ANALYSIS OF THE BURDEN, DETERMINANTS AND CONTROL RESPONSES FOR POST KALA-AZAR DERMAL LEISHMANIASIS IN SOUTH SUDAN:

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Uganda

48th International Course in Health Development
September 19, 2011 – September 7, 2012

KIT (ROYAL TROPICAL INSTITUTE)
Development Policy and Practice/
Vrije Universiteit Amsterdam

ANALYSIS OF THE BURDEN, DETERMINANTS AND CONTROL RESPONSES FOR POST KALA-AZAR DERMAL LEISHMANIASIS IN SOUTH SUDAN

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Public health

By

Charles Abongomera

Uganda

Declaration:
Where other people's work has been used either from printed source, internet or any other source this has been carefully acknowledged and referenced in accordance with departmental requirements.
The thesis analysis of the burden, determinants and control responses for Post Kala-azar Dermal Leishmaniasis in South Sudan is my own work.

Signature: ……..

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Development Policy and Practice/ Vrije Universiteit Amsterdam, The Netherlands

September 2012

Organised by:

KIT (ROYAL TROPICAL INSTITUTE), Development Policy and Practice Amsterdam, the Netherlands

In cooperation with:

Vrije Universiteit Amsterdam/ Free University of Amsterdam (VU) Amsterdam, the Netherlands

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Acknowledgments

I would like to thank the Course management for all the support during the year. I would also like to thank my teachers for all the support that I have received. Special thanks also go to my adviser and back stopper and the following people that helped in different aspects of this thesis. Sjoukje de Wit, Dr. Oleko Richard, Dr. Allan Mpairwe, Dr. Tullia Battaglioli, Dr. Christo Lado, Dr. Jill Seaman and Prof. Zijlstra E. E.

ABSTRACT:
In South Sudan, Post kala-azar dermal leishmaniasis (PKDL) is a neglected disease without effective methods of control while it is considered to contribute to increased transmission of Visceral Leishmaniasis (VL, kala-azar), a lethal disease when untreated.
This study aims to identify the burden, determinants, PKDL control responses and the cheapest and safest treatment options for PKDL in South Sudan.
The methodologies used are a literature review, a data analysis of treatment duration and outcome of two different PKDL treatment regimens used by Médecins Sans Frontières in South Sudan, and a cost minimisation analysis of the two regimens. The main findings show the burden of PKDL is under estimated: burden in 2010/2011 is estimated at 57,692, whilst only 1,052 cases were reported. There is no strategy for VL control, limited funding, shortage of human resources, few treatment facilities, and poor surveillance reporting. Treatment of severe PKDL with a Sodium Stibogluconate (SSG) and Paromomycin combination gives better cure rates and shorter duration of treatment than SSG alone (97.4% versus 89.8% p=0.02 and 30 days versus 36 days p value <0.0001). The combination therapy is cheaper than SSG, though not statistically significant (147 US$ versus 165 US$, p=0.07). Due to its toxicity, current treatment options are not suitable for public health control.
A comprehensive multi-sectorial approach is required for control: a VL /PKDL control strategy, donor funding, task shifting, integration of PKDL treatment in other facilities, involvement of NGOs. There should be advocacy for development of safer drugs and better diagnostic tests.

Key words: Post-kala-azar dermal leishmaniasis, Visceral leishmaniasis, South Sudan, burden, determinants

Word count: 12000

List of Abbreviations:

ACF……. Action Contre la Faim
ART…… Anti retroviral therapy
CFR……. Case fatality rate
CHW…… Community Health Worker
CPA……..Comprehensive peace agreement
DANIDA……Danish Agency for International Development
DFID……Department for International Development
ECHO…….European Commission for the Coordination of Humanitarian affairs
FBOs……..Faith based organisations
GOS…….Government of Sudan
GOSS…….Government of the Republic of South Sudan
HMIS……..Health management information system
HR…….Human resources
IDSR……..Integrated disease Surveillance and response
L-Amb……..Liposomal Amphotericin B
MF…….Miltefosine
MOH …… ……Ministry of Health, Government of South Sudan
MSF…….Médecins Sans Frontières
NBS…….South Sudan National Bureau of Statistics
NGOs……..Non Governmental Organisations
NSCSE……..New Sudan Centre for statistics and evaluation
PCR……. Polymerase chain reaction
PHCCs……...Primary Health care centres
PHCUs……Primary health care Units
PKDL.....Post-kala-azar dermal Leishmaniasis
PM ……..Paramomycin
SSCCSE……Southern Sudan Commission for Census, Statistics and Evaluation
SSAC……Southern Sudan Aids commission
SSG ……..Sodium Stibogluconate
UNICEF…….United Nations Children Fund
UNMIS……..United Nations Mission in the Sudan
UNOCHA……..United Nations Office for the coordination of Humanitarian Affairs
UNOPS ……..United Nations Office for Project Services
US$.....United States Dollars
VL ……..Visceral Leishmaniasis
WFP…….World food Programme
WHO……World Health Organisation

Chapter 1: Introduction

I am a medical doctor who graduated from Makerere University in Kampala, Uganda in 2001. I then did a one year internship at Mulago National Referral hospital in Kampala. From 2002-2005, I worked as medical officer at the Gulu Regional Referral hospital in Gulu district and Rubaga Hospital in Kampala.

I was interested in developing a career in international health and tropical medicine so in 2005/2006 I studied tropical medicine and international health at the Institute of Tropical medicine in Antwerp-Belgium. I then joined Médecins Sans Frontières (MSF), an international medical humanitarian organisation. Since 2006, I have worked in various positions, projects and countries.

In order to further develop my knowledge and skills in public health I decided to pursue the Master of Public Health at the Royal Tropical Institute in Amsterdam. This thesis is done in partial fulfilment of the degree of Master of Public Health. The thesis is an analysis of the burden, determinants and control responses for post-kala-azar dermal leishmaniasis (PKDL) in South Sudan. PKDL is considered as an immunological complication of Visceral leishmaniasis (VL) also known as Kala-Azar (Zijlstra *et al*., 2003).

I have chosen this topic because PKDL is a neglected disease without effective methods of control in place while PKDL is considered to contribute to increased transmission of VL, a lethal disease when untreated (Zijlstra *et al.,* 2003). The general objective of this thesis is to analyse the burden, determinants and control responses for PKDL in South Sudan in order to contribute to recommendations for its effective control that shall be used in VL programmes in South Sudan.

PKDL is considered a reservoir of Leishmania parasites and probable cause of VL epidemics (El Hassan and khalil, 2001; Zijlstra *et al*., 2003). Annually in the world there are 0.2-0.4 million new cases of VL, 20-40,000 deaths and 1,974,000 healthy years of life lost or disability adjusted life years (DALYs) lost (WHO, 2008; Alvar *et al*., 2012). In 2004, in Sudan, 99,000 DALYs lost were attributed to Leishmaniasis (WHO, 2009a).In Western Upper Nile (presently Unity State) during a VL epidemic (1984-1994), an estimated 100,000 people died amongst 280,000 people (Seaman *et al*., 1996).

MSF, the Ministry of Health of the government of South Sudan (MOH) and the World Health Organisation (WHO) all recognise PKDL as a neglected disease and are all committed to innovative efforts for its effective control (WHO, 2007; WHO,2012a; MSF,NOT DATED; MOH,2012a)

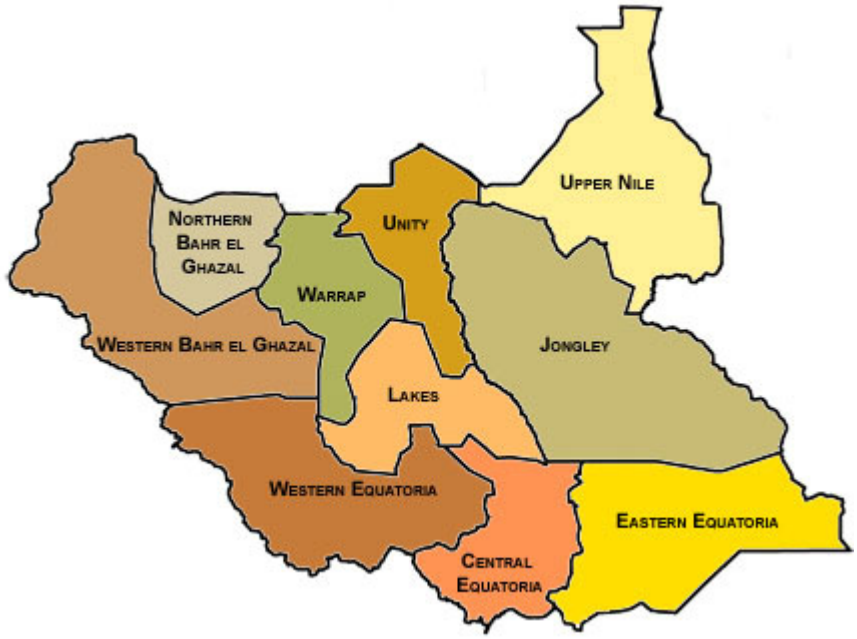
PKDL and VL are diseases that affect poor people worsening their economic situation. PKDL/VL occurs mainly in four States of South Sudan namely Jonglei, Upper Nile, Unity and Eastern Equatoria. Poor people are not well represented at the policy making level while the four States are not representative of the country. From an equity perspective this health problem ought to be controlled (Alvar *et al*., 2006; MOH, NOT DATED-a).

Chapter 2: Background information on South Sudan:

2.1 Administration

South Sudan is a newly independent African country. It became independent on the 9th of July 2011 (GOSS, 2011a). It occupies an area of 644, 329 square kilometres and is bordered to the south by Kenya, Uganda and the Democratic Republic of Congo to the east by Ethiopia, the north by Sudan and west by Central African Republic (NBS, 2012).
The country is divided into ten States as shown in the map below. The States most affected with VL and PKDL are Upper Nile, Jonglei, Unity and Eastern Equatoria (SSCCSE, 2007; Jan *et al*., 2008).

Fig. 1: <u>Map showing the States of South Sudan:</u>



Source: GOSS, 2011b

2.2 Demography:

The population is 8.26 million people, 16% are younger than five years and 49% are younger than 17 years. Males constitute 52% of the population and females 48% (SSCCSE, 2009). Life expectancy is 42 years in both sexes. The crude birth rate is estimated at 35.9 births per 1000 population, the crude death rate at 8.9 per 1000 population, population growth at 4.7%. The indicators are not expected to improve in the next few years (SSCCSE, 2009; MOH, 2012a).

2.3 Politics:

Before independence South Sudan was part of the Republic of Sudan a time in which it was at war with the northern part of the country for 39 years, 1955-1972 and 1983-2005 (GOSS, 2011a). Consequences of the war of 1983-2005 were 2 million deaths, 4 million internally displaced population and 600,000 refugees (UNMISS, 2011). Already an

undeveloped setting the war worsened this situation further by destruction of infrastructures, flight and killing of professionals along with destruction of the community social structure (MOH, 2007a; Muchomba and Sharp, NOT DATED; MOE-GOSS, 2011; Taylor-Robinson, 2002). Despite the signing of the Comprehensive peace agreement (CPA) in 2005, armed violence continues at the Sudan and South Sudan borders (UNOCHA, 2012).

