PZQ treatment is shown in Table 4.3.3.1. Overall, the cure rate for *S. haematobium* was 88.5%. The parasitological cure rate was independent of gender, p = 0.728 and age categories, p = 0.376. Most of the light and heavy infections were cleared or some heavy infections reversed to light infections with 3 sets of exceptions. Firstly, some light infections remained with light infection (n = 41). Secondly, two individuals who had light infections at base line were found with heavy infection at six weeks post treatment survey. Thirdly, one individual had heavy infection at both baseline (500.00 egp10 ml urine) and six weeks post treatment survey (697.67 egp10 ml urine). Overall there was a significant reduction in geometric mean egg intensity from 21.6 egp 10 ml urine at baseline to 1.2 egp10 ml urine at six weeks post treatment ($t = 39.7$, $p = < 0.001$).

Table 4.3.3.1: Parasitological cure rate in *Schistosoma haematobium* after a single oral dose of 40mg/kg praziquantel in relation to infection intensity among primary school children in rural and commercial farming areas in Zimbabwe

S. haematobium infection level Pre-treatment (egp10 ml of urine)	No. of patients Treated	No of patients cured (%)	No. of patients not cured		
			Light Infection	Heavy infection	All infections
Light intensity infection (< 50 egp10 ml urine)	414	371 (89.6)	41	2	43
Heavy intensity infection (≥ 50 egp10 ml urine)	210	181 (86.2)	28	1	29
Overall	624	552 (88.5)	69	3	72

4.3.4 Follow up of children treated at six weeks post treatment survey

Of the 72 participants diagnosed *S. haematobium* positive at six weeks after receiving treatment at baseline, 68 (94.4%) were successfully followed up and screened again at four and half months later. Among these 68 children, 46 (67.6%) had no *S. haematobium* eggs in their urine whilst 22 participants who remained positive received a third oral single dose of PZQ treatment at this point in time and they were diagnosed *S. haematobium* negative six months later.

4.3.5 Side effects following praziquantel treatment

Table 4.3.5.1 shows side effects reported 24 hours following treatment. Out of 675 children who received treatment 534 (79.1%) responded to the questionnaire regarding side effects. Among those who responded to the side effects questionnaire 352 (65.9%) had light infection and 182 (34.1%) had heavy infection. The side effect reported most often was stomach discomfort, 191 (35.8%), followed by nausea accounting for 102 (19.1%). Two hundred and ninety (54.3%) reported single transient side effects whilst 59 (11.0%) reported two or more side effects but these did not take a longer time to resolve. Side effects were independent of infection intensities.

Table 4.3.5.1: Number (%) of reported side effects among patients who complained of one or more side effects soon after administration of praziquantel in relation to *S. haematobium* pre-treatment infection intensity.

Reported side effects	Pre-treatment infection intensity		χ^2	p-value
	Light (n = 352)	Heavy (n = 182)		
Stomach discomfort	129 (36.6)	62 (34.1)	0.348	0.555
Dizziness	23 (6.5)	10 (5.5)	0.224	0.636
Diarrhoea	23 (6.5)	16 (8.8)	0.903	0.342
Nausea	61 (17.3)	41 (22.5)	2.098	0.148
Headache	25 (7.1)	7 (3.8)	2.258	0.133
Vomiting	6 (1.7)	4 (2.2)	0.159	0.690
Itchy skin	1 (0.3)	2 (1.1)	1.426	0.232
Lethargy and sleepy	1 (0.3)	1 (0.5)	0.226	0.634
Swollen face	1 (0.3)	0	0.518	0.472

4.4 Efficacy of combined treatment on prevalence of polyparasitism, helminths infection intensities and anaemia (IV)

4.4.1 Diagnosis and treatment compliance of participants

Tables 4.4.1.1.a-c describe treatment compliance for children at baseline and each follow up survey. The tables describe reasons why some participants missed treatment they also illustrate treatment compliency for participants diagnosed positive for schistosomes, STHs and *P. falciparum* at 6, 12 and 33 months follow up surveys. The tables also show the number of children diagnosed positive for each specific parasite at each treatment time point (survey) in relation to the number of individuals enrolled into the study.

S. mansoni and *S. haematobium* infection was treated with the same drug (praziquantel). As a result, some children diagnosed negative for *S. mansoni* received praziquantel treatment because they had single infection from *S. haematobium.* The same explanation applies for those children found negative for *S. haematobium* but received treatment. A similar explanation is also true for the treatment of STHs (hookworms, *A. lumbricoides* and *T. trichiura*) since a single drug, albendazole, was used to treat infection for any one, any two or all of the 3 nematodes.

Tables 4.4.1.1(a): Diagnosis of parasites and treatment compliance of primary school children at each follow up time point

Parasite treatment category	Number of participants (%)			
	Baseline n (%)	6 months n (%)	12 months n (%)	33 months n (%)
S. haematobium				
Uninfected and untreated	448 (34.4)	853 (65.5)	903 (69.3)	606 (46.5)
Infected and treated	675 (51.8)	250 (21.9)	178 (13.7)	300 (23.0)
Infected but not treated	92 (7.1)	0	0	0
Uninfected but treated	64 (4.9)	40 (3.1)	43 (3.3)	56 (4.3)
Undiagnosed but treated	1 (0.1)	3 (0.2)	0	0
Undiagnosed and untreated	23 (1.8)	157 (12.0)	179 (13.7)	341 (26.2)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**
S. mansoni				
Uninfected and untreated	491 (37.7)	822 (63.0)	871 (66.8)	594 (45.6)
Infected and treated	182 (14.0)	63 (4.8)	54 (4.1)	85 (6.5)
Infected but not treated	32 (2.5)	0	0	0
Uninfected but treated	547 (42.0)	214 (16.4)	165 (12.7)	271 (20.8)
Undiagnosed but treated	39 (3.0)	15 (1.2)	2 (0.2)	0
Undiagnosed and untreated	12 (0.9)	189 (14.5)	211 (16.2)	353 (27.1)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**

Tables 4.4.1.1(b): Diagnosis of parasites and treatment compliance of participants at each follow up time point

Parasite treatment category	Number of participants (%)			
	Baseline n (%)	6 months n (%)	12 months n (%)	33 months n (%)
Hookworms				
Uninfected and untreated	1101 (84.5)	1056 (81.0)	1039 (79.6)	864 (66.3)
Infected and treated	133 (10.2)	43 (3.3)	39 (3.0)	78 (6.0)
Infected but not treated	4 (0.3)	0	0	0
Uninfected but treated	11 (0.0)	8 (0.6)	5 (0.4)	4 (0.3)
Undiagnosed but treated	2 (0.2)	0	0	0
Undiagnosed and not treated	52 (3.9)	196 (15.0)	222 (17.0)	357 (27.4)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**
P. falciparum				
Uninfected and untreated	792 (60.8)	916 (70.3)	869 (66.7)	815 (62.5)
Infected and treated	143 (11.0)	64 (4.9)	58 (4.5)	38 (2.9)
Infected but not treated	0	0	0	0
Uninfected but treated	0	0	0	0
Undiagnosed but treated	0	0	0	0
Undiagnosed and untreated	368 (28.2)	323 (24.8)	376 (28.9)	450 (34.5)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**

Tables 4.4.1.1(c): Diagnosis of parasites and treatment compliance of participants at each follow up time point

Parasite treatment category	Number of participants (%)			
	Baseline n (%)	6 months n (%)	12 months n (%)	33 months n (%)
A. lumbricoides				
Uninfected and untreated	1106 (84.9)	1056 (81.0)	1037 (79.6)	861 (66.1)
Infected and treated	12 (1.0)	10 (0.8)	8 (0.6)	4 (0.3)
Infected but not untreated	0	0	0	0
Uninfected but treated	132 (10.1)	41 (3.1)	36 (2.8)	82 (6.3)
Undiagnosed but treated	2 (0.2)	0	0	0
Undiagnosed and untreated	51 (3.9)	196 (15.0)	222 (16.9)	356 (27.3)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**
T. trichiura				
Uninfected and untreated	792 (60.8)	1056 (81.0)	1037 (79.6)	864 (66.3)
Infected and treated	13 (1.0)	1 (0.1)	0	2 (0.2)
Infected but not treated	0	0	0	0
Uninfected but treated	131 (10.2)	50 (3.8)	44 (3.4)	81 (6.2)
Undiagnosed but treated	0	0	0	0
Undiagnosed and untreated	51 (3.9)	196 (15.0)	222 (16.9)	356 (27.3)
Total	**1303 (100)**	**1303 (100)**	**1303 (100)**	**1303 (100)**

4.4.2 Participants' compliance over 33 months follow- up period

Children successfully followed up from baseline through 6; 12 and 33 months follow up surveys were selected for the analysis aimed at determining the effect of treatment intervention on individual parasitic infections. Table 4.4.2.1 illustrates participants' compliance. Of the 1303 participants enrolled into the study, 906; 850; 850 and 772 were successfully followed up and diagnosed for *S. haematobium*, *S. mansoni*, hookworms and *P. falciparum* respectively from baseline through to 33 months follow up survey. *A. lumbricoides* and *T. trichiura* were left out of this analysis because they were diagnosed using the same method and slide preparation for the diagnosis of hookworms. Thus, the number of participants screened for hookworms is the same for the two parasites

Table 4.4.2.1: Diagnosis compliance of 1303 participants for specific parasites during the follow-up study

Participants' diagnosis compliance category	Number of participants (%)			
	S. haematobium	*S. mansoni*	Hookworm	*P. Falciparum*
Never diagnosed at all surveys	11 (0.8)	31 (2.1)	29 (2.2)	234 (18.0)
Diagnosed at:				
Baseline only	75 (5.8)	68 (5.2)	70 (5.4)	12 (0.9)
Baseline and 6 months	57 (4.4)	62 (4.8)	62 (4.8)	61 (4.7)
Baseline, 6 and 12 months	159 (12.2)	151 (11.6)	151 (11.6)	56 (4.3)
Baseline, 6, 12 and 33 months	**906 (69.5)**	**850 (65.2)**	**850 (65.2)**	**772 (59.2)**
Baseline and 12 months	30 (2.3)	34 (2.6)	34 (2.6)	0
Baseline and 33m	17 (1.3)	15 (1.2)	16 (1.2)	3 (0.2)
Baseline, 6 and 33 months	16 (1.2)	29 (2.2)	26 (2.0)	31 (2.4)
Baseline, 12 and 33 months	19 (1.5)	40 (3.1)	40 (3.1)	0
Some time point after baseline survey	13 (1.0)	23 (1.8)	25 (1.9)	134 (10.3)

4.4.3 Effect of treatment intervention on individual parasitic infections

Table 4.4.3.1a describes the effect of treatment intervention on the prevalence of *S. haematobium* at each treatment time point. Of the 906 participants screened for *S. haematobium* infection at all surveys, 543 (59.9%) received praziquantel treatment at baseline. Of these participants, 494 (90.1%) had urinary schistosomiasis. After following up all participants who received baseline praziquantel treatment at 6, 12 and 33 months follow up surveys; the overall prevalence reduction of *S. haematobium* was 77.5%, 79.1% and 61.6% respectively from baseline to 6, 12 and 33 months follow up survey respectively. The prevalence of *S. haematobium* was significantly higher in the rural than the farming area at baseline, 6 and 12 months follow up surveys, $\chi^2 = 0.001$, $\chi^2 = 0.001$ and $\chi^2 = 0.015$ respectively. Overall, the results show a sharp decline in prevalence of *S. haematobium* from baseline to 12 months follow up survey. However, the delayed 21 months follow up survey resulted in an increase in prevalence although this did not reach the pre-treatment level. These results are corroborated with a similar trend in decline of infection intensities for *S. haematobium* up to 12 months followed by an increase in prevalence with delayed treatment. Only light infection was predominant at 33 months follow up survey (Figure 4.4.4.1.1).

Of the 850 participants successfully followed up from baseline to 33 months follow up survey and diagnosed for *S. mansoni* at all surveys, 516 (60.7%) received praziquantel treatment at baseline. The prevalence of *S. mansoni* was significantly high in the farming area at baseline and at 33 months follow up survey $p = 0.001$. The overall prevalence reduction of *S. mansoni* from baseline to 6, 12 and 33 months follow up surveys was 79.4%, 73.8% and 65.5% respectively. However, compared to

the rural area, the prevalence of *S. mansoni* in the farming area rebounded to 17.2% following 21 months of delayed treatment where as the prevalence in the rural area continued to decline (0.4%).

Of the 772 participants successfully diagnosed for *P. falciparum* at baseline, 6, 12 and 33 months follow up surveys, 122 (15.8%) participants received treatment at baseline and they were followed up at each follow up survey. The prevalence of *P. falciparum* at each treatment time point is shown in table 4.4.3.1a. The prevalence reduction of *P. falciparum* infection was 85.2%; 82.8% and 92.6% respectively from baseline to 6, 12 and 33 months follow- up survey. The following participants reported to the nearest health facility (Burma valley clinic) for prompt malaria treatment between baseline and six months follow up survey (n = 8), between 6 months and 12 months follow up survey (n =24) and between 12 months and 33 months follow up survey (n = 56) treatment. Treatment was given based on signs and symptoms. The state registered nurse stationed at the clinic kept records of treatment given.

Of the 850 participants diagnosed successfully for hookworms at each survey through out the study, 110 (12.9%) received albendazole treatment at baseline. The effect of treatment intervention on the prevalence of hookworms is described in table 4.4.3.1a. The percentage reduction of prevalence of hookworms from baseline to 6, 12 and 33 months follow up surveys was 85.5%, 83.6 and 77.4% respectively. The participant who had hookworm infection in the rural area was cured after receiving treatment at baseline. The prevalence of hookworms in the farming area declined steadily up to

12 months follow up survey. It slightly increased following 21 months of delayed treatment. However, only light infection intensity was observed at 33 months follow up survey (Figure 4.4.4.3.1).

