The Prevalence and Impact of the Co-morbidity of Scabies and Other Neglected Tropical Diseases in Two Countries in the Asia-Pacific Region

Funafuti Atoll, Tuvalu

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Declaration on Ethics

The research presented and reported in this thesis was conducted within the guidelines for research ethics outlined in the *National Statement on Ethics Conduct in Research Involving Human* (1999), the *Joint NHMRC/AVCC Statement and Guidelines on Research Practice* (1997), the *James Cook University Policy on Experimentation Ethics. Standard Practices and Guidelines* (2001), and the *James Cook University Statement on Research Practice* (2001). The proposed research methodology received clearance from the James Cook University Experimentation Ethics Review Committee (**H2374**).

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Name Date

Statement of the Contribution of Others

The research included in this document was accomplished through collaboration with many individuals, agencies and organizations. I wish to acknowledge the contributions of the following for their invaluable input and technical support on the research projects described in this document.

From James Cook University

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Thank you and Merci!!

List of Abbreviations

µL	Micro litre
^{0}C	Degrees Celsius
AIDS	Acquired Immunodeficiency Syndrome
BMI	Body Mass Index
CHC	Community Health Centre
CSDH	Commission on Social Determinants of Health
DALYs	Disability-adjusted life years
DEC	Diethlycarbamazine
G	Gram
GAS	Group A Streptococci
GI	Gastrointestinal Illness
GN	Glomerulonephritis
GNP	Gross National Product
GPELF	Global Programme to Eliminate Lymphatic Filariasis
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
HSS	Health System Strengthening
ICT	Immunochromatogrophy Card Test
JCU	James Cook University
L	Litre
LF	Lymphatic Filariasis
MDA	Mass Drug Administration
MDG	Millennium Development Goals
Mg	Milligrams
mL	Millilitre
MoH	Ministry of Health

N	Sample size
NGO	Non-Governmental Organization
NTD	Neglected Tropical Diseases
NZ	New Zealand
PacELF	Pacific Programme to Eliminate Lymphatic Filariasis
PICTs	Pacific Island Countries and Territories
PNG	Papua New Guinea
$ppKM^2$	Persons per Square Metre
PSD	Parasitic Skin Diseases
PSGN	Post-streptococcal Glomerulonephritis
RHD	Rheumatic Heart Disease
RHF	Rheumatic Heart Fever
RR	Relative Risk
SAF	Sodium Acetate Formaldehyde
SD	Standard Deviation
SDH	Social Determinants of Health
SPHTMRS	School of Public Health, Tropical Medicine and Rehabilitation Sciences
STH	Soil Transmitted Helminths
TB	Tuberculosis
TTF	Tuvalu Trust Fund
WHO	World Health Organization

Abstract

The Prevalence and Impact of the Co-morbidity of Skin Infections and Other Neglected Tropical Diseases in the Asia- Pacific Region

Many people living in tropical settings in the developing world are burdened with neglected infectious diseases which remain unaddressed by the health sector. This study conducted baseline and follow-up surveys on a cohort of 900 children of Tuvalu to determine the prevalence and scope of skin infections and intestinal parasites; as well as cross-sectional survey of multiple sites in Timor-Leste.

Results indicated a high prevalence of infectious disease, especially skin infections in both countries with many participants presenting with multiple infections. Scabies and scabies co-infection with secondary bacterial or fungal diseases were the most common presentations in both populations. Intestinal parasites were present in 67% of the children surveyed in Tuvalu where one third of this cohort also had anaemia and abnormal urine results.

Overall these communities show a high burden of co-morbidity, the impact of which is unknown. However, the high proportion of multiple infectious diseases along with the clinical evidence suggests a negative health impact on these populations, which could benefit from multiple interventions in an integrated community-bases disease control programme.

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Chapter 1

Introduction to the Thesis

Structure of the Thesis:

The Doctor of Public Health degree is a professional doctoral degree and differs from the "traditional" doctoral thesis, as it is comprised of several components in order to demonstrate competencies in the broad discipline that is public health. This structure of this thesis is also non-traditional as this document is a collection of work in the area of public health with each chapter presented as a stand-alone item in whole or in part has been used in the production of a report, a project, or is being prepared for publication. Each of the chapters is therefore presented with its own introduction, methods section, results section, and discussion, and specific references for each chapter are provided at the end of each chapter, and may be duplicated in other chapters.

Content of the Thesis:

This thesis is a collection of original work carried out by me from 2005-2008 in Tuvalu and Timor-Leste. Reflected in this document is my personal interest in infectious disease surveillance, especially of skin infections. Through discussions with supervisors and collaborators the content has evolved to include intestinal parasites and throughout this process I realised that my research was framed within the framework of a particular group of diseases now referred to as the Neglected Tropical Diseases (NTD).

During my research I came to realise the broad scope that is public health also includes the emergence of life-style related chronic disease which are compounding the long-standing health issues posed by infectious diseases in developing countries in the tropical regions of Asia and the Western Pacific. While each chapter is an individual item this thesis is the collection of research with the common theme of the co-morbidity of NTD in two developing nations in the tropics.

The large-scale studies undertaken during my research required several collaborators and helpers all whom have contributed to this collection of work. I have included only material in this thesis which satisfies the following conditions:

1. I was personally involved in the study design.
2. I was directly involved in the collection of the data and samples.
3. I was directly involved in the data analysis
4. I was directly involved in preparing findings for publication. In most publications which have resulted, or will result from this thesis I have been, or will be first or corresponding author.

Readers may find that the writing style and vocabulary somewhat different from traditional "medical-scientific" publications due to the fact that this document is in essence a public health policy document, the content and context of which is supported by clinical evidence obtained from population-based surveys. It is my aim that readers view this document in the same light as the discipline of public health itself; broad in scope, multifaceted, and aiming to provide evidence to guide programming and interventions to improve the lives of entire populations.

Chapter 1 introduces the concept of multiple pathogens in tropical settings and the potential long and short-term health issues related to infection with one, or the co-morbidity of multiple diseases. This chapter also explains the social and economic factors which influence the spread of these diseases and how many diseases remain unaddressed by the health care sector due to lack of resources and other competing issues in resource-poor settings. The WHO estimates that these ignored diseases affect over 1billion people world-wide and are found in conditions of poverty, "neglected diseases of neglected populations"(WHO, 2007c). Collectively this group of up to 36 diseases are referred to as the Neglected Tropical Diseases (NTD), and WHO and other agencies are now pledging to address these pathogens through various programmes.

Chapters 2&3 are the baseline and follow-up surveys for intestinal parasites and skin diseases conducted in Tuvalu. These were the first comprehensive surveys of this kind which captured demographic, morphometric, and clinical variables (Hb, urine and stool) data from the child population of the main atoll of Funafuti in the Pacific Island nation of Tuvalu.

Chapter 4 is the first community-based survey of skin infections in Timor-Leste in over 30 years. This cross-sectional survey sampled from 4 of the country's 13 districts and also included urine sampling as a screening tool for possible kidney dysfunction related to bacterial pyoderma.

Chapter 5 provides an in-depth discussion on the epidemiology and importance of scabies in the public health context. This chapter outlines the inherent public health concerns related to the widely distributed parasite, *scarcoptes scabiei*, and the potential short and long-term health sequelae associated with this parasite. This chapter also explores the epidemiological and environmental health links between scabies and associated infectious diseases and their context within developing nations in the tropics.

Chapter 6 outlines recommendations to address the clinical and public health issues raised in this document. Again, this chapter is written within the framework of public health and acknowledges the multifaceted environmental and socioeconomic factors which contribute to the propagations of this disease. Hence, this chapter contains recommendations designed to address both treatment and prevention through the adoption of polices which aim to strengthen health systems and services, including public and environmental health infrastructure; to address both infectious diseases and the factors which their facilitate transmission.

Why Skin Infections?

Evidence shows that skin infections are an enormous health burden and are one of the most common reasons for presentation to health care facilities in developing nations (Currie and Carapetis, 2000; Mahe, 2001; Chimelli *et al.*, 2003; Mahe and Fanello, 2003; Shears, 2007). A review of the medical literature, conducted by WHO, supports the assertion that certain skin diseases are a commonly underestimated and growing health problem in developing countries. The most common conditions referred to in the review were pyoderma, ectoparasitoses, superficial mycoses, viral disorders, and dermatitis (WHO, 2005c).

It has been estimated that the rate of pyoderma in children can range from 10-90% in community and health care settings under conditions of poverty (Mahe and Fanello, 2003; Feldmeier *et al.*, 2005; Thomas *et al.*, 2005; WHO, 2005c). The WHO has declared that skin infections, including scabies are a major health concern in the Western Pacific Region (WHO, 2005b). Data from 18 bacteriological studies suggested group A streptococcal bacteria (GAS) remains the main etiological agent of pyoderma (either primary or secondary to scabies) in many tropical developing countries (Carapetis *et al.*, 2005; WHO, 2005c).

Group A streptococcal disease is a particular concern due to the risk associated with post-streptococcal glomerulonephritis (PSGN) and rheumatic heart fever (RHF), which can result in severe morbidity and death (Carapetis *et al.*, 1999; WHO, 2005c; National Heart Foundation, 2008). Infection with GAS can further lead to chronic cardiac and renal disease requiring significant health care resources and reducing the quality and often length of life for affected individuals.

Bacterial pyoderma is also closely related to incidence of the ectoparasite scabies (*scarcoptes scabiei*) as it is thought that the scratching related to scabies infection allows for bacterial colonization through micro-abrasions in the skin. Indicator data from the WHO databank indicates a high rate of scabies in some Pacific Island Countries and Territories (PICTs), and scabies is indicated as one of the top five reasons for presentations to health care facilities in Vanuatu, the Marshall Islands (WHO, 2008e).

Despite the high frequency of particular skin diseases in developing countries, they are often not regarded as a significant health problem which would benefit from a population based health intervention. Except for leprosy, this group of diseases are largely ignored by health care systems due to the incorrect assumption that skin diseases are a benign, non-threatening minor nuisance that do not merit measures which may appear out of proportion to the health priority. However, skin infections should be seen as diseases of poverty and inequity, as the three main factors associated with a high prevalence and incidence of common skin diseases in developing areas are: a low level of hygiene (including difficulties in access to water); climatic factors; and overcrowding (WHO, 2005c). Children and women bear the highest burden of infection.

Due to the above factors common skin conditions (scabies, pyoderma, and fungal infections) need to be addressed in population-based public health programmes such as leprosy, tuberculosis, or soil transmitted helminth (STH). Skin infections have been shown to be diseases of poverty, to be easily treated or prevented, and are currently ignored by the health care system, hence, they meet the criteria of neglected tropical diseases (NTD) and should be included into this group and addressed within the WHO framework for this category of diseases.

There are limited data on skin infections and their impact on affected populations, especially in the developing world where they are most prevalent. The body of work in this thesis was undertaken with the objective of assessing the prevalence and impact of skin conditions, (and other relevant co-morbidities) which has not been attempted; and to use the surveillance information to guide evidence-based interventions in affected communities.

Chapter 1

Addressing multiple pathogens in tropical settings

1.1 Introduction to the tropical environment

Tropical regions are unique physical and social environments due to their climate and geography, which support a wider range of flora and fauna than colder regions. Islands in tropical climates are further distinguished by their closed ecosystem. In this setting, infectious pathogens (some of which are unique to tropical environments) flourish in the warm and humid conditions (Ohta, 2006). Another major contribution to disease in the tropics is insects, many of which only exist in tropical and subtropical environments, and which serve as vectors for several pathogens. Social and cultural practices in tropical environments also play a role in disease dynamics. By nature, populations in these settings spend more time out of doors and have increased intimate interaction with land (soil) and marine environments. Tropical areas contain pathogens that are ubiquitous in all populations but are more prevalent in these areas due to the social and environmental conditions, in addition to pathogens that are exclusively endemic to these settings – hence the broad scope of infectious disease within tropical environments.

However, global trends indicate that most countries are experiencing an epidemiological transition as the burden of disease shifts from communicable disease to non-communicable disease. Infectious diseases are still prevalent and relevant, and are seen as an 'unfinished portfolio' by the World Health Organization (WHO) (WHO, 2008a; PAHO, 2009), but are now coexisting with increasing rates of lifestyle-related, non-communicable diseases, including obesity, cardiovascular disease, hypertension and diabetes (Lippe *et al.*, 2007; Misra and Khurana, 2008; Hossain *et al.*, 2009).

This shift in health epidemiology creates a complex and dynamic situation where multiple disease pathogens and other conditions overlap, with the potential to cause significant co-morbidity. This combination also poses a significant challenge for health-care systems in already overburdened settings with limited resources.

Social and economic factors strongly influence the dynamics of infectious diseases by creating and sustaining an environment that allows for optimal propagation and transmission. The majority of people living in tropical regions (including the Pacific region) live in low- to middle-income countries (Hotez *et al.*, 2007a) where WHO estimates that more than one billion people live in poverty and are at risk for infection with tropical illnesses (WHO, 2007c). Poverty has now been recognised as one of the most important determinants of ill health (Leon and Watt, 2001; Gupta and Kumar, 2007) and arguably the most influential factor in the propagation of infectious diseases (Folch *et al.*, 2003; Ezzati *et al.*, 2004; Tausig *et al.*, 2006).

At the national and regional levels, the socioeconomic status of nations impacts on health-care infrastructure, availability, quality and accessibility, and the availability and efficacy of public health programmes and interventions (Campbell and Campbell, 2007; Shears, 2007; Yusuf *et al.*, 2007). In their attempt to generate economic growth and increase industry and employment, resource-poor nations are likely to consent to environmental policies and practices that can facilitate disease transmission and impair interventions. Examples include the building of dams and canals, logging and deforestation, the placement of settlements near areas of disease exposure, and mining – just to name a few.

At the individual level, poverty impacts on autonomy through decreased knowledge and through socioeconomic barriers. These can impair an individual's ability to understand the dynamics of infectious diseases, identify risk factors and behaviours, or obtain health care or other services when required. Low socioeconomic status can further contribute to poor health status through poor nutrition, overcrowding, limited access to potable water and sanitation facilities, and decreased access to health care and other related services (Campbell and Campbell, 2007; Gupta and Kumar, 2007). Individuals and communities living in poverty may not have control over their own circumstances and hence engage in behaviours, activities and employment for survival that are detrimental to their health.

1.2 Spatial overlapping of multiple common infectious pathogens in the Pacific

As indicated in the previous section, there is a wide range of viral, bacterial and parasitic pathogens that thrive in the warm, moist conditions of the tropical environment. Under the aforementioned conditions of climate and poverty, the emergence and recrudescence of infectious disease continues in the tropical setting. Although by no means comprehensive, the following is a list of categories of unaddressed or under-addressed diseases of interest that are endemic to most of the Western Pacific region and to parts of Southeast Asia.

1.2.1 Vector-borne diseases

This group of pathogens are transmitted from one host to another via an insect acting as a transport intermediary (Haymann, 2004). Malaria is the most well known of this group of diseases. Currently, malaria is present in only a few Melanesian countries in the Pacific, but it is extensively endemic in Southeast Asia. Other vector-borne diseases, such as dengue fever and lymphatic filariasis, are more widely endemic in Pacific Island countries and territories (PICTs). Currently, dengue and dengue haemorrhagic fever are a growing problem in the region due to rapid urbanisation and poor standards of housing (WHO, 2008c).

Lymphatic filariasis (LF) is a mosquito-borne parasitic disease. The global burden of LF is estimated to be around 120 million. It is present in 83 countries in the tropics and subtropics, including 15 countries in the Pacific region (Ottesen, 2006; Hotez *et al.*, 2008; Ottesen *et al.*, 2008). LF has a very wide clinical spectrum. Many cases have few or no overt symptoms but still suffer from covert lymphatic damage and renal disease (Melrose, 2002). Sporadic acute attacks of fever, lymphadenitis and lymphangitis, and the inflammation of the scrotal contents in males, are common in infected people and can cause the sufferer to be absent from school or work for several days. The most severe manifestations of LF are elephantiasis – a chronic disfiguration resulting from swelling of limbs, genitalia or breast – and hydrocele. These chronic manifestations can cause immense suffering, ostracism, psychosocial dislocation, marital relationship breakdown, and economic hardship (Dreyer *et al.*, 2002; Perera *et al.*, 2007; Weissharr *et al.*, 2008; Pearson *et al.*, 2009).

The cumulative effect of these acute attacks can have a devastating socioeconomic effect on communities (Rajan, 2005), and hence WHO has classified LF as the second-most-common cause of long-term disability after mental illness. It is estimated that LF also causes the loss of five million disability-adjusted life years (DALYs) every year (Ohta, 2006; Mathers *et al.*, 2007; Hotez *et al.*, 2008). Like all nematode infections, LF commonly causes varying degrees of immunosuppression that can lead to increased susceptibility to other diseases, such as TB and HIV, and reduce the efficacy of vaccination (Melrose, 2002; Borkow and Bentwich, 2008) .

It is now recognised that the progression from asymptomatic disease to early reversible lymphoedema and elephantiasis is due to a complex, poorly understood immunological interaction between the human host and the parasite (Melrose, 2002) and, very importantly, secondary bacterial and fungal infections. Hygiene measures (to ameliorate acute filarial attacks), together with mild exercise and limb elevation, slow and may prevent progression of disease (Dreyer *et al.*, 2002; Shenoy, 2002; McPherson, 2003; Shenoy, 2008).

In 1997, the World Assembly passed a resolution calling for the elimination of LF as a public health problem by the year 2020. Shortly thereafter, the Global Programme to Eliminate LF (GPELF) was devised by WHO in partnership with a number of corporate and academic bodies. The Pacific Programme to Eliminate LF (PacELF) commenced in 1999 (Ichimori *et al.*, 2007). Merck, the manufacturer of Mectizan®, donated the medications for programme usage (Ottesen *et al.*, 2008), assisting the elimination programme in community-wide, mass drug administration (MDA) with a combination of albendazole and diethlycarbamazine (Ottesen, 2006).

GPELF has been successful in its goal to reduce the global burden of LF. More than 1.9 billion treatments have been given to individuals in 48 out of the 83 endemic countries for LF. It is further estimated that 9.5 million people have been prevented from developing overt symptoms of the disease, a saving of 32 million DALYs (Ottesen *et al.*, 2008). In the Pacific region significant progress has been made, with all but two of the LF-endemic countries having an MDA programme. The MDA programme has be successful in the Western Pacific Region. Most Pacific nations have completed five rounds of MDA and the prevalence of LF is nearing the elimination target of <1%. One of the major concerns in the region is that Papua New Guinea (where the prevalence of LF has been found to exceed 80% in some areas) (Melrose *et al.*, 2000), has only completed two rounds of MDA in a few localised areas, and has not

implemented a national programme (Ichimori *et al.*, 2007). However, there has been a reduction in prevalence of LF in the Miisima Province in PNG(Melrose, 2007).

1.2.2 Soil-transmitted helminths

Soil-transmitted helminths (STHs) are intestinal nematodes that require warm temperatures and soil to complete their life cycle. Most STH infection follows the faecal-oral route of transmission: eggs or larvae arrive in the environment via faeces (Bethony *et al.*, 2006; Ezeamama *et al.*, 2008), and human infection results from ingestion of eggs from contaminated food, water or inadequate hand-washing, or from heat-seeking larvae that burrow into the skin of the host (Heymann, 2004).

Without treatment and an improvement in sanitary conditions and hygiene practices, infection with these pathogens is maintained (Heymann, 2004; Thomas *et al.*, 2005; Bethony *et al.*, 2006). Community infection is maintained through environmental contamination resulting from constant exposure to faeces contaminated with STH eggs or larvae, ensuring constant re-infection. STHs are therefore considered diseases of poverty as they thrive in settings of overcrowding, poor sanitation and inadequate hygiene.

Soil-transmitted helminths of public and clinical health importance are *Necator americanus* and *Ancylostoma duoduale* (hookworms), *Trichuris trichiura* (whipworm) and *Ascaris lumbricoides* (large roundworm), and *Strongyloides stercoralis* (Bethony *et al.*, 2006; Hotez *et al.*, 2008). Long considered to be a ‘fact of life’ for people living in the least developed countries, there is now much evidence that these parasites are an important cause of morbidity and mortality, especially in children and pregnant women. The number of people infected globally is staggering: 807 million have ascariasis, 604 million have trichuriasis and 576 million have hookworm – and these are probably conservative estimates (Hotez *et al.*, 2008) – with a loss of 300 million DALYs (Ohta, 2006).

The major burden and subsequent morbidity of STHs have the greatest impact on children. Childhood infection with STHs has been shown to result in malnutrition, growth retardation and stunting, impeded physical and cognitive development, and anaemia (Stephanson *et al.*, 1990; Hall, 1993; Harms and Feldmeier, 2002; Bethony *et al.*, 2006; Hall *et al.*, 2008). Iron-deficiency anaemia has traditionally been associated with hookworm infection, but the literature demonstrates that the other three common species also contribute to anaemia (Ramdath *et al.*, 1995; Stephanson *et al.*, 2000; Bethony *et al.*, 2006).

Current research also suggests that anaemia is especially problematic where there is a high prevalence of multiple STHs, a condition known as polyparasitism (Ezeamama *et al.*, 2005; Ezeamama *et al.*, 2008). Research has established that STH infections decrease cognitive ability and performance and increase school absenteeism. Findings also indicate that de-worming school children can result in improvements in school performance and learning ability (Simeon *et al.*, 1995; Gardner *et al.*, 1996; Raj *et al.*, 1997; Sakti *et al.*, 1999; Di Silva, 2003; Sur *et al.*, 2005; Jardim-Botelho *et al.*, 2008).

STH-associated (especially hookworm-related) anaemia is an important problem in pregnant women. It has been estimated that between a third and a quarter of all pregnant women living in sub-Saharan Africa are infected with hookworm and at risk from hookworm-related anaemia. It is speculated that these figures can be applied across many parts of the developing world (Ayoya *et al.*, 2006; Bethony *et al.*, 2006; Hotez *et al.*, 2008; Ndyomugyenyi *et al.*, 2008). Anaemia is especially dangerous to women of child-bearing age, as those who experience significant blood loss during and after childbirth are at greater risk of postpartum complications if their iron stores are already depleted (Kayle *et al.*, 2008).

STH infections are also associated with a range of other conditions. The migration of *A. lumbricoides* and hookworm larvae through the lungs can cause Loeffler's syndrome and asthma. Adult *A. lumbricoides* can also migrate into the bile ducts, resulting in bilary obstruction, and a large bolus of worms can result in bowel obstruction or perforation. Heavy infection (>10,000 eggs/grams of faeces) (Huges *et al.*, 2004) with *T. trichura* is known to cause bleeding from the rectal mucosa and occasionally results in rectal prolapse (Khuroo, 1996; Stephanson *et al.*, 2000; Bethony *et al.*, 2006).

A critical aspect of helminth infection (STH and LF) is the ability of these pathogens to modulate the host's immune response against its own antigens and the antigens of other organisms (Bethony *et al.*, 2006; Hotez *et al.*, 2008). Evidence indicates that helminth infections can increase an individual's susceptibility to tuberculosis, therefore increasing the risk of severe pulmonary disease (Borkow and Bentwich, 2000).

The implications of HIV and STH co-infection are less clear, but some researchers believe that control of helminths is an essential part of the fight against HIV and AIDS (Fincham *et al.*, 2003; Borkow *et al.*, 2007; Tian and Zhou, 2008). The effects of helminth co-infection on malaria remain controversial, but recent evidence suggests that helminth infections can have an adverse effect on malaria infection through the process of immune suppression (Jackson *et al.*, 2009).

It has been proposed that parasite-induced immunosuppression also has the potential to reduce the efficacy of vaccination, leading to incomplete immunity against disease and economic loss due to vaccine inefficiency and wastage (Harms and Feldmeier, 2002; Kamal and Khalifa, 2006; Borkow and Bentwich, 2008). In response to the global burden of STHs, WHO initiated a control programme based on the de-worming of school-aged children, commencing in 2000. The programme aims to reduce both the prevalence and intensity of STH infection in children, the most affected population (WHO, 2003). Several studies have documented STH infection in PICTs (Huges *et al.*, 2004; Thomas *et al.*, 2005; Speare *et al.*, 2006), including in Tuvalu.

1.2.3 Common skin infections

Evidence shows that skin infections are an enormous health burden and among the most common reasons for presentation to health-care facilities in developing nations (Currie and Carapetis, 2000; Mahe, 2001; Chimelli *et al.*, 2003; Mahe and Fanello, 2003; Shears, 2007). It has been estimated that the rate of pyoderma in children can range from 10% to 90% in community and health-care settings under conditions of poverty (Mahe and Fanello, 2003; Feldmeier *et al.*, 2005; Thomas *et al.*, 2005; WHO, 2005c). Despite the high frequency of particular skin diseases in developing countries, they are often not regarded as a significant health problem that would benefit from a population-based health intervention.

The limited attention given to dermatological conditions results in large part from the incorrect assumption that skin diseases are benign and do not merit measures given to competing health conditions and priorities. In many countries national control measures for skin infections are non-existent, with the exception of long-established leprosy programmes in endemic areas. Skin infections should be seen as diseases of poverty and inequity, as the three main factors associated with a high prevalence and incidence of common skin diseases in developing areas are a low level of hygiene (including difficulties in access to water), climatic factors and overcrowding (WHO, 2005c). Children and women bear the highest burden of infection.

A review of the medical literature conducted by WHO supports the assertion that certain skin diseases remain underestimated but are a growing health problem in developing countries (WHO, 2005c). The most common conditions referred to in the review were pyoderma, ectoparasitoses, dermatophytes (superficial mycoses), viral disorders and dermatitis. Data from 18 bacteriological studies suggested group A streptococcal (GAS) bacteria remains the main etiological agent of pyoderma (either primary or secondary to scabies) in many tropical developing countries, followed by *Staphylococcus aureus* (Carapetis *et al.*, 2005; WHO, 2005c).

Group A streptococcal disease is a particular concern due to the risk associated with post-streptococcal glomerulonephritis (PSGN) and rheumatic heart fever (RHF), which can result in severe morbidity and death (Carapetis *et al.*, 1999; WHO, 2005c; National Heart Foundation, 2008). Infection with GAS can further lead to chronic cardiac and renal disease requiring significant health-care resources and reducing the quality and often length of life for affected individuals. It is estimated that the global burden of GAS results in over 500,000 deaths annually due to complications including PSGN, RHF and other invasive infections, with the majority of deaths due to rheumatic heart fever (WHO, 2001; National Heart Foundation, 2008).

Scabies (*Sarcoptes scabiei*), an ectoparasitic mite that burrows under the skin of mammalian hosts (Becherel *et al.*, 1999), contributes to the prevalence of bacterial pyoderma in developing countries. The parasite is found worldwide and is a disease of human and veterinary importance. Like other neglected tropical diseases, scabies is recognised as a condition of severe poverty as it spreads rapidly in conditions of overcrowding and decreased standards of hygiene (Becherel *et al.*, 1999; Campbell and Campbell, 2007; Hafner, 2009). The disease is transmitted directly through contact with a person infected with scabies, or by fomites (objects such as bedding and clothing) that are contaminated with the mites (Flinders and De Schweinitz, 2004).

Pruritis (itching), the hallmark symptom of infection with scabies mites (Becherel *et al.*, 1999; Carapetis *et al.*, 2004; Hengge *et al.*, 2006), frequently results in abrasions of the skin due to intense scratching (Weissharr *et al.*, 2008; Hafner, 2009). These micro-breaks in the skin facilitate the colonisation of bacteria, including GAS. There are numerous epidemiological links between scabies and pyoderma, with an abundance of evidence that the two pathogens frequently coexist in conditions of poverty and a reduced standard of living (Currie and

Carapetis, 2000; Hay, 2003; Carapetis *et al.*, 2004; Heukelbach *et al.*, 2004; Walton *et al.*, 2004). Furthermore, the co-morbidity of scabies and pyoderma has been implicated in the development of renal and cardiac disease in areas where they are both hyper-endemic; the majority of this evidence derives from Australian Aboriginal communities (Carapetis, 1998; Carapetis and Currie, 1998; Carapetis *et al.*, 1999).

The literature also indicates a global trend where epidemics of post-streptococcal renal disease have been shown to follow epidemics of scabies in tropical settings (Whittle *et al.*, 1973; Thevenieau, 1981; Reid and Poon-King, 1990; Berrios *et al.*, 2004; Heukelbach *et al.*, 2004; Lawrence *et al.*, 2005). The most convincing evidence of the link between scabies, pyoderma and renal disease is observed in studies where incidence of renal damage decreased to almost zero after mass chemotherapy treatment of scabies with ivermectin (Brooks and Grace, 2002; Carapetis *et al.*, 2004; Lawrence *et al.*, 2005; CRCAH, 2006).

The role of scabies in disease progression and negative health outcomes may be larger than originally assumed. The repeated association between scabies and pyoderma suggests a synergistic interaction between the two pathogens that produces an additive effect greater than either pathogen alone. One proposed explanation is that those with an underlying scabies infection may be predisposed to becoming hyper-infected with bacteria, especially GAS, resulting in more severe disease (Bisno and Stevens, 1996; Carapetis *et al.*, 1999; Brooks and Grace, 2002; Carapetis *et al.*, 2005). Another hypothesis suggests an interaction between scabies and specific strains of group A streptococci serotype-M (beta haemolytic), which are clinically linked with PSGN (Reid and Poon-King, 1990; Goodfellow *et al.*, 1999; Berrios *et al.*, 2004). The suggested mechanism of interaction between scabies and pyoderma is poorly understood, as is the role of scabies in the pathogenesis of more severe disease; hence, the scabies mite itself cannot be excluded as the pathological agent (Hay, 2003).

Dermatophyte infections (superficial mycosis or fungal infections) may be the most prevalent infectious agents worldwide (Brasch and Hipler, 2008). These infections appear to be endemic, particularly in children in poor developing countries (Seebacher *et al.*, 2008) and especially in tropical settings, where they often represent a public health concern and are difficult to treat due to humid conditions (Chimelli *et al.*, 2003). Dermatophyte infections cause intense pruritis (itching) and consequently can result in micro-abrasions in the skin and, similar to scabies, can facilitate the colonisation of the skin by bacteria, thereby encouraging the carriage of group A streptococci in tropical environments. Parallel to scabies infection, dermatophytes can serve as the first step to the acute and long-term complications associated with GAS.

1.3 Implications of co-morbidity in resource-poor settings

As previously discussed, the endemic infectious diseases present in the Pacific region cause significant morbidity, social and economic disruption and mortality. What is recently being recognised is the potential impact of co-morbidity as a consequence of the compounding effects of multiple diseases. Although the pathology resulting from the interaction between one or more of the previously mentioned parasitic and skin diseases is not always clearly understood, the interactions between multiple pathogens may be causing greater morbidity and mortality than any of these diseases alone, at both the individual and community level. Furthermore, co-morbidity with multiple disease pathogens presents challenges to health-care services and disease-control programmes in poorer nations. The impact on the health of these communities may then be further exacerbated by nutritional issues, such as malnutrition or over-nutrition, as observed in the recent surge in chronic lifestyle diseases such as obesity and other non-communicable conditions (Misra and Khurana, 2008).

The role of poverty, and poverty-related conditions, in infectious disease is clear: overcrowding, decreased sanitation and access to clean water, substandard housing, limited resources and mal-distribution of health services (Anon., 2003; Ehrenberg and Ault, 2005; Dodd and Cassels, 2006; Gupta and Kumar, 2007) all have a role in maintaining the human reservoir and facilitating the transmission of endemic infectious diseases in the tropics. The impact of infectious disease is usually measured in morbidity and mortality, but that is only one aspect of the infectious disease burden in developing nations. Morbidity and mortality from infectious disease are high in tropical settings due to the multitude of infectious diseases and poor living conditions. Death and disability of adult and child family members can cause severe social and economic devastation and leave families (especially women and children) vulnerable if key income earners are lost. Both morbidity and mortality directly result in decreased income and resources through lost wages from employment and decreased productivity of manual labour in subsistence lifestyles.

Indirectly, illness contributes to decreased productivity by impacting education and training. Decreased attendance and performance in educational settings hinders the ability to improve the knowledge, capacity and skills of individuals and entire communities. As children bear the greatest burden of infectious disease (Global Health Council, 2009), the potential loss of human capacity through impeded education and training due to illness and death is enormous. The other indirect costs associated with infectious disease are more difficult to measure.

The social, cultural and human costs of constant illness, death and hardship are immeasurable, as is the impact on the psyche of individuals affected in these settings.

The relationship between poverty and infectious disease could be viewed as cyclical rather than just a linear cause-and-effect dynamic. Poverty creates the conditions that propagate infectious disease, but the overall burden of illness from infectious disease maintains the conditions of poverty through lost productivity, income and human potential, and therefore perpetuates the cycle of poverty and infectious disease in tropical settings. This cycle is depicted in Figure 1.1.

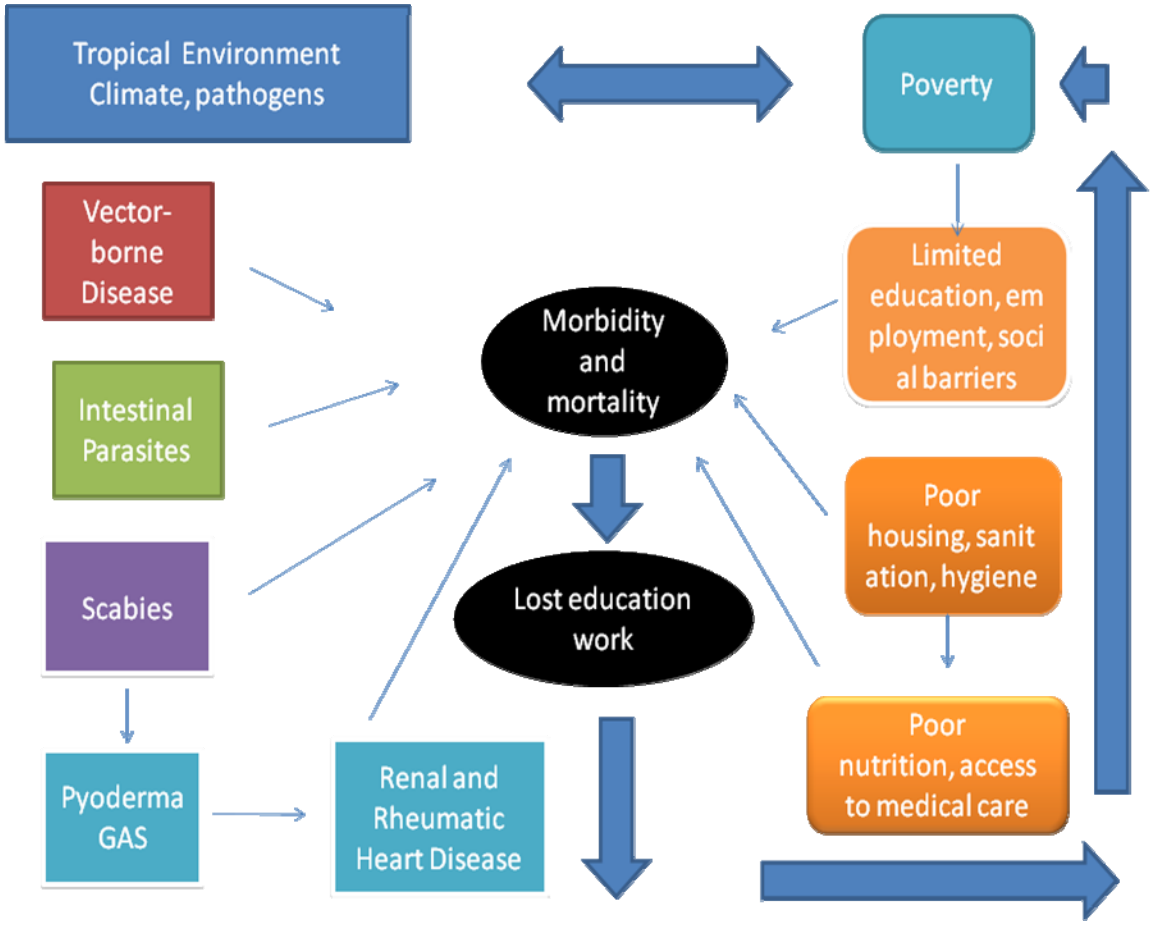

Figure 1.1: The dynamic cycle of poverty and infectious disease in tropical settings.

1.4 Traditional disease control strategies

The existing model of disease control and intervention is largely built on the ‘one disease, one programme’ principle. The majority of current programmes involve interventions or a series of interventions including, but not limited to, surveillance, epidemiology, education, detection and treatment, preventive measures, community development, and changes to policy and infrastructure. Many of these programmes are financially and resource intensive, allocating millions of dollars and employing thousands of people worldwide. The most well known are WHO and Global Fund programmes.

Historically, infectious disease control programmes developed from rudimentary surveillance and quarantine strategies and operated largely with disease-specific agendas that remained independent of one another despite medical, epidemiological and technical advances. The majority of disease control strategies exist in developing countries where the need is greatest. Often there are several disease control programmes in operation in the same area that are often run by the same agency, which runs multiple programmes and projects. Additionally, parallel programmes and projects are operated by different agencies completely independent of each other. This can, and often does, result in duplication of services and an inability to offer other essential services, which confuses the local population while consuming significant financial and human resources.

The evolution of single-disease strategies has been shaped by agencies, political and individual agendas and, ultimately, funding. Funding for interventions and programmes is almost exclusively disease-based, and frequently requires specific targeted activities and interventions. Therefore, the flexibility to include activities that are not directly related to programme mandates is limited in disease control strategies. This perpetuates the cycle of single-focus strategies by limiting the scope of interventions and activities that organisations are willing to undertake in order to ensure continued funding. Hence, the whole process is driven by form rather than function.

It should be noted that any intervention or project aimed at reducing the morbidity and mortality of any one disease or condition has the potential to have a positive impact on a population by improving the conditions and lives of communities. This is especially true of community development projects that aim to increase infrastructure, knowledge, capacity, economic development or environmental sustainability. All of these can result in improved environmental conditions which favour disease reduction.

There are a few examples of programmes that result in secondary benefits in addition to their main objectives. MDA programmes can have the additional benefit of treating secondary conditions and supporting other ongoing programmes. Usually these additional advantages are a sideline to the principal disease control objective; the fact remains that the majority of disease control strategies normally do not purposely incorporate multi-disease control initiatives into their programme design and implementation.

The WHO elimination programme for lymphatic filariasis uses a combination of DEC and albendazole in most parts of the world, including the Pacific. In Africa, a combination of ivermectin and albendazole is used because DEC can cause severe adverse reactions in people who are co-infected with *Loa loa* or onchocerciasis. Albendazole and ivermectin are also active against intestinal helminths, and the former is widely used in the WHO programme to de-worm school-aged children (PacELF, 2008). Ivermectin is also very effective against scabies (Brockerie *et al.*, 2000; Lawrence *et al.*, 2005; Merck, 2007).

The existence of parasitic and skin pathogens is again a complex interaction of environmental and social factors that facilitate the transmission of each disease and further amplify the effects of their interactions. This complex combination of factors requires disease control and outbreak management measures to be dynamic and adaptive to particular tropical island environments in order to be effective. Thus it has recently been recognised that a new model of infectious disease control is required that aims to improve the overall health of communities while making the most of increasingly limited resources in developing nations in the tropics.

1.5 Paradigm shift to integrated disease control strategies

1.5.1 Healthy Islands

The need for an adaptive and evolving approach to health, especially in island environments, is a theme that developed from the global health-related conferences held during the early 1990s. The 'Healthy Islands' concept was recognised by WHO and, as part of its Healthy Settings and Environments initiative, developed and introduced by the Western Pacific Regional Office of WHO during the meeting of Pacific health ministers in Fiji in 1995 (WHO, 2006a). The concept was designed to be flexible and not based on specific region-wide strategies but rather a conceptual framework for achieving an overall environment of health across all communities that make up Pacific nations. The framework addresses the integral relationship between health and the environment, and the sustainability of an age of rapid change and economic development in developing nations (Galea *et al.*, 2000).

As outlined in the Yanuca Island Declaration during the 1995 meeting in Fiji (WHO, 1995b), healthy islands are places where:

- children are nurtured in body and mind;
- environments invite learning and leisure;
- people work and age with dignity; and
- ecological balance is a source of pride.

