

PROTOCOL

Big SHIFT – Big Skin Health Intervention: Fiji Trial
Northern Division Scabies Control Project

Does Mass Drug Administration for Scabies Result in
Control of Serious Bacterial Complications? A Proof
of Concept Towards Global Elimination

Protocol Version 4.2
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Statement of Compliance

This document is a protocol for a research project. This study will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

CONTENTS

PROTOCOL SYNOPSIS	6
GLOSSARY OF ABBREVIATIONS.....	8
1. ADMINISTRATIVE INFORMATION	8
1.1. Trial registration	8
1.1.1. Registry.....	8
1.2. Sponsor	8
1.3. Expected duration of study	8
1.4. Contributorship	9
2. INTRODUCTION AND BACKGROUND	9
2.1. Background and rationale for study	9
2.1.1 Scabies as a neglected tropical disease	9
2.1.2 Ivermectin as mass drug administration.....	10
2.1.3 Rationale for research plan.....	10
2.2. Aim(s)	11
3 STUDY OBJECTIVES	11
3.1 Primary objective	11
3.2 Secondary objectives.....	12
4 STUDY DESIGN.....	12
4.1 Type of Study.....	12
4.2 Study Setting	13
5 PARTICIPANTS AND RECRUITMENT	14
5.1 Number of Participants	14
5.2 Eligibility Criteria.....	14
5.2.1 Inclusion criteria	14
5.2.2 Exclusion criteria	14
5.3 Recruitment and identification of potential participants	14
5.4 Consent	15
6 INTERVENTION	16
6.1 Treatment arms.....	16
6.2 Intervention(s).....	16
6.2.1 Dosage and route of administration.....	16
6.2.2 Dose modification	17
6.2.3 Preparation and administration of study drug	17

6.2.4	Dispensing and product accountability	18
6.2.5	Measurement of participant compliance	18
6.2.6	Excluded medications and treatments	18
7	RANDOMISATION AND BLINDING	18
7.1	Concealment mechanism	18
7.2	Breaking of the Study Blind	18
8	STUDY VISITS AND PROCEDURES.....	18
8.1	Surveillance	19
	8.1.1 Surveillance of primary outcome measures	19
	8.1.2 Surveillance of scabies and impetigo.....	19
8.2	Assessments during mass drug administration	20
	8.2.1 Assessment of contraindications to ivermectin including pregnancy and contraindications to permethrin	20
	8.2.2 Measurement of height	20
8.3	Reviewing health economics of mass drug administration	20
8.4	Assessing acceptability	21
8.5	Study timeline	22
	Schedule of assessments.....	24
8.6	Screening.....	24
8.7	Baseline	24
8.8	Visits	25
8.9	Final study visit	25
8.10	Withdrawal visit.....	25
8.11	Unscheduled visit	25
8.12	Participant Withdrawal.....	25
8.12.1	Reasons for withdrawal.....	25
8.12.2	Handling of withdrawals and losses to follow-up.....	25
8.12.3	Replacements.....	25
8.13	Halting MDA	25
8.14	Continuation of therapy	26
9	OUTCOMES.....	26
9.1	Primary outcome.....	26
9.2	Secondary outcome(s).....	26
10	ADVERSE EVENTS AND RISKS.....	27
10.1	Definitions	27
10.2	Assessment and documentation of adverse events	27

10.3	Eliciting adverse event information.....	27
11	DATA MANAGEMENT	28
11.1	Data Collection	28
11.1.1	Source Data	28
11.1.2	Data Capture Methods	29
11.2	Data Storage.....	29
11.3	Record Retention	29
12	STUDY OVERSIGHT	30
12.1	Governance structure.....	30
12.2	Independent Safety Committee	30
12.3	Quality Control and Quality Assurance.....	30
13	STATISTICAL METHODS	31
13.1	Sample Size Estimation.....	31
13.2	Statistical Analysis Plan.....	31
13.2.1	Population to be analysed.....	31
13.2.2	Methods of analysis.....	31
13.3	Interim Analyses.....	32
14	ETHICS AND DISSEMINATION	32
14.1	Research Ethics Approval	32
14.2	Modifications to the protocol.....	32
14.3	Protocol Deviations	33
14.4	Confidentiality	33
14.5	Participant Reimbursement.....	33
14.6	Financial Disclosure and Conflicts of Interest	33
14.7	Dissemination and translation plan	33
15	REFERENCES	34
16	LIST OF APPENDICES.....	36
	APPENDIX 1: Participant information sheet and consent form for hospital surveillance (child)	37
	APPENDIX 2: Participant information sheet and consent form for hospital surveillance (adult)	41
	APPENDIX 3: Participant information sheet and consent form for storage of biological specimens (child)	45
	APPENDIX 4: Participant information sheet and consent form for storage of biological specimens (adult)	49
	APPENDIX 5: Participant information sheet and consent form for village skin examination (child).....	53

APPENDIX 6: Participant information sheet and consent form for village skin examination (adult)	57
APPENDIX 7: Information sheet and informed consent for Quality of Life community survey	61
APPENDIX 8: Iver P® (ivermectin tablet) product information leaflet	63
APPENDIX 9: Mectizan® (ivermectin tablet) product information leaflet	65
APPENDIX 10 Lyclear® (permethrin cream) product information leaflet	67
APPENDIX 11: Diagnostic Criteria for Acute Rheumatic Fever from Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention	68
APPENDIX 12: Definitions of rheumatic heart disease from Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention	69
APPENDIX 13: Case definitions for Invasive Group A Streptococcal Disease and Staphylococcus aureus Disease	70
APPENDIX 14: Child information sheet and consent form for village skin examination	71
APPENDIX 15: Child information sheet and consent form for hospital surveillance	75
APPENDIX 16: Child information sheet and consent form: Storage of biological specimens	77
APPENDIX 17: Ministry of Health consent form for school distribution.....	80
APPENDIX 18: Information sheet for MDA	82
APPENDIX 19: Interview Guide for Community Member	84
APPENDIX 20: Interview Guide for Key Informant.....	89
APPENDIX 21: Participant information sheet for in-depth interview: community member.....	92
APPENDIX 22: Participant information sheet for in-depth interviews: key informant.....	94
APPENDIX 23: Dermatology Life Quality Index (DLQI) questionnaire	96
APPENDIX 24: Children's Dermatology Quality of Life Index Questionnaire.....	97
APPENDIX 25: AQoL-6D Questionnaire.....	99
APPENDIX 26: Adolescent AQoL-6D questionnaire	103
APPENDIX 27: Infant's Dermatitis quality of life index- modified for skin diseases	109

PROTOCOL SYNOPSIS

TITLE	Does Mass Drug Administration for Scabies Result in Control of Serious Bacterial Complications? A Proof of Concept Towards Global Eradication
OBJECTIVES	<p>Primary Aims:</p> <ol style="list-style-type: none"> 1. To evaluate the impact of ivermectin-based mass drug administration (MDA) on admission to hospital with skin and soft tissue infections (all ages) 2. To evaluate the impact of ivermectin-based MDA on other serious bacterial complications of scabies (bloodstream, kidney and heart disease in children aged less than 15 years) <p>Secondary Aims:</p> <ol style="list-style-type: none"> 1. To evaluate the impact of ivermectin-based MDA on scabies and impetigo prevalence, and on presentation to primary health care clinics with impetigo and scabies. 2. To evaluate the impact of ivermectin-based MDA on other serious bacterial complications of scabies (bloodstream kidney and heart disease in all ages) 3. To evaluate the safety of ivermectin-based MDA in a large population at risk of scabies 4. To evaluate coverage, acceptability and feasibility of large-scale ivermectin-based MDA 5. To evaluate the cost-effectiveness and affordability of large-scale ivermectin-based MDA compared to standard care
DESIGN	A before-after intervention trial of two doses of ivermectin-based MDA delivered to the whole population of the Northern Division of Fiji. In the 12-month periods pre and post intervention, data collection around hospital admissions for serious bacterial infections as well as presentations to primary health care clinics for scabies and impetigo will be collected. In addition to this evaluation of population coverage, incidence of serious adverse events, cost effectiveness and local acceptance of the program will be undertaken.
OUTCOMES	<p>Primary outcome measures:</p> <ul style="list-style-type: none"> • The number of patients (all-ages) with skin and soft tissue infection (STI) requiring hospital admission in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior) 1. The number of cases of other severe bacterial complications (invasive disease caused by <i>Streptococcus pyogenes</i> and <i>Staphylococcus aureus</i>, glomerulonephritis and rheumatic fever in children <15 years) presenting to hospitals in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)

	<p>Secondary outcome measures:</p> <ol style="list-style-type: none"> 1. Prevalence of scabies and impetigo in survey sites at 12 months compared to baseline 2. The number of presentations with scabies and impetigo to primary health care clinics by age group in 12 months after MDA compared to the 12 months prior 3. The number of cases of other severe bacterial complications (invasive disease caused by <i>Streptococcus pyogenes</i> and <i>Staphylococcus aureus</i>, glomerulonephritis and rheumatic fever in all age groups presenting to hospitals in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior) 4. Counts of all deaths, unexplained deaths and stillbirths in the year following MDA compared to 5 years prior, and number of emergency presentations to hospital in the week after MDA. 5. Population coverage of the programme 6. Acceptability and feasibility of the programme 7. Incremental cost-effectiveness ratios (cost per quality-adjusted life years gained) and budget impact (measured in financial streams of cost over a budget cycle) comparing MDA to standard care. <p>Incremental cost-effectiveness ratios (cost per quality-adjusted life years gained) and affordability (measured in financial streams of cost over a budget cycle) comparing MDA to standard care.</p>
STUDY DURATION	36 months
INTERVENTIONS	Ivermectin-based MDA will be offered to all individuals living in the Northern Division of Fiji. This will involve 2 doses administered 7-14 days apart through a network of trained community-based MDA distributors. Ivermectin will be substituted by topical permethrin cream in individuals who are less than 90cm tall, women who are pregnant, potentially pregnant, women breastfeeding infants less than 1 week of age and individuals on warfarin.
NUMBER OF PARTICIPANTS	135,000 approximately
POPULATION	All individuals living in the Northern Division of Fiji who agree to participate.

GLOSSARY OF ABBREVIATIONS

ABBREVIATION	TERM
AE	Adverse Event
CHW	Community Health Worker
HREC	Human Research Ethics Committee
IMCI	Integrated Management of Childhood Illness
ISC	Independent Safety Committee
LF	Lymphatic Filariasis
MCRI	Murdoch Children's Research Institute
MDA	Mass Drug Administration
MOHMS	Ministry of Health and Medical Services
NTD	Neglected Tropical Disease(s)
NHMRC	National health and Medical Research Council
PATIS	Patient Information System
PHIS	Public Health Information System
PSGN	Post Streptococcal Glomerulonephritis
RCH	Royal Children's Hospital
SAE	Serious Adverse Event
SHIFT	Skin Health Intervention Fiji Trial
SSTI	Skin and Soft Tissue Infections
UNSW	University of New South Wales
WHO	World Health Organisation

1. ADMINISTRATIVE INFORMATION**1.1. Trial registration****1.1.1. Registry**

This trial is registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) under the trial identifier of ACTRN12618000461291

1.2. Sponsor

Study Sponsor	Murdoch Children's Research Institute (MCRI)
Contact name	Professor Andrew Steer
Address	Royal Children's Hospital, 50 Flemington Rd, Parkville VIC 3052, Australia

1.3. Expected duration of study

The study will be conducted over 3 years from 2018-2020. A lead-in period of 6 months will take place during which, data collection protocols, public awareness measures and local training will be undertaken. Subsequent to this, data collection and surveillance for the period prior to intervention will commence for 12 months. The intervention will take place after this 12- month surveillance period with 2 doses of oral ivermectin approximately 1 week apart to be administered towards individuals who have given informed consent and are eligible to be involved in the trial. In the 12-month period following intervention, the same methods of data collection and surveillance will be undertaken.

1.4. Contributorship

Name	Summary of contribution
Professor Andrew Steer	Principal Investigator, Theme Director, Infection and Immunity, MCRI
Dr. Mike Kama	Principal Investigator, Medical Superintendant, Twomey Hospital, Fiji Ministry of Health
Dr. Margot Whitfield	Co-Investigator, Dermatologist and Senior Lecturer, UNSW
Professor John Kaldor	Co-Investigator, Epidemiologist, Kirby Institute, UNSW
Dr. Lucia Romani	Co-Investigator, Public Health researcher, Kirby Institute, UNSW
Dr. Aalisha Sahukhan	Co-Investigator, Acting Head of Health Protection, Fiji Ministry of Health
Associate Professor Joseph Kado	Co-Investigator, Head of Paediatrics, Fiji National University
Associate Professor Handan Wand	Co-Investigator, Biostatistician, UNSW
Professor Ross Andrews	Co-Investigator, Epidemiologist, Menzies School of Health Research
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Dr. Daniel Engelman	Co- Investigator, Paediatrician, MCRI
Dr. Meciusela Tuicakau	Co-Investigator Dermatologist, Tamavua Twomey Hospital, Fiji Ministry of Health and Medical Services
Dr. Rachel Devi	Co-Investigator, Acting Subdivisional Medical Officer for Macuata, Fiji Ministry of Health
Dr. Adam Jenney	Co-Investigator Infectious Diseases Physician and Clinical Microbiologist, Alfred Health, Melbourne
Dr. Li Jun Thean	Principal Research Coordinator, MCRI

2. INTRODUCTION AND BACKGROUND

2.1. Background and rationale for study

2.1.1 Scabies as a neglected tropical disease

Scabies is a recognised neglected tropical disease (NTD) by the World Health Organisation (WHO). It is caused by cutaneous infestation by a small mite of the species *Sarcoptes scabiei* var. *hominis* which is transmitted through close personal contact. The mite burrows under the epidermis and deposits eggs resulting in a host immune response leading to intense pruritus. (1) Scabies leads to economic disadvantage, reduced quality of life and a substantially increased risk of serious complications due to secondary bacterial skin and soft tissue infection with mainly *Staphylococcus aureus* and *Streptococcus pyogenes* in turn resulting in sepsis, post Streptococcal glomerulonephritis (PSGN) and rheumatic fever. (1) It is a major cause of morbidity and mortality in many developing countries with a global prevalence of 300 million people.(2) Scabies incidence is disproportionately high in vulnerable populations with low income and political marginalisation. (3)

Standard scabies treatment comprises of 2 applications of topical permethrin 5% or benzyl benzoate 25%, 7 days apart in affected individuals, family members and close contacts. It is also recommended that clothes and linen are washed and subject to heat. (4) Adherence to effective treatment is often poor in settings of economic disadvantage in the context of resource limitations (clean water for hygiene, medications, etc.) and overcrowding. Treatment of individuals with scabies and primary contacts is unlikely to result in population control of this disease. (1)

Setting a precedent for this trial is the recent Skin Health Intervention Fiji Trial (SHIFT), published in the New England Journal of Medicine in 2015, which demonstrated that Mass Drug Administration (MDA) using oral ivermectin led to a reduction in scabies prevalence in a small island community by 94% one year post intervention (previous prevalence over 32%, to less than 2%) compared to a reduction by 67% in the permethrin MDA arm and 49% in the standard care control arm.(5) The Big SHIFT will be conducted in a population of more than 135,000 people in Fiji (200 times the size of the initial SHIFT) to assess the impact of ivermectin MDA on the secondary bacterial complications of scabies. This will be the first definitive study of the impact of scabies MDA on serious infectious complications of the condition. Evidence from this study will progress the move towards scabies elimination as a global health problem.

2.1.2 Ivermectin as mass drug administration

Ivermectin is an antiparasitic agent that is effective against a range of nematodes and ectoparasites. It is classed as an ivermectin acaricide with its mode of action being interrupting the closure of class of ligand gated chloride ion channels in the scabies mite. It is postulated that this results in excessive release of the gamma-aminobutyric acid (GABA) neurotransmitter resulting in death of the parasite. It is not ovicidal and therefore a second dose of ivermectin is required to ensure total eradication in the treatment of scabies mite infestation. In Australia it is approved by the Therapeutic Goods Administration (TGA) for treatment of scabies, onchocerciasis and strongyloidiasis. (6)

Ivermectin has been found to be a very safe drug and has led on to a long history of being used in MDA programmes. A dose escalation study showed that the administration of 10 times the Food and Drug Administration (FDA) approved maximum dose of 200 μ g per kilogram did not precipitate any adverse effects. (7) According to the WHO report on Onchocerciasis Control, there have been no severe adverse reactions out of the more than 19 million doses of ivermectin administered. (8) In the preceding SHIFT, adverse events were more common in the ivermectin group compared to the permethrin group (15.6% vs 6.8%), the majority of complaints were itch and headache. There were no serious adverse events. A Cochrane review looking at efficacy of different agents for scabies treatment showed that one trial demonstrated that a single dose of Ivermectin (200 μ mg/kg) was more effective than placebo with less incidence of treatment failure.(2) There was one trial included that compared a single dose of ivermectin (200 μ mg/kg) with a single dose of permethrin which showed that permethrin was more effective raising a subsequent discussion that a higher dose or a 2nd dose of ivermectin may result in efficacy equal to topical permethrin.(2, 9)

2.1.3 Rationale for research plan

Although scabies and impetigo result in significant morbidity in their own right, the case for population wide MDA would be greatly reinforced if there was a meaningful reduction in the less common, but more severe, life-threatening and costly complications that have been linked to scabies in observational studies. To demonstrate this, a large population must be offered MDA intervention and observed over an extended time for the occurrence of these conditions.

Fiji already has extensive experience with national MDA programmes for NTD control including yaws elimination in the 1960s, and the lymphatic filariasis (LF) programme, which commenced in 2003, providing annual doses of albendazole and diethylcarbamazine, and achieving 80% national coverage. This existing infrastructure provides an ideal setting to scale up ivermectin-based MDA for scabies. The Northern Division was chosen because of its population size, relative isolation and high scabies prevalence. The demographic features of the Northern Division are broadly representative of the national population.

The before-after design is the only feasible way to assess if the massive reduction in scabies and impetigo prevalence observed in the SHIFT will result into meaningful reductions in the serious complications that result from secondary bacterial infection. Data from the SHIFT strongly indicates that ivermectin MDA will be effective and therefore randomisation including standard care is no longer ethical. Even if randomisation could be ethically justified, the units would need to have very large populations and be separated to minimise the likelihood of re-infestation from neighbouring zones and to minimise the possibility that people resident in one area would present at a health facility in another, especially in more densely populated urban and peri-urban areas. A randomised trial on this scale would also be logistically difficult and extremely expensive because of the number and size of the population units required. The before-after design has limitations, particularly regarding control for confounding, but has increasingly found favour for evaluation of health service and public health interventions including MDA programmes.[\(10-12\)](#)

2.2. Aim(s)

Co-primary aims;

1. To evaluate the impact of ivermectin-based MDA on admission to hospital with skin and soft tissue infections (SSTI) in all ages
2. To evaluate the impact of ivermectin-based MDA on other serious bacterial complications of scabies (bloodstream kidney and heart disease in children aged less than 15 years)

Secondary aims:

1. To evaluate the impact of ivermectin-based MDA on scabies and impetigo prevalence and on presentations to primary health care clinics with impetigo and scabies
2. To evaluate the impact of ivermectin-based MDA on other serious bacterial complications of scabies (bloodstream kidney and heart disease in all ages)
3. To evaluate the safety of ivermectin-based MDA in a large population at risk of scabies
4. To evaluate the coverage, acceptability and feasibility of large-scale ivermectin-based MDA
5. To evaluate the cost-effectiveness and budget impact of large-scale ivermectin-based MDA compared to standard care

3 STUDY OBJECTIVES

3.1 Primary objective

1. To measure the number of patients of all ages with SSTI requiring hospital admission in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)
2. To measure the number of cases of other severe bacterial complications (invasive disease caused by *S. pyogenes* and *S. aureus*, glomerulonephritis and rheumatic fever in children <15years) presenting to hospital in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)

3.2 Secondary objectives

1. To measure the prevalence of scabies and impetigo in survey sites at 12 months post-intervention compared to baseline
2. To measure the number of presentations with scabies and impetigo to primary healthcare clinics by age group in the 12 months after MDA compared to the 12 months prior
3. To measure the number of cases of other severe bacterial complications (invasive disease caused by *S. pyogenes* and *S. aureus*, glomerulonephritis and rheumatic fever in all ages presenting to hospital in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)
4. To measure counts of all deaths including unexplained deaths and stillbirths in the year following MDA compared to 5 years prior, and the number of emergency presentations to hospital in the week after MDA
5. To evaluate population coverage of the programme
6. To evaluate acceptability and feasibility of the programme
7. To determine cost-effectiveness ratios (cost per quality-adjusted life year gained) and budget impact (measured in financial streams of cost over a budget cycle) of MDA compared to standard care

4 STUDY DESIGN

4.1 Type of Study

This study is a before-after intervention trial of two doses of ivermectin-based MDA delivered to the whole population of the Northern Division of Fiji (estimated population 135,000). This design is the only feasible way to assess whether the massive reduction in scabies and impetigo prevalence observed in the SHIFT trial is translated into meaningful reductions in the occurrence of much more serious but less common endpoints.

All residents of the Northern Division will be invited to receive the intervention. Participants will be offered two doses of oral ivermectin at 200 μ g/kg, two weeks apart, unless the individuals fall under a demographic where safety data on ivermectin is limited. If so, ivermectin will be replaced by topical permethrin cream in children <90cm height, women who are, or may be pregnant, women who are breastfeeding infants under 1 week old and individuals on warfarin.

Each of the two doses of the intervention will be delivered 7-14 days apart. The outcome measures of this study will be compared in this same population from the 12-month surveillance periods pre and post intervention.

In September 2018, the Northern Division underwent their third Transmission Assessment Survey after their last round of MDA for lymphatic filariasis (LF) in 2012. Findings from the survey showed that prevalence was above the acceptable 1% threshold, meaning that MDA for LF was required in the Northern Division in 2019. According to the most recent WHO guideline for MDA, treatment with three agents; ivermectin, diethylcarbamazine (DEC) and albendazole instead of standard dual agent therapy was indicated. The combination of these three medications as a regimen for MDA is commonly referred to as “IDA” or triple therapy (13)

In view of this, the decision was made between the Fiji Ministry of Health and Medical Services (MOHMS) and the project’s investigators that there would be integration of the ivermectin-based MDA and the IDA-based MDA that was required in the Northern Division for LF. Dosage and inclusion criteria for ivermectin and permethrin as stated in this protocol will be implemented during the integrated MDA program. That is: the first dose of scabies treatment (ivermectin or permethrin) will be incorporated into the IDA for LF, and the 2nd dose of scabies treatment will be delivered 7-14 days afterwards.

4.2 Study Setting

The study will take place in the Northern Division of Fiji. It was selected after consultation of the Fijian members of the research team and other senior representatives of the Fiji Ministry of Health. It is a suitable setting for this project for many reasons. The division has a substantial population size estimated around 135,000 people. It is relatively isolated with a high scabies prevalence of 28.5% with higher prevalence in rural (31.1%) compared to urban areas (12.2%).⁽¹⁴⁾ The demographic features of the Northern Division are broadly representative of the national population. The region already has established infrastructure for mass drug administration through the previous work done through the lymphatic filariasis eradication programmes. The Northern division includes Vanua Levu which is the second largest island of Fiji. The Northern Division is comprised of four sub-divisions namely: Macuata; Cakaudrove; Bua and Taveuni sub-divisions which are further divided into 36 nursing zones. Labasa located in Macuata subdivision is the capital of the division. Labasa hospital has the most advanced facilities and treats the highest patient load of the region.

