IMPROVING THE DIAGNOSIS OF SCABIES IN LOW-RESOURCE SETTINGS

Millicent Osti

ORCID 0000-0002-0588-9238

Master of Philosophy

January 2020

Department of Paediatrics, Faculty of Medicine, Dentistry and Health Sciences

The University of Melbourne

Submitted in total fulfilment for the degree of Master of Philosophy

Abstract

Scabies is a parasitic disease and a global health problem that predominantly affects disadvantaged communities in low-resource settings. Scabies significantly impacts the health and quality of life of those with the disease. To accurately assess the global burden of disease and to compare data across regions, standardised diagnosis with consistent disease definitions is necessary. In low-resource settings, diagnosis by clinical assessment is the principal diagnostic method. In the absence of available experts, non-expert health workers are likely to play critical roles in diagnosis, including for prevalence mapping. Currently, standardised processes for clinical diagnosis for scabies do not exist. This thesis explores the diagnosis of scabies in low-resource settings and the role and utility of non-expert health workers in the diagnosis of scabies.

Chapter 3 describes the evaluation of non-expert health workers in the diagnosis of scabies and impetigo using clinical criteria. The diagnosis of four briefly-trained nurses was compared to the consensus diagnosis of two experienced doctors. The sensitivity of the nurses' diagnosis compared to the reference standard was 55.3% for scabies with a specificity of 89.9% Sensitivity for moderate to severe scabies was 93.5% with a specificity of 74%. The accuracy of diagnosis by non-expert health workers is promising and may be acceptable for scabies and impetigo disease mapping in low-resource settings.

Chapter 4 describes the development and evaluation of a training protocol for the diagnosis of scabies and impetigo for non-expert health workers. The aim of this study was to measure the change in knowledge and confidence of the participants and explore their experience and perceptions of the training. Training was evaluated using a case-based test, a questionnaire and semi-structured interviews. The overall results of the case-based test were 90% for scabies and 75.5% for impetigo. The mean score for both self-reported knowledge and confidence

increased from 2.5 to 4.5 following training and scores increased for all nurses (mean difference 2, 95%CI 1.1-2.9, P=0.005). The study showed that training local health staff in scabies diagnosis was enjoyable for participants and led to improvements in self-reported knowledge and confidence.

Chapter 5 investigates the prevalence of scabies and impetigo using a cross-sectional study in a primary school in Gizo in the Solomon Islands. Using the International Alliance for the Control of Scabies (IACS) diagnostic criteria the classified the diagnosis of scabies. The prevalence of scabies was 54.3% and prevalence of impetigo was 32.1%. 63.5% of those with impetigo had scabies, corresponding to a population attributable risk of 11.8%. The study highlighted the extremely high burden of these diseases supporting the need for interventions for scabies in this community.

Chapter 6 evaluates the methods of data collection, analysis and display for describing in detail the distribution of scabies lesions in a pilot study. The study used a novel technique of representation of dermatological lesions in the form of a choropleth map. The study found that the methods used were feasible for a larger population and would describe valuable detailed information on specific lesion location in scabies. The study will provide information on lesions at specific body sites to determine if simplified examinations are appropriate for prevalence surveys.

The public health control of scabies requires identification of high-prevalence communities to target interventions, as well as methods to monitor the effectiveness of interventions. Such programs would be dependent on accurate and standardised diagnosis for population mapping. This thesis suggests methods to improve the diagnosis of scabies in low-resource settings. Modifications to training and diagnostic methods are likely to improve diagnostic accuracy.

Improvements to scabies diagnosis will contribute to efficient collection methods and reliability of prevalence data.

Declaration

I hereby declare that:

1. This thesis comprises only my original work towards the degree of Master of Philosophy except where indicated in the preface;
2. Due acknowledgement has been made in the text to all other material used; and
3. The thesis is fewer than 50,000 words in length, exclusive of tables, maps, bibliographies and appendices.

Signed:

Millicent Osti

Date:

Preface

This thesis represents my original work.

I was the first author in the published manuscripts (Chapters 3 and 5) and made the major contribution to study design, implementation, analysis and writing. All co-authors have authorised the inclusion of these manuscripts within this thesis.

Chapters 1, 2, 4, 6 and 7 are entirely my work, supervised by Professor Andrew Steer and Dr Daniel Engelman. Additional assistance with graphics in Chapter 6 was provided by Fraser Daniell.

This work has not been submitted for any other qualifications.

No third-party editorial assistance was used in the preparation of this thesis.

Acknowledgements

I wish to thank the children of Gizo, Solomon Islands, and their families and teachers at Gizo Primary School. Without their involvement and support this research would not have been possible. I am grateful for their generosity in welcoming me into their community. I hope that this research will contribute towards improving health outcomes for the people of the Solomon Islands.

I wish to thank the local team, including staff Sana Bisili, Stephen Tiazi, Arthur Keremama, Winter Sino and Una Gagahe. I would like to thank Deanne Seppy, the local study coordinator and Nester Thugea the headmistress of Gizo Primary School. I also wish to thank Christina Gorae and Dickson Boara from the Western Province Ministry of Health and Oliver Sokana from the National Ministry of Health for their local expertise and support of this work.

I feel extremely privileged to have worked with the entire Tropical Diseases team at Murdoch Children's Research Institute. I am especially grateful to Matthew Parnaby and his logistical and programmatic assistance, as well as his good humour. I am also especially grateful to have shared an office space with Myra Hardy, Jun Thean, Jane Hawtin and Susie Lake, who provided encouragement, assistance and ongoing friendship.

I am very thankful to Dr Margot Whitfeld for her support, advice and enthusiasm, especially on the ground in the Solomon Islands.

I wish to thank Professor John Kaldor for his invaluable contributions to these studies and to Sophie Phelan for her help and companionship while in the Solomon Islands.

I want to thank Associate Professor Michael Marks for all of his contributions, especially his help and enthusiasm in Gizo.

I also wish to thank Anneke Grober for her assistance with statistics and data analysis.

I am very grateful to Fraser Daniell, who generously provided graphic design assistance.

I want to thank my advisory committee, Professor David Burgner and Associate Professor Catherine Satzke for their expertise, insights and helpful suggestions.

Notably, I am so very thankful to my supervisors Professor Andrew Steer and Dr Daniel Engelman.

Andrew gave me the most incredible opportunity to undertake this Master's and for that I will always be grateful. His support and advice was always grounded in positivity, kindness and openness. I feel extremely privileged to have had this opportunity to learn from him.

Dan was a constant source of advice and assistance helping me through every issue no matter how big or small. He challenged me to think and work in new ways and because of this I have learnt more than I could have imagined possible over the past two years.

I am inspired by Andrew and Dan's enthusiasm and passion for their work, their work ethic and their commitment to reducing health inequalities. Through the encouragement and opportunities they have provided to me, I have grown so much as a researcher, a clinician and a global citizen.

Most importantly, I want to thank my family for the education and opportunities they have provided me with, and for supporting me through all my endeavours. Especially to James, for encouraging me to seek out and pursue this, for his genuine interest in my work and for his unwavering support.

Publications and Presentations arising from this thesis

Publications

Osti MH, Sokana O, Gorae C, Whitfeld MJ, Steer AC, Engelman D. **The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy.** *PLoS Negl Trop Dis*. 2019;13(8):e0007635.

Osti MH, Sokana O, Phelan S, Marks M, Whitfeld MJ, Gorae C, et al. **Prevalence of scabies and impetigo in the Solomon Islands: a school survey.** *BMC Infect Dis.* 2019;19(1):803.

Presentations

Oral presentations

Scabies and impetigo in the Solomon Islands: a school survey using new diagnostic criteria, Australian College of Dermatology Rural Meeting, Orange, September 2019

Three-minute thesis, RCH Grand Rounds. Heat Runner Up and People's Choice, August 2019

Poster presentations

Accuracy of Non-expert Examiners in the Diagnosis of Scabies and Impetigo, World Congress of Dermatology, Milan, June 2019

Accuracy of Non-expert Examiners in the Clinical Diagnosis of Scabies and Impetigo, Australian College of Dermatology Annual Scientific Meeting, May 2019

Table of contents

Lists of Figures

List of Tables

Note: Additional Figures and Tables included in published works are not shown in these lists.

List of Abbreviations

DNA	Deoxyribonucleic acid
GIS	Geographic Information System
GTMP	Global Trachoma Mapping Project
HTLV-1	Human T-cell lymphotropic virus
HIV	Human Immunodeficiency Virus
IACS	International Alliance for the Control of Scabies
MDA	Mass drug administration
NGO	Non-governmental organisation
NTDs	Neglected tropical diseases
USD	United States Dollar
WHO	World Health Organization

Chapter 1. Background

Scabies is a parasitic skin disease caused by infestation with the mite *Sarcoptes scabiei* var. *hominis.* The 2016 Global Burden of Disease Study estimated a prevalence of 147 million, with an associated 3.8 million disability adjusted life years.[1, 2] In 2017, The World Health Organization added scabies to its list of Neglected Tropical Diseases (NTDs), outlining the need for large-scale control strategies.

Scabies causes itch, and with resultant scratching leads to broken skin and infection with bacterial pathogens, especially *Streptococcus pyogenes* and *Staphylococcus aureus.*[3] Bacterial co-infection of the skin may lead to more serious complications such as deep tissue infections or sepsis. Skin infection with *S. pyogenes* can also result in immune mediated complications including glomerulonephritis and possibly rheumatic heart disease.[4, 5]

The International Alliance of the Control of Scabies outlined the need for accurate global disease burden data in order to engage with relevant stakeholders and develop effective control measures.[6] A standardised approach to the diagnosis of scabies is required for reliable comparison of prevalence data across different time periods and regions. Beyond population mapping, standardised diagnosis is also needed for public health intervention trials, individually randomised clinical trials and disease surveillance.

A series of prevalence studies has demonstrated that scabies is a common condition in the Solomon Islands.[7-10] Scabies is recognized as a public health problem by the Solomon Islands Ministry of Health and Medical Services, although no formal control program is in place. Three trials of the community-based control of scabies have been conducted in the Solomon Islands, and provide an evidence base for future public health initiatives.[9, 10]

This thesis will investigate diagnostic methods for scabies in low-resource settings and explore ways to improve and standardize diagnosis through the training and utilisation of non-expert examiners.

1.1 Setting

1.1.1 Solomon Islands

The Solomon Islands is a Pacific nation comprised of 997 islands, positioned approximately 1800 kilometres to the north of Australia (Figure 1). The population of the Solomon Islands is approximately 520,000, with 80% of the population living in non-urban areas, mostly small rural villages.[11] The capital, Honiara, has a population of 64,600 and is situated on the island of Guadalcanal, one of six main islands.[11]

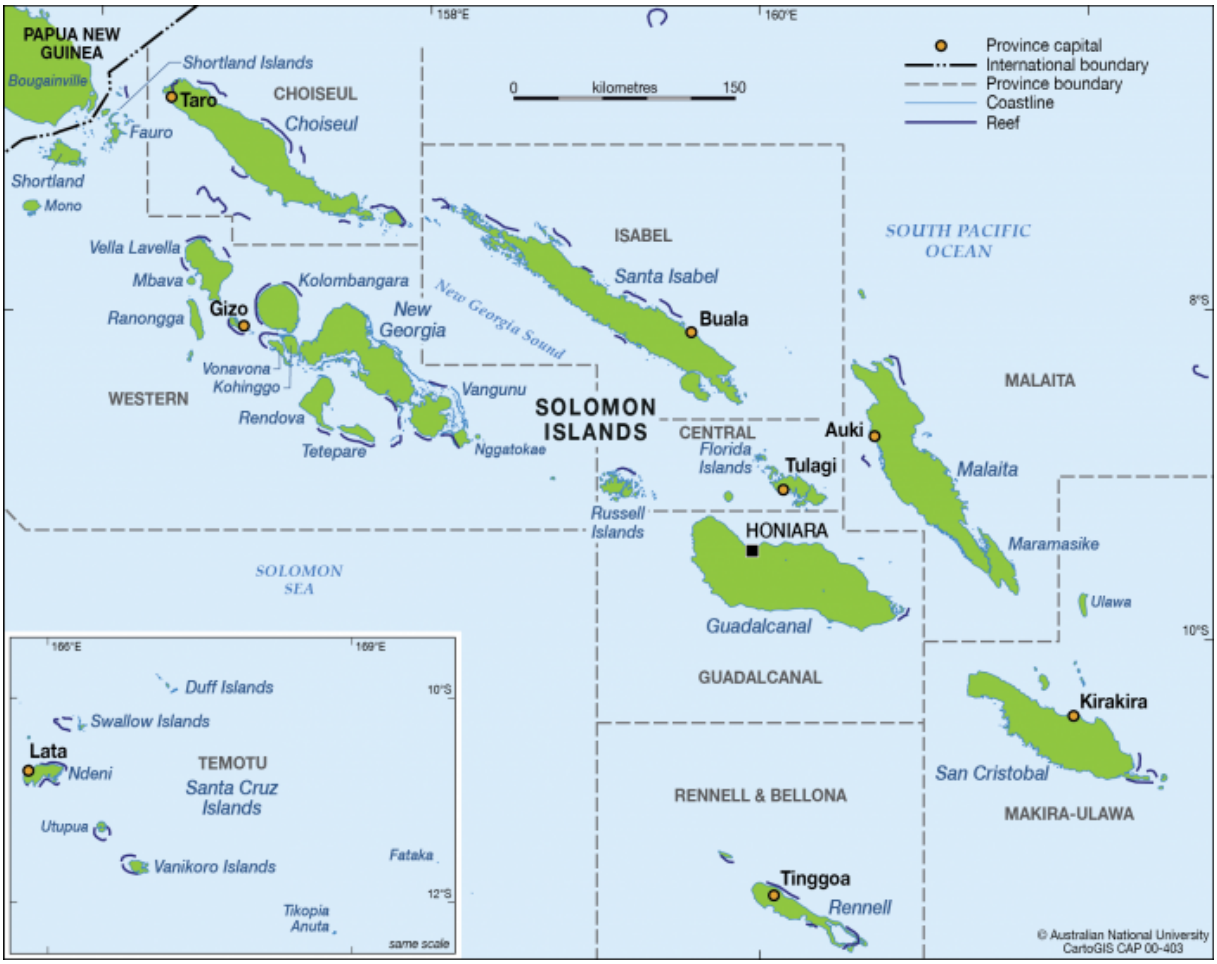


Figure 1. Map of the Solomon Islands

CartoGIS Services, College of Asia and the Pacific, The Australian National University[12]

Following independence from Britain in 1978, the Solomon Islands established a parliamentary democracy government with a constitutional monarch. The Queen is the head of state, represented in country by a Governor-General. A Prime Minister is elected by the Members of Parliament, with Parliament being a single chamber legislature made up of 50 single-member constituencies, elected every four years.[13] Local government is divided into the nine provinces; Central, Choiseul, Guadalcanal, Isabel, Makira-Ulawa, Malaita, Rennell-Bellona, Temotu and Western; and Honiara as a tenth administrative centre (Figure 1).