Table 4.4.3.1a: Effects of treatment intervention on prevalence of individual parasitic infections among children successfully followed up at all surveys

Parasite combination	Percentage (95%CI)			
	Baseline	6 months	12 months	33 months
S. haematobium				
Farming area (n = 261)	86.6 (81.8-90.5)	14.2 (10.2-19.0)	14.6 (10.5-19.4)	31.4 (25.3-37.4)
Rural area (n = 282)	95.0 (91.8-97.3)	25.9 (20.1-31.4)	22.7 (17.9-28.0)	37.6 (31.9-43.5)
Overall (n = 543)	90.1 (88.2-93.2)	20.3 (17.0-23.9)	18.8 (15.6-22.3)	34.6 (30.6-38.8)
S. mansoni				
Farming area (n = 257)	34.2 (28.5-40.4)	3.5 (1.6-6.5)	6.2 (3.6-9.9)	17.2 (12.7-22.3)
Rural area (n = 259)	16.2 (11.9-21.3)	6.9 (4.2-10.8)	6.9 (4.2-10.7)	0.4 (0.0-2.1)
Overall (n = 516)	25.2 (21.5-29.2)	5.2 (3.5-7.5)	6.6 (4.6-9.1)	8.7 (6.4-11.5)
Hookworm				
Farming area (n = 109)	92.7 (86.0-96.8)	7.3 (3.2-14.0)	9.2 (4.5-16.2)	14.7 (8.6-22.7)
Rural area (n = 1)	100 (0.25)*	0	0	0
Overall (n = 110)	92.7 (86.2-96.8)	7.2 (3.2-13.8)	9.1 (4.5-16.1)	14.7 (8.6-22.7)
P. falciparum				
Farming area (n = 122)	100 (97.0)*	14.8 (9.0-22.3)	17.2 (11.0-25.1)	7.4 (3.4-13.5)

*= One sides 97.5% Confidence Interval,

Table 4.4.3.1b describes the effect of treatment on the prevalence of *A. lumbricoides* and *T. trichiura*. The prevalence reduction of *A. lumbricoides* from baseline to 6, 12 and 33 months follow up surveys was 87.6%, 75.4 and 100% respectively. Of the 110 participants who received albendazole treatment, 10. 9% had *T. trichiura* at baseline. The prevalence declined to zero at 6, 12 and 33 months following treatment.

Table 4.4.3.1b: Effects of treatment intervention on prevalence of parasitic infections among children successfully followed up at all surveys

Parasite combination	Percentage (95%CI)			
	Baseline	6 months	12 months	33 months
A. lumbricoides				
Farming area (n = 110)	7.3 (3.2-13.8)	0.9 (0.0-5.0)	1.8 (0.2-6.4)	0
T. trichiura				
Farming area (n = 110)	10.9 (5.8-18.3)	0	0	0

4.4.4 Effect of treatment intervention on helminths infection intensities

Participants, who received treatment for each specific parasitic infection at baseline and successfully followed up at all surveys providing samples for diagnosis, were selected to determine the effect of treatment intervention on helminths infection intensities.

4.4.4.1 Effect of treatment intervention on *S. haematobium* intensity

Stratification of 494 participants who had *S. haematobium* and received treatment at baseline, into infection intensity categories showed that 321 (65%) and 173 (35.0) had light and heavy infection intensities respectively. The effect of treatment intervention at baseline and at each follow up survey on the prevalence of *S. haematobium* infection intensities is shown in Figure 4.4.4.1.1 Treatment intervention resulted in the steady decline in *S. haematobium* infection intensity during the first 12 months after which the prevalence of light infection slightly increased following 21 months of delayed treatment. The same trend was observed for heavy *S. haematobium* infection intensity although the prevalence was lower than that of light infection at each treatment time point. The percentage reduction of light infection intensities from baseline to 6, 12 and 33 months follow up surveys was 72.2%, 75.4% and 50.7% respectively. The percentage reduction of heavy infection intensities from baseline to 6, 12 and 33 months follow up survey was 93.7%; 91.4% and 88.8% respectively.

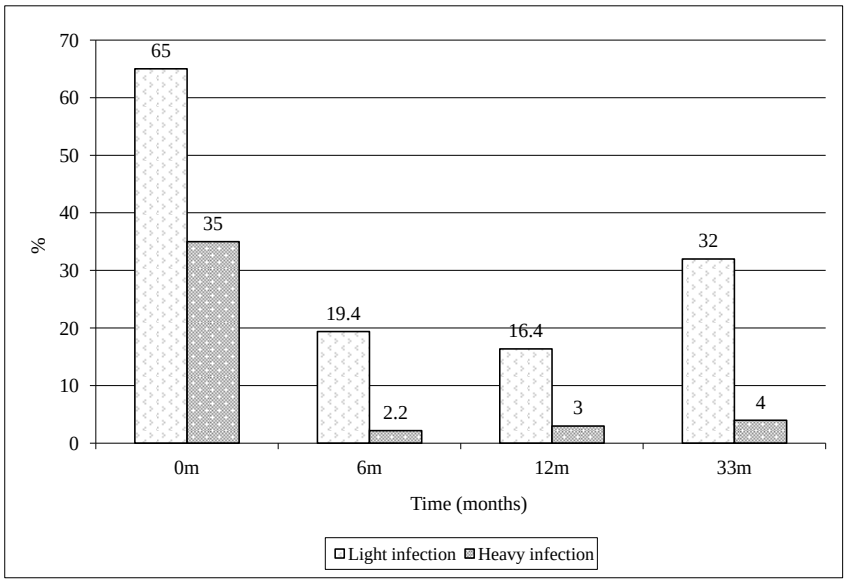

Figure 4.4.4.1.1: Effect of treatment intervention on prevalence of *S. haematobium* infection intensity

4.4.4.2 Effect of treatment intervention on *S. mansoni* infection intensity

Of the 850 participants diagnosed successfully for *S. mansoni* at each survey over 33 months, 516 (60.7%) received praziquantel treatment at baseline. Of these, 88 (17.1%) participants had intestinal schistosomiasis infection as demonstrated by the presence of *S. mansoni* eggs in the Kato Katz thick smear slides preparations. Stratification of 88 participants into infection intensity categories showed that 43 (48.9%), 28 (31.8%), 17(19.3%) had light, moderate and heavy infection respectively at baseline (Figure 4.4.4.2.1). At 6 months follow up survey *S. mansoni* was not detected using the Kato Katz technique. Only moderate infection was detected at 12 months follow up survey and light infection at 33 months follow up survey. The percentage reduction of heavy infection was 100% at 6, 12 and 33 months follow up surveys following praziquantel treatment at baseline. Percentage reduction of light infection intensity was 100% at both 6 and 12 months follow up survey. However, it reduced to 79.1% following 21 months of delayed screening and treatment.

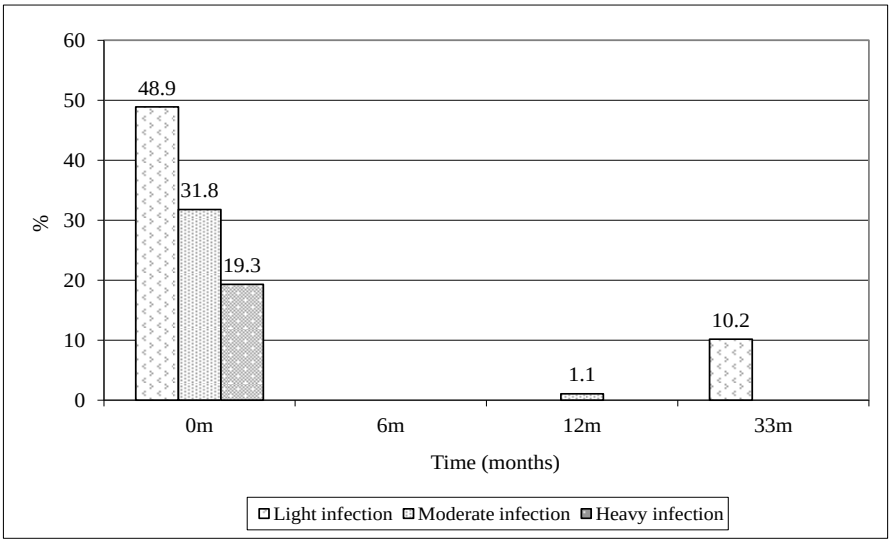

Figure 4.4.4.2.1: Effect of treatment intervention on prevalence of *S. mansoni* infection intensities

4.4.4.3 Effect of treatment intervention on hookworm infection intensities

Of the 850 participants diagnosed successfully for hookworms at each survey over 33 months, 110 (12.9%) received albendazole treatment at baseline. Of these, 73 (66.4%) participants had hookworm infection as demonstrated by the presence of hookworm eggs in the Kato Katz thick smear slides preparations. Stratification of 73 participants into infection intensity categories showed that 64 (87.3%), 8 (11.0%), 1 (1.4%) had light, moderate and heavy infections respectively at baseline. The effect of school based treatment intervention on hookworm infection intensity at each survey over 33 months is shown in figure 4.4.4.3.1. Moderate to heavy infection intensities declined to zero after the first round of treatment at baseline. The percentage reduction of light infection from baseline to 6, 12 and 33 months follow up surveys was 96.9%; 96.9% and 82.8%.

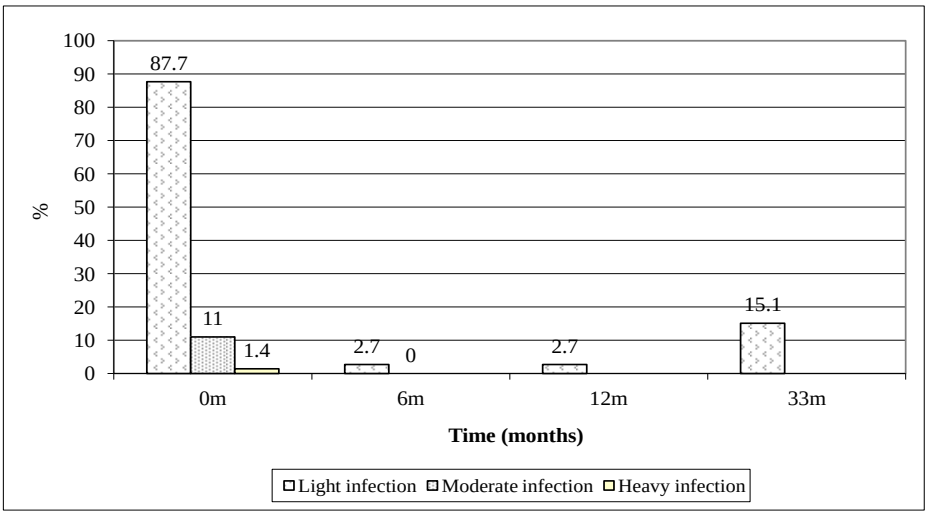

Figure 4.4.4.3.1: Effects of treatment intervention on prevalence of hookworm infection intensities

4.4.4.4 Effect of treatment intervention on co-infections

Of the 1303 participants enrolled into the study, 682 (52.3%) participants were successfully diagnosed for schistosomes, STHs, *P. falciparum* and helminths-*Plasmodium* co-infections at baseline, 6, 12 and 33 months follow- up surveys. Of these, 475 (71.7%) had at least a single parasitic infection and they received treatment at baseline, 171 (25.1%) were diagnosed negative for all parasites at baseline and the remaining 36 participants had infection but did not receive treatment at baseline. Four hundred and seventy five (475) participants were stratified into co-infection combinations and received the corresponding combined treatment at baseline and at any other follow up survey if found infected. Of the 36 participants who did not receive treatment at baseline, 3 participants were co-infected with schistosomes and *P. falciparum*, 2 participants were co-infected with schistosomes and STH and 31 participants had schistosomiasis infection only.

Table 4.4.4.4.1 describes different parasitic infection combinations observed after stratifying 475 participants that received treatment at baseline. After the first round of

treatment of these 475 participants, 63.6% of them turned negative for all parasites at 6 months follow up survey and they did not receive treatment at this follow up point in time. The proportion of children with no infection increased to 70.5% after treatment at baseline and six months follow up surveys.

There was a steady decline in prevalence of children infected with schistosomes only from 59.4% at baseline through 20% at 6 months to 17.3% at 12 months follow up survey. However, it increased to 33.3% following 21 months of delayed treatment. The prevalence reduction percentage of different parasite infection combinations at 12 months and 33 months follow up surveys is shown in table 4.4.4.4.1. Higher prevalence reduction percentages were observed among children with helminths-*Plasmodium* co-infections during the first year of treatment intervention. The highest prevalence reduction percentage of co-infections occurred among children co-infected with schistosomiasis, STH and *P. falciparum* at 12 months follow up survey.

Table 4.4.4.4.1: Effect of combined treatment intervention on co-infections among 475 participants successfully treated and followed up

Parasite combination	Percentage (95%CI)					
	Baseline (n = 475)	6 months (n = 475)	12 months (n = 475)	33 months (n = 475)	% reduction PR1	PR2
Not infected by any parasite	0	63.6 (59.1-67.9)	70.5 (66.2-74.6)	50.9 (46.4-55.5)		
Infected with SCH only	59.4(54.8-63.8)	20.8 (17.3-24.8)	17.3 (14.0-21.0)	33.3 (29.0-37.7)	70.9	43.9
Infected with STHs only	5.1 (3.3-7.4)	4.8 (3.1-7.2)	2.1 (1.0-3.8)	3.6 (2.1-5.7)	58.8	29.4
Infected with *P. f* only	7.2 (5.0-9.9)	7.6 (5.4-10.3)	5.5 (3.6-7.9)	2.3 (1.2-4.1)	23.6	68.1
Infected with SCH + STH	11.2 (8.5-14.3)	1.3 (0.5-2.7)	2.3 (1.2-4.1)	6.3 (4.3-8.9)	79.5	43.8
Infected with SCH + *P. f*	10.9 (8.3-14.1)	0.8 (0.2-2.1)	1.9 (0.9-3.6)	2.1 (1.0-3.8)	84.6	80.7
Infected with STH + *P. f*	1.3 (0.5-2.7)	0.8 (0.2-2.1)	0.2 (0.0-1.1)	0.4 (0.1-1.5)	91.7	69.2
Infected with SCH+ STH + *P. f*	5.1 (3.3-7.4)	0.2 (0.0-1.2)	0.2 (0.0-1.1)	1.1 (0.3-2.4)	96.1	78.4

PR1 = Percent prevalence reduction from baseline to 12 months follow up survey
PR2 = Percent prevalence reduction from baseline to 33 months follow up survey.

4.4.4.5 Effect of combined treatment intervention on the overall haematological characteristics.

Table 4.4.4.5.1 summarises the changes in mean Hb concentration and anaemia at 6, 12 and 33 months follow up surveys among 475 participants successfully followed up at all surveys after receiving treatment at least at baseline survey. Paired t-test showed a significant increase in the overall mean Hb concentration from baseline to 6, 12 and 33 months follow up surveys respectively (11.7-12.4g/dL, t = - 10.466, p < 0.001); (11.7- 12.5g/dL, t = - 11.162, p < 0.001) andn(11.7- 12.9 g/dL, t = - 17.277, p < 0.001). There was no significant increase in mean Hb concentration from 6 months to 12 months follow up survey (p = 168). A significant increase in mean Hb concentration was observed from 6 months to 33 months follow up survey (12.4-12.9 g/dL, t = - 9.096, p < 0.001) and from 12 months to 33 months follow up survey (12.5-12.9 g/dL, t = - 8.227, p < 0.001).