2.4 Physical environment and livelihood zones:

The climate is sub-humid, temperatures are between 25 to 35 degrees centigrade and rains vary from 200 to 2200 mm annually (Muchomba and Sharp, NOT DATED).The dry season is from January till April, a time, pastoralists migrate with their animals in search for water, grazing land and fishing areas. They return at the beginning of the rainy season. Floods and drought cycles are common and the population is adapted to overcoming it (Muchomba and Sharp, NOT DATED).

The river Nile forms a large swamp occupying most of the country. The river is a source of fish but the swampy area contributed to high prevalence of schistosomiasis and malaria (Muchomba and Sharp, NOT DATED). The south western part of the country is humid. This is suitable for Tsetse flies, the vectors of human african trypanosomiasis. The eastern flood plains have a lot of acacias and savanna woodlands while Eastern Equatoria also has termite mounds that are suitable for sandflies, the vectors of Leishmaniasis (Muchomba and Sharp, NOT DATED; Hoogstraal and Heyneman, 1969). Table 1 below shows the seven livelihood zones, characteristics of the inhabitants and respective location in the different States.

Table 1: Livelihood zones of South Sudan:

Livelihood Zones	**Characteristics of inhabitants**	**States**
Green belt	Crop farming batter trade and use of root crops	Western Equatoria , Central Equatoria
Iron stone plateau	Crop farming. Get extra food from green belt	Western Equatoria , central Equatoria Western Bahr-El -Ghazal Northern Bahr-El-Ghazal
Hills and mountains	Crop farming and pastoralism	Central Equatoria Eastern Equatoria, Jonglei
Arid / pastoral	Pastoralism	Eastern Equatoria, Jonglei
Nile-Sobat rivers	Crop farming, pastoralism, fishing and wild food collection	Upper Nile, Jonglei, Unity, lakes
Western flood plains	Crop farming, pastoralism, fishing and wild food collection	Warrap, Unity, lakes, Northern Bahr-El-Ghazal
Eastern flood plains	Crop farming, pastoralism, fishing and wild food collection	Jonglei, Upper Nile, Unity

Source: Muchomba and Sharp (NOT DATED)

2.5 Socio-economic:

The Gross national income is 888 US dollars (US$) per capita. About 98% of government revenue is from oil revenue and the rest from customs and taxes. Oil production is at its maximum and expected to decline. Oil revenue is expected to fall to 50% over the next 5 years (GOSS, 2011c). About 50.6% of the population live in poverty defined as less than 1 US$ per day. About 24 % of the urban population and 55 % of the rural population live in poverty (SSCCSE, 2010; MOH, 2012a).
Only 27% of the population is literate. Literacy rates are 53% in urban areas and 22% in rural areas (NBS, 2012).

2.6 Health services, water and Sanitation:

During the war until 2005 at the Signing of the CPA the health system was managed by Non Governmental Organisations (NGOs) and Faith based organisations (FBOs). Today the MOH is starting to take charge of the health system (MOH, 2012a). Table 2 below shows poor health indicators in South Sudan in 2010 (SSCCSE, 2007; SSCCSE, 2010, MOH, 2012a).

Table 2: Health Indicators in South Sudan in 2010

Indicator	Value
Maternal mortality ratio	2054
Infant mortality rates	75 per 1000 live births
Under five mortality rate	105 per 1000 live births
Total fertility rate	6.7
Skilled attendance at birth	19%
Contraceptive prevalence rate	4%
(Diptheria, Pertussis and tetanus DPT 3 coverage	15.1%
Acute Malnutrition prevalence	22.7%
Children 12-23 months completely vaccinated	6.3%

Source: (NBS, NOT DATED; SSCCSE, 2007; MOH, 2012a)

Malaria, pneumonia, diarrhoea, tuberculosis, malnutrition and neglected tropical diseases such as leishmaniasis form a significant burden of diseases (MOH, 2012a).
The health policy aims for a healthy and productive population through management of communicable and non communicable diseases, prioritising the care of women and children and management of the health system through partnerships with stakeholders. Leadership and management skills are limited within the MOH due to low numbers of qualified personnel (MOH, 2007a; MOH, 2012a).
The government expenditure on health is low; The total expenditure on health as percentage of total government expenditure is 4.0% and the government per capita expenditure on health is 9 US$. The rest of the

financing is as shown in table 3 below (WHO, 2012b; Sarah Fox and Alex Manu, 2012).

Table 3: Health financing indicators in Sudan in 2010

Total Expenditure on Health (THE) as a percentage of GDP	6.3 %
General Government Expenditure on health as percentage of THE	29.8%
Private Expenditure on Health (PvtHE) as percentage of THE	70.2%
Out of Pocket Expenditure as percentage of PvtHE	95.7%

Source: WHO, 2012b

There is critical shortage of human resources (HR) with one doctor for 33,308 people, one nurse for 3718 people and one midwife for 15,947 people. About 20% of primary health care facilities are not operational due to lack HR. Training schools are few, not well funded and lack HR (MOH, 2011; MOH, 2006) There is recurrent shortage of medicine due to poor forecasting and irregular supply. There are some counterfeit medicines and medical supplies within the local market (MOH, 2012a). Health facilities are insufficient and inequitably distributed with low quality of care. The utilisation rates are low at 0.2 visits per inhabitant per year (MOH, 2012a, MOH, 2011).

Free health services are provided in 60% of the health facilities, 34% charge user fees for specific services while in 5% all the services are paid (MOH, 2011). A significant proportion of the population uses traditional medicine (Mija-tesse Ververs, 2010). The health management information system is weak and characterised by late, incomplete reporting and limited supervision (MOH, 2012a).

Only 5.6% of the population use both improved water sources and sanitation facilities. About 68.7% of the population use improved drinking water sources while 7.4 % use improved sanitation facilities (NBS, NOT DATED).

The other ministries working along with the MOH are finance, agriculture and forestry, water resources and irrigation, gender, child and social welfare, education, housing and physical planning, transport and legal affairs and constitutional development. They are all aiming for development in their respective sectors (MOH, 2011; MOE-GOSS, 2011; Ministry of Water Resources and Irrigation, 2009; Ministry of Agriculture, 2011).

2.7 Infrastructures:

Outside the major towns all roads are unpaved. During the rainy season from May to December they become very muddy and unusable. They are mainly accessible during the dry season January to April (UNOPS, not dated). The rest of the infrastructures are also limited (World Bank, 2011).

Chapter 3: Problem statement, justification, research questions, objectives and methodology:

3.1 Problem statement and justification:

VL is caused by a protozoa *Leishmania donovani* and transmitted through the bite of female sandflies, *Phlebotomus orientalis* and *Phlebotomus martini.* Although there may be unknown animal reservoirs for the *Leishmania* parasite in South Sudan, transmission is predominantly anthroponotic. PKDL patients are considered to be important parasite reservoirs during inter-epidemic periods, and play a key role in transmission of VL (El Hassan and Khalil, 2001; Zijlstra *et al*., 2003).

In South Sudan, PKDL is a neglected disease without effective methods of control in place while it is considered to contribute to increased transmission of VL, a lethal disease when untreated (Zijlstra *et al*., 2003; El Hassan and Khalil, 2001).

Sandflies which were fed on skin lesions of PKDL patients got infected (Kirk and Lewis, 1955; Everard *et al.*, 1933).

PKDL is prevalent in areas with *Leishmania donovani* namely East Africa (Sudan, South Sudan, Ethiopia and Kenya) and Indian subcontinent (India, Nepal and Bangladesh) (Zijlstra *et al.,* 2003). In South Sudan, PKDL occurs equally among both sexes at a mean age of six years. PKDL occurs 0 to 6 years following VL treatment (Zijlstra *et al*., 2000; Musa, 2002; El Hassan *et al*., 1992)

PKDL pathogenesis is largely unknown and considered an immunological complication of VL. It is not known why some patients develop it and others do not but it is more common and severe in children younger than five years (Collin *et al*., 2003; Zijlstra *et al*., 2003)

PKDL is characterised by macular, papular and nodular lesions and is generally self-healing. In most cases the lesions are not harmful for the patient, and treatment is not indicated except for severe forms of PKDL, with severe facial involvement, ulceration, or mucosal involvement (Musa *et al*, 2002; Zijlstra *et al*., 2003).

In South Sudan, 50-60% of PKDL cases present after completion of VL treatment, 18% at onset of VL or during VL treatment while 8% present without history of VL, probably due to subclinical infection (Zijlstra *et al*. 1995, Zijlstra *et al*., 2000; Zijlstra *et al*., 2003).

Treatment of PKDL takes longer than treatment of VL and current national treatment recommendations are pentavalent antimonium (Sodium Stibogluconate or SSG) injections for 30-60 days. This long treatment requires long hospitalisation, which is expensive and very inconvenient for the patient, considering that PKDL is a non-fatal disease (WHO, 2010a, MOH, NOT DATED-a, MSF, 2012). Also it is very unfortunate that PKDL patients, having a non-fatal disease, are exposed to longer and therefore potentially more toxic treatment than VL patients (WHO, 2010a; MOH, NOT DATED-a).

Annually in the world there are 0.2-0.4 million new cases of VL, 20-40,000 deaths and 1,974,000 healthy years of life lost or disability adjusted life years (DALYs) lost (WHO, 2008; Alvar *et al*., 2012). In 2004,

in Sudan, 99,000 DALYs lost were attributed to Leishmaniasis (WHO, 2009a). In Western Upper Nile (presently Unity State) during a VL epidemic (1984-1994), an estimated 100,000 people died amongst 280,000 people (Seaman *et al*., 1996).
Current treatment regimens are based on compassionate grounds and limited published data from small cohorts. Cost minimisation analyses (CMA) of the various therapies have not been done (Zijlstra *et al*., 2003; WHO, 2010). Clinical trials have not been done as PKDL is a non-fatal complication of VL, and therefore even more neglected. Secondly clinical trials in PKDL are methodologically very complex as PKDL is generally self-healing, the inclusion of a placebo study arm raises ethical complications and there is no appropriate test-of-cure to determine when to stop treatment. Parasitological and even current polymerase chain reaction (PCR) techniques lack sensitivity (Chappuis *et al.*, 2007).
An effective public health control of PKDL meaning active case detection and treatment of all cases should be facilitated by treatment that is safe, effective, short, with minimal side effects and outpatient based (Lucio *et al.*, 2012).
PKDL and VL affect poor people and worsen their economic situation. PKDL/VL increases the burden of disease in the four States of Jonglei, Upper Nile, Unity and Eastern Equatoria. Poor people are not well represented at the policy making level while the four States are not representative of the country. From an equity perspective this health problem ought to be controlled (Alvar, *et al*., 2006; MOH, NOT DATED-a). Evaluation of the burden, determinants and gaps in current control responses will help in effective control of PKDL and VL in South Sudan (WHO, 2007).