In 2017, the Solomon Islands were ranked 152 of 189 countries and territories on the United Nations Human Development Index, with a value of 0.546, correlating to the low human development category.[14]The main industries in the Solomon Islands are agriculture, fish and forestry, with the main source of income for most households being the sale of fish, crops or handicrafts.

1.1.2 Health and education status

In 2009, the average number of births per woman was 4.7. Infant mortality rate is 22 per 1000, compared to 3.1 per 1000 in Australia, and under-five mortality is 28 per 1000, compared to 3.5 in Australia.[11, 15, 16]

Life expectancy at birth is 66.2 years for males and 73.1 years for females. The maternal mortality ratio is 143 (per 100,000 live births), compared to 23 in Australia.[11, 17]The most recent Solomon Islands census in 2009, estimated that 56% of the population completed primary education, and 21% of males and 16% of females completed secondary education.[11]

1.1.3 Health care services

The Ministry of Health and Medical Services is the major provider of services across the Solomon Islands, supplemented by faith-based and local and international Non-Governmental Organizations (NGOs). There are five levels of health care; level 1: nurse aide posts, level 2: rural health clinics, level 3: area health centres, level 4: provincial hospitals and level 5: The National Referral Hospital (in Honiara). There are public provincial hospitals in eight of the nine provinces. However, most health care is provided by trained nurse aides in rural villages.[18] These nurse aides deliver basic primary care and facilitate referral to higher-level services when necessary.[18]

1.1.4 Western Province

The Western Province of the Solomon Islands has a population of approximately 77,000. The capital of the Western Province is Gizo town, located on the Island of Gizo. Gizo town has a population of around 3,500, making it the fifth largest urban centre in the Solomon Islands.[11]

The mortality rate for children aged less than five years is 29 per 1000 in Western Province, compared to 28 per 1000 nationally. Life expectancy at birth is 65.7 years for males and 72.5 years for females, 0.5 years and 0.6 years lower than the national average for males and females respectively.[19]

In the Western Province, only 56% of households have access to a toilet facility, such as a flush toilet, water sealed toilet or a pit latrine. Most households (76%) use kerosene lamps for lighting, and just 12% of households are connected to the electricity grid.[19]

1.2 Scabies in the Solomon Islands

There are no country-wide data for scabies in the Solomon Islands, but provincial prevalence studies have been conducted. A survey conducted in ten villages in the Western Province in 2014, which included 1908 participants, estimated a scabies prevalence of 19.2% and an impetigo of prevalence of 32.7%.[8] A 2018 study conducted in Malaita province of 1291 individuals, found a prevalence of scabies of 9.2-11.8%.[9] In Choiseul province, following assessment of 1399 individuals in 2015, the prevalence of scabies was found to be 18.7%.[10]

1.2.1 Control of scabies

There have been public health programs for other NTDs in the Solomon Islands, including for a national program for trachoma control. There is currently no department of NTDs with the Ministry of Health or control program for scabies, but scabies has been incorporated into the

draft NTD management plan. However, research interventions for scabies using mass drug administration (MDA) with ivermectin have been conducted in Malaita and Choiseul.[9, 10] Benzyl benzoate is on the Essential Medicines List in the Solomon Islands but due to limited resources and logistic difficulty it is not available at all health centres. Permethrin cream is not available in the Solomon Islands. Ivermectin is available but is limited to specialist use at the National Referral Hospital and some provincial hospitals.

1.3 Aims and overview of the thesis

1.3.1 Overall aims

The over-arching aims of this thesis are to investigate the diagnosis of scabies in low-resource settings and to improve standardisation of clinical diagnosis through training and utilisation of non-expert examiners in the diagnosis of scabies. This thesis aimed to inform clinical diagnosis of scabies in low-resource settings by non-expert examiners. The main chapter of my thesis (Chapter 3) aimed to evaluate the role of non-expert health workers in the diagnosis of scabies. The three additional chapters of my thesis (Chapters 4, 5 and 6) investigated the burden of scabies and impetigo in the Western Province of the Solomon Islands, aimed to describe effective training package for diagnosis of scabies and explored a novel method of mapping the body distribution of scabies lesions.

1.3.2 Literature review (Chapter 2)

This literature review explores the current modalities used for the diagnosis of scabies and evaluates their strengths and weaknesses. It also investigates the use of clinical diagnosis for scabies and reviews the clinical features of the disease which may inform diagnosis.

1.3.3 Study of diagnostic accuracy (Chapter 3)

This study aims to determine the diagnostic accuracy of the diagnosis of scabies and impetigo by non-expert examiners after brief training. This chapter provides evidence for the utilisation of non-expert examiners in low-resource settings where expert examiners or other diagnostic methods are not available.

1.3.4 Study of a training package for the diagnosis of scabies (Chapter 4)

This chapter describes the development delivery and evaluation of a training package in scabies diagnosis, used in the diagnostic accuracy study (Chapter 3). The aims of this study were to measure the change in knowledge and confidence of participants before and after training, and to explore their experience of the training.

1.3.5 Study of prevalence of scabies in school children (Chapter 5)

This study aims to investigate the prevalence of scabies in a primary school cohort using clinical examination. This chapter extends the use of novel diagnostic criteria for scabies by applying them to school screening.

1.3.6 Study of the body distribution of scabies (Chapter 6)

This chapter investigates a novel approach to presentation of the body distribution of scabies using a choropleth methodology. This pilot study aimed to explore the feasibility of this method of data collection, analysis and visual presentation of scabies lesion distribution.

1.3.7 Discussion and conclusions (Chapter 7)

This chapter highlights synthesises the key findings of each of the preceding studies. This chapter also discusses conclusions, implications and recommendations based on the reported findings.

Chapter 2. Literature Review: The diagnosis of scabies

2.1 Overview

Human scabies is a parasitic disease caused by the microscopic mite, *Sarcoptes scabiei* var. *hominis*. Estimated prevalence of scabies is thought to be close to 150 million[1] with high associated morbidity.[2]

The scabies mite infests humans by using lytic secretions to penetrate into the host's skin. Once it has burrowed into the skin, it resides in the epidermis and ingests host cells, lay eggs and leaves behind faecal matter.[20] The presence of the mite and its products within the skin causes significant itching, especially at night. It has been associated with irritability in children, sleep disturbance and poor concentration throughout the day.[21, 22] The rash associated with scabies can lead to stigmatization of effected individuals, further contributing to reduced quality of life.[21]

Additionally, infestation with scabies is associated with bacterial co-infection, most commonly with *Streptococcus pyogenes* and *Staphylococcus aureus*.[3] Bacterial infection arises due to a compromised skin barrier caused by scratching. Skin infection can predispose individuals to more serious complications including cellulitis or sepsis. *S. pyogenes* can also cause other serious immune mediated complications including glomerulonephritis[4] and rheumatic fever[5], which can both progress to chronic diseases with high associated mortality.[23, 24]

Several effective treatments are available for scabies. However, case-control treatment strategies do not seem to have substantial impact on populations with high scabies prevalence.[25, 26] In these populations, community wide mass drug administration with anti-scabetic agents such as ivermectin appear to be successful for the control of scabies[27, 28]. In order for such

programs to be implemented, accurate prevalence mapping for scabies is needed for initial assessment, to determine which control strategies are required and for ongoing monitoring to evaluate effectiveness of control strategies.[29]

A systemic review of the global prevalence of scabies identified areas of high endemicity, mostly in disadvantaged populations in tropical and subtropical regions.[3] The review also found there were no data available for many regions of the world. The International Alliance for the Control of Scabies has outlined the need for accurate prevalence data to engage with stakeholders and to work towards the development of control guidelines.[6] To allow comparison and ensure reliability, standardized diagnosis for scabies is required.

Diagnosis of scabies is currently limited by the lack of a simple diagnostic test. A systematic review of diagnostic tests for scabies concluded that there are currently no reliable diagnostic methods.[30] Furthermore, a systematic review of methods used to diagnose scabies in clinical trials found a lack of consistency amongst the methods of diagnosis used.[31] Finally, a systematic review on the global prevalence of scabies outlined the poor quality and lack of diagnostic criteria among population studies included in the review.[3]

A definite diagnosis of scabies requires mite identification using magnification techniques such as microscopy or dermoscopy.[32] However, these techniques are not usually available in low-resource settings where scabies is endemic. In these settings, the diagnosis of scabies is usually based on clinical features.[3]

In 2018, the International Alliance for the Control of Scabies published a set of diagnostic criteria for scabies developed through a formal Delphi process (Table 1). These criteria incorporate a range of diagnostic certainty, from suspected scabies, clinical scabies and confirmed scabies, and highlight different methods used for diagnosis of scabies across this range.[33] The criteria specify that the categories of suspected scabies and clinical scabies are

based on the presence or absence of typical features of scabies, without the use of any diagnostic tool, while confirmed scabies requires direct visualisation of a mite, using a magnification tool. The criteria provide a highly valuable framework to guide diagnosis. However, they have not yet been validated and there are components of the criteria which require further explanation, including the definition of typical lesions and typical distribution.

Table 1. The 2018 International Alliance for the Control of Scabies Criteria[33]

	IACS subcategory
A:	**Confirmed scabies**
A1:	Mites, eggs or feces on light microscopy of skin samples
A2:	Mites, eggs or feces visualised on individual using high powered imaging device
A3:	Mite visualised on individual using dermoscopy
B:	**Clinical Scabies**
B1:	Scabies burrows
B2:	Typical lesions affecting male genitalia
B3:	Typical lesions in a typical distribution and two history features
C:	**Suspected Scabies**
C1:	Typical lesions in a typical distribution and one history feature
C2:	Atypical lesions or an atypical distribution and two history features
	History Features
H1:	Itch
H2:	Close contact with an individual who has itch or typical lesions in a typical distribution
A diagnosis of scabies should only be made if other differential diagnoses are considered less likely than scabies.	

This literature review will explore the diagnosis of scabies by investigating the components which form part of the assessment of clinical diagnosis. It will then investigate and describe the different methods and techniques that can be utilised for diagnosis of scabies.

2.2 Clinical diagnosis

2.2.1 Background

In primary health care settings where individuals may not be trained to use dermatoscopes or perform skin sampling, diagnosis is usually clinical. In low-resource settings, where access to specialists or diagnostic equipment is limited, diagnosis is also reliant on assessment of clinical signs and symptoms.

The clinical features of scabies are diverse with multiple lesion types and varied rash distributions. A systematic review of the diagnosis of scabies in clinical trials included 71 trials, 53 of which were conducted in a resource-limited country.[31] Of the trials included, 37% used clinical and testing methods for diagnosis, 20% used only clinical examination and 24% did not specify whether the diagnostic method. Of those that used clinical features as part of their diagnostic criteria, 55% included the presence of burrows, 50% included papules, 23% included nodules, 30% included pustules and 15% included excoriations. There was no common collection of clinical features used as diagnostic criteria in these trials. This lack of consistency makes interpretation of data difficult and comparison between studies complex.

Furthermore, there are very few data to inform assessment of the accuracy of clinical diagnosis for scabies. A systematic review performed in 2011 identified only one study that investigated the accuracy of history and examination for scabies diagnosis.[30] A review article outlined a 100% sensitivity and 97% specificity for "a history of diffuse itching and visible lesions associated with at least two typical locations of scabies, or a household member with itching".[30, 34] However, this study had several limitations including a poorly defined reference standard.