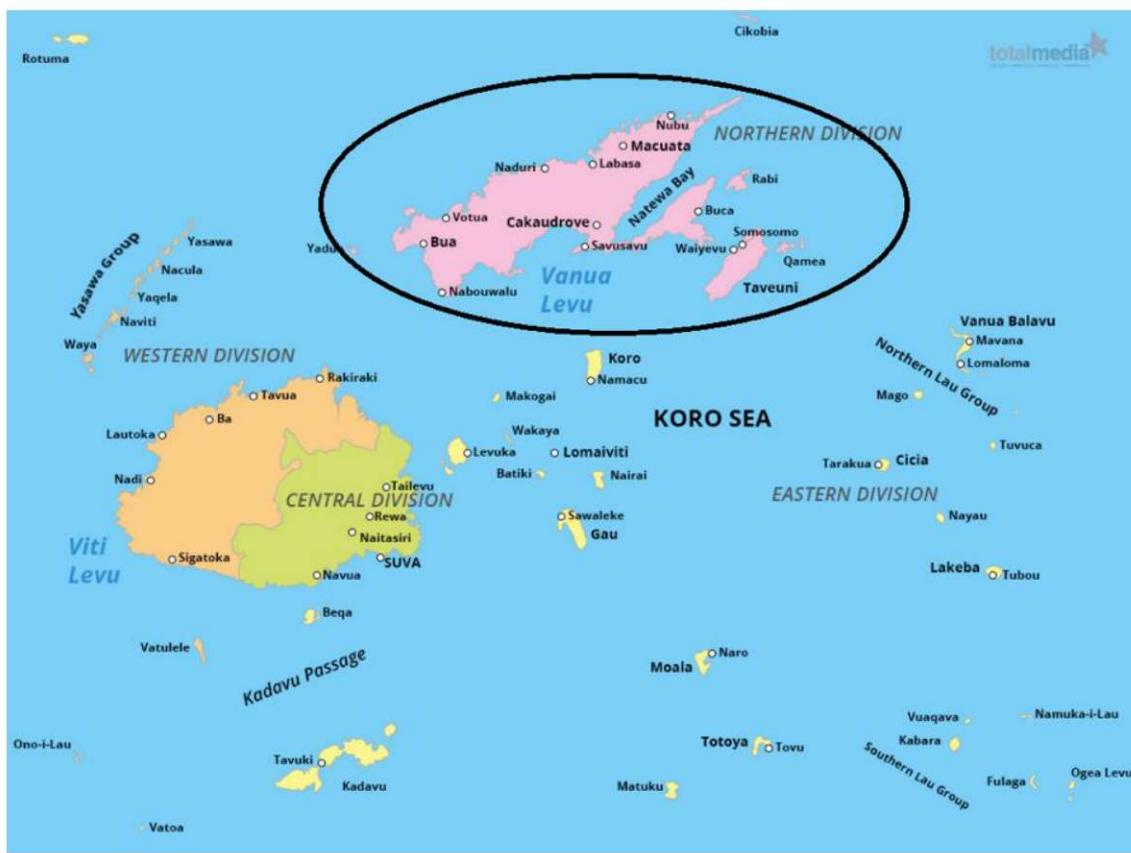


Figure 1. Community chosen for the study. Map sourced from Fiji Ministry of Health website http://www.health.gov.fj/?page_id=1612

The intervention will be distributed via an established network of trained, community-based MDA distributors, overseen by their respective zone nurse, who will in turn report to sub-divisional medical officers who will work supported by the project's Principal Research Coordinator.

Data will be collected in a variety of healthcare settings. Surveillance for serious bacterial complications of scabies will be undertaken by collecting data prospectively on admissions for severe SSTIs, bone and joint infections, glomerulonephritis, rheumatic fever or invasive infection caused by *S. pyogenes* and *S.*

aureus to Labasa Hospital. Surveillance will also take place through the microbiology laboratory in Labasa Hospital (which receives all microbiological specimens for the Northern Division) to identify patients with invasive infections caused by *S. pyogenes* and *S. aureus*.

To determine scabies and impetigo prevalence, community-based skin examinations for scabies and impetigo at baseline and 12 months post intervention will be undertaken within randomly selected villages and settlements. Prospective collection of data on clinic presentations and treatment for scabies and bacterial skin infection at primary health care clinics (nursing stations, health centres and primary care clinics held at the 4 hospitals) will also take place by reviewing routinely collected data in the form of monthly reports. Data will also be collected from routine infant health checks conducted by Maternal and Child Health Care nurses who routinely collect information on skin disease in children.

5 PARTICIPANTS AND RECRUITMENT

5.1 Number of Participants

The intervention will be offered to the entire population of the Northern Division of Fiji (population of approximately 135,000 people). Participants included in the study will be consenting individuals of mass drug administration in the Northern Division of Fiji. Assuming 80% response rate, the total number of participants will be approximately 108,000 participants.

5.2 Eligibility Criteria

As a community-based study of mass drug administration, all community members that have given verbal consent to participants are eligible for treatment.

5.2.1 Inclusion criteria

All community members are able to be included in the study

5.2.2 Exclusion criteria

The option of permethrin will be given to patients who are seriously ill: inpatients in hospital and bedridden in the community.

5.3 Recruitment and identification of potential participants

Participants will be identified via nursing census data that is collated into a 6-monthly report and updated on a more regular basis. Prior to the scheduled intervention, the study team will work alongside the Fiji MOHMS to establish a comprehensive program for information dissemination to ensure that the community members are aware of the MDA program and have the opportunity to raise issues that may be of concern.

Translated, written information regarding the MDA program will be displayed at nursing stations and health centres and handouts available for distribution at these centres. Information in regards to this program will be disseminated through existing public health mechanisms to relevant clinical staff to answer queries from the public around the program. Further communication to the public will be undertaken via radio and social media platforms. Information will also be distributed through schools via the existing public health nursing staff allocated to school health care.

We will use exactly the same strategies as used in a number of our previous collaborations in Fiji. Competency will be assessed on the basis of the legal age of consent in Fiji which is 18 years. In order for individuals under this age to be included in any aspect of the trial, informed consent will be sought from a parent/guardian. In addition, for children between the age of 12-17 years old, we will seek assent. This is standard practice for health research in Fiji and reflects our practice in previous studies.

Should an individual be older than 18 years but judged by investigators to potentially lack the capacity to give informed consent, informed consent will be sought from a parent/guardian. Should there be no parent or guardian identified, the person providing day to day care will be deemed suitable to provide consent on their behalf.

For hospital inpatients recruited to the study, competency will be assessed by the treating clinicians. In the field setting study personnel will directly check competency using the above criteria

5.4 Consent

Written informed consent will be sought for the various aspects of the study related to clinical examination or other individual-level evaluation components and are outlined below. These are:

- Documentation of cases of inpatients with conditions described in the outcome measures: skin and soft tissue infections, invasive *streptococcus pyogenes* and *Staphylococcus aureus* infections, post streptococcal glomerulonephritis, acute rheumatic fever and rheumatic heart disease at Labasa Hospital
- Storage of cultures for group A, C and G streptococci obtained from invasive sites
- Skin examinations at selected villages
- Quality of life surveys
- Semi-structured interviews

Informed consent for receiving MDA will follow national programmatic procedures and be verbal. Written third party consent will be obtained by the MOHMS for children receiving MDA in school from their parent or guardian.

Informed and written consent will be obtained from patients admitted to the Labasa Hospital for presentations of SSTIs, bone and joint infections, invasive Group A *Streptococcal* and *Staph aureus* infections. Consent will be obtained to review their medical records and if applicable, store clinically collected samples for further analysis for the purposes of the study. If a sample obtained from an invasive site yields a positive culture for group A, C and G streptococci, informed consent will be sought by the study nurses to store, export and analyse their samples for emm-typing. (see appendix 1-4 for information statements and consent forms). Explanation about the trial and obtaining consent will be done by the study nurse in the patient's own language which will most likely be English, Fijian or Hindi. The study nurses hired to perform this process will be local and fluent in required languages. The patient will need to provide written consent for the study team member to proceed with storage of their bacterial isolates.

Informed and written consent will also be obtained from individuals residing in the villages selected for skin examination and quality of life surveys. Informed consent will include consent from the participant to provide basic socio-demographic information such as age, sex, ethnicity, number of household members, education level, income and employment and a brief medical history including comorbidities. If the individual does not have the capacity to give written, informed consent, this will be sought from their legal guardian or next of kin. (see appendix 5-7 for information statements and consent forms)

In both settings, the study personnel that conducted the consent discussion will also sign the informed consent form. A copy of the consent form will be given to the subject or their legally acceptable representative and the fact that the subject has been consented to the study will be documented in the subject's record.

The MOHMS staff and community health workers (CHWs) trained for MDA distribution will conduct the informed consent process for mass drug administration. All nurses will receive prior training from the

Principal Research Coordinator and National LF coordinator on the due process required for informed consent. The consent process will describe the purpose of the MDA program, the procedures to be followed and the risks and benefits of participation. Due to the scale of the project and the study intervention being integrated as part of a national public health programme, verbal consent will be obtained from participants to receive MDA – skin examinations will not be conducted among these participants. (see appendix 18 for information sheet). If consent is not granted, this will be recorded on the coverage document, which will be informed by the nursing registry. Reasons for declining the intervention will be noted to inform acceptability of the intervention. Individuals who are too unwell to participate in the study will be noted against the coverage document.

Informed and written consent will be obtained from individuals residing in the villages and key informants participating in semi-structured interviews. Prospective participants will be informed about the research aims, inclusion criteria (age, residence location), interview process, potential risks and commitment by an independent researcher. During this process, prospective participants will be informed that their participation is voluntary and that all efforts will be made to ensure their confidentiality and anonymity is protected. Participants will also be told that they are free to not participate, and to withdraw at any time during the research, until the point of publication of findings. Please see appendices 5,6, 7, 14,21 and 22 for participant information statements and consent forms.

All consent will be voluntary and free from coercion.

6 INTERVENTION

6.1 Treatment arms

As this is a before – after trial there is only a single treatment arm of ivermectin-based MDA with permethrin cream used as a concurrent substitute where required but not for comparison.

6.2 Intervention(s)

The first dose of ivermectin will be supplied by the Mectizan Donation Program with the MOHMS as the recipients. Ivermectin for the second dose will be sourced from Fundación Mundo Sano and permethrin will be sourced locally.

Ivermectin 200 μ g/kg

Mectizan® is an ivermectin product manufactured and donated by Merck which is prepared in 3mg tablets. It also contains microcrystalline cellulose, pregelatinised corn starch, butylhydroxyanisol, anhydrous citric acid and magnesium stearate.

Iver P® is an ivermectin product manufactured by Laboratorio Elea which is prepared as 3mg tablets. It also contains lactose hydrate, Cellactose 80, Talc, sodium starch glycolate and Magnesium sterate. It has been used clinically in Argentina, Trinidad and Tobago and in clinical trials in Kenya. (see appendix 7 for product information)

Topical 5% permethrin cream (Lyclear®)

Topical 5% permethrin (Lyclear ®) cream for scabies is supplied in a 30g tube. The cream is applied all over the body including from neck to toe and washed off after a minimum of 8 hrs. Permethrin is applied for a maximum of 4 hours in infants under 2 months. (see appendix 8 for product information)

6.2.1 Dosage and route of administration

Ivermectin will be taken orally as directly observed therapy either swallowed whole or crushed and mixed with yoghurt/custard. The recommended dose for scabies is 200micrograms/kg. This trial is

designed to represent a large-scale national MDA programme and will need to assess feasibility utilising resources that are already available within the local health system. The ivermectin will be distributed by trained MOHMS nurses. The nurses will directly observe the first dose of ivermectin which will be given alongside DEC and albendazole as part of the integrated MDA program. The second dose of ivermectin will be dispensed at this visit. The second dose of ivermectin 7-14 days later will be directly observed by community health workers (selected village members who perform a variety of social duties such as census data collection) who will report back to zone nurses who will in turn report back to the Principal Research Coordinator and national LF coordinator during MDA. Training of community healthcare workers and zone nurses with regards to MDA distribution will be coordinated by the study team and the National LF Team at least 1 month prior to the time of MDA. Due to the large scale of the MDA and lack of local resources for weighing scales, the intention will be to dose according to height measured with a height stick with dosing brackets calculated according to local weight for height correlations.

Height (in centimeters)	Single oral dose Number of 3mg Iver P® tablets
90 to 112 cm	1 tablet
113 to 133 cm	2 tablets
134 to 146 cm	3 tablets
147 to 156 cm	4 tablets
157 to 164 cm	5 tablets
165 to 200 cm	6 tablets

Table 1. Ivermectin dose by height schedule by Death to Onchocerciasis and Lymphatic Filariasis (DOLF)

Participants with severe or crusted scabies will be treated with 2 doses of ivermectin (except if ivermectin is contraindicated as outlined above) in conjunction with twice weekly permethrin cream for 1 month, with review at 1,2,3,12 and 24 months. Efforts will be made to control these cases intensively to prevent the high mite load of infection associated with crusted scabies from diminishing the effect of the MDA. These cases will be followed up by the Principal Study Coordinator and referred to the appropriate subdivisional hospital.

Adult individuals who are assigned permethrin will receive a tube and will be asked to apply the cream from neck to toes and leave it on for a minimum of 8 hours and maximum of 24 hours if possible. For children measuring less than 90cm in height, parents will be asked to apply cream as directly observed therapy. Parents of infants under 2 months age will be advised to apply the permethrin for 4 hours only.

Prior to being offered the drug, participants will be informed of potential adverse reactions that may result from taking ivermectin as part of the public awareness and consent process. These reactions may be in relation to the ivermectin itself, but also more commonly as result of the destruction of parasites by the intervention. They will be informed to seek care from their local healthcare facility if required.

6.2.2 Dose modification

Doses will be titrated to height. Local height for weight correlations will be used to calculate the dose ranges. No other dose modifications will be necessary for the purposes of the study intervention.

6.2.3 Preparation and administration of study drug

Shortly prior to the scheduled MDA, ivermectin and permethrin will be transported to and stored at the nursing stations throughout the Northern Division. Dispensing of medications will be done by MOHMS

nurses, other health cadres and CHWs trained for MDA distribution. The MDA will be distributed from house to house, schools workplaces and at a suitable meeting point in the community with the public advised of the venue in advance.

6.2.4 Dispensing and product accountability

Prior to import and distribution of the ivermectin, authorisation for the Iver P® will be sought from the Medicines Regulatory Authority which is part of the Fiji Pharmaceutical and Biomedical Services Centre, Ministry of Health to ensure the product meets national standards. Permethrin which is already used widely locally will be sourced from local private pharmacies with prior notice so as not to disrupt local permethrin supply.

Ivermectin will arrive in the country by ship. The order request will be checked with the supplies delivered. The delivery notice number, delivery date, expiration date and the medications batch number will be recorded in a log book. Medications will be transported to Labasa Hospital by boat or road and stored in their pharmacy until close to the date of MDA. Prior to the scheduled MDA medications will be transported by road and boat to the divisional hospitals and distributed from there to the various nursing stations. Distributing nurses will maintain a log of all medicines dispensed that can be cross-checked against participants study records. Reasons for departure from the expected dispensing regimen will be recorded. At the end of the study there will be final reconciliation of study drug received, dispensed, consumed and returned. Any discrepancies will be investigated, resolved and documented by the study team.

6.2.5 Measurement of participant compliance

Ivermectin will be administered as directly observed therapy. Permethrin cream will be administered as directly observed therapy in children measuring less than 90cm in height. This will account for the majority of participants in the intervention. Compliance will be monitored via pill counts and observation of taking the ivermectin tablets and application of permethrin cream. The only group of people whereby treatment will not be directly observed is permethrin cream application on pregnant women, breastfeeding women with infants under 1 week of age and adults on warfarin.

6.2.6 Excluded medications and treatments

Ivermectin will be replaced by topical permethrin cream in the following groups:

- Children less than 90cm in height
- Pregnant women or women who think they may be pregnant
- Mothers nursing infants during the first week of life (15)
- Individuals taking warfarin(16)
- Very ill- too unwell to perform activities of daily living

7 RANDOMISATION AND BLINDING

7.1 Concealment mechanism

Not applicable.

7.2 Breaking of the Study Blind

Not applicable

8 STUDY VISITS AND PROCEDURES

8.1 Surveillance

8.1.1 Surveillance of primary outcome measures

During the surveillance periods of the study, two study nurses will perform daily visits to the wards of Labasa Hospital to review admissions and record cases that meet criteria for the conditions included in the study namely: severe skin and soft tissue infection (excluding diabetic foot ulcers), invasive infections from *Streptococcus pyogenes* and *Staphylococcus aureus* (including bone and joint infections), bacteraemia, post streptococcal glomerulonephritis and rheumatic fever. Information will be recorded by these nurses into the study database created for this study with case definitions for invasive group A streptococci and *S. aureus* infections, post streptococcal glomerulonephritis developed by A. Steer and A. Jenney.(17, 18) Criteria for rheumatic fever and rheumatic heart disease will be adopted from the Fiji Guidelines for acute rheumatic fever and rheumatic heart disease (see appendix 11). Once identified, informed and written consent will be sought from these patients to be included in this study. The study nurses will also review laboratory results daily as an added layer of surveillance for detection of cases to be included in the study. The Labasa Hospital laboratory processes all microbiological specimens from the Northern Division. Positive cultures for group A, C and G streptococci will be stored for analysis to review subtype prevalence for the purposes of the study with informed and written consent of the patient.

Routinely collected data regarding the number of admissions during the pre and post surveillance period for the conditions included in our primary outcome measures will be collected from the other two divisional hospitals of Fiji (Colonial War Memorial Hospital and Lautoka Hospital). This will be to determine if there are background variations in incidence during the period of surveillance that are unrelated to the intervention.

8.1.2 Surveillance of scabies and impetigo

Data on prevalence of scabies and impetigo pre and post intervention will be collected from community-based skin examinations at randomly selected villages at baseline and 12 months post intervention. At each time point, the sampling units will be randomly selected from the stratified population groups in the Northern Division. Participants from a subset of the sampling units will be offered quality of life questionnaires as part of the health economic evaluation of the intervention. The sampling units in which this is undertaken will be preserved for the 12 months post intervention surveys with new communities selected otherwise. These population groups are the urban and rural populations of the four subdivisions. One sampling unit will be selected per 5000-7500 people which amounts to 16-26 sampling units for the Northern Division. Communities with a population size within a range of 50-400 will be randomly selected as sampling units within these groups using probability proportional to size. This sample size will have at least 80% power to detect a 50% change in the prevalence of scabies and impetigo between baseline and at 12 months post intervention.

Residents of selected villages and settlements will be invited to participate through our public awareness campaign. After informed consent, participants will be asked to provide basic socio-demographic information such as age, sex, ethnicity, number of household members, education level, income and employment and a brief medical history including comorbidities. Participants' skin will be examined by expert examiners, following procedures used in the SHIFT trial. The examiners recruited will be required to pass a standardised assessment of their diagnostic skills before commencing examination of participants in study villages. A senior expert will supervise initial period of examination to ensure high quality diagnostic standards.

The diagnostic criteria from the consensus guideline of the International Alliance for the Control of Scabies will be used as the reference for clinical examination and diagnosis of scabies and impetigo.

(19) Scabies will be defined without the use of microscopy or dermatoscopy, but rather based on typical clinical findings, that is, pruritic inflammatory papules in a typical distribution. Impetigo is defined as papular, pustular or ulcerative lesions surrounded by erythema, with or without crusts, pus or bullae.

Routinely collected data on clinic presentations and treatments for scabies and bacterial skin infection at primary health care clinics (nursing stations, health centres and emergency departments at the 4 subdivisional hospitals) will be obtained. This will be through the submission of monthly reporting forms submitted through routine reporting mechanisms. Data from IMCI health presentations and school health visits in regard to skin disease will be collected through the extracting entries from the Public Health Information System.

8.2 Assessments during mass drug administration

8.2.1 Assessment of contraindications to ivermectin including pregnancy and contraindications to permethrin

All participants will be screened for contraindications for ivermectin. Participants will be asked whether they are pregnant, breastfeeding an infant under 7 days of age or taking warfarin. If a participant is pregnant or may be pregnant, breastfeeding an infant aged less than one week or taking warfarin, topical permethrin cream will be offered instead of oral ivermectin. Based on the recommendation of Fijian colleagues during SHIFT, drug administration will be offered to occur in a private area, so that the pregnancy status of participating females will not become known to others.

8.2.2 Measurement of height

During MDA participants will have their height checked against a height stick. Readings will be used to guide dosage of ivermectin.

8.3 Reviewing health economics of mass drug administration

Data on direct medical costs of hospitalisations and outpatient clinic visits i.e. the number and type of diagnostic procedures performed, the quantity of drugs and supplies used, and the length of hospital stay will be extracted from medical records at the 4 subdivisional hospitals, health centres and nursing stations. Unit costs of clinic visits, hospital bed day, emergency room visits, medications and diagnostics will be obtained from national price lists, national pharmacy and clinic and hospital invoices, supplemented with estimates from the literature. The costs of administering MDA will be estimated considering unit price and number of doses of ivermectin and topical permethrin cream, training of MDA distributors, materials, supervision and logistic costs, and based on study protocols.

Quality of life will be measured in a subset of participants during the community-based skin examinations. Age appropriate versions of the Dermatology Life Quality Index (DLQI) and the Assessment of Quality of life (AQoL)-6D questionnaires will be made available in Fijian and Hindi and will be administered by the study team. Members of the community who satisfy the case definition for scabies infection during the sentinel site exams will be consented and supplied with age appropriate disease-specific (DLQI) and generic (AQoL) quality of life questionnaires (Table 2). Given the high prevalence of other underlying skin conditions in the population, each individual with scabies that is surveyed will be age-matched with 2 types of controls: an individual without scabies or any other type of skin condition; an individual without scabies but with another skin condition. All controls (12 years and over) will be asked to complete the age-appropriate generic quality of life questionnaire (AQoL), and controls with other skin conditions will also be asked to complete the age-appropriate disease-specific quality of life questionnaire (DLQI) (Figure 2). Copies of the questionnaires are in Appendices 23-27. The estimated sample size will be 600-900 people including controls.