3.2 Research questions:

In order to address the problem statement of this thesis which is that, in South Sudan, PKDL is a neglected disease without effective methods of control in place while it is thought to contribute to increased transmission of VL, a lethal disease when untreated (Zijlstra *et al*., 2003, El Hassan and Khalil, 2001).The following are the study questions being asked.

(1) What is the burden of PKDL in South Sudan and its impact on VL epidemiology?
(2) What are the determinants of PKDL in South Sudan?
(3) What are the PKDL control responses in South Sudan?
(4) What is the cheapest and safest treatment option of PKDL in South Sudan?

3.3 Objectives

The main and specific objectives of this thesis are outlined below.
Main objective:
To analyse the burden, determinants and control responses for PKDL in South Sudan in order to contribute to recommendations for its effective control to be used in VL programmes in South Sudan.
Specific objectives:

(1) Analyse the burden of PKDL in South Sudan and its impact on the VL epidemiology.
(2) Explore and analyse the determinants of PKDL in South Sudan.
(3) Explore and analyse PKDL control responses and gaps to the current responses in South Sudan.
3.1 Explore PKDL control responses in South Sudan
3.2 Explore and analyse MSF control responses in Jonglei, Unity and Upper Nile States by doing a data analysis
3.3 Conduct a CMA based on the findings from the data analysis
(4) Review possible strategies and give recommendations for comprehensive and effective response for PKDL/VL control in South Sudan.

3.4 Methodology:

In order to answer the research questions I used the following methodologies:

3.4.1 Literature review for the burden, determinants and control responses of PKDL in South Sudan.

For the study on the determinants of PKDL I have used the Lalonde model as a guide. To find articles I used the VU library and the following search engines: Pub Med, Google scholar and Google. I also used the Vu library. I used the following key words or their combinations: "leishmaniasis'', "visceral leishmaniasis'', kala-azar, "Post-kala-azar dermal leishmaniasis'', Sudan, "South Sudan'', burden, determinants, conflict, health services education, nutrition, cultural, economic, gender, feeding practices.
I did not limit my search to year of publication as this is a neglected disease with similar issues repeated over several years and I also reviewed unpublished documents. I limited myself to English language publications, not being fluent at other languages.
My Limitations are that as South Sudan only recently became independent finding information specific to South Sudan is challenging and so I have sometimes used information from the former Republic of Sudan for this analysis. Furthermore as it is a post conflict/conflict setting it is difficult to access all the necessary information.

3.4.2 Methodology for the Data analysis

The study population were PKDL patients treated by all the existing MSF health facilities in Jonglei, Upper Nile and Unity States in South Sudan from 2002 to 2008. The health facilities were Primary health care units (PHCUs), Primary health care centres (PHCCs) and hospitals, staffed with doctors, nurses and Community Health Workers (CHWs). Doctors and nurses were only working in the PHCC and Hospitals.
Patients were treated either as per WHO protocol with SSG at a dose of 20 mg/kg/day (minimum daily dose 200 mg, no maximum dose) or as per an MSF experimental protocol with SSG and Paromomycin (PM). For the latter protocol, the SSG dose was as above while that of PM was 15 mg/kg/day for 17 days (minimum daily dose 50 mg, maximum dose

1,150 mg) (MSF, 1999; WHO, 1996). SSG is a 30 ml vial with 100 mg/ml and is given intramuscularly (IM). PM is a 2 ml vial containing 500 mg/ml of PM sulphate equivalent to 375 mg/ml PM base and is given IM (WHO, 2010a). SSG and PM were supplied by the International Dispensary Association (IDA) based in Amsterdam, the Netherlands. The decision of starting a patient on either SSG or SSG and PM was decided by the health facility that the patient visited. If the health facility had a doctor then the patient received SSG and PM. This decision was made as it was deemed difficult for a CHW to follow this rather complicated protocol with more than one drug. It is important to note that during this time SSG and PM was being used for treatment of VL based on a small study by Jill Seaman and the DNDI study was ongoing to determine the efficacy of SSG and PM in comparison to SSG alone in the treatment of VL (Seaman *et al*., 1993). The case definition and discharge diagnosis were defined according to WHO guidelines (MSF, 1999; WHO, 1996).

Demographic details, treatment history and discharge date and diagnosis date were documented for all patients.

Data were entered into a computerised MSF data collection sheet. Data cleaning was done by MSF staff working at the health facilities. The Statistics generated by the monthly reports were compared with the data records at the treatment facilities. Missing and conflicting information was clarified. An excel data set containing information from all health facilities was created.

This study is based on such excel data set, containing data from 2002 to 2008.

Data were analyzed using EpiInfo (Centres for Disease Control and Prevention (CDC)) version 3.5.3.

Statistical analysis:

Hypothesis testing; The null and alternative hypothesis.

Null hypothesis: There is no difference in duration of treatment between SSG and a combination of SSG and PM for the treatment of PKDL.

Alternative hypothesis: There is a difference in duration of treatment between SSG and a combination of SSG and PM for the treatment of PKDL.

Medians and interquartile ranges (IQR) and means and standard deviations were calculated. In order to compare the median treatment duration and age (continuous data, not normally distributed) in the two independent treatment groups, the non-parametric Kruskall Wallis test for two groups was used. Differences in the proportions of outcomes and gender in the two treatment groups were tested with chi square test or Fisher exact test when required. The level of significance was set at $p<0.05$.The 95% confidence intervals of the proportions were calculated.

The study is a retrospective analysis of routine data and has been reviewed and approved by the MSF scientific committee.

3.4.3 Cost minimisation analysis

The CMA was done on the same data set mentioned above. The medicine and other supplies mostly used are SSG and PM, needles, syringes, gloves and hospital facility. The audience of this analysis are the policy makers. It is a provider perspective and only direct medical costs are considered. An average PKDL patient weight of 24 kg is used for the analysis. The following costs have been considered as the necessary costs.

1. Drugs: The costs of SSG is 1.3 US$ per day, SSG and PM is 0.5 US$ per day (WHO, 2010a)
2. Syringes/needles: Disposable syringes with needles gauge 21 is 3 pounds for 100 pack. This is equivalent to 4.68 US$ and so 0.05 US$ per needle and syringe (Durbin PLC, NOT DATED; Reuters, 2012).
3. Gloves: The price of gloves is 2.42 Pounds per 100 pack (100 pieces) which is equivalent to 3.77 US$ and so 0.07 US$ per pair of gloves. (Durbin PLC, NOT DATED; Reuters, 2012)
4. Hospitalisation costs: 3.2 US$ per Day (Personal communication with Filip Meheus)

Statistical analysis:
Hypothesis testing; The null and alternative hypothesis
Null hypothesis: There is no difference in costs of treatment between SSG and a combination of SSG and PM for the treatment of PKDL.
Alternative hypothesis: There is a difference in costs of treatment between SSG and a combination of SSG and PM for the treatment of PKDL.
In order to compare the median treatment cost (continuous data, not normally distributed) in the two independent treatment groups, the non-parametric Kruskall Wallis test for two groups was used. The level of significance was set at $p<0.05$.

Chapter 4: Study results and findings

4.1 The burden of PKDL in South Sudan and its impact on the VL epidemiology:

The burden of PKDL is human and economic. In 2010 there were 513 cases of PKDL, 8916 cases of VL and 236 deaths. In 2011 there were 539 cases of PKDL, 7662 cases of VL and 273 deaths (WHO, 2010b; WHO, 2011, WHO, 2010c). These cases occurred in the four PKDL and VL affected states (WHO, 2010b; WHO, 2011). The tables 4 and 5 below show the number of PKDL, VL and deaths in the affected States of South Sudan in 2010 and 2011. Jonglei is the most affected, followed by Upper Nile, Unity and then Eastern Equatoria (WHO, 2010b; WHO, 2011).

Table 4: The number of cases of VL and severe PKDL in affected States of South Sudan in 2010:

	Jonglei	Upper Nile	Unity	Eastern Equatoria	Total
PKDL, n (%)	500 (97.50%)	13 (2.50%)	0 (0.0%)	0 (0.0%)	513(100%)
VL, n (%)	7560 (84.80%)	1047 (11.70%)	103 (1.20%)	206 (2.30%)	8916(100%)
Deaths, n (%)	132 (56%)	90 (38.10%)	12 (5.10%)	2 (0.80%)	236 (100%)

Source: WHO, 2010b; WHO, 2011

Table 5: The number of cases of VL and severe PKDL in affected States of South Sudan in 2011:

	Jonglei	Upper Nile	Unity	Eastern Equatoria	Total
PKDL, n (%)	519 (96.30%)	18 (3.30%)	2(0.40%)	0(0.00%	539(100%)
VL, n (%)	5965 (77.9%)	735 (9.6%)	677(8.8%)	285(3.70%)	7662(100%)
Deaths, n (%)	207(75.80%)	30(11.00%)	34(12.50%)	2(0.70%)	273(100%)

SOURCE: WHO, 2010b; WHO, 2011, SSCCSE, 2009

Several epidemics of VL occur in South Sudan with many deaths (Seaman *et al*., 1996). A significant number of VL deaths is not even noticed. In 1998 to2002 an estimated 91% (2409/2649) of deaths occurring in the catchment area of MSF projects were not noticed (Collin *et al*., 2006) The case fatality rate (CFR) in patient with VL and PKDL was 2.5% in 2010 and 3.2% in 2011. The table 6 below shows the CFR in the four States (WHO, 2010b; WHO, 2011).

Table 6: Case fatality rates in patients with VL and severe PKDL in four States of South Sudan in 2010 and 2011:

	Jonglei		Upper Nile		Unity		Eastern Equatoria	
	2010	2011	2010	2011	2010	2011	2010	2011
CFR	1.60%	3.20%	8.50%	4.00%	11.60%	5.00%	1.00%	0.70%

Source: (WHO, 2010b; WHO, 2011)

Both VL and PKDL affect mostly children and both sexes equally (Zijlstra *et al*., 2000; Musa, 2002; El Hassan *et al*., 1992) In 2004, in Sudan, 99,000 DALYs lost, 72,083 DALYs among males and 26,852 among females (WHO, 2009a; WHO, 2009b; WHO, 2009c).The most affected Counties in the four States and respective populations are presented in the table 7 below (MOH, 2012b; MOH, 2012c; SSCCSE, 2009).

Table 7: The most PKDL and VL affected counties in the four States of South Sudan:

State	Counties	Total populations
Jonglei	Old Fangak, Khorfulus, Ayod, Duk, Wuror, Nyirol, Akobo and Pibor	985,946
Upper Nile	Melut, Longochuk, Ulang, Baliet and Malakal	371,945
Unity	Pariang, Rubkona, Guit, Koch, leer and Mayendit	397,351
Eastern Equatoria	Kapoeta North, kapoeta East, Kapoeta South and Budi	445,750
	23 counties	2,200,992

Source: MOH, 2012b; MOH, 2012c and SSCCSE, 2009

Table 8 below shows the proportion of population affected by PKDL and VL in the affected counties of South Sudan. Jonglei is the most affected (WHO 2010b; WHO, 2011; SSCCSE, 2009).