2.2.2 Components of clinical history taking for the diagnosis of scabies

The IACS Criteria outline features of clinical history as a core component of clinical diagnosis of scabies.[33] In order to make a positive clinical diagnosis of scabies, the IACS Criteria call for at least one of the following features on history: 1) itching and; 2) positive contacts with itch or scabies.

2.2.2.1 Itch

Itch is a characteristic feature of scabies and results from hypersensitivity to mites and mite products, including saliva, faeces and ova, driven by infiltration of CD4 T cells.[35]. Itch was reported to be moderate to severe in 60-75% individuals with scabies [35, 36] and experienced by patients in all age groups, including infants (as evidenced by observation of scratching or presence of skin excoriation).[37, 38]

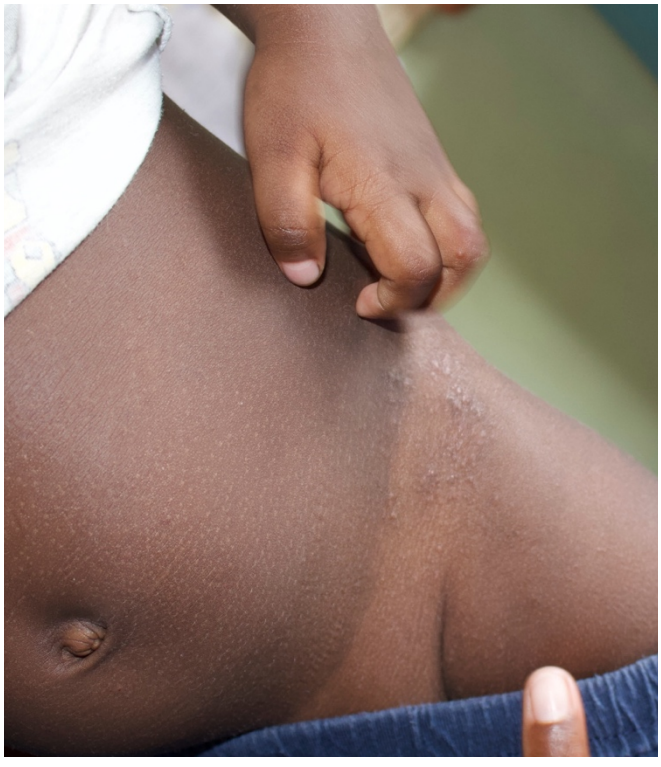


Figure 2. An infant with scabies, scratching lesions on his hip

(Image: Millicent Osti)

Itch caused by scabies is frequently experienced in the evening or prior to sleep [39-41], with up to 89% of those with scabies experiencing nocturnal itch leading to sleep disturbances in affected adults and children.[36, 42] In one study, as many as 88% of individuals complained of sleep difficulty due to nocturnal itch, and in another study 22% of children aged less than two years exhibited sleep disturbance.[35, 42]

2.2.2.2 Contact history

Multiple studies have reported that patients with scabies have a history of contact with at least one other individual with itch, with a range of 50% to 55%.[40, 42] The inclusion of a positive contact history of itch has been shown to improve sensitivity in scabies diagnosis.[34]

2.2.2.3 Overcrowding

Overcrowding is considered a risk factor for the transmission of scabies infection. A prospective study of children presenting to hospital in the remote regions of Western Australia found that individuals living in households with greater than 5 members had a higher risk of scabies infestation than those living in smaller households.[43] Similarly, in Egypt, larger families and night time crowding was associated with higher prevalence rates of scabies infection.[44] Although household overcrowding is not included as a diagnostic component of the IACS Criteria, it should heighten the suspicion of scabies in a clinical setting.

2.2.3 Rash or lesion appearance

The morphologic appearance of the rash of scabies is diverse, with most individuals exhibiting more than one type of lesion and over 60% exhibiting three or more.[21, 39] Commonly described scabies lesions include papules, nodules, vesicles and pustules. Scabies is also commonly associated with lesions that are considered “secondary lesions”, that is, those that develop as a

result of changes to primary lesions including excoriation, eczematisation, crusting and infective skin changes.

2.2.3.1 Papules

Papules are solid, palpable lesions less than 1cm in diameter.[45] In scabies they are commonly erythematous or the same colour as the surrounding skin. They are the most common lesion type of scabies, reported in 70-100% of individuals.[21, 46, 47 35]

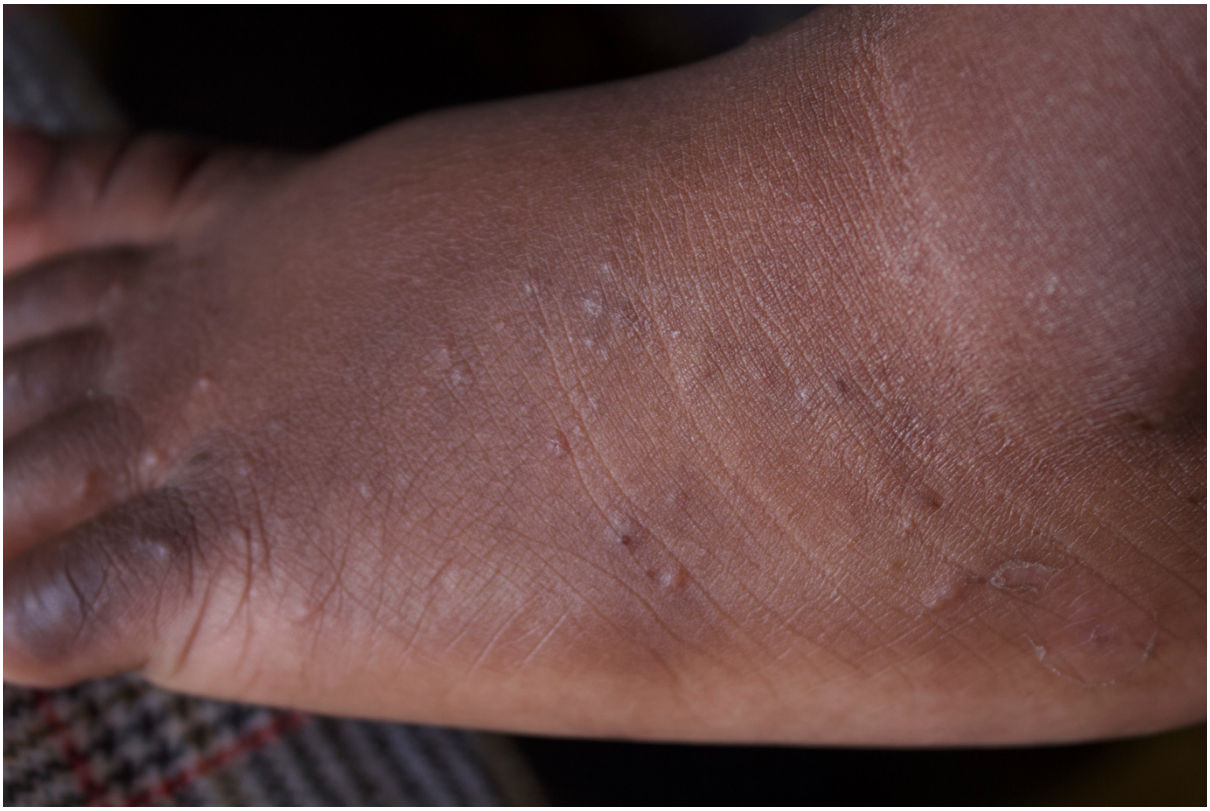


Figure 3. Papular lesions over the foot of a child with scabies

(Image: Millicent Osti)

2.2.3.2 Nodules

Nodules are solid, elevated palpable lesions greater than 1cm in diameter.[45] Nodules may be present as a primary feature of the scabies rash or they may develop as part of a persisting clinical occurrence after successful treated scabies infection. Nodules have been reported frequently in scabies[40, 46] seen in up to 44% of individuals with scabies.[22] However, in other studies nodules were seen less commonly and overall, appear to be reported less frequently than papules.[21, 35, 39, 47]

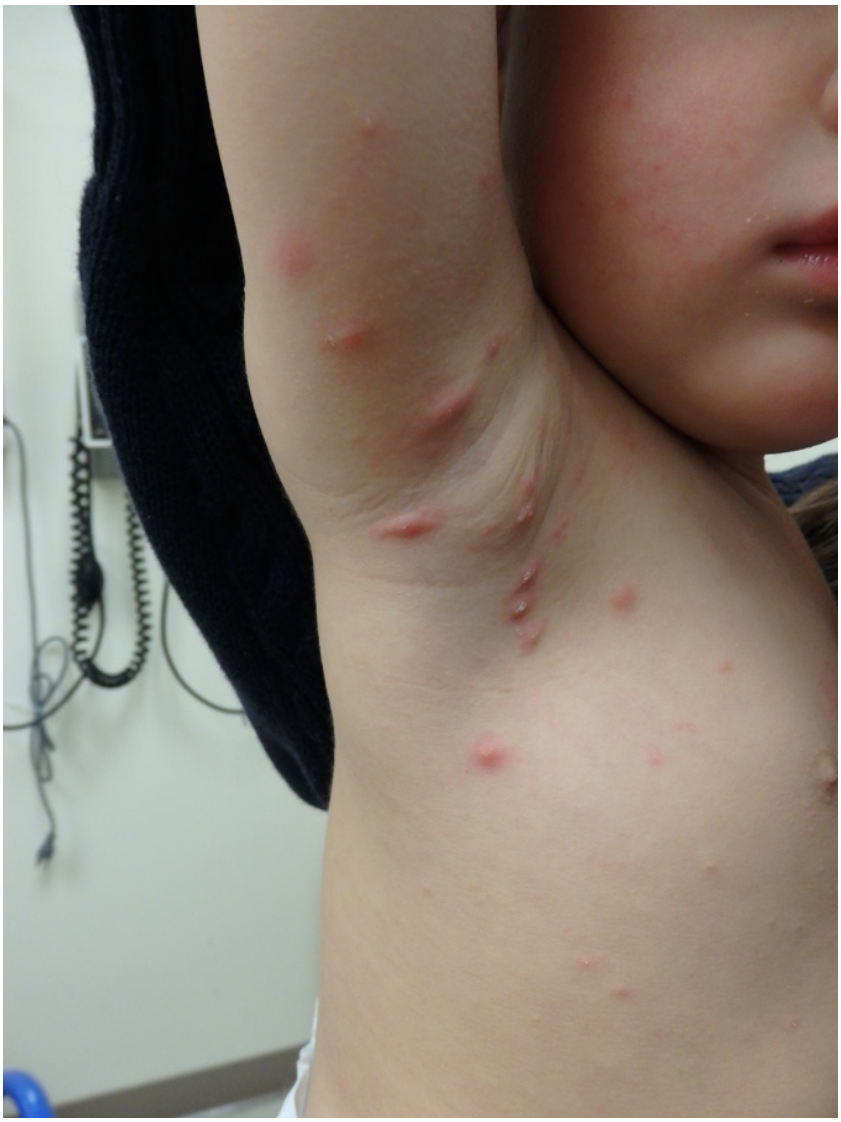


Figure 4. Nodules on the axilla of a child with scabies

(Image: Wingfield Rehmus, International Alliance for the Control of Scabies)

2.2.3.3 Vesicles and Pustules

Vesicles are small blister-like lesions (containing clear fluid) and pustules are fluid-filled lesions that contain pus. Both vesicles and pustules have been described as common rash morphologies of scabies. Pustules may be caused by inflammation alone and be sterile (that is, absent of any bacterial superinfection). Multiple studies have reported vesicles as a common manifestation in patients with scabies, in up to 68% in one report [39, 42, 46], while other studies have reported vesicles as being uncommon.[21, 35, 42, 46] Fewer studies have reported pustules as a manifestation of scabies, with a prevalence range of 16% to 43%.[37, 48, 49]

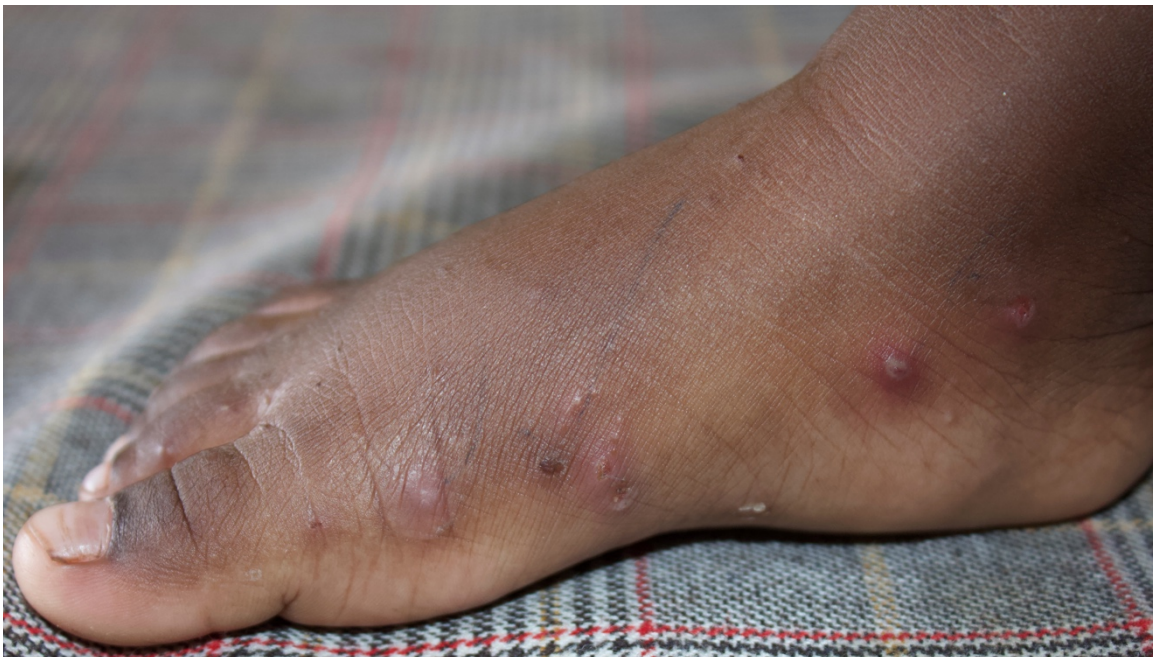


Figure 5. Papules and pustules on the foot of a child with clinical scabies

(Image: Millicent Osti)