The Healthy Islands concept aims to address broader concepts of health and wellness by building on the fundamental principles outlined in the Ottawa Charter, which focus on 'not merely the absence of disease' but the promotion and protection of health and the recognition that wellness is a combination of physical, mental, spiritual and environmental factors (WHO, 1997a). The approach embraces these concepts and encourages initiatives, projects and policies that move the entire community towards an increased state of wellbeing within their island context.

Further initiatives in the Western Pacific region are finally addressing the interplay of health issues and approaching them more strategically. The WHO Regional Office for the Western Pacific has developed four themes and 17 focuses in its action plan to impact and improve people's lives in the region. The first two themes outlined in the regional plan for action, 'Combating Communicable Disease' and 'Building Healthy Communities and Populations' (WHO, 1997a; WHO, 1997b), recognise the need to improve health through addressing infectious disease.

These two major themes address the burden of communicable diseases and aim to achieve improvement in health through the overall WHO 'settings approach', of which Healthy Islands is recognised as one settings that can be improved through integration methods and a strong focus on community action. Although there are many facets of health under this framework, reducing the overall burden of disease in developing nations would greatly improve the quality of life for individuals and have a positive cascade effect on the entire population in all areas of life, from physical health to economic and spiritual growth. Further suggestion of an integrated approach to controlling communicable disease in the Pacific is demonstrated by the recommendation of addressing multiple diseases, malaria and other vector-borne diseases though combined surveillance and response initiatives, referred to as 'cross-cutting' in the infectious disease framework (WHO, 1997a).

1.5.2 Millennium Development Goals

Arguably the greatest impact on infectious disease and other health-related issues in developing nations will result from the development of and commitment to the Millennium Development Goals (MDGs), which were introduced in 2000. This historic commitment to eradicate extreme poverty and improve the health and welfare of the world's poorest nations by 2015 has the potential to reduce the economic, social, educational and environmental conditions and barriers that propagate the existence and transmission of multiple infectious diseases and other contributing health problems.

The programme's stated goals are:

Goal 1: Eradicate extreme poverty and hunger

Goal 2: Achieve universal primary education

Goal 3: Promote gender equality and empower women

Goal 4: Reduce child mortality

Goal 5: Improve maternal health

Goal 6: Combat HIV/AIDS, malaria and other diseases

Goal 7: Ensure environmental sustainability

Goal 8: Develop a partnership for development

By acknowledging that poverty has a severe impact on health in poorer developing nations, and that improved health is essential to the global agenda of reducing poverty, the MDGs are the first global policy and strategy to address the interaction of a multitude of issues that contribute to the cycle of disease and poverty by allowing one to maintain the other. In regards to the relationship between the MDGs, development and health, five key opportunities and challenges have been identified (Dodd and Cassels, 2006).

These are, first, that the goals provide a common set of priorities on how to tackle poverty. Second, it is acknowledged that health is at the heart of the MDGs. Third, the MDGs are measureable and hence progress can be measured against set targets. Fourth, it is possible to calculate the cost associated with achieving the objectives and hence highlight the funding gaps that impede resource-poor countries. Fifth and finally, the final goal calls for a global partnership and recognises that rich countries must take action if poor countries are to achieve goals in order to move towards global security and prosperity (Dodd and Cassels, 2006).

The key challenges in addressing the existing barriers to improved health, including reducing the global burden of infectious disease, are:

1. To strengthen health systems
2. To ensure that health is prioritised within overall development and economic policies
3. To develop health strategies that respond to the diverse and evolving needs of countries
4. To mobilise more resources for health in poor countries
5. To improve the quality of health data in order to assess and measure progress

In addition to clearly stating the disease–poverty association, the MDGs go beyond traditional disease control strategies by focusing on the purposeful need to address health as a broader concept, and the requirement for policies and actions to address this with overarching policies and plans. Thus, in essence the MDGs can be seen to be advocating for infrastructure and resources, which provide the foundation for functional health systems that crosscut all areas of disease, reflecting the global need to combat co-morbidity. Although certain diseases of priority are directly mentioned, the MDGs further respond to the issue of multiple infectious pathogens by not limiting the goals to specific diseases or other specific health issues, thus creating inherent flexibility in action plans that previously did not exist.

1.5.3 WHO commitment to eradiating neglected tropical diseases

The second most influential policy to address co-morbidity of infectious diseases in resource-poor settings is outlined in WHO's Global Plan to Combat Neglected Tropical Diseases (NTDs). Neglected tropical diseases (and zoonoses) are a collection of 14 diseases that affect an estimated one billion people, causing untold suffering and mortality, and that can be prevented, eliminated or eradicated. The 14 NTDs are Buruli ulcer, Chagas disease, cholera/epidemic diarrhoeal diseases, dengue/dengue haemorrhagic fever, dracunculiasis (guinea worm), endemic treponematoses (yaws, pinta, endemic syphilis), human African trypanosomiasis (sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, and trachoma (WHO, 2008a).

This group of diseases are deemed neglected as they affect people in the poorest countries and do not often result in epidemic emergencies, and hence are not usually subjected to routine surveillance and reporting despite the fact that they are among the most common infections worldwide and frequently coexist in certain environments. For these reasons, NTDs have a devastating effect and are an enormous obstacle to human and economic development in already-impoverished nations. There is even a growing body of evidence suggesting that control of this group of diseases could directly contribute to the achievement of several of the MDGs by reducing the number of working and educational days lost to illness, reducing the number of health-care dollars for visits and hospital stays, and reducing maternal, infant and child mortality (WHO, 2007c).

The Global Plan to Combat NTD echoes the MDG recognition of the link between poverty and disease and expands upon Goal 6, 'Combat HIV/AIDS, malaria and other diseases', by identifying the severe burden of illness in impoverished nations caused by these neglected diseases, alone and in combination. WHO has placed the control of these infections on the international agenda, despite the fact that they (and many others) have been overshadowed by higher-profile diseases such as 'the big three' – malaria, tuberculosis and HIV – which are the focus of the Gates Global Fund's activities.

The initiative also goes one step beyond by advocating for a comprehensive and innovative strategy to address NTDs, which includes the following principles: a multi-pronged approach; a focus on populations rather than specific diseases; and a multi-disease, inter-sectoral and inter-programmatic approach (WHO, 2007c). The progression of this and the above-mentioned strategies represents a clear departure from many existing disease control efforts and indicates a strong commitment to the integration of operational infectious disease control.

1.6 Current state of integrated disease control programmes

The first influential policy papers highlighting the hidden global burden of neglected tropical diseases, and the need to address these diseases in an integrated and coordinated manner, were published between 2004 and 2006 (Molyneux, 2004; Molyneux and Nantulya, 2004; Fenwick *et al.*, 2005; Molyneux *et al.*, 2005; Hotez *et al.*, 2006a; Hotez *et al.*, 2006b; Lammie *et al.*, 2006). Since then, evidence of a shift in public health policies towards a more comprehensive approach is demonstrated in the current trend, which favours an increasing number of integrated operational disease control strategies.

Since 2004 integrated disease control strategies have been put under way in parts of Africa (Hotez *et al.*, 2007b), Latin America and the Caribbean (Holveck *et al.*, 2007) and the Western Pacific (Urbani and Palmer, 2001), along with a commitment in 2007 from the Asian Development Bank of USD180 million to combat NTDs in Laos, Cambodia and Vietnam (Hotez *et al.*, 2007b).

Currently, the most commonly employed integrated disease control strategy is 'rapid-impact mass chemotherapy' – the mass distribution of a combination of 4–6 medications specifically targeting overlapping NTDs in targeted communities. The strategy is referred to as 'rapid-impact' because the drugs target multiple infectious diseases simultaneously and because treatment packs can be quickly distributed via community-based distribution, result in rapid improvements in community health, and can interrupt or even eliminate transmission through a rapid decrease in disease reservoirs. Furthermore, through partnership programmes and donations from pharmaceutical manufacturers it is estimated that the cost for delivering treatment packs would be 26–47% less than non-integrated strategies (Hotez *et al.*, 2006b; Hotez *et al.*, 2007a).

Early successes in integrated control have been observed in the Global Programme to Eradicate LF though the use of albendazole and diethlycarbamazine (DEC). Mass treatment with these two drugs has not only reduced the prevalence of LF but resulted in the observation of a significant decrease in the prevalence of multiple STHs in the Western Pacific region (Urbani and Palmer, 2001), and of STHs and schistosomiasis in China, Japan and Korea (Yokogawa, 1985; Seo, 1990). More recent evidence of the benefits of this model of disease control has been documented by observed decreases in both LF and STHs in India, Indonesia and Haiti (Lammie *et al.*, 2006). Further investigations in these communities have demonstrated that high-coverage mass chemotherapy leads to decreased incidence of STHs, which may be sustainable through annual treatments.

GPELF continues to be viewed as an entry point upon which to 'piggyback' integrated control measures (Molyneux and Nantulya, 2004; Gyapong, 2005; WHO, 2005d). The initial impetus was based on the ancillary benefits of ivermectin for the control of onchocerciasis in Africa, and its increased effectiveness against parasites including STHs and schistosomiasis, in addition to the original use against LF (Utzinger and Keiser, 2004; Gyapong, 2005).

More recently, the benefits of ivermectin to stop the itching caused by scabies and head lice are seen as an important strategy against morbidity and mortality, through the reduction in the prevalence of scabies and the potential to reduce the burden of illness associated with group A streptococci bacteria by reducing bacterial colonisation facilitated by scabies infection (Heukelbach *et al.*, 2004; Speare and Durrheim, 2004; Carapetis *et al.*, 2005; Lawrence *et al.*, 2005).

The actual human and financial benefits of integrated disease control programmes are as yet unquantified, and whether the political will and economic support required to expand these programmes will continue, and include the wider scope of neglected diseases, is unknown. However, the model of purposefully combined and multi-purpose disease control has enormous potential to drastically and rapidly reduce the global burden of infectious diseases where it is most needed.

1.7 Objectives of this study

Reliable, consistent and comparable information about the aetiology and impact of disease and injuries in populations, and how these are evolving, is critical to identifying and developing agendas and priorities in health systems and services. Despite the documentation that neglected tropical diseases (including parasitic and skin pathogens) are a major public health concern, the epidemiological data on these infections is generally fragmented, incomplete and inconsistent, and its reliability is questionable (Mathers *et al.*, 2007). Increased knowledge of the dynamics of infectious diseases in these specific environments will help tailor interventions to achieve control.

The overall objective of this study is to determine the prevalence, aetiology and impact of specific neglected tropical diseases (common parasitic and skin diseases) in two developing countries in the Asia-Pacific, Timor-Leste and Tuvalu, to determine if these countries would benefit from disease control strategies to address these pathogens. The study objective(s) were met by inclusion of the following:

- establishing baseline surveillance for targeted STH and skin conditions scabies, pyoderma and dermatophytosis, and leprosy and yaws in Timor-Leste;
- determining the impact of single-dose mass chemotherapy of mebendazole on reducing intestinal parasites in school-aged children; and
- providing epidemiological information for evidence-based public health control programmes for these conditions.

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Chapter 2

Baseline survey of soil-transmitted helminths and skin infections of school-aged children on Funafuti Atoll, Tuvalu

2.1 Introduction to Tuvalu

The Pacific Island nation of Tuvalu, formally known as the Ellice Islands, lies in the southwest Pacific Ocean, north of the Fiji Islands and northeast of Australia, between latitudes 5 and 11 degrees south and longitudes 176 and 180 degrees east. The nation is comprised of nine low-lying coral atolls with an area of approximately 26 square kilometres (Cannon, 2007), making it the world's fourth-smallest country. The atolls were formed from volcanic activity and the two main ones, Funafuti and Nukufetau, are extinct volcanoes. Tuvalu's nine atolls (or islands, as they are referred to locally) situated from north to south are Nanumea, Niutao, Nanumanga, Nui, Vaitupu, Nukufetau, Funafuti, Nukulaelae and Niulakita.

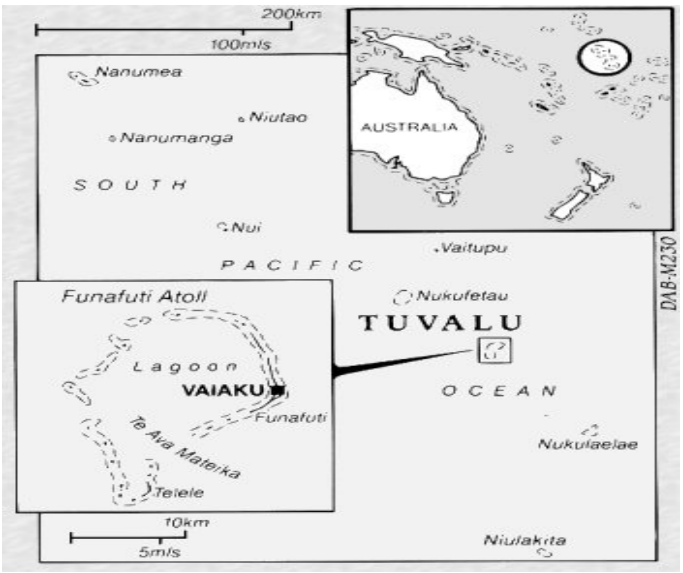

Figure 2.1: Combined map of Tuvalu (Government of Tuvalu, Central Statistics Division, 2006)

2.1.1 Land

Tuvalu has a tropical climate with an average daily temperature of 28.7°C and an average annual rainfall of 259.4 mm, creating a mostly hot and humid environment (Table 2.1). The average temperature does not fluctuate greatly throughout the year but rainfall is variable, with distinct ‘wet’ and ‘dry’ seasons. The islands are true coral atolls containing coral dust and sand; the only true soil was imported from Fiji to build a sporting field in 2003 (Conway, 2007).

Figure 2.2: Funafuti is the main island of Tuvalu.

Figure 2.2 shows the view of Funafuti Atoll when approaching the landing strip (clear line on the widest part of the island) by air. Funafuti Atoll is roughly annular, with the inhabited portion of the atoll on the right and the lagoon encircled by narrow strips of land on the left. The population of Funafuti lives in the widest portion of the island, which is roughly 800 metres across at maximum width.

The highest point in the entire country is just 4 metres above sea level, which is of great concern with global warming and rising sea levels. Experts predict that if current trends in rising sea levels continue, Tuvalu will no longer exist in 50 years as it will be completely engulfed (Roberts, 2007). The threat of their country no longer being in existence in less than one generation may make Tuvaluans (along with Maldivians) the first-ever environmental refugees (Assaf, 2006; Roberts, 2007).

Year	Annual average rainfall	Annual temperature (°C)		
		Min	Max	Annual average
2000	200.7 mm	26.0	31.1	28.6
2001	231.3 mm	25.9	31.3	28.6
2002	298.2 mm	26.2	31.5	28.9
2003	294.5 mm	26.4	30.9	28.7
2004	232.6 mm	26.1	31.6	28.8
2005	299.1 mm	26.3	31.5	28.9
Average	259.4 mm	26.2	31.1	28.7

Table 2.1: Annual rainfall and daily temperature in Tuvalu (Government of Tuvalu, 2006).

2.1.2 People

The majority of the country's 9,561 inhabitants are of Polynesian descent, with the exception of those living on the atoll of Nui, who are mostly descendants of Micronesians from the island of Kiribati, formerly the Gilbert Islands (Cannon, 2007). It is accepted that most of the ancestors of the people of Tuvalu came from neighbouring Polynesian countries, including Samoa, Tonga and Uvea (Wallis Island). Historically, there were several dialects and local languages, which can be categorised into three main language groups: the northern group of Nanumea, Niutao and Nanumanga; Nui, where the language is largely derived from the I-Kiribati language; and the central and southern group. Present-day Tuvaluans predominantly speak English and Tuvaluan, which is a Polynesian language strongly influenced by the Samoan language. Local languages or dialects are spoken on the smaller atolls, usually by older individuals, and I-Kiribati is spoken almost exclusively on Nui (Government of Tuvalu, 2006).

The country experiences dense urban population on the main atoll of Funafuti, which supports 4,492 people, almost half of the nation's population (47%) (Table 2.2). The overall population density of the nation is high, at 405.0 persons per square metre (pp km^2). This level of population density is considerably higher than that of other highly populated countries, such as China (138.7 pp km^2) and Japan (338.7 pp km^2), and significantly higher than neighbouring Pacific nations such as Kiribati (131.0 pp km^2) and Fiji (45.7 pp km^2) (United Nations, 2008) . In 2002, the national census indicated a population density on Funafuti Atoll of 1,610 pp km^2, making it one of the world's most densely populated capital cities.

The remaining 5,069 inhabitants live remotely on the outer atolls, which are accessible only by private vessels and inter-island cargo ships. Government statistics indicate that the average household population density is 6–7 persons per household (Government of Tuvalu, 2006). However, calculations based on census data indicate a variation in population density throughout the country ranging from 4.4 to 7.0 persons per household. Tuvaluans are a highly mobile population who undertake frequent travel between the outer islands and Funafuti. The data on household population density based on population averages do not reflect the actual conditions on Funafuti, where overcrowding is becoming the norm due to limited land and housing that do not accommodate the influx of the population to the small atoll.

Funafuti has eight principal villages; from north to south they are Lofeagai, Teone, Nanumasa, Fakaifou, Senala, Alapi, Vaiaku and Tekavatoetoe (Figure 2.3). The villages have both social and political significance as they are often populated by people from the outer islands and are also used as geographical boundaries for census and survey programmes. The population and habitation of each village varies. Fakaifou, Vaiaku and Alapi are located near the central hub of the atoll and have the highest population density.

Tuvalu has a high level of education and literacy. School is compulsory from ages 5-15 and has resulted in an adult (both men and women) literacy rate of 98%(Globaled, 2009).Children from all of the villages attend one of two primary schools: the government-run Nauti Primary School or the Seventh-day Adventist primary school. Preschools are more localised, and there is at least one in each village that is run either by the government or privately. The majority of older students attend the government high school located on the island of Vaitupu, and some attend the Seventh-day Adventist school located on Funafuti.

Island of enumeration	Total population			Tuvaluans			Non-Tuvaluans			House-holds	Land area (km^2)	Population density (pp km^2)	People per household (calculated from census data)
	T	M	F	T	M	F	T	M	F				
Total	9,561	4,729	4,832	9,358	4,617	4,741	203	112	91	1,568	25.63	373	6.1
Nanumea	664	305	359	661	303	358	3	2	1	128	3.87	172	5.2
Nanumanga	589	276	313	582	272	310	7	4	3	119	2.78	212	4.9
Niutao	663	314	349	652	312	340	11	2	9	143	2.53	262	4.6
Nui	548	263	285	540	262	278	8	1	7	108	2.83	194	5.1
Vaitupu	1,591	799	792	1,579	791	788	12	8	4	237	5.6	284	6.7
Nukufetau	586	286	300	582	285	297	4	1	3	118	2.99	196	5.0
Funafuti	**4,492**	**2,281**	**2,211**	**4,343**	**2,190**	**2,153**	**149**	**91**	**58**	**639**	**2.79**	**1,610**	**7.0**
Nukulaelae	393	186	207	384	183	201	9	3	6	68	1.82	216	5.8
Niulakita	35	19	16	35	19	16	0	0	0	8	0.42	83	4.4

T = total; M = males; F = females

Table 2.2: Island of enumeration by nationality and sex, number of households, land area and population density, 2002
(Government of Tuvalu, Central Statistics Division, 2002; Tuvalu Island statistics online, 2008).

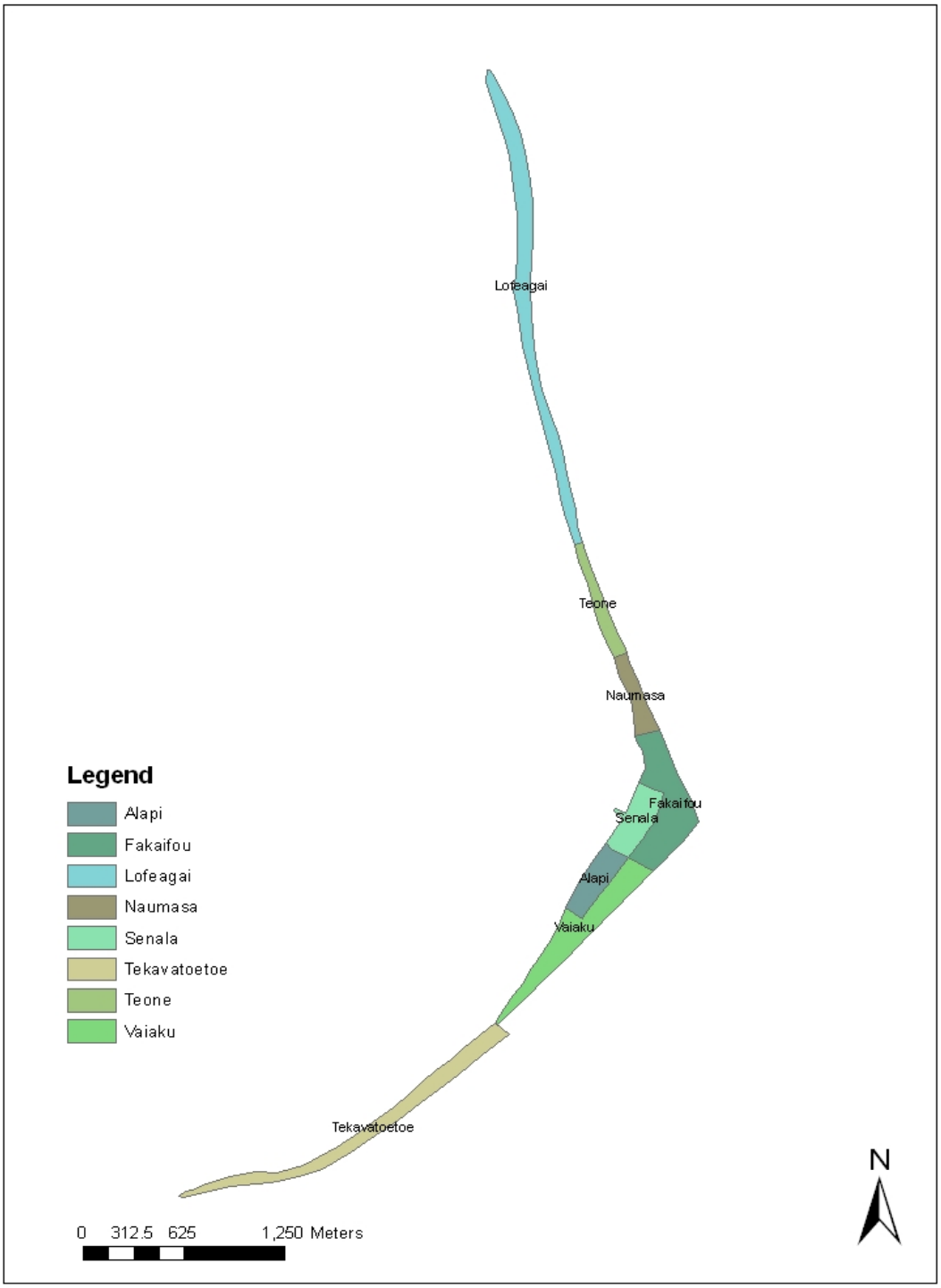

Figure 2.3: Map of villages on Funafuti Atoll.

Tuvalu has a young population with a median age of 23.7 years; 36.2% of residents are under 15 years, which is consistent with other developing nations (Table 2.3). One anomaly is the decreased population of 25–35-year-olds, which is inconsistent with the typical age distribution in developing nations. The reduction may be due to the small population size or to emigration: this age group likely represents educated and skilled young adults, who are most likely to emigrate as skilled migrants. The male-to-female ratio is 0.9 to 1.0, with approximately 21% of the female population falling within the child-bearing years of 15–44 (Figure 2.4). Combined with a relatively low death rate there is potential for significant population growth, emigration from Tuvalu notwithstanding.

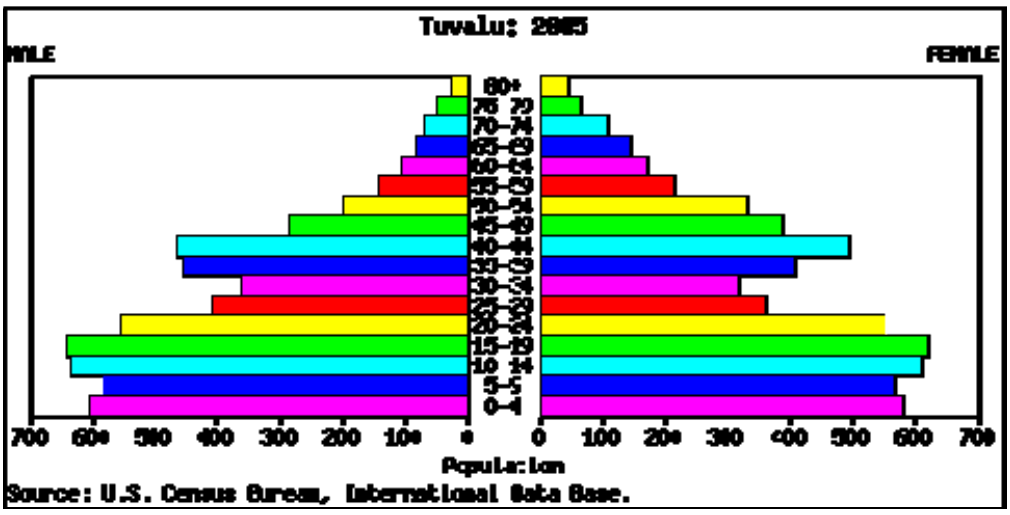

Figure 2.4: 2005 population pyramid for Tuvalu – age and sex distribution (US Census Bureau, 2008).

Population	**9,561**
Sex distribution	Males 49.5% Females 50.5%
Age breakdown 0–4 years	12.3%
5–9 years	12.6%
10–14 years	11.3%
15–19 years	8.6%
20–29 years	12.6%
30–39 years	12.9%
40–49 years	13.4%
50–59 years	7.8%
60–69 years	5.1%
70+ years	3.4%
Median age (years)	23.7
Crude birth rate per 100,000 population	27.1
General fertility rate per 100,000	3.7
Crude death rate per 100,000	9.9
Average life expectancy at birth (years)	Males 61.7 Females 65.1
Infant mortality rate per 100,000 births (under 1 year)	Males 41 Females 28
Mortality rate for children under 5 years of age per 100,000 live births	Males 6.5 Females 11.7
Rate of annual growth (1991–2002)	0.6

Table 2.3: Tuvalu demography and vital statistics 2002 (Government of Tuvalu, Central Statistics Division, 2002; Tuvalu Island statistics online, 2008).

2.1.3 Economy

The gross national product (GNP) per capita for this small nation is AUD2,500, which ranks Tuvalu 130th out of 224 nations (2005), classifying it as a middle- rather than a low-income nation. This GNP per capita ranking results from funds secured from the Tuvalu Trust Fund (TTF) and remittances from overseas employment (World Fact Book, 2008). The TTF is an international trust fund that was established in 1987 by Australia, New Zealand and the United Kingdom and later supported by Japan and South Korea. Initially the fund contained AUD17 Million but due to careful investment it was worth an estimated AUD77 million in 2006. Included in the latter figure is an additional AUD2 million generated from the sale of the internet domain name 'tv'. The TTF contributes to the annual government budget and compensates for the country's very limited income from exports and production (World Fact Book, 2008).

Like many small Pacific Island nations Tuvalu has a dual economy, with 36% of its inhabitants surviving largely on subsistence fishing and the harvesting of coconut products, and 64% employed in formal sector employment. Of those who have formal employment, 69% work for the Government of Tuvalu (the country's largest employer), 28% work in the private sector and 3% are employed by non-governmental organisations (NGOs) (Fakavae, 2007).

Remittances from Tuvaluans living abroad have been and still are an important part of Tuvalu's economic and social development. Historically, the main remittances from Tuvaluan nationals abroad have been those of: 1) seafarers, 2) contract phosphate workers in Nauru, and 3) Tuvaluans who have permanently migrated to Australia, NZ, Fiji or other nations. Currently Tuvaluans working internationally as seafarers are the largest source of remittances, followed by nationals who have permanently relocated (Fakavae, 2007).

Seafarers' annual remittances have increased significantly in the last decade: statistics show they increased from $743,790 to $3,680,490 in 2003 (Fakavae, 2007), demonstrating their vital importance to the small nation. Often a seafarer is the sole family income earner and supports an extended family household of up to 20 people. The loss of this vital income would be socially and economically devastating to the population.

2.1.4 Migration

Tuvaluans are a highly mobile population. Historically there has been frequent intra-island travelling for fishing and agriculture, and to maintain social and cultural ties. More recently, Tuvaluans have travelled to Funafuti for education, health care, international travel and employment opportunities. Funafuti is the site of the only hospital, the airport, government services and the majority of employment. The influx of inhabitants from the outer atolls is resulting in increased population density and the strain of urbanisation is becoming apparent. Land on Funafuti is scarce and those from outer atolls who are not traditional landowners are unable to build housing. Rental properties are rare and expensive, thus creating severe overcrowding in existing Funafuti households and placing further demands on water, electricity and sanitation services (Faagai, 2006).

In response to the lack of employment, scarcity of land and poor opportunities for young people, many younger Tuvaluans, especially those with skills and trades, are emigrating. In 1998 there were 1,899 resident departures, and these steadily increased to over 2,700 in 2003 (Fakavae, 2007). The main reasons for temporary migration are (in order of resident departures) extended visits for social/family reasons, government-related travel, education, and employment (Government of Tuvalu, 2006). While permanent emigration eases the population burden on Funafuti, it can also result in a shortage of skilled and educated labourers, which can become critical in a small population.

Climate change and the possible threat of losing their islands have prompted many Tuvaluans to consider emigration. There is currently no official immigration plan from any nation specifically for residents of Tuvalu despite international and regional discussion on the issue. New Zealand offers 75 places annually for citizens of Tuvalu under its Pacific Access Countries quota (New Zealand Ministry of Foreign Affairs & Trade, 2008) and the majority of migrating Tuvaluans choose New Zealand for permanent residence (Fakavae, 2007).

2.1.5 Health-care system

Tuvalu has a centralised health-care system with a 25-bed hospital, the Princess Margaret Hospital (Figure 2.5), located centrally on Funafuti Atoll. The hospital contains a staffed laboratory, outpatient clinics, a surgical theatre, a pharmacy and allied health services, such as dentistry, nutrition and other public health services and programmes. All medical services, both inpatient and outpatient, are provided free to Tuvaluan citizens. However, patients may incur minor fees for some allied health services.

Figure 2.5: Princess Margaret Hospital and Chief Health Officer Dr Takaai Nelesone, July 2003.

Each outer island has an outpost clinic staffed by senior nurses who provide basic primary health care to residents (Figure 2.6). Medical advice and support are provided remotely by doctors on Funafuti, and serious cases are referred to the central hospital for further treatment. However, in emergency situations medical evacuation is available only by boat – either cargo ship or naval patrol vessel. This system is very costly and inefficient due to the long turnaround time to retrieve patients, and can result in negative outcomes for critically ill patients.

Figure 2.6: The clinic on Nukufetau, the only health facility on the atoll, November 2005.

2.1.6 Health

As a developing nation in a tropical setting, the pattern of disease in Tuvalu is typical of a society undergoing epidemiological transition and experiencing both infectious and non-communicable diseases. There are several infectious diseases, including those that are distinct to tropical environments (such as LF) and those that are found elsewhere but commonly occur in low- to middle-income countries due to the reduced standard of living. Notably, there is evidence of parasitic diseases: scabies, intestinal helminths and lymphatic filariasis. Each parasite on its own can result in severe morbidity and personal discomfort and has the potential to result in serious long-term health issues.

Lymphatic filariasis is considered a significant health risk in Tuvalu, and the nation has been participating in PacELF since 2001 (PacELF, 2008). Historically there have been documented cases of elephantiasis (the most severe clinical manifestation of the disease) and of acute filarial attacks throughout Tuvalu, prompting the initiation of MDA, which has been conducted annually for the past six years throughout the country (Government of Tuvalu, 2004; PacELF, 2008). Fever and lymphoedema, hallmark symptoms of an episode of LF, are two of the eight reportable syndromes in the country's syndromic surveillance system (Nelesone *et al.*, 2006). There have been no reported cases of LF syndrome since 2003 (Government of Tuvalu, 2004; Government of Tuvalu, 2005).

Additionally, infection with LF has been shown to cause subclinical renal disease in patients who do not exhibit other classic symptoms or signs (Dreyer *et al.*, 1992; Dreyer *et al.*, 2002; Perera *et al.*, 2007).

Although data are incomplete and inconsistent throughout the Pacific region, Tuvalu has a comparatively high initial baseline prevalence of LF (22.5%) among the 11 PICTs considered to be endemic for the parasite, but has also demonstrated the most significant decrease (a reduction of 10%) in prevalence as reported from midterm surveillance and monitoring activities. The most recent survey, conducted in February 2008 after six treatments, indicates the prevalence of LF to be approximately 10% (Melrose, 2007).

Country	Population	Baseline prevalence (antigen)	Midterm prevalence (antigen)	Final assessment	Rounds of MDA
American Samoa	57,881	16.5 % (1999)	13.5% (2003)	Unavailable	4
Cook Islands	13,905	8.6% (1999)	0.4% (2002)	1.27% (2005)	6
Fiji	776,173	16.6% (2002–2003	11.4% (2005)	Unavailable	4
French Polynesia	252,900	13.8% (2000)	Ongoing	Unavailable	6
Kiribati	84,494	1.7% (1999–2000)	Unavailable	Unavailable	5
Niue	1,639	3.1% (1999)	1.3% (2001)	0.2% (2004)	4
Papua New Guinea	5,190,786	6% (2001–2004)	Unavailable	Unavailable	Varies by province
Samoa	176,848	4.5% (1999)	4.5% (2002)	1.1% (2004)	5
Tonga	97,784	2.7% (1999–2000)	2.5% (2003–2004)	Unavailable	5
Tuvalu	9,561	22.5% (1999)	12.1% (2004)	Pending	6
Vanuatu	186,678	4.8% (1997–1998)	8.0% (2002)	Pending	5

Table 2.4: Lymphatic filariasis prevalence for each of the 11 PICTs declared endemic by the PacELF programme (PacELF, 2008).

Although often unaddressed, bacterial and other skin infections are serious health problems in developing countries, especially in tropical settings. Previous research indicates that the prevalence of skin infections can range from 10% to 90% in Australian Aboriginal communities (Feldmeier *et al.*, 2005). Depending on the health care setting, between 7% and 70% of patients in tropical settings may present with skin lesions of infectious origin (Hengge *et al.*, 2006; WHO, 2008f). Previous studies also indicate that while the frequency and aetiology of fungal, bacterial and parasitic skin infections vary according to location, bacterial infections always play a significant role in skin presentations (WHO, 2005c).

Pyoderma is the most common bacterial skin condition, usually resulting from infection with staphylococcal or streptococcal bacteria (Carapetis *et al.*, 1999; Heymann, 2004; WHO, 2005c). The literature shows that the majority of pyoderma is due to streptococcal bacteria, including specific Group A streptococcal infections (Carapetis *et al.*, 1999; Carapetis *et al.*, 2005; WHO, 2005c). Research conducted in Aboriginal communities in northern Australia indicated that 80% of pyoderma lesions were culture positive for GAS (Currie and Carapetis, 2000; Shelby-James *et al.*, 2002). In addition to superficial skin presentations there are other clinical implications of GAS infection, including severe systemic infection leading to bacterial sepsis (Bisno and Stevens, 1996; Carapetis *et al.*, 1999; Brook, 2002; Carapetis *et al.*, 2005). Infection with GAS bacteria can also result in acute and chronic renal dysfunction, including post-streptococcal glomerulonephritis (Carapetis *et al.*, 1999; Feldmeier *et al.*, 2005; McDonald *et al.*, 2007), and can predispose some infected individuals to rheumatic heart disease (Ogunbi *et al.*, 1978; Rajajee, 1990; Carapetis, 1998; National Heart Foundation, 2008). The link from cutaneous lesions containing GAS to severe clinical complications with possible chronic sequelae has been established in resource-poor settings in the Pacific, most notably Aboriginal communities in Australia (Carapetis and Currie, 1998; Currie and Carapetis, 2000; Currie and Brewster, 2001; Carapetis *et al.*, 2004).

Furthermore, the epidemiology suggests that scabies plays an important role in this physiological pathway by facilitating colonisation with GAS and other bacteria through breaks in the skin caused by repeated scratching to relieve pruritis, the chief symptom of scabies infection (Brook, 2002; Flinders and De Schweinitz, 2004).

Data on skin infections in the Pacific region are limited and inconsistent, with the majority of information obtained from research and other sporadic surveys rather than routine surveillance activities. Historically, the literature indicates that the prevalence of skin infections, especially scabies and pyoderma, is similar to other tropical settings with similar conditions of poverty. Previous surveys found the prevalence of scabies to be 10% in Samoa (White and Barneston, 1998) and 12% on the island of Tanna in Vanuatu (Harris *et al.*, 1989). A high prevalence of scabies and associated conditions (bacterial pyoderma and PSGN) were documented in New Caledonia in 1981 (Thevenieau, 1981). A survey conducted on a remote island in Fiji concluded that scabies was present in 32% of schoolchildren and that 2% had impetigo, a specific streptococcal skin infection (Thomas *et al.*, 2005).

Several early studies conducted in Papua New Guinea and the Solomon Islands indicate that a wide range of skin infections, especially bacterial infections, are a public health issue. One study in Eastern Highlands Province in PNG found that 55% of the children surveyed had scabies, 34% had infected scabies (scabies and pyoderma co-infection) and 10% had ulcers (Montgomery, 1985). A further study in Goroka, PNG demonstrated that 95% of the infected lesions from a cohort of children were culture positive for group A streptococci (Bowness *et al.*, 1984). Findings from the Solomon Islands found that pyoderma was present in 52% of children aged less than 15 years and that dermatophyte infections were also universal in adults and children; they were absent in only very young children aged less than four years (Eason and Tasman-Jones, 1985).

More recent data from Pacific countries indicate that the prevalence of skin infections, especially scabies, has increased during the last 30 years. WHO has declared that skin infections are a major health concern in the Pacific region (WHO, 2005b; WHO, 2005c). Recent data from the WHO databank show that scabies was in the top five reasons for presentation at health-care facilities in Vanuatu and the Marshall Islands (WHO, 2008e). Finally, a recent study in Fiji estimated that one-fifth (20%) of the entire population is infected with scabies (Whitfield, 2008).

Data collected from outpatient visits to the Princess Margaret Hospital (PMH) on Funafuti and from outpost nursing clinics on each of Tuvalu's outer islands indicate that skin infections are contributing to the burden of illness in Tuvalu. Reports from 1997 to 2001 indicate that septic sores and wounds were among the top five most common presentations to health-care providers (Government of Tuvalu, 2006).

Since 2002 the Central Statistics Division has collected more detailed surveillance data for both communicable and non-communicable diseases. Analysis of the 2004 and 2005 data demonstrated that the category of 'septic sore/wound' was the leading cause of visits to health-care centres in both years (Table 2.5).

Further examination of the data over a two-year period showed that skin infections were a significant cause of morbidity, and bacterial skin infections in particular were the leading cause of morbidity in both 2004 and 2005, with fungal infections (all tinea species ringworm, athletes foot, ect,. are included in this classification and presented as aggregated data by the Ministry of Health) contributing to a lesser extent. Combining all categories of reported communicable diseases that fall under dermatological or 'skin' conditions, the true impact of these diseases on the health-care system of Tuvalu is startling. Skin conditions resulted in 76.5% of all outpatients seen (over 32,000 patient visits) for communicable diseases within the two-year period (Government of Tuvalu, 2004; Government of Tuvalu, 2005). Discussions with helath care providers attribute the increase in skin infections to increased crowding on Funafuti and lack of water.The statistics show the enormous burden of these infections upon both the population and the resource-constrained health-care system.

According to the country's health statistics, intestinal parasitic infections (chiefly caused by soil-transmitted helminths) are not a leading cause of morbidity, as STHs are seldom identified as a cause of gastroenteritis. However, on average there are approximately 500 reported cases of diarrhoea per year. This is likely only a fraction of the actual burden of illness in the community, as the literature suggests that episodes of acute gastrointestinal illness (GI) are greatly under-reported (Roy *et al.*, 2006; Flint *et al.*, 2007). Diarrhoea, the principal symptom of acute GI, is one of the eight conditions under surveillance in Tuvalu (Nelesone *et al.*, 2006).