Table 8: The proportion of population with PKDL and VL in affected counties of South Sudan in 2010 and 2011

	Jonglei		Upper Nile		Unity		Eastern Equatoria	
	2010	2011	2010	2011	2010	2011	2010	2011
PKDL	0.05%	0.05%	0.003%	0.005%	0.0%	0.0005%	0.0%	0.0%
VL	0.80%	0.60%	0.30%	0.20%	0.02%	0.20%	0.05%	0.06%

Source: WHO 2010b; WHO, 2011 and SSCCSE, 2009

The treatment duration is long with toxic drugs (MOH, NOT DATED-a). PKDL and VL increase the burden of the already poor population (SSCCSE, 2010).The provision of care for PKDL and VL has an economic cost. This cost is either for the patient together or to the health care provider (WHO, 2011).

Most of the health care is provided freely by NGOs. However those that charge user fees may be leading people deeper in to poverty (Rijal *et al*., 2005; Alvar *et al*., 2006; Anoopa *et al*., 2006).

Patients have to forego their work and also pay some goats to a porter in order to be carried to the health facility. Death of financial providers in families leads to more poverty (SSCCSE, 2010). The peak VL season is during harvest season therefore ill health compromises the food security in homes (Muchomba and Sharp, NOT DATED).

Tables 9 and 10 below show the costs of VL and PKDL drugs used in South Sudan. It includes the dosage and durations of the drugs (WHO, 2010a).

Table 9: The costs of some PKDL drugs currently used in South Sudan

PKDL treatment (mean patient weight 24 kg)

Drug	Dose	Duration	Cost (US$)
SSG	20mg/kg/day	30-60 days	38.2 – 76.5
SSG + PM	PM: 15mg/kg/day + SSG 20mg/kg/day	17 days 17-60 days	29 - 84
L-Amb	2.5 mg/kg/day	20 days	630
Miltefosine	2.5 mg/kg/day	28 days	30 - 70

Source: WHO, 2010a

Table 10: The costs of some VL drugs currently used in South Sudan:

VL treatment (mean patient weight 35 kg):

Drug	Dose	Duration	Cost (US$)
SSG	20mg/kg/day	30 days	55.8
SSG + PM	20mg/kg/day for SSG and 15 mg/kg/day for PM	17 days	44
L-Amb	5 mg/kg/day	6 doses	378
Miltefosine	2.5 mg/kg/day	28 days	45 - 100

Source: WHO, 2010a

The average cost of hospitalisation in South Sudan is estimated at 3.2 US$ per day (personal communication with Filip Meheus). The need for the control of PKDL and VL further compromises the critical shortage of HR (MOH, 2012a).

The Millennium development goals poverty reduction, gender equality, reducing child morbidity and mortality, reduction of burden of HIV and diseases such as PKDL, global partnerships are all compromised by the burden of PKDL and VL (WHO, 2010c).

In conclusion, PKDL and VL cause a significant burden on the lives of patients, health system providers and compromise the achievement of some millennium development goals (WHO, 2010b; WHO, 2011; WHO, 2010c).

4.2 The determinants of PKDL in South Sudan:

4.2.1 Political environment:

The states of VL and PKDL affected States were four of the seven States most affected during the war (WFP, 2006).The war resulted in destruction of infrastructure such as health facilities, schools and water and sanitation facilities. Professionals such as health professionals and teachers were killed while others fled. There was destruction of the social structure of the community resulting in orphans, vulnerable women and elderly. People were unable to move around freely and carry out their regular activities meaning agriculture, business, education and health facilities all came to a halt (MOH, 2007a; Muchomba and Sharp, NOT DATED; MOE-GOSS, 2011; Taylor and Robinson, 2002).

People hid for safety in the acacia woodlands getting bitten by Sandflies and contracting PKDL or VL. Populations from endemic areas fled to non endemic areas and vice versa (Seaman *et al*., 1996; Zijlstra *et al*., 1991). As South Sudan prepared for the referendum, large numbers of South Sudanese living in the northern part of Sudan and other countries returned. Upper Nile has received 74,946, Jonglei 21,739, Unity 88,049 and Eastern Equatoria 13,690. These returnees are at risk of VL and PKDL in these States as they have a low immunity to leishmaniasis (UNOCHA, 2012).

Armed conflicts still continue within the country mostly across the border with Sudan (UNOCHA, 2012; GOSS, 2011c). About 30% of the government budget is for security compared to 4% for health (GOSS, 2011c). The political environment is the distal determinant of VL and PKDL affecting the rest of the determinants as elaborated further below. The return of some peace offers an opportunity for tackling PKDL and VL (Rumunu *et al*., 2009).

4.2.2 Physical environment:

There are two foci of VL and PKDL in South Sudan, a northern focus comprising of Jonglei, Upper Nile and Unity and a southern focus consisting of Eastern Equatoria (Malaria Consortium, 2010).The northern focus has black cotton soil that favours the growth of *acacia seyal* and *balanites aegyptica* forests. Both the cracked black cotton soil and acacia-balanites forest are suitable breeding and resting sites for the sandfly *Phlebotomus orientalis* the vector of *Leishmania donovani* the cause of VL (Hoogstral and Heyneman, 1969). In the southern focus the main vector is *Phlebotomus martini* which is associated with termite mounds its resting ground (Minter *et al*., 1962; Wijers and Minter 1966).This physical environment is absent in the other parts of South Sudan and is what favours the transmission of leishmaniasis in the counties of the four States.

In addition to the above, maximum daily temperature of 34-38 degrees centigrade and annual rainfall of 400-1200 mm are factors that promote the presence of the vector (Thomson *et al*., 1999). Malnutrition leads to

decrease in immunity and increased likelihood of developing VL and PKDL (Ritmeijer and Davidson, 2003) Other than Eastern Equatoria with acute malnutrition rates of 13.7%, all the rest have acute malnutrition rates above 15% a humanitarian emergency threshold as shown in table 11 below (SSCCSE, 2007; IPC Global Partners, 2008).These could partly explain the higher severity of the VL and PKDL in those States compared to Eastern Equatoria.

Table 11: Acute wasting prevalence, in children younger than 5 years, in States of South Sudan, in 2010:

State	**Acute Wasting prevalence (% <-2 SD)**
Jonglei	31.2%
Upper Nile	21.5%
Unity	35.4%
Eastern Equatoria	13.7%

Source: NBS, NOT DATED

There are eight ecological zones in South Sudan that determine the livelihood patterns of its residents. In the dry season, during droughts and flooding the local population migrate with their animals in search of grazing areas, water and fishing areas. In this process they travel through the acacia forests sustaining sand fly bites contracting PKDL and VL (Seaman *et al*., 1996; Muchomba and Sharp, NOT DATED).The Sand fly lives in the acacia forests or in villages close to the forest and their numbers rise during the middle of the dry season and falls during the rainy season. The increase in numbers coincides with the migration through these forests facilitating the spread of infection. Biting time is between dusk and shortly after dawn (Hoogstral and Heyneman, 1969). In the northern focus wild food collection in the acacia woodlands predispose the population to sand fly bites and infection (Seaman *et al*., 1996; Muchomba and Sharp, not dated). The war in South Sudan affected seasonal migration, crop farming, batter trade leading to lack of food and thus malnutrition (Muchomba and Sharp, not dated; WHO, 2000). Additionally it also increased dependence on wild foods that meant searching for it in the acacia forests getting bitten by sandflies and getting infected with PKDL and VL (seaman *et al*., 1996).

4.2.3 Health services:

There are few health facilities providing PKDL and VLN treatment as shown in table 12 below. This compromises access to treatment and increase the spread of PKDL and VL (WHO, 2011; MOH, 2011; Zijlstra *et al*, 2003).

Table 12: The number and proportion of health facilities providing VL and PKDL treatment in four States of South Sudan in 2011

State	Number of health facilities providing VL and PKDL treatment	Total number of health facilities in the different states	Proportion of health services providing PKDL and VL treatment.	Health facilities compared with population in at risk counties
Jonglei	14	213	7%	70,425
Upper Nile	8	107	7%	46,493
Unity	2	66	3%	198,675
Eastern Equatoria	2	109	2%	228,875
	26	495	5%	

Source: (WHO, 2011; MOH, 2011)

Access to health services is hindered by the poor road net work, insecurity and flooding (MOH, 2012a). Overall numbers of health facilities are few. Jonglei state has the best ratio of number of facilities to the population. This could explain its better outcomes in case of mortality related to VL and PKDL. Inability to treat VL and PKDL increases the duration of illness and infectiousness and thus acts as a facilitator of VL. This low number of facilities could partly explain the high incidence of PKDL and VL (WHO, 2011; MOH, 2011).

The critical shortage of HR of health in the four States compromises the treatment of VL and PKDL (MOH, 2011). This is shown in the table 13 below.

Table 13 Critical shortage of HR in the four states of south Sudan in 2011:

State	Population per doctor	Population per Nurse
Upper Nile	24,727	2,026
Jonglei	41,170	10,956
Unity	195,267	4,506
Eastern Equatoria	181,225	6,813
Total	33,308	3,718

Source: MOH, 2011

In general the utilisation of health services is low and traditional treatment is one of the preferred options of the treatment. This prolongs the illness and duration of infectiousness (Mija-tesse Ververs, 2010; Zijlstra *et al*., 2003). The majority of health services are provided by NGOs so most are free at the point of service. Free health services are

provided in 60% of the health facilities, 34% charge user fees for specific services while in 5% all the services are paid (MOH, 2011). Low utilisation of services and inability to access care because of cost result prolongs illnesses and infectiousness.
Most of the drugs currently available for the treatment of PKDL are toxic so not all patients are started on treatment meaning a significant proportion remain reservoirs of infection. Furthermore the supply of these drugs is quite irregular which compromises the situation further.
Malnutrition and HIV are all immunosuppressive so increase the risk of PKDL and VL (Ritmeijer and Davidson, 2003; MOH, 2012a, MOH, 2012b). Table 14 below shows high HIV prevalence in the four states in 2012.

Table 14 HIV Prevalence in the four states of South Sudan in 2012:

State	HIV prevalence
Jonglei	2.1%
Upper Nile	2.7%
Eastern Equatoria	3.3%
Unity	1.6%

Source: SSAC, 2012

Only 32.2% own at least one long lasting insecticide treated net (NBS, NOT DATED). Table 15 below shows low bed net use in South Sudan in 2010.

Table 15: Percentage of house hold with long lasting insecticide treated net in 2010

States	Percentage of households owning one long lasting bed net.
Jonglei	21.7
Upper Nile	32.8
Unity	20.0
Eastern Equatoria	48.0

Source: (NBS, NOT DATED)

4.2.4: Socio-cultural:

4.2.4.1 Culture/traditions:

Seasonal migration with animals through acacia forests predisposes them to sand fly bites and leading to PKDL and VL (Seaman *et al*., 1996; Muchomba and Sharp, NOT DATED). Sleeping outside especially in the middle of the dry season coincides with the peak of sandflies and increased biting and Leishmania transmission (Hoogstral and Heyneman, 1969).
Traditional treatment consists of making incisions in the abdominal skin over the enlarged spleen. This prolongs the illness and the duration of infectiousness (Mija-tesse Ververs, 2010; Zijlstra *et al*., 2003).