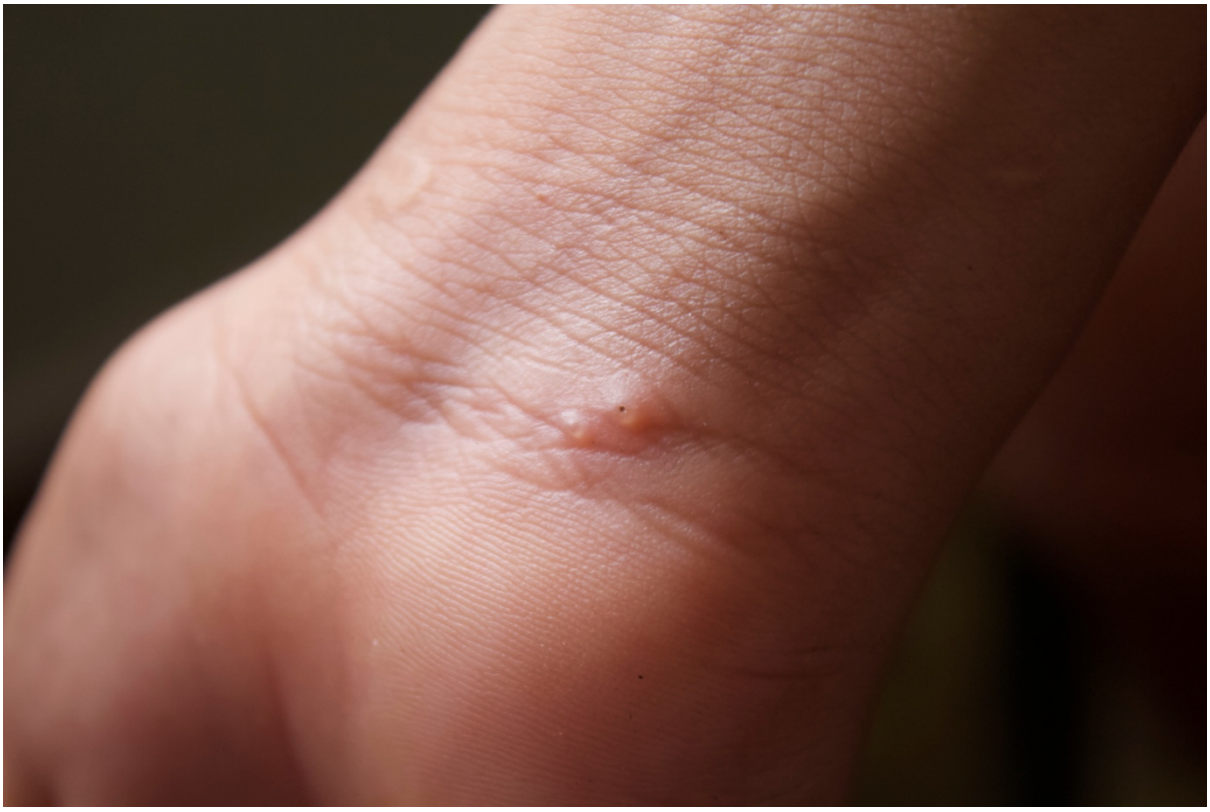


Figure 6. Vesicles on the wrist of an individual with suspected scabies

(Image: Millicent Osti)

2.2.3.4 Burrows

The scabies mite uses digestive enzymes and propulsive movements to invade the human host and tunnel into the stratum corneum, the outer most layer of the epidermis. Once the mite is located within the stratum corneum it continues to move through the skin, digesting human tissue and laying eggs as it travels.[50, 51] This action causes short, grey linear structures known as burrows.[52]

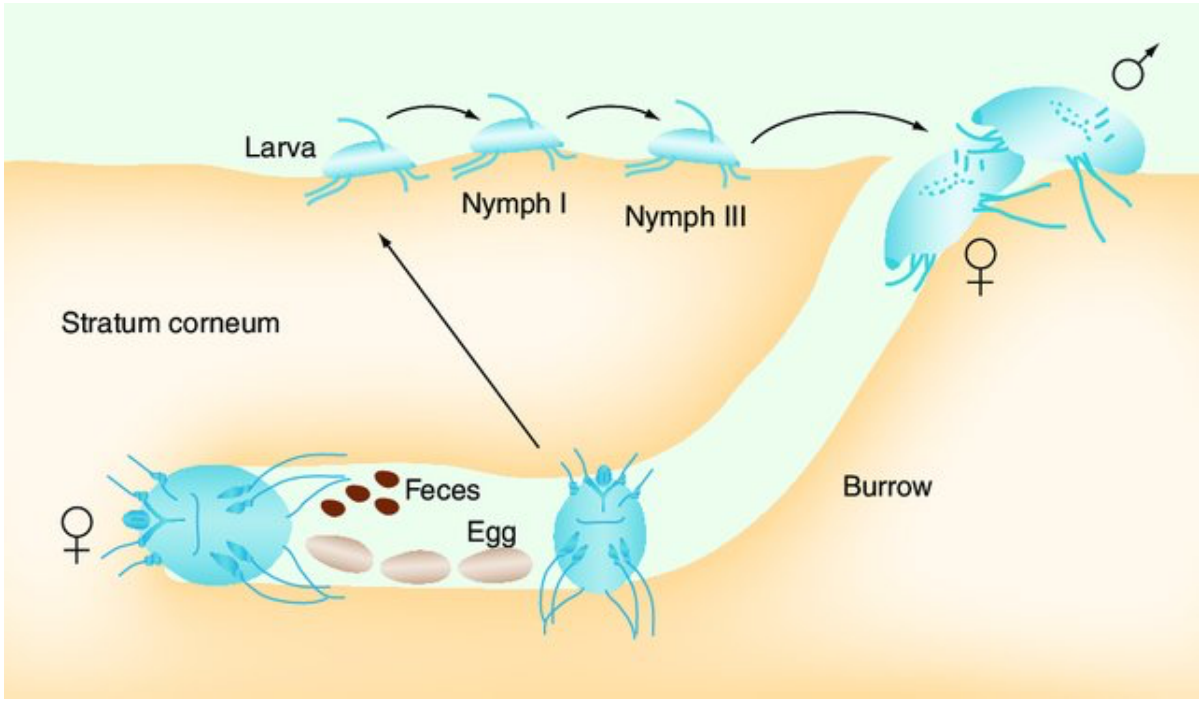


Figure 7. The life cycle of the scabies mite and the burrow

(Image: *New insights into Scabies and pediculosis*, Mumcuoglu et al[53])

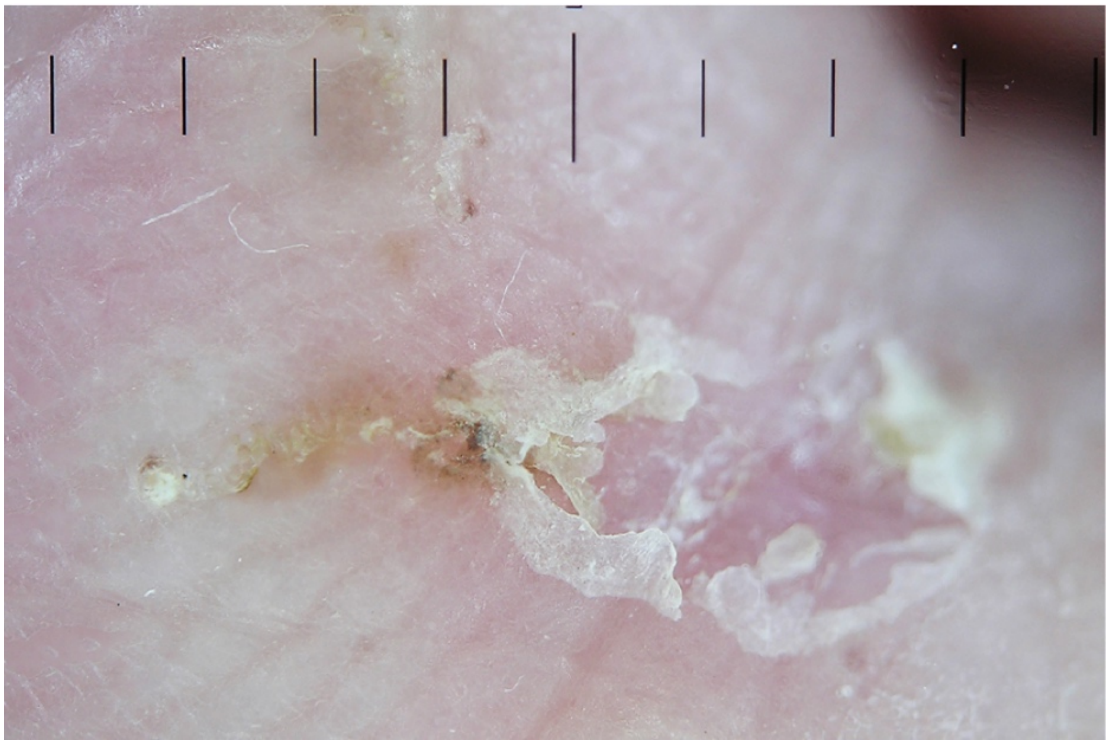


Figure 8. A magnified image of a burrow

(Image: Rie Yotsu, International Alliance for the Control of Scabies)

Burrows are difficult to see without magnification. Although considered pathognomonic, the sensitivity and specificity of the burrow as a diagnostic sign for scabies has not been evaluated. The prevalence of burrows in those with active scabies is inconsistent in the literature, ranging from 18 to 78%.[40, 42, 46, 47, 54, 55] However, many experts assert that burrows are observed less commonly in populations in whom scabies prevalence is very high, including in tropical areas.[20, 39]

2.2.3.5 Wake Sign

The 'wake sign', is a clinical finding specific to scabies which may assist in clinical diagnosis.[56] The wake may be visualized more easily with the naked eye than a burrow, seen as an area of scaling and inflammation trailing the burrow, in the shape of a wake as formed by a ship on water.

Figure 9. A wake behind a boat

(Image: By Edmont - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=6920796)

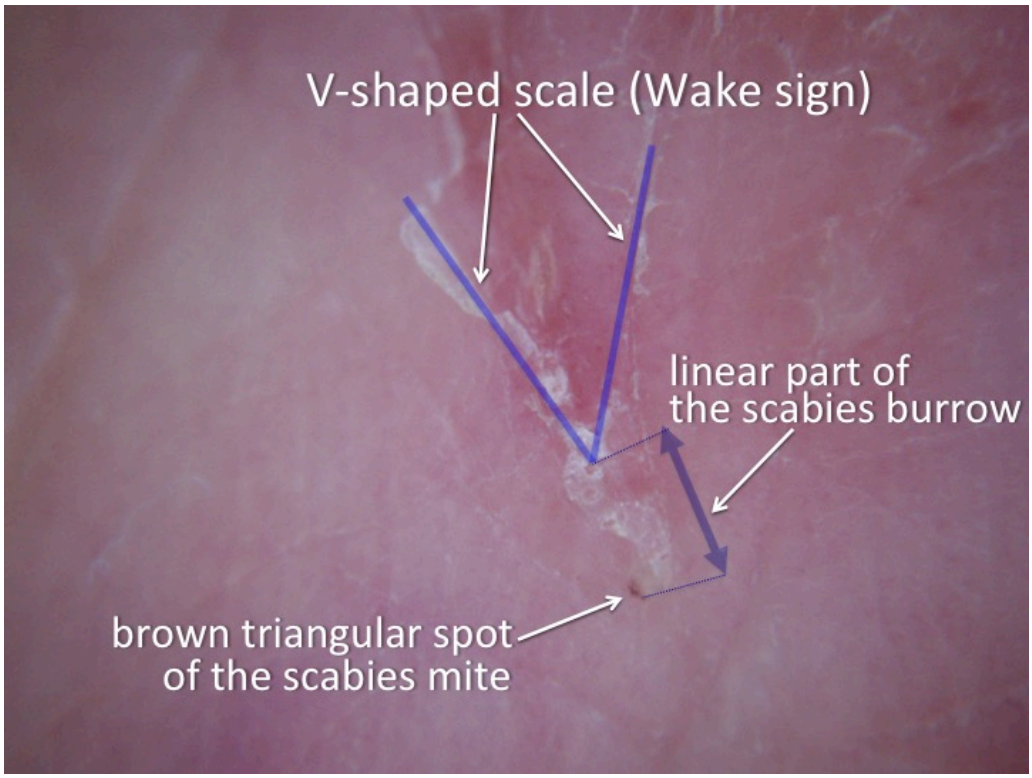


Figure 10. Pictorial explanation of the 'wake sign'

(Image: Junko Yoshizumi, International Alliance for the Control of Scabies)

2.2.3.6 Other lesion types

Some lesion morphologies, including macules and blisters, are described only rarely in the literature. In one study, macules were described in in 43% of individuals with scabies, but this morphology appears to be isolated to this study only.[39] In another study, blisters were reported in 4.3% of patients with classic scabies. Bullous scabies is a well described but infrequent atypical variant of scabies infestation. In the study mentioned above, it may have been possible that the blisters described may have represented common vesicles or a bullous variant of the disease rather than common scabies lesions.[42]

2.2.4 Secondary features of scabies

Secondary features of scabies include excoriations, eczematisation, crusting and infective changes. These features may obscure the appearance of typical lesions.