Only two surveys of STHs have been conducted in Tuvalu (Huges *et al.*, 2004; Speare *et al.*, 2006). A study of schoolchildren in the Pacific showed that STHs were present in all of the 13 countries where the surveys were conducted, and that Tuvalu had the highest prevalence (97%) of all PICTs (Huges *et al.*, 2004). The more recent cross-sectional faecal survey of the population, including adults and children, on the atoll of Nukufetau detected STHs in 69.9% of the survey participants despite three rounds of annual treatment with the anti-parasitic drugs diethlycarbamazine (DEC) and albendazole (Speare *et al.*, 2006). In both surveys only hookworm and whipworm (*Trichuris trichiura*) eggs were found.

Tuvalu, like the rest of the South Pacific, is experiencing an epidemiological transition, where the bulk of the disease burden is shifting from communicable disease to non-communicable disease. Increasing rates of lifestyle-related non-communicable diseases, including obesity, cardiovascular disease, hypertension and diabetes (Lippe *et al.*, 2007; Misra and Khurana, 2008; Hossain *et al.*, 2009), now coexist with the traditional infectious diseases described earlier. This shift in health epidemiology creates a complex and dynamic situation where multiple disease pathogens and other conditions overlap, with the potential to cause significant co-morbidity.

Age / Condition	<28 days		<1 year		1–4 years		5–14 years		15–25 years		Over 25 years		Yearly total
	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	
Conjunctivitis	0	0	10	15	35	49	93	121	32	30	169	124	678
Filariasis	0	0	0	1	0	0	0	1	2	1	21	30	56
Hepatitis B	0	0	1	0	0	5	0	1	0	0	3	2	12
ARI (unspecified)	10	0	283	185	776	575	636	415	213	154	1,513	614	5,374
Diarrhoea	2	0	57	46	245	179	180	167	96	78	445	304	1,799
Influenza	1	1	86	107	234	192	399	153	200	48	1,035	375	2,831
Cough	4	3	166	83	409	205	440	201	189	70	707	329	2,806
Septic sore/wound	**8**	**10**	**116**	**99**	**395**	**372**	**943**	**799**	**606**	**621**	**3,111**	**1,606**	**8,686**
Boils	**3**	**1**	**19**	**19**	**77**	**25**	**82**	**38**	**64**	**20**	**365**	**181**	**894**
Abscess	**0**	**0**	**71**	**32**	**108**	**56**	**89**	**78**	**59**	**61**	**368**	**212**	**1,134**
Otitis media	**1**	**0**	**34**	**5**	**87**	**62**	**143**	**128**	**47**	**39**	**184**	**152**	**882**
Fungal infection	**0**	**0**	**5**	**6**	**23**	**32**	**88**	**52**	**78**	**59**	**379**	**269**	**991**
Skin rash	**1**	**6**	**79**	**40**	**85**	**48**	**74**	**22**	**13**	**8**	**119**	**70**	**565**
Dhani/tinea	**0**	**0**	**5**	**1**	**2**	**8**	**26**	**24**	**35**	**30**	**104**	**93**	**328**
Ringworm	**0**	**0**	**0**	**0**	**7**	**5**	**44**	**19**	**127**	**63**	**239**	**195**	**699**
UTI	0	0	2	0	5	0	18	5	45	36	226	126	463
Gastritis	0	0	2	0	1	0	7	3	16	16	112	85	242
Other	11	7	118	71	268	186	288	320	265	291	1,475	2,528	5,828
Total	41	25	1,054	710	2,757	341	3,550	2,547	2,087	1,625	10,575	7,295	34,268

Table 2.5: Outpatient visits in Tuvalu 2004–2005 by age of patient (Government of Tuvalu, Central Statistics Division, unpublished report, 2004–2005).

For the purposes of this survey the definition of medical co-morbidity has been adapted; it is defined as: 1) the presence of one or more disorders (or diseases) in addition to a primary disease or disorder, and 2) the effect of such additional disorders or diseases, referring to the synergistic effect of multiple pathogens. In a broader public health context, co-morbidity can be viewed as the complex environmental and physiological interactions of multiple agents and diseases.

Each of the previously mentioned infectious diseases can result in significant morbidity and possible mortality. In a setting where several of these diseases exist, the physiological and socio-environmental interactions of infectious and non-communicable disease may be predisposing individuals and the population as a whole to serious and long-term negative health outcomes. The prevalence and impact of these conditions are poorly understood and under-investigated.

With a profile of skin infections, lymphatic filariasis and intestinal parasites leading to anaemia, subclinical renal dysfunction and other acute and chronic manifestations, it appears that the population of Tuvalu is currently experiencing co-morbidity from multiple infectious diseases. The prevalences and their associated burden of illness of these infectious diseases, alone and in combination, and in conjunction with other non-communicable conditions such as obesity, diabetes, anaemia, cardiac disease and nutritional status, are currently unknown.

2.2 Methods

The objective of this study was to determine the prevalence and impact of parasitic and skin diseases in the community in Tuvalu. In order to quantify the true prevalence and burden of these neglected diseases in the community, a survey of school-aged children was conducted to determine the baseline prevalence of parasitic and common skin infections on Funafuti Atoll, the most populated island. The study was undertaken by a team from the School of Public Health, Tropical Medicine and Rehabilitation Sciences at James Cook University (JCU), in collaboration with the Tuvalu Ministry of Health (MOH) and Ministry of Education. Within the MOH, the Department of Public Health was the lead agency. Children were targeted as this particular survey was conducted in conjunction with the implementation of the WHO De-worming Programme for School-aged Children, and because skin infections are most commonly found in children (Mahe, 2001; Chimelli *et al.*, 2003; WHO, 2005c; Seebacher *et al.*, 2008). Hence, this age group serves as an indicator for disease within a community.

Consecutive convenience sampling of all schoolchildren (2–15 years) on Funafuti was employed in the survey. Children were surveyed while at school for convenience of sampling, with research teams going from class to class from preschool to year 8 at the primary schools and preschools. There were six components to the survey: demographics, morphometrics, haemoglobin, faecal testing for nematode parasites, urine testing and clinical skin examination.

Permission was granted by both ministries, and ethical approval was granted by the James Cook University Ethics Committee (Appendix 1). The parents or guardians of all children were informed via the schools and the Department of Public Health through verbal communication and radio announcements. Verbal consent was obtained from the parents of all participating children. Children who were absent on the day the team visited their class were informed of a 'catch-up' session held at the end of the survey period.

All children, regardless of their participation in the study, were treated for intestinal nematodes with mebendazole (with parental permission) as part of the WHO programme to de-worm school-aged children; this occurred at the end of the survey period after the deadline for returning samples. Public health nurses continued with the treatment campaign throughout the outer islands. Data from the Department of Public Health indicated that they achieved a coverage rate of 96% of all children within the target age group within 60 days of the initial survey (Conway, 2007).

The survey was conducted over a four-week period in October 2006 at all primary schools and preschools on Funafuti. A survey team went from classroom to classroom conducting a child health check consisting of age, gender, height and weight. These biometric variables were then used to calculate height-for-age and weight-for-height as an indicator of the general health of the child population. Calculations were done in Microsoft Excel 2000. Full first and last names were used as unique identifiers and consecutive sample numbers were assigned to each unique participant. The names were removed once the data had been reconciled and duplicates and unknowns were removed.

Haemoglobin (Hb) was collected by finger-prick using diabetic lancets and was analysed on a portable machine, the HemoCue 201®. Finger-prick sampling is an established method for point-of-care tests; it measures the level of peripheral blood haemoglobin in real time in the absence of laboratory facilities (Munoz *et al.*, 2005).

Finger-prick is less painful and invasive than traditional veni-puncture blood sampling and reduces the risk of needle-stick injuries and blood-borne infection. The HemoCue 201® has shown greater power in detecting anaemia than micro-Hct techniques (Mendrone *et al.*, 2009) and is therefore the preferred method for screening in the field. Haemoglobin was collected as a health indicator at baseline, and later as a monitoring and evaluation indicator for the de-worming programme, as well as to compare levels of anaemia between children who were positive for STHs and those who were not.

Skin examinations were conducted for three targeted common skin infections, bacterial pyoderma, scabies and dermatophyte infections, according to the survey case definitions (Table 2.6). Skin infections were determined by clinical diagnosis by a trained team member who conducted all of the skin examinations to maintain consistency of diagnosis. Parents of children who required treatment of any kind were informed and referred to the outpatient clinic at the hospital, and children who were found to have more serious health conditions were taken directly to the hospital by a teacher or team member and their parents were informed immediately.

Skin disease	**Definition**	**Type of diagnosis**
Pyoderma	Any superficial bacterial skin infection (e.g. impetigo, impetigo contagiosa, ecthyma, folliculitis, furuncle, carbuncle, tropical ulcer, etc.)	Clinical
Scabies	Presence of lesions, nodules, burrows, papules, vesicles or crust characteristic of *Sarcoptes scabiei* infection with evidence of pruritis (itching)	Clinical
Dermatophyte (fungal) infection	Presence of lesions, maceration and inflammation characteristic of infection with dermatophyte species on the skin	Clinical and skin scraping for microscopic examination if required

Table 2.6: Case definitions of skin diseases used in survey.

Urine specimens were collected in a 5 ml yellow screw-topped plastic vial, and a 25 ml opaque brown screw-topped container was provided for faecal specimens; both were labelled with the participant's name and unique sample number. Verbal and written instructions in English and Tuvaluan were provided. Participants or their parent/guardian were asked to bring fresh urine and faecal samples to the hospital laboratory, and it was emphasised that urine samples needed to be received at the lab within one hour of providing the sample to ensure accurate results.

Urine samples were analysed for blood and protein using Multistix® 2820 (Bayer) urinalysis dipsticks (Lot #6C15D). Samples were refrigerated at 4ºC as soon as possible after delivery and dipstick testing was done in the PMH laboratory every afternoon. All stool samples were preserved in a 10% sodium acetate formaldehyde (SAF) fixative, transported to Australia and examined at JCU using a modified Kato-Katz method to calculate eggs per gram (Appendix 2). A modified Kato-Katz method was used as the samples were preserved rather than fresh – the modified methodology has been shown to be as effective as the original method (Melrose, 2009).The intensity of infection was graded as light, moderate or heavy using WHO criteria (Huges *et al*., 2004) (Table 2.7).

Level of infection	**Light**	**Moderate**	**Heavy**
(eggs per gram/faeces)	(1–1,000)	(1,000–10,000)	(>10,000)

Table 2.7: Intensity of *Trichuris trichiura* infection in schoolchildren on Funafuti Atoll.

Eighteen soil samples were collected near toilets, in damp and wet places such as gardens and between houses, and from high-traffic public locations to determine the presence of parasite eggs, assess the level of soil contamination and identify locations that may present a higher risk of transmission for STHs. Approximately 25 grams of soil per site was collected using wooden tongue depressors and placed into 50 ml brown-topped plastic sample jars similar to those used for the stool samples. Because unsterilized soil samples cannot be imported into Australia, an equal amount of a 10% SAF fixative was added to each sample and thoroughly mixed. Specimens were packaged for travel and shipped to JCU for testing.

The usual method for recovering parasite eggs from soil samples is by flotation (Tiyo *et al.*, 2008), but previous experience in our laboratory has shown that eggs fixed in formalin do not float well, making the method less effective (Speare, 2009). It was thus decided to use a flotation method and a direct examination method. Two soil samples collected near our laboratory were artificially contaminated with sheep faeces containing eggs of *Haemonchus contortus*, treated with SAF, and examined in the same way as the samples collected in Tuvalu to serve as controls.

Approximately 50 g of the fixed soil sample was transferred to a 70 ml wide-mouthed plastic container and mixed with enough water to form a pourable slurry. The slurry was filtered through two layers of surgical gauze into a 50 ml tube to remove vegetation, pieces of stone, and so on. The tube was centrifuged at 500 xg for 10 minutes and all of the supernatant removed. The resulting wet soil sample was thoroughly mixed with an applicator stick. Two 2 g portions were weighed out and each portion was transferred to a 10 ml plastic graduated centrifuge tube.

For the direct examination method, one tube was filled to the 10 ml mark with water and thoroughly mixed with a vortex mixer, and 0.1 ml was transferred to a glass slide and cover slipped. The slide was examined for parasite eggs using an x20 objective. Nine additional 0.1 ml aliquots were examined from the same tube and the number of eggs per gram of soil was calculated.

For the flotation method, the second of the two tubes was filled to the 9 ml mark with zinc sulphate solution with a specific gravity of 1.2 (Oge and Oge, 2000). The tube was mixed with a vortex mixer and then centrifuged for 10 minutes at 500 xg. The surface layer was carefully removed with a pipette, transferred to a microscope slide and examined for parasite eggs. Results were expressed as eggs per gram of soil.

Data were recorded by the research teams on data collection sheets and then transferred into a Microsoft Excel database and analysed using SPSS version 16. Demographic data were analysed using descriptive statistical tests, including: frequency, mean, proportion, confidence interval, chi-square tests, and odds ratios for relative risk associations. Categorical data were analysed using cross-tabulations and chi-square tests, and numerical data were analysed using t-tests assuming normally distributed data.

For the purposes of this study all results were considered to be significant when p-values > 0.05. All electronic data will be stored on a secure server with limited access within the School of Public Health, Tropical Medicine and Rehabilitation Science for a period of five years.

2.3 Results

2.3.1 Survey population

Participants were recruited from the two primary schools and nine preschools. A total of 921 children aged 2–14 years were included in the survey, representing 78% of the targeted population (Table 2.8). Males and females were equally represented, with 50% (460/921) and 49.9% (459/921) respectively. Gender was not recorded for two cases. The age profile of the children was 0–5 years 15.2% (140/921), 6–10 years 54.1% (498/921) and 11–15 years 30.6% (282/921) (Figure 2.7). The survey population was normally distributed in regards to the categorical variable of age.

		Age group			**Total**
		0–5	**6–10**	**11–15**	
Gender	**Male**	65	261	134	460
	Female	74	237	148	459
		140	498	282	**921**
Total		**15%**	**54%**	**31%**	

Table 2.8: Survey population on Funafuti by age and gender, 2006.

Seven of the eight villages on Funafuti Atoll were represented in the survey, with the majority of participants residing in the main villages of Fakaifou, Vaiaku and Alapi (Figure 2.8). There were no children identified in the survey from the village of Lofeagai, which may be due to the fact that Lofeagai has a small population and hence the few children in the target population were missed during the survey. Recording of the village may have been omitted during the data collection and children from the village may have been listed under ‘unknown’ for residence.

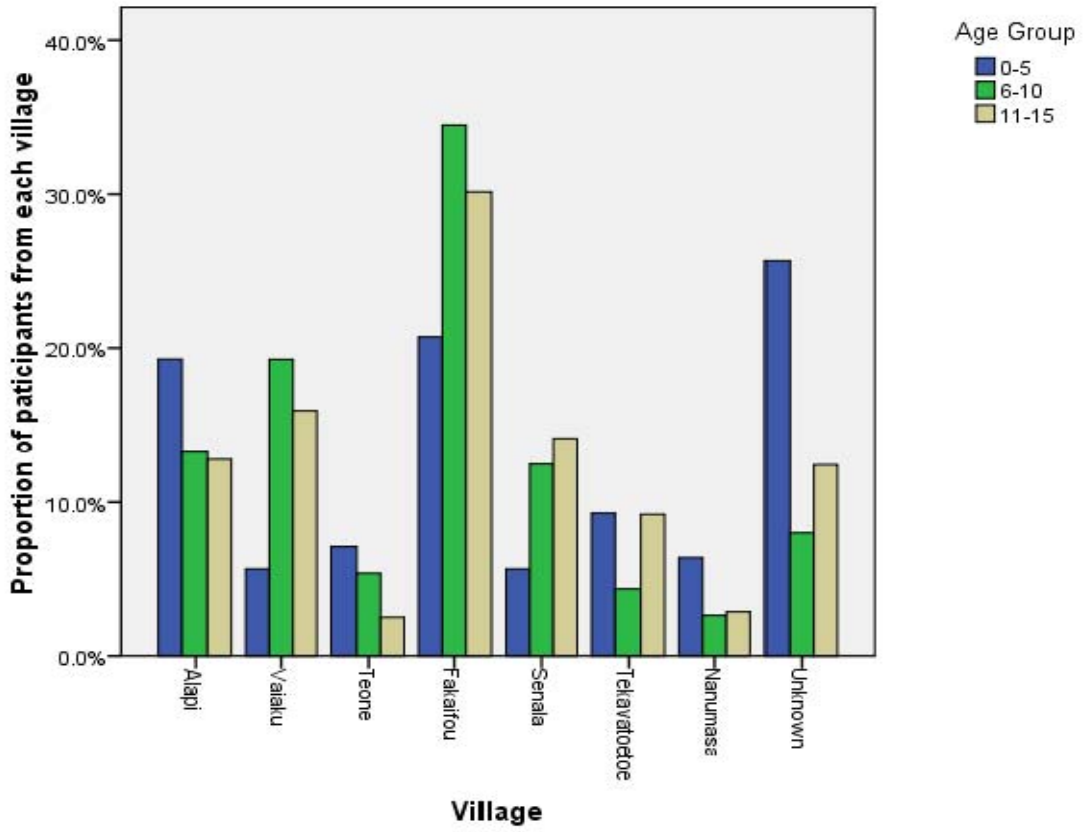

Figure 2.7: Proportion of survey participants from each village on Funafuti by age group, 2006.

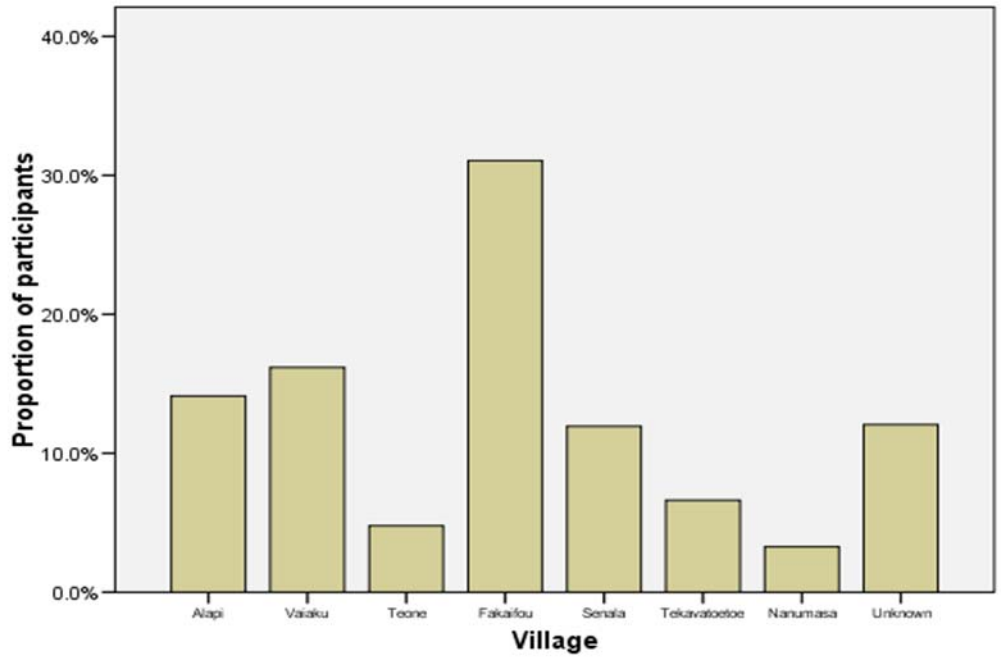

Figure 2.8: Survey population on Funafuti by village, 2006.

2.3.2 Morphometrics

Analysis of height, weight and age indicated that all children except one were of normal height for their age and there was only one case of stunting as determined by established WHO height-age-weight ratios. Based on WHO criteria for child body mass index (BMI) (WHO, 2006c), 46.7% were within the normal range (BMI = 18–24) and less than 1% were considered to be thin or severely thin (BMI <16). However, 42% of children were considered to be overweight (BMI >+1SD), 11% were obese (BMI >+2SD) and 7% were morbidly obese (BMI >+3SD). Only 3% were below the median and considered underweight (Table 2.9).

	Frequency	Percentage	BMI	Classification
-3 SD	1	0.11	>16	Severe thinness
-2 SD	5	0.54	16–17	Thinness
-1 SD	27	2.9	17	Normal range
Median BMI	405	43.8	18–24	Normal range
+1 SD	220	23.9	25	Overweight
+2 SD	100	10.9	30	Obese
+3 SD	66	7.1	40	Morbidly obese

Table 2.9: Distribution of BMI for schoolchildren 5–15 years of age on Funafuti, 2006.

2.3.3 Anaemia

Analysis of haemoglobin by age group indicated a range of values from 62 to 147 g/l. The data indicated that 60.5% of children surveyed met the WHO criteria for anaemia according to their age group (WHO *et al.*, 2001) (Table 2.10). Anaemia was present in all three age categories and was most common in those over five years of age. The current WHO standards for child anaemia do not differentiate between males and females under 13 years of age, and analysis of participants over 13 years indicated no differences between males and females.

Age group	Threshold for anaemia*	Mean Hb	% anaemia within age group
0–5 years	Hb > 110 g/l	108.7 (CI 106.7–110.7)	52.9%
6–10 years	Hb > 115 g/l	109.2 (CI 108.1–110.4)	65.4%
11–15 years	Hb > 120 g/l	116.8 (CI 115.2–118.4)	58.2%

* Based on WHO Standards 2005

Table 2.10: Prevalence of anaemia on Funafuti by age group and gender, 2006 (CI = 95%).

2.3.4 Skin diseases

More than half (51.4%) of children had at least one skin infection. Five per cent presented with more than one infection (most commonly seen were scabies infections with a secondary bacterial or fungal infection) and 4.5% presented with all three skin conditions: scabies, pyoderma and a fungal infection (Table 2.11). The majority of skin infections (66%) were seen in participants less than 10 years of age (t-test mean age 8.75 years).

Skin infection	Frequency	Percentage	Confidence intervals (95%)
No infection	351	38.1%	37.2–39.2%
Scabies uncomplicated	77	8.4%	7.5–9.6%
Pyoderma	352	38.4%	37.5–39.5%
Scabies (co-infection)	35	3.8%	2.9–5.1%
Fungal infection	6	0.7%	0.21–1.9%
No exam	100	10.6%	8.5–12.6%
Total	921	100.0%	

Participants may have been counted more than once if they had more than one skin condition.

Table 2.11: Prevalence of skin infections among schoolchildren on Funafuti, 2006.

Pyoderma was the most commonly seen skin presentation within the Funafuti survey population, with 38.4% of participants showing evidence of a superficial bacterial infection. The second most common condition was scabies (12.2%), which included presentation of uncomplicated cases (8.4%) and those who presented with scabies with a secondary bacterial (pyoderma) or fungal infection (3.8%). By far the least common of the skin presentations were fungal infections (dermatophyte infections); these were observed in less than 1% of the children (six cases).

Figure 2.9 includes the number of diagnosed presentations, not the number of discrete participants. The 'No exam' category included children who were initially missed or whose parents refused a clinical examination

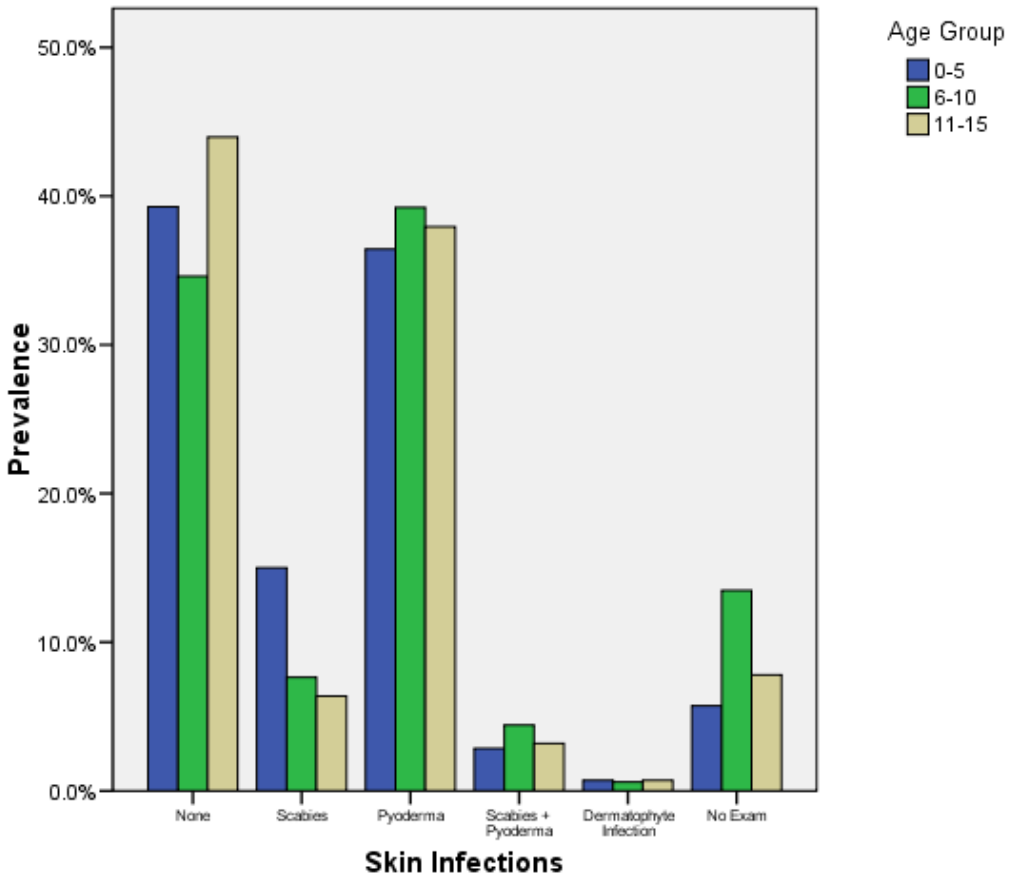

Figure 2.9: Prevalence of skin infections on Funafuti by age group, 2006.

Pyoderma and scabies were present across all age groups, and pyoderma was the most common skin presentation within each group (Figure 2.9). The proportion of cases was highest in those aged 0–5 years, with 15% in this group presenting with a bacterial infection, 7.6% in the 6–10 years group and 6.3% in those aged 11–15 years (Figure 2.12). Scabies was present in approximately one-third of all participants in every age group, and there was no significant difference between males and females (Pearson chi-square p-value 0.476) between the age groups (Pearson chi-square p-value 0.591). Analysis of the prevalence of skin infections by village showed that scabies, pyoderma and scabies co-infection were all present in each of the eight villages (Table 2.10).

Skin infection	**0–5 years**	**6–10 years**	**11–15 years**
None	39.0%	35.0%	43.0%
Scabies	15.0%	8.0%	7.0%
Pyoderma	36.0%	39.0%	39.0%
Scabies + pyoderma	3.0%	4.0%	3.0%
Dermatophyte infection	1.0%	1.0%	1.0%
No exam	6.0%	14.0%	8.0%
Total	100.0%	100.0%	100.0%

Table 2.12: Prevalence of skin infections on Funafuti by age group, 2006.

Within the villages, the proportion of cases of scabies ranged from 5.5% in Senala to 14.8% in Tekavatoetoe. The highest proportions of skin infections were found in Tekavatoetoe and Nanumasa (14.8% and 13.3% respectively), but the difference was not significant (Pearson chi-square p-value 0.885).

The frequency of pyoderma was more consistent throughout the atoll. Within each village the prevalence ranged from 36.8% in Fakaifou to almost one-half (46.7%) in Nanumaga. Again, the highest prevalence of pyoderma was seen in the villages of Nanumasa (46.7%), Teone (44.2%) and Tekavatoetoe (41.0%); however, the difference was not significant (Pearson chi-square p-value 0.579).

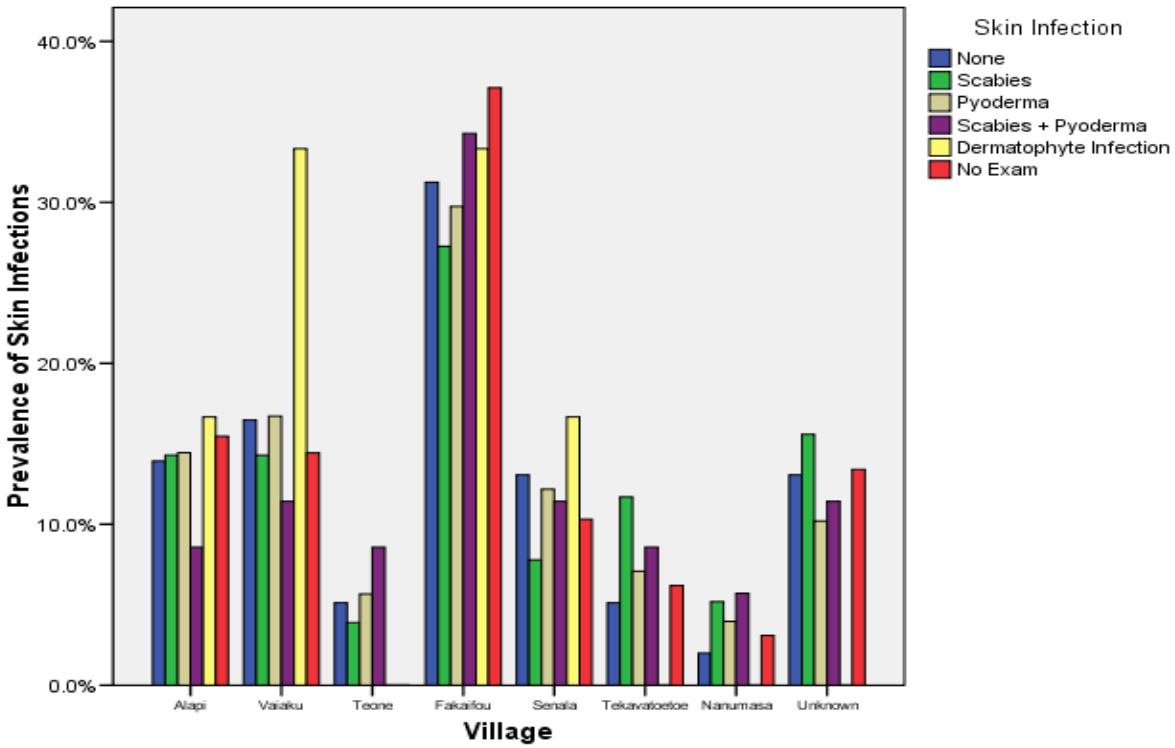

Figure 2.10: Prevalence of skin infections by village on Funafuti, 2006.

Figure 2.10 includes the number of diagnosed presentations, not the number of discrete participants. The 'No exam' category included children who were initially missed or whose parents refused a clinical examination. Table 2.13 shows the proportion of skin infections by village.

Skin infection		Village								
		Alapi	Vaiaku	Teone	Fakaifou	Senala	Tekavatoetoe	Nanumaga	Unknown	Total number of cases
None	Number of cases	**49**	**58**	**18**	**110**	**46**	**18**	**7**	**45**	**35**
	% within village	37.7	39.2	41.8	38.6	41.8	29.5	23.3	41.3	38.3
Scabies	Number of cases	**11**	**11**	**3**	**21**	**6**	**9**	**4**	**12**	**77**
	% within village	8.5	7.4	7.0	7.4	5.5	14.8	13.3	11.0	8.4
Pyoderma	Number of cases	**5**	**59**	**19**	**105**	**43**	**25**	**14**	**35**	**351**
	% within village	39.2	39.9	44.2	36.8	39.1	41.0	46.7	32.1	38.3
Scabies + pyoderma	Number of cases	**3**	**4**	**3**	**12**	**4**	**3**	**2**	**4**	**35**
	% within village	2.3	2.7	7.0	4.2	3.6	4.9	6.7	3.7	3.8
Fungal infection	Number of cases	**1**	**2**	**0**	**2**	**1**	**0**	**0**	**0**	**6**
	% within village	0.8	1.4	0.0	0.7	0.9	0.0	0.0	0.0	0.7
No exam	Number of cases	**15**	**14**	**0**	**35**	**10**	**6**	**3**	**13**	**96**
	% within village	11.5	9.5	0.0	12.3	9.1	9.8	10.0	11.9	10.5
Total	Number surveyed in village	**130**	**148**	**43**	**285**	**110**	**61**	**30**	**109**	**916***

Table 2.13: Prevalence of skin infections in school-aged children by village on Funafuti, 2006.

* Four cases were excluded from the analysis due to incomplete information.

2.3.5 Urine results

Four hundred and fourteen urine samples were submitted for analysis, of which 35.7% had proteinuria and 30.2% haematuria. Of the samples with proteinuria, 76.2% (112/147) had a trace amount of protein, 15.6% (23/147) had a moderate level of protein (30–100 g/L) and 8.2% (12/147) had a high level of protein (300–2000+ g/L). Haematuria was detected in 128 samples (30.2%), of which 55.5% had a trace or small amount of blood, 35.2% had a moderate amount and only 9.3% had a large amount present. Approximately 5% (42 cases) were positive for both haematuria and proteinuria. There was no significant difference between males and females (Pearson chi-square p-value 0.540 for haematuria, and for proteinuria 0.407). There was a significant difference in the mean age for haematuria, indicating that the prevalence of haematuria was significantly higher in those under eight years of age (t-test 7.95 years, p-value 0.047). There was no significant difference in the mean ages for those with proteinuria.

A subset of 376 participants (who both submitted a urine sample and had a skin examination) was analysed to investigate the broader impact of existing health and skin conditions on the child population. The strength of association between the measured clinical variables and haematuria and proteinuria is shown in Table 2.14, with the significant associations presented in bold.

Clinical variable and association	Relative risk	Confidence interval (95%)
Pyoderma + Haematuria	0.77	0.59–0.99
Pyoderma + Proteinuria	1.1	0.90–1.39
Scabies + Haematuria	**1.75**	1.04–2.94
Scabies + Proteinuria	**1.72**	1.03–2.87
Scabies + Pyoderma + Haematuria	1.21	0.46–3.22
Scabies + Pyoderma + Proteinuria	**2.23**	0.90–5.55
Overweight + Haematuria	1.09	0.73–1.63
Overweight + Proteinuria	0.97	0.66–1.43
Obese + Haematuria	1.28	0.66–2.54
Obese + Proteinuria	1.0	0.53–2.01

Table 2.14: Odds ratios indicating relative risk for haematuria and proteinuria and pyoderma infection.

The strongest association for abnormal urine results was seen in participants with proteinuria who had scabies and pyoderma co-infection (RR = 2.23) compared to those who had none of the conditions, or either condition alone; the difference, however, was not significant (Pearson chi-square p-value = 0.188). There were also stronger associations between both haematuria and proteinuria in participants with scabies (RR = 1.75 and RR = 1.72) compared to those who did not have scabies, although the difference was not statistically significant (Pearson chi-square p-value 0.703 and 0.715 respectively).

2.3.6 Intestinal helminths

A total of 327 stool samples were submitted during the survey (a return rate of 36%), which ranged between the age groups from 24.8% to 40.4%. The highest sample return rate originated from participants aged 6–15 years (Table 2.15). *Trichuris trichiura* eggs were present in approximately 70% (229/327). Hookworm eggs were present in 15 (4.9%) of the samples, and 1.3% of samples were positive for an unknown trematode species that may have been *Heterophyes heterophyes*. Approximately 5% of the population was positive for more than one intestinal helminth, and one sample was positive for three different parasite species. Analysis for hookworm and the unknown parasites was not conducted due to the small sample size.

	0–5 years	**6–10 years**	**11–15 years**	**Total**
Proportion of samples submitted	28.4%	40.4%	40.2%	36%
Number positive for *T. trichiura*	34	146	43	223
% positive within age group	71.0%	73.0%	61.4%	70.0%
Number positive for hookworm eggs	1	10	4	15
% positive within age group	2.0%	8.0%	4.9%	4.9%
Total population of age group	139	498	282	919*

* Two cases were not included due to missing information on age.

Table 2.15: Prevalence of *Trichuris trichiura* and hookworm by age group on Funafuti, 2006.

There were 223/327 samples positive for *Trichuris* (68.2%) with a consistently high frequency of distribution across the three age groups, ranging from 61.4% to 73.0%. The portion of positive samples was highest in those under 10 years of age, with a decrease of roughly 10% in 11–15-year-olds. There was no significant difference between males and females (Pearson chi-square p-value 0.937). The prevalence of *T. trichiura* in each village varied from 21.3% to 39.5%, with a mean of 25.2%. The rates in all of the villages were similar; they differed by less than 2% from each other with the exception of Teone village, which was higher at 39.5% (Figure 2.11). However, there was no significant difference in the proportion of *T. trichiura* between the villages (Pearson chi-square p-value 0.160).

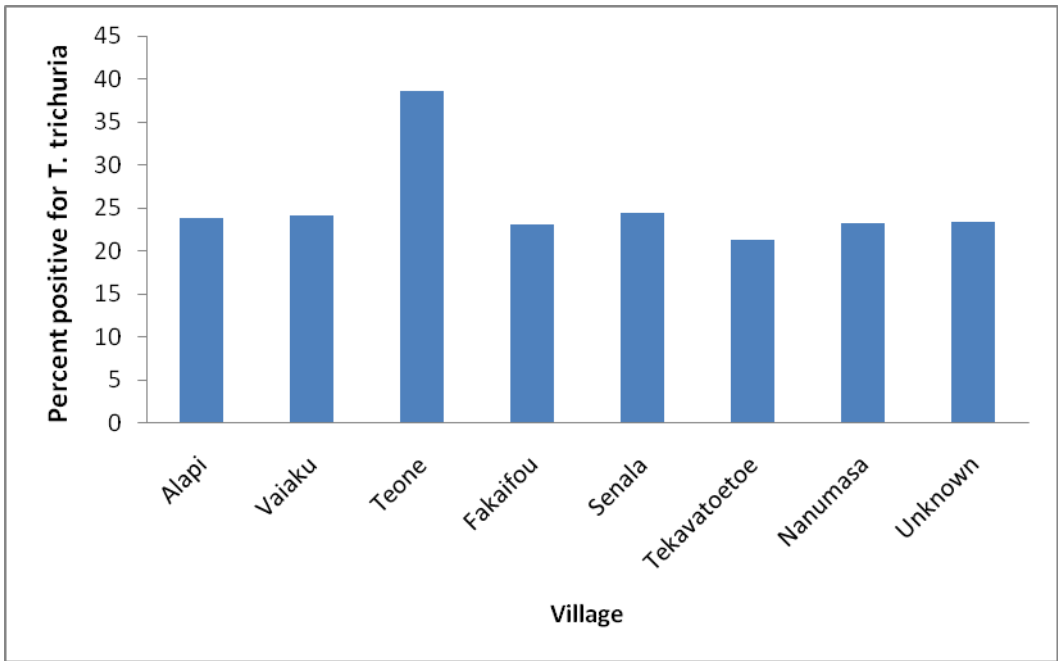

Figure 2.11: Prevalence of *Trichuris trichiura* by village on Funafuti, 2006.

Further examination of the stool specimens (n = 327) for the level of intensity based on the number of eggs per gram of faeces revealed that that majority of samples (78.6%) contained light levels of infection, 20% were classified as moderate infections, and two cases (1.4%) were deemed to be heavily infected with *T. trichiura* eggs (Table 2.16).

Level of infection	**Light** (1–1,000)	**Moderate** (1,000–10,000)	**Heavy** (>10,000)
Cases	180	46	2
% of sample	78.60%	20.0%	1.40%

Table 2.16: Intensity of *Trichuris trichiura* infection in schoolchildren on Funafuti, 2006.

Analysis of participants who submitted a faecal sample showed that 65% of those who were positive for *T. trichiura* also had anaemia. Odds-ratio analysis also indicated an association (1.2) between those who were anaemic and also positive for the parasite compared to those who were anaemic but not positive for the parasite (Table 2.17).

		Positive for *T. trichiura*	
		Yes	No
Anaemia	Yes	142	53
	No	77	49
	RR = 1.2		

RR = 1.2 CI at 95% (1.01–1.54) for anaemia and infection with *T. trichiura.*

Table 2.17: Relative risk for infection with *Trichuris trichiura* and anaemia.