Some feeding traditions negatively affect the nutritional status of individuals do exist. In some areas, pregnant women and children younger that five years don't eat eggs for fear of muteness. In the first 24 hours after birth the child is fed with cow's milk and water and colostrums are poured away. Women and children do not eat poultry, carrots or eggplants (GOAL, 2008; Mija-tesse Ververs, 2010). These feeding habits lead to malnutrition (WHO, 2003).

4.2.4.2 Gender:

In South Sudan the burden of leishmaniasis is higher among men than women (WHO, 2009b; WHO, 2009c).The is probably because males spend more time shepherding in the acacia woodlands and getting bitten by sandflies (Hassan *et al*., 2004).

Other than feeding children, women are also responsible for the household chores such as collecting firewood, water and wild food; agriculture, petty business and alcohol brewing. Therefore children are fed when the mother is available (ACF, 2007; Mija-tesse Ververs, 2010). Inadequate feeding of children leads to malnutrition (WHO, 2003).

4.2.5: Socio-economic:

4.2.5.1 Income and social status

Poverty is wide spread all over the four States. It is highest in Unity state and lowest in Upper Nile as shown in the table 16 below (SSCCSE, 2010).

Table 16: Proportion of population living in poverty in four States of South Sudan in 2009

State	Proportion of Population living in poverty (%)
Upper Nile	25.7
Jonglei	48.3
Unity	68.4
Eastern Equatoria	49.8

Source: SSCCSE, 2010

Poverty is associated with malnutrition as shown in the table 17 below (SSCCSE, 2007).

Table 17: Malnutrition Indicators by level of wealth, in Sudan, in 2006:

Wealth quintiles	**Underweight prevalence(% < -2 SD)**	**Stunting prevalence (% < -2 SD)**	**Wasting prevalence(% < -2 SD)**	**Total number of children (0-59 months)**
Poorest	**35.7**	**34.7**	**22.2**	**901,937**
Second	37.3	37.9	17.5	1,076,894
Middle	**34.0**	**36.5**	**12.9**	**1,138,063**
Fourth	27.0	29.4	11.0	1,169,554
Richest	**18.1**	**20.8**	**10.2**	**779,224**

Source: SSCCSE, 2007

Inability to pay for health care is also a determinant of VL and PKDL. Patients not able to afford health services remain infectious for longer and

as a result are reservoirs of infection for the rest of the population (Alvar, 2006, WHO, 2010a).

4.2.5.2: Literacy:

The higher the mother's education level the lower the possibility of malnutrition in the child as shown in table 18 below (SSCCSE, 2007).

Table 18 Malnutrition Indicators by level of mother's education in Sudan, in 2006:

Mother's education	Underweight prevalence(% <-2 SD)	Stunting prevalence (% <-2 SD)	Wasting prevalence(% <-2 SD)	Total number of children (0-59 months)
None	**35.1**	**36.6**	**16.9**	**2,917,020**
Primary	27.3	28.9	11.9	1,302,308
Secondary +	**18.9**	**20.1**	**11.2**	**659,446**

Source: (SSCCSE, 2007)

Table 19 below shows low literacy levels in the four States (NBS, 2012).

Table 19 Literacy rates in States of South Sudan in 2009:

State	Literate
Upper Nile	45%
Jonglei	16%
Unity	26%
Eastern Equatoria	19%

Source: NBS, 2012

All four States have very low levels of literacy. The association of low literacy with malnutrition could be a contributing factor to VL and PKDL (NBS, NOT DATED).

4.2.6: Water and sanitation:

The four States affected by PKDL all have low use as shown in the table 20 below (NBS, NOT DATED).

Table 20: Proportion of population using improved water and sanitation facilities in four states of South Sudan in 2010

State	Improved drinking water and sanitation
Upper Nile	7.2
Jonglei	5.8
Unity	7.0
Eastern Equatoria	4.3

Source: NBS, NOT DATED

Water is for drinking and preparation of meals while appropriate sanitation facilities aids waste disposal avoiding contamination of food. Low usage leads to development of diseases and malnutrition a risk factor for VL and PKDL (Sandy *et al*., 2010)

4.2.7: Biology and Genetics:

Low immunity in children and adults from non endemic areas is a risk factor for VL and PKDL. Therefore the returnees are at risk of developing VL and PKDL (Ritmeijer and Davisson, 2003). Leishmania in the northern focus presents is more virulent and may explain the lower prevalence and burden in Eastern Equatoria in comparison with the other States (Postiga, 2010)

There is emerging evidence that genetics may have a role in susceptibility to PKDL and VL. A few studies show that some tribes are more vulnerable to VL and PKDL than others (Jenefer *et al*., 2004; Mohamed *et al*., 2003; Bucheton *et al*., 2003; Mohamed *et al*., 2004).

4.3 What are the PKDL control responses in South Sudan?

4.3.1 Governance:

The MOH coordinates the VL response with support of WHO (MOH, 2012b) There is no policy and strategic plans for the control of VL/PKDL in South Sudan. Guidelines for diagnosis, treatment and prevention of VL is finalised by the MOH and its partners and will be soon be distributed to the treatment facilities (MOH, NOT DATED-a).

The response towards the control of VL in South Sudan has been divided among a few key actors. The management of cases is by the MOH and NGOs. NGOs currently treat almost 95% of the cases. Capacity building by the WHO and NGOs, MSF and WHO are responsible for the supply of the VL drugs, diagnostic kits and other supplies. The World food programme (WFP) and UNICEF are responsible for the supply of supplementary food and therapeutic food. Water, sanitation and hygiene is the responsibility of UNICEF and medair while logistics is supported by WHO and UNOCHA (MOH, 2012b).

The MOH priorities in the control of PKDL and VL are prevention of sand fly bites, diagnosis and treatment of cases (MOH, NOT DATED-a).

As a result of the war there are few competent public health managers within the MOH. The organisational structures are not well specified, staff supervision is poor, payment of staff is irregular, and absence from duty is common. There is poor financial management and health management information system (HMIS) is not well managed. Coordination of NGOs is problematic and supervision of lower health services hardly practiced (MOH, 2012a).

4.3.2 Health Financing:

Oil is the main government revenue and is expected to decline to about half in the next 5 years. Currently, only 4.0% of total government

expenditure is spent on health and 9.0 US$ per capita. This is very low (GOSS, 2011c, Sarah and Alex, 2012).
Donor funding is a main form of funds for the health system; contributing an estimated two thirds of the health budget. The donors include United States agency for International development (USAID), CHF (Common Humanitarian fund), Danish Agency for International Development (DANIDA) and European Commission for Humanitarian Affairs (ECHO) (MOH, 2012b).
Aid effectiveness is important and mechanisms are currently in place to ensure that funds are used appropriately. The WHO and other organisations are some of the main implementers of aid as the government needs some time to improve its technical capacity.
The way foreign aid is distributed in South Sudan follows either, project funding, programme funding, sector wide approach and some general budget support (UNOCHA, 2011).
The government is also aiming for the alignment of the aid with its development plan of 2011-2015 (GOSS, 2011c).
The country has been divided among the donors as shown in table 21 below.

Table 21: Donors in the different states of South Sudan in 2012:

State	**Type of donor**
Upper Nile	World Bank
Jonglei	World Bank
Eastern Equatoria	Pooled funds
Unity	Pooled funds

Source: Sarah and Alex, 2012

One of the main donors is the CHF. This is pooled funds that are donated by a number of countries e.g UK-DFID, Sweden, Norway, Netherlands, Spain, Austria, Ireland and Denmark. They contributed 48% of the entire health sector funding in 2011.The VL projects are integrated into the rest of the health facility activities so there is no funds ear marked for VL control only. The table in appendix: below shows the CHF funded projects tacking PKDL/VL control in South Sudan in 2012 (UNOCHA, 2011; UNDP, 2012).
The MOH has planned to have a health financing strategy developed by the end of 2012. They also aim to achieve a total percentage government expenditure on health of 15% by 2015 (MOH, 2012a).

4.3.3 Human resources for health:

Currently there is critical shortage of HR. NGOs have trained Community health workers (CHWs) and lay people to perform various tasks such diagnostic test, treatment and health promotion. The majority of the staff prefer to live in the urban areas avoiding the rural areas were the PKDL and VL cases exist (MOH, 2011; MOH, 2012a; MOH, 2006).

There is limited staff supervision from the MOH and WHO. MOH staffs are irregularly paid and compensation of the staff due to work related problems is mostly dependent on NGOs (MOH, 2006; MOH, 2012a). There are more professionals returning back but to the country but not necessarily to these VL/PKDL affected areas (MOH, 2006; MOH, 2011).There is high turnover of staff and increased work absenteeism (MOH, 2012a).
About 66% of the medical staff is male. Since its integrated projects several staff has so much work (MOH, 2006).
There are no standard HR policy guidelines. However the MOH is committed to improving the production, performance and productivity of its HR and it has planned to finalise its HR for health policy and strategy by the middle of 2012 though the final report if not yet out (MOH, 2012a).

4.3.4 Service delivery:

The main providers are MSF, Sudan medical relief, Christian Mission Aid (CMA), Coordinamento delle Organizzazioni per il Sevizio Volontario (COSV), Diocese of Torit (DOT), Malaria Consortium and medair (Malaria Consortium, 2010).
All sorts of services are given at different levels of the health system. The number of VL treatment centre has increased from 9 in 2009 to 26 in 2012(MOH, 2012b; Rumunu *et al*., 2009).MOH treatment guidelines have just been finalised and shall be distributed shortly to the health facilities (MOH, NOT DATED-a, MOH, 2011).
Health services are not equitably distributed. They perform passive case detection and have few diagnostic and treatment capacity (Rumunu *et al*., 2009; MOH, 2012b, WHO, 2010b, WHO, 2011). It is mainly NGO facilities that provide most of the care and because of limited overall coverage are therefore not comprehensive. Some facilities lack referral capacity (MOH, 2012a).
The effectiveness is improving as noted by fall in CFR from 15% in previous years to current 3.2% (MOH, 2012b). Utilisation in general is low and traditional treatment is also popular (MOH, 2012a; MOH, 2012b).
Improving health service delivery and access is a priority for the MOH. The MOH is planning on improve coverage of basic services, reducing inequalities, capacity building, resource mobilisation and development of policies for PKDL and VL (MOH, 2012a).

4.3.5 Health management and information system:

The integrated disease surveillance and response unit (IDSR) is responsible for identification of cases, reporting, investigation of potential outbreaks and response to control of the VL outbreaks (MOH, 2012b).
The MOH has prepared patient registers and treatment cards. All health facilities should compile a monthly report on the VL/PKDL cases seen within their catchment areas. During epidemics the frequency is increased to weekly reporting. All the reports are sent to the IDSR at the MOH and

WHO (MOH, NOT DATED-a). Most of the health facilities have reporting forms (MOH, 2012b).
In 2011 frequency of reporting was 3% in Upper Nile, 18% in Jonglei, 46% in Unity and 54% in Eastern Equatoria (MOH, 2012b).
The WHO case definition of VL is used but there is no definition of PKDL. The registration of cases is done in MOH formats and also NGO formats. Some NGOs reportedly do not hand in their data as they only use their formats (MOH, 2007b).
At the MOH central level lack of standard supervision checklist, limited skill, lack of transport, lack of incentives, poor coordination and limited awareness of the importance of supervision result in limited and ineffective supervision (MOH, 2007b).
There is limited data analysis at the health facility level however this is higher in NGO facilities. This is due to few staff, heavy work load, limited super vision and feedback (MOH, 2007b; MOH, 2012a).
Poor communication infrastructures such as the poor roads result in delay in receiving information. The MOH aims to strengthen the HMIS (MOH, 2012a).