Children living in the farming area had significantly lower Hb concentration compared to those living in the rural area at baseline 11.5 g/dL vs 12.1 g/dL, t = - 4.988, p < 0.001); 12 months (12.2 g/dL vs 13.0 g/dL, t = - 7.523, p < 0.001) and at 33 months follow up survey (12.8 vs 13.2 g/dL, t = -2.903 g/dL, p = 0.004). There was no difference in mean Hb concentration between the farming area and the rural area at 6 months follow-up survey (p = 0.891).

The prevalence of anaemia was significantly high in the commercial farming area compared to the rural area at baseline, 6, 12 and 33 months follow up surveys (p < 0.001, p = 0.022, p < 0.001, and p < 0.001 respectively).

McNemar's test showed a significant decrease in the overall proportion of anaemic children from baseline to 6, 12 and 33 months follow up surveys ($p < 0.001$). The decline in severity of anaemia stratified by site from baseline to 33 months follow up survey is also described in Table 4.4.4.5.1. Severe anaemia was not observed in the rural area at all surveys.

Table 4.4.4.5.1: Effect of combined helminths de-worming and malaria treatment on haematological characteristics among 475 primary school children who received treatment at baseline and were successfully followed up to 33 months follow up survey.

Haematological characteristics	**Baseline (T_0)**	**6 months (T_1)**	**12 months (T_2)**	**33 months (T_3)**
mean Hb (95%CI)				
Overall (n = 485)	11.7 (11.6-11.8)	12.4 (12.3-12.5)	12.5 (12.4-12.6)	12.9 (12.8-13.0)
Farming area (n = 312)	11.5 (11.3-11.7)	12.4 (12.3-12.5)	12.2 (12.1-12.3)	12.8 (12.7-12.9)
Rural area (n = 163)	12.1 (11.9-12.3)	12.4 (12.3-12.5)	13.0 (012.9-.13.1)	13.2 (13.0-13.4)
Anaemia prevalence (95%CI)				
Overall (n = 475)	45.7(41.1-50.3)	18.5(15.1-22.3)	20.0(16.5-23.9)	15.4(12.2-18.9)
Males (n = 230)	46.1(39.5-52.8)	13.0(9.0-18.1)	18.7(13.9-23.3)	13.0(9.0-18.1)
Females (n = 245)	43.3(39.0-51.8)	23.7(18.4-29.5)	21.2(16.3-26.9)	17.6(13.0-22.9)
Farming area (n = 312)	55.8(50.1-63.4) *	21.5(17.0-26.5)*	27.2(22.4-32.5)*	19.9(15.6-24.7)*
% none anaemic	44.2	78.8	72.1	80.1
% mild anaemia	44.6	18.6	23.7	19.2
% moderate anaemia	10.3	2.6	4.2	0.6
% severe anaemia	1.0	0.0	0.0	0.0
Rural area (n = 163)	26.4(19.8-33.8)*	12.9(8.2-19.0)*	6.1(3.0-11.0)*	6.7(3.4-11.8)*
% none anaemic	73.6	87.1	93.9	93.3
% mild anaemia	23.9	11.0	6.1	6.7
% moderate anaemia	2.5	1.8	0.0	0.0
% severe anaemia	0.0	0.0	0.0	0.0

*P- value < 0.05 for the χ^2 test of significance difference of anaemia between males and females; and between the farming and rural areas.

4.4.4.6 Effect of combined treatment on anaemia

In order to determine the effect treatment intervention of co-infections on anaemia, participants screened for anaemia, schistosomes, STHs, malaria, helminths-*Plasmodium* co-infections and those diagnosed negative for all parasite at baseline were considered. Table 4.4.4.6.1 shows the effect of combined treatment intervention of different co-infection combinations on anaemia over the study period.

The treatment intervention strategy reduced the prevalence of anaemia by 55.8 %, $p < 0.001$ in the first year and by 67.9 %, $p < 001$, at 33 months follow up survey among children infected with schistosomes only. The prevalence reduction of anaemia during the first 12 and 33 months follow up surveys in the group of individuals infected with STHs only was not significant, $p = 0.727$ and $p = 0.688$ respectively. The reduction of anaemia from baseline to 12 and 33 months follow up survey among individuals with singled infection from *P. falciparum* was significant $p < 0.001$.

Prevalence reduction percentages of anaemia among participants with different co-infection combinations are shown in Table 4.4.4.6.1. McNemar's test showed that the intervention strategy significantly reduced the prevalence of anaemia by 53.1%; $p < 0.001$ both in the first year and at 33months follow up survey among children co-infected with schistosomes + STHs. In the group of individuals co-infected with schistosomes + *P. falciparum* the prevalence of anaemia was significantly reduced from baseline to 12 and 33 months follow up surveys, $p < 0.001$. A greater percentage reduction in prevalence of anaemia from baseline was observed at 33 months follow up survey in the same group of individuals. Participants with STHs –*Plasmodium* co-

infections had the highest prevalence of anaemia at baseline (83.3%) and this was 4.6 times the prevalence observed in the uninfected group (18.1%). Although there were very few participants co-infected with STHs + *P. falciparum*, the prevalence reduction of anaemia from baseline to 33 months follow up survey was highest in the same group (80%). Overall, participants with helminths-*Plasmodium* co-infections benefited more from the treatment intervention compared to participants with single infections or non-infected individuals.

Table 4.4.4.6.1: Effect of combined helminths de-worming and malaria treatment intervention on anaemia

Parasite combination	Percentage (95%CI)					
	Baseline	6 months	12 months	33 months	% reduction PR1	PR2
Not infected (n = 171)	18.1 (12.7-24.7)	15.2 (10.2-21.5)	15.8 (10.7-22.1)	20.5 (14.7-27.3)	12.7	-
SCH only (n = 282)	31.2 (25.8-37.0)	15.2 (11.3-20.0)	13.8 (10.0-18.4)	10.0(6.7-14.0)	55.8	67.9
STHs only (n = 24)	37.5 (18.8-59.4)	25.0 (9.8-46.7)	29.2 (12.6-51.1)	25.0 (9.8-46.7)	22.0	33.3
P. f only (n = 34)	70.6 (52.5-84.9)	26.5 (12.9-44.4)	14.7 (5.0-31.1)	23.5 (10.7-41.2)	79.2	66.7
SCH + STH (n = 53)	60.4 (46.0-73.5)	22.6 (12.3-36.2)	28.3 (16.8-42.3)	28.3 (16.8-42.3)	53.1	53.1
SCH + *P. f* (n = 52)	76.9 (63.2-87.5)	19.2 (9.6-32.5)	38.5 (25.3-53.0)	19.2 (9.6-32.5)	49.9	75.0
STH + *P. f* (n = 6)	83.3 (35.9-99.6)	33.3 (4.3-77.2)	33.3 (4.3-77.2)	16.7 (0.4-64.1)	60.0	80.0
SCH+ STH + *P. f* (n = 24)	79.2 (57.8-92.9)	25.0 (9.7-46.7)	29.2 (12.6-51.1)	20.8 (7.1-42.2)	63.1	73.7

4.5 Effectiveness of school based health education primary school children's KAP in relation to schistosomiasis, STHs and malaria (V).

4.5.1 Demographic characteristics of participants included in the KAP study

One hundred and seventy-two (172) grade 3 children responded to the KAP questionnaire. The mean age (SD) of children included in the study was 9.8 (1.25) years, range (7-15 years). The proportion of females (53.5%) was significantly more than that for males (46.5%), $\chi^2 = 6.699$, $p = 0.010$. Of the 172 grade 3 children who responded to the questionnaire, 88.4% were Christians.

4.5.2 Schools' amenities

In all schools there was no water point with running water and soap for hand washing after toilet or before eating food. There was virtually no water supply at Kaswa primary school located in the farming area. Children were asked to bring their own drinking water from home. Valhalla was supplied with water pipe and a tape water point for drinking purposes only. There was a borehole in the nearest vicinity at Msapa primary school although this was shared with the surrounding community. Nyamaropa primary school was supplied with a borehole although the water level was too low. Children were asked to bring water in containers for watering the school vegetable garden, a sign of lack of running water in the school. Nyamaropa had ventilated pit latrines whilst schools in the farming area had non-ventilated pit latrines. Schools in the commercial farming area were situated near the clinic compared to Nyamaropa primary school in the rural area that was located about 10 km away from Madziwa rural hospital.

4.5.3 Sources of water for drinking and washing or bathing

After stratifying sources of water by school, it became evident that piped water was predominantly used in the commercial farming areas for drinking and cooking with the highest percentage of use of piped water being recorded for children living in farming areas surrounding Valhalla primary school 27/37 (73.0%). The percentage of piped water use by children attending Msapa, and Kaswa primary schools were 51.9% (14/27) and 40.9% (9/22) respectively. Children attending Nyamaropa Primary school frequently used boreholes and wells, 51.9% (44/86) and 32% (28/86) respectively. Washing and bathing were conducted at different water sources to that used for drinking or cooking. The percentages of respondents who indicated that they bathed or washed in the river/stream/dam were 74.1% (20/27), 72.7% (16/22), 45.9 (17/37), and 31.8% (31/86) for Msapa, Kaswa, Valhalla and Nyamaropa respectively. Overall, 63.2% (55/87) of respondents in the farming areas and 36.5% (27/85) of respondents in the rural area used unsafe water (river, stream/dam) for washing/bathing.

4.5.4 Sanitary facilities used by participants at home

The sanitary facilities used by respondents at home are shown in Figure.4.5.4.1. Of the 172 respondents, 12% used bush toilets whilst 88% used either pit, VIT or water closet types of toilets.. Of the 12% that used the bush toilets, 5.7% were living in the commercial farming area and 20.0% lived in the rural area. Communal pit and VIP toilets were commonly used in the commercial farming areas.

Only 4 (4.6%) respondents in the commercial farming area reported that they used water closet type of toilet. The same was not used in the rural area.

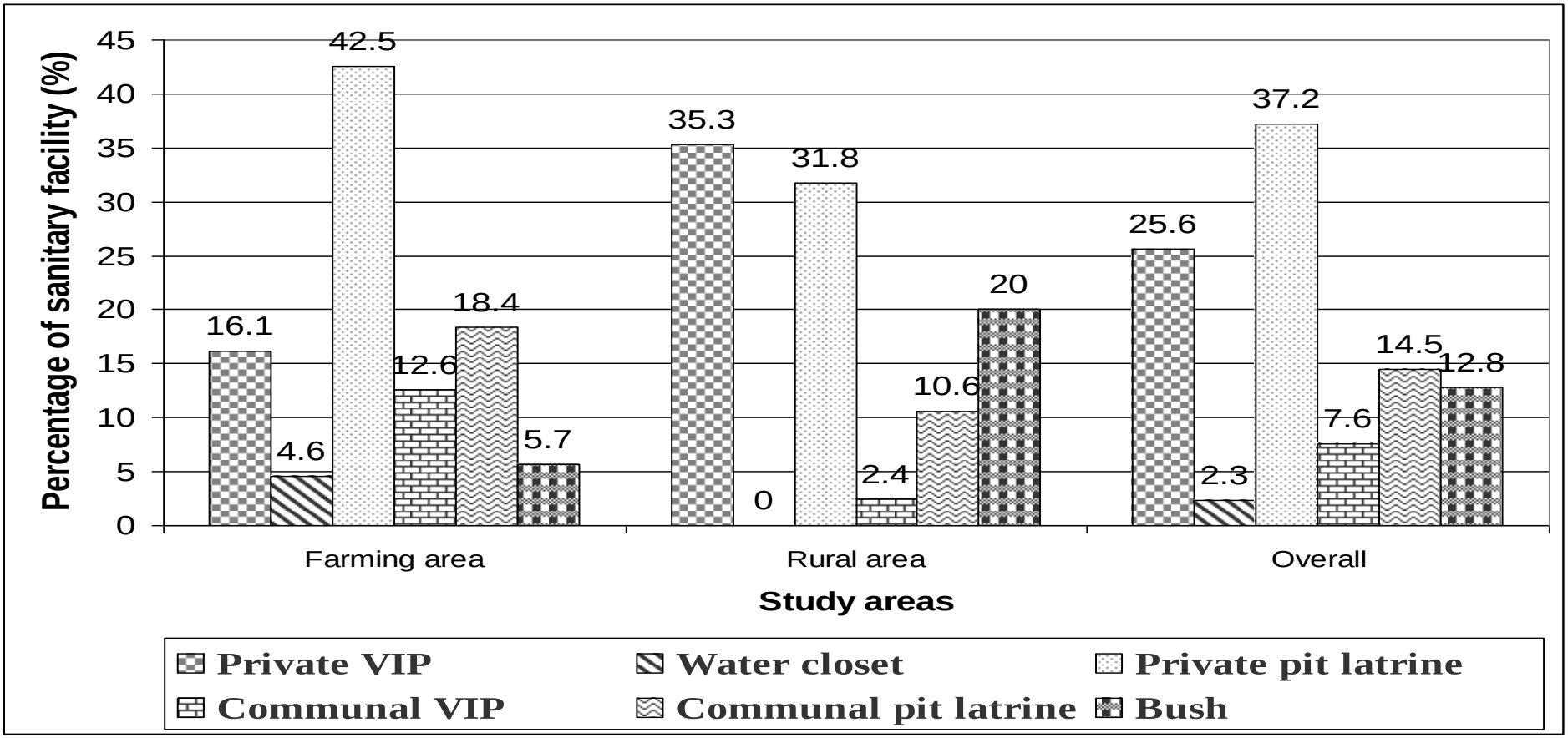

Figure.4.5.4.1: Types of toilets used by respondents at home

4.5.5 Participants' knowledge on causes of helminths and malaria

Table 4.5.5.1 describes the responses given by participants in relation to causes of schistosomiasis, STHs and malaria respectively. Whilst multiple responses were accepted, they were classified into correct or incorrect responses in relation to schistosomiasis, malaria and STHs causes. Of the 172 respondents 55 (32.0%; 95% CI: 25.1-39.5) had correct knowledge of the causes of schistosomiasis. There was no significant difference between the proportion of children in the farming area and those in the rural areas who knew the correct causes of the disease (36.8% vs 27.1; χ^2 = 1.869, p = 0.0.172). Thirty-three children (19.2%, 95% CI: 13.6-25.9) correctly knew the causes of malaria and this comprised of 26.4% (95% CI: 17.6-37.0) and 11.8 (95% CI: 5.8-20.6) of participants living in the farming and rural areas respectively (χ^2 = 5.969; p = 0.015). Only 7 respondents, (4.1%; 95% CI: 1.7-8.2) knew the causes of STHs.