2.2.4.1 Crusting

Crusts may represent dried serum, blood or pus. Diverse terminology, including "crusted papules", "crusting" and "scale", has been used across many studies, without clear definitions. Furthermore, the term crusting is confusing in the literature because of the potential for mis-classification with the severe atypical form of scabies known as "crusted scabies (see below), and also crusting that can appear with secondary bacterial infection (see below). Nonetheless, crusted papules or lesions have been reported in a number of studies, with a range of 19 to 82% of individuals in these studies.[39, 46, 57]

2.2.4.2 Eczema

Eczema associated with scabies may represent acute inflammatory changes or chronic thickened and dry skin. One study reported this feature in almost 50% of individuals with scabies.[58] Another study of nursing home staff and residents with scabies reported "dry skin" in 53.9% of individuals, which may represent eczematisation.[59] Most studies of the clinical features of scabies however rarely report eczematisation, ranging from 0-8%.[39, 55, 60]

2.2.4.3 Excoriations

Excoriations are linear breaks in the skin caused by scratching and are common in patients with scabies as a result of pruritus. Excoriations may alter the appearance of burrows or characteristic primary lesions.[21] Excoriations are very frequently reported, present in 41-85% of individuals with scabies.[21, 35, 37, 39, 55] One study reported a high proportion (52%) of patients with scabies exhibited excoriations at sites not infested with mites, indicating the presence of pruritus of healthy skin.[39] Although the direct mechanism of this is unknown is likely

represents a systemic delayed hypersensitivity immune reaction.[20] Lichenification, thickened skin from rubbing, was also seen in 10% of individuals in one study.[55]

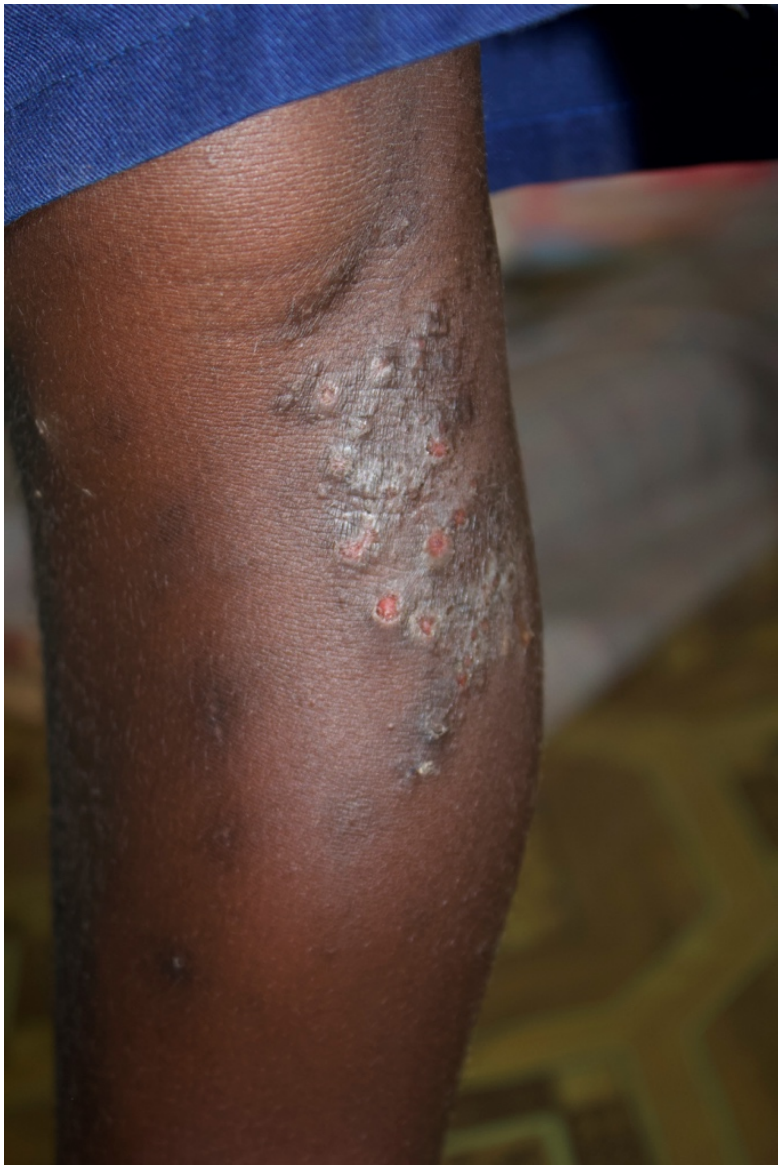


Figure 11. Excoriated scabies lesions on the lower leg with areas of lichenification likely from rubbing

(Image: Millicent Osti)

2.2.4.4 Bacterial co-infection

Mite burrows and the intense itching and associated excoriation impairs the skin barrier. This provides a route for bacteria to enter the skin, predisposing individuals to subsequent bacterial infection of the skin (impetigo). Bacterial skin infection may appear as lumps or sores with pus, crusting or redness, and may change the appearance of typical scabies lesions such that the diagnosis of scabies can be more complicated. In a national study in Fiji, the prevalence of impetigo was 19.6%, and as high as 34.2% in young children.[57] Secondary bacterial infection of scabies is common; in a study in Brazil 37% of patients with scabies had impetigo [39] and in American Samoa this proportion was 68%.[61]

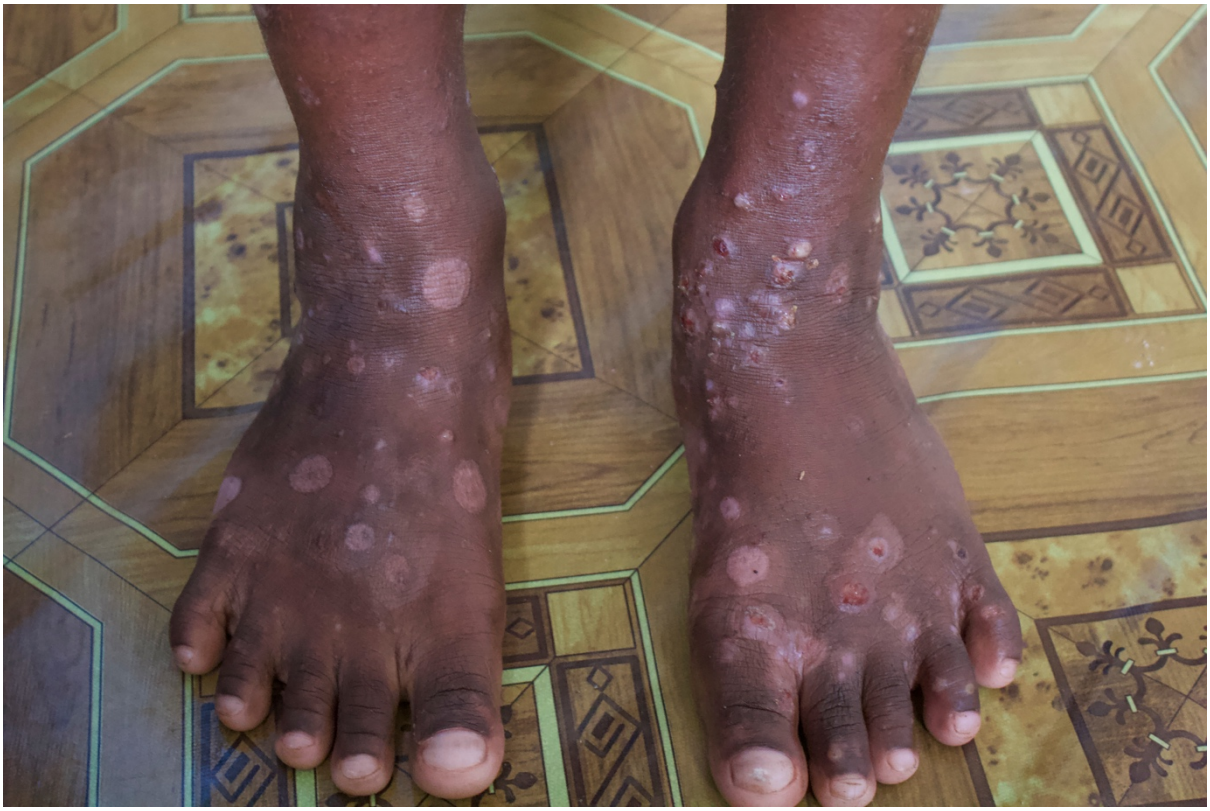


Figure 12. Severe scabies on the feet and ankles with infected lesions

(Image: Millicent Osti)

2.2.4.5 Lesion number

The majority of patients with scabies have less than ten lesions.[62] Greater lesion numbers represent more severe infections. Most individuals have less than ten lesions, however in cases which are more severe individuals have been reported to have more than twenty or even more than fifty lesions in very severe cases.[8, 39, 57]

2.2.5 Lesion distribution

Although the lesion burden in scabies is usually low, the associated rash can affect a multitude of sites.[35, 39, 63] It has been reported that the location of the rash in scabies does not always correlate with mite location.[64] However, burrows are only seen where a mite has been present and mites or mite products have been identified in nodules following biopsy.[65, 66] It has also been suggested that the lipid composition of the tissue may affect mite's choice of location,[50, 67] although these studies have been of *Sarcoptes scabiei* var *canis,* a mite that predominately affects dogs and foxes.

Commonly reported sites of scabies lesions are the interdigital spaces, wrists, dorsum of the hand, axillae, groin, genitals and abdominal area.[68, 69]

The upper limb is the most common site of lesions of scabies.[35, 62, 70, 71] The hands and wrists are more frequently affected than the forearms and upper arms.[22, 72] Lesions involving the interdigital webbing is considered highly characteristic of scabies and is reported to affect up to 80% of individuals with scabies.[46, 73] It has been suggested that individuals with lesions at their finger webs had a higher chance of correct diagnosis of scabies than those without involvement of this region.[74]

Figure 13. Scabies lesions affecting the hands and fingers

(Image: Millicent Osti)

Involvement of the wrists is also very common, supported by a number of studies which report wrist lesions in 13- 82% of affected individuals [35, 39, 42, 46, 49, 55] Many experts assert that the volar wrist is more commonly involved than the dorsal wrist, but there are few data to support this.[75]

The lower limbs are commonly reported to be involved in scabies, however there is wide variation in published reports (less than 1% to greater than 50%).[39, 42, 49, 70, 72] Retrospective analysis of data from the Solomon Islands and Fiji, showed that the feet and lower legs were much more commonly affected (49.7%, 48.3%) than the upper legs (22.6%).[76]

The abdomen has been reported as another frequently affected site in multiple studies.[39, 77] The abdomen has been reported to be involved in 60-80% of individuals with scabies.[35, 39 42] Some

studies report lower levels of involvement of this area. Many studies do not report involvement of the abdomen because it is often not examined due to sensitivities of exposing this area.

Lesions on the penis, including papules, nodules and burrows, are considered typical of scabies infestation.[75, 78] Multiple studies confirm that lesions on the genitals are common, with between 6 to 75% of male adult patients having lesions on the penis.[39, 46, 47, 55, 58] A study detailing microscopic examination for mites and/or eggs and/or faecal matter in 89 patients, reported that 66.7% of adult males had mite or mite products at their genitals and 51% had mite or mite products retrieved from their scrotum.[79] Therefore it is important to ensure that this site is treated.

A study of women presenting with vulval itch to a vulval dermatology clinic, reported a 7.5% prevalence of vulval scabies among their study population. Although this is a very specific population, the study highlights vulvar itch as a feature of scabies that may not otherwise be considered.[80] The lack of detailed data on genital involvement in females compared to males may be due to issues of privacy required for examination.

The involvement of fingernails and toenails in scabies has been infrequently reported.[81, 82] Mite or mite products have also been isolated from subungual areas of the fingers in asymptomatic individuals with mild scaling at the nails.[79] The subungual area may be overlooked on application of topical medication and therefore may be a source of persisting mites and reinfection.