2.3.7 Environmental samples

Results from environmental samples (soil, sand and other ground samples) indicated the presence of *Trichuris* and *Ascaris* eggs in the environment. Trichuris eggs were found in 29.4% of the samples tested and Ascaris eggs in 17.6%; two samples contained eggs from both species. Nematode eggs were found in samples from both public and private locations (Table 2.18). Overall egg counts were categorised as low intensity.

Sample no.	Source	Direct method Eggs per gram	Flotation method Eggs per gram
1	Private home, lagoon side – Senala	Nil	Nil
2	Nauti Primary School – faille	Nil	Nil
3	Nauti Primary School – toilet block	Nil	Nil
4	Main church – Vaikau	Nil	Nil
5	Private home – Fakaifou	Trichuris 70	Nil
6	Private home, near water tank – Vaikau	Nil	Nil
7	Sand from beach, lagoon side – Vaikau	Nil	Nil
8	No sample		
9	Maniapa (main community centre) – Vaikau	Trichuris 4	Nil
10	Salina Preschool – Alapi	Nil	Nil
11	Private home, lagoon side – Tekavatoetoe	Nil	Nil
12	South end of runway – lagoon side	Trichuris 20	Trichuris 2
13	Sports field	Trichuris 40 Ascaris 2	Nil
14	Between private homes – Fakaifou	Ascaris 1	Nil
15	Private home – Teone	Trichuris 8 Ascaris 1	Nil
16	Between private homes – Teone	Nil	Nil
17	Ferry passenger terminal, wharf	Nil	Nil
18	Sand from beach, ocean side – Teone	Nil	Nil
Control 1	JCU	49	2
Control 2	JCU	7	Nil

Table 2.18: Results of analysis of environmental samples taken on Funafuti Atoll, 2006.

2.4 Discussion

This survey is the largest to date of the prevalence and impact of skin infections and other neglected tropical diseases on the child population of Tuvalu. As the survey was conducted on a small isolated population, the possibility of sampling bias was considered in interpreting the results. However, the survey was conducted on the capital atoll of Funafuti and captured almost 80% of the target population and the power of the study was calculated to be 0.9. It is therefore suggested that the results are representative of all children aged 2–14 years in Tuvalu.

Almost half of the children on Funafuti were overweight according to WHO body mass index guidelines, which is consistent with the current worldwide trend towards child and adult obesity, even in developing nations (Misra and Khurana, 2008). The high prevalence of anaemia (60%) found in the population is also consistent with findings in other developing countries (Yip, 2002). However, it is unknown whether the anaemia is due to malnutrition from the lack of iron-rich foods, a high rate of parasitic infection, or a combination of factors.

Two-thirds of stool samples contained *Trichuris trichiura* eggs (including cases of heavy infection), which has been established as an associative factor in iron-deficiency anaemia (Despommier *et al.*, 2000; Huges *et al.*, 2004; Borkow *et al.*, 2007).

Approximately half of all children surveyed had at least one skin condition, and several cases of co-morbidity were identified. The presentation of skin infections in order of decreasing prevalence was pyoderma (38.4%), scabies (8.4%), pyoderma and scabies co-infection (3.8%) and fungal infections (>1%). The prevalence of scabies presentations was likely underestimated due to the difficulties in field diagnosis, especially in those participants with severe bacterial co-infections (Becherel *et al.*, 1999).

The prevalence of scabies (approximately 14%) was similar to that in other developing countries, where it is estimated that up to 9% of the community and 21% of those attending health-care centres are infected in underprivileged settings (Hengge *et al.*, 2006). One of the sequelae of community-wide scabies infection is the facilitation of bacterial colonisation, in which individuals and communities are predisposed to hyper-infection with GAS and other bacterial skin infections.

This may explain the levels of pyoderma seen in the children on Funafuti. Scabies as a health issue is not well addressed by Tuvalu's health-care system as the only treatment currently available is topical benzyl benzoate (and this is not consistently available), which historically has a low rate of compliance (Brockerie *et al.*, 2000; Brooks and Grace, 2002; Lawrence *et al.*, 2005).

The findings of pyoderma are also consistent with other studies in developing settings, including Australian Aboriginal communities and other Pacific nations, where the rate of pyoderma in children can range from 10% to 90% in community and health-care settings under conditions of poverty (Feldmeier *et al.*, 2005; Thomas *et al.*, 2005; WHO, 2005c). Skin swabs of sores were not taken in this survey. However, research has shown that most bacterial skin infections in resource-poor settings are caused by GAS bacteria.(Carapetis, 2005; Carapetis, 1998; WHO, 2005; Lawrence *et al*., 2005) These findings are of particular concern due to the established associations of GAS, including the acute conditions of post-streptococcal glomerulonephritis and rheumatic fever, both of which can progress to serious chronic disease (Carapetis, 1998; Carapetis and Currie, 1998; Berrios *et al.*, 2004; Lawrence *et al.*, 2005; Chin, 2006; National Heart Foundation, 2008).

A handful of cases of rheumatic fever have been documented in Tuvalu, including a 14-year-old patient. A recent increase in the number of patients receiving treatment for rheumatic heart disease has prompted public health officials to conduct ultrasound screening for this condition on Funafuti and the outer atolls, as the true burden of disease is unknown (Simeona, 2007). The exact burden of streptococcal disease in Tuvalu remains unknown, but the combined evidence from epidemiological, clinical and research data suggests that acute streptococcal infections and their associated outcomes are affecting the population.

One-third of all urine samples were positive for proteinuria and/or haematuria. These findings are suggestive of an underlying pathology in the population that may have a deleterious impact on child health. Haematuria is defined as the presence of red blood cells in the urine; however, there is no consensus on the clinical quantification of haematuria (Ledingham and Warrell, 2000). Abnormal proteinuria is considered to be in excess of 0.5 g/day, which coincides with a positive dipstick test for albumin, which has a lower detection limit of 150 mg/L (0.15 g/L) (Walmsley, 2004).

Proteinuria is often a transient phenomenon and can be indicative of benign causes, such as pyrexia, intensive physical activity or acute illness including urinary tract infection (Carroll and Temte, 2000; Ledingham and Warrell, 2000). It is also a symptom of more serious illness, such as glomerulonephritis or other acute kidney dysfunction, which is associated with certain strains of GAS infection (Whittle *et al.*, 1973; Thevenieau, 1981; Verma *et al.*, 1983; WHO, 2005b). Findings demonstrated a higher-than-expected prevalence of abnormal urine results in the samples obtained from the children on Funafuti. Repeated cohort studies in Japan and China have shown the presence of urine abnormalities was >5% upon initial dipstick screening for children without diabetes (Yangagihara *et al.*, 2007; Zhai *et al.*, 2007).

Studies conducted in tropical settings have shown that commercial urine reagent strips have a sensitivity of 95% and a specificity of 75% for detecting proteinuria (Figueroa *et al.*, 1996). However, the limitations of the methodology did not allow for determination of the aetiology of proteinuria. There were 12 children who had both high haematuria and proteinuria, which suggests that the glomerular basement membranes had allowed the passage of red blood cells and albumin, or that these participants may have had a urinary tract infection at the time of collection. The high rates of trace haematuria and proteinuria could also be residual effects of PSGN, which can persist for up to two years (Ledingham and Warrell, 2000), with haematuria persisting longer. The possible diagnosis of post-streptococcal glomerulonephritis is further supported by the high rate of pyoderma presenting during the survey.

There are several confounding factors and limitations to consider, especially as the majority of positive protein results were positive for a trace amount. Contamination, especially from female participants, could also be a contributing factor as urine specimens were not collected in a clinical setting. Other confounding factors that can result in abnormal urine results, such as lymphatic filariasis (Dreyer *et al.*, 2002) and obesity (Filler *et al.*, 2007), were considered. Lymphatic filariasis can result in acute and chronic renal dysfunction even in patients who are otherwise asymptomatic (Dreyer *et al.*, 1992). The most recent published figures found that the prevalence of LF in Tuvalu was 12.1% in 2004 (PacELF, 2008), although it is likely lower due to the additional four rounds of MAD since the last figures were published (Melrose, 2007).

Historically, LF is observed more frequently in adults than children (Ramaiah *et al.*, 2000; WHO, 2005d; Ottesen, 2006) and preliminary unpublished data from the national survey for LF conducted in February 2008 indicated that fewer than 10 children aged under 15 years were ICT card positive for the parasite (Melrose, 2007). The literature and the low prevalence of this disease in the population suggest that LF is not likely to be contributing significantly to renal dysfunction in Tuvaluan children.

Obesity is another possible confounding factor for proteinuria, as this condition is known to cause renal disease (Nelaj *et al.*, 2008; Lamacchia *et al.*, 2009). A study from a Canadian paediatric nephrology clinic concluded that obesity in children was a significant factor in paediatric renal disease (Filler *et al*., 2007). Results demonstrated that there was not an association between being overweight (categorised by a BMI >25) and proteinuria (RR ~1). There was a stronger relative risk (RR 1.28) between haematuria and obesity (BMI >30) than haematuria and overweight (BMI >25); however, the difference was not significant (Pearson chi-square p-value 0.870).

The relative risks for abnormal urine results against presentations for pyoderma showed weak associations (0.77 and 1.1 for haematuria and proteinuria respectively) for those who had pyoderma versus those who did not have the bacterial infection. The strength of association was stronger for scabies infections (RR 1.75 for haematuria and RR 1.72 for proteinuria), suggesting that those who had scabies infection were ~1.75 times more likely to have abnormal urine results than those who were not infected. However, neither association was statistically significant. Real-world clinical and epidemiological patterns indicate a link between these two organisms despite the pathology of synergy between the two infections being poorly understood. These findings suggest that scabies could be more of a contributing factor to the findings of abnormal urine results (the majority of which had trace quantities of protein or blood) than bacterial infections, due to a systemic pathology associated with scabies infection.

Findings also demonstrated that the strongest relative risk for proteinuria among survey participants was observed in participants who were co-infected with scabies and pyoderma, suggesting the possibility that the interaction of the two diseases may produce an additive effect in causing systemic disease that is greater than either infection on its own. One explanation is that individuals with an underlying scabies infection may be predisposed to becoming hyper-infected with bacteria, including strains of GAS that result in more severe disease.

Although the survey did not demonstrate a statistically significant association between systemic disease (as indicated by proteinuria and haematuria) and the targeted skin infections, it did demonstrate a higher-than-expected prevalence of abnormal urine results, and a high prevalence of parasitic and skin infections – all of which are clinically, socially and economically relevant to this population. Overall the urine results suggest that there is a high level of proteinuria and haematuria in the child population and that there are likely to be a multitude of pathologies. The impact of co-morbidity of multiple infectious diseases and other conditions is only recently becoming recognised (Huchinson *et al.*, 1997; Brook, 2002; Folch *et al.*, 2003; Berrios *et al.*, 2004; Feldmeier *et al.*, 2005; Lawrence *et al.*, 2005; Thomas *et al.*, 2005; Hengge *et al.*, 2006).

The three villages with the highest proportions of bacterial infections are located in 'dumping areas' or areas where household and other waste accumulates. This is particularly true of the villages of Nanumasa and Teone, which are situated around 'borrow pits' (Figure 2.12). These pits were created during coral excavation in order to provide materials to construct the runway on Funafuti during World War II. The resulting holes, where children frequently wash and swim, are consistently filled with a mixture of rain and sea water and have consequently become filled with waste from the community. Additionally, pig enclosures are situated on the edge of the pits, causing effluent to be washed into them and adding bacteria and organic matter to the pools.

Figure 2.12: Village of Teone on Funafuti, near the borrow pits, January 2008.

Houses are small, and made of wood and stone. The borrow pits fill with water as tide rises, and also contain rubbish.

These areas are not desirable for habitation; consequently, their occupants are usually non-traditional landowners of Funafuti. Therefore, houses built near the pits are less likely to have sewage systems or water tanks, hence limiting the residents' access to clean water and adequate sanitation. Statistics from the public health department reveal that approximately 30% of all households do not have running water or sanitation facilities, and the majority of such households are located in these communities (Faagai, 2006).

Results indicate that the environment is contaminated with several species of nematode eggs: 29.4% of samples were contaminated with *Trichuris* eggs and *Ascaris* eggs were found in 17.6% of samples. It was not possible to determine the level of contamination or risk association with any particular location, or whether the source of the eggs was human or animal.

Informal surveys conducted by Environmental Health have revealed that up to 30% of the population admit to defecating on the ground, a practice that would result in the environment being continuously contaminated with nematode eggs and perpetuating a cycle of re-infection (Faagai, 2006).

Based on this information and the high prevalence of *T. trichiura* in the survey population, it seems likely that the human population is the source of the Trichuris eggs. Survey results did not identify *Ascaris* eggs in any of the samples, suggesting that the eggs identified in the environmental samples may originate from an animal source. Further studies of the adult and animal population are suggested to assess the community-wide prevalence of STHs and possible zoonotic contamination of the environment.

Limited sanitation facilities are likely the reason for the continued practice of defecating on the ground. The village of Tekavatoetoe has the highest number of households without a septic system, or a toilet of any kind. Hence, residents have to use public toilets or urinate and defecate on the ground. Heavy rains increase the level of water in these areas and residents, especially children, are in more frequent contact with contaminated water. Individually and combined, these environmental factors are likely contributors to the increased proportion of parasitic and bacterial skin infections.

The aetiology of parasitic and skin infections is multi-factorial. The combination of environmental conditions such as those mentioned above, a hot tropical climate and overcrowding are providing ideal conditions for these highly contagious diseases to flourish. This dangerous combination of conditions is the proverbial ‘ticking time bomb’ of existing and emerging infectious diseases and modern-day lifestyle diseases such as obesity and diabetes.

This multi-dimensional co-morbidity may already be having a clinical and subclinical impact on the health of the population, as suggested by the negative health indicators already measurable in the community. The long-term potential consequences resulting from the interactions of these conditions are currently unknown, but the potential to cause disastrous public health issues in Tuvalu exists. In addition to the complications from GAS and scabies, the impact of STHs (and anaemia) has been proven to affect school performance and vaccine efficacy, and to cause increased allergies, increased susceptibility to HIV and tuberculosis (Borkow and Bentwich, 2000; Borkow and Bentwich, 2008) and the possibility of post-partum complications for women as they enter their child-bearing years (Brooker *et al.*, 2008).

Social determinants of health – such as poverty, adequate housing, sanitation and access to clean water, health, and education and community awareness – are contributing to the prevalence of infectious disease in Tuvalu. These factors are facilitating disease transmission in a tropical environment that already favours the existence of those agents. These environmental health issues are likely to be ongoing due to the 'urbanisation' of Funafuti from the outer islands as Tuvaluans relocate to the capital atoll for employment, education and access to services.

Climate change and global warming are predicted to have a direct impact on the islands of Tuvalu (Roberts, 2007). Rising tides and ocean levels will further reduce living space, contribute further to overcrowding, and add additional strain to the country's already limited resources. Rising water levels will also increase the amount of ground water seeping up through the coral, particularly in and around the 'borrow pits'. This will reduce the land area even further and lead to increased flooding (localised or general), which has the potential to result in a greater decrease in sanitation and further faecal contamination.

In summary, the survey findings indicate that Tuvalu has a dual portfolio of infectious and chronic diseases, as seen by the high rates of parasitic and skin conditions in conjunction with the observed high rates of childhood obesity. The global trend of increasing chronic diseases related to obesity has been clearly documented in developed and some middle-income nations (CDC, 2008; Misra and Khurana, 2008; Worley, 2009). While chronic diseases are a significant and emerging public health issue in developing nations, the burden of infectious disease still remains due to socioeconomic and environmental factors. The pattern that is emerging in developing nations is not simply an epidemiological shift from infectious to chronic disease but rather a situation of overlapping of infectious and lifestyle-related conditions (Misra and Khurana, 2008; PAHO, 2009; US Department of State, 2009a).

The epidemiological transition towards emerging chronic disease may further impede the elimination of infectious diseases, especially neglected tropical diseases, as these already under-addressed conditions are likely to be further ignored due to the competing health issues caused by obesity and other lifestyle-related diseases. The compounding effects of these diseases are still unknown but could place enormous strain on already resource-constrained health systems, pave the way for a global health crisis and threaten already-fragile economies (PAHO, 2009; Worley, 2009).

The evidence shows that Tuvalu is a country with the worst conditions of both the developed and developing worlds. A substantial reservoir of parasitic and skin infections demonstrates that neglected tropical diseases have been identified as part of this dual portfolio, and should no longer be ignored by the health-care system. The existing socioeconomic and environmental factors in Tuvalu that are contributing to the transmission of these diseases will pose significant challenges in their eradication. Further information on the epidemiology and scope of these common infections is required in order to gain a comprehensive understanding of the larger communicable-disease picture to understand their impact on the population. Therefore, the following future activities are suggested:

- follow-up of the child cohort on Funafuti 12 months after active case finding and treatment with mebendazole;
- a faecal survey of adults to establish the STH prevalence in the wider community;
- swabs to confirm pyoderma is group A streptococci;
- laboratory confirmation of abnormal urine results for those who screen positive with dipsticks; and
- consideration of oral treatment for scabies to reduce the reservoir of scabies and hence the prevalence of bacterial infections.

The baseline survey was the first step in providing the evidence needed to identify public health issues in the community, to establish a clear baseline for future surveillance activities and to identify gaps in the health-care system and health services. Once available, this information can be used to make evidence-based decisions and to develop specific cost-effective interventions best suited to this resource-constrained country.

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Chapter 3

A follow-up survey of school-aged children on Funafuti for parasite and skin infections after a single round of mebendazole

3.0 Introduction

Figure 3.1: Aerial photo of Funafuti Atoll, Tuvalu (Endou, 2007) .

Tuvalu is a small tropical island nation consisting of nine coral atolls located in the Western Pacific. There is evidence that this isolated population is experiencing a high proportion of parasitic and skin infections, as indicated anecdotally by health-care staff, hospital outpatient clinic data, and a baseline survey conducted in school-aged children in October 2006. The 2006 baseline study was the first comprehensive survey to evaluate the scope and prevalence of intestinal parasites and common skin infections (such as bacterial pyoderma, scabies and dermatophyte infections) in the child population. Additionally, children were evaluated for basic health indicators, including height-for-weight, height-for-age and haemoglobin.

The baseline study recruited 921 children aged 2–14 years. Findings indicated that 51.4% of the survey population had at least one of the targeted skin conditions, and 5% presented with more than one condition (most commonly seen were cases of scabies with a secondary bacterial infection). Bacterial pyoderma was the most commonly seen skin infection, which was most likely due to infection with group A streptococcal and staphylococcal bacteria (Carapetis *et al.*, 2005; WHO, 2005c; Hengge *et al.*, 2006). Intestinal parasites were present in 68.2% of the stool samples. Eggs of the soil-transmitted helminth (STH) *Trichuris trichiura,* or whipworm, were identified in approximately 70% of the samples. Hookworm was detected in a small portion of the samples (4.8%), as well as a few unidentifiable trematode species.

Further evidence of the impact of these pathogens on the child population is suggested by the high prevalence of anaemia in participants, 60% whom met the WHO criteria for anaemia; which is strongly associated with STH infection (Huchinson *et al.*, 1997; WHO *et al.*, 2001). Additionally, approximately 30% of urine samples were dipstick positive for proteinuria and/or haematuria. Both of these findings can be indicative of systemic infection, including infection with group A streptococcal bacteria (Carapetis *et al.*, 1999; Feldmeier *et al.*, 2005).

After sample collection, 97% of all school-aged children on Funafuti Atoll were treated with a standard dose of 400 mg of the antihelminth drug mebendazole, as recommended by WHO to reduce or eliminate helminth loads (WHO, 2003; WHO, 2007a). All active cases of bacterial pyoderma, scabies and dermatophyte infection were referred to the outpatient clinic at Princess Margaret Hospital for treatment. Parents and caregivers present during the survey examinations were educated on the conditions of interest and given advice on hygiene relating to the infections.

The baseline survey indicated a high prevalence of infectious disease, anaemia, abnormal urine results and obesity. Results also revealed that many participants were co-infected with more than one disease, and that co-morbidity with multiple infectious diseases and other conditions appears to have a negative physiological impact on this population. Additional surveillance is required to confirm the prevalence of the targeted infectious diseases and associated conditions to further establish the impact of co-morbidity on the population, and to assess the impact, if any, of the screening and treatment conducted during the baseline assessment.

3.1 Methodology

This study is a follow-up to the initial survey of school-aged children conducted in 2006. It had the following objectives:

- to resurvey for STHs and infectious skin conditions (scabies, pyoderma and dermatophytosis);
- to determine the impact of single-dose mass chemotherapy with mebendazole on reducing intestinal parasites; and
- to provide epidemiological information for evidence-based public health control programmes for these conditions.

The follow-up survey of school-aged children on Funafuti Atoll was carried out by a multidisciplinary team from the School of Public Health, Tropical Medicine and Rehabilitation Sciences from James Cook University. It was conducted over five weeks starting in February 2008, 14 months after the initial survey, and was done in conjunction with the WHO-mandated national survey for lymphatic filariasis (LF)(WHO, 2009c). The surveys were conducted simultaneously to maximise limited human and financial resources as well as minimise distress and disruption to the participants, especially the children.

The situation also provided the opportunity to combine, or 'piggyback', the parasite and skin infection survey with an existing disease control programme, allowing for the evaluation of an integrated multidisciplinary public health strategy.

The national LF survey aimed to screen the entire population of Funafuti (two years and older) and to treat positive cases of LF. Positive LF cases were defined as those who were both ICT card positive and confirmed positive by the presence of microfilaria on a 60 µL blood slide obtained after 3 p.m., as historically in the Pacific region this has been shown to be the most effective time to isolate the parasite in the peripheral blood (Iyengar, 1959; Sasa, 1976). The national survey employed community-based sampling by having designated testing sites in each of the eight villages throughout the atoll. School-aged children (2–14 years) were recruited for the follow-up survey from primary schools and preschools rather than at the community collection points with adults, in order to sample the highest proportion possible of this population while minimising disruption to the children and the school system.

It was thought that these objectives would not be achieved if the children were constantly leaving the classroom to go to their village testing site.

Permission was again granted by the ministries of health and education, and the survey was conducted under the previous ethics approval H2374 granted by the James Cook University Ethics Committee (Appendix 1). The parents of all schoolchildren were informed via the schools and the Department of Public Health through verbal communication and radio announcements. Verbal consent was obtained from the parents of all participating children. Children who were absent on the day the team visited their class were informed of a 'catch-up' session held at the end of the survey period. Participants who required treatment of any kind were referred to the outpatient clinic at Princess Margaret Hospital. Those who presented with more serious health conditions were taken directly to the hospital by a teacher or team member, and their parents were immediately informed. Children who were ICT card positive for LF were retested at community collection points after 3 p.m. for confirmatory diagnosis.

All children in Tuvalu registered in primary school or preschool were treated after data collection with 400 mg of mebendazole, regardless of their participation in the survey. Participants who were positive for LF after confirmatory testing were additionally treated according to WHO treatment protocols. The survey employed consecutive convenience sampling by travelling from classroom to classroom at Nauti and Seventh-day Adventist primary schools and the eight registered preschools (one preschool had closed since the baseline survey).

The survey consisted of a child health check (data included age, gender, height and weight), a skin examination, and requests for blood, urine and stool samples. The biometric variables were then used to calculate height-for-age, weight-for-height and BMI as indicators of the general health of the child population. A peripheral blood sample of approximately 125 µL was obtained by finger-prick using a diabetic lancet. One hundred µL was allocated for the ICT card and 25µL was allocated to assess peripheral haemoglobin (Hb) and analysed on a portable machine (manufactured by HemoCue®). Finger-prick sampling is an established method for point-of-care testing and measures the level of peripheral blood haemoglobin in real time in the absence of laboratory facilities (Munoz *et al.*, 2005).

Finger-prick is less painful and invasive than traditional veni-puncture blood sampling and reduces the risk of needle-stick injuries and blood-borne infection. The HemoCue 201® has shown greater power in detecting anaemia than micro-HcT techniques (Mendrone *et al.*, 2009) and is therefore the preferred method for screening in the field.

Skin examinations were conducted for the following common skin infections: bacterial pyoderma, scabies and dermatophyte infections. Scabies and dermatophyte infections were diagnosed clinically by a trained team member who conducted all of the skin examinations to maintain consistency of diagnosis. All protocols in the survey were the same as those used in the baseline survey; refer to the methods of Chapter 2 for details, including case definitions for skin diseases (Table 2.6).

For the collection of urine and stool specimens, participants or their guardians were given a 5 ml yellow-topped urine specimen container and a 25 ml opaque brown-topped faecal specimen container, both labelled with the participant's unique sample number. Verbal and written instructions in English and Tuvaluan were provided to participants, or to guardians requesting them, to submit both fresh urine and faecal samples to the hospital laboratory. It was emphasised that urine samples needed to be received at the lab within one hour of sample collection to ensure accurate results. Urine samples were stored refrigerated at 4°C. Urine samples were analysed for haematuria and proteinuria using Multistix 10 SG urinalysis dipsticks (manufactured by Bayer; lot #7H09C). This product replaced the former Multistix® 2820, which are no longer manufactured.

Stool samples were collected to test for the presence of STHs. All samples were preserved in 10% sodium acetate formalin (SAF) for transportation to Australia. The samples were then analysed at James Cook University using a modified Kato-Katz method (Appendix 2) as the samples were fixed rather than fresh, which was a requirement for taking the samples into Australia. Data was entered and analysed in SPSS version 15. First and family names were used as a unique identifier, and consecutive sample numbers were assigned to each unique participant. The names were removed once the data had been reconciled with duplicates and unknowns had been removed. For the purposes of this study, results were considered significant if the p-value was >0.05.

3.2 Results

3.2.1 Survey population

A total of 964 children aged 2–14 years were recruited from the two primary schools and eight preschools, representing 78% of the total target population. Males and females were equally represented (482 males and 482 females). The age distribution of the survey participants was consistent with the previous survey, with 13% (126/964) of those recruited aged 0–5 years, 60% (578/964) 6–10 years and 27% (260/964) 11–14 years. Males and females were also equally represented within each of the age groups, and the data was normally distributed according to the numerical variable of age (Table 3.1).

	2006				2008			
Gender	**0–5**	**6–10**	**11–15**	**Total**	**0–5**	**6–10**	**11–15**	**Total**
Male	65	261	134	460	64	295	123	482
Female	74	237	148	459	62	283	137	482
	140	498	282	921	126	578	260	964
	15.0%	54.0%	31.0%		13.0%	60.0%	27.0%	

Table 3.1: Survey population by age and gender, 2006 and 2008.

The follow-up survey recruited and recorded participants from all of the eight villages: Alapi, Vaiaku, Teone, Fakaifou, Senala, Lofeagai, Tekavatoetoe and Nanumasa. The majority of survey participants (54.7%) resided in Fakaifou (23.1%), Senala (17.5%) and Alapi (14.1%), which was only a slight change from the previous survey and was due to a minor demographic shift in the community boundaries for the villages (Figure 3.2).

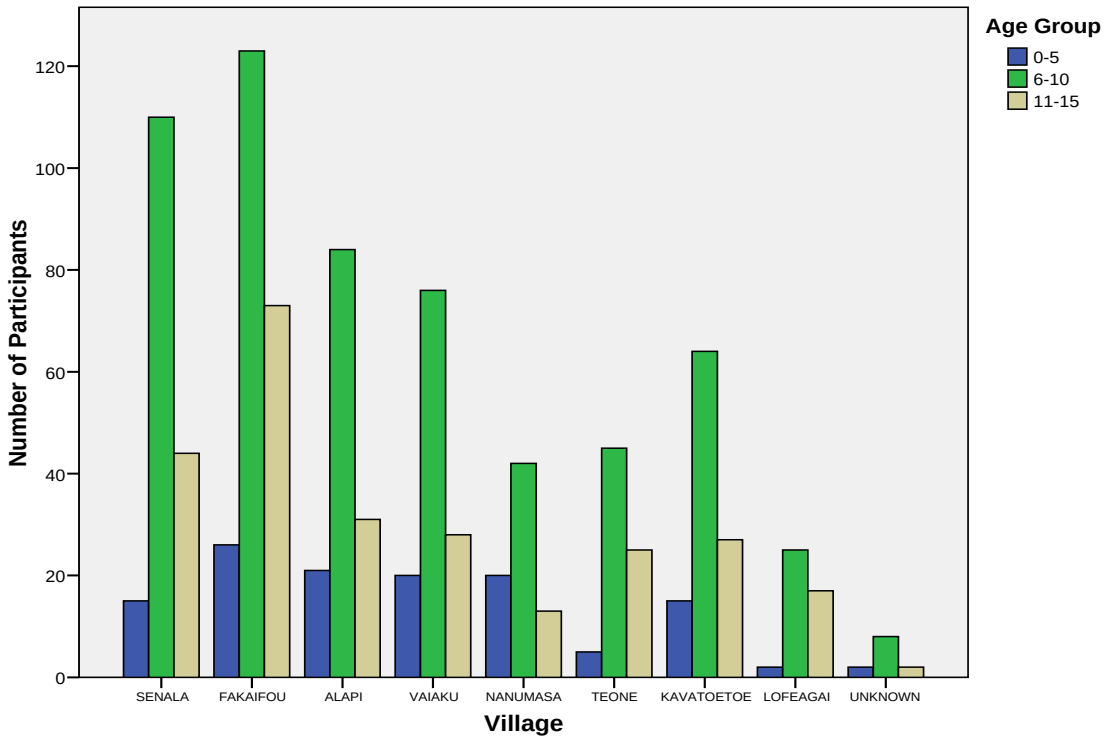

Figure 3.2: Number of participants by age group and village.

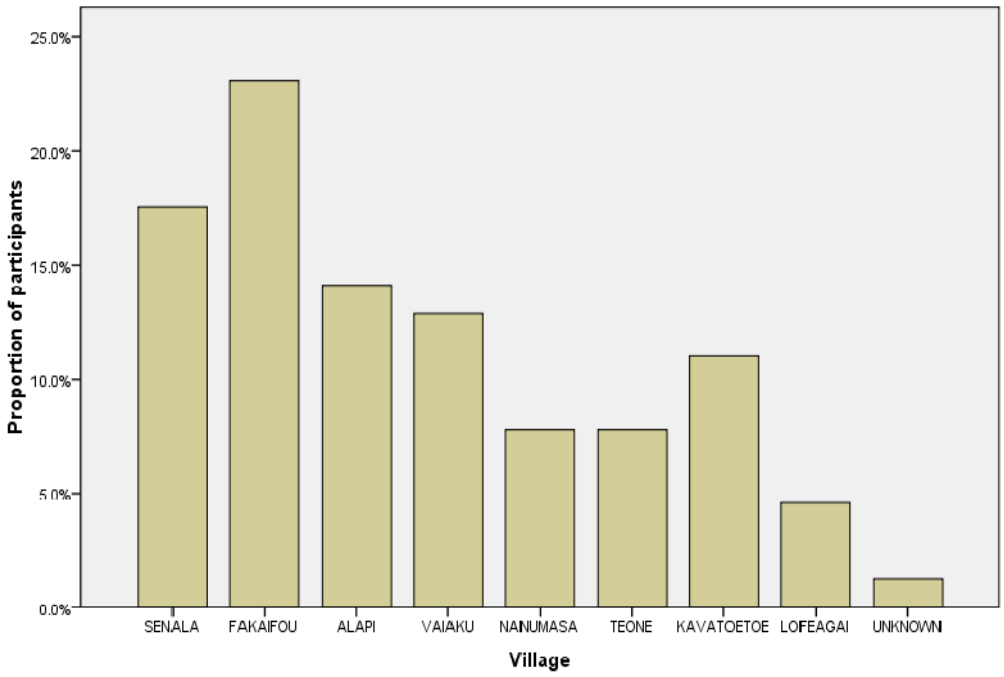

Figure 3.3: Proportion of survey participants by village.

3.2.2 Morphometrics

Analysis of height, weight and age indicated that all survey participants were of normal height for their age; there were no observed cases of stunting as determined by WHO's height-age-weight ratios (WHO, 2006c). The prevalence of obesity remained high, with 34% overweight (BMI>25) and 11.4% obese (BMI>30). There was, however, an overall decrease of 8% in those who were more than +1 SD from the median BMI from the previous survey in 2006.

	Frequency	Percent	BMI	Interpretation
-3 SD	0	0		Severe thinness
-2 SD	10	1		Thinness
-1 SD	34	3.5		Normal range
Median BMI	506	52.5	18–24	Normal range
+1 SD	218	22.6	25	Overweight
+2 SD	78	8.1	30	Obese
+3 SD	32	3.3	40	Morbidly obese

Table 3.2: Distribution of BMI for children aged 5–15 years on Funafuti, 2008.

3.2.3 Anaemia

Haemoglobin results ranged from 68 g/l to 154 g/l , with an overall prevalence of anaemia of 30% according to the WHO definition (WHO *et al.*, 2001), which is a 20% decrease from the previous survey (Pearson Chi-square p-value 0.215). Findings from this survey did not indicate a significant difference in the prevalence of anaemia between males and females (Pearson Chi-square p-value 0.887) or between the age groups with combined males and females (Pearson Chi-square p-value 0.224).

The decrease in the prevalence of anaemia from the baseline survey to the follow-up survey was observed in both males and females, and within most of the age groups. The only exception was in males aged 0–5, where the prevalence remained stable. The observed difference between the age groups was not significant (Pearson Chi-square p-value 0.86).

Age group	Threshold for anaemia*	Mean Hb (CI 95%)	% Anaemia within age group
0–5 years	Hb > 110 g/l	112 (110.0–114.8)	35.0%
6–10 years	Hb > 115 g/l	120 (119.6–120.9)	27.7%
11–15 years	Hb > 120 g/l	124 (122.8–128.8)	31.2%

* Based on WHO Standards 2001

Table 3.3: Prevalence of anaemia by age group in 2008.

	2006				2008			
Age group	**Number surveyed**	**Total anaemia**	**Female**	**Male**	**Number surveyed**	**Total anaemia**	**Female**	**Male**
0–5 years	136	52.9%	53.0%	46.7%	123	35.0%	27.9%	41.9%
6–10 years	493	65.4%	47.6%	52.4%	571	27.7%	27.8%	27.6%
11–15 years	281	58.2%	52.5%	47.5%	260	31.2%	33.1%	29.1%
Unknown	*11				*10			
Total	921	50.0%	456	454	964	30.0%	480	474

Table 3.4: Prevalence of anaemia by age group and gender, 2006 and 2008.

There were two cases in the 2006 data set and 10 cases in the 2008 data set that were recorded without age or gender.

3.2.4 Skin diseases

Skin examinations of participants showed that 63.8% (613 cases) had at least one skin infection, which is an overall increase of approximately 5% from the baseline survey. There were 467 cases (48.4%) that presented with more than one skin condition, and 6.1% (59 cases) presented with all three targeted infections: scabies, pyoderma and dermatophytosis. Scabies was the most commonly seen presentation (41.2%), followed by pyoderma (40.8%) and dermatophyte infections (15.0%). Scabies co-infection (scabies with a secondary bacterial or dermatophyte infection) was seen in 24.7% of the participants, an increase of 21% from the previous survey. Scabies and pyoderma co-infection was the most common co-infection (22.9%), while scabies with a dermatophyte co-infection had a prevalence of 7.8% (75 cases). Skin infections were again most prevalent in those younger than 10 years of age, with 77% presenting with at least one infection (T-test mean 8.86 years). There was no significant difference in the prevalence of skin infections between the age groups (ANOVA mean 8.5 years p-value 0.197), or between males and females (Pearson chi-square p-value 0.105).

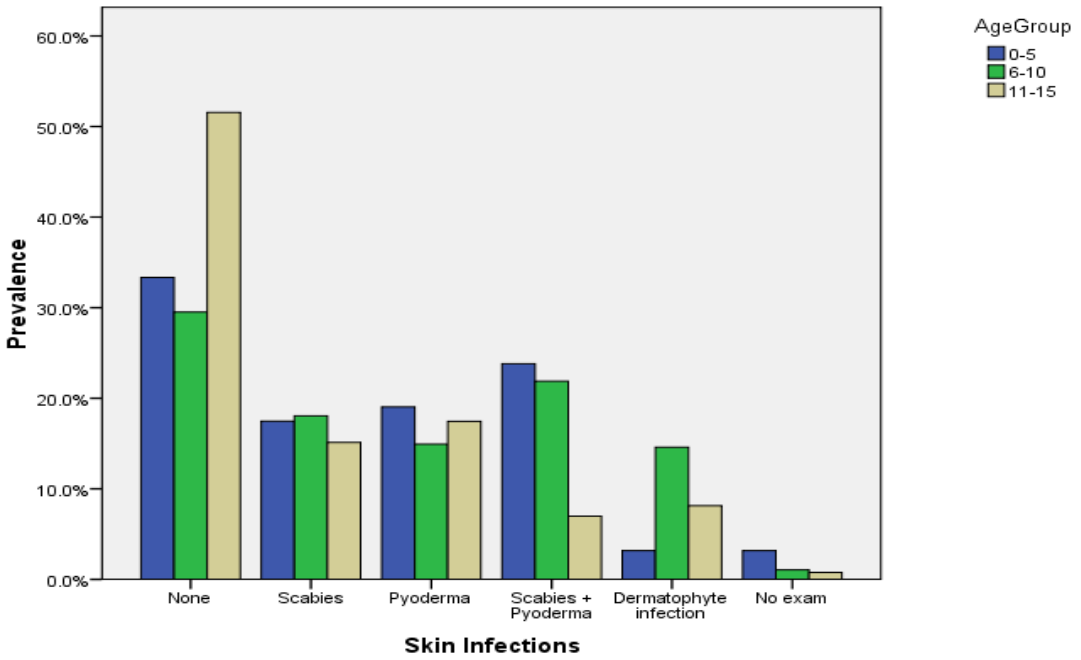

Figure 3.4: Prevalence of skin infections by age group on Funafuti, 2008.

	2006		2008			
Skin condition	**Frequency**	**Percent**	**Frequency**	**Percent**	**Confidence interval (95%)**	**Difference**
No infection	351	**38.10%**	347	**36.10 %**		**-2.00%**
Scabies	77	**8.40%**	397	**41.20 %**		**32.80%**
Pyoderma	352	**38.40%**	393	**40.80 %**		**2.40%**
Scabies co-infection	35	**3.80%**	238	**24.70 %**		**21.00%**
Dermatophyte infection	6	**0.70%**	145	**15.00 %**		**14.30%**
No examination	100	**10.60%**	12	**1.25%**		**-9.40%**
Total	921	**100.00%**	960	**100.00 %**		

Table 3.5: Comparative prevalence of skin infections among survey participants on Funafuti, 2006 and 2008.

A significant increase (32.8%) in the prevalence of scabies (Pearson Chi-square p-value 0.049) and dermatophyte infections (14.3%) (Pearson Chi-square p-value 0.019) was observed between the baseline and follow-up surveys. There was also a significant increase in scabies, and scabies co-infection with pyoderma was seen within each age group, ranging from 8% to 40%; the largest increase (40%) was observed in those younger than 10 years of age (Pearson Chi-square p-values all <0.05). Dermatophyte infections were more common in older participants and the proportion was highest in 6–10-year-olds (Table 3.5). Pyoderma was the only skin infection to remain unchanged (40%).

	No infection		**Scabies**		**Pyoderma**		**Scabies (infected)**		**Dermatophyte**	
Age group in years	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**
0–5	39.3%	**33.3%**	15.0%	**43.6%**	36.4%	**44.4%**	2.9%	**26.2%**	0.7%	**6.3%**
6–10	34.6%	**30.0%**	7.6%	**48.0%**	39.2%	**46.20%**	4.4%	**28.5%**	0.6%	**18.5%**
11–15	44.0%	**50.0%**	16.4%	**24.0%**	37.9%	**26.0%**	3.2%	**8.5%**	0.7%	**11.1%**

Table 3.6: Comparative prevalence of skin infections by age-group on Funafuti, 2006 and 2008.

The prevalence of scabies in the villages varied from 11.9% in Alapi to 22.7% in Lofeagai, and the prevalence of pyoderma ranged from 12.0% in Nanumasa to 24.5% in Kavatoetoe. The prevalence of scabies and pyoderma co-infection showed the greatest variability between villages, ranging from 18.1% in Fakaifou to 40.0% in Nanumasa. However, none of the differences in the prevalence of the above-mentioned skin diseases between the villages was significant (Pearson Chi-square p-values were greater than 0.05).