Tables 4.5.5.1: Responses of grade 3 primary schoolchildren regarding their knowledge about causes of schistosomiasis, STHs and malaria

Schistosomiasis	**n***	**(%)**	**Malaria**	**n ***	**(%)**	**STHs**	**n**	**(%)**
No idea	87	49.3	No idea	110	64.0	No idea	155	90.1
Swimming in river or dam	31	17.5	Mosquito/mosquito bite	33	19.2	Drinking dirt water	4	2.3
Playing in the river or dam	13	8.0	Eating with dirty hands	3	1.7	Eat with dirt hands	2	1.2
Drinking dirt water	9	5.1	Eating green mangoes	3	1.7	Playing in dirt water	2	1.2
Eating salt	7	4.0	Cold	3	1.7	Playing in the river	2	1.2
Germs or worms in water	7	4.0	Playing in the rain	3	1.7	Drugs	1	0.6
Entering toilet without shoes	3	1.7	Hot weather	3	1.2	Infected water	1	0.6
Contact with river water	2	1.1	Dirty water/water	2	1.2	Not eating too much	1	0.6
Snails	2	1.1	Drinking dirty water	2	1.2	Stepping in water	1	0.6
Stepping on urine	2	1.1	Playing in dirty water	2	1.2	Water	1	0.6
Jumping over fire	2	1.1	Headache	2	1.2	Eating rotten food	1	0.6
Eating green mangoes	1	0.6	Fishing	2	1.2	Dirty water	1	0.6
Stepping in vomit	1	0.6	Eating maize meal	1	0.6			
Going to the river	1	0.6	Poor hygiene	1	0.6			
Moving blood	1	0.6	Spontaneous disease	1	0.6			
Not wearing shoes	1	0.6	Swimming in the river	1	0.6			
Stepping in witches place	1	0.6	Toilet	1	0.6			
Urinating in water	1	0.6	Getting in water	1	0.6			
Waterborne disease	1	0.6						
Sugar	1	0.6						
In abdomen	1	0.6						
Total	**176**	**100**		**174**	**100**		**172**	**100**

* Multiple responses were given.

4.5.6 Participants' knowledge on prevention measures of helminths and malaria

Table 4.5.6.1 describes the best ways to prevent schistosomiasis, STHs and malaria. Of the 172 grade three children who responded to questions regarding the best ways to prevent schistosomiasis, malaria and STHs, 38 (22.1%; 95% CI: 16.1-20.0); 33 (19.2%; 95% CI: 13.6-25.9) and 10 (5.8%; 95% CI: 2.8-10.4) new the best ways to prevent schistosomiasis, malaria and soil transmitted helminthiasis, respectively.

Table 4.5.6.1: Responses of grade 3 primary schoolchildren regarding their knowledge about prevention of schistosomiasis, STHs and malaria

Schistosomiasis	**n***	**(%)**	**Malaria**	**n***	**(%)**	**STHs**	**n**	**(%)**
No idea	126	71.6	No idea	131	75.3	No idea	156	90.7
Take drugs	18	10.8	Take antimalarial medicines	23	13.2	Take medicines	7	4.1
Avoid playing in water	10	5.7	Visit health care centre	4	2.3	Visit health centre	3	1.7
Avoid swimming in rivers	6	3.4	Sleep under ITN	3	1.7	Don't play in water	2	1.2
Avoid too much salt	4	2.3	Bun herbal plants	2	1.1	Don't use dirt water	1	0.6
Visit health care centre	3	1.7	Clean toilets	1	0.6	Use holy water	1	0.6
Enter toilet wearing shoes	2	1.1	Use mosquito repellents	1	0.6	Don't drink water	1	0.6
Use herbs	2	1.1	Stay indoors during rain	1	0.6	Infected water	1	0.6
Wear shoes	2	1.1	Practice good hygiene	1	0.6			
Drink clean water	1	0.6	Do not play in dirty water	1	0.6			
Avoid water contact	1	0.6	Do not play in rubbish dumb	1	0.6			
			Take prophylactic drugs	1	0.6			
			Drink clean water	1	0.6			
			Wash hands	1	0.6			
			Wash hands before eating	1	0.6			
			Avoid defecating anywhere	1	0.6			
Total	**176**	**100**		**174**	**100**		**172**	**100**

*Multiple responses were given

4.5.7 Association of participants' knowledge, experience and practices with urinary schistosomiasis

The association between participants' knowledge, experience and practices with schistosomiasis is shown in Table 4.5.7.1. There was a significant association between people who reported that they had suffered from schistosomiasis with *S. haematobium* infection as diagnosed parasitologically (OR = 2.60, 95% CI = 1.36-4.96, p = 0.003). Although many respondents who said their urine was red were *S. haematobium* positive, there was no significant association between this response and *S. haematobium* infection based on microscopic examination of urine for schistosome ova. Neither was there any association between swimming in the river with schistosomiasis infection (Table 4.5.7.1).

Table 4.5.7.1: Association between water sources, knowledge, experience and participants' practices with *S. haematobium* infection

Parameter	***S. h* positive n(%)**	***S. h* negative n(%0)**	**Odds Ratio**	**p-value**
Condition of water sources				
Safe water	51 (59.3)	35 (40.7)		
Unsafe water sources	53 (63.1)	31 (36.9)	1.18 (0.60-2.28)	0.612
Knowledge on schistosomiasis				
Had no knowledge about schistosomiasis	34 (54.8)	28 (45.2)		
Knew about schistosomiasis	70 (64.8)	38 (35.2)	1.52 (0.80-2.87)	0.199
Whether participant suffered from schistosomiasis				
Had not suffered from schistosomiasis	47 (51.1)	45 (48.9)		
Suffered from schistosomiasis	57 (73.1)	21 (26.9)	2.60 (1.36-4.96)	0.003
Swimming in the river, pond or dam				
Do not swim in the river	47 (59.5)	32 (40.5)		
Swims in the river, pond or dam	57 (62.7)	34 (37.4)	1.14 (0.62-2.12)	0.675
Whether or not participants urinate near the river				
Do not urinate near the river	58 (58.0)	42 (42.0)		
Urinate near the river	46 (65.7)	24 (34.3)	1.39 (0.74-2.61)	0.310
Whether participant had seen their urine red or not				
Not seen their urine red	49 (59.0)	34 (41.0)		
Have seen their urine red	55 (63.2)	32 (36.8)	1.19 (0.64-2.21)	0.576
Whether or not participant's urine was red				
Reported that their urine was not red	59 (55.7)	47 (44.3)		
Reported that their urine was red	45 (70.3)	19 (29.7)	1.89 (0.98-3.65)	0.058

4.5.8 Association of participants' knowledge, experience and practices with malaria

The association between participants' knowledge, experience and practices with malaria is shown in Table 4.5.8.1. Malaria infection as diagnosed by microscopy of the thick blood smear for parasites was associated with participants' awareness and experience with the disease.

Tables 4.5.8.1: Association between participants' knowledge, experience and practice with malaria diagnosed parasitologically

Parameter	***P. f positive***	***P. f* negative**	**Odds ratio**	**p-value**
Awareness of malaria disease				
Not aware of malaria	2 (4.7)	41 (95.3)		
Aware of malaria	23 (30.7)	52 (69.3)	9.07 (2.02-40.71)	0.001
Experience with malaria				
Not suffered from malaria	1 (2.3)	42 (97.7)		
Suffered from malaria	24 (32.0)	51 (68.0)	19.77 (2.57-152.25)	< 0.001
Knowledge about causes of malaria				
Did not know causes of malaria	18 (19.1)	76 (80.9)		
Knew causes of malaria	7 (29.2)	17 (70.8)	1.74 (0.63- 4.82)	0.284
Knowledge about malaria prevention measures				
Did not know malaria prevention measures	19 (20.0)	76 (80.0)		
Knew malaria prevention measure	6 (24.0)	19 (76.0)	1.26 (0.44-3.60)	0.661
Participants' awareness about ITNs				
Knew about ITNs	8 (20.5)	31 (79.5)		
Did not know about ITNs	17 (21.5)	62 (78.5)	1.06(0.38-3.17)	0.900
Participants' use of ITNs				
Used ITNs	2 (10.5)	17 (89.5)		
Did not use ITNs	23 (23.2)	76 (76.8)	2.57 (0.54-24.45)	0.214

Key: P. f = Plasmodium falciparum

4.5.9 Effect of health education on knowledge of grade three children about the causes of schistosomiasis, STHs and malaria

The effect of school based health education on knowledge of participants about causes of schistosomiasis, STHs and malaria is described in Table 4.5.9.1. The results show that of the 172 grade 3 children interviewed at pre-intervention, a small proportion of them new the causes of schistosomiasis, malaria and STHs. Only 2.4% of the children living in the rural area knew about causes of STHs. The results also revealed that at pre-intervention, children living in the farming area had more knowledge about the causes of the diseases under investigation compared to those living in the rural area. At baseline, children living in the commercial farming area had significantly higher knowledge about causes of malaria compared to children living in the rural area (Table 4.5.9.1). Knowledge attitudes and practice studies after school based health promotion campaign combined with chemotherapy showed an overall improvement in children's knowledge about the causes of schistosomiasis, malaria and STHs (Table 4.5.9.1). However, as opposed to the pre-intervention study, the results revealed that a significantly higher proportion of children living in the rural area knew the correct causes of schistosomiasis, STHs and malaria after intervention (Table 4.5.9.1).

Table 4.5.9.1: Schoolchildren's knowledge about causes of schistosomiasis, STHs and malaria before and after school based health education

Disease	Aspect	Overall % (95%CI) n	Farming area % (95%CI) n	Rural area % (95%CI) n	χ^2 –test (p-value)
Schistosomiasis	Correct knowledge about causes* before intervention (2004)	32.0 (25.1-39.5) 172	36.8 (26.7-47.8) 87	27.1 (18.0-37.8) 85	0.172
	Correct knowledge about causes after intervention (2006)	67.4 (59.9-74.4) 172	56.3 (45.3-66.9) 87	78.8 (68.6-86.9) 85	0.002
Malaria	Correct knowledge about causes* before intervention (2004)	19.2 (13.6-25.9) 172	26.4 (17.6-37.0) 87	11.8 (5.8-20.6) 85	0.015
	Correct knowledge about causes after intervention (2006)	71.5 (64.1-78.1) 171	66.7 (55.7-76.4) 87	76.5 (66.0-85.0) 85	0.169
STH	Correct knowledge about causes before intervention (2004)	4.1 (1.7-8.2) 172	5.7 (1.9-12.9) 87	2.4 (0.3-8.2) 85	0.084
	Correct knowledge about causes after intervention (2006)	55.8 (48.1-63.4) 172	51.7 (40.8-62.6) 87	60.0 (48.8-74.5) 85	0.260

* McNemar's test of significant difference, $p < 0.05$.

4.5.10 Effect of health education on knowledge of grade three children regarding control measures for schistosomiasis, STHs and malaria

Table 4.5.10.1. describes the effect school based health education intervention on the knowledge of children regarding the best ways to prevent schistosomiasis, STHs and malaria. The results show an improvement of knowledge of children regarding the diseases. McNemar's test showed that school based health education and treatment intervention improved knowledge of children about the prevention measures for schistosomiasis, malaria and hookworms ($p < 0.001$). The results also showed that a greater proportion of children living in the rural area had significantly acquired knowledge about the best practice to control schistosomiasis and STHs compared to those living in the farming area. The results demonstrate a greater improvement in the proportion of children who knew the best ways to prevent malaria in the rural area compared to the farming area following health education intervention (76.5%; 95% CI: 66.0-85.0 vs 66.7%; 95% CI: 55.7-76.4). However, the difference was not significant.

Table 4.5.10.1: Schoolchildren's knowledge about prevention measures for schistosomiasis, STHs and malaria before and after school based health education

Disease	Aspect	Overall	Farming area	Rural area	χ^2–test p-value)
Schistosomiasis					
	Correct knowledge about preventive measures before intervention (2004)	*22.1 (16.1-29.0) 172	26.4 (17.6-37.0) 87	17.6 (10.2-27.4) 85	0.16
	Correct knowledge about preventive measures after intervention (2006)	69.2 (61.7-76.0) 172	54.0 (43.0-64.8) 87	84.5 (75.3-91.6) 85	<.001
Malaria					
	Correct knowledge about preventive measures before intervention (2004)	* 19.2 (13.6-25.9) 172	25.3 (16.6-35.7) 87	12.9 (6.6-22.0) 85	0.040
	Correct knowledge about preventive Measures after intervention (2006)	66.3 (58.7-73.3) 172	64.4 (53.4-74.4) 87	68.2 (57.2-77.9) 85	0.630
STH					
	Correct knowledge about preventive before intervention (2004)	*5.8 (2.8-10.4) 172	8.0 (3.3-15.9) 87	3.5 (0.7-10.0) 85	0.206
	Correct knowledge about preventive measures after intervention (2006)	59.3 (51.6-66.7) 172	50.6 (39.6-61.5) 87	68.2 (57.2-77.9) 85	0.022

* McNemar's test of significant difference, $p < 0.05$

4.5.11 Effect of school based health education on practice of children in relation to schistosomiasis and STHs transmission

4.5.11.1 Hand washing before eating food and after toilet

Practices of children in relation to schistosomiasis and STHs before and after school based health education are described in Table 4.5.11.1. The results revealed that a greater proportion of the 172 respondents reported that they always washed their hands before eating food at pre-intervention compared to those who reported a similar practice after intervention (75.6%; 95% CI: 68.5-81.8 vs 48.8; 95% CI: 41.2-56.6 respectively). Among those who indicated that they sometimes or always washed their hands before eating food, only 11.6 % (95% CI: 7.2-17.4) reported that they always washed their hands with soap, 44.8% (95% CI: 37.2-52.5) of the respondents reported that they never used soap when washing hands and 43.6% (95% CI: 36.1-51.4) used soap sometimes. After intervention, a majority of the respondents (69.8%, 95% CI: 62.3-76.5) indicated that they sometimes washed their hands with soap before eating food and only 6.4% (95% CI: 3.2-11.2) stated that they always used soap when washing their hands before eating food.

Among those children who said they always or sometimes washed their hands after toilet, a greater proportion of respondents (47.1%; 95% CI: 39.5-54.8) indicated that they did not use soap to wash their hands and only 9.9% (95% CI: 5.9-15.4) said they always washed their hands with soap after toilet following school based health education.