2.2.6 Atypical presentations

Scabies has many varied presentations. Although the majority of cases present with the classic features described above, some individuals may present with other, atypical manifestations of scabies infestation. These manifestations are rare but can pose diagnostic challenges for

clinicians. Atypical scabies presentations include crusted scabies, nodular scabies, bullous scabies and scabies incognito.

Crusted scabies is a disease caused by hyper-infestation of the scabies mite and presents with hyperkeratotic crusting of the skin. Compared to the low mite burden seen in classic scabies, a patient with crusted scabies may be host to over one million mites. Crusted scabies is reported to have a 50% five-year mortality.[83] It is considered a separate disease entity to classic scabies and the intricacies of presentation and diagnosis are complex.

Nodular scabies is a clinical variant of scabies which presents primarily with erythematous or hyperpigmented nodules, which are elevated lesions greater than 1cm. There are two hypotheses as to the cause of nodular scabies. First, it may be caused by a persistent hypersensitivity reaction to non-viable mite products in treated scabies infection.[20] Second, it may be due to persistent scabies infection in nodular lesions.[66]

Bullous scabies is a rare presentation which mimics the features of bullous pemphigoid. It is usually seen in elderly patients, is more common in males, and is poorly responsive to immunosuppressant therapy.[84]

Scabies incognito is a form of classical scabies in which the typical features have been masked by the incorrect administration of topical or systemic steroids. It is a common occurrence, especially in populations were steroids are easily accessible, and may also result in features of Cushing's due to excessive steroid use.[85, 86]

2.2.7 Other factors influencing clinical presentation

Scabies can present differently in different populations, with variation by sex, age, skin type, setting and co-morbidities of the individual with scabies. Therefore, the approach to diagnosis may need to be modified based on the setting or the population.

2.2.7.1 Sex

Male and female individuals infected with scabies present similarly, although some differences in the prevalence and appearance of the rash have been reported. Analysis of the Global Burden of Disease Study 2015 demonstrated that the burden of scabies is evenly distributed between sexes in most regions.[44, 87, 88] Some studies report increased frequency in females, including among women of child bearing age.[89] A study conducted in Palestine also observed a higher incidence in females aged 31-50 years, however no gender difference was seen in other age groups.[88] In contrast to these findings, a small number of studies report increased prevalence in males when compared to females.[90, 91]

Scabies frequently involves the breasts in females. One study found a significant difference between females and males for lesions located at the nipples and breasts (40.2% vs 15.5%).[39] Another study reported that mites or mite products were present on the breasts in 60.5% of females with scabies enrolled in the study, comparted to only 4% of males.[79] Otherwise, the rash distribution of scabies is similar in males and females.[35]

2.2.7.2 Age

Across most studies of scabies, children exhibit the highest prevalence[3] with young age frequently identified as an independent risk factor for prevalence and severity.[88, 89] Among children, scabies prevalence is generally highest among school aged children.[3] There are some

studies, including in the Northern Territory of Australia among indigenous populations that have observed that scabies has a peak prevalence in infants.[35, 41, 62, 92]

The type of lesions seen with scabies infestation may vary according to the age of the individual. Lesion type in children can be more varied than in adults, and the predominant lesion type among children may be influenced by their age.[39]

Scabies can present quite differently in young children, particularly infants, compared to adults. First, the primary complaint by a parent of an infant with scabies may be poor feeding and irritability, rather than rash.[93] Second, the rash may present differently in infants. Nodules have been reported to be more frequent among infants compared to older age groups,[42, 93] although papules are still frequently seen.[37, 94] Third, excoriations may be less common in infants, possibly due to lack of an effective pincer grasp and inability to scratch.[48] Fourth, burrows have also been reported to be more common in infants, which may also be due to the absence of effective scratching and therefore reduced likelihood of overlying excoriations that may obscure the burrows.[42] Fifth, children are more likely to develop bacterial superinfection than adults.[39, 41] Infants appear to be at highest risk. Finally, infants frequently have involvement of more body areas than older children and adults.[39] The head, scalp and face are common sites for scabies infestation in infants (Figure 14). This may be due to physical differences in skin at these sites between infants and older children, or because of direct transmission from the mother to the child's face while breastfeeding.[42, 62, 94]

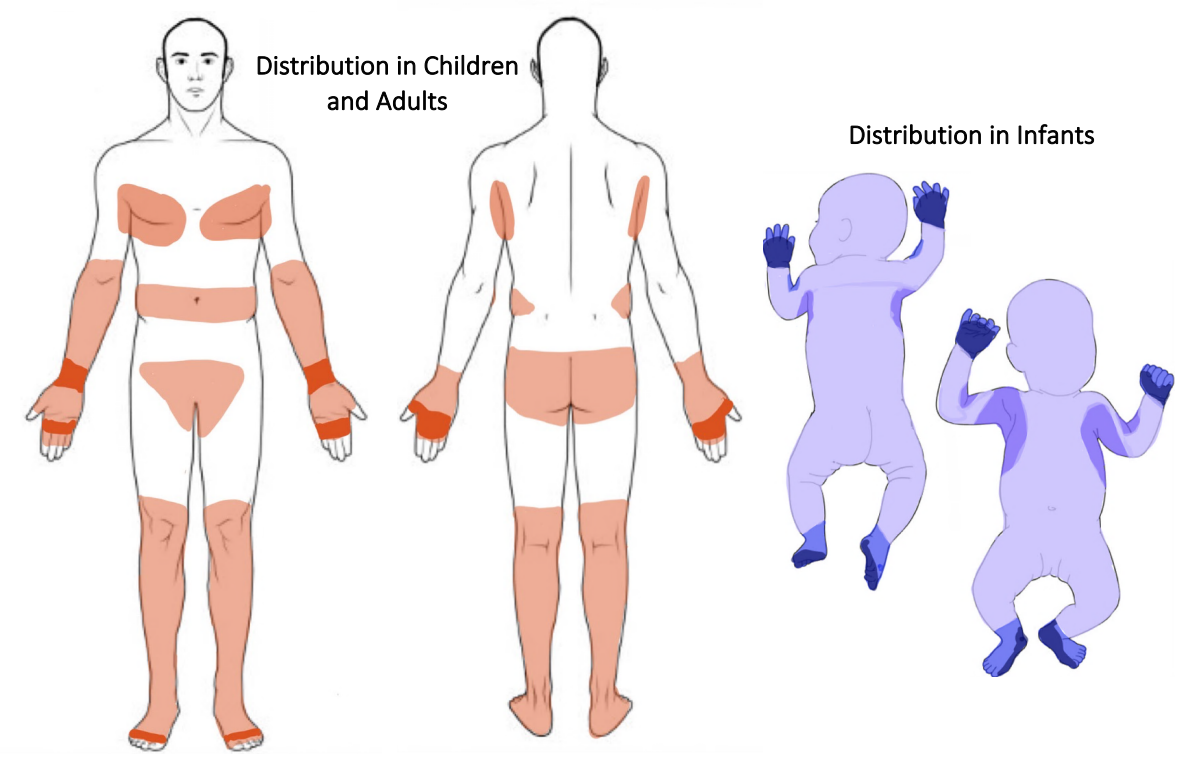


Figure 14. Distribution of scabies lesions in adults and children and infants

(Image: adapted from image by Daniel Engelman)

2.2.7.3 Climate

The majority of studies that have investigated seasonal variation in scabies prevalence have shown no relationship between season and scabies.[63, 89, 95] However, these studies have mostly been conducted in regions with small temperature variations throughout the year. A study conducted in Malawi reported an increased incidence of scabies during the cold season, consistent with historical data from Denmark that showed peaks of prevalence in winter and troughs in summer.[96, 97] An explanation for these observations may be an increased risk of transmission in in colder weather due to indoor crowding. A study in the Northern Territory of Australia reported no correlation between prevalence of bacterial co-infection of scabies with dry or wet season.[98] In contrast, the abovementioned study in Malawi observed a higher incidence of pyoderma during the hot season.[96]

2.2.7.4 Co-morbidities

Individuals with an ineffective immunological response may be unable to provide an appropriate immune response to mite infestation resulting in uninhibited mite reproduction and inhabitance.[99] This may be iatrogenic (due to oral or topical steroids), due to chronic disease, heavy alcohol use, lymphoma or leukaemia or infection with HTLV-1 and HIV.[83] As a result of immune suppression, the rash associated with scabies infection may also have an atypical appearance in these individuals.[100, 101] Immunosuppressed individuals may have an increased risk of progression to more severe scabies, including crusted scabies, and on the other hand may present with scabies incognito.[20, 86]

Individuals with scabies and a background of neurological or sensory disturbances may have an unusual presentation.[102] Neurocognitive dysfunction, as in seen with dementia, has been associated with more severe of disease and also with the absence of itch.[103, 104] Neurocognitive dysfunction may impair the experience of or ability to itch, and so the mite is not scratched from the skin, possibly increasing mite survival.[103]

2.3 Non-clinical diagnosis

Although clinical diagnosis remains crucial to scabies diagnosis in many settings, other techniques may provide useful information to contribute to diagnosis. A clinical diagnosis of scabies can be confirmed upon visualisation of the scabies mite or mite products including ova (eggs) or scybala (faeces). Depending on the method used, mite or mite products can be visualised while in the skin or can be removed and visualised external to the skin.

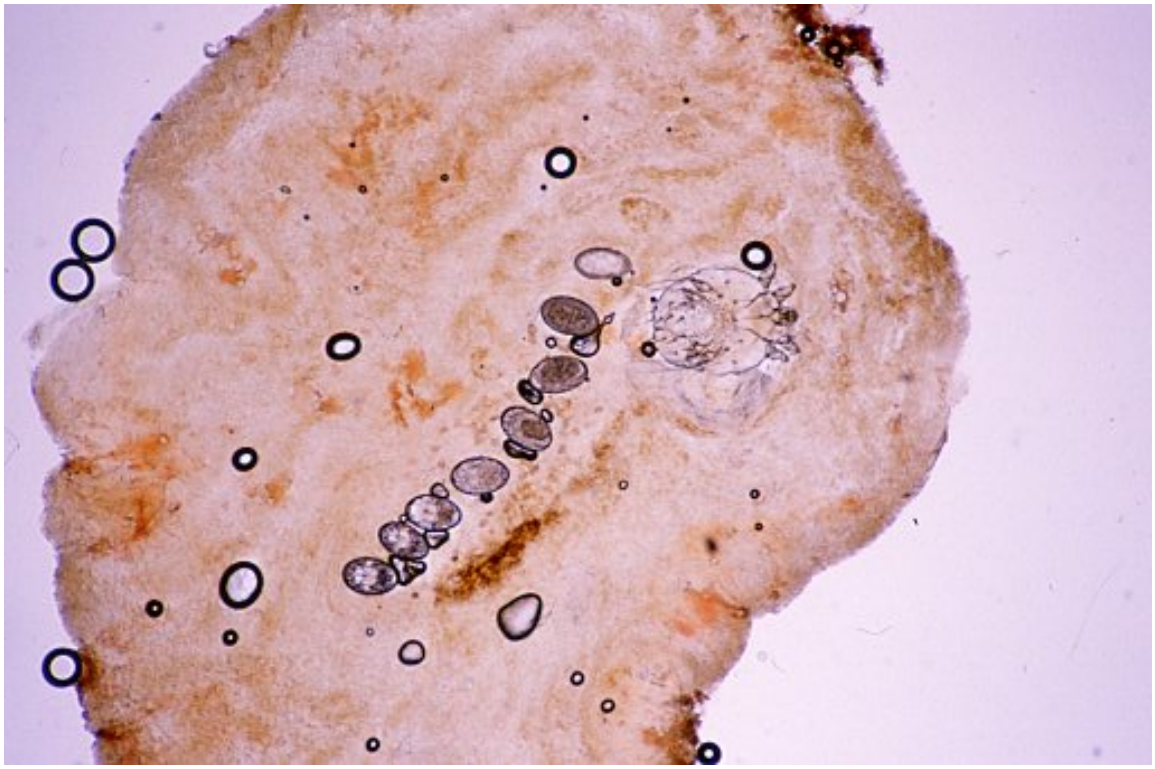


Figure 15. Microscopy of a scabies mite and ova

(Image: Norisha Ishii, International Alliance for the Control of Scabies)

2.3.1 Mite visualisation ex vivo

2.3.1.1 Skin scraping

Scabies mites can be removed from the skin using various skin sampling methods including skin scraping, biopsy or the adhesive tape test. In a dermatological outpatient setting scabies is often diagnosed by microscopic identification of the mite or mite products via a skin scraping.[90] However, the reliability of microscopic diagnosis of scabies is dependent on the sample of skin which is taken for microscopic examination and if dermoscopy is used to orientate scrapings.[101, 105] One study showed the microscopic evaluation of skin scrapings had a sensitivity of 90%, with a specificity of 100%.[40] This high sensitivity likely reflects the fact that in this study the examiners took repeated skin scrapings with the assistance of dermoscopy until the operator was satisfied with the negative result. Another study found a much lower sensitivity of 46%

and did not use dermoscopy orientated scrapings.[106] Therefore, the sensitivity relies on the use of repeated or orientated skin sampling which can be time consuming.