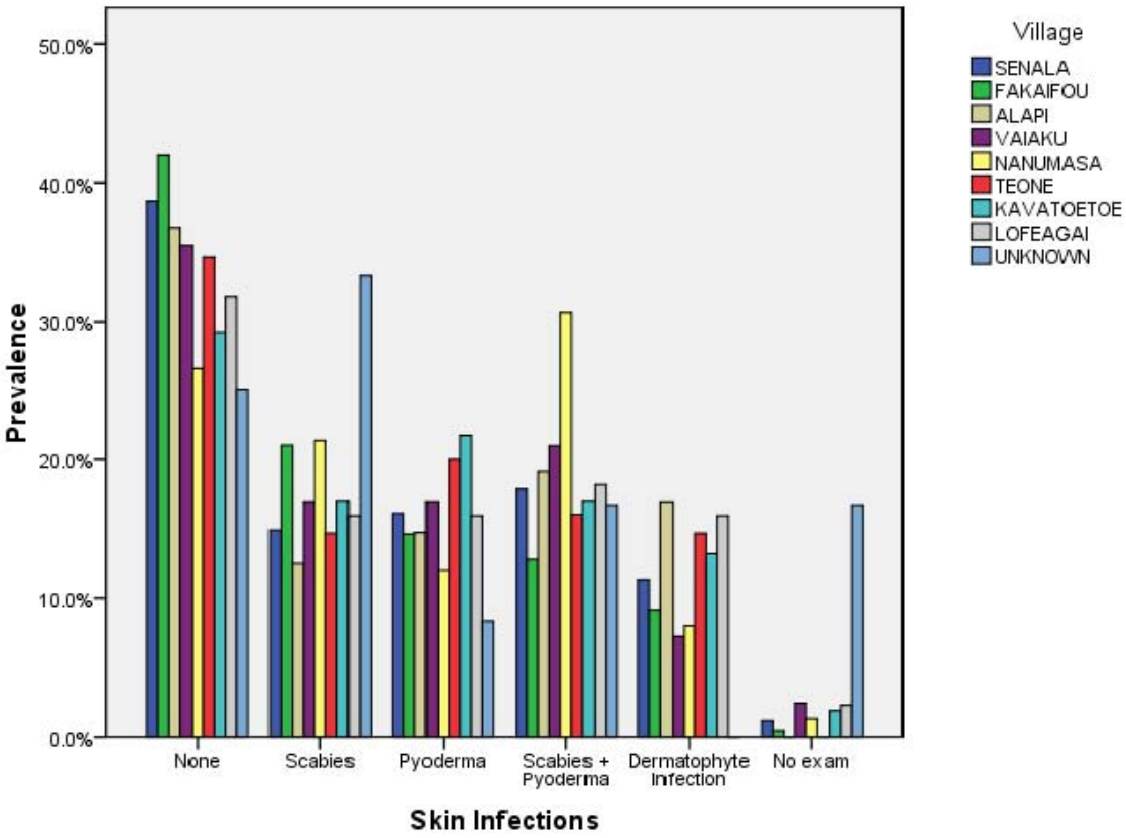

Figure 3.5: Prevalence of skin infections by village, 2008.

Table 3.7: Comparative prevalence of skin infections by village on Funafuti Atoll, 2006 and 2008.

		No infection		Scabies		Pyoderma		Scabies (infected)		Dermatophyte infections	
		2006	2008	2006	2008	2006	2008	2006	2008	2006	2008
SENALA	Number of cases	46	62	46	23	43	31	4	41	1	8
	% within village	41.8%	37.1%	41.8%	13.8%	39.1%	18.6%	3.6%	24.6%	0.9%	4.8%
FAKAIFOU	Number of cases	110	91	21	48	105	37	12	40	2	4
	% within village	38.6%	41.2%	7.4%	21.7%	36.8%	16.7%	4.2%	18.1%	0.7%	1.8%
ALAPI	Number of cases	49	51	11	16	51	18	3	37	1	13
	% within village	37.7%	37.8%	8.5%	11.9%	39.2%	13.3%	2.3%	27.4%	0.8%	9.6%
VAIAKU	Number of cases	58	44	58	21	59	22	4	32	2	2
	% within village	39.2%	35.5%	39.2%	16.9%	39.9%	17.7%	2.7%	25.9%	1.4%	1.6%
NANUMASA	Number of cases	7	20	4	15	14	9	2	30	0	0
	% within village	23.3%	26.7%	13.3%	20.0%	46.7%	12.0%	6.7%	40.0%	0.0%	0.0%
TEONE	Number of cases	18	24	3	12	19	17	3	17	0	5
	% within village	41.8%	32.0%	7.0%	16.0%	44.2%	22.7%	7.0%	22.7%	0.0%	6.6%
TEKAVATOETOE	Number of cases	18	28	9	18	25	26	3	25	0	7
	% within village	29.5%	26.4%	14.8%	17.0%	41.0%	24.5%	4.9%	23.6%	0.0%	6.6%
LOFEAGAI	Number of cases	N/A	12	N/A	10	N/A	6	N/A	13	N/A	2
	% within village	N/A	27.3%	N/A	22.7%	N/A	13.6%	N/A	29.6%	N/A	4.5%
UNKNOWN	Number of cases	45	3	12	4	35	1	4	2	0	0
	% within village	41.3%	25.0%	11.0%	33.3%	32.1%	8.3%	3.7%	16.7%	0.0%	0.0%

3.2.5 Urine results

The sample return rate for both urine and stool samples were lower in 2008 than the previous survey in 2006. There were 326 returned urine samples (return rate of 34%). The overall prevalence of haematuria decreased from 30.2% in 2006 to 21% in 2008, while the overall prevalence of proteinuria increased to 51.2% from 35.7% in 2006. There was also an increase in the proportion of participants who were positive for both, from 5% in 2006 to 13% in 2008. All of the above changes were not statistically significant as the Pearson Chi-square vales were all greater than 0.05.

Haematuria was quantified as trace in 74.2% (52/70), moderate in 12.9% (9/70) and large in 12.9% (9/70) according to the gradient on the dipstick. These results were similar to findings from the initial survey, as demonstrated in Table 3.8. There was no significant difference in the prevalence of haematuria between males and females (Pearson Chi-square p-value 0.887) or between age groups (Pearson Chi-square p-value 0.224). The overall prevalence of proteinuria (<1.5 g/L) was 51.2% (167). According to the gradient on the dipstick, 82.6% were quantified as trace protein, 13.8% were moderate (30 to 100 g/L) and 3.6% were large (300 to 2000 g/L).

	Quantified haematuria by category			**Quantified proteinuria by category**		
	Trace	**Moderate**	**Large**	**Trace**	**Moderate**	**Large**
2006	55.5%	35.2%	9.3%	76.2%	15.6%	8.2%
2008	74.2%	12.9%	12.9%	82.6%	13.8%	3.6%

Table 3.8: Comparison of the proportion of haematuria and proteinuria by category, 2006 and 2008.

Further analysis was conducted of the subset of survey participants who submitted a urine sample and had a skin examination (n=317) to determine if there was an association between any of the targeted conditions and haematuria or proteinuria (Table 3.9).

Clinical variable and association	Relative risk 2006	Relative risk 2008	Pearson Chi-square p-value
Pyoderma + haematuria	0.77 (CI 0.59–0.99)	**1.24 (CI 0.99–1.56)**	1.180
Pyoderma + proteinuria	1.1 (CI 0.90–1.39)	0.97 (CI 0.79–1.2)	0.900
Scabies + haematuria	**1.75 (CI 1.04–2.94)**	1.1 (CI 0.08–1.47)	0.786
Scabies + proteinuria	**1.72 (CI 1.03–2.87)**	0.8 (CI 0.66–0.09)	0.531
Scabies + pyoderma + haematuria	1.21 (0.46–3.22)	**1.29 (CI 0.8–1.9)**	0.219
Scabies + pyoderma + proteinuria	**2.23 (0.90–5.55)**	**1.59 (CI 1.2–2.4)**	0.269
Overweight + haematuria	1.09 (0.73–1.63)	1.1 (CI 0.08–1.94)	**0.036**
Overweight + proteinuria	0.97 (0.66–1.43)	1.2 (CI 0.08–1.69)	**0.049**
Obese + haematuria	1.28 (CI 0.66–2.54)	1.2 (CI 0.56–2.86)	0.623
Obese + proteinuria	1.00 (CI 0.5–2.01	1.2 (CI 0.56–2.86)	0.062

Table 3.9: Relative risk for haematuria and proteinuria and pyoderma infection, 2006–2008.

Statistical analysis of the association between abnormal urine results and the targeted conditions once again indicated that the strongest association was observed in participants with proteinuria who were also co-infected with scabies and pyoderma (RR 1.59), compared to participants who did not have any of these conditions or had either condition alone. The two other notable associations were seen in patients with haematuria who presented with either pyoderma (RR 1.24) or pyoderma and scabies co-infection (RR 1.29), compared to participants who did not present with these skin infections. There was a significant association observed between participants who had either haematuria or proteinuria and who were also obese (BMI>25), compared to those participants who were not obese (Pearson Chi-square p-value 0.036 and 0.049).

3.2.6 Soil-transmitted helminths

A total of 214 faecal samples were submitted, which is a return rate of 22% and a reduction of 14% from the previous survey. Laboratory analysis of the stool specimens indicated that 59% (126/214) were positive for STHs, a decrease of 10% from 2006 (Pearson Chi-square 0.555). The most commonly seen infection was again *T. trichiura* (58%); however, there was an 11% decrease in prevalence from the previous survey. There was also a 3% decrease in the prevalence of hookworm eggs, from 5% in 2006 to 2% in 2008. Four samples were positive for both *Trichuris* and hookworm eggs, also a decrease from the baseline survey. There were two samples with unknown trematode species that may have been *Heterophyes heterophyes*. Analysis for hookworm and the unknown parasites was not conducted due to the small sample size.

	2006				2008			
	0–5 years	6–10 years	11–15 years	Total	0–5 years	6–10 years	11–15 years	Total
Proportion of samples submitted	28.4%	40.4%	40.2%	36.0%	8.8%	73.6%	17.6%	22.0%
Number positive for *T. trichiura*	34	146	43	223	9	91	22	122
% positive within age group	71.0%	73.0%	61.4%	70%	47.4%	57.0%	62.8%	58.0%
Number positive for hookworm eggs	1	10	4	15				
% positive within age group	2.0%	8.0%	4.9%	4.9%				
Total population of age group	139	498	282	919*	126	568	269	964

Table 3.10: Prevalence of *Trichuris trichiura* by gender and age group on Funafuti.
Four cases were not included due to missing information on age.

The majority of samples (73.6%) were submitted from the 6–10-year-old age group. It was observed that the prevalence of *Trichuris* increased with age and the highest prevalence was seen in the 11–15-year-old group. The difference between the age groups was not significant (Pearson Chi-square p-value 0.503). Infection with *T. trichiura* was significantly higher in females (67%) than males (42%) (Pearson Chi-square p-value <0.05) and the number of samples submitted from males and females was equal, 104 and 109 respectively. The decrease in the prevalence of *Trichuris* infection was observed in all age groups but was only significant in 0–5-year-olds (Pearson Chi-square p-value <0.05).

The prevalence of *Trichuris* in the villages ranged from 6.8% to 21.1%, although the difference was not significant (Pearson Chi-square p-value 0.887). The mean prevalence of Trichuris infection decreased from 22% in 2006 to 12.7% in 2008, and decreases were seen in all villages (Pearson Chi-square p-value 0.256). A graph of the 2008 survey results indicates that the prevalence of *T. trichiura* is proportional to population size with the exception of the village of Tekavatoetoe, which had the highest prevalence per population (Figure 3.6).

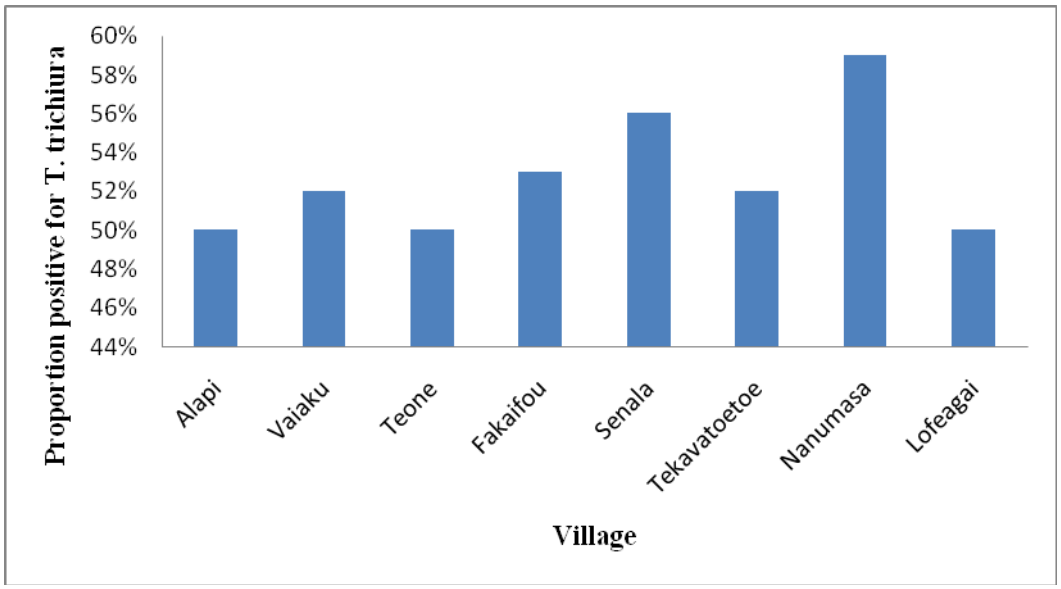

Figure 3.6: Prevalence of *Trichuris trichiura* by village on Funafuti, 2008.

	Level of infection	Light (1–1,000)	Moderate (1,000–10,000)	Heavy (>10,000)
2006	Cases	180	46	2
	% of positive samples	78.6%	20.0%	1.4%
2008	Cases	108	11	0
	% of positive samples	84.0%	16.0%	0.0%

Table 3.11: Intensity of *Trichuris trichiura* infection in schoolchildren on Funafuti, 2008.

(Category of intensity based on Huges *et al*., 2004)

Examination of the 124 faecal samples that were positive for *T. trichiura* eggs indicated that the majority of samples (84%) could be categorised as light infections (<1000 eggs per gram of faeces), 16% indicated moderate infection (1,000–9,999 eggs per gram of faeces) and there were no cases of heavy infection (>10,000 eggs per gram of faeces). This represents a reduction in the intensity of infection of *T. trichiura* in the stool samples obtained during the follow-up survey.

A shift in the proportion of moderate cases to light cases was also observed. Overall, there was a decrease in intensity of infection as the geometric mean number of Trichuris eggs per gram of stool decreased significantly from 227.5 eggs per gram in 2006, to 32.2 eggs per gram in 2008 (Mann-Whitney p-value 0.00).

		Positive for *T. trichiura*	
		Yes	No
Anaemia	Yes	34	83
	No	23	73

RR=1.1

Table 3.12**: Odds ratio of the relative risk for infection with *T. trichiura* and anaemia.**

RR=1.1 CI at 95% (0.87–1.45) for anaemia and infection with *T. trichiura*.

Further analysis of participants who submitted a faecal sample did not demonstrate a significant association between those who were anaemic and infected with *T. trichiura* and those who were not positive for the parasite (Pearson Chi-square p-value 0.403). The weak association between these two variables was observed in both surveys.

3.3 Discussion

This large-scale survey was a follow-up survey on Funafuti Atoll of the prevalence and impact of skin infections and other neglected tropical diseases on a cohort of children aged 2–15 years. This survey, parallel to the baseline survey, captured a high proportion of the target population (78%) and therefore the results can be considered representative of the true burden of disease in the child population of Tuvalu.

Results of the follow-up survey indicated a high prevalence in the survey population of multiple infectious pathogens and chronic diseases as well as co-morbidity. The prevalence of overweight and obese children remained unchanged at 45.4%, with approximately one-third being overweight and 11.4% obese. This finding supports the conclusion that the level of childhood (and likely adult) obesity in Tuvalu is consistent with global trends that indicate that obesity is on the rise in developing nations (Misra and Khurana, 2008; WHO, 2008d; Francais *et al.*, 2009). Overweight and obesity in childhood can lead to serious long-term health consequences, including diabetes, cardiac disease, and renal disorders (CDC, 2008; WHO, 2008d). In addition to the negative physiological outcomes of obesity, the literature indicates that overweight and obese individuals suffer from social stigmatisation and ridicule, and in general are prone to reduced quality of life (CDC, 2008; Latner *et al.*, 2009; Zabelina *et al.*, 2009).

As a developing nation, Tuvalu has limited resources to allocate to health and medical services. There is one tertiary health-care centre located on the main atoll of Funafuti, limited medical staff and no facilities for dialysis. Given the prevalence of obesity indicated in this population, the burden of disease it creates through patient care and consequences from the associated outcomes, obesity alone has the potential to exceed the health-care capacity of this small country.

The 20% decrease in the prevalence of anaemia was paralleled by a decrease in both the prevalence and intensity of *Trichuris trichiura* infection from the baseline survey in 2006. Infection with *T. trichiura* has been strongly associated with anaemia (Despommier *et al.*, 2000; Huges *et al.*, 2004; Borkow and Bentwich, 2008). It is possible that the reduction in the prevalence of anaemia is highly attributable to a reduction in the prevalence and intensity of this parasite due to the mass treatment with mebendazole. The decrease in anaemia may also be attributed to dietary changes, such as an increase in the consumption of iron-rich foods; however, as the population's dietary habits were not included in the survey it is not possible to determine the cause of the decrease in anaemia.

There was an increase in the number of children presenting with infectious skin diseases in 2008. A particular concern is the increase in scabies to 40%, indicating that the proportion of scabies now parallels the proportion of bacterial infections in children. There was also an increase in the presentations of co-infection with scabies and pyoderma. The follow-up survey confirmed that the prevalence of scabies and other skin infections is similar to that in other developing nations (Feldmeier *et al.*, 2005; WHO, 2005c; WHO, 2005b; Hengge *et al.*, 2006), especially in tropical settings (Mahe, 2001; Tyring, 2006; Campbell and Campbell, 2007). Overall survey findings demonstrated that skin infections, scabies and dermatophyte infections, in particular, are on the rise in Tuvaluan children.

The overall increase in skin infections, especially scabies, may be a reflection of several factors. Scabies and other skin infections are diseases of overcrowding and decreased hygiene (Becherel *et al.*, 1999; Heymann, 2004). Increased migration to Funafuti Atoll from the outer atolls (Government of Tuvalu, 2006) has resulted in increased overcrowding of households throughout Tuvalu (Faagai, 2006). Overcrowding is placing a strain on an already resource-constrained environment, especially on the availability of adequate housing and clean water. The rise in population has increased the average number of individuals living in each household, and the scarcity of land places limitations on the building of new homes.

The increase in population has also decreased the availability of water for bathing and other hygienic functions for each individual within a household environment, as one-third of all households on Funafuti do not have running water or sanitation facilities (Faagai, 2006). The combination of increased population density and decreased sanitation creates ideal conditions for skin and parasitic diseases (Despommier *et al.*, 2000; Carapetis *et al.*, 2004; Flint *et al.*, 2007).

The increase in the prevalence of scabies and dermatophyte infections could also be attributed to the limited treatment options available in Tuvalu. During both surveys it was observed that the hospital pharmacy did not stock treatment for dermatophyte infections and had only limited quantities of benzyl benzoate for scabies treatment. Benzyl benzoate liquid is an effective topical treatment for scabies when used appropriately. However, it produces a burning sensation when applied to broken skin, which is a frequent condition in patients with scabies. Like other topical treatment, it requires two applications for effective treatment of the parasites. Therefore, compliance is often low with this treatment, as described in the literature (Brockerie *et al.*, 2000; Brooks and Grace, 2002; Lawrence *et al.*, 2005). Discussions with the local public health department indicate that scabies is a common presentation at the hospital outpatient clinic and the supply of topical scabies treatment is often inadequate and inconsistent (Conway, 2007). Compliance issues notwithstanding, survey results suggest that the current supply of scabies treatment could not meet the burden of disease in the community. Considering the high burden of disease and the compliance issues associated with topical treatments, an alternative treatment for scabies could be considered.

The high prevalence of scabies is also a likely contributor to the prevalence of pyoderma observed in the study population. Pruritis (itching), the hallmark symptom of scabies infection (Becherel *et al.*, 1999; Carapetis *et al.*, 2004; Hengge *et al.*, 2006), frequently results in abrasions of the skin due to intense scratching (Weissharr *et al.*, 2008; Hafner, 2009). These micro-breaks in the skin facilitate the colonisation of bacteria, including group A streptococcal bacteria (GAS).

The literature states that the rate of pyoderma in children can range from 10% to 90% in community and health-care settings under conditions of poverty (Mahe and Fanello, 2003; Feldmeier *et al.*, 2005; Thomas *et al.*, 2005; WHO, 2005c). The results from Tuvalu are consistent with these global findings as the data from both surveys indicates a high prevalence of pyoderma (40%). The profile of age and geographic distribution of this skin disease remained consistent during both surveys, suggesting the distribution of pyoderma is community-wide and pointing to the existence of a sustainable reservoir of bacterial pyoderma in the community.

A collective review of the burden of pyoderma demonstrates that the majority of pyoderma in developing countries is attributable to GAS (Carapetis *et al.*, 1999; Carapetis *et al.*, 2005; Lawrence *et al.*, 2005; WHO, 2005c). Colonisation with GAS can lead to a range of acute bacterial infections that vary in severity from topical dermatological infections, such as impetigo, cellulitis and even bacterial sepsis caused by invasive GAS (Bisno and Stevens, 1996; Carapetis *et al.*, 1999; Currie and Carapetis, 2000; Brook, 2002; Hengge *et al.*, 2006; Weissharr *et al.*, 2008).

Infection with GAS can also lead to more serious acute health outcomes, including post-streptococcal glomerulonephritis (PSGN) and rheumatic heart fever; which in turn can lead to the chronic conditions of cardiac and renal dysfunction (Carapetis, 1998; Carapetis and Currie, 1998; Currie and Carapetis, 2000; Currie and Brewster, 2001; WHO, 2005b; Chin, 2006; McDonald *et al.*, 2007; National Heart Foundation, 2008). Skin or throat carriage of GAS bacteria can also predispose individuals to long-term complications, including life-long impairment of renal and cardiac function, and even mortality (Rajajee, 1990; Jasir *et al.*, 2000; WHO, 2001; WHO, 2005b; CRCAH, 2006). Clinical cases of rheumatic fever have already been documented in Tuvalu, including a 14-year-old patient. An increase in the number of patients receiving treatment for rheumatic heart disease prompted public health officials to conduct ultrasound screening for this condition on Funafuti and the outer atolls (Simeona, 2007).

Repeated urinalysis indicated the overall prevalence of abnormal urine results remained consistent at approximately 30%. Survey results indicated a 30% prevalence of abnormal urine results in Tuvaluan children, which is higher than the established prevalence of 5% or less in children in developing settings (Yangagihara *et al.*, 2007; Zhai *et al.*, 2007), where the sensitivity and specificity of commercial urine reagent strips for detecting proteinuria is 95% and 75% respectively (Kaiser *et al.*, 1992).

The consistent findings of haematuria and proteinuria are suggestive of underlying pathology in the population that may be having a deleterious impact on child health. Proteinuria is protein in the urine in excess of 0.5 g/day (Walmsley, 2004) and is often a transient phenomenon that can be indicative of common causes such as pyrexia, intensive physical activity or acute illness, including urinary tract infection (Carroll and Temte, 2000; Ledingham and Warrell, 2000). Haematuria, the presence of red blood cells in urine, is not found under normal conditions (Ledingham and Warrell, 2000).

Both findings can be indicative of more serious pathology, including systemic infections and conditions such as PSGN, an acute renal disorder associated with certain strains of GAS (Rajajee, 1990; Shelby-James *et al.*, 2002; WHO, 2005b; WHO, 2005c).

Further support for the hypothesis of PSGN is demonstrated by the association between scabies, pyoderma and abnormal urine results. The highest relative risk (RR) coefficients, and hence the strongest associations with abnormal urinalysis, were seen in patients who had scabies, pyoderma or co-infection with both skin diseases, compared to those who did not have these infections. Also, the highest RR for abnormal urine results was associated with those who were co-infected with both scabies and pyoderma, compared to those who did not have these infections or those who had either infection alone. This result was observed in both surveys. Assuming that the majority of pyoderma is attributable to streptococcal bacteria (WHO, 2005b; WHO, 2005c; Tyring, 2006), then the observed association between proteinuria and haematuria and pyoderma infection in this study is consistent with PSGN, as described in the literature (Carapetis *et al.*, 1999; Goodfellow *et al.*, 1999; Currie and Brewster, 2001; Berrios *et al.*, 2004; Carapetis *et al.*, 2005; Feldmeier *et al.*, 2005; Lawrence *et al.*, 2005).

The associations observed in both sets of survey data also suggest that scabies has a larger role in PSGN than originally thought. While the literature supports the link between pyoderma and PSGN (Whittle *et al.*, 1973; Goodfellow *et al.*, 1999; Lawrence *et al.*, 2005; WHO, 2005b), the underlying pathology of scabies infection remains unclear. Historical research in developing settings has demonstrated an epidemiological link between scabies epidemics being followed by epidemics of PSGN in Nigeria (Whittle *et al.*, 1973), New Caledonia (Thevenieau, 1981), Papua New Guinea (Bowness *et al.*, 1984; Montgomery, 1985), Trinidad (Svartman *et al.*, 1972; Reid and Poon-King, 1990), Chile (Berrios *et al.*, 2004) and Peru (Rodriguez, 2004).

The repeated association between scabies and pyoderma observed in the surveys also suggests the existence of an interactive pathological mechanism from these diseases, which in combination produce an additive effect greater than either infection on its own. One possible explanation is that individuals with an underlying scabies infection may be predisposed to becoming hyperinfected with bacteria, including strains of GAS, which can result in more severe disease (Bisno and Stevens, 1996; Carapetis *et al.*, 1999; Brook, 2002; Carapetis *et al.*, 2005). Another theory suggests an interaction between scabies infection and certain strains of GAS serotype-M, which is linked with PSGN (Reid and Poon-King, 1990; Goodfellow *et al.*, 1999; Berrios *et al.*, 2004).

There are numerous examples in the last 40 years that have recognised the epidemiological and clinical link between the scabies mite and bacterial pyoderma attributed to GAS, and the subsequent negative health outcomes, such as acute and chronic renal and cardiac disease (Whittle *et al.*, 1973; Verma *et al.*, 1983; Carapetis, 1998; Brook, 2002; Feldmeier *et al.*, 2005; Hengge *et al.*, 2006; McDonald *et al.*, 2007; Weissharr *et al.*, 2008). The majority of evidence that supports the pathway of disease progression with scabies and GAS leading to chronic renal and cardiac dysfunction comes from Australian Aboriginal communities (Carapetis, 1998; Carapetis and Currie, 1998; Carapetis *et al.*, 1999; Currie and Carapetis, 2000; Currie and Brewster, 2001; Shelby-James *et al.*, 2002; CRCAH, 2004; McDonald *et al.*, 2007; National Heart Foundation, 2008).

Perhaps the most convincing evidence of the link between scabies, pyoderma and renal disease is seen in the results of the study conducted by Lawrence *et al*. (2005) in the Solomon Islands, which demonstrated that the prevalence of renal damage decreased to almost zero following a 96% decrease in the prevalence of scabies after mass treatment with ivermectin. The potential role of scabies as a direct or synergistic contributor to PSGN has only recently been recognised and is being more actively investigated. As the role of scabies and host immune response is presently not well understood, the parasite cannot be excluded in the pathogenesis of renal disease (Hay, 2003).

The survey methodology did not allow for differentiation of the aetiology of proteinuria. Results demonstrated an increase in the prevalence of proteinuria, and an increase in the proportion of children who had both proteinuria and haematuria. This could be indicative of leaking in the glomerular basement membrane, allowing the passage of red blood cells and albumin, and could be a residual effect of PSGN. It is also possible that participants may have been experiencing a urinary tract infection at the time of sample collection. However, considering the higher-than-expected prevalence of haematuria and proteinuria, in conjunction with the generalised distribution of pyoderma (40%) in this population, it is suggestive of PSGN.

There are a number of confounding factors that could have contributed to the findings of abnormal urinalysis. The specimens were not collected in a clinical setting, allowing for the possibility that samples may have been contaminated, especially from female participants. Another confounding factor to be considered is lymphatic filariasis, which is endemic in Tuvalu and most of the Western Pacific region (PACELF, 2008). Infection with LF, even subclinically, can result in proteinuria due to lymphatic impairment (Dreyer *et al.*, 1992; Dreyer *et al.*, 2002).

Recent figures, however, suggest that the national prevalence of LF in Tuvalu is less than 8% (Melrose, 2007), which is supported by the national survey for LF conducted in February 2008. Findings from this survey indicated that there were fewer than 10 children aged younger than 15 years who were ICT card positive for the parasite. The low prevalence of the disease in both the child and adult population suggests that LF is not likely to be a significant contributor to renal dysfunction in children.

Obesity is known to result in renal disease and hence to contribute to abnormal urine results (Nelaj *et al.*, 2008; Lamacchia *et al.*, 2009). A retrospective Canadian study of overweight and obese children found obesity to be a significant factor in paediatric renal disease (Filler *et al.*, 2007), and the high prevalence of childhood obesity in Tuvalu means it should be considered in this analysis. Based on RR, there was a moderate association between participants who were overweight or obese and who were positive for either proteinuria or haematuria during both the baseline and follow-up surveys (RR ranged from 0.97 to 1.28), compared to those who were not overweight or obese. Additionally, results from the follow-up survey demonstrated a statistically significant association between participants who had proteinuria or haematuria and were obese, compared to those participants who were not obese (Pearson Chi-squared p-values <0.05).

The overall decrease in both the prevalence and intensity of *T. trichiura* infection throughout the entire cohort, and the parallel decrease in anaemia, was an expected result after mass chemotherapy with the antihelminth drug mebendazole. The decrease in infection was observed 14 months after one round of treatment and likely was more significant immediately after the participants were treated, owing to possible re-infection from a heavily infected environment.

The findings support the effectiveness and rapid benefits from de-worming initiatives and highlight the need for expanding the programme to include multiple treatments of the entire population to continually reduce the reservoir and burden of soil-transmitted helminths; while improving sanitation and hygiene.

In summary, the follow-up survey confirms that the prevalence of skin and parasitic infections in the cohort of primary-school children of Tuvalu is consistent with other developing nations in similar settings in tropical environments. The follow-up survey also confirms the dual portfolio of infectious and chronic disease and that the child population and likely the adult population are experiencing a high prevalence of co-morbidity of infectious disease, chronic conditions and their associated outcomes. The infectious diseases observed in this population are neglected tropical diseases that are diseases of poverty, overcrowding and other socioeconomic determinants of health, which are not currently addressed by the health sector.

The combination of multiple pathogens, overcrowded dwellings and inadequate water and sanitation has resulted in a high burden of acute disease and discomfort, with conditions that have demonstrated the capacity to have long-term chronic effects at the population level. Clinical findings from the surveys and information provided by the Ministry of Health indicate that this population is already experiencing some of the known sequelae from the individual infections, including anaemia, renal damage and cardiac disease. The impact of the co-morbidity of multiple infections on individuals and on the population as a whole remains unclear, but research is beginning to acknowledge the issues of co-morbidity of neglected tropical diseases and the need to address them (Huchinson *et al.*, 1997; Huges *et al.*, 2004; Lawrence *et al.*, 2005; Thomas *et al.*, 2005; Gupta and Kumar, 2007).

What is needed is a comprehensive, integrated disease control strategy to address all of the conditions indicated, as well as the underlying issues that propagate these infections. This intervention strategy needs to be efficient and cost-effective while addressing the burden of illness within the community, rather than just a single disease programme. Current research and reviews of scientific literature recognise the global burden of neglected tropical diseases and advocate the introduction of integrated disease control strategies to address multiple overlapping co-existing pathogens in affected populations (Mathers *et al.*, 2007).

Overall integrated disease control strategies for neglected tropical diseases aim to prevent, control and eliminate neglected tropical diseases by addressing the diseases and the social and economic conditions that propagate them (Ehrenberg and Ault, 2005; Campbell and Campbell, 2007; Holveck *et al.*, 2007; Hotez *et al.*, 2007a). As these diseases affect the poorest countries, integrated disease control strategies also aim to target multiple diseases simultaneously to achieve maximum coverage and efficiency while minimising the strain on already resource-constrained settings (Ehrenberg and Ault, 2005; Dodd and Cassels, 2006; Gupta and Kumar, 2007).

Early evaluation has shown the success of these campaigns, especially those initiatives that utilise combined mass chemotherapy. Combined mass chemotherapy provides mass treatment for multiple diseases, to achieve maximum treatment coverage with a single distribution. This is achieved through the distribution of pre-prepared 'combi-pack' drug treatment packages, and through the utilisation of multipurpose medications, such as ivermectin, that have the capacity to treat multiple pathogens with overlapping spatial distribution (Lammie *et al.*, 2006; Hotez *et al.*, 2007a).

The following initiatives have been identified as a priority in order to address the burden of infectious diseases in Tuvalu: ongoing disease surveillance; integrated treatment for co-morbidity for the entire population at risk to reduce disease reservoirs; education on disease control, hygiene and nutrition; improvements to infrastructure to improve access to clean water and sanitation; and monitoring and evaluation of interventions to assess efficacy. The comprehensive multi-pronged approach that has been suggested will require time and resources to implement all of the complementary components. It is therefore suggested that the control strategy be implemented in two phases. Phase 1 would see the initiation of disease surveillance and treatment initiatives to reduce the burden of disease on individuals, and to reduce the reservoir of pathogens in the community. Phase 2 would see the implementation of initiatives to improve infrastructure and the social determinants of health to reduce the environmental and social conditions that facilitate the transmission of these infectious diseases.

Based on the findings from the surveys and the scope and prevalence of infectious disease in Tuvalu, it appears that the most effective initial course of action would be to initiate a community-based mass treatment with the antiparasitic drug ivermectin. Ivermectin is a safe and effective drug that has been used for over 30 years to treat various parasitic diseases worldwide (Brooks and Grace, 2002; Heukelbach *et al.*, 2004; Speare and Durrheim, 2004).

It has been shown to be a safe and effective treatment for scabies, some soil-transmitted helminths, and lymphatic filariasis (Brockerie *et al.*, 2000; Despommier *et al.*, 2000; Fincham *et al.*, 2003; Carapetis *et al.*, 2004; Lawrence *et al.*, 2005).

Community-wide treatment with ivermectin could reduce the prevalence of scabies and consequently reduce the prevalence of bacterial pyoderma in the community (Heukelbach *et al.*, 2004; Speare and Durrheim, 2004). The reduction in the carriage of streptococci bacteria could greatly reduce the renal and cardiac damage resulting from GAS (Lawrence *et al.*, 2005).

Mass treatment would also greatly reduce the intensity of *T. trichiura* as well as the community reservoir of this parasite. In time, with repeated application a reduction in the community prevalence will lead to a reduction in the prevalence of this species of soil-dwelling parasite, thus breaking the cycle of infection via environmental contamination (Urbani and Palmer, 2001). Ivermectin, however, would likely have a minimal impact on the prevalence of hookworm (Gyapong, 2005; Moncayo *et al.*, 2008; Massa *et al.*, 2009). The rapid results of mass chemotherapy, and their impact on the health of a population, are documented in the literature (Brockerie *et al.*, 2000; Carapetis *et al.*, 2004; Lawrence *et al.*, 2005) and were observed in the results from the Tuvalu follow-up survey. Additionally, the use of ivermectin would support the PacELF programme to reduce the prevalence of lymphatic filariasis, which is ongoing in Tuvalu.

Baseline and follow-up surveys have confirmed the need for an efficient and cost-effective disease control strategy to address the burden of multiple neglected tropical diseases in Tuvalu. The co-morbidity of multiple pathogens is impacting the population, and the potential for long-term negative outcomes exists. A multifaceted integrated disease control strategy has been recommended focusing on treatment, control and prevention of parasitic and skin diseases to reduce the disease burden in this population.

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Chapter 4

A cross-sectional baseline survey for common skin conditions in Timor-Leste

4.1 Introduction to Timor-Leste

Timor-Leste is a newly independent country and the world's youngest nation after being officially granted independence from Indonesia in 2002. The island of Timor is part of the Malay Archipelago and the largest and easternmost of the Lesser Sunda Islands. It is situated approximately 600 km north-east of Australia in the Timor Sea, occupying 15,000 km^2. The Indonesian province of Nusa Tenggara lies to the west. The small East Timorese enclave of Oecussi is located in West Timor, resulting in an immense geographical separation from the remainder of the country.

Figure 4.1: Political map of Timor-Leste with map of extreme South-East Asia and Australia embedded to show Timor-Leste in relation to the region (Government of Timor-Leste, 2007).

4.1.1 The land and the people

Five years after independence, approximately 1,000,000 people live in this nation, which is divided into 13 districts, 65 subdistricts and 507 villages (Government of the Democratic Republic of Timor-Leste, 2005). Typical of demographic profiles of developing countries, Timor-Leste has a young population, with almost 20% younger than five years of age, slightly more than 50% under 15 years and about two-thirds under 25 years old. There are more males than females, with a ratio of 1.07:1. The average life expectancy is 57 years (UNICEF, 2002a; Timor-Leste Ministry of Health *et al.*, 2004; UNICEF, 2007a). Approximately 30% of the population lives in urban centres and 21% lives in the capital city of Dili (Timor-Leste Ministry of Health, 2005).

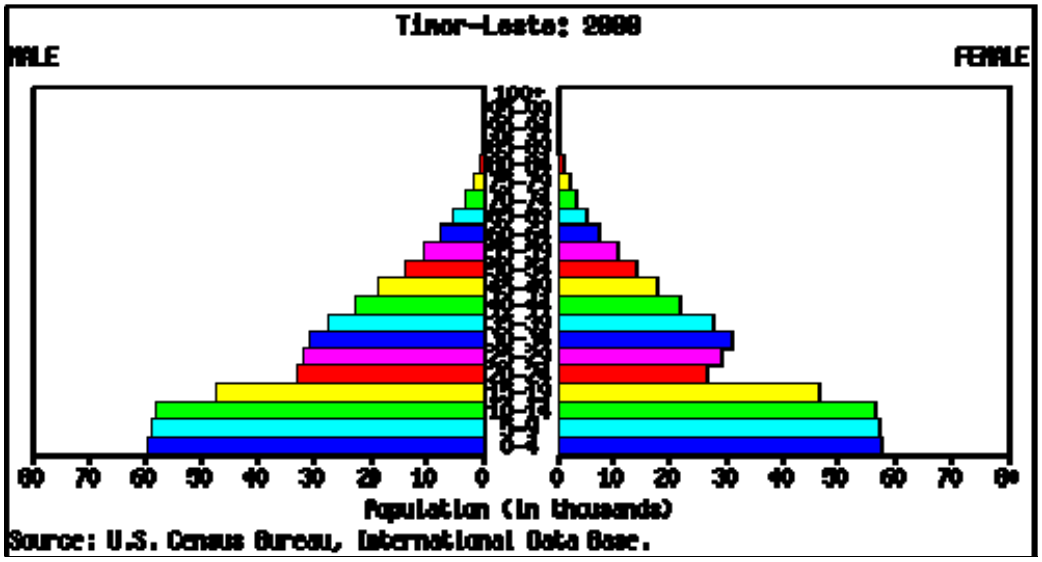

Figure 4.2: Population pyramid for Timor-Leste 2000 by age and sex (U.S. Census Bureau, 2008).

The capital, largest city and main port is Dili, and the second-largest city is the eastern town of Baucau, with estimated populations of 177,410 and 119,651 respectively (Timor-Leste Ministry of Health, 2005). The topography ranges from flat coastal areas to a mountainous interior with thick jungle. The highest point of Timor-Leste is Mount Tatamailau at 2963 metres. The local climate is tropical and generally hot and humid, characterised by distinct rainy and dry seasons. During the dry season the northern parts of the country are prone to drought, which reduces crop yields and affects food supplies, resulting in severe food shortages for four months annually: October–November and February–March (World Food Programme, 2008).