Table 4.5.11.1: Participants' practice in relation to STHs, schistosomiasis and malaria transmission before and after school health education

Practice	Before intervention		After intervention	
	n	%	n	%
Hand washing before eating food				
Every time	130	75.6	84	48.8
Sometimes	42	24.4	88	51.2
Hand washing with soap before eating food				
Always	20	11.6	11	6.4
Sometimes	75	43.6	120	69.8
Not at all	77	44.8	41	23.8
Hand washing after using toilet				
Always	74	43.0	70	40.7
Sometimes	69	40.1	79	45.9
Not at all	29	16.9	23	13.4
Hand washing with soap after toilet				
Always washes hands with soap	24	14.0	17	9.9
Sometimes washes hands with soap	29	16.9	59	34.3
Do not wash hands with soap after toilet	90	52.3	81	47.1
Do not wash hands after toilet	29	16.9	15	8.7
Swimming in the river/ dam				
Yes	92	53.5	43	25.0
No	80	46.5	129	75.0

4.5.12 Swimming and disposing of excreta near the river

Table 4.5.12.1 describe the practice of respondents in relation to schistosomiasis transmission. Before school based health education about schistosomiasis causes and its control measures, 53.5% (95% CI: 45.7-61.1) indicated that they swam in streams, rivers or dams. The proportions of children who reported that they swam in the same water sources after health education significantly declined after health education (25.0%; 95% CI: 18.7-32.2). The proportion of children who reported that they did not swim in the river or dams significantly increased from 46.5% (95% CI: 38.8-54.3) to 75.0% (95% CI: 67.8-81.3). The respondents also demonstrated that they reduced their frequency of swimming in the rivers or dams after school health educations (Table 4.5.12.1). Similar trends in reduction of pre-disposing practices to schistosomiasis were observed when respondents were asked if they urinated or defecated near the river before and after intervention.

Table 4.5.12.1: Participants' practice in relation to schistosomiasis and STH transmission before and after school health education

Practice	Before intervention		After intervention	
	n	%	n	%
Use of ITNs				
Yes	27	15.7	38	22.1
No	145	84.3	134	77.9
Participants' frequency of swimming				
Does not swim in the river/pond	80	46.5	116	67.4
Once/twice per week	50	29.1	15	8.7
Every other day	18	10.5	15	8.7
Once/twice per month	9	5.2	16	9.3
Everyday	8	4.7	2	1.2
Once every two months	7	4.1	8	4.7
Urinating near the river				
Yes	71	41.3	39	22.7
No	101	58.7	133	70.3
If participants defecate near the river				
Yes	51	29.7	23	13.4
No	121	70.3	149	86.6
If participants' have shoes				
Yes	124	72.1	135	78.5
No	48	27.9	37	21.5
Conditions when participants do not wear shoes (Multiple responses)				
When at home	102	59.3	93	54.1
During recreation	53	30.8	28	16.3
During farming	44	25.6	38	22.1
In classroom	24	14.0	2	1.2
When fishing	12	7.0	4	2.3

4.5.13 Effect of school based health education on practice of children in relation to hookworms and malaria transmission

There was an insignificant increase in the proportion of children who reported that they used ITNs before and after health education (15.7%, 95% CI: 10.6-22.0) and (22.1, 95% CI: 16.1-29.0) regardless of children's improved knowledge about causes and preventive measures for malaria.

Of the 172 participants, 82.6% (95%CI: 76.0-87.9) reported that they helped their families farming at home before intervention. The proportion of children who gave a similar response slightly decresed after school based health education (79.7%, 95% CI: 72.9-85.4). Also observed was an insignificant increase in proportion of respondents who reported that they wore shoes from pre-intervention (72.1%, 95% CI: 64.8-78.7) compared to post intervention (78.5%, 95% CI: 71.6-84.4). Respondents who said they sometimes or always wore shoes were asked when they would not wear shoes. Of 172 respondents, 59.3% (95% CI: 51.6-66.7) and 54.1% (95% CI: 46.3-61.7) reported that they removed shoes when at home. Also 30.8 % (95% CI: 24.0-38.3) and 16.3% (95% CI: 11.1-22.7) reported that they removed shoes during recreation. Of the 172 respondents, 25.6 (95% CI: 19.2- 32.8) and 22.1% (95% CI: 16.1-29.0) reported that they removed shoes during farming at pre- and post intervention surveys respectively.

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CHAPTER 5: DISCUSSION

Helminths infections and malaria are widespread in the tropics and the subtropical areas. The spatial and temporal distribution of helminths and malaria infections often overlaps, and hence, polyparasitism from these parasitic diseases is a common phenomenon. Recent studies suggest helminths infections may increase susceptibility to malaria (Le Hesran *et al*., 2004; Sokhna *et al.*, 2004**)**. Whilst over the years most research has concentrated on single species parasite infections, recently there has been a resurgence of interest in contextual predictors of co-infcetions and an increased recognition of the global burden of disease attributable to neglected tropical diseases (NTDs). This has lead to the demand for revitalization of polyparasitism research in order to elucidate issues of co-infections (Hotez *et al.,* 2006; Mwangi *et al.,* 2006). While this is one of the recent studies focusing on concomitant parasitic infections, it is among the very few that have determined co-infections with schistosomiasis, soil transmitted helminths and *P. falciparum* at the same time and space. The study determined the extent of helminths–*Plasmodium* co-infections and their effect on anaemia. It also assessed the effectiveness of integrated intervention strategies for helminthic-*Plasmodium* co-infections on co-morbidity (anaemia) and prevalence of single and concomitant infections among primary school children living in rural and commercial farming areas in Zimbabwe.

The main observations of this study can be summarised as follows: (1) Co-infections with helminths and *Plasmodium falciparum* existed in the farming area only and was not observed in the rural area. (2) The prevalence of anaemia was high in children with *P. falciparum* and increased with increasing helminths egg intensities. The prevalence of anaemia also increased

from children with single infections to almost double in individuals with helminths-*Plasmodium* co-infections.

(3) Chemotherapy with praziquantel, the current priority strategy for the control of schistosomiasis, showed high cure rates in treatment of the predominant *S. haematobium* species infection among primary schoolchildren in Zimbabwe. (4) Regular combined 6 monthly praziquantel, albendazole and prompt malaria treatment resulted in a linear decline in prevalence of parasitic infection in the first 12 months follow up period. However, 21 months delayed treatment resulted in a rebound of prevalence of helminths infection although the prevalence did not reach pre-intervention levels. Light helminths infections rebound following 21months (almost 2years) of delayed treatment. (5) Combined school based praziquantel, albendazole and prompt malaria treatment resulted in decline of polyparasitism. (6) The prevalence and severity of anaemia declined in response to clearance of polyparasitism over time following treatment. (7) Grade three children showed pre-intervention poor knowledge and risk behaviour in relation to schistosomiasis, STHs and malaria transmission. Whilst school based health education substantially improved their knowledge. However, health education intervention alone could not change children's practices with regards to washing hands with soap, wearing of shoes and use of ITNs.

5.1 The burden of single parasitic infections and co-infections (I)

Baseline prevalence studies on helminths and *Plasmodium* demonstrated that *S. mansoni*, *S. haematobium*, hookworms, *A. lumbricoides*, *T. trichiura* and *P. falciparum* were commonly found in the commercial farming area. Only *S. mansoni* and *S. haematobium* were found in the rural area. Helminths and helminths –*Plasmodium* co-infections were common in the commercial

farming areas in Burma Valley and were not observed in the rural area. These findings suggest a need to determine the extent of single and co-infections in different geographical settings in order to identify areas where co-infections occur from those with single parasitic infections as a first step in planning cost effective integrated control methods for parasitic diseases in the developing world where resources are limited. Co-infections observed in the commercial farming areas could be due to the overlap of conditions including crowded settlements that favour existence of all parasites investigated. Our findings are corroborated by previous studies in the same area although different investigators focused their research on single parasite infections (Chandiwana *et al.,* 1983; Taylor and Makura, 1985; Taylor and Mutambu, 1986; Bradley *et al*., 1992; Mutapi *et al* 2000; Mduluza *et al*., 2001).

Burma Valley farming activities include largely banana plantations and to some extent growing of tobacco and flowers. The area is supplied with perennial rivers that flow from the mountain range in the west to the east. These, together with dams are reservoirs of both schistosome intermediate host snails. Owing to the communal nature of toilets in the farming area, many people prefer bathing and washing their clothes in the rivers than using toilets as bath rooms making schistosomiasis transmission inevitable. Year round banana irrigation activities and high annual rain falls keep wet soils in the area and maintain water ponds where vector mosquitoes can lay their eggs, breed and multiply enhancing malaria transmission. The wet soils constantly support survival of *A. lumbricoides*, *T. trichiura* ova and hookworm larvae that are indiscriminately deposited in stool on the ground by the inhabintants.

Although there has been a reduction in the number of families sharing a single toilet to 4 per Blair toilet (Chandiwana *et al*., 1983; personal observation, 2004-2007), it is common that cleaning communal toilets is seldom, making them unsuitable for use especially in the rain season. In such conditions, people tend to prefer defecating in the bush or banana plantations contaminating the environment with helminths eggs thereby enhancing transmission of STHs in the farming area.

In the rural areas, toilets are mainly privately owned at each household. Subsistence farming is practiced and people depend on natural rains for their farming activities. The area is dry during the dry season and people are also dispersed. These conditions do not favour transmission of helminths and malaria.

The clustering of polyparasitism in the same community as observed in the commercial farming area, household and same individuals, justifies preventive chemotherapy recommended by the World Health Organization in 2006. Preventive chemotherapy encourages cost effective delivery of different drugs for the treatment of different infections as a single package in order to provide integrated control of neglected tropical diseases (WHO 2006a). However, integration of NTDs control with the so called "big three diseases"(malaria, tuberculosis and HIV/AIDS has been proposed (Molyneux *et al.*, 2005; 2006, Hotez *et al*., 2006). In this study, researchers were able to provide combined treatment for schistosomiassis, STH and malaria among children with co-infection.

The urine filtration technique used to diagnose *S. haematobium* is currently the widely used method due to its field applicability and sensitivity (WHO 2002a). A conclusive diagnosis of urinary schistosomiasis infection status was based on examination of urine specimens provided by each individual on at least two successive days between 10:00 am and 2:00 pm in order to reduce bias due to misdiagnosis and also due to daily variability in egg excretion or circardian egg excretion (Doehring *et al.,* 1983; Engels *et al*., 1996). The urinary schistosomiasis diagnostic technique used in this study is widely recommended (Mott *et al.,* 1982; WHO, 2002a).

Generally, at least three stool samples collected on three or more successive days are examined in order to give a conclusive diagnosis of intestinal helminths including intestinal schistosomiasis using the Kato Katz technique (Engels *et al.,* 1996). In our study we only collected stool specimens from each participant on two successive days due to logistical reasons. However, the Kato Katz method was complemented with the formal ether concentration technique that was performed concurrently. The formal ether concentration technique is more sensitive especially in identifying light infections since intestinal worms infestations are diagnosed from a larger amount of stool (about 1 gram) as opposed to 41.7 mg used for Kato Katz (WHO, 2002a). The formal ether concentration technique concentrates eggs such that even light infections can be detected where as the Kato Katz's sensitivity declines in light infections (when egg intensity falls below 100 epg stool). Combination of multiple diagnostic techniques has been shown to improve sensitivity in diagnosis of intestinal helminths (Yu *et al*., 1998; Santos *et al.,* 2005; Goodman *et al*., 2007).

5.2 Effect of polyparasitism on anaemia (II)

The hypothesis of this study was that, the effect resulting from helminths-helminths or helminths –*Plasmodium* co-infections on anaemia among primary school children may be additive or multiplicative. Despite a geographic overlap in disease distribution and identification of common risk factors of infection, few studies have explicitly focused on determining the effects of single helminthic or *Plasmodium* infections on anaemia (Brooker *et al*., 1999; Koukounari *et al*., 2007; Takem *et al.,* 2010). Those few studies that have investigated the effect of co-infection on anaemia have focused on different combinations of infections than what was studied in our study, for example concomitant infection with multiple species of STHs (Ezeamama *et al*., 2005; Gilden and Mascie-Taylor, 2001), schistosomiasis and STHs co-infection (Brito *et al*., 2006; Guyatt *et al.,* 2001). Since multiple infections with schistosomiasis; STHs and/or *Plasmodium* is pervasive among primary school children, making data available on the effect of such co-infections on co-morbidity (prevalence and severity of anaemia) is warranted as this can help health managers in planning appropriate targeted school health interventions.

Baseline data in Burma Valley commercial farming area with schistosomiasis, STHs and malaria co-endemicity showed that anaemia was associated with *P. falciparum* infection, increasing *S. haematobium* and hookworm egg intensities. It also revealed that the prevalence of anaemia increased from single parasitic infection through helminths-helminths co-infections to helminths -*Plasmodium* infections. The highest prevalence of anaemia was observed in individuals with schistosomiasis + STHs + *P. falciparum* co-infections (80.8%). Our study has therefore, demonstrated the multiplicative effect of helminths – *Plasmodium* co-infections on anaemia.

The limitation of our study is that we did not take food samples consumed by the study population for the determination of other factors associated with anaemia (B12, folate, riboflavin and iron) since the etiology of this disease is multi-factorial. The prevalence and impact of other diseases such as HIV/AIDS on anaemia was not assessed in the study population due to ethical reasons. However, the stratification of the study population into groups of individuals with no parasitic infection, single and co-infections allowed us to demonstrate the importance of these parasitic co-infections in the etiology of anaemia. Stratification of participants into different co-infection combinations revealed a additive effect of helminths-*Plasmodium* co-infections on anaemia. Thus, priority should be given to rigorous screening of communities for helminths–*Plasmodium* co-infections in order to prioritise resources effectively in integrated control of anaemia in tropical countries co-endemic for helminths and *Plasmodium.* Our results show that estimating the extent of anaemia in a community, assuming single parasitic infections only, may result in exaggeration of the effect of single infections on anaemia that in reality could be due to unchecked co-infections.

5.3 Praziquantel efficacy (III)

Zimbabwe has drafted a plan of action for the national control of schistosomiasis and soil transmitted helminthiasis (MOHCW, 2010) indicatingpriority given to the control of these diseases as specified in the National Health Strategy (2009-2013). The Government's interest to control schistosomiasis and STHs was also in response to the global demand (54^{th} WHA, 2001). Wide-spread use of praziquantel is, therefore, anticipated in Zimbabwe at the time when there is growing global concern of possible emergence of resistance to praziquantel, the sole drug of choice available (Renganathan and Cioli, 1998). Recommendations have therefore been made to regularly assess efficacy of praziquantel against its wide spread use that is now imminent in the

developing world (WHO, 2005a; Fenwick and Webster, 2006). Thus, the drug efficacy study conducted in our study was not only warranted but also timely.

Results from the efficacy study on 624 primary school children that were diagnosed *S. haematobium* positive, received treatment at baseline and followed up 6 weeks later, revealed a remarkable praziquantel cure rate of 88.5%. In general, the cure rates for praziquantel ranges from 70-90% (Gryseels *et al.,* 1987, Utzinger *et al.,* 2000a).