Age range	DLQI version	AQoL-6D version
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0-4 years	ISQOL- modified	N/A
4-12 years	CDLQI	N/A
12-15 years	CDLQI	AQoL-6D_Adolescent
15-18 years	DLQI	AQoL-6D_Adolescent
>18 years	DLQI	AQoL-6D

Table 2. Survey versions for various age ranges

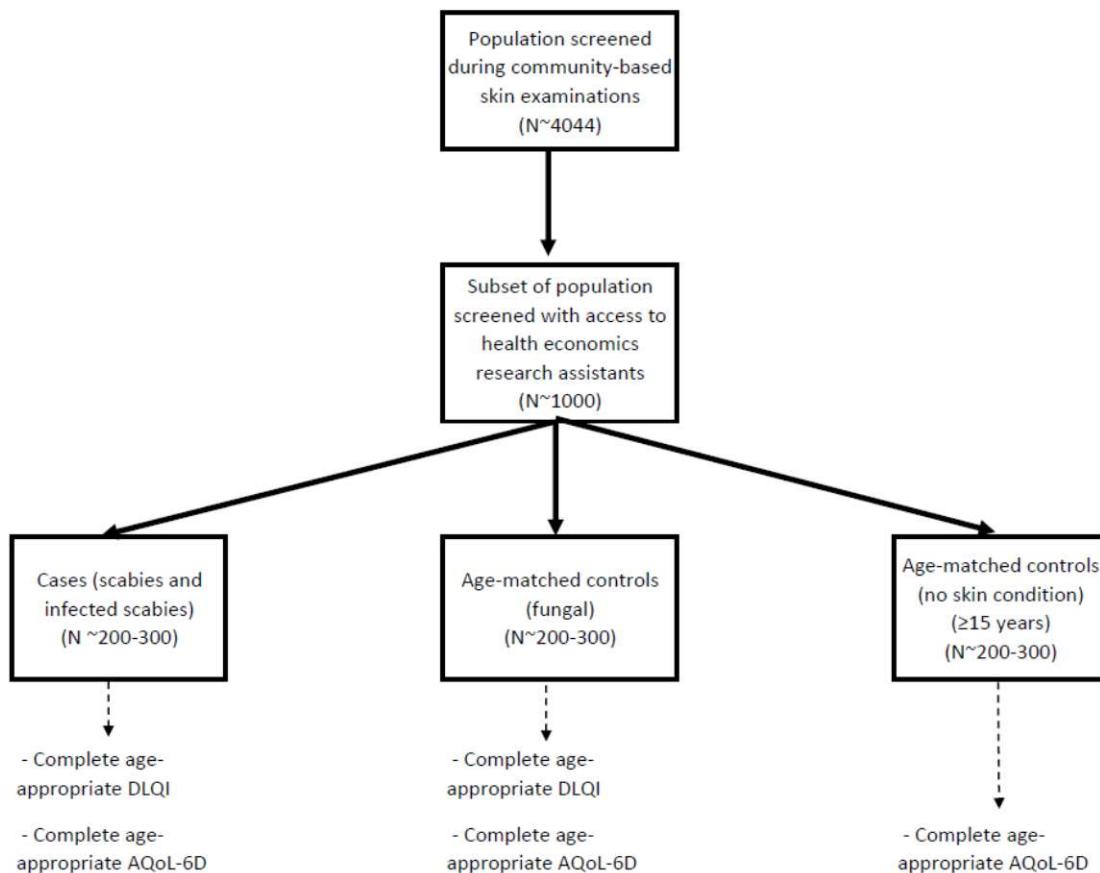


Figure 2. Sampling for health economics questionnaires

8.4 Assessing acceptability

Semi-structured interviews will explore the sociocultural beliefs and behaviours that sustain and enhance the transmission of LF, scabies and impetigo and assess the acceptability of MDA for LF, scabies and impetigo control in Fiji. The duration of each interview will take between 1 to 1.5 hours. The participants will represent two different groups:

- Community members: Individual or paired interviews will be conducted with up to 24 community members across 6 locations (settlements or villages) – aged 18 years or over (see Appendix 19 for discussion guide).

- Key informants: Individual interviews will be undertaken with 10 key informants working in the health sector (e.g. clinical staff, health service managers and policy makers) in Fiji (see Appendix 20 for discussion guide).

8.5 Study timeline

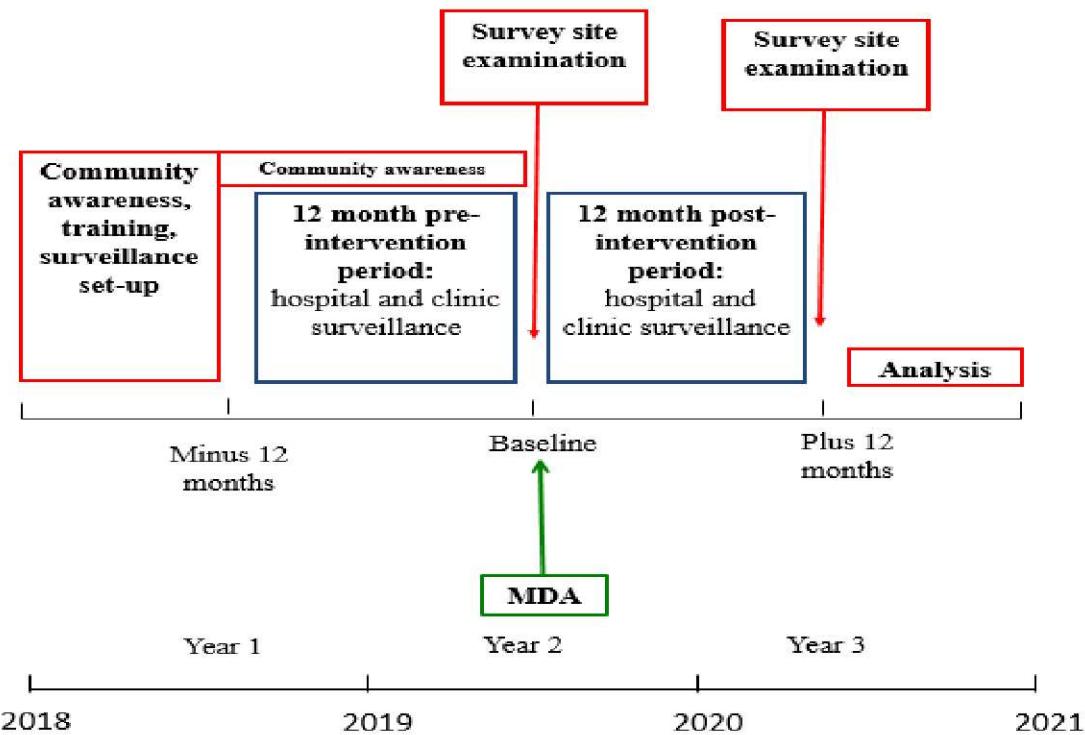


Figure 3. Study timeline

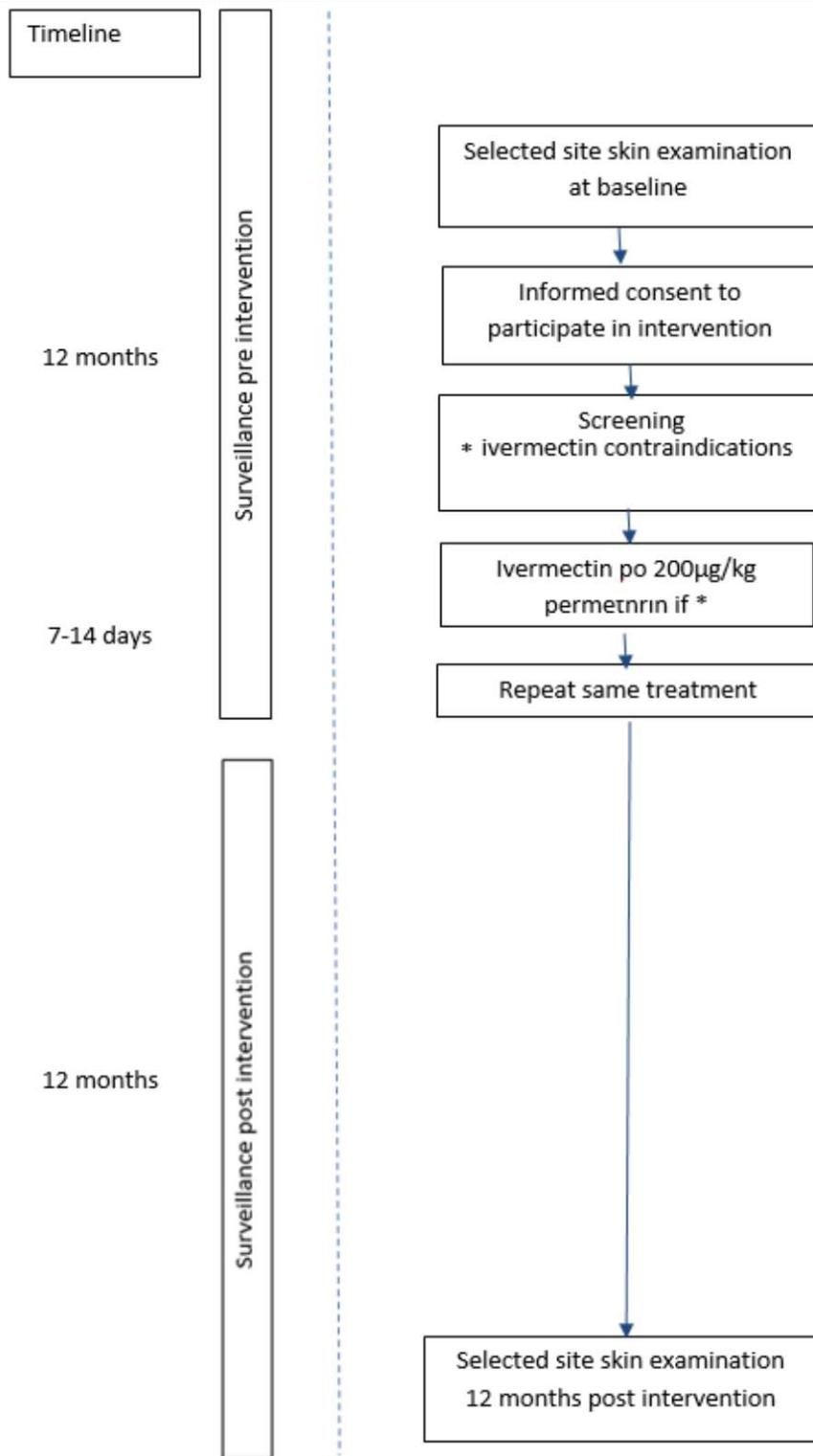


Figure 4. Study design and treatment flowchart from baseline to 36 months

*Standard ivermectin contraindications for mass drug administration are: pregnancy (known or suspected), women who are breastfeeding infants under one week of age, children less than 90cm in height and individuals receiving warfarin therapy.

Schedule of assessments

Study period	Pre MDA (months 1-12)	MDA		
Visit number	Visit 1 Skin examinations and quality of life surveys	Visit 2 Dose 1	Visit 3 Dose 2	Visit 4 Skin examinations and quality of life surveys
Timing	Month 11	Month 12	Month 12	Month 23
Admissions with SSTI				
Admissions with rheumatic fever	●			●
Admissions with PSGN	●			●
Admissions with invasive GAS and Staphylococcus aureus infections	●			●
Presentations with scabies	●			●
Presentations with impetigo	●			●
Informed consent	X* X**	X	X	X*
Examination for scabies and impetigo	X*			X*
Quality of life survey	X			X
Demographic information		X	X	
Height measurement		X	X	
Contraindication check		X	X	
Study drug administration		X	X	

* Only in selected villages, approximately 3,000 to 5,000 people (2.6 % randomly selected sample)

** Only in randomly selected adults in selected villages, approximately 300 people (5% of adults in the selected villages)

8.6 Screening

Individuals who have informed consent to receive the intervention will be screened for any contraindications for ivermectin by the MDA distributors. Their height, pregnancy status, breastfeeding status and if they are taking warfarin will be reviewed and if any criteria are met to be excluded from ivermectin administration, permethrin treatment will be administered instead.

8.7 Baseline

Information that will be collected from consenting individuals for MDA will be: demographic data, height, pregnancy status and whether they are taking warfarin.

8.8 Visits

The first study visit will be for surveillance purposes to collect data on baseline prevalence of scabies and impetigo in 16-26 randomly selected communities of population size between 50-400 people. For individuals who have given informed consent, demographic data will be collected, and skin examinations will be conducted. These visits will take place 1-2 months prior to the intervention. Quality of life questionnaires will take place during this visit. The participants being individuals who have been randomly selected and have given informed, written consent. Semi-structured interviews with community members and key informants will also take place during this time.

The second and third visits will be for the purposes of mass drug administration. These will be to the whole Northern Division of Fiji. During these visits, individuals who provide informed consent will be offered 2 doses of ivermectin (or permethrin if ivermectin is contraindicated) 8-14 days apart. This will take place over a 6-week period. Due to the limitations in staffing and resources, a mop up period will not be feasible.

The forth visit will happen 12 months post the MDA. This will be to collect data on prevalence of scabies and impetigo as well as to repeat the quality of life surveys post intervention in 16-26 villages selected using the same random sampling method as those at baseline. The same procedures will apply to those followed during the pre-intervention period.

8.9 Final study visit

Not applicable

8.10 Withdrawal visit

Only 2 doses of ivermectin or permethrin are involved in this study, administered 7-14 days apart. Should a participant who has given consent previously chooses to withdraw prior to receiving the second dose, they will no longer be offered the second dose of MDA.

8.11 Unscheduled visit

Not applicable

8.12 Participant Withdrawal

8.12.1 Reasons for withdrawal

Study participation is voluntary and study participants can withdraw at any time. The number of withdrawals will be recorded and only data collected prior to withdrawal will be included in the analysis. Reason for non-participation will be recorded for review of feasibility of the intervention.

8.12.2 Handling of withdrawals and losses to follow-up

Only data collected prior to withdrawal or loss to follow-up will be included in the analysis.

8.12.3 Replacements

Not applicable.

8.13 Halting MDA

The trial is planned to run over a total period of 36 months with a 24-month period of data collection for surveillance (pre and post intervention) and MDA scheduled after a preceding 12 months of surveillance. The 6-month period prior to the commencement of surveillance will be used to set up data collection systems for surveillance, train staff and commence a public awareness program for the project. The 6-month period post surveillance will be used for data analysis. Monitoring for safety will incorporate the safety of IDA therapy.

In addition to effectiveness data, data relating to all deaths, unexplained deaths and stillbirths in the year following the MDA will be collected and compared to the preceding 5 years. Data from hospital

records for emergency presentation in the week following MDA will be collected and compared to the preceding week. All serious adverse events that occur within 24 hours of the MDA will be reported to the Principal Research Coordinator by local health staff. These reports will be assessed and reviewed by the Principal Research Coordinator for any causal relationship of the adverse event to the MDA. If there is a cluster of serious adverse events that occurs 24 hours following MDA, this will be reported to the Principal Investigator and Independent Safety Committee for further review of safety data.

It should be noted that in this study only 2 doses of the ivermectin/permethrin will be administered 7-14 days apart. Because there will be no ongoing delivery of drugs beyond this, stopping and terminating rules are applicable over the period of MDA.

The circumstances under which the MDA can be halted prematurely are:

- There is a life threatening or fatal serious adverse event (SAE) which is, in the view of the Principal Investigator or the Independent Safety Committee (ISC), attributable to the intervention
- There is an unusual cluster of SAE's that, in the view of the Principal Investigator or the ISC, attributable to the treatment
- Evidence emerges from another study that indicate either of the regimens being investigated in the study are unsafe

8.14 Continuation of therapy

Not applicable.

9 OUTCOMES

9.1 Primary outcome

The co-primary outcome measures are:

1. The number of patients (all ages) with SSTI requiring hospital admission in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)
2. The number of cases of other severe bacterial complications (invasive disease caused by *Streptococcus pyogenes* and *Staphylococcus aureus*, glomerulonephritis and rheumatic fever in children <15 years) presenting to hospitals in the post-intervention period (12 months after MDA) compared to the pre- intervention period (12 months prior)

9.2 Secondary outcome(s)

The secondary outcome measures are:

1. Prevalence of scabies and impetigo in survey sites at 12 months compared to baseline
2. The number of presentations with scabies and impetigo to primary health care clinics by age group in the 12 months after MDA compared to the 12 months prior
3. The number of cases of other severe bacterial complications (invasive disease caused by *Streptococcus pyogenes* and *Staphylococcus aureus*, glomerulonephritis and rheumatic fever in all age groups presenting to hospitals in the post-intervention period (12 months after MDA) compared to the pre-intervention period (12 months prior)
4. Counts of all deaths, unexplained deaths and stillbirths in the year following MDA compared to 5 years prior, and number of emergency presentations to hospital in the week after MDA
5. Population coverage of the programme

6. Acceptability and feasibility of the programme
7. Incremental cost-effectiveness ratios (cost per quality-adjusted life year gained) and budget impact (measured in financial streams of cost over a budget cycle) of MDA compared to standard care.

10 ADVERSE EVENTS AND RISKS

10.1 Definitions

Adverse Event (AE): Any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment. (20)

Serious Adverse Event (SAE)

Adverse events are classified as serious or non-serious

A SAE is defined as any AE that:

- results in death; or
- is immediately life threatening; or
- causes or prolongs hospital admission; or
- results in persistent or significant disability, incapacity; or
- results in misuse or dependence (20)
- is a congenital anomaly/ birth defect

Cluster

A cluster is two or more cases of the same or similar event related in time, geography, and/or medicine administered. (20)

10.2 Assessment and documentation of adverse events

Assessment of adverse events will be performed according to the Common Terminology Criteria for Adverse Events (CTCAE v4.0)(21)

Adverse events will be graded according to severity

- Grade 1: Mild
- Grade 2: Moderate
- Grade 3: Severe – requiring medical care or hospitalisation
- Grade 4: Life-threatening or disabling
- Grade 5: Death

Adverse events will be assessed for the likely relationship to treatment

- Not related to treatment
- Unlikely to be related to treatment
- Possibly related to treatment
- Probably related to treatment
- Definitely related to treatment

10.3 Eliciting adverse event information

Doctors and nurse working in the local healthcare facilities will be briefed in the period preceding MDA to report all SAEs that occur within 24 hours of MDA contemporaneously to the Principal Research Coordinator who will record the details of the event. These notifications will also serve to alert the study coordinator to a cluster of SAEs occurring in the 24-hour period post MDA. Should a cluster be identified, the Principal Research Coordinator will report within 24 hours to the Principal Investigator and trial Steering Committee to review safety data. A report will be prepared for the Independent Safety Committee and if there are upcoming sites for ivermectin MDA within the project, a decision about whether to proceed, delay or halt MDA will be made by the Independent Safety Committee.

Doctors and nurses working in local healthcare facilities will be briefed in the period preceding MDA to notify the Principal Research Coordinator if made aware of participants who are pregnant and have been found to have been inadvertently given administered IDA during the MDA. As part of safety monitoring, the outcomes of the pregnancy will be followed up by the Principal Research Coordinator and a report generated to submit to the Independent Safety Committee. The Principal Research Coordinator or local study coordinator will liaise with local health staff to aid in providing support for these individuals.

Data regarding counts of all deaths, unexplained deaths and stillbirths in the year following MDA compared to 5 years prior, and number of emergency presentations to hospital in the week after MDA will be collected retrospectively sourcing from routinely collected data.

11 DATA MANAGEMENT

11.1 Data Collection

Case report forms will be checked for completeness and accuracy by the study coordinator against the source data. Original case report forms will be used when entering information into the computer database. The database will be checked against the case report forms for accuracy. No investigation of the data will begin until an accurate database has been assured.

11.1.1 Source Data

Source data will be collected from a variety of sources outlined below:

Information regarding hospital or health centre admissions for SSTIs, bacteraemia, invasive infections from group A streptococci and *Staphylococcus aureus* in Labasa hospital will be gathered via active surveillance methods. Relevant cases will be highlighted through liaison between clinical and laboratory staff and the employed study nurses. Information pertaining to patient demographics, reason for admission, past medical history and site of infection will be gathered through review of clinical and laboratory records.

Positive cultures for group A streptococci and *Staphylococcus aureus* from blood and invasive fluid specimens that had been collected clinically will be recorded by the study nurses. If the sample was obtained from an inpatient at the Labasa Hospital this will be cross checked with cases found on the wards and if found to be a new case, the patient will be approached for consent to be included in the study. No sample will be kept for the purposes of the study if informed consent is not obtained to do so. Their admission and diagnosis this will be recorded for the purposes of the study, but no further medical information will be actively sought. Information regarding cases presenting to the other subdivisional hospitals and health centres will be gathered through the Patient Information System (PATIS) or PHIS which is fed through monthly nursing reports that are already routinely collected. This information will be entered in to the study database with each case assigned a case number for the purposes of maintaining confidentiality.

In order to account for changes in incidence that are independent of MDA, routinely collected data of admissions during the pre and post MDA periods of surveillance will be collected from the other 2 divisional hospitals in Fiji (Colonial War Memorial Hospital and Lautoka Hospital). The conditions for which the admission data will be sought will be for skin and soft tissue infections, invasive infections (from *Staphylococcus aureus*, group A, C and G streptococcus) and post infectious complications from group A streptococcus identified through ICD-10 coding. Overall admission numbers at Labasa Hospital will also be collected to determine if monthly fluctuations of admissions for the primary and secondary outcome measures are reflective of general hospital attendance.

Information in regards to presentations with scabies and bacterial skin infection to nursing stations, health centres and outpatient departments will be obtained through monthly reporting forms submitted through established reporting mechanisms. Routinely collected data from the Public Health

Information system regarding IMCI presentations for scabies and bacterial skin infection during the pre and post MDA periods of surveillance will be collected as a measure of reliability for the study's monthly reporting system.

Information on prevalence of scabies and impetigo will be collected through clinical documentation during site examinations at the 30 selected villages. Documentation will initially be on a paper form but will be collated and subsequently entered into the study database.

Information on **sociocultural beliefs and behaviours that sustain and enhance the transmission of LF, scabies and impetigo** and acceptability of the study will be during semi-structured interviews by an independent interviewer with clinical staff, community members including MDA distributors, health service managers at all levels of the Ministry of Health and relevant non-governmental organisations such as the WHO regional office.

11.1.2 Data Capture Methods

Data collected by the study nurses in regard to hospital admissions for the studied conditions will be entered directly into the study database by them. The study database will be password protected, only accessible to the research staff, principal investigator and study statistician. Paper forms will be transported and stored securely only accessible to research staff and investigators.

Responses from the paper record for the quality of life surveys will be transferred into an electronic excel spreadsheet with identifying information kept in a separate database to the survey responses.

11.2 Data Storage

Data collected about the patients and surveyed individuals will be coded and re-identifiable and held in strict confidence. All results will be presented in a way which does not allow individuals to be identified. No information concerning the study of the data will be released to any unauthorised third party.

Storage and access will be through a password-protected database, held at the Murdoch Children's Research Institute. Data will be entered into the study database with restricted access to the study coordinator, principal investigator and the study statistician. The paper data forms will be kept in a locked room. Only the investigators and the study staff will have access to the raw data during and after the study.

11.3 Record Retention

The paper data forms will be kept in a locked room in a locked and secure filing system at our office in Labasa, Fiji. Both paper consent forms from hospital surveillance and data forms from quality of life surveys will be kept for the duration of the study, then destroyed through shredding. Raw electronic data will be stored at the Murdoch Children's Research Institute under password-protection in the study database. All extracted electronic data will be kept in a password protected database. Only the Principal Investigator, study statistician and Principal Research Coordinator will have access to the raw data during and after the study. For participants over the age of 18 during the trial, data will be destroyed or deleted after 15 years, for participants under 18 years of age during the trial, data will be kept for 25 years according to the National Health and Medical Research Council and in accordance with Fiji data storage policy.

For the acceptability component, signed consent forms and hard-copy de-identified interview data will be stored separately in a locked filing cabinet and electronic data will be stored on a password-protected computer. Data will only be accessible to staff employed in the project and study investigators. Data will be destroyed 7 years after the completion of the project.

If data is published, only aggregate results will be analysed. Reports and publications will not disclose the identity of participants.

12 STUDY OVERSIGHT

12.1 Governance structure

The study has been endorsed by the Fijian Ministry of Health through discussion at the Deputy Secretary Health Services Meeting in Fiji on 16th February 2017 during which the project was met with unanimous committee support and consensus for the proposed project to be adopted in the Northern Division. The project has also been approved by the Fijian Interim Leadership Team (ILT) on 7th November 2017. Ethics approval will be sought from the Fiji Research Ethics Committee and the Royal Children's Hospital (RCH) Human Research Ethics Committee who will review all study protocols. The study will be overseen by the trial investigators with representation from national and divisional local health authorities.