Timor-Leste is one of the poorest nations in South-East Asia, with the average person earning about USD1.20 per day in the larger centres and less in rural areas (Aarons, 2007). It is estimated that 50% of the population is either unemployed or inadequately employed (The Royal Norwegian Embassy in Jakarta, 2009). In 2007 the World Bank ranked Timor-Leste 176th out of 177 nations, with a gross national product (GNP) of only USD395 million (World Bank Group, 2008). However, this figure is only an estimation, and may be inflated due to the revenues from recently discovered oil and gas reserves (US Department of State, 2009b). Revenue from this source is paid to the Timorese government but does not greatly contribute to the local economy or ease the rate of unemployment, as there are no processing facilities in Timor-Leste and the products are piped directly to Australia (Geographic, 2007).

Food insecurity is common and widespread due to the combination of drought, low crop yields, lack of income, underdeveloped markets, transport issues and civil unrest. Over 30% of the population experiences regular food shortages (World Food Programme, 2008). Over two-thirds of the population live in rural areas and their access to food is further restricted by transportation costs and reduced income potential, as those in rural areas are more likely to earn closer to USD0.55 per day (World Food Programme, 2008) than their urban counterparts.

4.1.2 Health and the health-care system

The vast majority of the population resides in poverty in rural areas with limited access to infrastructure, including comprehensive medical services (Government of the Democratic Republic of Timor-Leste, 2005). Health indicators in Timor-Leste are among the lowest in East Asia and communicable diseases are a significant component of the major health problems (UNICEF, 2002b).

Food insecurity is apparent, with 40% of the general population exhibiting signs of malnutrition (Aarons, 2007). A study of malnutrition in children concluded that 47% of children under five were chronically malnourished (stunted) and 43% were severely malnourished (underweight), and the national rate of wasting was 12% (World Food Programme, 2008). These results were some of the highest in Asia – the national rates for stunting in Myanmar, Cambodia and Laos were 32%, 35% and 42% (Timor-Leste Ministry of Health *et al.*, 2004; World Food Programme, 2008). Overall, approximately 12% of children will die before the age of five years (Aarons, 2007).

Past civil unrest and military occupation have greatly damaged infrastructure and health-care services, and many long-standing public health programmes established during Indonesian rule have collapsed. This has allowed for the resurgence of several infectious diseases. The Timorese government, with the help of international agencies, is working to restore services and programmes. Control programmes for tuberculosis, leprosy, and soil-transmitted helminths (STHs) have historically been in place (UNICEF, 2007a). A strategic plan to train health-care professionals and strengthen the health-care system has been developed and implementation is under way (Timor-Leste Ministry of Health, 2005).

4.1.3 Skin conditions

Data on the prevalence and aetiology of skin infections in Timor-Leste is limited. In September/October 1970 a dermatological survey was conducted in two subdistricts in the districts of Baucau and Manufahi. Almost 3000 people were examined for a variety of conditions, and more than a third of participants in Baucau (38.9%) and 20% in Manufahi were found to have a skin disease. Among these, the majority had a transmissible skin disease (Picoto, 1970). The most common infectious skin diseases were scabies and superficial fungal infections. In Manufahi 61.3% of the individuals examined had scabies, while 30.7% had scabies in Baucau. The prevalence of fungal infections was also high (24% in Baucau and 49.5% in Manufahi). The overall rate of leprosy in the two subdistricts was 41.8 per 10,000 population (Picoto, 1970).

Chevalier *et al.* (2000) reported the first confirmed cases of cutaneous leishmaniasis, a parasitic disease spread by the bite of infected sandflies. If undiagnosed or not treated, this disease can lead to severe disfigurement (Hayman, 2004). A tropical medicine unit from the French military diagnosed 46 cases during free medical clinics conducted in November 1999. The cases were diagnosed using microscopic analysis of tissue smears on site, and samples were sent to Europe for confirmation (Chevalier *et al.*, 2000).

Cutaneous leishmaniasis rarely presents in South-East Asia (Maguire *et al.*, 1998; Despommier *et al.*, 2000; Heymann, 2004). However, the known insect vector – sandflies from the genus *Phelbotomus* – is found worldwide (Ashford, 2000) and has been identified in Thailand (Apiwathnasorn, 1993). Isolated localised cases of cutaneous and visceral leishmaniasis have been documented in South-East Asia, including Singapore (Tan *et al.*, 2000); the first indigenous case of visceral leishmaniasis was found in an infant in southern Thailand (Thisyakorn *et al.*, 1999).

While these were isolated cases of the disease in Timor-Leste, they were identified by professionals with experience in tropical medicine using established clinical and laboratory diagnostic techniques (Chevalier *et al.*, 2000). Evidence from other countries in the region indicates the presence of the elements (capable known vectors and documented transmission) necessary for localised foci of leishmaniasis and sporadic outbreaks of the disease. The cluster of cases in Timor-Leste may have resulted from cases imported from neighbouring Indonesia. One can conclude from the cases identified in 1999 that cutaneous leishmaniasis was, and may still be, present at low prevalence in Timor-Leste, and the potential exists for it to become a pressing health issue under the right conditions. Since this initial report there have been no subsequent reports of cutaneous leishmaniasis at health-care centres or in the community. However, there is no active surveillance programme for the disease.

Lim (2005) examined the impact of dermatological infections on the Australian peacekeeping forces sent into Timor-Leste in 2000. He found that 25% of all the deployed soldiers' medical consultations were dermatologically related and that bacterial and fungal infections were the most common presentations. In 2006, the Timor-Leste Ministry of Health (MoH) reported nationally that 48,221 people had visited health facilities with skin problems (skin ulcers, scabies, etc.) and more than 50% of these patients were aged under 15 years (Government of the Democratic Republic of Timor-Leste, 2006b).

Leprosy is a potentially disfiguring and debilitating disease caused by the bacterium *Mycobacterium leprae*; it affects the skin, peripheral nerves and airways (Heymann, 2004). Transmission is believed to be through airborne droplets released from the respiratory tract of infected individuals. Left untreated, it can progress to severe disfigurement, progressive debilitation and mortality. Leprosy is a neglected tropical disease and the leading cause of permanent disability worldwide. It predominantly affects poor and marginalised populations (WHO, 2008b).

Historically, the disease has been endemic in southern and South-East Asia, but recent efforts towards the global elimination of leprosy have resulted in all but two countries (Nepal and Timor-Leste) meeting the elimination target (Lobo and Narain, 2005; WHO, 2008b).

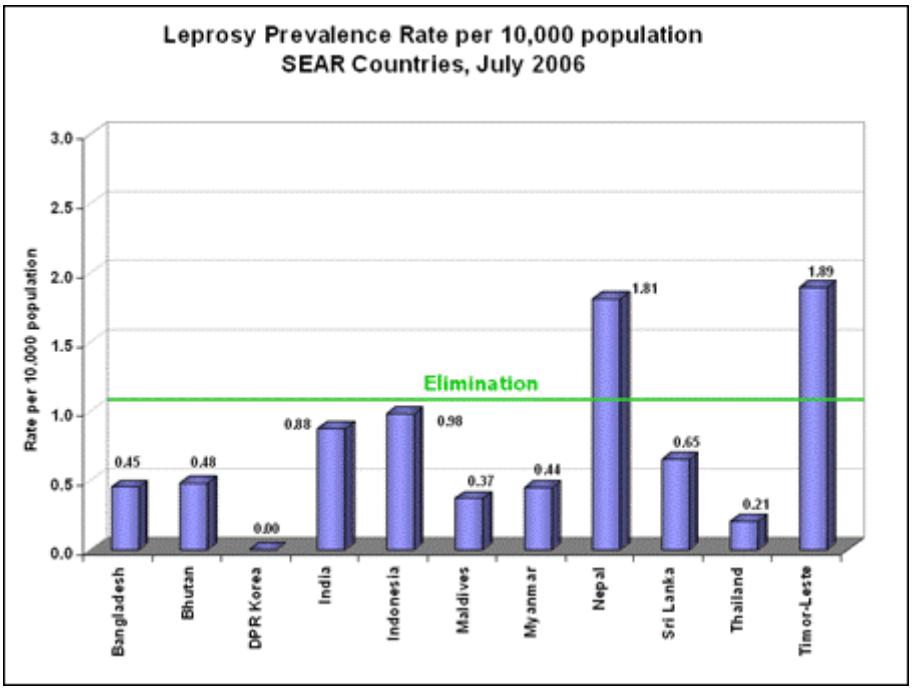

Figure 4.3: Leprosy rates in the South-East Asian region as of July 2006 (WHO, 2008b).

Yaws is an endemic disease with a few isolated active foci in three countries in the South-East Asian region: India, Indonesia and Timor-Leste. It is said that yaws begins where the road ends, indicating that it is a disease of poverty associated with warm and humid tropical environments, poor sanitation and overcrowding (WHO, 2008f).

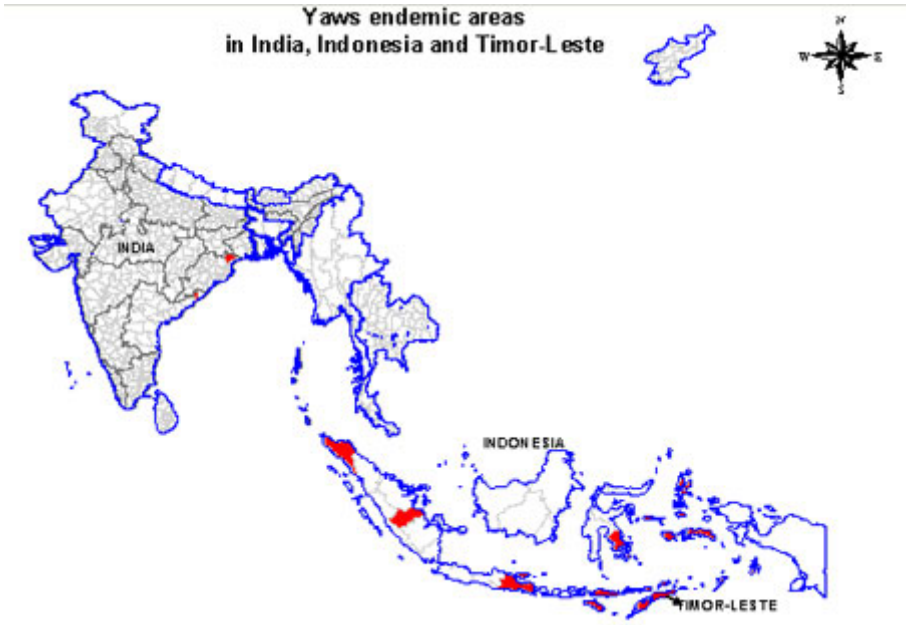

Figure 4.4: Map of active foci of yaws activity in South-East Asia (WHO, 2008f).

Yaws is a contagious non-venereal infection caused by treponemal bacteria. It usually affects children under 15 years, with incidence peaking at 6–10 years (Heymann, 2004). The disease is spread via person-to-person contact, which allows the bacteria to enter the dermis through cuts or abrasions in the skin. Yaws results in skin ulcerations (which are contagious if not scabbed over) and normally remains limited to the skin (WHO, 2008f). However, more serious outcomes can occur, including early bone and joint involvement, due to the systemic dissemination of the bacteria. On average 10% of untreated cases may develop destructive lesions involving bone, cartilage, skin and soft tissue, similar to those seen in tertiary syphilis, 5-10 years after infection (WHO, 2008f). There is no official data on cases of yaws in Timor-Leste, but survey data indicates the disease is present in six of the 13 districts.

4.2 Methods

The objective of this study was to determine the baseline prevalence of skin diseases in Timor-Leste in order to assess the burden of these infections on the community, and to determine if a public health intervention is warranted. The survey was conducted by a multidisciplinary team from the Timor-Leste MoH and the World Health Organization (WHO) in Timor-Leste, together with the School of Public Health, Tropical Medicine and Rehabilitation Sciences (SPHTMRS) from James Cook University in north Queensland, Australia. Team members included local nurses and translators, a leprosy specialist from the Indonesian MoH, members of the leprosy team from the Timor-Leste MoH, a laboratory technician and a medical epidemiologist.

A cross-sectional survey was designed utilising consecutive convenience sampling, to determine the baseline prevalence and aetiology of skin infections in Timor-Leste. The study used convenience sampling because the majority of the population of Timor-Leste lives in remote villages that are difficult to access individually. The screening was conducted over a four-week period during September 2007. Fourteen sites in four geographically diverse districts (Oecussi, Bobanaro, Cova-Lima and the island of Atauro in the district of Dili) were selected (Figure 4.5). These areas included coastal, inland and mountainous environments. The isolated enclave of Oecussi in West Timor was selected because of its historical higher rates of leprosy and its isolation from the rest of Timor-Leste. Subdistricts were selected for geographic and culturally diversity. Sampling was conducted in urban, sub-urban and rural settings to be representative of the general population. Districts were also selected based on safety, as some areas of the country are prone to political instability.

Participants were recruited from hospitals, community health centres (CHCs) and primary schools, as these are focal points that serve multiple villages and are accessible to the majority of individuals. All participating individuals provided oral consent prior to being visually examined. Local nurses and community health-care workers were present to help translate and ensure that participants were able to understand and provide informed consent. Participants were examined for the five targeted skin conditions – scabies, pyoderma (superficial bacterial infections), dermatophyte infections, leprosy and yaws (also known as framboesia tropica) – using standardised case definitions. Clinical case definitions were developed and applied (Table 4.1) and all unknown conditions were photographed and examined by staff at SPHTMRS for confirmatory diagnosis. Participants were given a 5 ml yellow screw-topped plastic vial and asked to provide a fresh urine sample in order to test for proteinuria. Urine samples were analysed on site by a laboratory technician for protein using Bayer Uristix® urinalysis dipsticks.

Ethical approval was obtained from the Timor-Leste MoH, WHO and the James Cook University Research Ethics Committee (approval H2374). Anyone found to have a skin infection or a medical symptom or condition of concern was either treated by the team at the time of examination or referred to the CHC for treatment. Full first and last names were used as a unique identifier and consecutive sample numbers were assigned to each unique participant. The names were removed once the data had been reconciled and duplicates and unknowns had been removed.

The data was entered into a Microsoft Access® database and analysis was conducted using Access and SPSS® version 16. Demographic data was analysed using descriptive statistical tests, including frequency, mean, proportion, confidence interval, Chi-square tests, and odds-ratios for relative risk associations. Categorical data was analysed using cross-tabulations and Chi-squared tests.

Skin disease	Definition	Type of diagnosis
Pyoderma	Any superficial bacterial skin infection (e.g. impetigo, impetigo contagiosa, ecthyma, folliculitis, furuncle, carbuncle, tropical ulcer, etc.)	Clinical
Scabies	Presence of lesions, nodules, burrows, papules, vesicles or crust characteristic of *Sarcoptes scabiei* infection with evidence of pruritis (itching)	Clinical
Dermatophyte fungal infection	Presence of lesions, maceration and inflammation characteristic of infection with dermatophyte species on the skin	Clinical and skin scraping for microscopic examination if required
Leprosy	Presence of hypopigmented or reddish skin lesions and evidence of loss of sensation, not attributable to trauma or other disease process	Clinical
Yaws	Presence of one or more of: 1. erythrematous ulcer with scab papillomas 2. palmar/plantar hyperkeratosis (thickening)	Clinical

Table 4.1: Table of case definitions of skin diseases used in survey.

4.3 Results

4.3.1 The survey population

A total of 1535 participants aged between four months and 97 years of age were examined. The highest number of participants was recruited in Oecussi (664/1535, 43.2%), followed by Bobanaro (525/1535, 34.2%), Cova-Lima (228/1535, 14.9%) and Dili (Atauro) (118/1535, 7.7%) (Figure 4.5). The sample population was comprised of a relatively equal proportion of 855 males (55.7%) and 680 females (44.3%) (Table 4.2). The majority of participants (36%) were between the ages of 11 and 20 (Table 4.3).

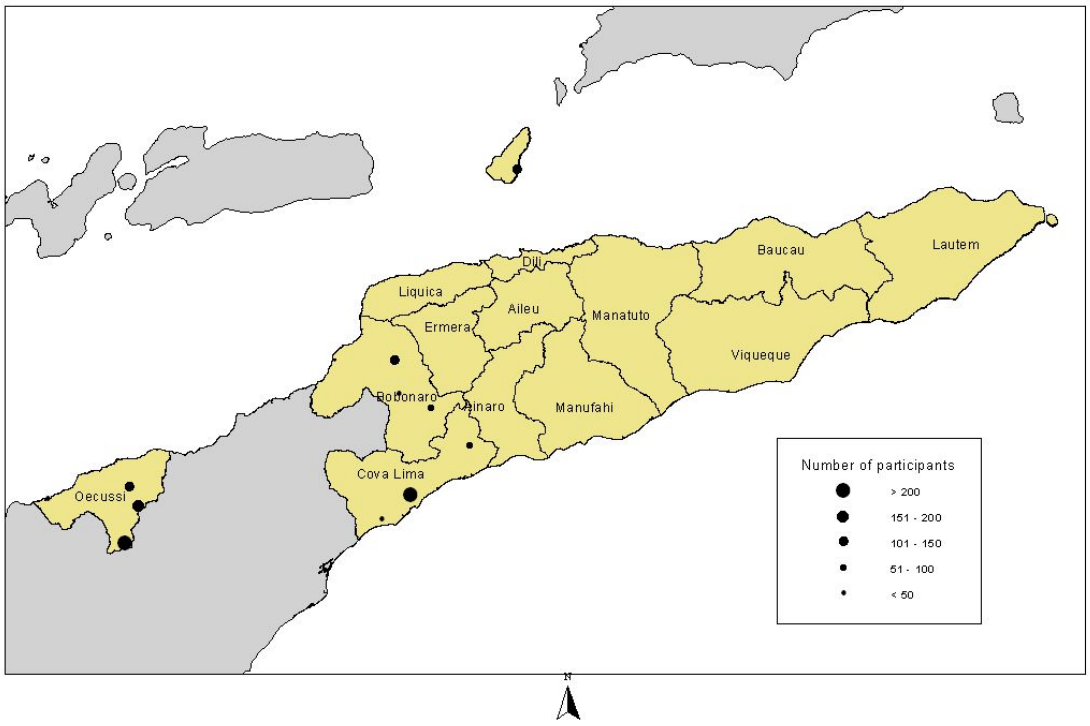

Figure 4.5: Number of survey participants by subdistrict.

District	Subdistrict	Site	Number of male participants	Number of female participants	Total
Oecussi	Oesilo	Oesilo CHC	94	101	195
Oecussi	Passabe	Passabe CHC	179	94	273
Oecussi	Passabe	Malelat Hospital	26	48	74
Oecussi	Nitibe	Boaconana CHC	79	43	122
Oecussi	Panta Makasar	Baqui CHC	45	32	77
Bobanaro	Bobanaro	Bobanaro CHC	91	39	130
Bobanaro	Calico	Calico CHC	11	10	21
Bobanaro	Maliana	Maliana Hospital	52	22	74
Cova-Lima	Zumalai	Zumalai	33	6	39
Cova-Lima	Tilomar	Salele CHC	170	159	329
Cova-Lima	Suai	Seran Cote School	16	27	43
Cova-Lima	Suai	Suai CHC	27	29	56
Atauro	Macadade	Macadade CHC	20	37	57
Atauro	Belquqi	Belquqi CHC	12	33	45
		Total	**855**	**680**	**1535**

Table 4.2: Geographical distribution of survey participants by sex.

Age group	Frequency		Percent	Percent of survey population	Cumulative percent	Percent of age group within total population
0–5	Female	38	38.4%			
	Male	61	61.6%	6.40%	6.40%	0.05%
	Total	**99**				
6–10	Female	68	68.0%			
	Male	78	78.0%	9.50%	15.90%	0.09%
	Total	**146**				
11–15	Female	235	48.7%			
	Male	248	51.3%	31.50%	47.40%	0.30%
	Total	**483**				
16–20	Female	189	38.8%			
	Male	298	61.2%	31.70%	79.10%	0.40%
	Total	**487**				
21–25	Female	21	21.0%			
	Male	18	18.0%	2.50%	81.60%	0.05%
	Total	**39**				
26–30	Female	37	60.7%			
	Male	24	39.3%	3.80%	85.40%	0.09%
	Total	**61**				
31–35	Female	13	44.8%			
	Male	16	55.2%	1.90%	87.30%	0.05%
	Total	**29**				
36–40	Female	18	35.3%			
	Male	33	64.7%	3.30%	90.60%	0.09%
	Total	**51**				
41–45	Female	18	52.9%			
	Male	16	47.1%	2.20%	92.80%	0.07%
	Total	**34**				
46–50	Female	16	41.0%			
	Male	23	59.0%	2.50%	95.30%	0.09%
	Total	**39**				
50+	Female	27	40.3%			
	Male	40	59.7%	4.70%	100.00%	0.06%
	Total	**67**				

Table 4.3**: Distribution of survey population in Timor-Leste by age and sex (n=1474)**

(61 participants were not included in this table due to incomplete data).

4.3.2 Skin infections

Overall, the majority of those screened (58.9%) had at least one of the skin conditions targeted in the survey: 38.9% had a dermatophyte infection, 17.3% had scabies, and 7.3% had pyoderma. There were 29 new cases of leprosy (1.9%) and six cases of yaws (0.4%) discovered during the survey examinations. The most commonly identified condition was dermatophytosis, with men and women affected in equal proportions (Figure 4.6). Approximately 10% had two or more infections. When participants were co-infected, the two most common co-infections were scabies with pyoderma (38%) and scabies with a fungal infection (35.2%).

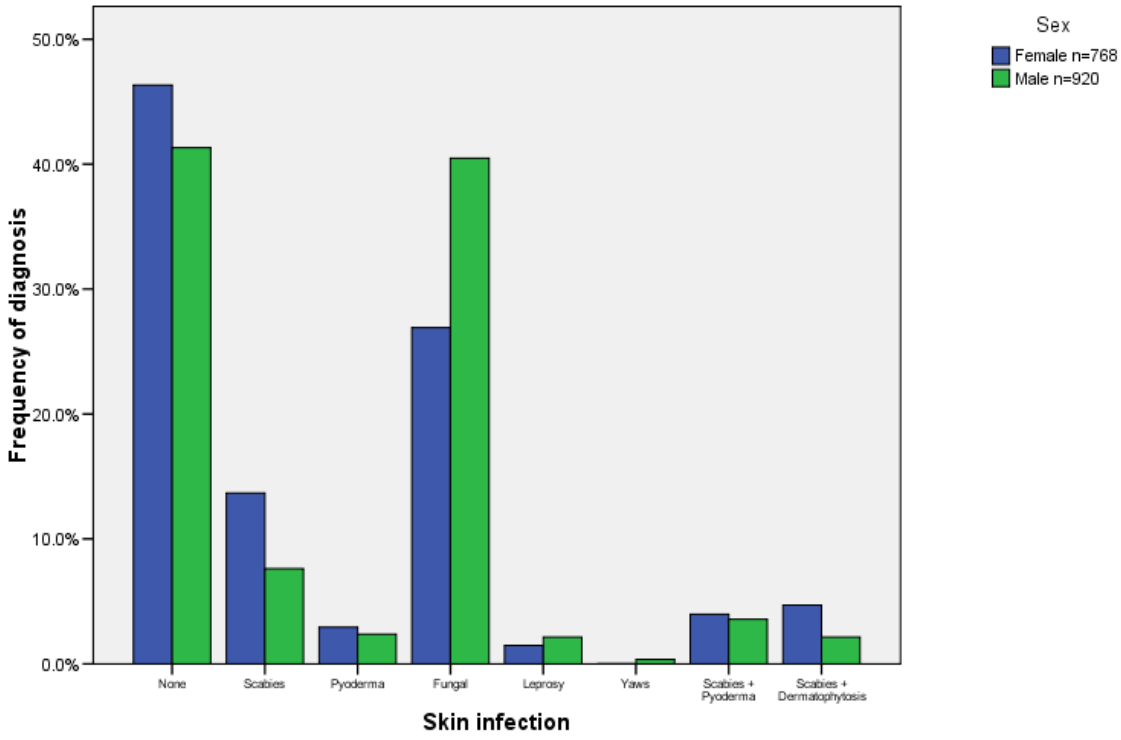

Figure 4.6: Frequency of skin infections by sex (n=1474)

(61 participants were not included in this table due to incomplete data).

The prevalence of dermatophyte infections was lowest among young children (under 10 years) and gradually increased with age. The highest prevalence was found among participants in mid-adulthood (31–35 years). Approximately 20% of all people screened and 37% of children aged less than 10 years were found to have scabies. Figure 4.7 shows the distribution of skin infections by age.

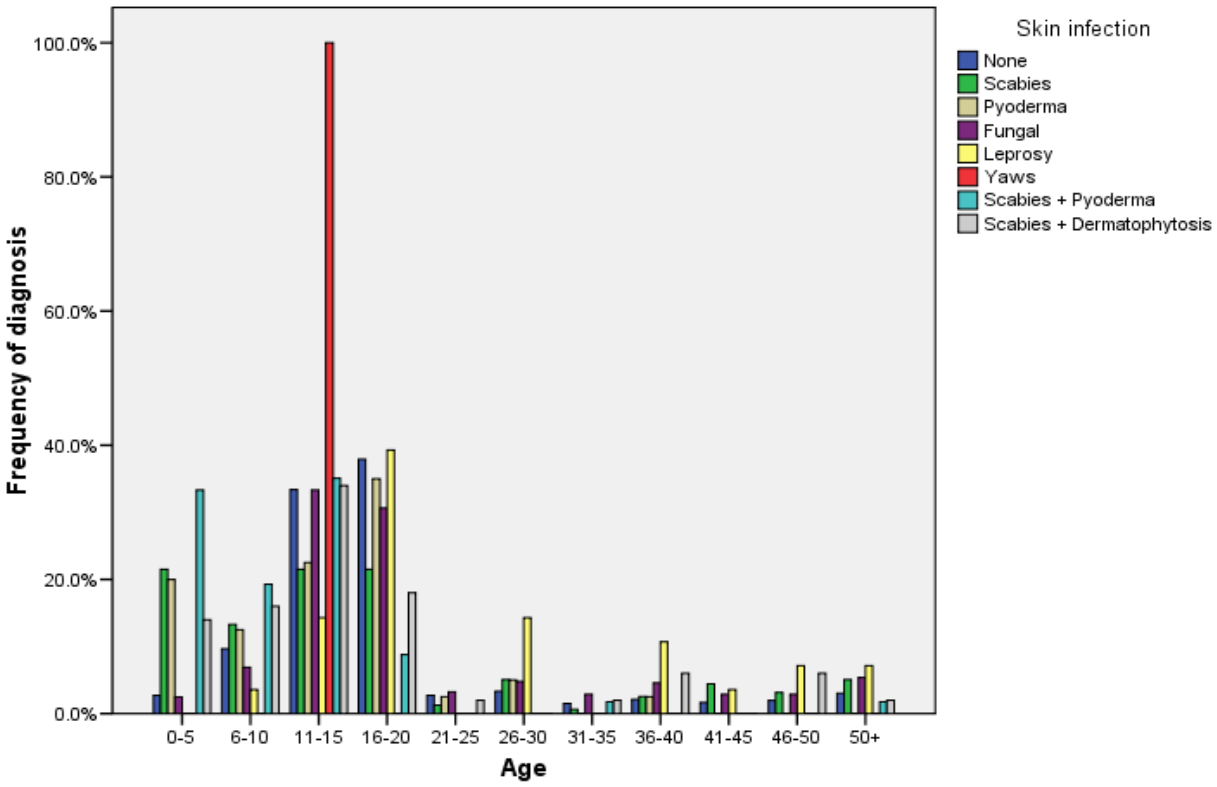

Figure 4.7: Skin infections by age.

The survey identified 29 previously undiagnosed cases of leprosy; the youngest was an eight-year-old female from Oecussi. Leprosy was identified in all age groups but was most prevalent in those aged 16–20 years. Eighteen of the 29 cases were males and the majority of cases (19/29) resided in Oecussi. There were six cases of yaws detected; all but one case were male and all were aged 6–15 years. Table 4.4 shows the distribution of infections by age group and sex.

Age group in years	Sex	No infection identified Cases (%)	Dermatophytosis Cases (%)	Scabies Cases (%)	Pyoderma Cases (%)	Leprosy Cases (%)	Yaws Cases (%)
0–5	Male (n=61)	13 (21.3)	10 (16.4)	35 (57.3)	18 (29.5)	0 (0.0)	0 (0.0)
	Female (n=38)	4 (10.5)	14 (36.8)	17 (44.7)	12 (31.6)	0 (0.0)	0 (0.0)
	Total (n=99)[a]	**17 (17.1)**	**24 (24.2)**	**52 (52.5)**	**30 (30.3)**	**0 (0.0)**	**0 (0.0)**
6–10	Male (n=78)	34 (43.5)	31 (39.7)	12 (15.3)	7 (9.0)	0 (0.0)	3 (3.8)
	Female (n=68)	30 (44.1)	13 (19.1)	26 (38.2)	11 (16.1)	1 (1.5)	0 (0.0)
	Total (n=146)[a]	**59 (40.4)**	**44 (30.1)**	**38 (26.0)**	**18 (12.3)**	**1 (0.7)**	**3 (2.0)**
11–15	Male (n=248)	119 (48.0)	103 (41.5)	29 (11.7)	13 (5.2)	1 (0.4)	3 (1.2)
	Female (n=235)	107 (45.5)	92 (39.1)	42 (18.0)	21 (8.9)	3 (1.3)	0 (0.0)
	Total (n=483)[a]	**218 (45.1)**	**195 (40.4)**	**71 (14.7)**	**34 (7.0)**	**4 (0.8)**	**3 (0.6)**
16–20	Male (n=298)	147 (49.3)	119 (40.0)	25 (8.4)	10 (3.3)	8 (2.7)	2 (0.7)
	Female (n=189)	108 (57.1)	57 (30.1)	25 (13.2)	12 (6.3)	3 (1.6)	0 (0.0)
	Total (n=487)[*]	**245 (50.3)**	**176 (36.1)**	**50 (10.3)**	**22 (4.5)**	**11 (2.3)**	**0 (0.0)**
21 to25	Male (n=18)	5 (28.0)	12 (67.0)	0 (0.0)	1 (5.5)	0 (0.0)	0 (0.0)
	Female (n=21)	13 (62.0)	7 (33.3)	3 (14.2)	1 (4.8)	0 (0.0)	0 (0.0)
	Total (n=39)[*]	**18 (46.2)**	**19 (48.7)**	**3 (7.7)**	**2 (5.1)**	**0 (0.0)**	**0 (0.0)**
26–30	Male (n=24)	6 (25.0)	14 (58.3)	2 (8.3)	0 (0.0)	2 (8.3)	0 (0.0)
	Female (n=37)	16 (43.2)	15 (40.5)	6 (16.2)	2 (5.4)	2 (5.4)	0 (0.0)
	Total (n=61)[*]	**22 (36.0)**	**29 (47.5)**	**8 (13.1)**	**2 (3.3)**	**4 (6.6)**	**0 (0.0)**
31–35	Male (n=16)	4 (25.0)	12 (75.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Female (n=13)	7 (54.0)	5 (38.5)	3 (23.0)	1 (7.7)	0 (0.0)	0 (0.0)
	Total (n=29)[*]	**11 (38.0)**	**17 (58.6)**	**3 (10.3)**	**1 (3.4)**	**0 (0.0)**	**0 (0.0)**
36–40	Male (n=33)	9 (27.2)	21 (63.6)	5 (15.1)	0 (0.0)	3 (9.0)	0 (0.0)
	Female (n=18)	8 (44.4)	7 (38.8)	3 (16.6)	1 (5.5)	0 (0.0)	0 (0.0)
	Total (n=51)[*]	**15 (29.4)**	**28 (54.9)**	**8 (15.7)**	**1 (2.0)**	**3 (5.9)**	**0 (0.0)**
41–45	Male (n=16)	5 (31.2)	10 (62.5)	1 (6.25)	0 (0.0)	0 (0.0)	0 (0.0)
	Female (n=18)	6 (33.3)	5 (28.0)	6 (33.3)	0 (0.0)	1 (5.5)	0 (0.0)
	Total (n=34)[*]	**11 (32.4)**	**15 (44.1)**	**7 (20.6)**	**0 (0.0)**	**1 (2.9)**	**0 (0.0)**
46–50	Male (n=23)	7 (30.4)	13 (56.5)	4 (17.4)	1 (4.3)	2 (8.7)	0 (0.0)
	Female (n=16)	7 (43.8)	6 (37.5)	5 (31.2)	0 (0.0)	0 (0.0)	0 (0.0)
	Total (n=39)[*]	**14 (35.9)**	**19 (48.7)**	**9 (23.1)**	**1 (2.6)**	**2 (5.1)**	**0 (0.0)**
over 50	Male (n=40)	17 (42.5)	19 (47.5)	5 (12.5)	1 (2.5)	2 (5.0)	0 (0.0)
	Female (n=27)	10 (37.0)	11 (41.0)	6 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)
	Total (n=67)[*]	**27 (29.9)**	**30 (44.8)**	**11 (16.4)**	**1 (0.9)**	**2 (3.0)**	**0 (0.0)**
Total		**646 (42.0)**	**597 (39.0)**	**266 (17.0)**	**112 (7.0)**	**29 (2.0)**	**9 (1.0)**

Table 4.4: Distribution of skin infections by age group and sex.

*individuals may be counted more than once if they had more than one condition.

Scabies, pyoderma and dermatophyte infections were present in all four districts and at all recruitment sites (Figure 4.8). The proportion of cases of dermatophytosis ranged from 24.6% on Atauro to 41.3% in Oecussi. Cases of scabies were more consistent at approximately 16%, with the exception of Atauro, where the proportion of participants presenting with the infection was 28%, double the mean of the other three districts. Cases of pyoderma were also consistent across the three districts on the mainland at approximately 7%, compared with Atauro, where the proportion was 13%. There was no statistical difference between the villages for any of the three above-mentioned conditions of scabies (Pearson Chi-square value 12.35), pyoderma (Pearson Chi-square value 14.89) and dermatophytosis (Pearson Chi-square value 11.70).

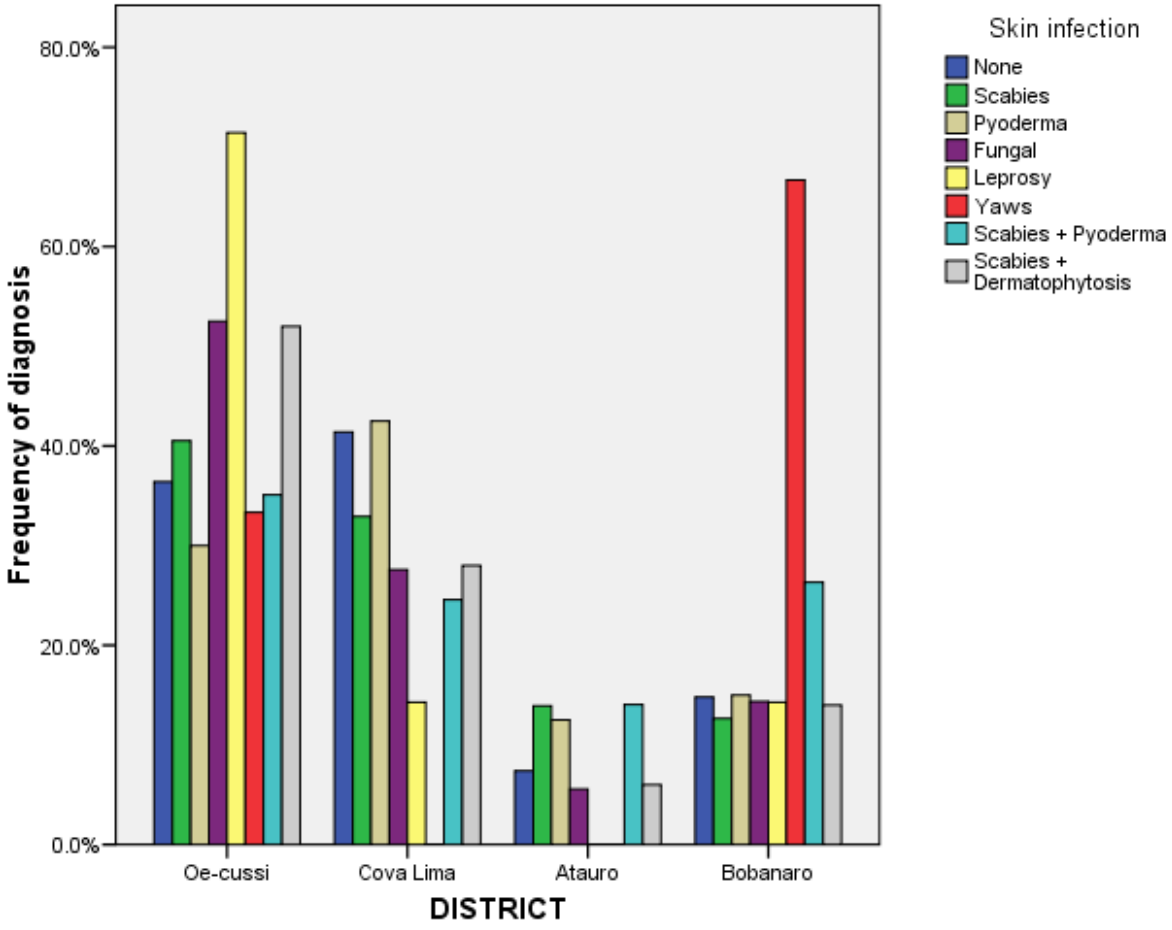

Figure 4.8: Frequency of skin infections by district.

4.3.3 Urinalysis

Urinalysis results on the 1047 submitted samples indicated that 41% (430) were positive for proteinuria. Of the samples positive for proteinuria, 83.5% (358/430) indicated a trace amount of protein, 16.3% (70/430) indicated a moderate level of protein (30–100 g/L) and 0.02% (2/430) had a high level of protein of (300–2000 g/L). Abnormal urine results were highest in those aged 11–15, and there was no significant difference between males and females (Pearson Chi-squared p value = 8.9).

Statistical analysis was conducted on those who both had a skin examination and submitted a urine sample (n=1047) to investigate the broader health impact of skin infections in the community. Table 4.5 outlines the associations between proteinuria and infection with scabies or pyoderma and co-infection with both skin diseases, compared to participants who did not have these conditions. Relative risk using odds-ratios suggests no association between pyoderma and proteinuria (RR=0.79) and a weak association with proteinuria in those who had scabies compared to those who did not have the infection (RR=1.02). The strongest association (RR=1.29) for proteinuria was identified in those who were co-infected with scabies and pyoderma. All of the RR values fell within the parameters of a confidence interval at 95%.

Chi-squared tests indicated a significant association between proteinuria and scabies infection when compared to those individuals with proteinuria who did not have a scabies infection. The relationship between proteinuria, and pyoderma- scabies co-infection was not significant.

Clinical variable and association	**Relative risk**	**Confidence interval (95%) for RR**	**Chi-squared test**
Pyoderma + proteinuria	0.79	0.47–1.33	p=0.379
Scabies + proteinuria	**1.02**	0.76–1.36	p=0.903
Scabies + pyoderma + proteinuria	**1.29**	0.75–1.60	p=0.486

Table 4.5: Relative risk table for urinalysis results.

4.4 Discussion

This survey appears to be the only community-based skin survey to have been undertaken in Timor-Leste in more than 30 years. A high proportion of the participants were identified as having at least one of the five targeted skin conditions. The results showed a higher proportion of skin infections than documented in the previous survey, which was conducted in 1970 (Picoto, 1970). These findings were consistent with other studies in developing countries, which demonstrate a high rate of skin infections in these settings. Skin conditions are known to be among the most common presentations at health-care facilities in the developing world (Mahe, 2001).

Dermatophytosis (superficial fungal infection) was the most commonly seen presentation among survey participants. This result is consistent with other findings, which state that dermatophytes may be most the prevalent infectious agents worldwide (Brasch and Hipler, 2008) and appear to be endemic, particularly in children in poor developing countries (Seebacher *et al.*, 2008). This is especially true in tropical settings, where skin infections often represent a public health concern (Chimelli *et al.*, 2003). Unlike the other conditions of interest in this survey, dermatophytosis was seen less often in younger children and prevalence increased with age, possibly resulting from repeated exposure to these agents over time.