The prominent side effects reported by children were stomach discomfort (35.8%), and nausea (19.1%). These are common side effects of praziquantel treatment that clear off within 24 hours (Stelma *et al*., 1995; Utzinger *et al.,* 2000a; Raso *et al*., 2004, Cioli and Mattoccia, 2002). The immunological response to many schistosome antigens exposed to the body when praziquantel treatment disrupts and kill worms cause side effects (Utzinger *et al*., 2003; Cioli and Mattoccia, 2002). It is fortunate that only one oedematous swelling was reported in our study. Such side effects could be more worrisome to the community especially during national mass treatment campaigns anticipated in Zimbabwe. Thus, any praziquantel mass treatment should be supported with stocks of medicines that treat for adverse events in order to encourage community compliance and participation in such national programmes. The public also need to be informed about the side effects associated with praziquantel treatment so that they know what to do when such adverse events occur during mass treatment campaigns. Awareness campaigns should therefore be conducted prior to mass praziquantel administration.

Parasitological cure and egg reduction rates used in the assessment of praziquantel efficacy in treatment of *S. haematobium* in our study is field applicable and has been widely used (Stelma *et al.*, 1995; Utzinger *et al.*, 2000a; Utzinger *et al*., 2000b; N'goran *et al*., 2003; Raso *et al*., 2004). However, care must be taken to examine multiple specimens on successive days in order to improve sensitivity of the current parasitological tests. This is important especially when the drug has cleared many but not all worms after treatment. Low infections can best be detected after examination of multiple specimens collected from an individual.

In our study we observed that sensitivity of the urine filtration technique improved with increasing number of urine examination days until day 3. We also observed that the single urine examination resulted in an overestimated cure rate of 97.3%, which declined to 88.5% on the third day of urine examination. For logistics reasons and compliance issues, we did not continue to collect more urine specimens after the third day. Had we done so, probably the cure rate could have been further reduced. Whilst determination of schistosome circulating anodic antigens (CAA) and circulating cathodic antigen (CCA) that clear in circulation within 10-21 days of successful antischistosomal treatment are sensitive methods to monitor schistosomiasis treatment efficacy, the technology required to determine these circulating antigens, Enzyme Linked immunosorbent Assay (ELISA) is not field applicable (De Jonge *et al.*, 1989; van Lieshout *et al*., 1991; 1993). Thus, the parasitological cure and egg reduction rates methods may continue to be used in efficacy studies until schistosome circulating antigen detection methods become field applicable.

The observed positive *S. haematobium* infected individuals (n = 72) at 6 weeks following treatment could be due to maturation of worms that were at varying pre-patent developmental

stages when treatment was given at baseline (Xiao *et al*., 1985; Xiao *et al.,* 1987; Cioli and Mattoccia, 2002; Utizinger, 2003). This is because the baseline prevalence of *S. haematobium* of 66.8% and 52.3% in the rural and commercial farming areas respectively, indicates ongoing high schistosomiasis transmission according to the Word Health Organization guidelines (WHO, 2002a). Praziquantel has low activity against pre-patent schistosomes and, thus, they do not respond well to treatment (Xiao *et al.,* 1987; Utizinger *et al*., 2003). Thus, pre-patent schistosomes could have matured a week or later after treatment, thereby, causing false treatment failure in these high transmission areas.

The best way to improve schistosomiasis treatment efficacy in high transmitting areas would be through combination chemotherapy in which two drugs with different mechanisms of action are used to target different developmental stages of schistosomes in order to enhance cure and egg reduction rates (Utzinger *et al.,* 2003). The two drugs should also be broad spectrum, being able to cure all schistosome species (Utzinger *et al.,* 2000) so that they can be applied in different geographical areas with different schistosome species. Stage specificity laboratory studies on susceptibility of schistosomes to praziquantel, oxamanquine and artemisinin derivative (artemether) revealed that whilst oxamanquine and praziquantel exhibit high activities against cercariae, very young schistosomula (less than 5 days) and adult worms, atermether have high activity on young schistosomula age range, 5-35 days (Utzinger *et al*., 2003). Combination therapy with praziquantel and oxamanquine cannot yield desired results (high cure and egg reduction rates) in this regard. Oxamanquine is also mono species-specific targeting *S. mansoni* only. Thus, only praziquantel and atermisinin derivatives can best be used in schistosomiasis combination chemotherapy since they are all broad spectrum (Utzinger *et al*., 2003).

The co-endemicity of schistosomiasis and malaria especially in sub–Saharan Africa (Mazigo *et al*., 2010), imposes difficulties in approving wide spread use of combination chemotherapy with artemisinin. This is because artemisinins are the only few remaining drugs against malaria that require careful protection in order to minimize chances of development of malaria drug resistance (Utzinger *et al*., 2001; WHO report on malaria 2009). Although field studies have shown promising use of artemether in prophylactic treatment of schistosomiasis the control strategy can only be applied in malaria non endemic countries like Brazil and Egypt. It can not be applied in the majority of sub - Saharan African countries where schistosomiasis and malaria are pervasive (Mazigo *et al*., 2010; Raso *et al*., 2004; Brooker *et al*., 2007a, Utzinger *et al*., 2000b).

5.4 Effect of combined treatment on polyparasitism and anaemia (IV)

Study (IV) was conducted to determine the effect of combined helminths and malaria treatment intervention on the prevalence and infection intensities of individual parasitic infections. It was also conducted with the aim to determine the effect of combined treatment intervention on the prevalence of polyparasitism. The effect of clearance of polyparasitism on anaemia was also determined. The discussion of these studies is therefore divided into two sections: (i) effect of treatment intervention on prevalence of single and co-infections as well as helminths infection intensities and (ii) effect of treatment of co-infections on prevalence and severity of anaemia.

5.4.1 Effect of combined treatment intervention on single infection and polyparasitism

Our results exhibit a steady decline in prevalence of *P. falciparum* from baseline to 33 months follow up surveys. This is despite the fact that there was a 21 months delay in following up the

study population between 12 and 33 months. There are some explanations to this. Firstly, malaria treatment was based on parasitological results when the team was in the field. Secondly, children were health educated about malaria signs and symptoms. They were educated to seek prompt malaria treatment basing on their ability to recognize signs and symptoms of malaria during the absence of the research team. This could have had such a beneficial impact on transmission of malaria in the study population. However, very low numbers of children who sought prompt malaria treatment was reported (n = 8; n = 24; n = 56) at the clinic between baseline and 6 months, 6 and 12 months and 12 and 33 months respectively.

Malaria itself is an acute disease whose symptoms that include fever, severe headache and joint pains influence patients to seek medical treatment on their own. Health seeking behaviour due to the acuteness of the disease may also have contributed to the decline in prevalence of malaria. The 6, 12 and 33 months follow up surveys were conducted in December 2004, June 2005 and March 2007. In Zimbabwe, malaria transmission occurs in December and peaks in March (Taylor and Mutambu, 1986, National malaria control programme, 2008, National Health Profile, 2002-2008). Thus, naturally we would expect more children to be infected during the follow up surveys conducted in December 2004 and March 2007. These months are characterised by high temperatures and high rainfall, conditions that favour breeding of mosquitoes and, thus, transmission of malaria. The research technicians who examined malaria slides at baseline were maintained throughout the study in order to minimize chances of observer bias.

Another intervention measure that was outside our influence was the indoor residual spraying (IRS), undertaken by the Ministry of Health and Child Welfare annually in malaria endemic

districts just before malaria season. Spraying occurs just before the onset of rain season between October and November and if delayed the exercise can spill into December. Spraying is targeted in malaria endemic districts and Mutare is among the 33 malarious districts in Zimbabwe where IRS intervention is annually implemented (National Malaria Control Programme, 2008). This intervention could have reduced the risk of malaria infection among participants. Guyatt *et al.,* (2002) showed that sleeping in a room sprayed with insecticide reduced the risk of *P. falciparum* infection by 75%. The combination of prompt malaria treatment and health education with annual IRS strategies could have caused such a steady decline in prevalence of malaria even in the malaria peak month (March) as observed in this study in 2007.

The decline in prevalence of schistosomiasis and STHs over 12 months was in response to regular six monthly-combined praziquantel and albendazole treatment. However, the prevalence of helminths rebounded following 21 months of delayed treatment. Analysis of infection intensities for *S. haematobium, S. mansoni* and hookworms showed that only light infection intensities rebound after almost 2 years of delayed treatment. More importantly, the proportion of heavy infections were either completely cleared as for hookworms and *S. mansoni,* for *S. haematobium* the prevalence of heavy intensity was 4.0% almost 2 years later compared with 35% before treatment (Figures. 4.4.4.1.1; 4.4.4.2.1 and 4.4.4.3.1). Our results are corroborated with findings from studies conducted in Burkina Faso (Toure *et al*., 2007, Zhang *et al*., 2007). Thus, if the primary objective for preventive chemotherapy is to reduce morbidity by maintaining low levels of heavy infection intensities, then a revision of regular treatment cycles from annual treatment in high schistosomiasis transmission to a much more cost effective biannual treatment may need to be considered (Montresor *et al*., 1999; WHO, 2006a).This is

particularly important in the developing world where limited resources have stalled progress in comprehensive national schistosomiasis control programs (WHO, 1999).

Helminths re-infection observed in this study confirm that environmental contamination with schistosomes and hookworms continued especially in the farming area where pit latrines were still being shared and not regularly used. Our results reveal that without provision of alternative safe water sources and protective clothing (shoes and ITNs), re-infection with schistosomiasis, STHs and malaria is inevitable. In a separate comparative study of two IPTi trials that used the same study design, follow-up intervention, procedures and assessment of outcomes, in Tanzania and Mozambique, children were randomised to receive either SP or placebo administered 3 times alongside routine vaccinations delivered through the Expanded Program on Immunisation. Characteristics of the two areas and efficacy on clinical malaria after each dose were compared. The most relevant difference was in ITN's use; 68% in Ifakara and zero in Manhiça. In Ifakara, IPTi was associated with a 53% reduction in the risk of clinical malaria between the second and the third dose. During the same period, there was no significant effect in Manhiça. Similarly, protection against malaria episodes was maintained in Ifakara during 6 months after dose 3, but no effect of IPTi was observed in Manhiça. The authors concluded that the high ITN coverage in Ifakara is the most likely explanation for the difference in IPTi efficacy on clinical malaria (Menendez *et al*., 2007). Thus, health education about preventive measures of helminthiasis and malaria combined with treatment without provision of sanitary conditions and protective clothing (shoes and ITNs) may be a short term measures in control of helminthiasis and malaria (WHO, 1999; WHO malaria report, 2009).

The reduction of helminths and *P. falciparum* prevalence in response to combined intervention strategy was corroborated with corresponding reduction in prevalence of co-infections (Table 4.4.4.4.1**)**. However, unlike helminths + *Plasmodium* co-infections that continued to decline steadily up to 33 months follow up survey, schistosome + STHs co-infection exhibited a rebound in prevalence to slightly more than half the baseline prevalence (Table 4.4.4.4.1). This characteristic pattern of schistosome + STHs co-infection combination follows a similar trend in individual parasite transmission pattern over 33 months (Table 4.4.4.4.1; Figures. 4.4.4.1.1; 4.4.4.3.1 and 4.4.4.2.1). These results show how difficult it is to re-establish helminths-*Plasmodium* co-infections when integrated control strategies are implemented in an area with polyparasitism. Study II shows a strong association of anaemia with helminths + *Plasmodium* co-infections. Thus, any strategy that disrupts polyparasitism will ultimately control anaemia and also the associated severe clinical outcomes resulting from helminths-*Plasmodium* co-infections (Druilhe *et al.,* 2005; Le Hesran *et al.,* 2004; Sokhna *et al.,* 2004)**.**

5.4.2 Effect of combined treatment intervention of co-infections on anaemia

The main hypothesis of this study was that anaemia changes in a predictable fashion with alterations in the burden of helminths, *Plasmodium* and helminths-*Plasmodium* co-infections following treatment intervention. Also, in order to determine the effect of intervention only those individuals diagnosed and treated at baseline and then followed up successfully at all surveys being screened for anaemia at each survey (n = 475) were considered. Overall, the prevalence of anaemia was 45.7%. After stratifying participants by site, the prevalence of anaemia predicted this stratification with anaemia being significantly higher in the commercial farming area compared to the rural area (55.8% vs 26.4%; $p < 0.001$), (Table 4.4.4.5.1). More importantly the

pre-intervention stratification of participants into separate groups of those participants not infected with any of the parasites, those with single parasitic infections and those with helminths-*Plasmodium* co-infections were also predicted by a significant increase in anaemia following the same fashion respectively (Table 4.4.4.6.1).

A further exploration was made in which the stratified groups of individuals were followed up over a period of 33 months after baseline and treatment was also given at each survey when infection was observed parasitologically. Haemoglobin levels and anaemia were determined among these individuals at baseline; 6; 12 and 33 months follow up surveys respectively. Our data show that there was no marked increase on Hb levels and prevalence of anaemia from baseline to 33 months follow up survey among individuals not infected with any parasite. When the different groups of individuals infected with single parasites and those with co-infections were also followed up, a decline in prevalence of single and co-infections was predicted by a corresponding decrease in anaemia (Table 4.4.4.6.1). Improvement of anaemia was more apparent in individuals who had schistosomiasis, *P. falciparum* single infections and those who had different helminths –*Plasmodium* co-infections at baseline. This was in response to the decline in prevalence of single infections and helminths- *Plasmodium* polyparasitism.

At baseline survey, we also observed that children in the commercial farming area had already been introduced to school based supplementary feeding three months earlier with porridge prepared from powder fortified with iron (8 mg ferrus fumerate). This was being prepared daily and given to children at break time. Due to ethical reasons, our study also lacked a control group of infected individuals that was either given a placebo or not treated at all. We did also not take

portions of food samples eaten by the participants to determine, iron, vitamin B12 and folate content due to logistical reasons. These factors could have biased our findings. However, the stratification of children into different infection combinations showing a slight decrease in anaemia among children not infected with any parasite compared to substantial anaemia percentage prevalence reduction in those individuals in the same area but who had single and helminths- *Plasmodium* co-infections enabled us to observe the contribution of polyparasitism on the burden of anaemia.

Following up stratified children from baseline to 33 months enabled our observation of the subsequent effect of treatment intervention on Hb levels and anaemia. Studies conducted elsewhere show the synergistic effect of supplementary iron and parasite control on anaemia confirming our observations. For example, in a study conducted to determine the effect of antihelminthic treatment on helminths and anaemia among female tea pluckers in Bangladesh, Gilgen and Taylor observed that the group that was given albendazole only showed a mean rise in Hb of 1.94 g/l between pre- and post treatment survey. However, in the group receiving both albendazole and 24 weekly doses of iron supplementation a rise of 7.78 g/l was seen in the 24 weeks of the study (Gilgen and Taylor, 2001). Another study was conducted in KwaZulu-Natal to determine the effect of different antihelminthic treatment regimens combined with iron supplementation on the nutritional status of schoolchildren (Taylor *et al.,* 2001). It revealed that children given triple doses of albendazole, praziquantel and ferrus fumerate 200 mg weekly for ten weeks had a significant increase in Hb levels from baseline level. Those children that received either placebo only or praziquantel and albendazole treatment only had no significant increase in Hb levels (Taylor *et al.,* 2001). These results collaborate our findings in the

commercial farming area where treatment and coincidental iron supplementation through iron fortified porridge was implemented concurrently.