4.3.6 Medicines and supplies:

All medicines and diagnostic kits for the control of VL and PKDL in South Sudan are procured by WHO or MSF. WHO supplies the MOH and other NGOs while MSF uses its own supplies (Malaria Consortium, 2010). International dispensary association (IDA) is the main supplier of MSF and probably WHO as well.
The WHO and MOH store their drugs and supplies within the central medical store for further distribution to the health facilities. There is limited storage capacity within the MOH facilities. MOH medicines and supplies are only sent on case by case basis to the respective health facilities (Malaria Consortium, 2010). Cold chain capacity is limited in Juba ware house and the health facilities compromising the storage of ambisome (MOH, 2012b). SSG, PM and Miltefosine are on the national essential drug list except Glucantime and Amphotericin B. MOH provides the rest of the drugs for the treatment of concurrent infections. Selection and quantification is done annually. South Sudan pharmaceutical quality control laboratory test the quality of the drugs (MOH, NOT DATED-b).
The MOH promotes the use of standard treatment guidelines among public and private sector however not operational at the moment. Shortage of drugs and diagnostic kits at health facilities is a problem (MOH, 2012a; Malaria Consortium, 2010).
Observations from other states which are probably as in the VL/PKDL affected states and are as follows; the supply chain is 54% push and 15% pull system. Only 39% of health facilities have necessary forms. Data from health facilities arrive late and incomplete. Inventory system is poorly understood and there is lack of stock cards. About 27% reported stock outs in the last three months. Only 35%of health facilities have minimally accepted drug storage requirements, 20% use drugs rationally,

no adverse drug reaction follow up. Only 19% of facilities have guidelines for disposal of expired drugs and most use pits for burning. Most positions are either vacant or filled by lay workers. Forecasting of national requirements is done manually (USAID, 2011).

4.3.7 Prevention of PKDL and VL:

There is primary and tertiary prevention of PKDL and VL. There are no methods of secondary prevention (MOH, NOT DATED-a; WHO, 2010a; MSF, 2012).

4.3.8 Primary prevention:

This consists of health education, bed nets distribution and use, universal precautions and early diagnosis and treatment of PKDL and VL (MOH, NOT DATED-a; MSF, 2012).

Health education promotes the use of bed nets and avoidance of sleeping outdoors. It informs about the signs and symptoms of PKDL and VL, availability and location of treatment centres, the transmission of VL and the prevention of HIV, malnutrition and maintenance of good health through the use of clean water, latrines, personal hygiene such as hand washing (MOH, NOT DATED-a, MSF, 2012).

Bed nets distribution and use is promoted however coverage is still low (MOH, NOT DATED-a; MSF, 2012).

Universal precautions promoted include, not sharing syringes and needles and screening of blood before transfusion (MOH, 2012a).

Early diagnosis and treatment is discussed further under tertiary prevention (MOH, NOT DATED-a; MSF, 2012).

4.3.9 Tertiary prevention:

The treatment of VL cannot be started without confirmation of diagnosis. PKDL is diagnosed clinically (MSF, 2012; MOH, NOT DATED-a; WHO, 2010a).

The diagnostic tests used are rk39, DAT, microscopy on bone marrow, spleen and lymph node aspirates. The level of health facility level were the tests should be used is not well defined (MOH, NOT DATED-a; MSF, 2012)

The MOH and partners are using the following drugs for the treatment of PKDL and VL as shown in table 22 below (MOH, NOT DATED-a; MSF, 2012).

Table 22: MOH and MSF VL and PKDL treatment protocols in 2012:

	MOH		MSF
	First line	Second line	
Primary kala-azar;	SSG and PM	SSG	SSG and PM
Relapse of kala-azar:	SSG and PM or SSG	Liposomal Amphotericin B deoxycholate (ambisome) or Amphotericin B deoxycholate	SSG and PM
PKDL:	SSG or SSG and PM		PM +SSG
Leishmania and HIV co infection:	Liposomal Amphotericin B deoxycholate (ambisome) or pentavalent antimonials (SSG) in absence of amphotericin.		Primary/relapse VL and HIV positive: Ambisome +Miltesfosine
Treatment of severely ill patients and pregnant women	Liposomal Amphotericin B deoxycholate (ambisome)		Liposomal Amphotericin B deoxycholate (ambisome)

Source: (MOH, NOT DATED-a; MSF, 2012)

Supportive treatment is done for concurrent infections such as diarrhoea, vomiting, cough, tuberculosis, respiratory tract infections, bleeding, skin infections , HIV/AIDS, malaria, malnutrition and Iritis (MSF, 2012; MOH, NOT DATED-a) There is access to HIV treatment (MOH, 2012a).
The MOH has a case definition of VL but not that of PKDL (MOH, NOT DATED-a). Epidemic preparedness is planned at the central level but there is limited preparation at the health facility level (MOH, NOT DATED-a; MOH, 2012b).

4.4 Data and cost minimisation analyses:

Between 2002 and 2008, a total of 422 patients were treated for PKDL in MSF health facilities in South Sudan. Of these, 343 were treated with SSG and 79 with SSG+PM.

The table 23 below shows the results of the data and CMA.

Table 23: Data and Cost minimisation analyses results

		SSG	SSG +PM	P value	Statistical test
Number of patients		343	76		
Age (years):	**Median**	**6**	**3**	**P=0.0047 significant**	Kruskal-Wallis test for two groups
	IQR	2-18	1-9		
	Mean	11	8		
	standard deviation	11	10		
	Total	333	70		
Sex:	Females	164 (48.5%)	38 (51.4%)	P=0.659 Not significant	Chi square-uncorrected
	Males	174 (51.5%)	36 (48.6%)		
	Total	338 (100%)	74 (100%)		
Outcome	**Cured, n (%)**	**307 (89.8)**	**74 (97.4)**	**P=0.04 significant**	Fisher exact
	95% CI of difference (%)	**7.6 (0.6-11.7)**			
	Defaulted or died, n (%)	**35 (10.2)**	**2 (2.6)**		
	95% CI of difference (%)	**7.6 (0.6-11.7)**			
	Total, n (%)	342 (100)	76 (100)		
Duration of treatment (days)	**Median**	**36**	**30**	**P=0.0000 significant**	Kruskal-Wallis test for two groups
	95% CI of difference	**6 (3-9)**			
	IQR	30-50	21-39		
	Mean	40	33		
	standard deviation	14	14		
	Total	342	76		
Cost of treatment (US$)	**Median**	**165**	**147**	**P=0.07 Not significant**	Kruskal-Wallis test for two groups
	95% CI of difference	**18 (3-34)**			
	IQR	138-230	103-188		
	Mean	181	160		
	standard deviation	64	64		

Chapter 5: Discussion and Conclusions:

5.1 The burden of PKDL in South Sudan and its impact on the VL epidemiology:

DALYs is one of the main ways of measuring the burden of disease and widely used by policy makers for disease prioritisation and allocation of resources. The accurateness of DALYs depends on the incidence, duration of illness, morbidity and mortality data (Alvar *et al*., 2012). The incidence of VL and PKDL are reported by passive detection and thus there is a lot of underreporting. Under reporting of VL is considered severe in South Sudan about 4.2 to 8.1 folds the estimated figures (Alvar *et al*., 2012) Therefore reviewing the incidence of cases for 2010 and 2011 this could be 4.2 to 8.1 times. The PKDL burden can be estimated as 50% to 60% of the VL cases the new estimates are as shown in table 24 below (Zijlstra *et al*., 2003; Alvar *et al*., 2012; WHO, 2010b; MOH, 2012b).

Table 24: New estimates for the numbers of VL and PKDL in 2010 and 2011

	2010		2011	
VL	8916	37447 to 72,220	7662	32,180 to 62,062
PKDL	513	18,724 to 43332	539	16,090 to 37237

Source: (Zijlstra *et al*., 2003; Alvar *et al*., 2012; MOH, 2012b)

This is a very high burden for the states and must be controlled (Alvar *et al*., 2012; WHO, 2010b; MOH, 2011).
The case fatality rate of 2.7% and 3.2% are under reporting since they are only facility based. Estimates could get to 20% as shown in a study (WHO, 2010b; WHO, 2011; Zijlstra *et al*., 1994).
Ongoing surveillance has to be improved and occasionally supported by active case detection (Alvar *et al*., 2012; WHO, 2007). The drugs for the treatment of VL and PKDL are toxic meaning only severe forms of PKDL are treated (Zijlstra *et al*., 2003; MOH, NOT DATED-a).
Advocacy continues for investment in to safer drugs Amphotericin B or liposomal amphotericin B is very expensive but one of the best treatments. It is very important to obtain these drugs at an affordable cost to decrease the burden of disease (Alvar *et al*., 2006).
Early diagnosis and treatment also reduces the financial burden on the health system as patients rapidly improve and become less infectious. A healthy population free of VL and PKDL is able to work for the economic development of the nation which is the goal of the national health policy (MOH, 2007a; WHO, 2011c).
Low immunity in children and men mostly shepherding increases their burden (Hassan *et al*., 2004; Zijlstra *et al*., 2003).
Control of VL and PKDL contributes to achieving the millennium development goals by curing patients there is a work force that prevents hunger and poverty, gender empowerment integration in the control has

further reaching results, child morbidity and mortality is prevented goal, HIV/Co infected patients are treated, HIV is a risk factor for VL and PKDL. Global partnerships in the fight to combat neglected diseases improve global collaboration for public health (WHO, 2010c; Alvar *et al*, 2012). In conclusion, the true burden of PKDL is enormous but underestimated and achievement of the millennium development goals is compromised if this is not addressed. Health management information needs to be improved, occasional survey (annual) to get the real burden and better affordable drugs provided (WHO, 2010c; Alvar *et al*, 2012; WHO, 2010b; WHO, 2011).

5.2 The determinants of PKDL in South Sudan

The political environment is the distal determinant of VL and PKDL. The government should ensure that during conflict health facilities and medical professionals are not targeted. They should ensure that access to humanitarian aid is not prohibited. The Geneva conventions should be followed (MSF, 2002). Peace offers a possibility of controlling VL and PKDL (Rumunu *et al*., 2009).The returnees to South Sudan must be closely monitored and health education provided at arrival sites. Currently there is spread to areas initially unaffected by population migrations, which is sometimes due to conflict (UNOCHA, 2012).