Scabies (17%) and pyoderma (7%) were the second and third most prevalent conditions recorded during the survey, which is in line with the disease profile of other resource-poor settings in the tropics. It has been noted that scabies is present in 9–21% of those presenting at health-care centres in developing settings (Hengge *et al.*, 2006), and research conducted in Australian Aboriginal communities and other Pacific nations has indicated that pyoderma in children ranges from 10% to 90% in community and health-care settings (Feldmeier *et al.*, 2005; Thomas *et al.*, 2005; WHO, 2005c).

WHO compiled a review of community-based studies on the prevalence of scabies and pyoderma conducted since 1980; it documented that on the whole, the prevalence of pyoderma ranged from 1% to 20% in less developed countries but in the Pacific region provenances ranged from 40% to 90% (WHO, 2005b). Additional studies have suggested that the prevalence of scabies ranges from 1% to 10% in African and Asian countries but increases to 50% to 80% in the Pacific region (WHO, 2005b).

Overall, our survey results indicated that skin infections were most common in those under 20 and that males were affected more often than females. Four of the five conditions of interest were present in higher proportions in males than in females, except for dermatophyte infections, which were higher in females. The difference was not significant (p=11.7). Notably, females had a higher frequency of co-infection than males, but the difference was also not significant (p=18.0).

The higher proportion of skin infections in the younger population was expected for two reasons. First, the literature indicates that skin infections, especially scabies and pyoderma, most often affect children in the developing world; this is especially true in tropical environments (Chevalier *et al.*, 2000; Mahe, 2001; WHO, 2005c; WHO, 2005b). Community-based surveys conducted with school children in Ethiopia demonstrated that 84% of children surveyed at school had at least one skin infection (Figueroa *et al.*, 1996). Second, the findings could be attributed to the age and gender structure of Timor-Leste's population. The nation has a predominantly young population, of which 58% is aged younger than 20 years and males between the ages of 11 and 19 years comprise 12% (Government of the Democratic Republic of Timor-Leste, 2006a).

However, males aged 11–20 years were over-represented in the survey population, accounting on average for 0.35% of the survey population while all other age groups accounted for 0.06% (average). Thus, the results of the survey may not reflect the true epidemiology of the age and gender distribution of skin infections in Timor-Leste and it is difficult to know if they are representative of the entire population.

Despite the age and gender distribution of skin infections in Timor-Leste, it is still possible that the results may be an underestimation of the true burden of skin infections, and in particular of scabies infections. First, skin infections, especially scabies infections, are difficult to diagnose and require health-care providers who are skilled in their diagnosis (Becherel *et al.*, 1999; Flinders and De Schweinitz, 2004; Walton *et al.*, 2004). Second, the survey may have identified only severe cases of skin disease, as participants presenting at health facilities were more motivated to seek medical care than those with less severe infections. Third, as a result of the survey design, the team most commonly examined only one member of a household; however, when participants were asked about the health of their family members they often indicated there were other people in their household with similar symptoms.

Skin infections, scabies in particular, are easily transmitted from person to person and outbreaks are commonly associated with overcrowded living arrangements and a lack of access to water; both of these factors are common throughout Timor-Leste. The survey was conducted towards the end of the 'dry' season, when water sources in the participating districts are limited further – a situation that could increase the opportunity for household transmission. Given these factors, it is reasonable to expect more than one case of skin disease per household. Taking into account both the limitations of the survey design and the environmental conditions, it may be difficult to determine the extent to which the results of the survey accurately reflect the true burden of scabies and other skin infections.

The 29 previously undiagnosed cases of leprosy were expected. Leprosy is endemic in Timor-Leste, with a historically high prevalence, especially in the district of Oecussi where the majority of the cases were identified. Timor-Leste has had an active and successful leprosy control programme in place since 2003. The programme primarily focuses on early case detection (via active case finding) and treatment, ensuring that all patients have uninterrupted access to multi-drug therapy. As a result, all districts have reduced their incidence and rate of leprosy – the national rate has fallen from 4.7 per 10,000 population in 2003 to 2.4 per 10,000 population in 2006. In Oecussi the rate has fallen from 54.2 per 10,000 population in 2004 to 13.8 per 10,000 in 2006; this figure remains higher than other districts in the country (WHO, 2005a).

The survey demonstrated that the district of Oecussi (the isolated enclave located in Indonesian West Timor) continues to have a higher proportion of cases of leprosy than the rest of the country. This may be due to the district's geographical isolation, which may limit access to the diagnosis and treatment available to other districts in Timor-Leste. Another possibility for the higher proportion of cases is the large reservoir of cases that have been historically present. It has been suggested by locals (but not confirmed by any documentation) that Timor-Leste, and Oecussi district in particular, was once used as a leper colony by the Portuguese. The survey findings indicate that this district will remain a challenge for Timor-Leste to meet the objective for global leprosy elimination of less than 1 case per 10,000.

The discovery of the six cases of yaws is consistent with current regional knowledge that isolated foci of activity are present in Timor-Leste and neighbouring Indonesia. The survey identified cases in the districts of Oecussi and Bobanaro.

Both districts have previously reported cases of the disease (WHO, 2008b) and contain geographically isolated areas that are typical settings for yaws. Although it is difficult to assess the prevalence of the disease due to the lack of data, these cases are also likely to be an underestimation of the true disease burden. There are about 4000 new cases reported annually in Indonesia; hence, based on population, poverty levels, environmental factors and the destabilisation of Timor-Leste's health services due to recent conflict, it is estimated that the incidence of yaws in Timor-Leste is 1000 per annum (WHO, 2008b).

Further efforts are needed to locate pockets of infections that are continuing transmission. Some of the participants screened were opportunistically examined while presenting at community health centres for other health issues; however, most cases of leprosy and all but one case of yaws were discovered through examinations in schools. This highlights the importance of community-focused, rather than health-institution-based, control programmes to increase the efficacy of case-finding and reduce the number of undiagnosed individuals.

Atauro Island was identified as having prevalences of scabies and pyoderma that were twice the rate of the other three districts, despite having the smallest number of participants. These findings may be the result of environmental factors and infrastructure. Atauro is extremely dry and fresh water is limited, especially during the dry season. With no industry, employment is scarce on the remote island and residents live in extreme poverty; hence, overcrowding is common. This combination of overcrowding and decreased sanitation is likely contributing to the higher proportion of skin infections.

Health care is also limited on Atauro, a fact that is likely to have contributed to the higher case load of scabies and pyoderma. There are only three CHCs on the island and they are accessible to only half of the population by land, with the remainder of people having to travel by boat. The clinics were unattended for several years during the conflict; they are currently staffed part-time by two local nurses and a medical team run by Australian Aid International, which provides basic primary health-care services for two weeks each month.

There are further limitations in the survey design, and therefore limitations on how accurately the findings represent the actual burden of disease caused by skin infections in Timor-Leste. Although the survey aimed to include geographically and culturally diverse locations across the country in order to achieve a cross-sectional sample, it was only conducted in four of the 13 districts due to time and security. At the time of the study there was still ongoing conflict in Timor-Leste, and districts that posed an increased amount of risk to the survey team were not included. In order to increase participation and provide treatment to all those who required it, all willing participants were included in the survey. Hence, recruitment was not randomised, which may have resulted in a selection bias of participants.

Skin diseases were based on clinical diagnosis by a team of individuals, allowing for variation in the accuracy of identification. Diagnoses of skin conditions were also not confirmed via other methods, such as laboratory tests. Severity of skin diseases was not captured as grading or staging of the skin conditions was not conducted.

The most common infections – dermatophytosis, scabies and pyoderma – are causing discomfort among those who are infected, and all of the five conditions included in the survey have the potential to result in acute and possibly long-term negative health outcomes for the population of Timor-Leste. The high prevalence of scabies infection is likely to be an important contributing factor to the correspondingly high proportion of pyoderma observed, particularly among young children. The repeated scratching caused by a scabies infection can result in breaks in the skin, which in turn facilitate bacterial infection (pyoderma) (Heymann, 2004).

Pyoderma is the most common bacterial skin condition and usually results from infection with staphylococcal or streptococcal bacteria (Carapetis *et al.*, 1999; Heymann, 2004; WHO, 2005c). The literature shows that the majority of pyoderma is due to streptococcal bacteria, including streptococci pyogenes (Carapetis *et al.*, 1999; Carapetis *et al.*, 2005; WHO, 2005c). Research conducted in Aboriginal communities in northern Australia indicated that 80% of pyoderma lesions were culture positive for GAS(Currie and Carapetis, 2000; Shelby-James *et al.*, 2002).

Worldwide, the highest incidence of GAS infections occurs in countries with warmer climates, where housing is overcrowded and the opportunity to use soap and water is limited (Melrose and Rahmah, 2006). While the prevalence of GAS is not known in Timor-Leste, it is plausible that the high proportion of pyoderma seen during our survey was infections with GAS, which may be a contributing factor in the poor health of the Timorese population (WHO, 2005c).

Group A streptococcus is known to be the causal agent for a variety of conditions, ranging from mild superficial skin infections to life-threatening systemic diseases. Acute conditions include pyoderma, cellutitis, tonsillitis and septicemia. Infection with this group of bacteria can also result in acute conditions, which can then progress to chronic auto-immune illness in some individuals and some of which can also be fatal. Specific examples include post-streptococcal glomerulonephritis (PSGN), which may result in both acute and chronic kidney dysfunction (Benudiz, 2007), and rheumatic heart fever, another acute sequela that can progress to chronic and sometime fatal rheumatic heart disease (American Heart Association, 2009).

There is also evidence to suggest systemic disease within the population owing to the finding of a 40% prevalence of proteinuria among participants, which is higher than expected based on data from the region. Community-based screening of adults in Japan showed the highest prevalence of proteinuria to be 5.3% (Kunihiro *et al.*, 2008), and a Taiwanese study found that rapid urinalysis dipsticks have been shown to be 95% sensitive and 70% specific in field screening in Sudan (Kaiser *et al.*, 1992).

Renal disease, both acute and chronic, is multi-factorial, and there may be several confounding factors contributing to the abnormal urine results. The majority of the proteinuria was due to trace amounts of protein, which could be a transient phenomenon due to pyrexia, intensive physical activity or acute illness, including urinary tract infection (Carroll and Temte, 2000; Ledingham and Warrell, 2000). Subclinical renal damage can also be caused by infections, hypertension, diabetes (Carroll and Temte, 2000) and lymphatic filariasis (Dreyer *et al.*, 1992; Melrose and Rahmah, 2006). False positive results and contamination of specimens, especially from females, also need to be considered.

Unfortunately, the methodology did not allow for differentiation of the proteins identified in the urine. However, it is difficult to provide a definitive clinical interpretation on dipstick urinalysis alone without additional clinical information, such as blood pressure, data on hematuria or further laboratory analysis of urine.

However, considering the prevalence of pyoderma among participants it is possible that the proteinuria is the result of acute kidney damage caused by PSGN. As previously mentioned, acute nephritis following pyoderma is a well-recognised sequela of GAS infection (Rajajee, 1990; Lawrence *et al.*, 2005; WHO, 2005b). Either recent or past infections are possible owing to high rates of pyoderma in the community, as residual protein may be detected from an episode up to two years earlier (Ledingham and Warrell, 2000).

Odds-ratios tests revealed that there was no association between proteinuria and pyoderma. However, results did indicate a stronger association between proteinuria and those participants who were co-infected with both scabies and pyoderma than those who had either infection alone – a trend observed in both the baseline and follow-up surveys conducted in Tuvalu, presented in previous chapters. Although these results were not found to be statistically significant according to Pearson Chi-square tests, they have clinical significance to the populations that are living with the daily burden of the infections, and seem to confirm the growing body of knowledge that points to the global burden of skin infections.

The findings suggest that infection with scabies mites may contribute to systemic disease, as indicated by elevated protein in the urine, or there could be an underlying subclinical pathology with scabies infection that is compounded by co-infection with a streptococcal bacterial infection. The possibility of a link between scabies and renal pathology is supported by different lines of evidence. High rates of renal disease also have a high prevalence with scabies and pyoderma in underprivileged setting in tropical regions (Carapetis *et al.*, 1999; Currie and Brewster, 2001; Carapetis *et al.*, 2005; Feldmeier *et al.*, 2005).

It has been historically documented that seasonal fluctuations in scabies incidence are followed by similar patterns of newly diagnosed cases of PSGN (Whittle *et al.*, 1973; Verma *et al.*, 1983), and that epidemics of PSGN have paralleled epidemics of scabies in tropical settings (Svartman *et al.*, 1972).

The pattern of overlapping spatial distribution of scabies and PSGN in such settings has been documented over time in Chile (Berrios *et al.*, 2004) and Trinidad (Svartman *et al.*, 1972; Reid and Poon-King, 1990). Some of the most compelling evidence of a link between scabies and PSGN comes from a study conducted in the Solomon Islands, where mass treatment with ivermectin reduced the prevalence of scabies by 96% and the indicators of renal dysfunction to near zero (Lawrence *et al.*, 2005).

4.5 Conclusions

This survey has provided evidence that skin infections are a public health concern in Timor-Leste and that the population would benefit from a disease control intervention aimed at diagnosing, treating and ultimately reducing the prevalence of these infections in the community. Reducing the prevalence of skin diseases could result in an improved quality of life, reduce the impact of associated acute and chronic outcomes, and facilitate reaching global targets for the elimination of leprosy and yaws.

Research from northern Australia has documented the benefits of healthy skin programmes initiated in rural Aboriginal communities. Preliminary results have shown the following results (CRCAH, 2004; CRCAH, 2006):

- prevalence of scabies reduced from 30% to as low as 5% in some communities;
- prevalence of skin sores among children reduced from 50% to less than 25%, with the vast majority of remaining sores being mild/moderate rather than severe;
- reductions in antibiotic use and clinic presentations (skin infections are the major reason for child presentations in most Aboriginal communities); and
- potential reductions in skin-associated chronic or severe acute diseases (e.g. rheumatic fever / rheumatic heart disease, PSGN-associated renal disease, severe streptococcal and staphylococcal infections).

However, establishing disease control programmes in a country such as Timor-Leste is challenging. Programmes that require active case finding and subsequent follow-up, such as tuberculosis or leprosy control, are time- and resource-intensive operations. Despite these difficulties, there are successful disease control activities being undertaken; one example is the MoH's integrated programme to eliminate lymphatic filariasis (LF) and control intestinal parasitic infections. Therefore, it is suggested that an expansion of an existing programme be undertaken to include a healthy skin component.

A community-based healthy skin programme could be ‘piggybacked’ or integrated into the existing leprosy or LF control programmes – both have established procedures and logistics for active case-finding, treatment and onward referral within the public health system. Utilising the existing structures and personnel would increase interventions without greatly increasing the costs associated with the creation of a new stand-alone disease control programme. Existing staff could receive additional training and screen and treat for multiple diseases during site visits, thus increasing the efficiency of community visits while providing much-needed public health services.

The efficacy of community-based programming was highlighted by the detection of previously undiagnosed cases through opportunistic screening, which increases the surveillance catchment by targeting whole communities and not relying on individuals presenting at clinics or other health facilities, and allows for greater and earlier detection of cases, as shown by this survey. Community-based activities may also increase catchment by reducing social and geographic barriers that inhibit individuals from presenting to the health system.

In summary, the introduction of an integrated community-based healthy skin programme into one of the operational disease control programmes containing education, surveillance, treatment and other disease-control initiatives would reduce the prevalence of skin infections and their associated outcomes in Timor-Leste. Integration of the control of skin infections into an existing disease-control intervention would allow for the most efficient use of limited resources while achieving maximum health benefits for the population of Timor-Leste.

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Chapter 5

Scabies in the Pacific: The pathology and potential consequences of this neglected skin disease in Pacific Island nations

5.0 Abstract

This chapter is a review of the pathology of scabies (*Sarcoptes scabiei*) as a neglected tropical disease and as an underlying contributor to more complex public health issues in Pacific Island communities. It outlines the clinical presentations, impact and complications that can arise from scabies infection, and the potential wide-reaching public health implications resulting from the disease in developing nations within tropical settings. It also explores the gaps in knowledge concerning the true burden of the disease of scabies in the Western Pacific region.

5.1 Introduction

Sarcoptes scabiei is an ectoparasitic mite that burrows under the skin of mammalian hosts (Figure 5.1) (Becherel *et al.*, 1999). The parasite is found worldwide and is a disease of human and veterinary importance. Scabies, like other neglected tropical diseases, is recognised as a condition of severe poverty because it spreads rapidly in conditions of overcrowding and decreased standards of hygiene (Heymann, 2004; Hengge *et al.*, 2006). The disease is transmitted directly through contact with a person infected with scabies, or by fomites (objects such as bedding and clothing) that are contaminated with the mites (Flinders and De Schweinitz, 2004).

The prevalence of scabies is considered to be low in the general population in most industrialised nations. It is usually only considered to be a disease of public health importance in indigenous populations, the elderly, and immune-compromised individuals such as those living with HIV and AIDS (Walton *et al.*, 2004). Hence, scabies and other skin infections (with the exception of leprosy) remain largely overlooked as a public health issue.

Figure 5.1

Figure 5.1: *Scarcoptes scabiei* mite. Scratching bites from scabies mites can facilitate the spread of bacteria, which can result in serious clinical and public health outcomes.

Parasitic skin diseases, including scabies, are present in all climates; however, under conditions of poverty seen in developing nations, especially under tropical conditions, scabies and other ectoparasite infections are more frequent. It is estimated that at any one time up to 300 million people worldwide are infected (Haymann, 2004; Feldmeier and Heukelbach, 2009). In contrast to the general population, the prevalence of scabies is higher in vulnerable or disadvantaged communities, and vulnerable populations, as shown in Australian Aboriginal communities, Latin America, sub-Saharan Africa and homeless populations (Currie and Carapetis, 2000; Currie and Brewster, 2001; Chimelli *et al.*, 2003; Carapetis *et al.*, 2004; Heukelbach *et al.*, 2004; Heukelbach *et al.*, 2005; Lawrence *et al.*, 2005; Campbell and Campbell, 2007; Weissharr *et al.*, 2008).

5.2 Clinical presentations

Clinically, scabies typically presents as allergic dermatitis resulting from the hallmark symptom pruritis (itching), caused by the burrowing of the mite under the skin (Weissharr *et al.*, 2008). The intensity of infection and accompanying morbidity are variable and depend upon the level of mite infestation and host immune factors (Flinders and De Schweinitz, 2004; Burkhart, 2006). Scabies lesions or burrows are sometimes visible to the eye but subclinical and low-level infections are often difficult to diagnose, and these cases are often misdiagnosed or missed (Figure 5.2).

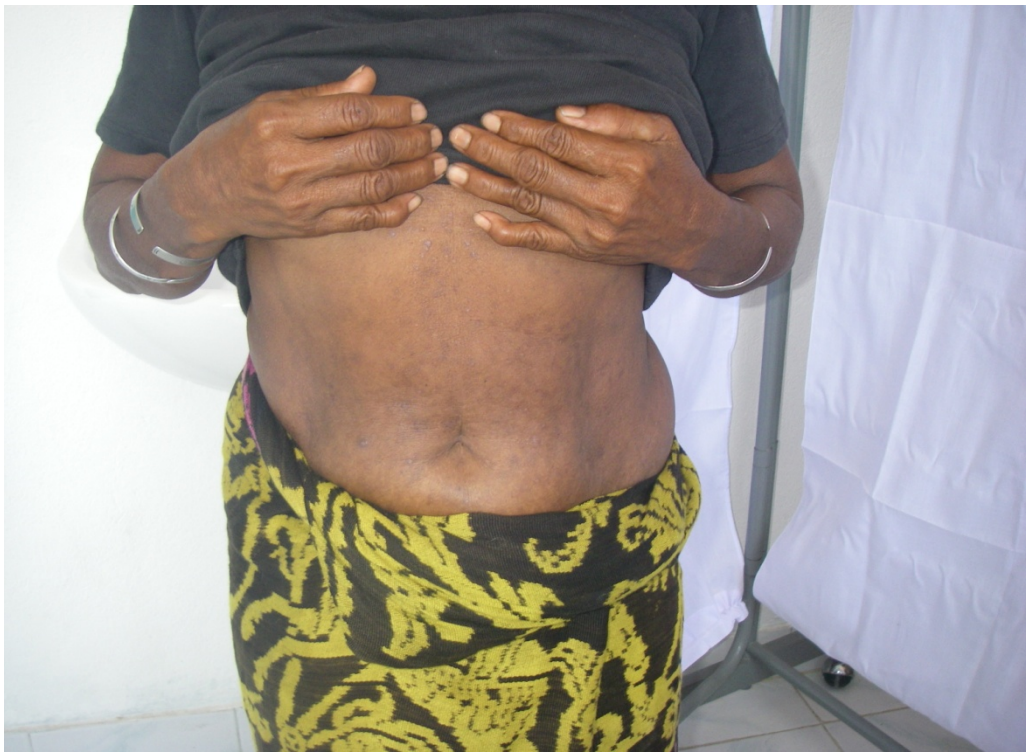

Figure 5.2: Adult female from Timor-Leste with scabies infection on abdomen, 2007. Lesions are seen as darker spots against the skin.

The most severe presentation of the disease is crusted or Norwegian scabies. This extreme manifestation is caused by hyper-infection with hundreds of mites, resulting in hyperkeratosis – the thickening and hardening of the skin (Figure 5.3) (Walton *et al.*, 2008). It is most often seen in immune-compromised individuals (people living with HIV and AIDS, the elderly, homeless populations) as those with a sub-optimal immune system are vulnerable to hyper-infection by mites (Josephine *et al.*, 2006).

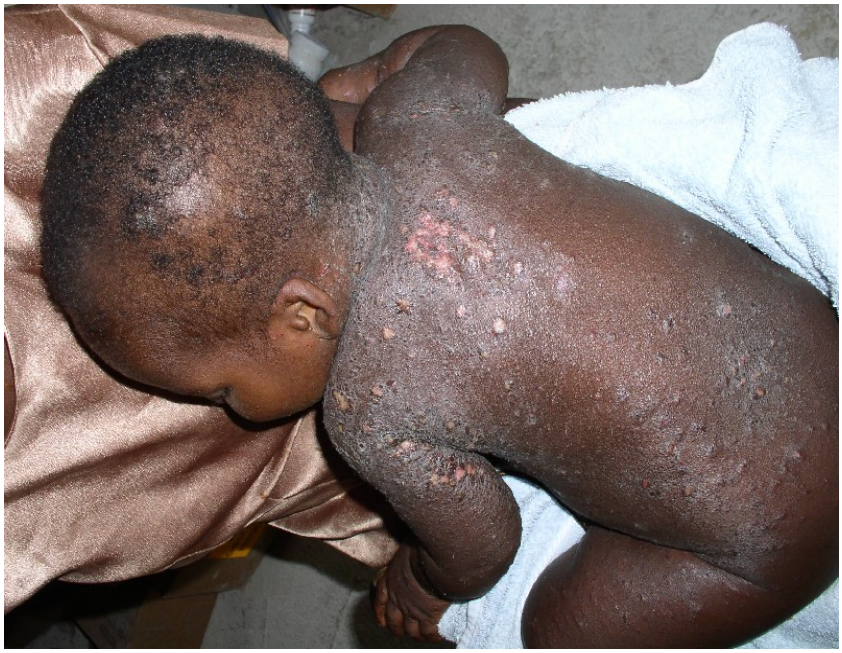

Figure 5.3: Baby with hyper-infection with scabies, Papua New Guinea, 2005.

5.3 Complications

The most common complication with scabies infestation is secondary bacterial (pyoderma) or fungal infection. Secondary infections are facilitated by breaks in the skin caused by the intense pruritis, allowing other pathogens an opportunity to colonise the skin (Hay, 2003; Carapetis *et al.*, 2004; Walton *et al.*, 2004; Hengge *et al.*, 2006; Weissharr *et al.*, 2008). The most commonly seen secondary infection is bacterial pyoderma. Co-infections with dermatophyte fungal species are less common (Sfia *et al.*, 2007). Figure 5.5 outlines the full extent of complications that can arise from scabies infection.

5.3.1 Pyoderma

Pyoderma is a superficial bacterial infection of the skin, including boils, ulcers, furuncles and carbuncles, which arise from infection with pyogenic bacteria, usually *Staphylococcus aureus*, *Streptococcus pyogenes* (GAS) or both (Carapetis *et al.*, 2005). Pyoderma is the complication that poses the greatest risk to public health, as bacterial infections cause a broad spectrum of disease that can range from simple boils and ulcers to more severe presentation, such as cellulitis and septicaemia (Tyring, 2006; McDonald *et al.*, 2007). The worldwide prevalence of bacterial pyoderma is estimated at 18.1 million cases, with 1.78 million new cases diagnosed each year (Carapetis *et al.*, 2005); these figures are considered to be an underestimation of the true global burden of the disease.

Research from the World Health Organization has indicated that the majority of bacterial pyoderma is attributed to streptococcal species, including GAS (WHO, 2005c). This is further supported by findings from Australian Aboriginal communities in which 10–90% of children had purulent skin sores, with GAS isolated as the primary pathogen in up to 80% of pyoderma lesions (Currie and Carapetis, 2000; Shelby-James *et al.*, 2002). In communities with high rates of GAS, children often experience repeated infections and it is common to have several episodes of pyoderma in the course of a year (Rodriguez, 2004). Also, Carapetis found that in cases with several pyoderma lesions present, each lesion was usually colonised by a different strain of GAS (Currie and Carapetis, 2000), thus amplifying the opportunity for systemic infection due to the tendency of GAS bacteria to spread into the deeper tissues of the body (Bisno and Stevens, 1996).

The exact factors that predispose individuals to pyoderma infection are not clear, but experience from several developing countries indicates that those from resource-poor communities who are living in conditions of crowding and have reduced access to clean water are at greater risk, especially children (Feldmeier *et al.*, 2005). The literature also indicates that pyoderma and scabies are most often found in children, especially children under the age of 10 years (WHO, 2005c; Seebacher *et al.*, 2008).

Global findings demonstrate a strong association between scabies and pyoderma. In settings where parasitic skin diseases are endemic, streptococcal colonisation of fingertips is frequent (Feldmeier *et al.*, 2005). In indigenous communities in northern Australia, scabies infection was found to be an underlying factor in 50–70% of streptococci-related pyoderma, and 80% of super-infected lesions contained GAS (Currie and Carapetis, 2000; Brook, 2002) According to Lawrence *et al.*, in the Solomon Islands, where the prevalence of scabies in children was found to 25%, 86% of swabbed fingertips were positive for streptococci and 71% were identified as GAS isolates (Lawrence *et al.*, 2005).

It has been suggested that GAS colonisation is facilitated by scabies not solely through micro-abrasions in the skin, but also from unknown factors inside the burrows that favour the survival and multiplication of GAS bacteria (Feldmeier *et al.*, 2005). This suggestion is attributed to the global association of GAS with scabies rather than other parasitic skin diseases (PSDs), even though other PSDs cause pruritis. Additionally, scabies is the only PSD to have documented long-term consequences of the colonisation of skin lesions by GAS (Feldmeier *et al.*, 2005).

For children residing in resource-poor tropical settings, evidence has shown that early colonisation and long-term carriage of GAS have the potential to result in hyper-infection of individuals and communities. They are also the basis for longer-term implications due to repeated and continuous exposure to multiple strains of GAS in highly endemic settings. The majority of these bacterial infections have been shown to be the result of underlying scabies infection (Bisno and Stevens, 1996; Heukelbach *et al.*, 2005; Feldmeier and Heukelbach, 2009).

5.3.2 Renal disease

Rheumatic heart fever and renal disease are two serious complications of GAS that have both acute and long-term clinical consequences. Acute renal disease is a documented complication following streptococcal infection, including post-streptococcal glomerulonephritis (PSGN) (Goodfellow *et al.*, 1999; Berrios *et al.*, 2004; Carapetis *et al.*, 2005). This syndrome is associated with acute inflammation of the nephron glomerulus due to the host immune response to specific strains of GAS. Symptoms usually appear 10–14 days after infection with GAS and most frequently include acute nephrotic syndrome, hypertension, haematuria, proteinuria, fever, malaise and oedema (Ledingham and Warrell, 2000).

Children aged 2–12 years are most often affected by PSGN, but the condition can develop at any age. It is estimated that 15% of patients will develop PSGN after infection with group A beta-hemolytic streptococci (Benudiz, 2007). This prevalence is likely to be an underestimation of the true burden of disease because of subclinical glomerulonephritis (GN), which frequently goes undetected. Lang and Towers estimated that the ratio of subclinical cases of GN to apparent GN was 4:1 to 10:1 (Lang and Towers, 2001), suggesting that the incidence of PSGN is greatly underestimated.

The majority of cases of PSGN (90%) in children are self-resolving. Microscopic haematuria often resolves within six months but proteinuria may linger for up to 10 years (Benudiz, 2007), suggesting long-term impact on the nephrons, even in resolved cases. A small percentage of cases experience more serious manifestations requiring hospitalisation. Permanent renal damage or renal failure are possible consequences of PSGN, requiring lifelong dialysis, or kidney transplantation in severe cases that have progressed to end-stage renal disease (ESRD) (Ledingham and Warrell, 2000; Herrera and Rodriguez-Iturbe, 2003).

Adult cases can have more severe outcomes, with a higher proportion experiencing residual and long-term renal impairment. Thirty to 50% of adults with PSGN can expect prolonged hypertension, renal dysfunction or abnormal urine results (Raff *et al.*, 2005). Progression to ESRD is seen in 3–5% of adult cases, and some unexplained cases of chronic nephritis have been linked to subclinical cases of PSGN (Haas, 2003) .

The exact mechanisms that lead to progression to PSGN after GAS infection in some individuals are unknown, and renal sequelae may not present until several years after exposure. Evidence from many developing countries in tropical climates illustrates a strong association between PSGN and underlying scabies infection. Scabies is the only parasitic skin disease to be linked to long-term consequences following GAS colonisation, with several studies in developing countries that document overlapping epidemics of scabies and PSGN. Examination of 20 years of registered cases of PSGN in Chile indicated that the spatial incidence of high rates of PSGN and high rates of scabies overlapped (Berrios *et al.*, 2004). Similar patterns were observed in Trinidad, where increasing prevalence of scabies over time was paralleled by a rising incidence of PSGN (Svartman *et al.*, 1972; Reid and Poon-King, 1990).

These findings, plus an abundance of evidence from Australian Aboriginal communities (Carapetis, 1998; Carapetis and Currie, 1998; Carapetis *et al.*, 1999; Goodfellow *et al.*, 1999; CRCAH, 2006), document and support the association between scabies and renal disease. Further support for this association is demonstrated by established patterns of seasonal variability, where the incidence of newly diagnosed cases of PSGN is preceded by parallel incidence of scabies cases (Whittle *et al.*, 1973; Verma *et al.*, 1983). The most convincing evidence for a causal relationship between scabies and PSGN is illustrated in a population-based study conducted in the Solomon Islands that showed that after a 96% decrease in scabies prevalence (after mass drug treatment with ivermectin), indicators of renal impairment decreased to almost zero (Lawrence *et al.*, 2005).

Experience points to mechanisms of scabies–pyoderma co-morbidity as aetiology of PSGN and accompanying renal impairment in affected communities. The dynamic pathology between these three conditions is still not completely understood, and GAS (particularly M-subtypes) is thought to be responsible for the development of glomerulonephritis. The role of scabies as an underlying factor of the progression to renal disease needs to be considered, and scabies itself as a causal agent in the development of PSGN cannot be ruled out (Hay, 2003).

5.3.3 Rheumatic heart disease

The global burden of rheumatic heart disease (RHD) is enormous, with data from numerous studies estimating that 282,000 new cases and 232,000 deaths annually can be attributed to this disease (Carapetis *et al.*, 2005). Rheumatic heart fever (RHF) and chronic RHD are the most severe clinical outcomes of infection with GAS, involving an inflammatory condition of the connective tissues of the heart, joints, skin and brain caused by a cross-reaction of host antibodies to specific strains of GAS (American Heart Association, 2009). This delayed immune response usually appears 2–3 weeks after infection with GAS bacteria (Kumar *et al.*, 2007). In up to one-third of all cases of RHD, the underlying streptococcal infection may be asymptomatic.

Acute RHF is a devastating disease that primarily affects children aged 5–15 years. It will develop in 0.03–3% of children and 20% of adults with untreated GAS infection (Chin, 2006; Porth, 2007). The major manifestations are fever, arthritis and carditis. Up to 40% of RHF patients will develop cardiac complications, including pancarditis and pericarditis. The major cause of morbidity and mortality from RHF is rheumatic disease caused by valve damage, with the mortality rate estimated at 2–5% (Chin, 2006). Approximately 60% of patients with rheumatic fever will progress to RHD and experience valve insufficiency in the form of valve stenosis, regurgitation, atrial dilation, arrhythmias and ventricular impairment (Carapetis *et al.*, 2005). Chronic RHD remains the leading cause of mitral valve stenosis (the narrowing of the orifice of the mitral valve(Dajani *et al.*, 1995; Cheng, 2007)) and valve replacement in adults in the developed world, and the estimated mortality rate for RHD is 1–10% (WHO, 2001; WHO, 2005b; Chin, 2006).

Incidence of pyoderma, RHF, and RHD has decreased dramatically in industrialised nations with the exception of vulnerable and indigenous populations, while RHD is a major health problem in the developing world. RHD remains one of the major causes of cardiac-related morbidity and mortality in resource-poor settings, and complications from this condition have a significant human and economic impact on affected populations (Carapetis *et al.*, 2005; Abbas and Person, 2008; Trabelsi *et al.*, 2008).

Cases of acute RHF require treatment with penicillin to manage streptococcal bacteria and reduce the potential for cardiac damage. It is estimated that 40% of paediatric patients who do not develop RHD will still require penicillin prophylaxis until the age of 21 to reduce streptococcal carriage and relapses of RHF (Dajani *et al.*, 1995; National Heart Foundation, 2008; Gerber *et al.*, 2009). Studies based on data from Aboriginal populations in Australia show the median age of the first onset of RHF is 11 years, requiring those without further complications to have, on average, 10 years of antibiotic prophylaxis (Carapetis *et al.*, 2005). Added to this burden of disease is the treatment required for the patients with RHD, including lifelong antibiotic treatment, management of stenosis, and cardiac surgery, including valve replacement.

Historically, RHD is associated with pharyngotonsillitis related to throat carriage of GAS, and PSGN is associated with pyoderma (Chin, 2006), but other evidence challenges this convention. An early study conducted in 1978, which surveyed almost 13,000 school-aged children in Lagos, concluded an association with GAS and carditis in tropical populations that required further investigation (Ogunbi *et al.*, 1978). More recent and compelling evidence of a link between streptococcal skin infections and RHD is obtained from studies with Aboriginal groups in northern Australia. These groups have some of the highest rates of RHF and RHD in the world. Pharyngitis and throat carriage of GAS is low but pyoderma is high, suggesting that skin-related streptococci are likely underlying the epidemic of rheumatic disease in these populations (Carapetis, 1998; Carapetis and Currie, 1998; McDonald *et al.*, 2007).

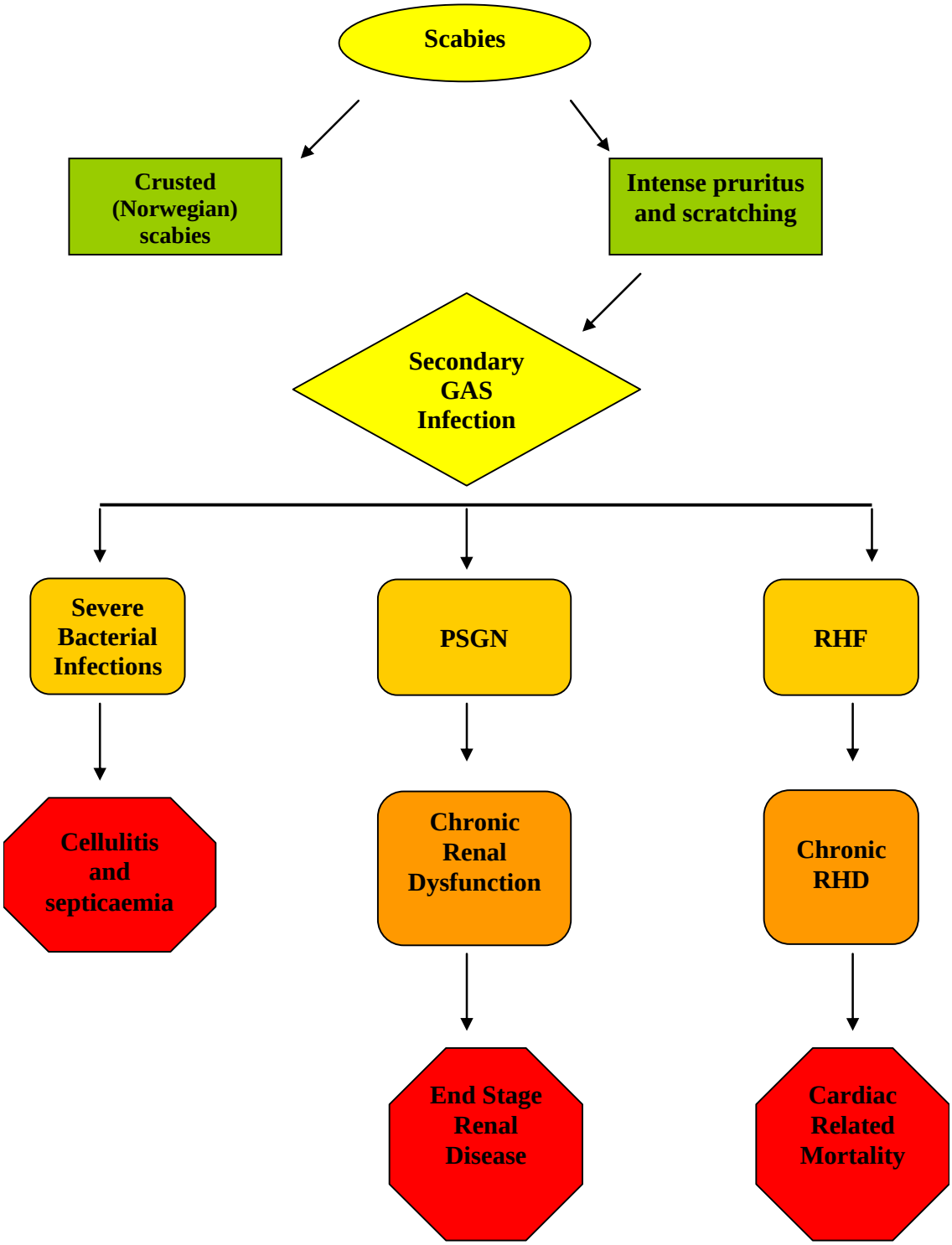

Figure 5.4: Flow Chart of group A streptococcal infection manifestations and complications underpinned by scabies infection.

5.4 Scabies in the Pacific

Skin infections are known to be prevalent in conditions of poverty, overcrowding and poor hygiene, and their propagation is further encouraged by climatic factors present in the humid tropical environment of the South Pacific. Data on skin infections is limited and inconsistent, as many of the 22 Pacific Island countries and territories (PICTs) do not conduct routine surveillance or report on skin diseases. The majority of data is obtained through patient records at health-care facilities, and periodic research and survey activities.

WHO has declared that skin infections, including scabies, are a major health concern in the Western Pacific region (WHO, 2005b). Indicator data from the WHO databank indicates a high rate of scabies in some PICTs: scabies is indicated as one of the top five reasons for presentations to health-care facilities in Vanuatu and the Marshall Islands (WHO, 2008e). An AusAID-initiated project conducted in 1996 and 1997 found the proportion of scabies in Samoa and Vanuatu to be 10% and 2% respectively (White and Barneston, 1998).

Current research illustrates that the rate of scabies is higher than previously assumed. A study undertaken in Fiji in 2008 found that up to one-fifth of all Fijians are affected by scabies (Whitfield, 2008). Findings in the Solomon Islands were similar, with 25% of those in sentinel villages infected with scabies mites. Unpublished research conducted in Tuvalu in 2007 and 2008 indicated the prevalence of skin infections in children aged 2–15 years was 60%: about one-third had scabies, and scabies co-infection with pyoderma was seen in 35% of the study population (Harmen *et al.*, 2008).