Once all ethics approvals are in place, the first year of pre-intervention observation will commence. Informed consent will be sought from the inpatients at Labasa Hospital if they have been identified through active case finding as a suitable case for inclusion in the study during active surveillance at Labasa hospital. Informed consent will also be sought from inpatients at Labasa Hospital if their positive pathology samples are collected and stored for analysis for the purposes of the study. On the lead up to the intervention, a comprehensive program of information dissemination will be established in consultation with local leaders, zone nurses and village health workers to ensure that community members are informed and have the opportunity to raise any issues of concern. This will be done in various ways including meetings lead by subdivisional medical officers liaising with community leaders through routine provincial meetings, distribution of written material, social media and radio segments.

Informed consent will be required to participate in the intervention phase. In the case of an individual lacking the capacity to give informed consent to participate, consent will be sought from their legal guardians or next of kin.

An Independent Safety Committee will be assembled to meet as required in the 12-month period following MDA. This committee will comprise of Fijian and Australian medical academics with expertise in relevant clinical and biostatistics fields.

A national team will comprise of the Fijian Acting Head of Health Protection, the Fijian Neglected Tropical Disease Officer, National LF Coordinator, Divisional Medical Officer the Principal Investigator and the local and principal study coordinators will be in charge of overseeing and guiding operations and reviewing processes as necessary.

Community stakeholders refers to provincial authorities, village chiefs, religious leaders, educational authorities, local clinical staff and community workers. They will be responsible for gauging and providing feedback in regards to community acceptability around the concept and operations of the project.

12.2 Independent Safety Committee

An independent Safety Committee will be established to oversee the safety and progress the trial.

12.3 Quality Control and Quality Assurance

The Principal Research Coordinator and local study coordinator will be responsible for overseeing and checking completeness and accuracy of data collection. Initial training of study nurses and community workers at skin inspection sites will be undertaken prior to commencement of the study. Review of accuracy of data collection will be undertaken by the study coordinators through routine crosschecks between clinical documents and entered data. Incomplete forms will be reviewed and further training to relevant staff responsible for data collection will be provided as required.

13 STATISTICAL METHODS

13.1 Sample Size Estimation

Primary endpoints: Based on information collected from the routine hospital reporting system at Labasa Hospital over the last 2 years, we anticipate that there will be 410 cases of hospitalisation for severe SSTI and 172 cases of the combined endpoint of invasive bacterial disease, rheumatic fever and glomerulonephritis in children < 15 years during the pre-intervention period, or annual rates of 293 and 123 per 100 000 respectively. We will have 90% power to detect a 50% reduction in the annual incidence of admissions of patients with severe SSTI from 293 to 147 per 100,000. We will have 80% power to detect a 40% reduction (from 123 to 74 cases per 100,000) in the combined endpoint of admissions in children aged less than 15 years with any of invasive bacterial disease, rheumatic fever or glomerulonephritis. Secondary endpoints: To achieve 90% power to detect a 50% reduction in scabies or impetigo prevalence, from 20% to 10%, or 30% to 15% after ivermectin-based MDA, we will need to examine approximately 3,000 to 5,000 people from 16-26 communities randomly selected from clusters based on the urban and rural populations of the four subdivisions of the Northern Division. This sample size will be sufficient to detect 50% reduction with at least 80% power in scabies/impetigo prevalence (i.e. from 30% to 15% and 20% to 10%) with an interclass correlation coefficient of 0.01/0.02.

13.2 Statistical Analysis Plan

13.2.1 Population to be analysed

The study population will be all individuals residing in the Northern Division of Fiji at month 0-24 of the study. Surveillance for SSTIs, bacteraemia, invasive bacterial infections, RF and PSGN will be performed on the entire population based on healthcare presentations to facilities in the Northern Division. Surveillance for scabies and impetigo will be carried out on consenting individuals from the villages and urban communities that will be randomly selected for this study. Intervention will be offered to all consenting individuals living in the Northern Division of Fiji.

13.2.2 Methods of analysis

Statistical analysis will be conducted using STATA software.

Co-primary outcome measures: We will calculate annual incidence rates of both primary endpoints (all ages) admissions with severe SSTI, and the combined endpoint of admissions with any of rheumatic fever, glomerulonephritis or invasive infection (in children aged less than 15 years). Data will be weighted to account for the stratified 2 stage cluster sampling design of the study. After this adjustment, incidence rates will be calculated separately for the 12 month pre- and post-intervention periods using census data for the Northern Division as the denominator. We will use Poisson models to assess the impact of MDA by calculating overall, age-specific and ethnicity-specific incidence rate ratios and 95% confidence intervals to compare the pre and post periods. Data will be analysed according to the statistical methods described in Hayes and Moulton (2009)(22) cluster level summaries will be calculated for all primary and secondary outcomes of interest.

Secondary outcome measures:

1. The prevalence of scabies and impetigo at survey sites will be calculated at 12 months after MDA and compared to the corresponding calculation at baseline. To obtain confidence intervals and test for significance ($\alpha=0.05$), we will use generalised estimating equations accounting for 2-level clustering within subdivisions and urban/rural settlements with Probability Proportional to Size applied to the first stage.

2. We will record and report deaths and emergency hospital admissions in the week following MDA and compare to average counts at corresponding time periods in other years.
3. We will use Poisson models to compare the number of presentations to primary care with scabies and impetigo in the pre- and post-intervention periods. Incidence rate ratios (post vs. pre) and 95% confidence intervals will be calculated. In addition, we will compare the quarterly point prevalence of scabies and impetigo in children aged < 1 year before and after MDA.
4. Population coverage (single dose and both doses) and feasibility of the programme will be measured by doses distributed to individuals divided by total population.
5. Responses from the qualitative interviews will be transcribed and analysed thematically and triangulated with quantitative results to contextualize them.
6. The cost effectiveness of ivermectin-based MDA compared to standard care will be assessed from the Fijian health care provider perspective by modelling direct medical costs and health outcomes associated with the intervention and standard care. A Markov decision tree model will be built using the software TreeAge, using a one-year time horizon in the base case analysis, with 5- and 10-year time horizons explored in scenario analyses to assess the longer-term impact of the intervention. Direct medical costs will be estimated from number of presentations to primary care, hospitalisations, number and type of diagnostic procedures performed, quantity and type of drugs and supplies used, and length of hospitalisation. Unit costs will be obtained from national price lists, hospital invoices, and published literature. Additional scenario analyses will be carried out to evaluate the impact of different prices of ivermectin, and number of MDA cycles needed over the long term. Results will be presented as costs per case (of scabies & impetigo) averted, cost per disability-adjusted life year (DALY) averted, and cost per quality-adjusted life year (QALY) gained. One-way, multivariable and probabilistic sensitivity analyses will be conducted to assess the impact of key parameters and assumptions on the results. Standard reporting procedures will be followed based on the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Guidelines. (23)

13.3 Interim Analyses

Due to the design of this study being a before-after trial, interim analysis is not applicable.

14 ETHICS AND DISSEMINATION

14.1 Research Ethics Approval

This protocol and the informed consent document and any subsequent modifications will be reviewed and approved by the human research ethics committee (HREC). A letter of protocol approval by HREC will be obtained prior to the commencement of the study, as well as approval for other study documents participant to HREC review. This protocol will be considered by the RCH HREC and the Fiji National Research Ethics Review Committee

14.2 Modifications to the protocol

Should modifications from the original protocol be required approval will be sought for amendments to the protocol and these will be described in the final reports. Protocol modifications will be reported to study investigators in accordance with standard GCP processes.

14.3 Protocol Deviations

Deviation from the original protocol is not anticipated, however, if this does occur approval will be sought for amendments to the protocol and this will be described in the final reports. Protocol modifications will be reported to study investigators in accordance with standard GCP processes.

14.4 Confidentiality

Subject confidentiality is strictly held in trust by the participating investigators, research staff, and the sponsoring institution and their agents. This confidentiality is extended to cover testing of biological samples and the clinical information relating to participating participants. The study protocol, documentation, data and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorised third party, without prior written approval of the sponsoring institution. Authorised representatives of the sponsoring institution may inspect all documents and records required to be maintained by the Investigator, including but not limited to, medical records (office, clinic or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records. All laboratory specimens, evaluation forms, reports and other records that leave the site will be identified only by the Participant Identification Number (PID) to maintain participant confidentiality. Clinical information will not be released without written permission of the participant, except as necessary for monitoring by HREC or regulatory agencies.

14.5 Participant Reimbursement

Not applicable

14.6 Financial Disclosure and Conflicts of Interest

There are no relevant financial or other conflict of interest to be disclosed

14.7 Dissemination and translation plan

Results of this trial will be made available via publication. Individual data will not be made public, but re-identifiable data may be made available for further analysis. Results of the study will be presented locally (including to the community) and made available to health policy decision makers and clinical staff.

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16 LIST OF APPENDICES

- APPENDIX 1: Participant information sheet and consent form for hospital surveillance (child)
- APPENDIX 2: Participant information sheet and consent form for hospital surveillance (adult)
- APPENDIX 3: Participant information sheet and consent form for storage of biological specimens (child)
- APPENDIX 4: Participant information sheet and consent form for storage of biological specimens (adult)
- APPENDIX 5: Participant information sheet and consent form for village skin examination (child)
- APPENDIX 6: Participant information sheet and consent form for village skin examination (adult)
- APPENDIX 7: Information sheet and informed consent for quality of life community survey
- APPENDIX 8: Iver P® (ivermectin tablet) product information leaflet
- APPENDIX 9: Mectizan® (ivermectin tablet) product information
- APPENDIX 10: Lyclear® (permethrin cream) product information leaflet
- APPENDIX 11: Diagnostic Criteria for Acute Rheumatic Fever from Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention
- APPENDIX 12: Definitions of rheumatic heart disease from Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention
- APPENDIX 13: Case definitions for invasive group A streptococcal disease and Staphylococcus aureus disease
- APPENDIX 14: Child information sheet and consent form for village skin examination
- APPENDIX 15: Child Information Sheet and consent Form: Hospital Surveillance
- APPENDIX 16: Child Information Sheet and Assent Form: Storage of Biological Specimens
- APPENDIX 17: Ministry of Health consent form for school distribution
- APPENDIX 18: Information Sheet for MDA
- APPENDIX 19: Interview Guide for Community Member
- APPENDIX 20: Interview Guide for Key Informant
- APPENDIX 21: Participant information sheet for in-depth interviews: community member
- APPENDIX 22 Participant information sheet for in-depth interviews: key informant
- APPENDIX 23: Dermatology Life Quality Index (DLQI) questionnaire
- APPENDIX 24: Children's Dermatology Quality of Life Index (CDLQI) questionnaire
- APPENDIX 25: Assessment of Quality of Life 6-dimension (AQoL-6D) questionnaire
- APPENDIX 26: Adolescent AQoL-6D questionnaire
- APPENDIX 27: Infant's dermatitis quality of life index- modified for scabies

**APPENDIX 1: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR
HOSPITAL SURVEILLANCE (CHILD)**

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer, Murdoch Children's Research Institute

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

We are inviting your child to take part in the hospital surveillance arm of the Northern Division Scabies Control Project ('the project'). Through this project, we aim to find out if treating an entire community for scabies will reduce the serious bacterial complications associated with it.

Surveillance means we are observing how often a particular condition occurs. In this case we are doing this to find out how common it is for people to have certain illnesses before and after they have taken the drug for scabies.

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A Streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems.

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD. RHD is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

We want to find out if treating scabies in a community will reduce serious complications related to scabies. The medication used in this study is called ivermectin. Ivermectin is a medicine that kills parasites like the scabies mite. The Skin Health Intervention Fiji Trial was recently carried out to look at different ways to treat scabies. Its results showed that ivermectin was the most effective way to reduce scabies infections when given to everyone in a community. This project will offer ivermectin to everyone in the Northern Division in mid-2019 to treat scabies and compare the number of cases of:

- scabies,
- skin infections, and
- serious bacterial complications.

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia

Why we are inviting you to be included:

We would like to include your child in the project because your community has been selected to receive mass drug administration as part of this study. In addition, your child has been admitted with one of the conditions that we are monitoring. If you agree for your child to be included in this study, we will collect information about them such as:

- age
- gender
- ethnicity
- details of why they have been admitted

We will collect this information by talking with you directly and reviewing your child's case file. This information will help us to see if the number of cases of the condition you are admitted with have fallen after MDA for scabies.

The information from this study will be important in helping to wipe out scabies in Fiji. This will benefit all adults and children in Fiji.

Protecting privacy:

Any information we collect for this research project that can identify your child will be treated as confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your child's name and give the information a special code number. Only the research team can match your child's name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqomate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project
- an Australian Human Research Ethics Committee
- the Fiji National Research Ethics Review Committee, Fiji.

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about your child. Their information will be kept for up to 25 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your child's information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that your child cannot be identified. No information concerning the study or the data will be released to any unauthorised third party.

Your choice to participate:

Your child does not have to take part in this trial. If you say no, your child will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Thank you very much for your time.

Yours sincerely,



Dr. Li Jun Thean
Principal Research Coordinator of Northern Division Scabies Control Project
Murdoch Children's Research Institute

If you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact:

Chair, Fiji National Research Ethics Review Committee, Fiji, Telephone (+679) 3221 424

Consent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 2.0 **Version Date:** 28/05/2018

- I have read this information statement and I understand its contents.
- I understand what my child and I have to do to be involved in this project.
- I understand the risks my child could face because of their involvement in this project.
- I voluntarily consent for my child to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Parent/Guardian Name

Parent/Guardian Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

**APPENDIX 2: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR
HOSPITAL SURVEILLANCE (ADULT)**

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

We are inviting you to take part in the hospital surveillance arm of the Northern Division Scabies Control Project ('the project'). Through this project, we aim to find out if treating an entire community for scabies will reduce the serious bacterial complications associated with it.

Surveillance means we are observing how often a particular condition occurs. In this case we are doing this to find out how common it is for people to have certain illnesses before and after they have taken the drug for scabies.

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems.

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD. RHD is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

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- serious bacterial complications.

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia.

Why we are inviting you to be included:

We would like to include you in the project because your whole community has been selected to receive medication for scabies. In addition, you have been admitted with one of the conditions that we are monitoring. If you agree to be included in this study, we will collect information about you such as your:

- age
- gender
- ethnicity
- details of why you have been admitted

We will collect this information by talking with you directly and reviewing your case file. This information will help us to see if the number of cases of the condition you are admitted with have fallen after MDA for scabies.

The information from this study will be important in helping to wipe out scabies in Fiji. This will benefit all adults and children in Fiji.

Protecting privacy:

We will treat any information we collect for this research project that can identify you confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your name and give the information a special code number. Only the research team can match your name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqomate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project

- an Australian Human Research Ethics Committee
- the Fiji National Research Ethics Review Committee, Fiji

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about you. Your data will be kept for 15 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that you cannot be identified. No information concerning the study or the data will be released to any unauthorised third party.

Your choice to participate:

You do not have to take part in this trial. If you say no, you will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Thank you very much for your time.

Yours sincerely,



Dr. Li Jun Thean
Principal Study Coordinator of Northern Division Scabies Control Project
Murdoch Children's Research Institute

If you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact:

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- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Participant Name

Participant Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

**APPENDIX 3: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR
STORAGE OF BIOLOGICAL SPECIMENS (CHILD)**

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer, Murdoch Children's Research Institute

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

We are inviting your child to take part in an aspect of the hospital surveillance arm, of the Northern Division Scabies Control Project ('the project'). This involves allowing us to store some of the bacteria that has grown from some of their body fluid. We will send this bacteria for further testing. As part of this project we are interested in finding out more about this bacteria that has made them unwell.

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD which is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

We want to find out if treating scabies in a community will reduce serious complications related to scabies. The medication used in this study is called ivermectin. Ivermectin is a medicine

that kills parasites like the scabies mite. The Skin Health Intervention Fiji Trial was recently carried out to look at different ways to treat scabies. Its results showed that ivermectin was the most effective way to reduce scabies infections when given to everyone in a community. This project will offer ivermectin to everyone in the Northern Division in mid-2019 to treat scabies and compare the number of cases of:

- scabies,
- skin infections, and
- serious bacterial complications

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia

Why we are inviting your child to be included:

We would like to include your child in the project because your community has been selected to receive MDA as part of this study. In addition, a sample taken from your child by their doctor has grown group A streptococci or similar bacteria like group C or G streptococci.

As we mentioned, group A streptococcus causes serious complications linked with scabies. We are looking into this because these bacteria make many people very sick. We want to learn more about the bacteria that are common in your community.

What is involved:

We will collect a sample of the bacteria that has grown in the laboratory from the blood/bodily fluid that has been collected by your child's doctor or nurse. We will then send these bacteria to our laboratory at the Murdoch Children's Research Institute in Australia. There, we will perform a test called 'emm typing' which will give us very detailed information about the identity of the bacteria. The results of this test are not relevant to the direct care that you are receiving from the doctors looking after you but will potentially help future research to develop new ways to fight this bacteria such as developing a vaccine.

Protecting privacy:

We will treat any information we collect for this research project that can identify your child confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your name and give the information a special code number. Only the research team can match your name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqomate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project.
- an Australian Human Research Ethics Committee.
- the Fiji National Research Ethics Review Committee, Fiji

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about your child. Their information will be kept for up to 25 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your child's information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that your child cannot be identified. No information concerning the study or the data will be released to any unauthorised third party.

Your choice to participate:

Your child does not have to take part in this trial. If you say no, they will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Thank you very much for your time.

Yours sincerely,



Dr. Li Jun Thean
Principal Study Coordinator of Northern Division Scabies Control Project
Murdoch Children's Research Institute

If you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact:

Chair, Fiji National Research Ethics Review Committee, Fiji, Telephone (+679) 3221 424

Consent Form

HREC Project Number: **HREC 38020A**

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 2.0 **Version Date:** 28/05/2018

- I have read this information statement and I understand its contents.
- I understand what my child and I have to do to be involved in this project.
- I understand the risks my child could face because of their involvement in this project.
- I voluntarily consent for my child to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Parent/Guardian Name

Parent/Guardian Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

**APPENDIX 4: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR
STORAGE OF BIOLOGICAL SPECIMENS (ADULT)**

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer, Murdoch Children's Research Institute

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

We are inviting you to take part in an aspect of the hospital surveillance arm, of the Northern Division Scabies Control Project ('the project'). This involves allowing us to store some of the bacteria that has grown from some of your body fluid. We will send this bacteria for further testing. As part of this project we are interested in finding out more about this bacteria that has made you unwell.

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems.

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD which is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

We want to find out if treating scabies in a community will reduce serious complications related to scabies. The medication used in this study is called ivermectin. Ivermectin is a medicine that kills parasites like the scabies mite. The Skin Health Intervention Fiji Trial was recently carried out to look at different ways to treat scabies. Its results showed that ivermectin was the most effective way to reduce scabies infections when given to everyone in a community.

This project will offer ivermectin to everyone in the Northern Division in mid-2019 to treat scabies and compare the number of cases of:

- scabies,
- skin infections, and
- serious bacterial complications

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia

Why we are inviting you to be included:

We would like to include you in the project because your community has been selected to receive MDA as part of this study. In addition, a sample taken from you by your doctors has grown group A streptococci or similar bacteria like group C or G streptococci.

As we mentioned, group A streptococcus causes serious complications linked with scabies. We are looking into this because these bacteria make many people very sick. We want to learn more about the bacteria that are common in your community.

What is involved:

We will collect a sample of the bacteria that has grown in the laboratory from the blood/bodily fluid that has been collected by your doctor or nurse. We will then send these bacteria to our laboratory at the Murdoch Children's Research Institute in Australia. There, we will perform a test called 'emm typing' which will give us very detailed information about the identity of the bacteria. The results of this test are not relevant to the direct care that you are receiving from the doctors looking after you but will potentially help future research to develop new ways to fight this bacteria such as developing a vaccine.

Protecting privacy:

We will treat any information we collect for this research project that can identify you as confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your name and give the information a special code number. Only the research team can match your name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqomate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project
- an Australian Human Research Ethics Committee
- the Fiji National Research Ethics Review Committee, Fiji

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about you. Your data will be kept

for 15 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that you cannot be identified. No information concerning the study or the data will be released to any unauthorised third party.

Your choice to participate:

You do not have to take part in this trial. If you say no, you will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Thank you very much for your time.

Yours sincerely,



Dr. Li Jun Thean
Principal Study Coordinator of Northern Division Scabies Control Project
Murdoch Children's Research Institute

If you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact:

Chair, Fiji National Research Ethics Review Committee, Fiji, Telephone (+679) 3221 424

Consent Form

HREC Project Number: **HREC 38020A**

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 2.0 **Version Date:** 28/05/2018

- I have read this information statement and I understand its contents.
- I understand what I have to do to be involved in this project.
- I understand the risks I could face because of my involvement in this project.
- I voluntarily consent to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Participant Name

Participant Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

For phone consent only:

Name of Clinician Facilitating Call

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

**APPENDIX 5: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR
VILLAGE SKIN EXAMINATION (CHILD)**

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer, Murdoch Children's Research Institute

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

Would like to invite your child to take part in the skin examination arm of the Northern Division Scabies Control Project ('the project). As part of the project we want to compare how common scabies and impetigo are among your community before and after ivermectin ('the medication) for scabies is given to everyone through mass drug administration (MDA).

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A Streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD. RHD is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

We want to find out if treating scabies in a community will reduce serious complications related to scabies. The medication used in this study is called ivermectin. Ivermectin is a medicine that kills parasites like the scabies mite. The Skin Health Intervention Fiji Trial was recently carried out to look at different ways to treat scabies. Its results showed that ivermectin was the most effective way to reduce scabies infections when given to everyone in a community.

This project will offer ivermectin to everyone in the Northern Division in mid-2019 to treat scabies and compare the number of cases of:

- scabies,
- skin infections, and
- serious bacterial complications

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia

Why we are inviting your child to be take part:

We would like to include your child in the project because your community will be receiving drug administration for scabies as part of this study. In addition, they live in one of the villages that has been randomly selected as a site for skin examinations. We are doing these examinations to find out how common scabies and impetigo are in the Northern Division. We will use the information from these examinations to see how much the scabies treatment given to everyone reduced scabies and impetigo in your community.

What is involved:

With your consent, a trained nurse will examine your child's skin for scabies and impetigo. They will ask you to provide basic information such as your child's:

- age
- sex
- ethnicity
- number of household members
- education level
- a brief medical history

This information will help us know about scabies and impetigo in your community. If the nurse examining your child thinks that they have either of these conditions, they will refer your child to the local health centre for assessment and treatment. If they agree that they have scabies, you will be given permethrin cream as treatment.

Protecting privacy:

We will treat any information we collect for this research project that can identify your child will be treated as confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your child's name and give the information a special code number. Only the research team can match your child's name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqamate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project.

- an Australian Human Research Ethics Committee.
- the Fiji National Research Ethics Review Committee, Fiji

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about your child. Their information will be kept for up to 25 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your child's information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that your child cannot be identified. No information concerning the study or the data will be released to any unauthorized third party.

Your choice to participate:

You do not have to give consent for your child to take part in this trial. If you say no, you will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Yours sincerely,



Dr. Li Jun Thean
Principal Study Coordinator of Northern Division Scabies Control Project

Murdoch Children's Research InstituteIf you have any concerns and/or complaints about the project, the way it is being conducted or your child's rights as a research participant, and would like to speak to someone independent of the project, please contact:

Chair, Fiji National Research Ethics Review Committee, Fiji, Telephone (+679) 3221 424

Consent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 2.0 **Version Date:** 28/05/2018

- I have read this information statement and I understand its contents.
- I understand what my child and I have to do to be involved in this project.
- I understand the risks my child could face because of their involvement in this project.
- I voluntarily consent for my child to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Parent/Guardian Name

Parent/Guardian Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

APPENDIX 6: PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR

VILLAGE SKIN EXAMINATION (ADULT)

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Principal Researcher: Professor Andrew Steer, Murdoch Children's Research Institute

Version Number: 2.0 **Version Date:** 28/05/2018

Dear,

Would like to invite you to take part in the skin examination arm of the Northern Division Scabies Control Project ('the project). As part of the project we want to compare how common scabies and impetigo are among your community before and after ivermectin ('the medication) for scabies is given to everyone through mass drug administration.