The physical environment presents a challenge to the control as there are not many effective methods of vector control. Bed net use is shown to be effective. Insecticide spraying may not be very effective as transmission is sylvatic. There is need to invest in existing methods and newer effective methods of vector control are required (WHO, 2010a; Ritmeijer *et al*., 2007). Malnutrition may be controlled through collaboration with the nutrition department and the agricultural sector that should ensure and improve food availability (MOH, 2012a).

The health services delivery is discussed further on. Cultural practices may be addressed through health promotion. Intersectoral collaboration with the department of water and sanitation, education and Ministry of gender are required to address these determinants. Provision of free health care and partnerships with poverty alleviation programmes may help prevent poverty and promote health (MOH, 2012a, GOSS-2011c).

5.2.1 Conclusion:

Several determinants have been noted but the most important determinants are the political environment, the physical environment, the health services, cultural habits and biology. The other determinants act through malnutrition a risk factor for PKDL and VL and these are socio economic situation and water and sanitation. Protection of health services during conflict, intersectoral collaboration and the use of available protective methods are the key to control (WHO, 2010c; MSF, 2002).

5.3 The PKDL control responses in South Sudan

5.3.1 Governance:

The MOH aims at improving governance through investment in institutional development and strengthening inter programmatic and intersectoral coordination (MOH, 2012a).

A VL/PKDL Control strategy needs to be developed to guide an effective control of VL and PKDL (WHO, 2007).

The MOH faces several governance problems and so will need support in developing the strategy. In the immediate term which is within six months, the MOH should be supported by the WHO and other partners in this process (MOH, 2012a).

The vision and principles of the strategy are in line with the global plan to combat neglected tropical diseases and also fit within the national health policy and health sector development plans (WHO, 2007; MOH, 2007a; MOH, 2012a).

The components of the strategy should be tailored to the challenges for the control of PKDL and VL within South Sudan and the global plan to combat neglected tropical diseases. These components are strengthening of the health system, intersectoral and interprogrammatic collaboration, quantifying the burden, increasing coverage with comprehensive packages of preventive efforts, research into new control strategies and advocacy for resource allocation and newer effective methods of control (WHO, 2007).

5.3.2 Health Finance:

Oil the current main source of government revenue is dropping and the taxation base is limited (GOSS, 2011c). Effective finance mechanisms have to be put in place to finance the health system (MOH, 2012a).

Donor aid is highly needed for the control of PKDL and VL in South Sudan. This is pertinent until the intermediate term (next two years) after which supplementation from funds of the MOH if they are able to advocate for more funds from government as stimulated in the health sector development plan. Other mechanisms could be taxation, contracting out and voucher schemes (MOH, 2012a).

Donors, MOH, finance and development partners shall all have to ensure timely financial planning, provision of funds and implementation of activities in order not to compromise service delivery. The MOH, NGOs, donors should all lobby for more funding of PKDL and VL control.

In the future taxes may contribute to significant funding. It is advantageous because it's an equitable and efficient form of financing. Training of the staff is needed as the HR shall need training in accounting and financial management. The disadvantages in South Sudan are that the majority of people are the informal sector. There is also avoidance of tax payment as observed in the previous years so a close follow up is very important (GOSS, 2011c). Fortunately with more returnees coming back the tax base should increase. In the meantime the follow-up should be

made on people working in the private sector to ensure that they are paying their taxes.
In the long term, Public private partnerships can be improved through contracting health facilities to NGOs and then the government pays for the services provided. The government can carry out a joint venture with private partners. Vouchers may be offered to PKDL and VL patients so that they may obtain free services from health providers. An example is the supply of bed nets can be done through vouchers.
User fees should not be an option because it will reduce access to health and cause catastrophic expenditures (Magaret *et al*., 2001; Alvar *et al*., 2006).

5.3.3 Human Resources for health:

The PKDL/ VL control strategy should be integrated with the HR strategy. There should be integration of human resource management activities such as human resource planning, recruitment and selection, performance management, training and development and employee relations (McCourt and Eldridge, 2003).
In the policy formulation all stake holders should be involved (MOH, 2012a). In the short term, NGOs should continue to work with CHWs and lay workers. An expected competency of these cadres needs to be defined (WHO, 2006).
Staffs should be given appropriate financial incentives. Providing better living conditions, safe and supportive working environments, outreach support, career development programmes and professional network. Public recognition measures are helpful in encouraging people to work (WHO, 2010c).
To ensure that staffs are always available, they should be given Job descriptions, told norms and codes of conduct, their skills matched with their tasks and they should be supervised. They should be appropriately rewarded for their services, acknowledged and be listened too. They must also be supplied with all the necessary tools and infrastructure needed to perform their tasks (WHO, 2010c).
The MOH should also put in place regulations enabling the staff to work in all areas. Compulsory service in rural areas can be implemented. People who accept to work in rural areas should be given scholarships. Hard ship allowances can also be provided (WHO, 2010c)
In order to attract female health workers, it is important to clarify the barriers to female participation to training and working. Provide suitable incentives favouring neither sex. Provide good working conditions for females. Provide maternity leaves, and breast feeding times. Liaise with the Ministry of education for the promotion of girl education (Hilary, 2000)
Basing on the HMIS data on case load in the respective areas HR can be allocated. Equity must also be considered (MOH, 2012a).
Training on work load analysis can be done (WHO, 2010d).

They should create health professional schools outside the major cities, and encourage medical internship rotations of nurses, doctors and clinical officers in rural areas. The medical curriculum should reflect rural health issues. There should be continuous professional development for rural health workers (WHO, 2010c).

5.3.4. Health services delivery:

The MOH should agree on a common agreement what services should be provided at the respective health system levels. This is in order to improve efficiency and quality of care. Provision of services could be health education, diagnosis and treatment of simple PKDL cases in the PHCU and referral to a PHCC or hospital if needed. The PHCC and Hospitals can provide the above services including HIV treatment (MSF, 2012; MOH, 2011).

The recently concluded health facility mapping can be used to identify functional health facilities in which integration could take place. Integration of PKDL/VL treatment into more health facilities increases the coverage of control. The following services can be integrated into the rest of the facilities; health education, diagnosis (clinical and use of diagnostic tests), treatment (including follow up treatments) and disease surveillances. This shall require training of staff and possibly more staff, provision of PKDL and VL treatment equipments.

5.3.5 Health management and information system:

There is an urgent need in Improvement of the functioning of the HMIS. A committee should be selected to review the functioning of the HMIS and make some proposals for improvement (WHO, 2004; Alvar *et al*., 2012; WHO, 2007).

In the immediate and short term NGOs and MOH should work together in improving HMIS. It is important to give training and the data collection tools to NGOs. Joint supervision can be done between NGO and MOH staff. NGOs should be allowed to supervise and also collect HMIS data from MOH health facilities and transfer them to the next reporting levels. In the intermediate to long term a whole assessment and evaluation of the HMIS should be done by the IDSR with support from the WHO. A review of the data collection tools should be made looking for the quality of data in terms of accuracy, completeness, adequacy and timeliness and problems encountered. Review of data processing, analysis and dissemination, supply, logistics and coordination (WHO, 2004).

The data needs should be specified for every health level and roles assigned. Appropriate follow up indicators designed and data flow and frequency outlined. The design of the tools and trainings should take into consideration competency of the staff. Pre-testing should be done under almost similar conditions. A monitoring and evaluation plan, data dissemination and feedback well organised and lastly continuous reviewing of the process (WHO, 2004).

5.3.6. Medicines and supplies:

In the short term and intermediate term WHO and MSF continue the supply. NGOs to work with MOH to develop the inventory management, improve stock conditions, supply chain, graduate to computerised system at the central level for quantification of national demands. Do training on the indicators for rational use and follow up supervision. Provide guidelines for drug disposal, first in and first out procedure to be used. Train CHWs and lay people in management of medicines and supplies. To ensure rational drug use and improved quality of care, MOH should be trained by the WHO or NGOs on the three sets of drug use indicators. These are health facilitator indicators, prescriber indicators and patient care indicators (WHO, 1993). The health facility indicators review the availability of essential drugs. Improvements can be made from the starting points. The prescriber indicators guarantee the rational prescription of drugs. The amount of drugs prescribed by the staff, the proportion of Injections, antibiotics and also the amount of drugs from the MSF essential drugs list are reviewed against the set guidelines (WHO, 1993). The patient care indicators evaluate quality of care to the patient through reviewing the average time of consultation, average dispensing time, percentage of drugs dispensed; percentage of drugs labelled and patient's knowledge of correct dosage. All these indicators help to improve the quality of care (WHO, 1993).

5.3.7 Prevention:

The control of reservoirs through case detection, diagnosis and treatment reduces morbidity and mortality (WHO, 2010a; Desjeux, 2004; Guerin *et al*., 2002; Chappuis *et al*., 2007). Passive case detection is insufficient in emergencies so active case detection should be done (WHO, 2010). The low coverage of bed nets can be improved through increasing service delivery as explained above (WHO, 2010a). Epidemic preparedness and response is also very crucial in the control of PKDL and VL and should be improved (MOH, 2012b; WHO, 2010a). A diagnostic policy should be implemented to improve the quality of care. An example is as table 25 below (WHO, 2010a).

Table 25: Diagnostic Policy at the different health service levels

Level of health service	Diagnostic test
PHCU	rK39 antigen based immunochromatogrpahic test
PHCU/ state/ county -hospitals	rK 39 antigen test, DAT Microscopy on bone marrow, spleen and lymphnode aspirates.
Tertiary hospital	rK 39 antigen test, DAT Microscopy on bone marrow, spleen and lymphnode aspirates, other serological tests (IFAT, ELISA) Culture or PCR

Source: WHO, 2010a

In PKDL Serological tests such as rK39, DAT and ELISA are often positive. (WHO, 2010a).The rk39 is easy to use but DAT is a bit complex requiring cold chain and experienced laboratory technician and hospital facility (Chappuis *et al*., 2007). The sensitivity of the microscopic exams on aspirates, Lymph node is 53-65%, spleen is 96% (93-99%) and bone marrow aspirates 53-86% To do this you need qualified medical personnel and possibility to manage bleeding complications (Zijlstra *et al*., 1992; Siding *et al*., 1996; Ho *et al*., 1948; Babiker *et al*., 2007; Kager and Rees, 1983).
HIV co infected patients are highly infectious to sandflies and their clinical presentation is atypical .Their treatment and prognosis is different. Antiretroviral therapy should be started in all HIV patients diagnosed. NGOs should support the MOH with this (WHO, 2010a).
Other prevention methods include avoiding times moving in the acacia forest during the evening and dawn; avoiding sitting on termite mounds and the application of repellents (WHO, 2010a).