5.5 Effectiveness of school based health education on Grade three children's KAP concerning schistosomiasis, STH and malaria (V)

Before conducting this study, our hypothesis was that grade three children had knowledge about schistosomiasis, STHs and malaria. It was assumed the information about the communicable diseases would be passed on to them by their parents. As a result, their KAP in relation to schistosomiasis, STHs and malaria would be a proxy of their parents and the community in which they lived. Surprisingly the data from our studies on KAP for grade 3 children showed that before school health education intervention was implemented, a small proportion of grade three children knew about the causes and preventive measures of schistosomiasis, STHs and malaria. These results demonstrate a deficiency in health education about malaria and helminthiasis in the high-risk age group and possibly little knowledge of the community about causes and preventive measures of these diseases. The results amply show that there was an increase in knowledge following school based health education about the causes and prevention measures of malaria, schistosomiasis and STHs. The majority of grade three children realized the benefits of protecting themselves against mosquito bites. For example whilst only 19.2% (95%CI: 13.6-25.9) of the 172 children provided correct answers about best measures to control malaria before intervention, 66.3% (58.7-73.3) were able to provide correct answers about best measures to control the same disease after school health education. For schistosomiasis, the students indicated that many of them no longer swam in rivers, defecate or urinate near the rivers following school based health education. The frequency of swimming was reduced following health education intervention.

Results on responses to the question regarding hand washing before eating showed that at pre-intervention 75.6% of participants indicated that they washed hands before eating food. It was anticipated that after school based health education, improved hygienic practice would be observed. However, the responses on hand washing following health education showed that only 48.8% indicated that they washed hands before eating food. This discrepancy was due to the fact that at baseline students associated hand washing with eating the main meal courses like dinner or lunch which traditionally their parents would always make water available for hand washing before and after eating such meals at home. It is actually a sign of disrespect for a child to eat a meal at dinner or lunch before washing hands where as eating any snacks as well as fruits even at home or packed lunches at school is done without one being monitored for hand washing. Our results therefore show that after health education, participants were now aware that anything they ate was referred to as food. This included snacks or packed lunches they brought to schools as well as fruit which they normally would eat before washing hands. This could explain the decline in the proportion of children who said they washed hands before eating food following health education.

The lack of proper school amenities such as running water and soap for hand washing, clean and ventilated pit latrines, safe water for drinking in schools, provide major challenges for school health promotion. This is because the main aim of health education is not for students to merely know and provide correct answers on questionnaires about good practices to prevent communicable diseases. It is however, the demonstration of outcome in terms of change in an individual's health related behaviour (Ekeh and Adeniyi, 1988). A small proportion of children that indicated that they always washed hands with soap before eating (11.6 % and 6.4%) or after

toilet (14.0% and 9.9%), before and after school health education respectively demonstrated that washing hands with soap was rare in both the farming and rural areas. This is a common phenomenon in the developing world where the low socio-economic status put soap beyond the reach of many people. These people may preserve whatever amount of soap they may have for washing clothes or bathing instead of hand washing (Curtis and Cairncross, 2003). However, hands serve as vectors, transmitting pathogens from feaces to surfaces, to foodstuffs, drinks and the mouths of susceptible hosts. It is, therefore, plausible to encourage effective hand washing with soap as it serves as a self-vaccine against pathogens that cause trichuriasis, ascariasis, shigellosis, cholera and dysentery.

The lack of significant increase in the proportion of children who reported that they used ITNs from baseline (15.7%, 95%CI: 10.6-22.0) to post intervention survey (22.1, 95%CI: 16.1-29.0) shows that health education alone would not make students own and sleep under mosquito nets. A weakness on the part of our intervention is that we did not have enough funding to at least procure mosquito nets for our study participants. Neither did we have resources for providing running water and soap for washing hands in schools. Parents too could not provide these enabling factors. Thus, our results show that, in order for the students to successfully translate their health behaviour into practice, the resources (ITNs, soap, running water and toilets) have to be accessible and available both at home and in schools so that children could replicate health changes observed in schools at home.

Due to ethical reasons, all children were subjected to the same health education material. We, therefore, did not have a control arm that could have better described the effectiveness of the

combined school based health education and treatment. However, the follow up design that provided results for pre-and post intervention KAP studies helped in circumventing this weakness.

5.6 Potential confounders and limitations of the pre- and post intervention study design

Limitations of the pre-and post intervention study design include possibilities of having other interventions not known to or beyond the control of the observer. Due to ethical reasons, participants in our study were not limited to receiving treatment from the research study only. They were also not monitored for the occurrence and treatment of other diseases such as tuberculosis and HIV that were beyond the scope of the study. All these are possible limitations that could have acted as confounders in our study. Data looking at different diseases concurrently in the same people and looking at the treatments presents problems of confounding. Correlated variables as a result of a third variable, for example for helminths infections there is a correlation between infection and age but this is not necessarily because age causes infection, but rather, the processes that cause infection (exposure to infective agents in water) increase with age giving the positive correlation between age and infection. There are possible ways of dealing with these confounders:

1. Step-wise analyses which include step-wise regression and ANOVA using sequential sums of squares. These will allow sequential decomposition of the effects of several explanatory sequentially so that the effects of confounding variables can be allowed for before testing for the effects of the variables of interest. In this way, we reduce the likelihood of spurious effects being significant.
2. Nested design, where cases of a disease that occur in a defined cohort are identified, and, for each, a specified number of matched controls is selected from among those in the

cohort who have not developed the disease by the time of disease occurrence in the case. In this study that would be people with schistosomiasis/STH matched with those without and similarly people with malaria matched with those without malaria infection. Given the high sample sizes of infected people, this would be less appropriate for these data and the step-wise analyses would be more applicable (Sokal and Rohlf, 1995).

5.7 Overall conclusions

Our results showed heterogeneity in distribution of parasites among primary school children living in rural and commercial farming areas. Polyparasitism with STHs, malaria and schistosomiasis was observed in the farming area where toilets are still being shared among at least 4 families, people are over-crowded, persistent irrigation and cultivation keep the soils wet sustaining STHs larval survival and ponds of water that support breeding of malaria vector mosquitoes. These conditions coupled with warm temperatures make Burma Valley conducive for transmission of STHs, malaria and schistosomiasis and the observed helminths-*Plasmodium* polyparasitism a norm in the commercial farming area. Schistosomiasis was pre-dominant in both the rural and commercial farming area.

Helminths-*Plasmodium* co-infections observed in the commercial farming area showed a multiplicative effect on anaemia whose prevalence increased from individuals not infected with any parasites, through single infections to those individuals with co-infections. The prevalence of anaemia was also positively correlated with egg intensities.

Six monthly combined praziquantel, albendazole and prompt malaria treatment in the first year of intervention resulted in high prevalence and infection intensity reduction percentages.

Twenty-one (21) months delayed treatment caused a rebound of light infections only and these did not exceed pre-treatment levels. These results show that delaying treatment over a period of 2 years in areas endemic for STHs, schistosomiasis and *P. falciparum* could be a cost-effective treatment intervention strategy for the control of helminths–*Plasmodium* polyparasitism.

Our data has also shown that integrated school based praziquantel, albendazole and prompt malaria treatment reduced the prevalence of single and co-infections to low levels. More importantly it has shown that anaemia responded in a typical fashion to clearance of co-infection and single infections over time. However, these results still need to be confirmed elsewhere as this is the first study to explore the efficacy of combined strategy to control helminths–*Plasmodium* polyparasitism on anaemia in Zimbabwe.

The praziquantel parasitological cure rate of 88.5% for *S. haematobium* demonstrated that praziquantel treatment is efficacious among primary school aged children in Zimbabwe.

Our data on KAP indicate that school health education improves children's knowledge in relationship to causes and prevention measures for communicable diseases that most often affect them. However, the results also show that when knowledge is not supported by enabling and reinforcing factors, desirable health changes in children's practices may not be realised. The results regarding failure of children to wash hands with soap before eating and after toilet, lack of ownership and use of ITNs by children after health education reveal unavailability of soap and running water in schools for hand washing. It also shows lack of support from parents at home

who should make available soap for hand washing, ITNs for children to sleep under and provide shoes for children to wear.

5.8 Recommendations

Our study has shown that schistosomiasis is pre-dominant in both the farming and rural areas in Zimbabwe with an overall prevalence of 60.0%. Given its effect on anaemia, cognitive potential among primary school children and other secondary morbidities including male and female genital schistosomiasis that are risk factors of HIV transmission (Kjetland et al 2006), we recommend urgent national control of schistosomiasis adopting a school based approach in Zimbabwe.

There is a need to prioritize further surveys in different regional locations in order to identify areas with schistosomiasis-STH and helminths-*Plasmodium* polyparasitism in Zimbabwe as this data is currently needed to plan cost effective integrated strategies for the control of neglected tropical diseases (schistosomiasis and STHs) and malaria (Hotez *et al*., 2006, Mwangi *et al*., 2006; Molyneux *et al*., 2005).

Our study is among the few studies that have explored the impact of co-infection on anaemia showing a multiplicative effect. However, there is need to conduct further studies with similar design but in different epidemiological settings in order to verify our observations on the changes of anaemia in a fashionable way in response to clearance of polyparasitism following treatment.

The timing of re-treatment cycles based on the prevalence of polyparasitism and intensity of parasites need to be evaluated elsewhere before recommendations are made to change helminths

treatment cycles stipulated by the World Health Organisation (WHO 2002; WHO 2006). Results from this study have shown that delaying treatment rounds by 21 months would results in a re-bound of mainly light infections that may not be important regarding development of morbidities (WHO 2002). Thus, considering that schistosomiasis, STHs and malaria affect populations with poor economies, carefully designed studies should be conducted to further explore the optimal and cost effective treatment and re-treatment cycles. Basing on our results we postulate that a two year combined de-worming cycle with prompt malaria treatment and provision of ITNs is efficacious and cost effective even if the prevalence of worms is $\geq 50\%$. We also recommend that health planners need to consider seriously identification of populations at risk of helminths-*Plasmodium* co-infections in order to integrate the usual costly vertical control programme for the sustainable and effective control of polyparasitism and anaemia.

Mass school based praziquantel treatment can be initiated in Zimbabwe as praziquantel has been proven efficacious (parasitological cure rate of 88.5%) among the high risk age group (5-15 years). However, there is need to provide health education to the communities about common side effects associated with praziquantel treatment and their transient nature in order to ensure community compliance in mass treatment campaigns.

School health education should be implemented in order to improve children's knowledge about the diseases that affect them and the children to adopt hygienic practices that corroborate efforts made by health managers in mitigating preventable communicable diseases such as schistosomiasis, malaria and STHs. These infections simply require avoidance of contamination of the environment for schistosomiasis and STHs, sleeping under an ITN or application of

mosquito repellents (for malaria) and a cost effective adequate hand washing with soap before handling or eating and after toilet for STHs. However, hand washing with soap after toilet has an ancillary benefit of preventing other diseases of major public health importance that include cholera, dysentery and shigellosis.

Provision of school amenities such as running water and soap for hand washing, toilets for sanitation and provision of safe drinking water are enabling factors that should be prioritized in schools in order to enhance school health. Parents should be involved in health promotion so that they are also motivated to provide enabling factors such as ITNs for children to sleep under. Health promotion to parents will enable them to change their attitudes towards making available shoes for their children to wear and to provide soap required for hand washing before eating and handling fruits as well as after toilet. Community participation will ensure that the changes observed in the school setting can be replicated in the students' home.

5.9 Future work

Our work has been conducted on primary schoolchildren. This is a high risk group for schistosomiasis, STH and malaria as well. We have for the first time determined and shown that helminths-*Plasmodium* polyparasitism is common among primary schoolchildren and has an additive or multiplicative effect on anaemia. We have also shown that anaemia responds in a fashionable way to clearance of single infections and polyparasitism. However, there is need for other field studies in diverse communities in Zimbabwe and elsewhere in order to identify populations at high risk of polyparasitism for control and also to confirm our findings on responses of anaemia to treatment of parasites. We also determined the efficacy of praziquantel

treatment on *S. haematobium* treatment among primary schoolchildren. Further studies need to be conducted in the adult population to confirm if the efficacy is within the same range.

The effect of school health education on primary schoolchildren KAP requires further investigations with study designs that include the control arms in order to better describe the effectiveness of this intervention. Care must also be taken to provide enabling factors such as soap, running water for hand washing in schools, provision of sanitation and ITNs for adequate exploration of the effect of school health promotion on behaviour changes of primary school children and the communities.

Finally it is my gratitude to indicate that the work in this study has been taken up by the Ministry of Health and Child Welfare of Zimbabwe to be implemented at national level and priority has been given to school based control of schistosomiasis and STHs. The title of the national programme: National Plan of Action for control of schistosomiasis and soil transmitted helminthiasis in Zimbabwe (Midzi *et al* 2010). The planning phase (National survey of schistosomiasis and STHs and drafting of a school based parasite control policy) were successfully undertaken in 2010 and 2011 with the author having been able to coordinate these programs. Preparations are at an advanced stage for the implementation phase that includes estimation of praziquantel and albendazole quantities for national mass drug administration. Medicines have already been imported. Training of trainers and primary school health masters is still to be undertaken.

5.10: Outstanding achievements resulting from this PhD work

The PhD work has resulted in five publications that contributes towards the chapters described in this thesis (Appendix E)

Ministry of Health and Child Welfare seconded the author as the National Focal person for schistosomiasis and soil transmitted helminthiasis control in Zimbabwe owing to the PhD work that influenced the National schistosomiasis and STH control program.

The author has managed to source 2.5 million praziquantel tablets and 2.4 million Albendazole tablets for the commencement of mass drug administration in Zimbabwe beginning in 2012. He successfully coordinated implementation of the comprehensive combined national schistosomiasis and STH survey including major urban areas for the first time in Zimbabwe (MOHCW-National schistosomiasis and STHs survey report 2011).

The author has also successfully organized a workshop to draft a policy for the control of schistosomiasis, STH and other NTDs in Zimbabwe, with support from the Ministry of Health and Child Welfare, Ministry of Education Sport Arts and Culture, University of Zimbabwe, Faculty of Medicine, Department of Community Medicine, Department of Medical Laboratory Sciences, WHO, UNICEF (18-21 July 2011).