Scabies:

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. About one in three people in the Northern Division are affected by scabies. Scabies causes an intense itch and broken skin. This can lead to a skin infection by bacteria if it is not treated properly. It can also lead to serious complications such as an infection in the blood and other body parts such as muscles, bones and joints.

A type of bacteria called group A Streptococci, commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease (RHD) and kidney disease. Someone with rheumatic fever may experience:

- fever
- joint pain
- rashes
- abnormal movements
- heart problems

People with rheumatic fever need many years of monthly injections with antibiotics in order to prevent RHD. RHD is permanent damage to the heart that often needs heart surgery. Through this project we want to find out if we are able to prevent some of these serious complications through scabies treatment.

What is this project about?

We want to find out if treating scabies in a community will reduce serious complications related to scabies. The medication used in this study is called ivermectin. Ivermectin is a medicine that kills parasites like the scabies mite. The Skin Health Intervention Fiji Trial was recently carried out to look at different ways to treat scabies. Its results showed that ivermectin was the most effective way to reduce scabies infections when given to everyone in a community. This project will offer ivermectin to everyone in the Northern Division in mid-2019 to treat scabies and compare the number of cases of:

- scabies,
- skin infections, and
- serious bacterial complications.

We will compare the number of cases over the 12 months before and 12 months after people have been given ivermectin.

Funding:

The project is funded by the National Health and Research Council of Australia

Why we are inviting you to be take part:

We would like to include you in the project because your community will be receiving mass drug administration for scabies as part of this study. In addition, you live in one of the villages that has been randomly selected as a site for skin examinations. We are doing these examinations to find out how common scabies and impetigo are in the Northern Division. We will use the information from these examinations to see how much the scabies treatment given to everyone reduced scabies and impetigo in your community

What is involved:

With your consent, a trained nurse will examine your skin for scabies and impetigo. They will ask you to provide basic information such as:

- age
- sex
- ethnicity
- number of household members
- education level
- income and
- employment
- a brief medical history

This information will help us know about scabies and impetigo in your community. If the nurse examining you thinks that you have either of these conditions, they will refer you to the local health centre for assessment and treatment. If they agree that you have scabies, you will be given permethrin cream as treatment.

Protecting privacy:

We will treat any information we collect for this research project that can identify you will be treated as confidential. We can disclose the information only with your permission, except as required by law. The information will be re-identifiable. This means that we will remove your name and give the information a special code number. Only the research team can match your name to the code number, if it is necessary to do so. The information will be entered in a password-protected computer database. Any paper data forms will be stored securely in a locked room at the Roqomate House in Labasa. The following people may access information collected as part of this research project:

- the research team involved with this project
- an Australian Human Research Ethics Committee

- the Fiji National Research Ethics Review Committee, Fiji

In accordance with Fijian National Health Research Policy 1999 and Health Information Policy 2011, as well as Australian and/or Victorian privacy and other relevant laws, you have the right to access and correct the information we collect and store about you. Your data will be kept for 15 years then destroyed in accordance with Fiji data storage policy. Please contact us if you would like to access your information.

When we write or talk about the results of this project, only group results will be analysed and information will be provided in such a way that you cannot be identified. No information concerning the study or the data will be released to any unauthorized third party.

Your choice to participate:

You do not have to take part in this trial. If you say no, you will still get the best possible care from the hospital. If you give consent and you change your mind you can do so at any time without telling us why. In that situation we will use any information already collected unless you tell us not to and we will not collect any additional information. Your decision will not affect any treatment or care they receive in the future

If you have any questions about the project, you can contact Dr. Li Jun Thean on +679 7412938. You can also email her at lijun.thean@mcri.edu.au.

Thank you very much for your time.

Yours sincerely,



Dr. Li Jun Thean
Principal Study Coordinator of Northern Division Scabies Control Project
Murdoch Children's Research Institute

If you have any concerns and/or complaints about the project, the way it is being conducted or your rights as a research participant, and would like to speak to someone independent of the project, please contact:

Chair, Fiji National Research Ethics Review Committee, Fiji, Telephone (+679) 3221 424

Consent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 2.0 **Version Date:** 28/05/2018

- I have read this information statement and I understand its contents.
- I understand what I have to do to be involved in this project.
- I understand the risks I could face because of my involvement in this project.
- I voluntarily consent to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Participant Name

Participant Signature

Date

Name of Witness to Participant's
Signature

Witness Signature

Date

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name

Research Team Member
Signature

Date

Note: All parties signing the Consent Form must date their own signature.

APPENDIX 7: INFORMATION SHEET AND INFORMED CONSENT FOR QUALITY OF

LIFE COMMUNITY SURVEY

(to be read to each respondent)

Good morning / afternoon, my name is _____. I am working with the Northern Division scabies project ('the project'). We would like to invite you to participate in a survey to find out what you think about your skin health. It is important that you understand why we are doing this survey. Please read this information sheet or listen carefully as I read it. If you have any more questions, please ask me, the surveyor and I will try to answer them for you.

Why we are inviting you to be included?

We would like to invite you to participate in this survey as your village has been selected at random from the list of villages in the Northern Division to participate in the skin examinations and this survey. We would like to find out about how your skin's health affects your day to day life. Having your opinion will be valuable to help us see if improving skin health makes a true difference to how people in Fiji study, work and have fun.

What is the purpose of the survey?

We are interested in what people in the Northern Division think about skin health in general and how it effects your life. As part of the Northern Division Scabies Control Project we are asking some people in the Northern Division to take part in a short survey. This is so we can find out more about how skin disease affects you.

How long will the survey take?

If you do choose to help with this study, we will need less than 10 minutes of your time to answer the survey. At any time during the survey, you are free to stop and withdraw from the study. You do not have to give me (the facilitator) a reason.

Your choice to participate

Your participation is entirely voluntary and you are under no obligation to participate. Whether or not you choose to participate, your status and access to health care will not be affected in any way. There are no anticipated risks or benefits for you if you choose to participate in this survey.

Your privacy

During the survey, your responses will be recorded on this paper or in our electronic database. We will not record your name during our discussion today and you will be assigned an identification number for our records. The information that you provide during our discussion will be completely confidential. All files will remain with the study coordinator and will be kept in a locked cabinet and all electronic files will be password protected. The main research team in this country from the Murdoch Children's Research Institute in Melbourne, Australia will access the study files and the ethics boards of the Fiji National Research Ethics Review Committee and The Royal Children's Human Research Ethics Committees is necessary.-----

I have read the information sheet provided or it has been read to me concerning this study and I understand what will be required of me if I participate in this study, which will be a verbal interview and discussion.

My questions regarding this study have been answered by: _____

I understand that at any time I may withdraw from this study without giving a reason and without having any effect on my access to health care.

I agree to take part in this study.

Signature of the respondent: _____

Signature of parent/ guardian if respondent under 18 years: _____

Signature of a witness: _____

Signature of the enumerator to indicate that the informed consent has been read and the information sheet given to the respondent: _____

APPENDIX 8: IVER P® (IVERMECTIN TABLET) PRODUCT INFORMATION LEAFLET

 <p>Lab. Elea S.A.C.I.F.A Sarandí 2353 - C1417 AZE Ciudad de Buenos Aires Tel: 4379-4300 / 4566-6111 Fax: 4379-4333</p>	<p>Producto : Iver P 3 mg Comprimidos - DOSSIER OMS</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Materia I</td> <td style="width: 30%;">Prospecto</td> <td style="width: 40%;">Código: 000000-00 reemplaza a</td> </tr> <tr> <td>Fecha: 29/04/15</td> <td>Nº Diseño: 8744/2</td> <td></td> </tr> <tr> <td>Medidas : 180x280 mm</td> <td>Plano:</td> <td>Escala: 100% specif. Técnicas: <input type="checkbox"/> LACA <input type="checkbox"/> CUÑO <input type="checkbox"/> BRAILLE</td> </tr> <tr> <td>Nº Colores : 2</td> <td>Citocromia <input type="checkbox"/></td> <td>Pantones : ■ P-286 U ■ Negro U</td> </tr> <tr> <td colspan="3">NOTAS: ■ El color representa al troquel. Los elementos representados con este color no deben imprimirse.</td> </tr> <tr> <td colspan="3">Motivo de emisión: Agrega texto de cápsula dehumidificadora en PRECAUCIONES/ PRESENTACIONES</td> </tr> </table> <p>LOS COLORES QUE SE VEN EN ESTA IMPRESIÓN PUEDEN TENER DESVIACIONES RESPECTO DE LOS COLORES PANTONE ESPECIFICADOS Y NO DEBEN USARSE COMO PATRÓN DE COMPARACIÓN</p>	Materia I	Prospecto	Código: 000000-00 reemplaza a	Fecha: 29/04/15	Nº Diseño: 8744/2		Medidas : 180x280 mm	Plano:	Escala: 100% specif. Técnicas: <input type="checkbox"/> LACA <input type="checkbox"/> CUÑO <input type="checkbox"/> BRAILLE	Nº Colores : 2	Citocromia <input type="checkbox"/>	Pantones : ■ P-286 U ■ Negro U	NOTAS: ■ El color representa al troquel. Los elementos representados con este color no deben imprimirse.			Motivo de emisión: Agrega texto de cápsula dehumidificadora en PRECAUCIONES/ PRESENTACIONES																				
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<p>Iver P® Ivermectin 3 mg</p> <p>Tablet</p> <p>Manufactured in Argentina Sold under prescription</p> <p>Formula Each tablet of Iver P® contains: Ivermectin 3 mg. Excipients: Lactose hydrate, Cellulose 80, Talc, Sodium starch glycolate, Magnesium stearate.</p> <p>Therapeutic action Iver P® 3 mg is a broad-spectrum semisynthetic antiparasitic agent for oral administration. ATC Code: P02CF.</p> <p>Indications Iver P® 3 mg is indicated for the treatment of the following parasitic diseases: onchocerciasis, intestinal strongyloidiasis, human scabies.</p> <p>Pharmacodynamics Ivermectin is a member of the avermectin class of broad-spectrum antiparasitic agents which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite. Compounds of this class may also interact with other ligand-gated chloride channels such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA). The selectivity of the avermectin class is different to the tools that some monovalents do not have glutamate-gated chloride channels and that the avermectins have a low affinity for mammalian ligand-gated chloride channels. In addition, ivermectin does not readily cross the blood-brain barrier in humans.</p> <p>Ivermectin stimulates the release of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) from the presynaptic nerve endings. Therefore, it inhibits, in the nematodes, the transmission of influx from the interneurons of the ventral nerve cord to the motor neurons. In arthropods, a similar mechanism inhibits the transmission of influx to the neuromuscular junction. Ivermectin does not easily penetrate the central nervous system of mammals. There is a dose-dependent interaction with GABA modulating transmission.</p> <p>In adult patients, a single dose reduces within a few days the number of microfilariae involving the skin of undetectable rates. After a single dose, the number of remaining microfilariae is, at least, 12 times lower to 10% of the number before treatment.</p> <p>This is the result of the combination of the microfilaricide effect and the temporary inhibition of the microfilariae from the womb of adult parasites. In patients with eye injuries, there is a significant decrease in introcular microfilariae.</p> <p>Its use has been also observed in the following cases:</p> <ul style="list-style-type: none"> • Patients of advanced age. • Treatment of endemic scabies. • Immunocompromised patients, who cannot easily be treated with topical treatments for scabies, with risk of failure. • Patients with forms of scabies that do not respond to conventional treatments. <p>Pharmacokinetics Each 3 mg Iver P® tablet has a mixture of, at least, 80% of 22,23-dihydroavermectin B1a and 20% of 22,23-thiomethylavermectin B1b. With single 12 mg ivermectin oral doses administered in tablets, the middle peak of concentrations of the main compound (H2B1a) in plasma was 46.6 (\pm 21.9) measured 4 hours after the product administration. Concentration in plasma increases as the dose increases in a proportional fashion. Ivermectin metabolizes in the liver and it is excreted, mainly in the urine, almost totally through feces (within 12 days). A dose of 12 mg of ivermectin oral dose is effective in vitro when using CYP3A4, CYP2D6 and CYP2E1 enzymes. Enzyme CYP450 1A2 and CYP2E1 were also shown to be involved in the metabolism of ivermectin, but with less intensity. In vitro studies suggest that clinically relevant effective concentrations of ivermectin do not specifically inhibit the metabolism activities of CYP3A4, CYP2D6, CYP2C9, CYP1A2, and CYP2E1. The plasma half-life of ivermectin in men is, approximately, 18 hours; the half-life of metabolites is, approximately, 3 days.</p> <p>Dosage and administration Strongyloidiasis The recommended dosage of 3 mg Iver P® tablets for the treatment of intestinal strongyloidiasis is 200 micrograms per kilogram of body weight (see the dosage guidelines table). Take a single dose with or without food. In children, take the dose in two halves in the morning or in any other time of the day, but food ingestion must be avoided two hours before and two hours after taking 3 mg Iver P® tablets. There are no other restrictions as regards food or concomitant drugs. If necessary and upon medical advice, repeat dose 15 days later.</p> <p>Dosage guidelines table for the treatment of onchocerciasis</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Weight (in kilograms)</th> <th>Single oral dose Number of 3 mg Iver P® tablets</th> </tr> </thead> <tbody> <tr> <td>15 to 24 kg</td> <td>1 tablet</td> </tr> <tr> <td>25 to 44 kg</td> <td>2 tablets</td> </tr> <tr> <td>45 to 64 kg</td> <td>3 tablets</td> </tr> <tr> <td>65 to 84 kg</td> <td>4 tablets</td> </tr> <tr> <td>> 85 kg</td> <td>150 micrograms per kilogram of body weight</td> </tr> </tbody> </table> <p>Dosage guidelines table for the treatment of scabies</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Weight (in kilograms)</th> <th>Single oral dose Number of 3 mg Iver P® tablets</th> </tr> </thead> <tbody> <tr> <td>15 to 24 kg</td> <td>1 tablet</td> </tr> <tr> <td>25 to 35 kg</td> <td>2 tablets</td> </tr> <tr> <td>36 to 50 kg</td> <td>3 tablets</td> </tr> <tr> <td>51 to 65 kg</td> <td>4 tablets</td> </tr> <tr> <td>66 to 79 kg</td> <td>5 tablets</td> </tr> <tr> <td>> 80 kg</td> <td>200 micrograms per kilogram of body weight</td> </tr> </tbody> </table> <p>If the weight is unknown, the dose of ivermectin for mass administration campaigns can be determined according to the height of the patients pursuant to the following information:</p> <p>Dosage guidelines table according to the patient's height</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Height (in centimeters)</th> <th>Single oral dose Number of 3 mg Iver P® tablets</th> </tr> </thead> <tbody> <tr> <td>90 to 119 cm</td> <td>1 tablet</td> </tr> <tr> <td>120 to 140 cm</td> <td>2 tablets</td> </tr> <tr> <td>141 to 158 cm</td> <td>3 tablets</td> </tr> <tr> <td>> 158 cm</td> <td>4 tablets</td> </tr> </tbody> </table> <p>In all the cases, strictly follow the physician's indication.</p> <p>Do not use the product after the expiration date that is clearly printed in the package.</p> <p>Contraindications Hypersensitivity to any of the formula components.</p> <p>Precautions and warnings After treatment with microlarval drugs, patients with hyperreactive onchodermatitis may be more likely than others to experience severe adverse reactions, such as edema and aggravation of onchodermatitis.</p> <p>Very rare reports of patients with onchocerciasis who are also heavily infected with Loa loa may develop a serious or even fatal angioedema either spontaneously or following treatment with an effective microfilaricide. In these patients, the following adverse effects have also been reported: neck and back pain, red eye, conjunctival hemorrhage, dysuria, urinary and fecal incontinence, ataxia, confusion, lethargy, seizures, and coma. This syndrome has been seen very rarely following the use of ivermectin. In individuals who warrant treatment with ivermectin for any reason and have had significant exposure to Loa loa-endemic areas (West and Central Africa), pre-treatment assessment for loiasis and careful post-treatment follow-up should be implemented.</p> <p>Each pack of the product contains aseptic canister/s as a desiccant to prevent tablets to get moisture. DO NOT SWALLOW THE CANISTER.</p>		Weight (in kilograms)	Single oral dose Number of 3 mg Iver P® tablets	15 to 24 kg	1 tablet	25 to 44 kg	2 tablets	45 to 64 kg	3 tablets	65 to 84 kg	4 tablets	> 85 kg	150 micrograms per kilogram of body weight	Weight (in kilograms)	Single oral dose Number of 3 mg Iver P® tablets	15 to 24 kg	1 tablet	25 to 35 kg	2 tablets	36 to 50 kg	3 tablets	51 to 65 kg	4 tablets	66 to 79 kg	5 tablets	> 80 kg	200 micrograms per kilogram of body weight	Height (in centimeters)	Single oral dose Number of 3 mg Iver P® tablets	90 to 119 cm	1 tablet	120 to 140 cm	2 tablets	141 to 158 cm	3 tablets	> 158 cm	4 tablets
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Drug interactions

According to post-marketing reports, ivermectin rarely increases the INR (International Normalized Ratio) in patients who are anticoagulated with warfarin.

Pregnancy

Category C. Ivermectin is not recommended for pregnant women; administration of ivermectin in doses similar or equal to maternotoxic doses result in fetal malformation in most lab animal species.

Ivermectin has been shown to be teratogenic in mice, rats, and rabbits when given in repeated doses of 0.2, 8, 1, and 4.5 times the maximum recommended human dose, respectively (on a mg/m²/day basis). Teratogenicity was characterized in the 3 species tested by cleft palate; clubbed forepaws were additionally observed in rabbits.

These developmental effects were found only at or near doses that were maternotoxic to the pregnant female. Therefore, ivermectin does not appear to be selectively fetotoxic to the developing fetus. However, there are no adequate and well-controlled studies in pregnant women. It is hard to determine from such studies the risk of one low dose.

Breastfeeding

Less than 2% of ivermectin dose is excreted in human milk. Safety has not been determined in infants. 3 mg Iver P® tablets should not be administered to breastfeeding mothers unless the expected benefit outweighs the possible risk to the newborn. Treatment of mothers who intend to breast-feed should be administered one week after the birth.

Carcinogenesis, mutagenesis, impairment of fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of ivermectin. Ivermectin was not genotoxic in vitro in the Ames microbial mutagenicity assay of *Salmonella Typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100 with and without rat liver enzyme activation, the Mouse Lymphoma Cell Line L5178Y (cytotoxicity and mutagenicity) assays, or the unscheduled DNA synthesis assay in human fibroblasts.

Ivermectin had no adverse effects on the fertility in rats in studies of repeated doses of up to 3 times the maximum recommended human dose of 200 mcg/kg (on a mg/m²/day basis).

Pediatric use

Safety and effectiveness in pediatric patients weighing less than 15 kg have not been established.

Geriatric use

Safety and effectiveness in this age group have not been established. According to clinical experience, differences in responses between the elderly and younger patients have not been identified. In general, treatment of elderly patients should be cautious, as they usually have decreased hepatic and renal functions, are under treatment with other drugs, or present comorbidity.

Adverse reactions and effects

In most cases, adverse effects are mild and temporary.

• Hypersensitivity reactions caused by the microfilariae death after treatment with ivermectin are the symptoms of Mazzotti reaction, pruritus, conjunctivitis, orthralgia, myalgia (including abdominal myalgia) fever, edema, lymphadenitis, adenopathies, nausea, vomiting, diarrhea, orthostatic hypotension, tachycardia, asthenia, rash and headaches.

These symptoms are rarely severe.

• Ophthalmological side effects are not frequent after treatment with 3 mg Iver P® tablets; however, occasionally, the following effects can appear during treatment: abnormal sensation in the eyes, eyelid edema, anterior uveitis, conjunctivitis, limbitis, keratitis, chorioretinitis or choroiditis. These symptoms are rarely severe; and, generally, disappear without corticosteroids.

• Somnolence and non-specific temporary ECG changes were reported.

• In some cases, temporary eosinophilia, high levels of transaminases (GPT) and hemoglobin increase are reported.

• Post-marketing reports include conjunctival hemorrhage (especially, when ivermectin was used in onchocerciasis treatment), orthostatic hypotension, worsening of bronchial asthma, toxic epidermal necrolysis, Stevens-Johnson syndrome, seizures, hepatitis, increase of liver enzymes, and increase of bilirubin.

Overdosage

Cases of accidental overdosage with ivermectin have been reported, but no death can be attributed to it. In case of severe intoxication with unknown doses (veterinary formulation), symptoms are those observed during the animal toxicology tests; mainly, mydriasis, somnolence, slow motor activity, tremors and ataxia.

In case of accidental poisoning, supportive therapy, if indicated, should include parenteral fluids and electrolytes, respiratory support (oxygen and mechanical ventilation if necessary) and pressor agents if clinically significant hypotension is present.

Induction of emesis and/or gastric lavage as soon as possible, followed by purgatives and other routine anti-poison measures, may be indicated if needed to prevent absorption of ingested material. Pursuant to the results of reports in humans, it seems appropriate to avoid GABA-receptor agonist drugs when treating accidental poisoning with ivermectin.

In case of overdosage, call your doctor or seek medical attention in the nearest hospital or the following poison control centers.

Presentation

Iver P® is supplied in 3 mg tablets, in packages of 6 tablets and 250 tablets (for hospital use) and a/some canister/s as a desiccant (do not swallow the canister).

Storage

Store at temperatures below 30°C (86°F). Store away from moisture.

KEEP THIS AND ALL MEDICINES OUT OF THE REACH OF CHILDREN. IF YOU HAVE ANY QUESTIONS, ALWAYS CONSULT YOUR DOCTOR OR PHARMACIST.

Medicinal product authorized by the Ministry of Health.

Certificate No. 55.983

Laboratorio S.A.C.I.F.y A.

Manufactured in: Sanobria 2353, City of Buenos Aires, Argentine Republic

Technical director: Fernando G. Tonéguzzo, Pharmacist.

Last update:

000000-00 1-pm-g



APPENDIX 9: MECTIZAN® (IVERMECTIN TABLET) PRODUCT INFORMATION LEAFLET

MECTIZAN® 3 mg, tablet (ivermectin, MSD)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet, you may need to read it again.
 - If you have further questions, if you have a doubt, ask your doctor or your pharmacist for more information.
- This medicine has been prescribed for you personally. You should not pass it on to others even if their symptoms are the same as yours. It may harm them.

1. DRUG IDENTIFICATION

a/ DENOMINATION

MECTIZAN® 3 mg, tablet

b/ QUALITATIVE AND QUANTITATIVE COMPOSITION

Ivermectin 3,00 mg
For a tablet

Excipients: microcrystalline cellulose, pregelatinized corn starch, butylhydroxyanisol, anhydrous citric acid, magnesium stearate.

c/ PHARMACEUTICAL FORM

Tablet.

d/ PHARMACOTHERAPEUTIC CLASS

ANTHELMINTIC

e/ NAME AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER AND RESPONSIBLE FOR PLACING THE DRUG ON THE MARKET



MSD France
34, avenue Léonard de Vinci
92400 Courbevoie
Medical Information: 01 80 46 40 40

f/ NAME AND ADDRESS OF THE MANUFACTURER

Merck Sharp & Dohme BV
Waarderweg 39
2031 BN Haarlem
Netherlands

or

Merck Sharp & Dohme-Chibret Laboratories
Route de Marsat
63200 Riom

2. IN WHICH CASE(S) SHOULD THIS DRUG BE USED?

This drug is an antiparasitic medication.