Although data in the region is limited, all of the research from 1997 to 2008 suggests that scabies is present in 2–35% of surveyed populations in the Pacific. Extrapolating the average of these figures combined with data from developing nations in other regions, it can be estimated that 20% of the population of Pacific Island nations is infected with scabies.

5.5 Future directions

The relationship between skin infections and RHD and renal disease remains speculative but cannot be discounted. In disadvantaged populations (especially in tropical settings), it is well documented that communities with a high prevalence of GAS have a correspondingly high prevalence of scabies infection, and subsequently a high prevalence of rheumatic and renal disease. From an early age vulnerable individuals are continually exposed and repeatedly infected with various strains of GAS (Feldmeier *et al.*, 2005), generating symptomatic and asymptomatic infection. Limited surveillance and reporting of all streptococci-related disease further compounds the lack of understanding of the epidemiology and pathogenesis of these conditions. Hence, in these settings, the role of skin infections, including scabies, needs to be considered as an underlying factor in the complex co-morbidity involving GAS and proceeding outcomes.

Scabies is a disease of human and veterinary importance and still the cause of significant global morbidity. The suggestion that scabies contributes to the carriage of GAS, or plays a larger role in a complex pathology when in co-infection with other pathogens, demonstrates the need for a disease control strategy. Scabies and other skin conditions (including leprosy) are diseases of extreme poverty and their impact on vulnerable populations is unrecognised. Therefore, scabies and other skin infections could be declared neglected diseases of neglected populations, and should be added to the formal list of neglected tropical diseases (NTDs).

Skin infections, like other NTDs, could benefit from integrated disease control strategies due to their common transmission factors and overlapping distribution with other diseases of poverty and decreased hygiene and sanitation. Control of skin infections could be integrated into existing community-based disease control programmes that periodically undertake community-wide active surveillance, case finding and treatment. Examples of programmes include the WHO programmes for leprosy (WHO, 2006b; Plianbangchang, 2008), tuberculosis (WHO, 2009g) and onchocerciasis (WHO, 2009d); the Global Programme for the Elimination of Lymphatic Filariasis (GPELF) (WHO, 2009c); and the WHO de-worming programme for soil-transmitted helminths (STHs) (WHO, 2009f).

All of the above programmes involve annual community-based interventions to control their mandated diseases. The leprosy, LF and TB programmes often involve door-to-door visits and follow-up to actively seek and treat all cases within affected communities and to capture the largest-possible portion of the targeted populations. Control strategies against onchocerciasis and leprosy are limited to their endemic regions; therefore, interventions for scabies and other common skin infections would be more effective if 'piggy-backed' onto a programme with wider global distribution, such as the global LF and TB programmes, which exist in some capacity in almost all developing settings in tropical climates.

Field teams could be trained to identify and treat common skin infections in addition to the primary targeted disease, thus greatly reducing the operational cost of surveillance and treatment for a stand-alone intervention. The efficiency and cost-savings would be further improved by teams delivering health promotion and education to communities on risk factors and behaviours common to multiple infectious conditions. Another benefit of this approach is the opportunity for early detection at community level – hopefully reducing morbidity and mortality and improving outcomes – rather than relying on patients to present to the health-care system. This proactive approach can be especially beneficial in resource-constrained settings where health resources are often mal-distributed and where those in rural and remote areas have limited or non-existent services.

Theoretically, there are no limits to the evolution of the model of integrated control. If adequately supported in principle and by funding, this strategy could be tailored to provide initiatives that address all NTDs specifically endemic to communities, and could even expand to address other conditions and lack of services, providing comprehensive solutions to achieve improved health that are both efficient and cost-effective.

The first step in addressing the co-morbidity of NTDs is also the first step in addressing the global impact of scabies and other skin infections through the development of 'rapid-impact' chemotherapy packs. This integrated disease control strategy combines 4–6 medications that specifically target the overlapping NTDs in the targeted communities (Fenwick *et al.*, 2005; Molyneux *et al.*, 2005; Hotez *et al.*, 2006a). They are referred to as 'rapid-impact' because the chemotherapy simultaneously targets multiple infectious diseases.

Treatment packs can be quickly distributed via community-based distribution, resulting in rapid improvements in community health while interrupting transmission through a rapid decrease in disease reservoirs. Delivery costs are estimated to be 26–47% less than non-integrated strategies through partner donation initiatives (Hotez *et al.*, 2006b; Hotez *et al.*, 2007a).

The inclusion of the anti-parasitic drug ivermectin in treatment packs against STHs and onchocerciasis (in Africa) has a hidden benefit as this drug is also a highly effective treatment for scabies (Walton *et al.*, 2004; Lawrence *et al.*, 2005; Walton *et al.*, 2008). Ivermectin has been shown to be more effective than topical treatments such as benzyl-benzoate or permethrin cream in treating scabies and more useful in high-prevalence settings, and to have higher compliance (Brooks and Grace, 2002). If high coverage is achieved, mass oral treatment drastically and quickly reduces the reservoir of the mites within communities, even in settings of poor hygiene and limited access to water (Brooks and Grace, 2002).

It is not surprising that the literature shows a recent trend in treatment for scabies in the developing world where the disease is endemic or hyper-endemic in impoverished communities; the trend favours the mass administration of oral ivermectin to treat entire populations, thereby reducing the prevalence of scabies, decreasing the community reservoir, and reducing the burden of disease associated with scabies and pyoderma (Brockerie *et al.*, 2000; Heukelbach *et al.*, 2004; Speare and Durrheim, 2004). Studies using mass treatment with ivermectin as an intervention for scabies have documented success at reducing the prevalence of the parasite, and this reduction in prevalence is followed by a reduction in pyoderma and pyoderma-associated outcomes, including acute renal damage (Carapetis *et al.*, 2004; Heukelbach *et al.*, 2004; Lawrence *et al.*, 2005; CRCAH, 2006).

The GPELF has been identified as an entry point for integrating the control of NTDs (Molyneux and Nantulya, 2004; Molyneux *et al.*, 2005) and is also the logical entry point for scabies control, based on mass chemotherapy with ivermectin to control LF in parts of Africa. Ivermectin replaces DEC in areas where LF is co-endemic with onchocerciasis, as DEC provokes a severe immune reaction, called the Mazzotti reaction, in individuals who are co-infected (Cooper *et al.*, 2002). Therefore, replacing albendazole with ivermectin in combination with DEC for mass chemotherapy for LF would expand the fight against NTDs by supporting the treatment of LF and reducing the prevalence of STHs while having a significant impact on the reduction of scabies (Speare and Durrheim, 2004; Molyneux *et al.*, 2005; Hotez *et al.*, 2007a).

Studies have shown that ivermectin is a highly effective treatment against LF (Ottesen, 2006; Ottesen *et al.*, 2008; Molyneux, 2009). Clinical reviews have found that ivermectin, in combination with DEC or albendazole, was equally if not more effective than albendazole with DEC in reducing the prevalence of microfilariae in infected patients, and in maintaining the reduction for up to 12 months after a single dose (Tisch *et al.*, 2005; Merck, 2007).

According to a systematic review, *Trichuris trichiura* shows an unsatisfactory response to single-dose albendazole (Keiser and Utzinger, 2008). Ivermectin has been shown to be effective against a wider variety of STHs and other intestinal parasites, including *Ascaris lumbricoides*, *Strongyloides stercoralis* and *Trichuris trichiura (Heymann, 2004; Omura, 2008)*, highlighting the benefits of this drug in settings where the prevalence of Trichuris is known to be high.

Ivermectin was approved for human use in 1987 (Keiser and Utzinger, 2008). Since then millions of doses have been given for the mass treatment of onchocerciasis, LF and other parasitic conditions. In mass treatment campaigns the drug has been shown to be safe with few contraindications and able to be given to children weighing over 15 kg, with few reported adverse reactions (Oyibo and Fagbenro-Beyioku, 2003; Heukelbach *et al.*, 2004; Gyapong, 2005; Molyneux, 2009). Fewer adverse reactions may result in greater compliance and coverage in mass treatment.

In summary, ivermectin is a more cost-effective solution than albendazole to a wider range of NTDs, including scabies. Therefore, the inclusion of ivermectin in the treatment protocols for the GPELF, and expansion of ‘rapid-impact’ mass chemotherapy into all areas at risk for multiple NTDs, have the potential to significantly reduce the prevalence and burden of several infectious diseases, including scabies and pyoderma and their associated outcomes.

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Chapter 6

Recommendations for addressing multiple pathogens in resource-constrained settings: A role for an integrated disease control programme

6.1 Background

The recommendations outlined in this chapter are based on the results of the surveys conducted in Tuvalu and Timor-Leste presented earlier. While the recommendations are based on specific findings from the two study locations, the context can be extrapolated and applied to other developing nations in tropical settings. Results from the health surveys indicated a high proportion of multiple infectious pathogens – specifically parasitic and skin infections – in both Tuvalu and Timor-Leste. The study also confirmed a high prevalence of scabies and bacterial pyoderma in both countries. This epidemiological profile is consistent with other developing nations (Mahe, 2001; Mahe and Fanello, 2003; WHO, 2005c; Feldmeier and Heukelbach, 2009).

As outlined in the previous chapters, several of the infectious agents identified during the surveys have the potential to cause both short- and long-term negative health outcomes. These include the associated sequelae from infection with GAS bacteria (as outlined in detail in Chapter 5), and the multitude of health problems associated with soil-transmitted helminth (STH) infections (Lawrence *et al.*, 2005; Sur *et al.*, 2005; WHO, 2005b; National Heart Foundation, 2008; Ndyomugyenyi *et al.*, 2008). Additionally, the potential impact from the combined co-morbidity of these co-endemic pathogens is concerning. Clinical findings from the study suggest that co-morbidity is impacting the health of the populations as a result of the higher-than-expected prevalence of anaemia in Tuvalu, and haematuria and proteinuria (suggesting the possibility of systemic disease) in both nations.

Skin infections (with the exception of leprosy) are currently not addressed in either country (or in most developing-country settings) by national programmes despite their frequency in the developing world, and competing health priorties. (Mahe and Fanello, 2003; WHO, 2005c; Tyring, 2006; WHO, 2008b; Feldmeier and Heukelbach, 2009). Lymphatic filariasis (LF) has been addressed in Tuvalu through the WHO Pacific Programme to Eliminate Lymphatic Filariasis (PacELF) since 2000, and in Timor-Leste since 1999 (WHO, 2005d; PacELF, 2008).

Control of intestinal parasites has been supported by WHO in Timor-Leste since 2004 and in Tuvalu in 2007 (WHO, 2007a; WHO, 2007c). The variability of programmes and interventions between countries illustrates the differences in disease priorities, and the inconsistency of disease control programmes, in developing settings.

Timor-Leste and Tuvalu are geographically and culturally diverse nations within the diverse Asia-Pacific region (Tuvalu is included in the Regional Office for the Western Pacific and Timor-Leste in the Regional Office for South-East Asia, according to WHO) (WHO, 2009a). However, present in both countries is the combination of environmental and socio-economic factors that contribute to the propagation of infectious diseases. Poverty is an underlying issue in all developing countries and impacts the social determinants of health: education, housing standards, infrastructure, nutrition, and access to health care (Anon., 2003; Dodd and Cassels, 2006; Campbell and Campbell, 2007). The presence and high prevalence of the diseases identified during the surveys are indicative of poverty and the environmental conditions mentioned above (Ezzati *et al.*, 2004; Heymann, 2004; Assaf, 2006; Campbell and Campbell, 2007; Hotez *et al.*, 2008).

Intestinal parasites, LF and leprosy form part of a group of illnesses and conditions now recognised as neglected tropical diseases (NTDs) by WHO (Hotez *et al.*, 2006b; WHO, 2007c; WHO, 2008a). This group of diseases has been expanded to include up to 36 conditions endemic in tropical settings that cause significant morbidity and/or mortality. In turn, this results in enormous physical, social and economic impact on large, resource-poor populations. Frequently, this group of diseases geographically overlap, causing co-morbidity. The impact of these diseases alone and in combination is largely overlooked by the health sector (Hotez *et al.*, 2006b; Hotez *et al.*, 2007a; WHO, 2008a).

The confirmed presence of multiple infectious pathogens in Tuvalu and Timor-Leste demonstrates the need for these nations to reconsider current disease control strategies. An expansion and modification of the scope of existing programmes is required in order to address skin diseases as an area of public health importance, thereby reducing the prevalence and negative health outcomes of parasitic and skin diseases.

6.2 Recommendations: Overview

Considering the high proportion of skin infections identified in the surveys (see chapters 2 and 4) and already identified in developing settings (Mahe, 2001; WHO, 2005c; Tyring, 2006), it can be expected that skin infections are co-endemic with other neglected tropical diseases. Therefore, skin diseases are likely co-contributors to the significant burden of illness in impoverished populations. As skin diseases are transmitted under the same socioeconomic conditions as other NTDs (Heymann, 2004; Tyring, 2006) and impact the same populations as other NTDs (Ehrenberg and Ault, 2005; Mathers *et al.*, 2007; Feldmeier and Heukelbach, 2009), it seems logical to address skin diseases under the same framework as the existing NTDs. Therefore, the first step in addressing these pathogens is to identify skin diseases, especially scabies, as a public health priority in the developing world and declare them to be NTDs. Once skin infections are officially considered as NTDs they can be addressed within the framework for the control of NTDs.

NTDs are diseases of poverty and are sustained through a complex interaction of social and environmental factors (see Figure 1.1 in chapter 1) that are linked to the social determinants of health (Hotez *et al.*, 2006b; Mathers *et al.*, 2007). It is unrealistic to assume that treatment initiatives alone will provide a long-term solution to reducing the disease burden of NTDs if the factors that sustain them remain unchanged. The proposed strategy recommends a broader approach to reducing the prevalence of these neglected diseases by not only treating them but by preventing their transmission by reducing or eliminating the conditions that favour their propagation. Overall, this would be accomplished by a two-tiered approach that aims to reduce the burden of NTDs (encompassing skin diseases) through detection and treatment initiatives, as well as developing broader community development initiatives that invest in the community and aim to improve the social and environmental conditions that are currently maintaining the cycle of disease and poverty.

Owing to the large amount of planning and resources involved in the recommended strategy, the intervention should be implemented in two stages. The first set of initiatives focuses on detection and treatment activities, aiming to result in an immediate reduction in the burden of acute illness of the targeted diseases, and the prevention of their chronic sequelae. Secondly, it is recommended that treatment-centred activities be simultaneously paired with, or followed up with, initiatives aimed at improving the social and environmental conditions in communities, thereby reducing the opportunity for disease transmission.

It is further recommended that the programme be community-based, as the Timor survey highlighted the benefits of increased and early detection of asymptomatic cases through community-based active surveillance.

In addition to multiple infectious diseases, survey findings from Tuvalu identified a high proportion of childhood obesity. This epidemiological profile of co-morbidity of infectious and lifestyle-related chronic disease is consistent with other developing settings (Lippe *et al.*, 2007; Misra and Khurana, 2008; Hossain *et al.*, 2009). The negative consequences of being overweight and obese have been documented (CDC, 2008; Misra and Khurana, 2008; Latner *et al.*, 2009; Zabelina *et al.*, 2009). It is probable that obesity, especially in children, is a contributing factor to ill health in this population; however, addressing obesity and other lifestyle-related chronic diseases is beyond the scope of this paper.

6.2.1 Strategic planning for neglected tropical diseases

The development of this overall strategic plan to adequately address NTDs (including skin infections) in developing settings is based on the urgent need to address these neglected conditions as demonstrated by the literature and the results from the survey. It is also needed due to a lack of existing policies and structures to address the NTDs. The strategic plan was guided by the evidence and current trends in public health and control of infectious diseases, especially NTDs. Contained within the overarching strategy are policies to address the disease burden of specific NTDs and improve the overall health and social and environmental conditions currently experienced across the Asia-Pacific region. In general, the recommended policies and proposed initiatives are not location-specific, as they are based on knowledge obtained in two different settings. However, all or parts of the document could be readily adapted and applied in similar settings.

The enormous resources required to achieve the objectives in this chapter are probably beyond the capacity of most resource-constrained settings, and the targeted diseases (especially skin infections) are usually considered to be a low priority. To overcome resource constraints, an integrated control strategy is recommended to improve the efficiency and cost-effectiveness of the control programme by combining or integrating control initiatives of multiple NTDs into one programme.

Current literature supports the integration of NTD control programmes in order to reach the targeted goals of the reduction and elimination of specific diseases, as this approach is more efficient and cost-effective in resource-limited settings (Ehrenberg and Ault, 2005; Hotez *et al.*, 2006a; Holveck *et al.*, 2007; WHO, 2007c). Recent reviews of such programmes have indicated that the approach has been successful in the expansion of mass treatment and other control initiatives and is having an impact on the burden of disease attributed to NTDs (Molyneux, 2004; Lammie *et al.*, 2006; Hotez *et al.*, 2007b; Ottesen *et al.*, 2008). Hence, the recommendations outlined here are in line with the current trend towards integrated control for NTDs.

Control of parasitic and skin diseases can be made more efficient and economical by integrating or 'piggy-backing' the control of skin infections into existing disease control programmes. Many developing nations in the Asia-Pacific region, including Tuvalu and Timor-Leste, have existing disease control programmes where the research surveys for this study were integrated or 'piggy-backed' onto the ongoing leprosy programme (Timor-Leste) and the Global Programme for the Elimination of Lymphatic Filariasis (GPELF) (Tuvalu). The research undertaken for this study provides supporting evidence that these pre-existing structures can be an effective starting point to address multiple health issues. In fact, GPELF has been identified as the most logical entry point for integration of disease control (Molyneux *et al.*, 2005; Hotez *et al.*, 2006a; Ottesen *et al.*, 2008), and due to the wide distribution and success of the programme (Ottesen *et al.*, 2008; PacELF, 2008) it is the most logical launching point to address skin diseases in the Asia-Pacific region. This will be discussed later in the chapter.

The recommendations outlined in this chapter take into consideration the current shift in public health policy that acknowledges the need for a broader approach in the fight against infectious diseases. This includes addressing the social determinants of health as well as socio-economic and environmental factors influencing NTDs. The Millennium Development Goals (MDGs) and other 'pro-poor' policies that strongly advocate for the global reduction of poverty in order to break the poverty–disease cycle are strong supporting policies for the control and elimination of NTDs and other infectious diseases (Molyneux *et al.*, 2005; Dodd and Cassels, 2006). This trend was apparent at the most recent (6th) European Congress on Tropical Medicine and International Health held in Verona, Italy in September 2009, whose theme was 'Equity, Human Rights, and Access to Care' (SIMET, 2009).

While poverty has been found to be a clear link in the cycle of infectious disease, and plays a significant role in the global burden of NTDs, specific poverty-reduction strategies are beyond the scope of this study. Current trends in health system development and policies support increased equity and access to health care as well as addressing the social determinants of health, and were taken into consideration in the development of the recommendations.

A strong supporting framework for the control of NTDs comes from the 2008 report of the WHO Commission on Social Determinants of Health (CSDH). CSDH was established in 2005 in response to the recognition that social factors were contributing to ill health and furthering inequities, and to support member states in addressing these social determinants of health (WHO, 2009e). The committee defines the social determinants of health as the 'conditions in which people are born, grow, live, work and age, including the health system' (WHO, 2009e). The world's political and international health leaders are recognising the urgent need to make a major, sustained commitment to strengthening health systems. This renewed political interest presents an important opportunity to make sustainable improvements across disease areas and health programmes, and to redouble global efforts to meet the challenge of achieving the MDGs (WHO, 2009e).

The first CSDH report published in 2008, simply titled 'Why treat people without changing what makes them sick?', identified three strategies to address the issue of ill health resulting from social, environmental and political inequities (CSDH, 2008):

1. improve daily living conditions;
2. tackle the inequitable distribution of power, money and resources; and
3. measure and understand the problem and assess the impact of action.

Another overarching framework used in the development of recommendations is the WHO initiative for health systems strengthening (HSS), which recognises the urgent need for countries to commit to the strengthening of health-care systems to provide the necessary services to meet the needs of their populations, adequately address the burden of ill health, and achieve the MDGs (WHO, 2009b). A WHO report on HSS published in 2007 outlines six targeted areas (described as building blocks) for the strengthening of health-care systems that are needed to meet the MDGs, achieve good health outcomes, and cope with the health-care crisis and challenges that arise (WHO, 2007b).

The six recommended building blocks are:

- good health services
- a well-performing health workforce
- a well-functioning health information system
- equitable access to essential medical products, vaccines and technologies
- good health financing
- leadership and governance.

Elements from the health policies and frameworks outlined in the WHO document were incorporated to develop a framework to address NTDs. The model outlined below for addressing NTDs (and possible other health issues) is recommended to address both diseases and their causal factors, and to develop short- and long-term solutions to NTDs, including parasitic and skin conditions. The individual country settings within the region will have specific disease and population profiles, and existing systems. Therefore, strategic programming must be adaptive to individual settings.

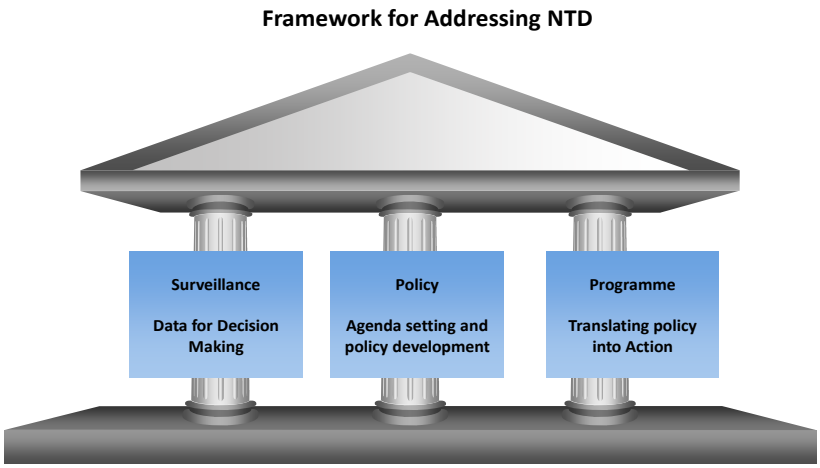

Figure 6.1: Framework for addressing NTDs.

The first stage (or pillar) recommends surveillance initiatives to provide the data required for evidence-based decision making. Data on parasitic and skin infections is limited in the Asia-Pacific region and surveillance activities need to provide the necessary demographic, prevalence, morbidity and other health-related data essential to build an epidemiological profile for each setting. Information obtained from surveillance activities identifies skin and parasitic diseases as issues of public health importance and will be crucial in generating awareness and political will, without which there will be little momentum or funding for a control strategy. Surveillance systems should be designed to capture and cross-examine all data required to build and maintain epidemiological profiles. The recommended surveillance system also needs to be flexible in order to adapt to the changing and evolving disease epidemiology and burden of illness.

The second stage (or pillar) is the overall development of a strategic plan that outlines the health agendas and priorities identified by surveillance data, and the policies that will address them. The creation of NTD-specific policies at the highest political level indicates the political will to address parasitic and skin diseases as public health priorities, and outlines the targets for the reduction or elimination of disease. Further recommendations will include development of broad-based policies that advocate the improvement of educational standards of health providers, increased public education and awareness, upgrading of health services, changes to treatment and procedure protocols, and upgrading of water and sanitation infrastructure. Within these policies lies the foundation for the creation of specific programme activities and initiatives to achieve the policy agendas.

The third pillar of the recommended model is programme development. This is the translation of policy into action through the implementation of activities, initiatives and interventions designed to meet the goals and objectives for the control of parasitic and skin diseases (along with other NTDs). All interventions and related activities will stem from direction given from the overarching strategic policy document, with the intention to contribute to the set overall goals and objectives.

The advantage of this model in the development of integrated disease control programmes is that it provides an overall structure for developing and strengthening health systems, thus allowing for the identification of multiple public health issues and development of policies and programmes that simultaneously address multiple health priorities and their root aetiology.

A further advantage is that the model can be adapted to a variety of settings and has the capability to address a range of complex health issues. Applying this template to strategic planning designed to address the co-morbidity of parasitic and skin diseases provides the opportunity to integrate disease control through the development of policies that, by definition, view this group of diseases, their interactions and adverse outcomes as a single health priority requiring a single programme with multiple corresponding activities.

6.3 Specific recommendations for an integrated parasitic and skin disease control programme

6.3.1 Surveillance

The limited data on parasitic and skin infections indicates that these diseases are not seen as a public health priority. Almost all data on these infections has been obtained through estimates based on occasional research initiatives, and from limited data from health-care settings. Existing data suggests that skin and parasitic diseases are a community-wide problem in developing countries. A comprehensive surveillance strategy for parasitic and skin infections is recommended to obtain data that is representative of the actual burden of these diseases in the community, in order to develop specific and appropriate intervention strategies and to evaluate their efficacy.

Surveillance activities can be divided into two categories: formal, ongoing, passive clinical-based surveillance of patients presenting to health-care facilities; and periodic, active community-based surveillance. The following surveillance initiatives are suggested:

- ongoing formal surveillance for parasitic and skin diseases based on patients presenting to clinical settings;
- ongoing syndromic surveillance for diarrhoea and rheumatic heart fever;
- annual community-based screening for parasitic and skin diseases;
- periodic community-based screening for rheumatic heart disease; and
- periodic urine screening of all school-aged children.

Once established, a formal ongoing surveillance system will provide baseline data on disease prevalence, epidemiological distribution, seasonal fluctuations, and patterns of health-seeking behaviour. This passive system will provide continual data to serve as a comparison for seasonal trends, alert officials to outbreaks, and aid programme monitoring and evaluation.

It is recommended that the following items be considered in the incorporation of parasitic and skin diseases into an existing surveillance system:

- Specific targeted skin and parasite diseases should be selected based on historical or current knowledge of disease epidemiology and regional or local information.
- Once specific diseases have been chosen, case definitions should be developed or adapted from existing definitions to allow for comparison within and between regional and national programmes.
- A core data set should be compiled that includes demographic, epidemiological, clinical and laboratory data, to establish a baseline data set and epidemiological profile of these diseases. This will serve as the template for all future comparisons.
- In addition to the actual targeted diseases, the scope of surveillance should be widened to include associated diseases and conditions that are indicative of the impact of the targeted infections (rheumatic heart fever, renal disease and diarrhoea).
- Data should be collected using standard collection tools, and should be collated and stored electronically at a central location for analysis.
- Disease data should be collected from all clinical settings, community health centres, clinics and in-patient and out-patient areas in hospitals.
- Enhanced surveillance activities, such as research, should be encouraged and undertaken at regular intervals to expand on the information obtained from the standard surveillance system.

Data obtained from ongoing passive surveillance requires a huge investment of resources, and often there is a lag in providing sufficient good-quality data to guide initiatives. Hence, active surveillance activities need to be undertaken in conjunction with establishing a public health surveillance system. Active community-based surveillance is labour intensive and therefore it is recommended that it be carried out periodically. Community-based surveillance will provide more accurate data on prevalence of skin diseases and parasites in the population, as it does not rely on patients presenting to health-care centres. Suggestions for community-based surveillance initiatives include:

- research surveys on selected populations;
- screening of school-aged children; and
- mass screening of the entire population.

The above-mentioned initiatives are labour and cost intensive. Therefore, it is recommended that mass screening activities be integrated or 'piggy-backed' onto existing successful disease control programmes. GPELF has been identified as the most logical entry point for integrated initiatives, due to the potential for the expansion of this programme in the developing world (Molyneux *et al.*, 2005; Hotez *et al.*, 2007a; Ottesen *et al.*, 2008). Increased efficacy in the control of skin and parasitic diseases could be achieved through the opportunistic distribution of mass drug chemotherapy during surveillance and screening initiatives.

6.3.2 Policy agenda to address parasitic diseases, skin infections and other NTDs

Policy development is the most influential phase in the strategic planning for control of NTDs. Therefore, in order to address the burden of illness caused by the co-morbidity of parasitic and skin diseases and other NTDs, it is crucial that the concept of integrated disease control be fully embedded into the strategic planning phase. Adoption of this concept during early policy development is essential in ensuring that the overarching policies, which ultimately govern all aspects of the strategy, reflect the goal of reducing the prevalence and impact of multiple diseases directly through treatment and through addressing the multitude of factors that encourage their propagation.

The annexing of a parasite and skin disease control programme into an established disease control programme is recommended because established disease control strategies are already in existence in most Asia-Pacific countries, and:

- some of these programmes operate at the national level and incorporate active community-based activities, such as door-to-door testing and treatment for entire communities;
- they employ local health-care workers who are already trained and experienced in public health campaigns, and who have established relationships with local communities;
- they have already established the logistics, protocols and equipment required for mass coverage of a population, and are designed to manage the challenges of accessing remote and isolated areas; and
- they are supported by larger, often global agencies, which means that core funding for the established programme is already in place. Integrating another disease control programme will require only a fraction of the funding required for developing a fully independent strategy.

The first step towards integration of disease control programming is to recognise and declare skin infections, including scabies, as an NTD so that they can be addressed within the framework of NTDs. Once skin infections are recognised as an NTD, the second policy agenda is a change to the treatment protocol within GPELF to replace albendazole with ivermectin. Ivermectin is a broader-spectrum anti-parasitic drug than albendazole and has been shown to be equally as effective in the treatment of LF as albendazole in reducing the density of microfilaria (Tisch *et al.*, 2005; Merck, 2007). It is also a highly effective treatment against many STHs (Heymann, 2004; Omura, 2008).

Mass treatment with ivermectin has shown the drug to be highly effective in reducing the prevalence of scabies in hyper-endemic communities (Brockerie *et al.*, 2000; Brooks and Grace, 2002; Lawrence *et al.*, 2005). Reducing the prevalence of scabies could subsequently reduce the prevalence of bacterial pyoderma, and hence the reservoir of group A streptococcus bacteria in these endemic settings and ultimately the acute and chronic burden of illness associated with these infections. Early studies have already indicated a reduction in both scabies and haematuria, which are associated symptoms of infection with GAS (Lawrence *et al.*, 2005).

The third policy agenda to address treatment of scabies and NTDs is the expansion of 'rapid-impact' mass chemotherapy, including ivermectin (and other medications for location-specific NTDs) to reduce the prevalence of scabies and STHs in settings where LF is not endemic and hence GPELF is not operating. This will expand the WHO school de-worming programme to include the entire community, not just schoolchildren, and introduce scabies and STH control to developing-country settings where an alternative programme (such as leprosy or tuberculosis) is in operation.

Addressing the larger socio-economic environmental conditions is central to sustainable reduction of infectious diseases. It is recommended that policies for NTDs set an agenda with the objectives of strengthening health systems and services and addressing some of the basic determinants of health that contribute to these diseases. It is therefore recommended that the policy agenda support improvements to the following areas: infrastructure, including water, sanitation and transport; clinical services; education; environmental health and housing; and public health. Specific policy objectives related to reducing parasitic and skin infections should include:

- improvements in clinical services in order to prevent, treat and manage cases of parasitic and skin diseases;
- training and up-skilling of practitioners to recognise, correctly diagnose and treat these infections, and the associated conditions indicative of this group of diseases (diarrhoea, rheumatic fever, renal dysfunction);
- development of a basic health service package that contributes to the overall health system, which also includes the requirements for addressing parasitic and skin diseases;
- updating treatment protocols to ensure treatments are current and effective, in order to increase primary treatment efficacy and reduce treatment failures;
- the addition of appropriate medications to the essential drug formulary to ensure a constant supply of effective treatment and supplies;
- equipping both urban and rural health facilities, especially outposts, with trained staff and ensuring an adequate supply of medications and supplies are constantly available for remote populations;

- improvements to housing conditions and access to affordable housing to reduce overcrowding and improve sanitation;
- infrastructure improvements to water and sanitation services to improve access to clean water and reduce waste contamination in areas of human population, thereby decreasing human exposure to contaminated waste products and reducing the cycle of STHs, and to encourage increased personal hygiene;
- improvement and maintenance of roadways and transportation to reduce barriers to community access to health-care facilities and the transport of medications and supplies to the entire population; and
- community education to educate the population about the factors contributing to disease transmission, signs and symptoms, when to seek health care, and tangible disease prevention and control measures.

6.4 Treatment-centred disease control initiatives

The initiatives outlined in this section are recommended to achieve a reduction in prevalence of parasitic and skin diseases, thereby reducing the burden of illness caused by these targeted diseases and their associated sequelae, as outlined in the policy agenda. The initiatives aim to achieve the objectives through detection and treatment, and by reducing or eliminating opportunities for transmission through improvements to health services and environmental conditions.

6.4.1 Integrated mass screening and treatment

Mass screening of a population is the most accurate way to determine the true prevalence of parasitic and skin infections and the true burden of disease. The most effective and efficient method of community-based screening of skin and parasitic diseases in the Asia-Pacific region would be to integrate detection and treatment of these targeted condition into GPELF through an existing national programme. GPELF is carried out annually in participating countries with the objective of capturing upwards of 80% of the population (PacELF, 2008). It is further recommended that mass screening for the targeted diseases be conducted door-to-door to reach a higher proportion of the target population.

If integrated into a national LF programme, mass screening and treatment for NTDs could be implemented quickly and efficiently, requiring the following initiatives:

- training of existing field teams to recognise the signs and symptoms of skin diseases for surveillance purposes and for further treatment referral;
- training in appropriate sampling techniques for STHs;
- training in adequate administration of 'rapid-impact' treatment packs containing ivermectin; and
- provision of appropriate medications and testing equipment to medical teams for immediate treatment of affected individuals; the teams could use this control initiative to restock local clinics, especially those in remote areas.

Mass distribution of 'rapid-impact' chemotherapy with ivermectin (and other medications for location-specific pathogens) would also be a highly effective option to address co-morbidity by treating multiple diseases simultaneously in areas where:

- LF is not endemic and disease control programmes are not in operation;
- scabies and STHs are known to be highly endemic or hyper-endemic; and
- there is a lack of capacity for STH testing.

6.5 Community development disease control initiatives

6.5.1 Education about and awareness of skin and parasitic infections

Raising awareness of parasitic and skin diseases in health-care providers and the general population is a priority due to the low profile of these diseases. Therefore, it is recommended to initiate both community and provider education programmes to increase awareness of the general personal hygiene related to the transmission of NTDs, including the diseases' life cycle and symptoms, and preventative measures for the diseases. Specific stand-alone education sessions could be undertaken, or they could be incorporated opportunistically into general health education or awareness sessions that include other diseases or health issues.

As these diseases have the biggest impact on children, it is logical to target health information

campaigns to women who are the primary care givers and hence have the most access to this target group. The literature shows that providing heath information to women and girls (as well as improved genral education) has the greatest improvement on health outcomes for the entire family, referred to as "*the double dividend of gender equality*"(UNICEF, 2007b; UNIFEM, 2010).
Suggested activities include:

- public information on general personal hygiene;
- public information sessions on parasitic and skin diseases;
- integrating information about these diseases into existing health education and hygiene programmes for schoolchildren;
- opportunistic patient education by health-care providers to patients or parents during clinic or hospital visits; and
- information given by public health nurses to new mothers or during child health checks.

Skin diseases and parasitic infections and their associated outcomes can be challenging to diagnose, requiring all health-care providers to acquire the capacity or upgrade their existing capacity to diagnose and treat these conditions before screening or other initiatives can commence. Practitioners will need to be aware of the local epidemiology and burden of disease in their communities. Suggested activities include:

- inclusion of training on parasitic and skin diseases and their associated outcomes in formal training of health-care providers, including community health workers;
- development of a national training programme for up-skilling existing providers in parasitic and skin diseases and associated conditions;
- specific training of health-care workers and field-team members of existing disease control programmes, such as the leprosy or LF team, to identify skin conditions and collect appropriate samples; and
- up-skilling of laboratory personnel and equipment to support diagnosis of the targeted conditions and to equip facilities to handle high specimen loads generated from a national programme.

6.5.2 Sanitation and hygiene initiatives

Following an increase in awareness and community education on hygiene, the next initiative is improving the standard of sanitation and hygiene within NTD-affected settings. The ultimate objective is provision of potable running water and contained sewerage systems to every household. This objective is almost unrealistic in resource-poor settings due to the limitations on financial and human resources and the challenges posed by local geography. The objective of improved community hygiene will require considerable investment in sanitation infrastructure and a long-term commitment to incremental improvements. Listed below are several long-term and short-term initiatives to improve overall sanitation and hygiene related to NTDs:

- improvements to water treatment in both urban and rural areas to ensure community water supply is potable;
- upgrading of sewerage infrastructure to achieve closed sewerage systems to contain raw sewage;
- upgrading of sanitation infrastructure to hospitals, health clinics and schools;
- initiatives to supply water tanks to households without running water;
- initiatives to install or upgrade sewerage facilities within households and communities;
- addition of community wells and communal sanitation blocks in densely populated and rural areas where main water access is not available;
- dispensing of soap or other hand-washing products during treatment or education campaigns; and
- education about and provision of closed footwear to schoolchildren, who are at greatest risk for STHs.

6.5.3 Improved housing initiatives

Inadequate housing and overcrowding are significant contributing factors to the transmission of infectious disease, including NTDs (Bloomfield and Scott, 2003; Heymann, 2004; Molyneux and Nantulya, 2004; Mimesh *et al.*, 2008; WHO, 2009e). The following initiatives, in conjunction with the other community development activities, are suggested to further improve the conditions that encourage NTDs:

- initiatives to repair screens, windows and roofing in schools, hospitals and community centres to reduce the risk of mosquito-borne disease;
- education and initiatives for repairs to household structures to reduce the risk of mosquito-borne disease;
- programmes to provide sound permanent housing for those residing in semi-permanent structures or structures fashioned from bush materials;
- provision of bed nets for those in rural areas or in areas where housing cannot be improved; and
- initiatives to provide affordable accommodation in areas undergoing urbanisation, to reduce the number of residents in each dwelling.

6.6 Summary

The policies, objectives and initiatives outlined above form part of a comprehensive strategic plan to integrate the control of parasitic and skin infections into the framework of NTDs, in order to reduce the enormous burden of illness resulting from these infections. By simultaneously targeting multiple co-endemic diseases and the socioeconomic and environmental conditions that propagate these diseases, this model of disease control is both cost-effective and efficient and therefore an ideal model for resource-constrained settings. Ultimately, the incorporation of the control of parasitic and skin diseases and other NTDs into a much broader health strategy has the potential to result in additional health, environmental and social benefits for resource-poor communities, and to become the framework for significant and sustainable change.

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Appendices

Appendix 1

Approval for research or teaching involving human subjects. - A dynamic public health approach to controlling parasites and reducing skin infections in the Pacific Island Nation of Tuvalu

ADMINISTRATIVE DOCUMENTATION HAS BEEN REMOVED

Appendix 2

Semi-quantitative egg counts on SAF-fixed samples using a modified Kato Katz method.

The Kato Katz method (Katz *et al.*, 1972) is widely used for doing egg counts in the field. The materials required are: a plastic template with a central hole, glass microscope slides, and cover slip-sized squares of cellophane that have been soaked in a mixture of glycerol and malachite green. The plastic template is placed on the glass slide forming a depression that can contain an average of 43.7mg of fresh faeces. The depression is filled with faeces, carefully levelled off, and the template removed. A square of cellophane is removed from the glycerol/malachite green, placed over the faeces on the slide, pressed down, and excess of glycerol wiped away. Slides are left for one hour to allow the glycerol to clear the preparation for easy visibility, the number of eggs is counted microscopically, and the number of eggs per gram calculated.

Although the Kato Katz technique is simple and convenient, it does have some drawbacks. It must be done in the field and that is not always convenient or safe. Fresh faeces pose an infection risk and fresh faeces cannot be imported into Australia. They must be fixed with a formalin-based fixative such as SAF (Sodium acetate-acetic acid-formaldehyde).

Appendix 3

List of Publications

Malena ML dos Santos, Salvador Armaral, Sonia Harmen, Hayley Gallagher , Jose L. Fernandes and Megan Counahan. “The prevalence of common skin infections in Timor-Leste: A cross sectional survey”. **Submitted to BMC Infectious Diseases December 2009.**

Rick Speare, Falatea Fab Latasi, Tekaai Nelesone, Sonia Harmen, Wayne Melrose, David Durrheim, Jorg Heukelbach. **Trichuris and hookworm prevalence on Tuvalu, a remote Pacific island, following three annual mass drug administration rounds with diethylcarbamazine and albendazole** . BMC Infectious Diseases, July 2006. 12;6:110.