6.0 CHAPTER 6 REFERENCES

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Zimbabwe Demography and Health Survey 2005-2006, Statistics Office, Harare, Zimbabwe

APPENDICES

APPENDIX A: SCHISTOSOMIASIS, SOIL TRANSMITTED HELMINTHIASIS AND MALARIA QUESTIONNAIRE

Interview Date ----/----/ ----- School Code ---------- I.D No ----------

1. Name: ---------- 2. Age: ---------- (yrs) 3. Sex M [ ] F [ ]

2. Village / Community: ---------- 5. House No: ----------

6. Occupation of your parent/guardian: [1] Farmer [2] Fisherman [3] Trader [4] Teacher

[5] Civil servant [6] Businessman [7] Unemployed [8] Other: ----------

7. What is your ethnicity [1] Shona [2] Ndau [3] Ndebele [4] Zezuru [5] Other ---------

8. What is your religion [1] Christian [2] Islam [3] Traditionalist [4] Other: ----------

General information

WATER

12. Do you have a water source inside your house? [1] Yes [2] No

13. What is your source of drinking water at home?

[1] Stream/river [2] Pond [3] Well/borehole [4] Pipe borne water [5] Spring

[6] Water tanker [7] Rain water [8] Other

14. What is your source of water for Bathing, washing clothes? [1] River/stream

[2] Well [3] Tape water [4] Borehole [5] Dam [6] Garden well

15. How close is the water source at home in community? [1] Available in the house

[2] Near my house [3] Far from house [4] Very far from house

SANITATION

16. Do you have a latrine inside your house? [1] Yes [2] No (if No, go to q18)

17. If yes, what is the type is of latrine? [1] KVIP [2] water closet [3] Pit

18. Do you have a latrine near your house? [1] Yes [2] No 9if no go to 20)

19. If yes, what is the type of latrine? [1] KVIP [2] water closet [3] Pit

20. Where do you defecate when at home?

Private toilet	**Public toilet**
[1] KVIP	[4] KVIP [7] Beach [8] Farm [9] Other ---------
[2] Water closet	[5] Water closet
[3] Pit	[6] Bush

Knowledge

21. Do you know of the following diseases? If yes, have you suffered from it?

	Knowledge	**Suffered**
Malaria	[1] Yes [2] No	[1] Yes [2] No
Bilharzia	[1] Yes [2] No	[1] Yes [2] No
Intestinal worms	[1] Yes [2] No	[1] yes [2] No

22. What courses the following diseases?

[1] Malaria_____

[2] Bilharzia_____

[3] Intestinal worms_____

23. What is the best way to control the following diseases?

[1] Malaria_____

[2] Bilharzia_____

[3]Intestinal worms_____

Attitude and Practice

24. Do you eat with your hands? [1] Yes [2] No

25. Do you wash your hands before eating [1] Every time [2] Sometimes [3] Not at all

(if not all, go to q28)

26. If every time or sometimes, do you wash your hands with soap before eating?

[1] Yes [2] No

27. Do you have shoes or sandals? [1] Yes [2] No [3] Sometimes (if no go to q31)

28. If yes do you wear shoes or sandals? [1] Yes [2] No [3] Sometimes (if no go to q31)

29. If yes or sometimes, when do you NOT wear shoes? (Accept multiple responses)

[1] At home [2] During recreation [3] In the classroom [4] In the farm

[5] Fishing

30. Do you wash your hands after toilet? [1] Always [2] Sometimes [3] Not at all

(if no go to q 33)

31. If always or sometimes, do you use soap after toilet? [1] Yes [2] No

[3] Sometimes

32. Where are you taken for health care when you are ill?

[1] Hospital [2] Health [3] Spiritualist [4] Chemical shop [5] Prayer camp

[6] Don't go anywhere

33. Where do you dispose your household garbage/rubbish? _____

34. How do you dispose of your waster [1] propose anywhere [2] Put in a bin

[3] Put in a bag [4] Other ----------

35. Do you help your family in farming? [1] Yes [2] No

36. Where do you normally defecate at School?

[1] KVIP [2] Water closet [3] Pit latrine [4] Bush [5] Beach [6] Dunghill
[7] River bank [8] Other ----------

37. Do you discuss health issues at home? [1] Yes [2] No [3] Sometimes

(if no go to q40)

38. If yes or sometimes, with whom do you discuss health issues at home?

[1] Father [2] Mother [3] Grand parents [4] Siblings [5] Friends [6] Other -----

39. Do you discuss personal health issues at school with teachers? [1] Yes [2] No (if no go to 42)

40. If yes select the health issues you discuss at school (Accept multiple responses)

[1] Diarrhoea [2] Bilharzia [3] Malaria [4] Intestinal worms

[5] Abdominal pains [6] Other-------

41. Do you know what an Insecticide Treated Bed Net is? [1] Yes [2] No

42. Do you use a Treated Bed net? [1] Yes [2] No

43. Do you swim in the river or pond [1] Yes [2] No (if no go to q46)

44. If yes, how often do you swim in the river or pond?

[1] Every day [2] Every other day [3] once/twice a week

[4] Once/twice a month [5] Less than once a month

45. Do you sometimes urinate near the river or pond [1] Yes [2] No.

46. Do you sometimes defecate near the river or pond [1] Yes [2] No.

47. Do you help your mother cooking at home? [1] Yes [2] No

48. Have you ever seen your urine red? [1] Yes [2] No

49. Do you easily get tired? [1] Yes [2] No

50. Have you had raised body temperature or felt cold in the last 3 days?

[1] Yes [2] No

51. Have you taken any medicine in the last 3 days [1] Yes [2] No.

APPENDIX B: HEALTH EDUCATION MATERIAL

CAUSES OF BILHARZIA

Bilharzia is caused by the following:

1. Penetration of bilharzia worms (cercariae) into our bodies when we get in contact with contaminated river water.
2. Playing in the river contaminated with freshwater snails
3. Swimming in the pond, stream, river or dam
4. Failing to cross the river by the bridge or to use stepping stones
5. Washing clothes or bathing in the river.
6. Urinating or defecating in or near the river.
7. Failure to use toilets for excretion
8. Fishing whilst standing in the river
9. Any contact with contaminated water in the pond, stream, river or dam with a naked body

Signs and Symptom of bilharzia

1. Loss of blood that appear in terminal urine or in stool.
2. Painful urination
3. Reduced school performance
4. General weakness and inactive
5. Bladder and liver cancer
6. Impaired growth
7. Infertility later in life
8. Death can also occur

Best ways to prevent bilharzia

1. Avoid swimming in stagnant water in ponds, streams, river or dam.
2. Stand by the river bank when fishing and avoid contact with river water.
3. Avoid playing in water
4. Avoid washing clothes or bathing in the stream, river or dam
5. Wear gumshoes when watering the garden
6. Clear the river banks or canals of grass or any vegetation that may harbour freshwater snails.
7. Kill freshwater snails using the chemical molluscicides
8. Seek medical treatment for bilharzia when infected

CAUSES OF SOIL TRANSMITTED HELMINTHIASIS

- Swallowing eggs of worms together with food or fruits.
- Eating food with dirty hands
- Failure to wash hands with soap after toilet
- Failure to wash hands with soap always before eating
- Eating dirty fruits
- Preferring to defecate in the bush instead of using the toilet
- Eating cold food that has not been covered or protected from flies
- Drinking dirty water
- Keeping long and dirty fingers
- Walking with bare foot in the field or around the school or home yard where children indiscriminately defecate

Signs and symptoms of soil transmitted helminthiasis

- Blocked stomach
- Stomach discomfort
- Nausea and reduced Vitamin A absorption
- Loss of appetite
- Reduced growth
- Anaemia
- Reduced school performance

Prevention measures

- Always wash hands with soap before handling or eating food and after eating food.
- Always wash hands with soap after using the toilet
- Always wash fruits and vegetables thoroughly with soap before eating
- Avoid eating food that has been unprotected from flies
- Avoid drinking dirty water
- Always use toilets when urinating and defecating and avoid using the defecating in the bush or the field
- Keeping finger nails short
- Seek medical treatment when infected worms

CAUSES OF MALARIA

Bites by female mosquitoes

Signs and symptoms of malaria

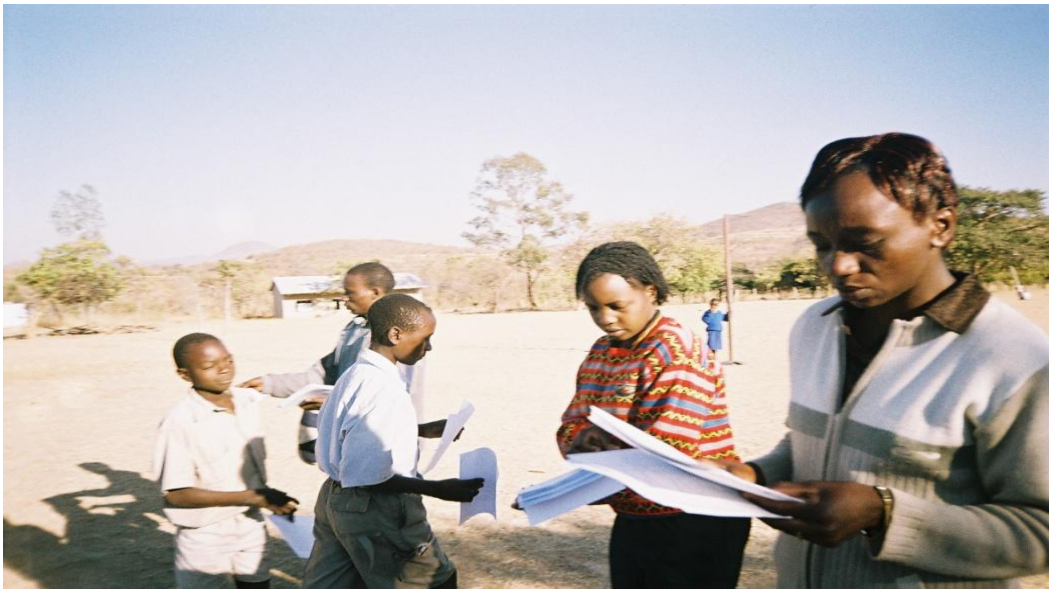
- Fever
- Severe headache
- Joints pains and general body weakness
- Nausea and vomiting
- Anaemia
- Flue like cough

Best measures to prevent malaria

- Always sleep under a treated mosquito net
- Spray mosquito repellents
- Wear long robes at night
- Spray indoors to kill resting mosquitoes
- Fill all open holes that can act as breeding places for mosquitoes
- When you experience symptoms of malaria promptly visit the clinic for treatment.

APPENDEX C: PICTURES OF ACTIVITIES UNDERTAKEN DURING THE STUDY

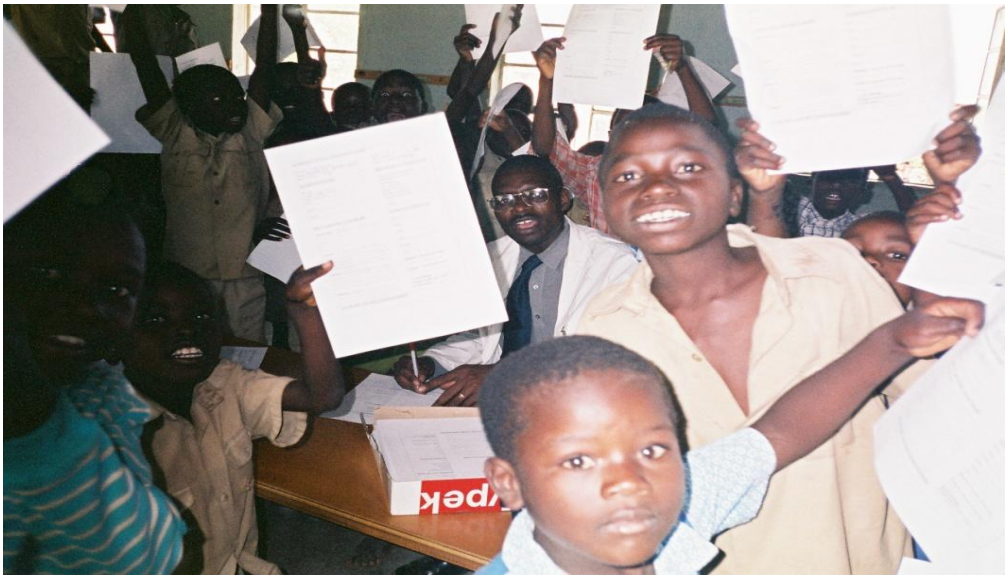
School health education was another component of the school based parasite control programme. The PI explains bilharzia life cycle to school children in presence of school head and teaching staff



Distribution of heath education leaflets about causes and best ways to control schistosomiasis, malaria and Soil transmitted helminthiasis to primary school children

Children were asked to read, share with family members and friends health education material on leaflets material about causes and best ways to prevent schistosomiasis, soil transmitted helminthiasis and malaria

School heads were left with health education flip charts for continuous health education in classes by teachers at their spare time



Songs promoting school health were also consolidated in school health activities. The project Investigator (PI) **N. Midzi** pictured centre singing together with primary school children.

Door to do home visits following up participants who failed to come to school

Door to door home visits following missing participants made this programme a success: Pictured is the PI explaining to parents why the child who enrolled into the study had to be successfully followed up at each follow up survey.

APPENDIX D: PAPERS PUBLISHED FROM THIS PhD WORK

- The burden of polyparasitism among primary schoolchildren in rural and farming areas in Zimbabwe. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* 2008, 102: 1039-1045

- Consequences of polyparasitism on anaemia among primary schoolchildren in Zimbabwe. *Acta Tropica.* 2010, 115: 103-111

- Praziquantel treatment against *Schistosoma haematobium* infection among primary school children in Zimbabwe. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2008. 102: 759-766

- Efficacy of integrated school based de-worming and prompt malaria treatment on helminths-Plasmodium falciparum co-infections: A 33 months follow up study. *BMC International Health and Human Rights* 2011, **11**:9.

- Knowledge Attitudes and Practices of grade three primary school children in relation to schistosomiasis, soil transmitted helminthiasis and malaria in Zimbabwe. BMC Infectious Diseases 2011, **11**: 169 doi: 10.1186/1471-2334-11-169.

APPENDIX E: APPROVAL LETTER FROM THE MEDICAL RESEARCH COUNCIL OF ZIMBABWE FOR THE PhD STUDY

APPENDIX F: APPROVAL LETTER FROM THE MEDICAL RESEARCH COUNCIL OF ZIMBABWE FOR THE NATIONAL SCHISTOSOMIASIS AND STH CONTROL PROGRAMME