This drug is indicated:

- for the treatment of onchocerciasis (a disease due to the infection caused by a parasite: the filaria *Onchocerca volvulus*);
- for the treatment of microfilariaemia in case of infection caused by *Wuchereria bancrofti* (lymphatic filariasis).

3. CAUTION!

a/ IN WHICH CASE(S) SHOULD THIS DRUG NOT BE USED?

This drug is an antiparasitic medication.

This drug is indicated:

- for the treatment of onchocerciasis (a disease due to the infection caused by a parasite: the filaria *Onchocerca volvulus*);
- for the treatment of microfilariaemia in case of infection caused by *Wuchereria bancrofti* (lymphatic filariasis).

3. CAUTION!

a/ IN WHICH CASE(S) SHOULD THIS DRUG NOT BE USED?

This drug SHOULD NOT BE USED in case of history of allergic reactions to any component of this product.

IN CASE OF DOUBT, IT IS NECESSARY TO ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE.

b/ SPECIAL WARNINGS

In African areas where there are also cases of the human parasitic infection caused by *Loa loa*, it is advisable not to use this medication concomitantly with diethylcarbamazine (DEC) because it may result in increased risk of side effects which may sometimes be serious.

This medicine should only be used when the infestation is proven or highly suspected. It has no efficacy in prophylactic use of the disease (prevention treatment).

IN CASE OF DOUBT, IT IS NECESSARY TO ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE.

c/ PRECAUTION FOR USE

IN CASE OF DOUBT, IT IS NECESSARY TO ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE.

d/ INTERACTIONS WITH OTHER DRUGS AND OTHER INTERACTIONS

IN ORDER TO AVOID POSSIBLE INTERACTION BETWEEN SEVERAL MEDICATIONS, IT IS NECESSARY TO INFORM YOUR PHYSICIAN OR YOUR PHARMACIST IF YOU ARE TAKING ANY OTHER TREATMENT.

e/ PREGNANCY – BREAST FEEDING

Pregnancy:

If you are pregnant, ask your doctor for advice before taking MECTIZAN.

Breast-feeding:

If you are breast-feeding, tell your doctor. If necessary, prescription should be delayed until one week after the birth of the child.

AS A GENERAL RULE, IT IS RECOMMENDED DURING PREGNANCY AND BREAST-FEEDING TO ALWAYS ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE BEFORE USING ANY DRUG.

f/ DRIVING AND USING MACHINES

The effect of MECTIZAN on the ability to drive or use machines has not been studied. In some patients, possible side effects such as dizziness, somnolence, vertigo and tremor that may affect the ability to drive or operate machinery, are not excluded (See section Side effects).

4. HOW SHOULD THIS DRUG BE USED?

a/ DOSAGE

Treatment of onchocerciasis:

The recommended dosage in the treatment of onchocerciasis is a single oral dose of 150 µg/kg of body weight.

For the treatment of individual patients, retreatment may be considered after a 3-months interval.

In mass distribution campaigns for onchocerciasis, the most commonly used dose interval is 12 months. However, in some areas it may be preferable to repeat the administration every 6 months according to the prevalence of the microfilarial density.

For guidance, the dose as established by the patient's weight is:

BODY WEIGHT (kg)	DOSE (Number of 3 mg tablets)
15 to 25	one
26 to 44	two
45 to 64	three
65 to 84	four

Alternatively, and if no scales are available, the dose of ivermectin for use in mass distribution campaigns may be established by the patient's height, as follows:

HEIGHT (cm)	DOSE (Number of 3 mg tablets)
90 to 119	one
120 to 140	two
141 to 158	three
> 158	four

Treatment of microfilaremia caused by *Wuchereria bancrofti* (lymphatic filariasis):

The recommended dosage for mass therapy campaigns of microfilaremia caused by *Wuchereria bancrofti* (lymphatic filariasis) is a single oral dose of 150 to 200 µg of ivermectin per kilogram of body weight once every 6 months.

In endemic areas where treatment can only be administered once every 12 months, the recommended dosage is 300 to 400 µg per kilogram of body weight to maintain adequate suppression of microfilaremia in treated subjects.

For guidance, the dose, as established by the patient's weight, is:

BODY WEIGHT (kg)	DOSE when given once every 6 months (Number of 3 mg tablets)	DOSE when given once every 12 months (Number of 3 mg tablets)
15 to 25	One	two
26 to 44	Two	four
45 to 64	Three	six
65 to 84	Four	eight

Alternatively, and if no scales are available, the dosage for use in mass therapy campaigns may be established by the patient's height as follows:

HEIGHT (cm)	DOSE when given once every 6 months (Number of 3 mg tablets)	DOSE when given once every 12 months (Number of 3 mg tablets)
90 to 119	one	two
120 to 140	two	four
141 to 158	three	six
> 158	four	eight

IN ALL CASES, FOLLOW STRICTLY YOUR DOCTOR'S PRESCRIPTION.

b/ METHOD AND ROUTE OF ADMINISTRATION

Oral route.

For children less than 6 years of age, tablets should be crushed before swallowing.

Treatment is one single oral dose taken with water on an empty stomach.

The dose may be taken at any time of the day but no food should be taken within two hours before or after administration, as the influence of food on absorption is unknown.

c/ FREQUENCY AND TIME WHEN THE DRUG SHOULD BE ADMINISTERED

This medicine is administered in one single dose.

d/ WHAT SHOULD YOU DO IN CASE OF OVERDOSE?

Consult a doctor.

5. UNDESIRABLE AND TROUBLESOME SIDE EFFECTS

AS WITH ANY ACTIVE INGREDIENT, THIS MEDICATION CAN, IN SOME PATIENTS, CAUSE MORE OR LESS TROUBLESOME EFFECTS:

Most often side effects are mild and transient but they may be higher in patients infested with several parasites particularly in case of infestation with *Loa loa*.

Following administration of ivermectin in patients infested with Onchocerca volvulus : itching, redness of the eyes, joint pains, fever, nausea, vomiting, swelling of lymph nodes, diarrhea, hypotension, vertigo, accelerated heart rate, fatigue, rash, headache, visual disturbances, may occur.

Following administration of ivermectin in patients infested with lymphatic filariasis, have been reported: fever, headache, asthenia, feeling of weakness, muscle and joint pains, body pains, digestive disorders such as loss of appetite, nausea, abdominal and epigastric pain, cough, feeling of respiratory discomfort, sore throat, hypotension when getting up, chills, vertigo, sweating, testicular pain or feeling of discomfort.

In patients also heavily infested with the filaria *Loa loa*, serious brain disorders have been reported exceptionally following administration of ivermectin.

Cases of expulsion of adult ascaris worms have been reported following administration of ivermectin.

Very rarely, serious skin reactions have been reported.

INFORM YOUR DOCTOR OR PHARMACIST ABOUT ANY UNDESIRABLE AND TROUBLESOME EFFECT NOT LISTED IN THIS PACKAGE INSERT.

6. CONSERVATION

a/ DO NOT EXCEED THE LIMIT DATE OF USE CLEARLY MENTIONED ON THE PACKAGING

b/ SPECIAL STORAGE PRECAUTIONS

Do not store above 30°C.

7. DATE OF REVISION OF THE PACKAGE LEAFLET

05 October 2011.

APPENDIX 10 LYCLEAR® (PERMETHRIN CREAM) PRODUCT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET

Lyclear® Dermal Cream**Permethrin**

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use Lyclear Dermal Cream carefully to get the best results from it.

Keep this leaflet. You may need to read it again.

Ask your pharmacist if you need more information or advice.

You must contact a doctor if the symptoms worsen or do not improve.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist straightaway.

In this leaflet:

- What Lyclear Dermal Cream is and what it is used for
- Possible side effects
- Storage
- Further information

1. What Lyclear Dermal Cream is and what it is used for

Lyclear Dermal Cream is used to treat infestations of scabies and crab lice on the body. It contains the ingredient permethrin which belongs to a group of medicines called pyrethroids which can kill mites such as scabies and crab lice.

2. Before you use Lyclear Dermal Cream

Take as directed by your doctor or pharmacist. Do not exceed the dose.

3. How to use Lyclear Dermal Cream

If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

Warning:

For cutaneous use only if do not swallow this medicine.

Avoid contact with eyes or mucous membranes or asthma or eczema.

Children up to 23 months of age:

Do not use Lyclear Dermal Cream on children under 23 months of age.

When not to use Lyclear Dermal Cream:

Tak as directed by your doctor or pharmacist - see below for dosage. Children up to 23 months of age:

- If you are allergic to pyrethroids or other compounds - see above for dosage. Children up to 23 months of age:

- If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

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Do not use Lyclear Dermal Cream on children under 23 months of age.

When not to use Lyclear Dermal Cream:

Tak as directed by your doctor or pharmacist - see below for dosage. Children up to 23 months of age:

- If you are allergic to pyrethroids or other compounds - see above for dosage. Children up to 23 months of age:

- If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

For cutaneous use only if do not swallow this medicine.

Avoid contact with eyes or mucous membranes or asthma or eczema.

Children up to 23 months of age:

Do not use Lyclear Dermal Cream on children under 23 months of age.

When not to use Lyclear Dermal Cream:

Tak as directed by your doctor or pharmacist - see below for dosage. Children up to 23 months of age:

- If you are allergic to pyrethroids or other compounds - see above for dosage. Children up to 23 months of age:

- If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

For cutaneous use only if do not swallow this medicine.

Avoid contact with eyes or mucous membranes or asthma or eczema.

Children up to 23 months of age:

Do not use Lyclear Dermal Cream on children under 23 months of age.

When not to use Lyclear Dermal Cream:

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- If you are allergic to pyrethroids or other compounds - see above for dosage. Children up to 23 months of age:

- If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

For cutaneous use only if do not swallow this medicine.

Avoid contact with eyes or mucous membranes or asthma or eczema.

Children up to 23 months of age:

Do not use Lyclear Dermal Cream on children under 23 months of age.

When not to use Lyclear Dermal Cream:

Tak as directed by your doctor or pharmacist - see below for dosage. Children up to 23 months of age:

- If you are allergic to pyrethroids or other compounds - see above for dosage. Children up to 23 months of age:

- If you are known to be allergic to pyrethroids or other compounds - you should only use Lyclear Dermal Cream after seeking advice from your doctor.

How and when should you use Lyclear Dermal Cream?
Lyclear Dermal Cream is for cutaneous use only.
Take cream not to allow the cream to get into the eye only, to mouth or over the genital region or open wounds. If accidental contact occurs, rinse thoroughly with water.
Adults should apply the cream to the whole body including the neck, joints, hands and soles of the feet. The head and face should be washed in warm water before applying the cream to the hair and scalp. If necessary, children should wash their hair.
There are no special instructions for children under 23 months of age.

For treatment of crab lice in adults:

Any facial hair (beards, moustaches and eyebrows) should be checked for the presence of eggs. Cream should be applied to any such hair, carefully avoiding eyes. If live lice or eggs are found on the eyelashes they should be removed.

Cream should apply the cream uniformly to the whole body, including the joints of the hands, soles of the feet, neck, elbow, knee, shoulder, back, and scalp. If necessary, children should wash their hair.

Keep your child from eating the cream until they have been washed. Treatment of children up to the age of 23 months should therefore only be treated under close medical supervision.

Elderly: Elderly patients over 65 years should use the cream in the same way as adults but in addition, the face, ears and scalp should also be treated. Care should be applied to any such hair, carefully avoiding eyes.

How long should you use Lyclear Dermal Cream?
One application of Lyclear Dermal Cream is usually sufficient.

Leave the cream on the skin for at least eight hours to wash away any excess. If you have to wash other parts of the body, wash the cream off first, then wash the hands and wrist area. The same applies if you have to wash other parts of the body, wash the cream off first, then wash the hands and wrist area.

After each application of cream, take a shower and wash the skin with soap and water. Provided these instructions are followed, a single application is generally sufficient for successful treatment. However, in cases of persistent or renewed infestation, it may be necessary to repeat the treatment after 14 days.

If you use too much:
If too much cream is applied, it should be washed off with soap and warm water. If there are any signs of irritation, talk to your doctor. If it continues, seek medical advice from the Doctor of a Medical and Emergency Department of the nearest hospital immediately.

4. Possible side effects
Like all medicines, Lyclear Dermal Cream can cause side effects, although not everybody gets them.

If severe hypersensitivity reactions occur, please consult a doctor immediately. In this case you must not use Lyclear Dermal Cream any more.

Common side effects affect 1 to 15% of people. These include reddening of the skin or unusual sensations on the skin (prickliness, such as stinging, pricking, skin burning sensation as well as dry skin). Moisturisers and oils or lotions are recommended as follow up treatment. The itching and a skin rash (red-cakes eczema) may persist for up to four weeks after the end of treatment. This is caused by a reaction to the dead scales mites. If after using Lyclear Dermal Cream you have the same reaction but the disease is persisting, please speak to your doctor before applying it again.

Headache can occur in 1 in 100 people.

Musculoskeletal pain may affect 1 to 10 in 10,000 people.

Very rarely, skin lesions (excoriations), inflammation of the hair follicles (folliculitis), and reduced skin pigmentation have been reported at the time Lyclear Dermal Cream is used.

Symptomless mites have been reported causing difficulties at the lime instances from the permethrin group were being used. These include redness and/or skin rash (urticaria). These reactions may also spread beyond the area of the mite infestation.

Nausea may appear. Clothing was not reported after the use of Lyclear Dermal Cream and is known in connection with other permethrin-containing drugs.

Reporting of side effects: If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report any side effects you think may be associated with this medicine. By applying the 'yellow card' on the patient information leaflet you will help to provide more information on the safety of this medicine.

Do not store above 25°C. Do not freeze. Keep the cream in the original carton. Do not use Lyclear Dermal Cream after the date printed after 'exp' on the carton, or if the expiry date has passed. Take the product back to your pharmacist for safe disposal.

Lyclear Dermal Cream is a white cream in a 30 g tube. Active substance: Permethrin (5% w/w).

Other ingredients: Coconut oil, glycerine monostearate, macrogol 6 ether, emulsifying wax E(231), sorbitol, myristate, lanolin, dibutyltin dilaurate, paraffin, menthol, benzyl alcohol, citric acid, fragrance, carbomer, sodium hydroxide and purified water.

Marketing Authorisation holder: Ongka Pharma Ltd., 1st Floor, 32 Vauxhall Bridge Road, London, SW1V 5SA, United Kingdom. Send all enquiries to this address.

Manufacturer: Medicom Biotech NV, Virgilius 21, BE-8560 Wetteren, Belgium.

Lyclear is a registered trademark. Date of text revision: Sep 2015.

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APPENDIX 11: DIAGNOSTIC CRITERIA FOR ACUTE RHEUMATIC FEVER FROM FIJI GUIDELINES FOR ACUTE RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE DIAGNOSIS, MANAGEMENT AND PREVENTION

Table 2:Fiji Criteria for ARF Diagnosis[1]

	Criteria
A: Diagnosis: initial ARF	2 major manifestations <u>OR</u> 1 major plus 2 minor manifestations <u>PLUS</u> evidence of GAS infection*
Diagnosis: recurrent ARF	2 major <u>OR</u> 1 major plus 2 <u>minor</u> <u>OR</u> 3 minor <u>PLUS</u> evidence of GAS infection*
B: Major criteria	<ol style="list-style-type: none"> 1. <u>Carditis</u> -Clinical and/or sub-clinical (on echocardiography) 2. Arthritis <u>Monoarthritis, polyarthritis or polyarthralgia</u> 3. Chorea** 4. Erythema marginatum 5. Subcutaneous nodules
C: Minor criteria	<ol style="list-style-type: none"> 1. <u>Monoarthralgia</u> (unless arthritis is included as a major manifestation) 2. Fever ($\geq 38^{\circ}\text{C}$) 3. ESR $\geq 30 \text{ mm/h}$ or white cell count $\geq 15 \times 10^6/\text{mL}$ 4. Prolonged P-R interval, for age (unless <u>carditis</u> is a major criterion)

*Evidence of preceding group A streptococcal infection is defined by at least one of the following:

1. Elevated ASOT above cut-offs by age determined for Fiji (see Table 3)
2. A rising ASOT defined as a twofold or greater difference between titres measured at presentation and when convalescent (2-4 weeks later generally)
3. A positive throat swab for group A streptococcus at presentation

** Note that ARF can be diagnosed on the basis of chorea without other manifestations or evidence of GAS infection.

**APPENDIX 12: DEFINITIONS OF RHEUMATIC HEART DISEASE FROM FIJI GUIDELINES FOR ACUTE
RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE DIAGNOSIS, MANAGEMENT AND
PREVENTION**

Table 9 Recommended secondary prophylaxis regimens

Category	Definition of category	Duration
	Minimum duration for all persons with ARF or RHD ¹	Minimum 10 years after most recent episode of ARF or until age 21 years (whichever is longer)
No RHD	No pathological mitral or aortic regurgitation, but may have minor morphological changes to mitral or aortic valves on echocardiography	Discontinue at the minimum duration ^
Mild RHD	Mild mitral or aortic regurgitation clinically and on echocardiography, with no clinical evidence of heart failure and no evidence of cardiac chamber enlargement on echocardiography	Discontinue after the minimum duration
Moderate RHD	<ul style="list-style-type: none"> • Any valve lesion of moderate severity clinically (e.g. mild–moderate cardiomegaly and/or mild–moderate heart failure) or on echocardiography • Mild mitral regurgitation, together with mild aortic regurgitation clinically or on echocardiography • Mild or moderate mitral or aortic stenosis • Any pulmonary or tricuspid valve lesion co-existing with a left-sided valve lesion 	Continue until 35 years of age
Severe RHD	<ul style="list-style-type: none"> • Any severe valve lesion clinically (e.g. moderate to severe cardiomegaly or heart failure) or on echocardiography • Any impending or previous cardiac valve surgery for RHD 	Continue until age 40 years, or longer*

¹ Patients >25 years of age who are diagnosed with RHD, without any documented history of prior ARF, should receive prophylaxis until the age of 35 years. At this time, they should be reassessed to determine whether prophylaxis should be continued. ^ Decisions to cease secondary prophylaxis should be based on clinical and echocardiographic assessment. * Risk of recurrence is extremely low in people aged >40 years. In some cases, for example, when the patient decides that they want to reduce even a minimal risk of recurrence, prophylaxis may be continued beyond the age of 40 years, or even for life. Continue prophylaxis for life (benzathine penicillin where not allergic) after valve replacement surgery.

APPENDIX 13: CASE DEFINITIONS FOR INVASIVE GROUP A STREPTOCOCCAL DISEASE AND STAPHYLOCOCCUS AUREUS DISEASE

Case definitions for invasive group A streptococcal (GAS) and Staphylococcus aureus disease	
Disease	
Definite	<p>Either of the following:</p> <ol style="list-style-type: none"> 1. The isolation of GAS or Staphylococcus aureus from a normally sterile site (e.g. blood, cerebrospinal fluid, or other sterile fluid/tissue) 2. Clinical presentation of necrotising fasciitis with evidence of GAS infection or Staphylococcus aureus disease (e.g. the presence of typical gram positive cocci on Gram stain or positive streptococcal serology)
Probable	<p>Any of the following</p> <ol style="list-style-type: none"> 1. A classic presentation of necrotizing fasciitis without microbiological confirmation 2. Cellulitis in a patient who is moderately or severely unwell (i.e. unwell and history of parenteral antibiotics and/or admission to hospital” and microbiological confirmation (i.e. GAS or Staphylococcus aureus culture of swab or positive streptococcal serology) 3. Other clinically significant infection in a patient who is moderately or severely unwell (i.e. unwell and history of parenteral antibiotics and/or admission to hospital), in conjunction with positive group A streptococcal culture from deep wound swab or biopsy from surgical infection site.

Big SHIFT Adolescent Information Sheet: Skin Examination.

Why am I being asked to be in this study?

Your community has been selected by chance to represent the Northern Division. We would like to find out how common scabies and impetigo are in your community. We are doing this to see whether there have been any changes in the presence of scabies and skin sores in your community before and after medication for scabies called ivermectin is given to everyone.

What will happen during the skin examination?

Once you agree to take part, a trained nurse will examine your skin to find out if you have scabies or skin sores. They will also ask you to provide some basic information which will help us know about scabies and skin sores in your community.

Do I have to take part in the study?

You can decide whether you want to take part in the skin examination or not. You can discuss your choice with your parents and feel free to ask us about any questions you have.

Will other people know about my information if I take part?

All information will be protected and not shared to other people. All information is only available to the people who are involved with the skin examination.

Who can I contact for any questions?

If you have any questions, you or your parent(s) can call us on Vodafone mobile number 2758444 or contact the study coordinator, Dr Li Jun Thean on 7412938.

Adolescent Consent Form

HREC Project Number : **HREC 38020A**

Research Project Title : Northern Division Scabies Control Project (Big SHIFT)

Version Number : 1.1 **Version Date:** 18/04/2019

- I have read and/or have received explanation about skin examination in the northern division.
- I understand what I have to do to be part of this research project
- I understand the risks I could face by taking part in this research project
- I am happy to take part in this research project
- I was given time to ask questions about the project and I am happy with the answers I got
- I understand that this research project has received ethics approval from Australia and Fiji
- I understand that I will get a copy of this information sheet and a consent form

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

(Sign your name here)

(Date)

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

.....
Research Team Member Name Signature Date

Note: All parties signing the Consent Form must write the date after signing.

Big SHIFT Adolescent Information Sheet: Hospital Surveillance

Why am I being asked to be in this study?



We want to find out how many people are admitted to hospital with illnesses similar to yours. We are doing this to see if less people get sick from your illness after your community receives medicine to reduce scabies.

Do I have to be in the study?

If you do not want to be in this study, you should tell parents why. Everyone can talk about what the right thing to do is. Please feel free to ask us about any questions you have.

You can change your mind after you start the study. All you have to do is to tell us. Your doctors will still look after you in the best way they can.

What will happen to me in this study?



By being in the study, we will look through your medical notes to take down information listed there. We may ask you and your family some questions about your health. No further tests, medicine or visits to the hospital will be needed by the study.

Who will get my information?

We will keep information about you on our computer system. Only people working on the study will be able to see this information.



Who can I contact with any questions?

If you have any questions, you can talk to any of the study team. You can also ask your parents to talk to us. You can call the study doctor, Dr Li Jun Thean on 741 2938.

Adolescent Consent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 1.0

Version Date: 06/09/2018

- I have read and/or have received explanation about this scabies research project in the Labasa Hospital
- I understand what I have to do to be part of this research project
- I understand the risks I could face by taking part in this research project
- I am happy to take part in this research project
- I was given time to ask questions about the project and I am happy with the answers I got
- I understand that this research project has received ethics approval from Australia and Fiji
- I understand that I will get a copy of this information sheet and a consent form

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

(Sign your name here)

(Date)

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

.....

Research Team Member Name Signature Date

Note: All parties signing the Consent Form must date their own signature.

Big SHIFT Child Information Sheet: Hospital Surveillance

Why am I being asked to be in this study?



We want to find out how many people are admitted to hospital with illnesses similar to yours. We are doing this to see if less people get sick from your illness after your community receives medicine to reduce scabies.