2.3.1.2 Biopsy

Although mite or mite products may be visible in skin biopsy samples, such as a punch or excisional biopsy, it is not commonly performed for the diagnosis of scabies. A study from a specialist dermatologist setting identified that only 2% of individuals with scabies were diagnosed using identification of scabies from a skin biopsy.[90] Those cases diagnosed using biopsy may have had a low clinical suspicion for scabies and therefore a biopsy was used to diagnose anther condition that requires biopsy, rather than a scraping as is sufficient with scabies.

2.3.1.3 Adhesive tape test

The adhesive tape test was first described by Katsumata and Katsumata in 2006.[107] It requires the use of strong adhesive packing tape, cut into the size of a microscope slide, placed onto scabies lesion and rapidly removed. This process is performed with the intention of collecting a mite or mite products which are present in the epidermis or mites on the surface of the skin. This sample can then be observed under microscopy. The adhesive tape test has a sensitivity reported to be around 68% when compared to diagnosis by mite visualisation on either skin scraping or adhesive tape test.[106] The adhesive tape test is less invasive than a biopsy or skin scraping, and can be performed by inexperienced examiners, although it still requires the use of microscopy for mite visualisation. The technique relies on the texture of the epidermis to stick to the tape, and therefore it has been suggested that the test is likely to be more reliable in patients with skin atrophy, such as the elderly, and on areas of skin where it is thin, such as fingers and toes.[106]

2.3.2 Mite visualisation in vivo

Multiple methods can be used for mite visualisation in the skin, including dermoscopy and videodermoscopy. Epiluminescence microscopy (ELM) allows the visualization and magnification of skin, using a dermatoscope or videodermatoscope, with the use of oil on the skin and a slide between the lens and the skin to reduce light reflection. Initially introduced for the observation of pigmented lesions, dermoscopy was suggested in 1992 to assist with scabies diagnosis.[108] Most dermatoscopes now employ a polarized light source, erasing the need for oil immersion. Traditional handheld dermatoscopes generally allow x10 magnification, however some newer models may allow up to x60 magnification.

2.3.2.1 Dermoscopy

Dermoscopy can facilitate the diagnosis of scabies by visualization of the burrow or scabies mite. The head and mouth parts of the mite are visible as a dark triangular structure described as a jet with contrail [109] The reported sensitivity of dermoscopy is high (83-91%) when compared to *ex vivo* microscopy as the criterion standard.[40, 106] Specificity of dermoscopy is reported to be 46% with a lower positive predictive value than other diagnostic methods.[106] Although these are reliable methods of diagnosis, training is required in order to operate these devices.[30] Dermoscopy is likely to play an important diagnostic role in well-resourced settings but are unlikely to greatly contribute to the diagnosis of the majority of scabies cases in low-resource settings.

Figure 16. Low magnification dermoscopy of a burrow and mite

(Image: Giuseppe Micali, International Alliance for the Control of Scabies)

2.3.2.2 Videodermoscopy

Videodermatoscopes are devices that allow non-invasive in vivo observation of the skin at very high magnifications. They can also allow capture of moving images. One study found that a videodermatoscope with a magnification of up to 600x was able to identify mites and burrows in 62% of children with scabies.[110] In this study, individuals were initially examined at lower magnification (100x) for a full body examination, which reportedly took 3 to 5 minutes. Suspicious lesions were then re-examined at higher magnification, allowing a more streamlined approach to the skin examination. Clearly, this technique requires operators with considerable expertise. Currently, the cost of a medical videodermatoscope is around USD$20,000.[32] A small study compared the diagnosis of scabies using a medically marketed videodermatoscope

with a much cheaper (approximately USD$30), publicly available videomicroscope.[111] Despite the lower resolution of the cheaper videodermatoscope, both devices were able to identify the scabies mite or products to confirm infection. Identification of scabies mites using a non-medical handheld digital video microscope has also been demonstrated in a low-resource setting.[112] Such devices may be useful in settings where more expensive devices are not available, however they are likely to require access to charging facilities which may be limited in some remote regions where scabies is endemic. Further experience with these devices is needed in order to justify their use in scabies field diagnosis.

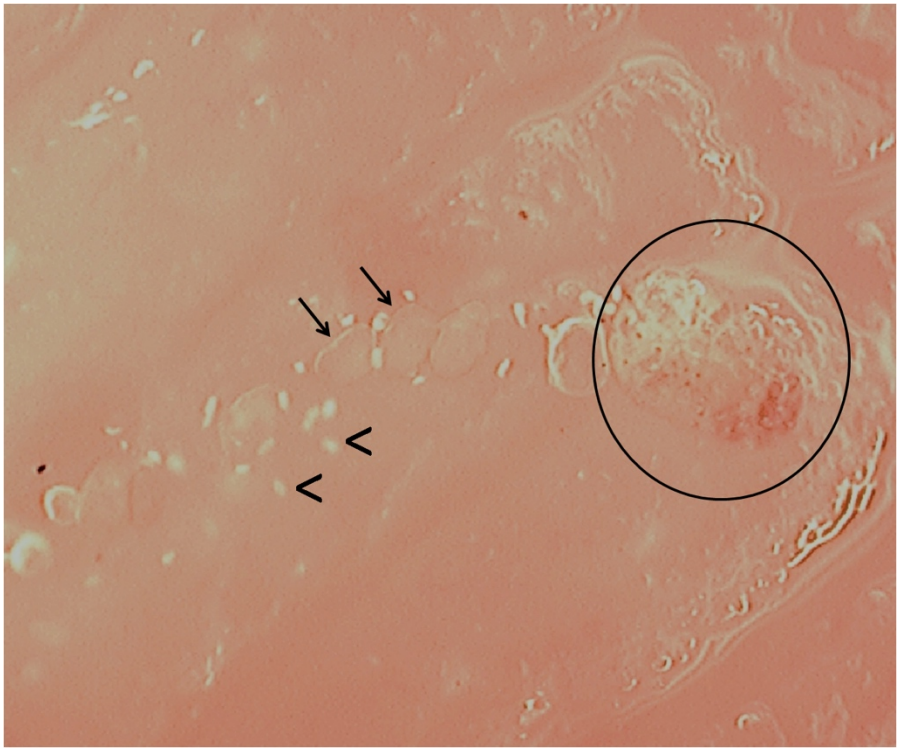


Figure 17. High magnification video dermoscopy (still image) featuring a scabies mite (circled), ova and faecal matter

(Image: Giuseppe Micali, International Alliance for the Control of Scabies)

2.3.2.3 Other imaging modalities

Reflectance confocal microscopy is an imaging technique that can produce a black and white in vivo two-dimensional image using lasers which reflected off structures according to their refraction index.[32] This allows histological analysis of these layers of skin without the need for

skin sampling. This technique has been described as a diagnostic tool for scabies and can provide visualization of mite peristaltic gastrointestinal activity which can confirm mite viability consistent with current infection.[113, 114] Other imaging modalities are unable to provide sufficient detail to determine if the mite is still alive within the skin, unless there is successive examination of the same area of skin to observe mite migration, or decomposition following treatment, but this is time consuming and requires individuals to represent at multiple time points for re-examaination.[115] No studies have been performed to identify the utility of confocal microscopy for the diagnosis of scabies in large cohorts. Reflectance confocal instruments are expensive (~USD$150,000) and only available in some high resource settings.[32]

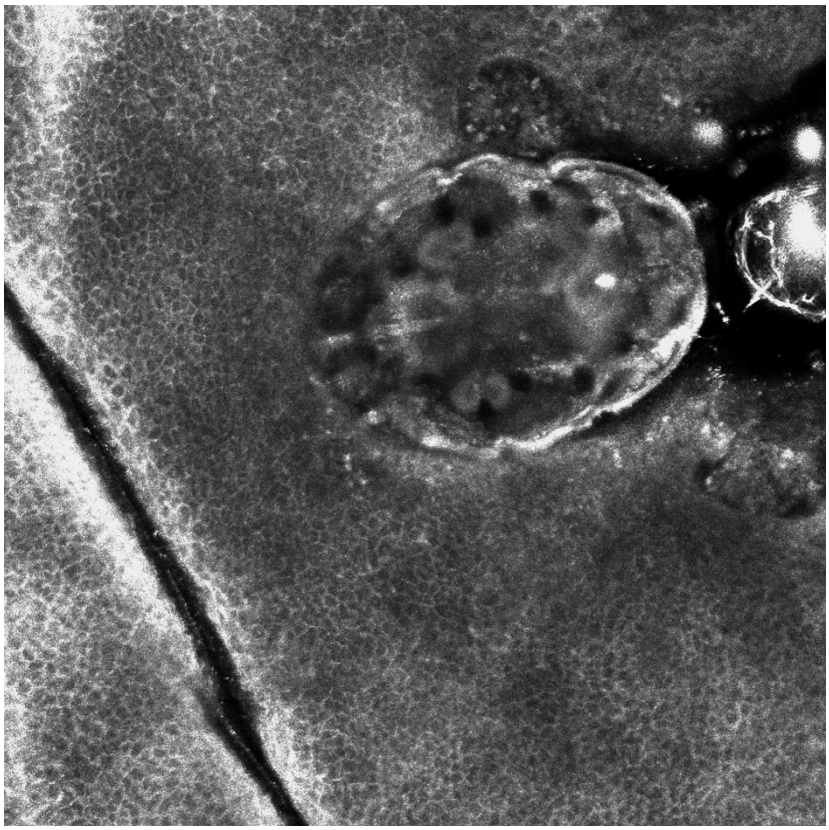


Figure 18. Reflectance confocal microscopy image of a scabies mite

(Image: Dev Tilakaratne, International Alliance for the control of scabies)

Similarly, optical coherence tomography is a newer method of mite visualization which can provide high-resolution cross-sectional images of the skin, with detailed visualization of mites and burrows.[116] However, optical coherence tomography instruments are similar in price to the confocal microscopy and only available in highly specialized settings. Optical coherence tomography requires around ten minutes for examination of each lesion. Although confocal microscopy and optical coherence tomography may be useful in tertiary settings to study mite behaviour or to confirm mite viability, they are unlikely to play a major role in mite diagnosis globally.

2.3.3 Other diagnostic modalities

2.3.3.1 Burrow ink test

The burrow ink test attempts to highlight burrows formed by the scabies mite which may not be visible without magnification.[117] It is performed by using a pen to cover a papule with ink, then wiping the ink off the skin using an alcohol wipe. If present, the ink will track down the burrow and will not be removed by wiping, producing a dark tortuous line, and allowing the burrow to be more easily visible. Although inexpensive, the process can be time consuming and relies on the presence of burrows.

2.3.3.2 Antigen and antibody detection techniques

Newer methods are under investigation for use in the confirmation of scabies infection by detection of scabies antigens (using enzyme linked immunosorbent assays) or DNA (using polymerase chain reaction) in *ex vivo* samples.[118-120] Substantial research and development is required for these techniques before they contribute to the diagnosis of scabies in most settings. Similarly, the detection of antibodies in serum to scabies antigens requires further research.[121] Two key barriers to successful development of serologic tests for scabies have been that there

is incomplete understanding of the immune response to scabies and the cross reactivity between scabies and house dust mite allergens.[122, 123]

2.4 Reference standard

According to the Standards for Reporting Diagnostic Accuracy Studies guidelines, a clinical reference standard is the "best available method for establishing the presence or absence of the target condition" with a gold standard being "an error-free reference standard".[124]

Based on this definition, no gold standard diagnostic method for scabies exists as no current diagnostic method is without error. It has been proposed that the clinical reference standard for scabies be *ex vivo* identification of the scabies mite, eggs or faeces under a microscope.[40, 106] Additionally, dermoscopy-guided skin sampling can increase sensitivity.[105] However, microscopy is not readily available in areas where the burden of scabies is high, and it is time consuming and not suitable for field surveys or clinical examination in these settings. Furthermore, microscopy can have a low sensitivity. In order to increase the robustness of the clinical reference standard, some experts have suggested that negative diagnoses should be followed up at a later stage and reassessed, a technique which was used in a small sample of the studies reviewed.[110, 125] However, this is often not practical, especially in areas where there is a high prevalence. Although the use of dermoscopy could be practical in some low-resource settings, most individuals are not trained in its use and do not have access to a dermatoscope because of cost.

There is a clear need for an alternate, simple clinical reference standard for settings where scabies is most prevalent that does not incorporate use of a sophisticated or expensive device. Clinical examination by expert examiners may be the most appropriate clinical reference standard in such settings.[126]

2.5 Conclusions

In settings where scabies is endemic, diagnosis depends on clinical assessment. Currently, there is little evidence to suggest that diagnostic tools may feasibly or significantly increase the accuracy of diagnosis in high prevalence settings. It is therefore important that the clinical diagnosis of scabies is investigated for accuracy. Additionally, clinical diagnosis requires international standardization so that burden of disease can be reliably measured and compared between regions and programs.