5.3.8 Data and cost minimisation analyses:

The diagnosis and follow up of the patients were done by doctors and CHWs in the SSG and PM group and SSG group respectively. Doctors are much more skilled than CHWs so this introduces an observer bias. It is not know what form of difference this has created. Generally patients are admitted with severe maculo popular rash sometimes involving the mucosa and discharged when the rash is markedly improved, not palpable (WHO, 1996, MSF, 1999).
Nutrition status and haemoglobin levels have not been added to the analysis because the data was incomplete. However they are risk factors for mortality and not treatment failure and since there were only three deaths it is unlikely that they have an impact on the outcome of this analysis (Collin *et al.*, 2003; Gorski *et al.*, 2010). PKDL grading has not been added since it is not shown to have any effect on the treatment duration (Collin *et al*., 2003).
Two patients received PM treatment for less than a week so were considered to have had spontaneous recovery. Another patient also on PM had 30 days of treatment which is unlikely since treatment is only for 17 days. The treatment duration of a patient on SSG was not recorded. These four patients were removed from the analysis.
The ages of 16 patients were missing, 10 in the SSG group and 6 in the SSG and PM group. The sexes of 7 patients were missing, 5 in the SSG group and two in the SSG and PM group. The patients in the SSG and PM group were probably younger because younger children suffer more from severe PKDL and were more likely to be seen by the doctor as the CHWs refer severe cases to the doctor.
A limitation of the study is that there was no systematic HIV testing at this time however HIV prevalence in this patient group was estimated at less than one percent (MSF, personal communication).

The results show that there is a difference in the outcomes of cure, defaulters and deaths in between SSG or SSG and PM combination treatment. The cure rate is 7.6% (95% CI 0.6-11.7) higher in SSG and PM combination treatment group than the SSG group, 97.4% versus 89.8%. The failure rate is 7.6% (95% CI 0.6-11.7) lower in the SSG and PM combination treatment group than the SSG group, 2.6% versus 10.2%.The p value is 0.04 which is significant.
The results also show that SSG and PM combination shortens the duration of treatment by about 6 days (95% CI 3-9). This is statistically significant, p value is <0.0001.
After stratification by age group, (cut offs at the 25^{th}, 50^{th}, 75^{th} percentile of the distribution of age in the whole population: ≤2 years, 3-5 years, 6-17 and >17 years), there was still a difference in duration of treatment in between the two treatment groups and most significantly in the younger age groups.
The costs of treatment with SSG and PM is 18 US$ (95% CI 3-34) cheaper than with SSG. However the difference is not statistically significant, p value is 0.07. This may need a bigger sample size to demonstrate. However shorter treatment duration is beneficial for the patient reducing opportunity costs and drug toxicity.
SSG is cardio-toxic, nephro-toxic, causes pancreatitis and lethal (Gasser *et al.,* 1994; Shahian and Alborzi, 2009; Zaghloul and Al-Jasser, 2004; den Boer *et al.*, 2009; Musa *et al.,* 2012). For the use in individual patients it may be appropriate for severe PKDL (Chappuis *et al.*, 2007). It is feasible to provide at primary health care unit level. The disadvantages are that the duration of treatment is long and longer than of treatment of VL thus potentially more risks of toxicity. It requires more laboratories monitoring than in VL patients. It is not suitable for the treatment of HIV co-infected patients (Ritmeijer *et al.,* 2006; den Boer *et al.,* 2009). It is administered by injections which are painful. Though it is cheap it is not suitable for public health control because mild and moderate grades are not treated. In case patients default there is increased risk of resistance (WHO, 2010a; den Boer *et al.,* 2009).
SSG and PM combination therapy is also beneficial for severe cases. Toxicity due to PM is rare (Chappuis *et al.,* 2007; den Boer *et al.*, 2009). It is feasible to provide at primary health care unit level and duration of treatment is shorter than SSG monotherapy however still treatment is longer than that of treatment of VL. Thus potentially more risks of toxicity than in VL patients. It is not suitable for the treatment of HIV infected patients (Ritmeijer *et al.,* 2006; den Boer *et al.,* 2009). It is also administered by painful injections. For public health control it is not suitable because mild and moderate grades are still not treated (WHO, 2010a; den Boer *et al.,* 2009).
Miltefosine has been shown to be effective in the treatment of two HIV infected PKDL patients (Dejenie *et al.,* 2006). It has few side effects so may be used for mild and moderate cases of PKDL as well. It can be used in HIV patients. It is administered orally and feasible to provide at

primary health care unit level. The disadvantages are that it is expensive and the duration of treatment is long as or even longer than that of VL. It is not suitable for pregnant PKDL patients because it may be teratogenic (Sundar and Olliaro, 2007; den Boer *et al*., 2009). It is not suitable for public health control as it requires pregnancy testing and provision of effective contraception during and at least four months after treatment for non-pregnant women of reproductive age. Lastly, because of its long half-life there is a high risk of resistance development if given as monotherapy (WHO, 2010a; den Boer *et al.,* 2009)

Liposomal amphotericin B has few side effects and may be used for all cases. It is administered intravenously, requires laboratories monitoring, only feasible in hospitals and requires cold chain (Hashim *et al*., 1995; den Boer *et al.*, 2009). The duration of treatment is a month however could be as short as two weeks. The duration of treatment is the same as of treatment of VL. Hospitalisation is not very convenient for the patient. It is very expensive so not suitable for public health control. It may be considered in patients in whom the previous three regimens are contraindicated such as pregnant women, HIV patients and VL patients younger than 2 years or older than 45 years (WHO, 2010a; Musa *et al.,* 2005; Hashim *et al*., 1995; den Boer *et al*., 2009).

In conclusion, for the treatment of severe PKDL; SSG and PM combination should be used instead of SSG as it offers shorter treatment duration and better outcomes (cure, defaulter and deaths) than SSG monotherapy. The SSG and PM combination treatment is cheaper than SSG monotherapy however the difference is not statistically significant and so would probably require a larger sample size to demonstrate.

In general, the drugs currently available are not ideal for treatment because of toxicity, resistance, high prices, long duration of treatment or inadequate mode of administration (den Boer *et al.,* 2009; Lucio *et al.,* 2012). For public health control, drugs should be efficacious in a wide variety of the population (young, immunosuppressed patients etc.), safe, benefits should outweigh the risks, have an easy mode of administration (preferably oral) and of short course to promote patient compliance (lasting a week).They should also not have a lot of monitoring requirements, be stable and should be cost effective. Advocacy for drugs meeting this target profile remains a priority (Lucio *et al.,* 2012; den Boer *et al.,* 2009; MSF, NOT DATED).

Chapter 6: Recommendations

The overall objective of a VL programme is to decrease the burden of PKDL/VL. This can only be achieved if the appropriate control mechanisms are in place. The following are the recommendations based on the conclusions of the findings. Immediate term means within the next 6 months, short term means within the next 1 year, intermediate within the next two years and long term means there after. The state with fewest staff and poor outcomes of patients is Unity and is a priority during this strategic planning (WHO, 2010b; WHO, 2011).

Governance for the control of these diseases has been highlighted as one of the weak areas. In the immediate term, the MOH should develop a comprehensive VL /PKDL control strategic plan with support from the WHO and other partners. This will help to bring all partners under one umbrella with a common vision and strategies to execute and in the long run achieve a decrease in the burden of PKDL and VL. The PKDL/ VL control strategy should include all the recommendations further below; financing, HR, service delivery, HMIS, medicines, intersectoral and interprogrammatic collaboration, prevention, research and advocacy (WHO, 2010c).

The government expenditure on health is quite low. From now till the intermediate term, donor funding shall be the main form of funding. MOH and partners working in PKDL control should lobby more for pooled funds and internationally for more funds for the control of PKDL. For the long term, donor funding may be supplemented with funds from taxation system, voucher schemes for bed nets and contracting out to private partners (WHO, 2010c).

Overall there is critical shortage of HR and this compromises the control of PKDL and VL. NGOs should work in collaboration with MOH. Within the immediate and short term the CHWs and lay workers should continue as the base of service providers. Their trainings should be comprehensively planned. More International staff support from NGOs. Female workers should be encouraged to apply for positions. NGOs should support MOH in Job descriptions/norms and codes of conduct and do joint supervisions. Appropriate incentives awarded. Medical internship rotations in VL affected areas. Rotations of MOH staff in NGO PKDL treatment sites in order to learn the treatment of PKDL/VL. In the long term; production of medical personnel from schools and location of training schools in rural areas. NGO may supervise and offer technical support to MOH staff. CHWs can work at all levels of the health system, PHCU, PHCC and Hospital while doctors and nurses at PHCC and Hospital only.

Service delivery is inequitable and has a low coverage. Therefore integration of PKDL/VL treatment into the rest of the services is important to increase coverage and must be started from Unity State. In the short term to the intermediate term, this should be progressive with a lot of support from the NGO facilities operational within the VL affected States and currently not treating PKDL and VL. The following services can be integrated, health education, diagnosis (clinical and use of diagnostic

tests), treatment (including follow up treatments) and disease surveillances.
HMIS is an important component that is not functioning well at the moment. In the short term it would be important to give training on the data collection tools to NGOs. MOH and NGOs can also participate in joint supervision. In the intermediate to long term a whole assessment and evaluation of the HMIS is necessary (WHO, 2004).
Currently there are shortages and irrational use of drugs. In the Short term and intermediate term WHO and MSF continue the supply. NGOs should support MOH in improving the management of its inventory and improve stock conditions. The staff at central level should be taught how to use soft ware for quantification of international orders. Do training on the indicators for rational use and follow up supervision. Guidelines for drug management should be provided (WHO, 1993).
The government should ensure that during conflict health facilities and medical professionals are not targeted. They should ensure that access to humanitarian aid is not prohibited. The Geneva conventions should be followed (MSF, 2002). A multi-sectorial approach is required to influence the determinants (WHO, 2010c).
In primary prevention the distribution and use of bed nets are low. This shall have to be increased to a wider coverage. Mass distribution of bed nets is an option that can be done within the short term. This has dual task for both malaria prevention and PKDL and VL prevention. There should be collaboration with the malaria control programme to increase coverage. Health education messages should be passed concurrently at these moments.
In tertiary prevention the drugs SSG or SSG and PM are currently used. From this analysis SSG and PM provides a shorter duration of treatment and thus a better option for the treatment of the patient and SSG toxicity (WHO, 2010a)
Overall all the drugs currently suitable available are not suitable for public health control because of duration of treatment and toxicity (WHO, 2010a).There is limited funding for research and advocacy for newer diagnostic, treatments and prevention strategies which is a priority.

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Chapter 8: Appendix

Table showing the CHF funded projects in south sudan in 2012:

NGO	state	Project title	Finance (USD)
Upper nile initiative and development organisation (UNIDO)	Unity	• provision of basic health services in four payams including mobile services • Surveillance and emergency response	190,280
THESO: The health support organisation	unity state:	• Controlling communicable diseases: emergency preparedness and response	397,211
Save the children in South Sudan (SCiSS):	Upper nile	• basic service provision for health and emergency preparedness and response • including surveillance and treatment of kala azar	282,455
Medair:	Upper Nile, Jonglei , Unity	• Preparedness and response to health related emergencies in South sudan	500,000
Goal:	Upper Nile	• provision of integrated primary health care for vulnerable populations	500,000
COSV	Jonglei	• support to basic services	200,000
WHO	All ten states	• emergency preparedness and response; Health cluster coordination at national, state and county level	299,980
WHO	High risk areas	• Strengthen epidemic preparedness and response capacity in high risk areas	250,000

Source: UNDP, 2012