Do I have to be in the study?

If you do not want to be in this study, you should tell parents why. Everyone can talk about what the right thing to do is. Please feel free to ask us about any questions you have.

You can change your mind after you start the study. All you have to do is to tell us. Your doctors will still look after you in the best way they can.

What will happen to me in this study?



By being in the study, we will look through your medical notes to take down information listed there. We may ask you and your family some questions about your health. No further tests, medicine or visits to the hospital will be needed by the study.

Who will get my information?



We will keep information about you on our computer system. Only people working on the study will be able to see this information.

Who can I contact with any questions?

If you have any questions, you can talk to any of the study team. You can also ask your parents to talk to us.

You can call the study doctor, Dr Li Jun Thean on 741 2938.

Assent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 1.0

Version Date: 21/08/2018

- I have read and/or have received explanation about this scabies research project in the Labasa Hospital
- I understand what I have to do to be part of this research project
- I understand the risks I could face by taking part in this research project
- I am happy to take part in this research project
- I was given time to ask questions about the project and I am happy with the answers I got
- I understand that this research project has received ethics approval from Australia and Fiji
- I understand that I will get a copy of this information sheet and a consent form

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

(Sign your name here)

(Date)

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

.....
Research Team Member Name Signature Date

Note: All parties signing the Consent Form must date their own signature.

Big SHIFT Adolescent Information Sheet: Storage of Biological Specimens



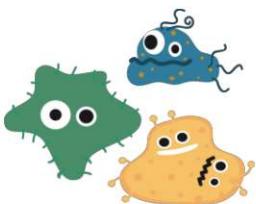
Why am I being asked to be in this study?

We want to find out more about the bacteria that has made you sick. We want to do this so that in the future we may be able to prevent other boys and girls from becoming ill through vaccines.

Do I have to be in the study?

If you do not want to be in this study, you should tell your parents why. Everyone can talk about what the right thing to do is. Please feel free to ask us about any questions you have.

You can change your mind after you start the study. All you have to do is to tell us. Your doctors will still look after you in the best way they can.



What will happen to me in this study?

We will store the bacteria that has grown from the blood/body fluid your doctor has already collected from you. We will send these bacteria to the Murdoch Children's Research Institute in Australia where we can run tests that will help us know more about the bacteria that has made you sick.

Even though these tests will not help you directly, the information we will get will help prevent many other people from getting sick from this bacteria in the future.

Who will get my information?

We will keep information about the bacteria we are storing from you on our computer system. Only people working on the study will be able to see this information.



Who can I contact with any questions?

If you have any questions, you can talk to any of the study team. You can also ask your parents to talk to us.

You can call the study doctor, Dr Li Jun Thean on 7412938.

Adolescent Consent Form

HREC Project Number: HREC 38020A

Research Project Title: Northern Division Scabies Control Project (Big SHIFT)

Version Number: 1.0

Version Date: 06/09/2018

- I have read and/or have received explanation about this scabies research project in the Labasa Hospital
- I understand what I have to do to be part of this research project
- I understand the risks I could face by taking part in this research project
- I am happy to take part in this research project
- I was given time to ask questions about the project and I am happy with the answers I got
- I understand that this research project has received ethics approval from Australia and Fiji
- I understand that I will get a copy of this information sheet and a consent form

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.

(Sign your name here)

(Date)

Declaration by researcher: I have explained the project to the participant who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

.....

Research Team Member Name Signature Date

Note: All parties signing the Consent Form must date their own signature.



Fiji Centre for Communicable Disease Control

Mataika House, Building 30, Tamavua Hospital Complex, G.P.O.Box 16346, Suva, Fiji.
Tel: (+679) 3320 066. Fax: (+679) 3320 344.

Mass Drug Administration Consent Form (School Distribution)

Dear parent or guardian,

Thank you for taking the time to read this information sheet and consent form for your child to receive medication at school as part of the mass drug administration (MDA) in the Northern Division. This MDA program is aimed to treat and prevent three conditions namely, scabies, lymphatic filariasis and soil transmitted helminths.

Lymphatic Filariasis (LF)

Commonly known as elephantiasis, LF is a painful and disfiguring tropical disease caused by thread-like worms (microfilariae) that live in the human lymphatic system and is transmitted through mosquitoes. The outcome of a recent survey conducted in the Northern Division has raised concerns due to the increase in positive cases surpassing the critical cut off. The Ministry of Health is therefore conducting Mass Drug Administration in the Northern division to stop transmission of Lymphatic filariasis and to avoid future health complications.

Scabies

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. Approximately 28.5% of people in the Northern Division are affected at any point in time. This is especially worse in children aged 5 to 9 years old with approximately 44% having scabies at any time. Scabies is spread by skin to skin contact. It causes intense itch and skin breakage which leads to skin infection by bacteria if not treated properly. Bacteria can not only cause skin infection but can lead to serious illness such as infection in blood and other body parts such as muscles, bones and joints. A type of bacteria (group A streptococci) that commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease and kidney disease. Giving treatment that kills the mite to everyone in your community will help to reduce the chance of getting scabies by preventing it from spreading.

Soil Transmitted Helminths (STH)

Also known as intestinal worms are worms that come from the soil and live in our intestines. They can cause stomach pain, tiredness, weight loss and poor growth in children. We can get STH from walking barefoot on soil or eating unwashed fruit and vegetables.

What is involved?

This MDA program will be giving treatment to everyone in the Northern Division at the same time. Health workers will be visiting schools to distribute the tablets that are effective against LF, scabies and STH. The medications given will be ivermectin, diethylcarbamazine and albendazole.

How will they benefit?

If your child has LF, scabies and/or STH these medications will treat their infection. If they don't have one of these infections, they will still benefit from everyone around them being treated at the same time as this will reduce the chance of getting any of these infections in the future through preventing spread.

Are there any risks?

Side effects from the medications are more likely if your child has LF, STH or scabies infection because their body is reacting to the dying worms and/or mites. They might experience itching and swelling of face, headache, joint pain, tiredness, weakness, dizziness, fainting, nausea, vomiting, stomach pain, diarrhea, fever, painful glands in groin/neck/armpits. These are infrequent and resolve by themselves and with simple medications such as Panadol. Skin rash, racing heart, or an allergic reaction (itchy rash, difficulty breathing, tightness in chest, swelling of face/tongue) are very rare.

If your child feels unwell you can present to your local health facility.

What you need to do

If you allow your child to be treated then please sign this form and have your child return it to his/her school. A single treatment per year is usually sufficient to ensure that all the adult worms have been killed. Consumption of these medications will help prevent scabies and its complications, illness from soil transmitted helminths and long-term health effects of Lymphatic filariasis.

If you have any questions about this Mass Drug Administration, you can contact your nearest health centre.

(Circle your choice)

ALLOW

DO NOT ALLOW

Child's Name: _____ Year: _____ Age: _____

Residential Address: _____

Parent/Guardian signature: _____

OR thumbprint

Date: _____



APPENDIX 18: INFORMATION SHEET FOR MDA



Fiji Centre for Communicable Disease Control

Mataika House, Building 30, Tamavua Hospital Complex, G.P.O.Box 16346, Suva, Fiji.

Tel: (+679) 3320 066. Fax: (+679) 3320 344.

Mass Drug Administration Information Sheet

Dear Sir/Madam,

Thank you for taking the time to read this information sheet to receive medication as part of the mass drug administration (MDA) in the Northern Division. This MDA program is aimed to treat and prevent three conditions namely, scabies, lymphatic filariasis and soil transmitted helminths.

Lymphatic Filariasis (LF)

Commonly known as elephantiasis, LF is a painful and disfiguring tropical disease caused by thread-like worms (microfilariae) that live in the human lymphatic system and is transmitted through mosquitoes. The outcome of a recent survey conducted in the Northern Division has raised concerns due to the increase in positive cases surpassing the critical cut off. The Ministry of Health is therefore conducting MDA in the Northern division to stop transmission of LF and to avoid future health complications.

Scabies

Scabies is a mite infection that is common in Fiji, especially in the Northern Division. Approximately 28.5% of people in the Northern Division are affected at any point in time. This is especially worse in children aged 5 to 9 years old with approximately 44% having scabies at any time. Scabies is spread by skin to skin contact. It causes intense itch and skin breakage which leads to skin infection by bacteria if not treated properly. Bacteria can not only cause skin infection but can lead to serious illness such as infection in blood and other body parts such as muscles, bones and joints. A type of bacteria (group A streptococci) that commonly causes infections in skin can also cause serious illness after infection such as rheumatic fever, rheumatic heart disease and kidney disease. Giving treatment that kills the mite to everyone in your community will help to reduce the chance of getting scabies by preventing it from spreading.

Soil Transmitted Helminths (STH)

Also known as intestinal worms are worms that come from the soil and live in our intestines. They can cause stomach pain, tiredness, weight loss and poor growth in children. We can get STH from walking barefoot on soil or eating unwashed fruit and vegetables.

What is involved?

This MDA program will be giving treatment to everyone in the Northern Division at the same time. Health workers will be visiting homes, workplaces and schools to distribute the tablets that are effective against LF, scabies and STH. The medications given will be ivermectin, diethylcarbamazine and albendazole.

Treatment may vary if you fall into a particular group:

1. Children under 2 years old
2. Children under 90cm tall
3. Women who are pregnant or may be pregnant
4. Women breastfeeding infants less than 7 days old
5. People who are severely ill- unable to perform activities of daily living, need family assistance due to illness
6. People on warfarin

Before we give you the medicine, please let us know if you are pregnant or may be pregnant, breastfeeding an infant under 7 days old or taking warfarin.

What to do if you find out you have taken any of the tablets while pregnant

If you find out that you were pregnant when you took the tablets, please notify the health facility that is taking care of you during your pregnancy. These medications have not been shown to cause harm to pregnant women or their babies. A doctor from our team will be available to answer any questions you have about the tablets and pregnancy and to document the outcome of your pregnancy.

How will you benefit?

If you or your family has LF, scabies and/or STH these medications will treat their infection. Even if you don't have one of these infections, you and your family will still benefit from everyone in your community being treated at the same time as this will reduce the chance of getting any of these infections in the future through preventing spread.

Are there any risks?

About 1 in 5 people who take the medication experience mild side effects from them. These side effects are mild and resolve by themselves with simple medication such as Panadol. Side effects from the medications are more likely if you have LF, STH or scabies infection because your body is reacting to fight the dying worms and/or mites. You might experience itching, headache, joint pain, tiredness, weakness, dizziness, fainting, nausea, vomiting, stomach pain, diarrhea, fever, painful glands in groin/neck/armpits. Skin rash, racing heart, or an allergic reaction (itchy rash, difficulty breathing, tightness in chest, swelling of face/tongue) are very rare. If you or your family feel unwell you/they can present to your local health facility.

What you need to do

If you would like to participate, medication will be dispensed to you. The person distributing the medications will observe you take the first dose. This is the only way that we can be sure that the community has been treated properly. A second dose of ivermectin or permethrin will be given to you and a member of the health team will return to observe you take it in 7-14 days. A single treatment per year is sufficient to ensure that all the adult LF worms have been killed. These medications will help prevent scabies and its complications, illness from soil transmitted helminths and long-term health effects of Lymphatic filariasis. If you have any further questions about the MDA, you can contact your nearest health centre or call the Northern Division Scabies Control Program on 7334532

APPENDIX 19: INTERVIEW GUIDE FOR COMMUNITY MEMBER

INTERVIEW GUIDE
COMMUNITY MEMBER

Theme	Purpose
Introduction	Obtain some basic demographic information and to build a relationship with the participant and get them used to start telling their story.
Knowledge of scabies	To assess the level of knowledge that community members have about LF, scabies and impetigo, including how it's transmitted, prevented and treated.
Experience with scabies	To understand their experiences with scabies, including reoccurrence of LF and scabies symptoms.
Management/Treatment	To understand their behaviours related to LF and scabies management and treatment (formal and informal strategies).
Impact	To understand the impact of LF, scabies/impetigo on their life, including health, economic and social factors.
Prevention and health promotion	To identify any preventative measures being used to prevent the spread of LF and scabies; examine individual, household and community efforts.
MDA	To determine people's thoughts and acceptance of MDA in their community.
Conclusion	Warm down participant and seek any missed views/ideas.

INTRODUCTION QUESTIONS

Purpose – Obtain some basic demographic information and to build a relationship with the participant and get them used to start telling their story.

1. Can you tell me a bit about yourself and your family?
 - o Ask about: age, marital status, religious affiliation, place of origin.
2. Where and with whom do you currently live?
3. How are you currently supporting yourself financially? What has been your usual occupation, way of making a living? *Probe – fishing or farming, daily labour, private employment, civil service, small scale enterprise etc.*
4. In Fiji we often have children, some of whom are biologically ours and others that aren't, but we still care for. Can you tell me about the number and different types of children that you have and care for?

KNOWLEDGE OF LF, SCABIES AND IMPETIGO

Purpose – To assess the level of knowledge that community members have about LF, scabies and impetigo, including how it's transmitted, prevented and treated.

1. Tell me about scabies and impetigo in your village? Is it common? Who does it affect? Why?
2. What words are used locally to talk about scabies and impetigo?
3. What have you been told about scabies and impetigo? *Probe – what do scabies look like?*
Difference between scabies and impetigo?
 - a) What causes scabies and impetigo? *Probe – small insects, dietary deficiency, dirt, change in the weather.*
 - b) How is it transmitted? *Probe – how does it move from person to person?*
4. Who usually gets scabies? *Probe – adults vs children vs grandparents vs other people? iTaukei (Indigenous) vs Indo-Fijian? Why?*
5. What do you know about scabies and impetigo treatment?
6. What do you know about how to prevent scabies and impetigo?
7. Where did you learn/hear this information? *Probe – health worker (nurse, doctor)? family, friends or colleagues? What was said?*
8. Repeat questions with focus on LF.

EXPERIENCE WITH LF, SCABIES AND IMPETIGO

Purpose – To understand their experiences with scabies, including reoccurrence of LF and scabies symptoms.

1. Tell me about scabies and impetigo in your family? Who is affected? With what symptoms? Frequency?
2. Have you or anyone in your family experienced a rash and intense itching on your skin that gets worse at night? *Probe for scabies symptoms – scabies rash (blisters, bumps or pimples), itching a rash between the fingers, on the arms, legs etc. If yes, who?*
3. Have these symptoms ever lead to skin sores? *Probe for impetigo symptoms – open sores, blisters filled with fluid, yellowish crust etc.*
4. Do you or anyone in your family have these symptoms now? If not, when was the last time anyone had these symptoms?
5. What do you think caused these symptoms? *Probe – small insects, dietary deficiency, dirt, change in the weather.*
6. Repeat questions with focus on LF.

MANAGEMENT/TREATMENT FOR LF, SCABIES AND IMPETIGO

Purpose – To understand their behaviours related to LF and scabies management and treatment (formal and informal strategies)

1. Have you ever done anything about these symptoms to make it better?
 - a. If no, why not?
 - b. If yes,
 - i. what did you do? *Probe around clinic, traditional medicine, other management.*

-
- ii. how long after the symptoms presented did you first do something about the symptoms? What was the tipping point?

 - 2. *If went to the clinic -*
 - a. What made you decide to go to the clinic? *Probe around severity of scabies or impetigo.*
 - b. Which clinic did you go?
 - c. Who did you see and what did they say about scabies/impetigo? Diagnosis?
 - d. How did that information help you or not?
 - e. How did you feel when you were told that you/someone in your family had scabies?
Probe for worries, relief, what was helpful, etc.
 - f. Did you receive treatment? If yes,
 - i. How did you feel about taking this treatment?
 - ii. What did you like/dislike about the treatment?
 - iii. Have you experienced any side effects? If yes, what side effect/s have you experienced and how have you coped with them?
 - iv. Did the treatment work?
 - v. Since taking the treatment have you experienced scabies/impetigo like symptoms?

 - 3. *If used traditional medicine –*
 - a. Some people in Fiji also use other types of medicine/therapy to treat illnesses. Have you used or are you using any other forms of treatment to manage scabies/impetigo? *Probe – herbal leaves to reduce itching, coconut oil etc.*
 - b. How has this helped? Has it reduced the severity of your symptoms etc?

 - 4. *Other management –*
 - a. What other ways have you managed scabies/impetigo? *Probe – hygiene/showers, change diet etc.*
 - b. How has this helped? Has it reduced the severity of your symptoms etc?

 - 5. Repeat questions with focus on LF.

IMPACT OF LF, SCABIES AND IMPETIGO

Purpose – To understand the impact of scabies/impetigo on their life, including health, economic and social factors.

- 1. Tell me about how scabies and impetigo has impacted on your life? *Probe – health, social, economic? Any difference between scabies and impetigo?*

- 2. How have scabies/impetigo symptoms disrupted your family's day-to-day life?
 - a. What impact has scabies/impetigo had on your/your family's health? *Probe – trouble sleeping, poor health, emotional wellbeing etc. Difference between scabies and impetigo?*
 - b. What impact has scabies/impetigo had on your/your family's income? *Probe – unable to work, cost of treatment etc. can you estimate Difference between scabies and impetigo?*

- c. What impact has scabies/impetigo had on your/your family's social life? *Probe – child's schooling, attending church or other social events etc. Difference between scabies and impetigo?*
- 3. Has scabies/impetigo had different impacts for different family members?
 - a. Children - *Probe – school, friends, teasing.*
 - b. Adults - *Probe – work, socialising, financially.*
 - c. Older family members – *Probe – wellbeing, skin issues*
- 4. Repeat questions with focus on LF.

PREVENTION OF LF AND SCABIES

Purpose – To identify any preventative measures being used to prevent the spread of scabies; examine individual, household and community efforts

- 1. What different things do people in Fiji do to prevent scabies? *Probe – individual, household, community levels*
- 2. What are you and other members in your household doing to prevent scabies?
 - a. Individual? *Probe – avoid close contact with relatives, shaking hands, hygiene etc.*
 - b. Household? *Probe – sleeping arrangements, no sharing towels, clothes etc., regularly washing bedding, towels, clothes etc.*
 - c. How do different members of your family deal with scabies prevention? *Probe – grandparents? Pass down knowledge? Children vs adults etc.*
- 3. Has your settlement/village ever worked together to prevent the spread of scabies? *Probe – village meeting to discuss scabies, mass cleaning of clothes and bedding when outbreak occurred etc.*
- 4. Some people in Fiji also use other types of medicine/therapy prevent illnesses. Are you using any other measures to help prevent people in your household from getting scabies?
- 5. Where did you learn about these prevention strategies?
- 6. Has the Ministry of Health, a nurse or a community-based organisation every come into your settlement/village and provided education around early recognition and awareness of scabies? *Probe – health promotion, promotion of community-based action around prevention etc.*
 - a. If yes, what did they share with you?
 - b. Was it helpful? Did it change the way your family manages scabies/impetigo?
- 7. Repeat questions with focus on LF.

MASS DRUG ADMINISTRATION INTERVENTION

Purpose – To determine people's thoughts and acceptance of MDA in their community

Soon, a new activity will be happening [name of community] where everyone, both adults and children, will be treated for scabies/impetigo and lymphatic filariasis. Health care workers will travel around and administer xxx doses of xxx. The goal is to eliminate scabies, impetigo and lymphatic filariasis from your community.

1. Have you heard about this activity before for treating scabies and impetigo? What about lymphatic filariasis?
2. What have you heard about it? Who told you?
3. Will you and your family be willing to take it? Why / why not? *Probe – confidence in the medication, acceptability of the number of tablets etc.*
4. What would encourage you to take this treatment? *Probe – health benefits, others taking it etc.*
5. What are people saying about this type of treatment? *Probe for positives and negatives.*
6. Even people who don't have any symptoms of scabies/impetigo/lymphatic filariasis will be asked to take part. How do you think people will feel about being asked to take medication for scabies/impetigo/lymphatic filariasis if they have no symptoms? Will they be happy to participate, or will they be worried or unsure?
 - a) If happy: Why are people happy to participate?
 - b) If worried / unsure: What might make people more comfortable with being treated for scabies/impetigo/lymphatic filariasis?
7. What would participating in the MDA program mean for your family and your community?

CONCLUDING THE INTERVIEW

Do you have any other recommendations for improving scabies and impetigo treatment in your area?

Is there anything you would like to add or elaborate on?

Is there any issue that you feel we haven't covered in this interview that is important to you that you would like to talk about?

APPENDIX 20: INTERVIEW GUIDE FOR KEY INFORMANT

INTERVIEW GUIDE

KEY INFORMANT

Theme	Purpose
Introduction	Obtain some basic information about the participant and their work.
Scabies and impetigo in Fiji	To assess the perceived scale of LF, scabies and impetigo in Fiji and its impact on the population
Transmission	To determine the geographical, structural and behavioural environments that facilitate and sustain LF and scabies transmission.
Health services	To determine successes and gaps in LF, scabies and impetigo treatment services.
Community-based interventions	To determine availability and strength of community-based interventions to prevent LF, scabies and impetigo.
Policy	To determine successes and gaps in LF, scabies and impetigo policy and service provision.
Conclusion	Warm down participant and seek any missed views/ideas.

INTRODUCTION QUESTIONS

Purpose – Obtain some basic information about the participant and their work

1. Can you tell me a bit about yourself?
 - a. Your role and responsibilities within the organisation?
 - b. How long you have worked in this role?
 - c. Which provinces in Fiji is your organisation currently working?
 - d. Which other organisations are you working with at local, provincial and national levels?

LF, SCABIES AND IMPETIGO IN FIJI

Purpose – To assess the perceived scale of LF, scabies and impetigo in Fiji and its impact on the population.

1. Tell me about scabies and impetigo in Fiji? Is it common? Who does it affect? Why?
2. What impact do scabies and impetigo have on the Fijian population? *Probe – health, financial and social.*
3. How do scabies/impetigo impact different people in Fiji?
 - a. Children - *Probe – school, friends, teasing.*
 - b. Adults - *Probe – work, socialising, financially.*
 - c. Older family members – *Probe – wellbeing, skin issues.*

-
4. How is scabies and impetigo perceived in Fiji? *Probe – normal part of life, big problem etc.*
 5. Repeat questions with focus on LF.

LF AND SCABIES TRANSMISSION

Purpose – To determine the geographical, structural and behavioural environments that facilitate and sustain scabies transmission

1. What are the main facilitators of scabies transmission in Fiji? *Probe – individual, household, structural factors.*
2. What do you see as the key social determinants of scabies transmission in Fiji?
 - *Probe – Overcrowded homes, poor hygiene, poverty, barriers to access to health services, mobility.*
3. How, if at all, do these issues differ across different communities in Fiji? Vanua Levu?
4. Who is most likely to contract scabies in Fiji? Vanua Levu? Why?
5. What is currently being done at a policy and programmatic level to address these issues? What else can be done?
6. Repeat questions with focus on LF.

HEALTH SERVICES

Purpose – To determine successes and gaps in LF, scabies and impetigo treatment services

1. What health services are available for scabies and impetigo in Fiji? Settlements vs villages? Capacities in different regions? Vanua Levu?
2. Under what circumstances do people seek medical treatment for scabies and impetigo? Why? Where do they go?
3. Which groups of people tend to access medical treatment?
4. What are the reasons you think people do not seek medical treatment? *Probe around barriers – individual, social, cultural, religious etc.*
5. What are the current strengths of scabies related treatment approaches in Fiji? What is working well? Why?
6. What are the main challenges of delivering scabies related treatment in Fiji?
7. What do you think could be done to strengthen scabies screening, diagnosis and treatment?
 - a. What is currently being done?
 - b. What is currently missing?
 - c. What aspects of service delivery could be improved? Why? How would this help?
8. Repeat questions with focus on LF.

COMMUNITY-BASED INTERVENTIONS

1. What community-based interventions exist to manage scabies and impetigo in Fiji? (MDA vs health promotion)
 - a. What is involved in each?
2. How successful have community-based scabies and impetigo interventions been to date? (MDA vs health promotion)
3. How have communities responded to community-based interventions? (MDA vs health promotion)
4. What have been some of the challenges to implementing MDA for treatment of scabies?
5. What do you think could be done to strengthen future community-based interventions? (MDA vs health promotion)
6. Are you aware of any other types of medicine/therapy people in Fiji are using to prevent or treat scabies and impetigo in Fiji?
7. Repeat questions with focus on LF.

POLICY IMPLEMENTATION

Purpose – To determine successes and gaps in LF, scabies and impetigo policy and service provision

1. In your view, what works well and what are the potential challenges and gaps in current scabies policy and service provision?
2. How can these policies, programs and services be improved?
 - a. Policy level?
 - b. Clinical setting?
 - c. Community setting?
 - d. Awareness and education?
 - e. Other support?
3. What advice would you give other service providers working with this population?
4. Repeat questions with focus on LF.

CONCLUDING THE INTERVIEW

Is there anything you would like to add or elaborate on?

Is there any issue that you feel we haven't covered in this interview that is important to you that you would like to talk about?

APPENDIX 21: PARTICIPANT INFORMATION SHEET FOR IN-DEPTH INTERVIEW: COMMUNITY MEMBER

With the Northern Division Scabies Control Project ('the project'), we will be offering medicine for scabies to everyone in the Northern Division. This process is called mass drug administration. We want to find out what effect this will have on scabies and its associated serious bacterial complications. As part of this project, we are asking some people who participated in that study to take part in an in-depth interview. It is important that you understand why we are doing this interview, so please read this information sheet carefully. If you have any more questions, ask the interviewer and they will try to answer them for you.

Why we are conducting this interview

We are interested in finding out what you thought about taking part in the mass drug administration for scabies and lymphatic filariasis. We also want to find out your experiences with lymphatic filariasis and scabies and how people, particularly you, understand lymphatic filariasis and scabies infection. This interview will help us understand what members of your community think about a mass drug administration program. It will also help us identify how people living in your community understand and deal with infections such as lymphatic filariasis and scabies and identify ways to improve how people get diagnosed and treated, how to make treatment more manageable and how to prevent other people becoming infected. Your participation is entirely voluntary and you are under no obligation to participate. Whether or not you choose to participate, your status and access to health care will not be affected in any way. There are no anticipated risks or benefits to participation in this study.

What the interview will involve

If you decide to take part in the research, we will ask you to take part in an interview. The conversation will be guided by the questions asked by the researcher where you will be asked about your experiences, thoughts and opinions around lymphatic filariasis and scabies, treatment, engagement and experience of services, and your suggestions around further improvements. There are no right or wrong answers to the questions we will ask – we are just asking you about your own thoughts and experiences. You can choose not to answer some of the questions if you want. You do not have to give the interviewer a reason. You can also stop the interview any time you want. The interview will take about one hour in a location where you feel happy, safe and where nobody will be able to hear what is being talked about.

Your privacy

The information that you provide during our discussion will be completely confidential. We will not record your name and you will be assigned an identification number for our records. We will take some written notes during our discussion. If you agree to participate in the interview, with your permission we would like to record the discussion using a digital audio-recorder so that we can capture your story. All files will remain with the study coordinator and will be kept in a locked cabinet and all electronic files will be password protected. The main research team in this country from the Murdoch Children's Research Institute in Melbourne, Australia will access the study files and the ethics boards of the Fiji National Research Ethics Review Committee and The Royal Children's Human Research Ethics Committees if necessary

I have read the information sheet provided or it has been read to me concerning this study. I understand what will be required of me if I participate in this study, which will be a verbal interview and discussion.

My questions regarding this study have been answered by: _____

I understand that at any time I may withdraw from this study without giving a reason and without having any effect on my access to health care.

I agree to take part in this study.

Signature of the respondent: _____

Signature of a witness: _____

Signature of the enumerator to indicate that the informed consent has been read and the information sheet given to the respondent: _____

PARTICIPANT INFORMATION SHEET

In-depth Interview: Key Informant

With the Northern Division Scabies Control Project ('the project'), we will be offering medicine for scabies to everyone in the Northern Division. This process is called mass drug administration. We want to find out what effect this will have on scabies and its associated serious bacterial complications. As part of this project, we are asking key informants working closely with the study population to take part in an in-depth interview. It is important that you understand why we are doing this interview, so please read this information sheet carefully. If you have any more questions, ask the interviewer and they will try to answer them for you.

Why we are conducting this interview

We are interested in finding out about community experiences and understandings of scabies and lymphatic filariasis infection, including acceptability of mass drug administration. We are also interested in learning more about scabies and lymphatic filariasis diagnosis and treatment in Fiji and the health seeking behaviours of the study population. You have been invited because as a key informant working closely with this identified population group, we believe you will provide important information from your experiences. This interview will help us understand community acceptability of mass drug administration and help us to identify ways to improve how people get diagnosed and treated, how to make treatment more manageable and how to prevent other people becoming infected. Your participation is entirely voluntary and you are under no obligation to participate. There are no anticipated risks or benefits to participation in this study.

What the interview will involve

If you decide to take part in the research, we will ask you to take part in an interview. The conversation will be guided by the questions asked by the researcher where you will be asked about your experiences, thoughts and opinions around scabies and lymphatic filariasis. For stakeholders like yourself, we will ask you about your knowledge of scabies and lymphatic filariasis; your experiences and involvement in providing scabies and lymphatic filariasis diagnosis and treatment; your knowledge and observations around the roll out of mass drug administration to control scabies and lymphatic filariasis in Fiji; and the health seeking behaviours in relation to people with scabies and/or lymphatic filariasis. Finally, we will ask you to discuss the issues faced as service providers and the suggestions around future improvements. There are no right or wrong answers to the questions we will ask – we are just asking you about your own thoughts and experiences. You can choose not to answer some of the questions if you want. You do not have to give the interviewer a reason. You can also stop the interview any time you want. The interview will take about one hour in a location where you feel happy, safe and where nobody will be able to hear what is being talked about.

Your privacy

The information that you provide during our discussion will be completely confidential. We will not record your name and you will be assigned an identification number for our records. We will take some written notes during our discussion. If you agree to participate in the interview, with your permission we would like to record the discussion using a digital audio-recorder so that we can capture your story. All files will remain with the study coordinator and will be kept in a locked cabinet and all electronic files will be password protected. The main research team in this country from the Murdoch Children's Research Institute in Melbourne, Australia will access the study files and the ethics boards

I have read the information sheet provided or it has been read to me concerning this study. I understand what will be required of me if I participate in this study, which will be a verbal interview and discussion.

My questions regarding this study have been answered by: _____

I agree to take part in this study.

Signature of the respondent: _____

Signature of a witness: _____

Signature of the enumerator to indicate that the informed consent has been read and the information sheet given to the respondent: _____

APPENDIX 23: DERMATOLOGY LIFE QUALITY INDEX (DLQI) QUESTIONNAIRE**DERMATOLOGY LIFE QUALITY INDEX (DLQI)**

Hospital No:

Date:

Name:

Score:

Address:

Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life
OVER THE LAST WEEK. Please tick (✓) one box for each question.

- | | | | | | | | | |
|--|-----------|--------------------------|----------|--------------------------|--------------|--------------------------|------------|--------------------------|
| 1. Over the last week, how itchy, sore, painful or stinging has your skin been? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 2. Over the last week, how embarrassed or self conscious have you been because of your skin? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 4. Over the last week, how much has your skin influenced the clothes you wear? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 5. Over the last week, how much has your skin affected any social or leisure activities? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 6. Over the last week, how much has your skin made it difficult for you to do any sport? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 7. Over the last week, has your skin prevented you from working or studying? | Yes | <input type="checkbox"/> | No | <input type="checkbox"/> | Not relevant | <input type="checkbox"/> | | |
| If "No", over the last week how much has your skin been a problem at work or studying? | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> | | |
| 8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 9. Over the last week, how much has your skin caused any sexual difficulties? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| 10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time? | Very much | <input type="checkbox"/> | A lot | <input type="checkbox"/> | A little | <input type="checkbox"/> | Not at all | <input type="checkbox"/> |
| | | | | | Not relevant | <input type="checkbox"/> | | |

Please check you have answered **EVERY** question. Thank you.

Trouble with Skin

The aim of the questionnaire is to measure how much your skin problem has affected you OVER THE LAST WEEK. Please tick ✓ one box for each question.

OVER THE LAST WEEK

Very much

Quite a lot

A little

Not at all



How itchy, 'scratchy', sore or painful has your skin been?

Very much

Quite a lot

A little

Not at all



How much has your skin affected your friendships?

Very much

Quite a lot

A little

Not at all



How much has your skin trouble affected going out, playing or doing hobbies?

OVER THE LAST WEEK

Very much

Quite a lot

A little

Not at all



How upset or embarrassed, self conscious or sad have you been because of your skin?

Very much

Quite a lot

A little

Not at all



How much have you changed or worn different or special clothes/shoes because of your skin?

Very much

Quite a lot

A little

Not at all



How much have you avoided swimming or other sports because of your skin trouble?

Children's Dermatology Life Quality Index



If school time: How much did your skin affect your **school work**?

If holiday time: How has your skin problem interfered with your **holiday plans**?

OVER THE LAST WEEK

Very much



Quite a lot



A little



Not at all



OVER THE LAST WEEK

Very much



Quite a lot



A little



Not at all



How much trouble have you had because of your skin with other people **calling you names, teasing, bullying, asking questions or avoiding you?**

How much has your **sleep** been affected by your skin problem ?

Hospital No.:

Name :

Age:

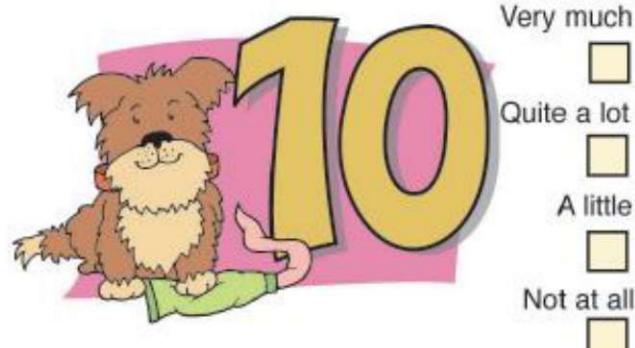
Address:

Diagnosis:

Date:

CDLQI SCORE:

CDLQI ©M.S. Lewis-Jones, A.Y. Finlay June 1993
Illustrations ©Media Resources Centre, UWCMD, Dec 1996



How much of a problem has the **treatment** for your skin been ?

Please check that you have answered **EVERY** question. Thank you.

APPENDIX 25: AQOL-6D QUESTIONNAIRE

AQoL-6D (Data Collection Copy Simplified)

Tick the box that best describes your situation as it has been over the past week

Q1 How much help do you need with jobs around your place of residence (eg preparing food, cleaning, gardening)?

- I can do all these tasks very quickly and efficiently without any help
- I can do these tasks relatively easily without help
- I can do these tasks only very slowly without help
- I cannot do most of these tasks unless I have help
- I can do none of these tasks by myself.

Q2 How easy or difficult is it for you to get around by yourself outside your place of residence (eg to go shopping, visiting)?

- getting around is enjoyable and easy
- I have no difficulty getting around outside my place of residence
- I have a little difficulty
- I have moderate difficulty
- I have a lot of difficulty
- I cannot get around unless somebody is there to help me.

Q3 How easy or difficult is it for you to move around (using any aids or equipment you need eg a wheelchair, frame or stick)?

- I am very mobile
- I have no difficulty with mobility
- I have some difficulty with mobility (for example, going uphill)
- I have difficulty with mobility. I can go short distances only.
- I have a lot of difficulty with mobility. I need someone to help me.
- I am bedridden.

Q4 How difficult is it for you to wash, toilet, dress yourself, eat or care for your appearance?

- these tasks are very easy for me
- I have no real difficulty in carrying out these tasks
- I find some of these tasks difficult, but I manage to do them on my own
- many of these tasks are difficult, and I need help to do them
- I cannot do these tasks by myself at all.

Q5 How happy are you with your close and intimate relationships?

- very happy
- generally happy
- neither happy nor unhappy
- generally unhappy
- very unhappy

Q6 Does your health affect your relationship with your family?

- my role in the family is unaffected by my health
- there are some parts of my family role I cannot carry out
- there are many parts of my family role I cannot carry out
- I cannot carry out any part of my family role.

Tick the box that best describes your situation as it has been over the past week

Q7 Does your health affect your role in your community (eg residential, sporting, church or cultural groups)?

- my role in the community is unaffected by my health
- there are some parts of my community role I cannot carry out
- there are many parts of my community role I cannot carry out
- I cannot carry out any part of my community role.

Q8 How often did you feel in despair over the last seven days?

- never
- occasionally
- sometimes
- often
- all the time.

Q9 How often did you feel worried in the last seven days?

- never
- occasionally
- sometimes
- often
- all the time.

Q10 How often do you feel sad?

- never
- rarely
- some of the time
- usually
- nearly all the time.

Q11 Do you normally feel calm and tranquil or agitated?

I am

- always calm and tranquil
- usually calm and tranquil
- sometimes calm and tranquil, sometimes agitated
- usually agitated
- always agitated.

Q12 How much energy do you have to do the things you want to do?

I am

- always full of energy
- usually full of energy
- occasionally energetic
- usually tired and lacking energy
- always tired and lacking energy.

Q13 How often do you feel in control of your life?

- always
- mostly
- sometimes
- only occasionally
- never.

Tick the box that best describes your situation as it has been over the past week

Q14 How much do you feel you can cope with life's problems?

- completely
- mostly
- partly
- very little
- not at all.

Q15 How often do you experience serious pain?

I experience it

- very rarely
- less than once a week
- three to four times a week
- most of the time.

Q16 How much pain or discomfort do you experience?

- none at all
- I have moderate pain
- I suffer from severe pain
- I suffer unbearable pain.

Q17 How often does pain interfere with your usual activities?

- never
- rarely
- sometimes
- often
- always

Q18 How well can you see (using your glasses or contact lenses if needed)?

- I have excellent sight
- I see normally
- I have some difficulty focusing on things, or I do not see them sharply. *E.g. small print, a newspaper or seeing objects in the distance.*
- I have a lot of difficulty seeing things. *My vision is blurred. I can see just enough to get by with.*
- I only see general shapes. *I need a guide to move around*
- I am completely blind.

Q19 How well can you hear (using your hearing aid if needed)?

- I have excellent hearing
- I hear normally
- I have some difficulty hearing or I do not hear clearly. *I have trouble hearing softly-spoken people or when there is background noise.*
- I have difficulty hearing things clearly. *Often I do not understand what is said. I usually do not take part in conversations because I cannot hear what is said.*
- I hear very little indeed. *I cannot fully understand loud voices speaking directly to me.*
- I am completely deaf.

Q20 How well do you communicate with others (talking, signing, texting, being understood by others and understanding them)?

- I have no trouble speaking to them or understanding what they are saying
- I have some difficulty being understood by people who do not know me. I have no trouble understanding what others are saying to me.
- I am understood only by people who know me well. I have great trouble understanding what others are saying to me.
- I cannot adequately communicate with others.

APPENDIX 26: ADOLESCENT AQOL-6D QUESTIONNAIRE

Adolescent AQoL- 6D Simplified

(Generic QoL for Adolescents)

This questionnaire has six sections:

1. Physical ability
2. Social and family relationships
3. Mental health
4. Coping
5. Pain
6. Vision, hearing and communication

You answer each question by ticking the box next to the response that best fits your situation.

Example answer



Most of the time Tom enjoys a good relationship with his family so he marks the second box from the top to show his answer:

How happy are you with your relationships with your family?

- very happy
- generally happy
- neither happy nor unhappy
- generally unhappy
- very unhappy
- this question is not relevant to me.

Physical ability

Questions 1 to 4 are about how well you are physically able to do things for yourself.

Q1 How much help do you need when you do jobs around where you live
(eg. cleaning, helping with meals, working in the garden)?

- I can do all these jobs very quickly and easily without any help
- I can do these jobs relatively easily without help
- I can do these jobs only very slowly without help
- I cannot do most of these jobs unless I have help
- I can do none of these jobs by myself
- I never do jobs where I live although I am able to do so. (*same score as second response*)

Q2 How easy or difficult is it for you to get around **by yourself** outside your home
(eg. at school, going out with my friends)?

- getting around is enjoyable and easy
- I have no difficulty getting around outside my house
- a little difficulty
- moderate difficulty
- a lot of difficulty
- I cannot get around unless somebody is there to help me.

Q3 How well can you walk or run?

- I find walking or running very easy.
- I have no real difficulty with walking or running.
- I find walking or running slightly difficult.
(*I cannot run to catch a bus or train, I find walking uphill difficult.*)
- Walking is difficult for me.
(*I walk short distances only. I have difficulty walking up stairs.*)
- I have great difficulty walking.
(*I cannot walk without a walking stick or frame, or someone to help me.*)
- I am bedridden.

Q4 How easy is washing yourself, going to the toilet, dressing, eating, and looking after your appearance?

- These tasks are very easy for me.
- I have no real difficulty in carrying out these tasks.
- I find some of these tasks difficult, but I manage to do them on my own.
- Many of these tasks are difficult, and I need help to do them.
- I cannot do these tasks by myself at all.

Social and family relationships

Questions 5 to 7 are about your relationships and involvement with your family, friends and local community, and how they are affected by your health.

Q5 How happy do your close friendships make you?

- very happy
- generally happy
- neither happy nor unhappy
- generally unhappy
- very unhappy

Q6 Does your health affect your relationship with your family?

- My relationship with my family is unaffected by my health.
- Some parts of my relationship with my family are affected by my health.
- Many parts of my relationship with my family are affected by my health.
- Every part of my relationship with my family is affected by my health.

Q7 How does your health affect your involvement in groups, clubs, sporting or school activities?

- My involvement with such groups is not affected by my health.
- There are some group activities I am not involved in because of my health.
- There are many group activities I am not involved in because of my health.
- I am not involved in any group activities because of my health.

Mental health

Questions 8 to 11 are about my mental health.

Q8 How often did you feel in despair (lost and hopeless) over the last seven days?

- never
- occasionally
- sometimes
- often
- all the time.

Q9 How often did you feel worried over the last seven days?

- never
- occasionally
- sometimes
- often
- all the time.

Q10 How often do you feel sad?

- never
- rarely
- sometimes
- usually
- nearly all the time.

Q11 How often do you feel calm or agitated (stressed)?

- always calm
- usually calm
- sometimes calm, sometimes agitated
- usually agitated
- always agitated.

Coping

Questions 12 to 14 are about my ability to cope with things.

Q12 How much energy do you have to do the things you want to do?

- always full of energy
- usually full of energy
- occasionally full of energy
- usually tired and lacking energy
- always tired and lacking energy.

Q13 How often do you feel you manage your life well?

- always
- mostly
- sometimes
- only occasionally
- never.

Q14 How much do you feel you can cope with life's problems (such as conflict with family or friends, doing exams etc.)?

- completely
- mostly
- partly
- very little
- not at all.

Questions 15 to 17 are about my experiences of physical pain.

Q15 How often do you experience serious physical pain?

- very rarely
- less than once a week
- three to four times a week
- most of the time.

Q16 How much physical pain or discomfort do you experience?

- none at all
- I have moderate pain
- I suffer from severe pain
- I suffer unbearable pain.

Q17 How often does physical pain interfere with your usual activities?

- never
- rarely
- sometimes
- often
- always.

Vision, hearing and communication

Questions 18 to 20 are about seeing, hearing and communicating.

Q18 How good is your vision (with your glasses or contact lenses if you wear them)?

- I have excellent sight.
- I see normally.
- I have some difficulty focusing on things, or I do not see them sharply.
(eg. small print, writing on the board or seeing objects in the distance)
- I have a lot of difficulty seeing things. *(My vision is blurred. I can see just enough to get by with.)*
- I only see general shapes. I need a guide to move around.
- I am completely blind.

Q19 How good is your hearing (with your hearing aid if you wear one)?

- I have excellent hearing
- I hear normally
- I have some difficulty hearing or I do not hear clearly. (*I have trouble hearing softly-spoken people or when there is background noise.*)
- I have difficulty hearing things clearly. (*Often I do not understand what is said. I usually do not take part in conversations because I cannot hear what is said.*)
- I hear very little indeed. (*I cannot fully understand loud voices speaking directly to me.*)
- I am completely deaf.

Q20 How well can you communicate with others (eg. by talking, listening, writing or using sign language)?

- I have **no** difficulty speaking to them or understanding what they are saying.
- I have **some** difficulty being understood by people who do not know me.
I have no trouble understanding what others are saying to me.
- I have **great** trouble understanding what others are saying to me.
I am understood only by people who know me well.
- I cannot communicate with others.

APPENDIX 27: INFANT'S DERMATITIS QUALITY OF LIFE INDEX- MODIFIED FOR SKIN DISEASES**Draft 7****INFANTS' SKIN DISEASE QUALITY OF LIFE INDEX (IDQOL modified)**

Name:
Address:

Date:**IDQOL
SCORE**

The aim of this chart is to record how your child's scabies has been. Each question concerns THE LAST WEEK ONLY. Please could you answer every question.

Dermatitis Severity

Over the last week, **how severe** do you think your child's skin disease has been?; i.e. how itchy, inflamed or widespread.

- Extremely severe
 Severe
 Average
 Fairly good
 None

Life Quality Index

- | | |
|--|--|
| 1. Over the last week, how much has your child been itching and scratching? | All the time <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
None <input type="checkbox"/> |
| 2. Over the last week, what has your child's mood been? | Always crying, extremely difficult <input type="checkbox"/>
Very fretful <input type="checkbox"/>
Slightly fretful <input type="checkbox"/>
Happy <input type="checkbox"/> |
| 3. Over the last week approximately how much time on average has it taken to get your child off to sleep each night? | More than 2 hrs <input type="checkbox"/>
1 - 2 hrs <input type="checkbox"/>
15mins - 1 hr <input type="checkbox"/>
0-15mins <input type="checkbox"/> |
| 4. Over the last week, what was the total time that your child's sleep was disturbed on average each night? | 5 hrs or more <input type="checkbox"/>
3 - 4 hrs <input type="checkbox"/>
1 - 2 hrs <input type="checkbox"/>
Less than 1 hour <input type="checkbox"/> |
| 5. Over the last week, has your child's skin disease interfered with playing or swimming? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
Not at all <input type="checkbox"/> |
| 6. Over the last week, has your child's skin disease interfered with your child taking part in or enjoying other family activities? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
Not at all <input type="checkbox"/> |
| 7. Over the last week, have there been problems with your child at mealtimes because of the skin disease? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
None <input type="checkbox"/> |
| 8. Over the last week, have there been problems with your child caused by the treatment? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
None <input type="checkbox"/>
Has not had treatment <input type="checkbox"/> |
| 9. Over the last week, has your child's skin disease meant that dressing and undressing the child has been uncomfortable? | Very much <input type="checkbox"/>
A lot <input type="checkbox"/>
A little <input type="checkbox"/>
None <input type="checkbox"/> |
| 10. Over the last week how much has your child | Very much <input type="checkbox"/> |

having skin disease been a problem at bathtime?	A lot	<input type="checkbox"/>
	A little	<input type="checkbox"/>
	None	<input type="checkbox"/>

Please can you check that you have answered every question.
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