Consensus diagnostic criteria for scabies were published by the International Alliance for the Control of Scabies in 2018 (IACS Criteria). However, these criteria have not yet been validated. Furthermore, there are no published consensus guidelines on what can be considered typical lesions and typical distribution of lesions, both critical elements to the IACS Criteria. Investigation of the use of these criteria to diagnose scabies by experts and non-experts is an important step in the development of robust clinical diagnostic methods for standardization and use in clinical trials. Investigating the common appearance and locations of scabies lesions will support the description of what is considered typical for lesion type and distribution.

Until other methods of diagnosis are available and acceptable in scabies endemic settings, standardisation of the clinical diagnosis of scabies is essential. This will require the development of standardized training, diagnostic criteria and examination methodology.

Chapter 3. The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy

Osti MH, Sokana O, Gorae C, Whitfeld MJ, Steer AC, Engelman D. The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy. *PLoS Negl Trop Dis*. 2019;13(8):e0007635.

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy

Millicent H. Osti[1,2,3], Oliver Sokana[4], Christina Gorae[4], Margot J. Whitfeld[5,6], Andrew C. Steer[1,2,3,7], Daniel Engelman[1,2,3,7]*

1 Tropical Diseases, Murdoch Children's Research Institute, Melbourne, VIC, Australia, **2** Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia, **3** Melbourne Children's Global Health, Melbourne, VIC, Australia, **4** Ministry of Health and Medical Services, Honiara, Solomon Islands, **5** Department of Dermatology, St Vincent's Hospital, Sydney, NSW, Australia, **6** School of Medicine, University of New South Wales, Sydney, NSW, Australia, **7** Department of General Medicine, Royal Children's Hospital, Melbourne, VIC, Australia

* Daniel.Engelman@rch.org.au

Abstract

Background

Although scabies is estimated to be one of the most common skin conditions globally, prevalence data is not available in most settings. Disease mapping is required to develop and monitor successful control programs. Non-expert health workers are likely to play an important role in scabies mapping activities in endemic settings.

Methodology

Four non-expert health workers were trained in the diagnosis of scabies and impetigo. The health worker diagnosis was compared to a reference consensus diagnosis of two doctors experienced in diagnosis. The study was conducted in a primary school in Gizo, Solomon Islands, in August 2018. The six examiners consecutively assessed school students, blinded to each other's findings. Training and diagnostic procedures followed criteria for scabies diagnosis established by the International Alliance for the Control of Scabies in 2018.

Principal findings

Amongst the 171 students who underwent clinical assessment the prevalence of scabies and impetigo according to the reference standard was 55% and 45% respectively. Sensitivity of the non-expert health workers' diagnosis compared to the reference standard was 55.3% for scabies (95% confidence interval [CI], 50.1–60.4) with a specificity of 89.9% (95% CI 86–93.1) and 52.6% for impetigo (95% CI 46.9–58.3) with a specificity 97.8% (95% CI 95.7–99). Sensitivity for moderate to severe scabies was 93.5% (95% CI 86.3–97.6) with a specificity of 74% (95% CI 70.2–77.5).

Conclusions

Following brief training, the diagnostic accuracy of non-expert health workers for scabies and impetigo was promising, especially for moderate to severe disease. Modifications to

OPEN ACCESS

Citation: Osti MH, Sokana O, Gorae C, Whitfeld MJ, Steer AC, Engelman D (2019) The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy. PLoS Negl Trop Dis 13(8): e0007635. https://doi.org/10.1371/journal.pntd.0007635

Editor: Katja Fischer, QIMR Berghofer Medical Research Institute, AUSTRALIA

Received: March 17, 2019

Accepted: July 16, 2019

Published: August 19, 2019

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: DE and ACS are supported by fellowships from the National Health and Medical Research Council of Australia. ACS is also supported by the National Heart Foundation of Australia. MHO is supported by an Australian Government Research Training Program (RTP) Scholarship. The funders had no role in study design, data collection and

analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

training and processes are recommended to further improve accuracy. The diagnosis by non-expert health workers may be acceptable for scabies and impetigo mapping in endemic areas.

Author summary

Scabies is a parasitic infection that leads to significant morbidity worldwide. Mapping of scabies prevalence would improve the understanding of the true burden of disease and the need for control programs in specific countries and regions. The diagnosis of scabies in low resource settings, where the disease is most prevalent, is reliant on clinical examination. A task shifting approach, utilizing local health staff, could substantially increase the feasibility to undertake mapping surveys in low-resource settings. In this study, we aimed to evaluate the diagnostic accuracy of clinical assessment of local health workers following brief training. Our study found that these non-expert health workers could diagnose scabies with moderate accuracy and diagnose more severe disease with high accuracy. Further work is needed to develop standardized training packages to ensure a high level of diagnostic accuracy by non-expert health workers.

Introduction

Human scabies is a parasitic skin condition caused by infestation with the mite *Sarcoptes scabiei* var. *hominis*. Scabies is a significant public health problem, affecting more than 200 million people globally, with the highest burden in low-resource settings in tropical and subtropical regions [1, 2]. Scabies frequently leads to bacterial skin infection (impetigo), which places individuals at risk of developing serious sequalae including invasive bacterial infections, poststreptococcal glomerulonephritis and possibly rheumatic fever [3–5].

The need for global control of scabies has been recognized by the World Health Organization with the recent addition of scabies to the Department of Neglected Tropical Disease (NTD) Control portfolio [6]. In order to achieve development and implementation of effective control programs, accurate burden estimates are needed. This requires development of an easily implementable protocol for standardized diagnosis in settings where scabies is endemic. Scabies disproportionately affects low resource communities, where clinical diagnosis remains the most commonly used method in programs and research, performed by experts or by local health staff such as nurses [7]. However, clinical diagnostic methods and case definitions are not consistent across studies [7, 8].

Diagnostic criteria, developed through a global Delphi consensus study, and published in 2018 by the International Alliance for the Control of Scabies (IACS), aim to improve the standardization of diagnosis for observational and interventional research [9]. The IACS Criteria enable diagnosis at three levels of diagnostic certainty: level A—Confirmed Scabies; level B—Clinical Scabies; or level C—Suspected Scabies (Table 1). Levels B and C aim to facilitate standardized diagnosis in settings where clinical assessment is the only available or practical diagnostic tool. In the absence of the development of a simple diagnostic test and an expected shortage of available experts, trained non-expert examiners are likely to play a central role in future population screening. This reflects the 'task shifting' approach suggested by the World Health Organization in order to maximize human resources by the reallocation of specific tasks to health workers with reduced training time and less qualifications [10]. Brief training of

Table 1. IACS Criteria for the diagnosis scabies.

A:	**Confirmed scabies**
A1:	Mites, eggs or feces on light microscopy of skin samples
A2:	Mites, eggs or feces visualized on individual using high powered imaging device
A3:	Mite visualized on individual using dermoscopy
B:	**Clinical Scabies**
B1:	Scabies burrows
B2:	Typical lesions affecting male genitalia
B3:	Typical lesions in a typical distribution and two history features
C:	**Suspected Scabies**
C1:	Typical lesions in a typical distribution and one history feature
C2:	Atypical lesions or an atypical distribution and two history features
	History Features
H1:	Itch
H2:	Close contact with an individual who has itch or typical lesions in a typical distribution

A diagnosis of scabies should only be made if other differential diagnoses are considered less likely than scabies.

https://doi.org/10.1371/journal.pntd.0007635.t001

health workers can improve their diagnostic ability following clinical assessment [11]. The clinical assessment of trained, non-expert examiners has been used for diagnosis and mapping for other NTDs including trachoma, leprosy and podoconiosis [12–14].

Although the IACS Criteria provide a consensus approach for scabies diagnosis, they have not yet been validated. The feasibility of implementing these criteria for scabies in a low-resource setting, and the accuracy of non-experts in using the criteria remain unknown. Therefore, we aimed to investigate the diagnostic accuracy of briefly trained, non-expert examiners in the diagnosis of scabies, using the IACS criteria.

Methods

Ethics statement

Ethics approval was granted by the Royal Children's Hospital Melbourne Human Research Ethics Committee (reference number 38099A) and the Solomon Islands Health Research and Ethics Review Board (reference number 05/18).

Study design and setting

This single site, prospective study of diagnostic accuracy took place in Gizo, a town in the Western Province of the Solomon Islands, with an estimated population of 7,177 [15]. The Solomon Islands is categorized as a low human development country, based on the United Nation's Human Development Index, ranking 156 out of 188 countries and territories [16]. A survey of scabies in the Western Province (but not including Gizo town) in 2014 estimated the prevalence of scabies to be 19.2% and the prevalence of impetigo to be 32.7% [17]. The study followed the STARD criteria for studies of diagnostic accuracy (S3 Table) [18].

Participants

The Western Province Ministry of Health recruited four nurses from surrounding towns to travel to Gizo for the study. The nurses provided informed written consent to participate.

Students from a single primary school were consecutively enrolled from August 21 to 24, 2018. Information was sent out to families in the weeks leading up to study. Members from the

study team attended a meeting with teachers and parents to answer any questions. Signed written consent was obtained from parents or guardians of all participating students. All students with parental consent were eligible for inclusion. There were no exclusion criteria.

All participants underwent six sequential, blinded clinical assessments (by four non-expert examiners and two expert examiners) at Gizo Primary School over four days. Each child was assessed by all examiners on the same day. Data were collected on skin examination and history features based on the components of the IACS Criteria.

Training

Four nurses were recruited to participate based on availability and pre-defined desirable attributes and skills, similar to the indicators used by the Global Trachoma Mapping Project (GTMP) [13]. These included effective communication skills, ability to work long days, capacity to work with technological devices and ability to travel for fieldwork. The nurses were current employees of the Ministry of Health working in local health centers clinics or hospitals. They were aware of scabies and impetigo through previous professional experience but had no formal training in diagnosis of these skin conditions prior to the study. In August 2018, the nurses participated in an intensive two-day training program led by two doctors with extensive experience in the clinical diagnosis of scabies and in training of skin disease. A third doctor provided background information on the public health importance of scabies. Training consisted of interactive tutorials focused on the clinical features of scabies, based on the IACS Criteria [9]. At the time of the study, only the basic criteria levels were published, and detailed information on the criteria (for example, how to define 'typical lesions' and 'typical distribution') was not available. Trainers therefore interpreted these terms using previous experience. Nurses were also trained in the diagnosis of bacterial skin infection, which frequently complicates scabies lesions (causing infected scabies), or can coexist as impetigo [19]. They were also trained to identify other locally relevant skin conditions that may present similarly to scabies.

Written assessment

As a component of training, the nurses took a written test consisting of 50 clinical cases, similar to the GTMP grader training slide-test [13]. Each case included one clinical photograph and relevant history features. Nurses were instructed to indicate the presence or absence of scabies and/or bacterial skin infection. Responses were marked against the consensus diagnosis of two experts. There was no minimum competency required in order to progress to the clinical assessment.

Clinical assessment

Supervised, practical training was then conducted in the school setting and included participants with and without the target skin conditions. Diagnosis relied on clinical assessment (IACS Criteria Level B, Clinical Scabies, and C, Suspected Scabies, Table 1). Neither microscopy nor dermoscopy were used by any examiner for reasons of logistics and cost, and to resemble the conditions that may be anticipated as part of a scabies mapping surveys in a low-resource setting. There was no specified time limit for clinical examination.

The clinical assessment was a focused skin examination of exposed areas. The children wore school uniforms consisting of shorts and a short-sleeved shirt or a short-sleeved school dress. Shoes (most often sandals) were removed prior to assessment. Therefore, exposed areas were neck, face and scalp, from fingers to upper arms, and from toes to upper thighs. The genitals were not examined so the IACS subcategory B2 (typical lesions affecting male genitalia) was not included.

For the purpose of this study, typical lesions were defined as multiple small lumps (papules, nodules or vesicles) occurring in the same area. Typical distribution of lesions was defined as lesions on the fingers, finger-webs, wrists, hands, forearms toe-webs, feet and legs. All examiners were provided with a body diagram outlining the regions considered typical for scabies lesions. Scabies severity was defined by number of lesions, consistent with previous studies [17, 20]: mild, 1–10 lesions; moderate, 11–49 lesions; or severe, $\geq$ 50 lesions.

Each examiner also assessed the two history components of the IACS Criteria (presence of itch, and contact history). A positive response to any of the four following questions was considered as a positive contact history: whether an individual lived with someone with itch; lived with someone with a rash that looked like scabies; had a friend or classmate with itch; or had a friend or classmate with a rash that looked like scabies. Students were shown reference photographs of typical scabies rashes to aide these questions.

Impetigo was defined as papules, pustules or ulcerative lesions with associated erythema, crusting or pustular exudate. Impetigo included both infected scabies lesions and discrete impetigo lesions. Severity of impetigo was defined as: very mild (1–5 lesions); mild (6–10 lesions); moderate (11–49 lesions); or severe ($\geq$ 50 lesions) [21].

Index test

The index test was the clinical diagnosis of scabies (and impetigo) by non-expert examiners (the four nurses) following training.

Reference standard

The reference standard was the diagnosis made by two medical doctors (a dermatologist and a pediatrician) with extensive experience in the diagnosis of scabies and tropical skin diseases. The two doctors independently assessed participants for scabies (using the IACS Criteria) and bacterial skin infection. Where there was disagreement on the presence of scabies or impetigo, the participant was re-examined by both doctors together to establish a consensus diagnosis.

Analysis

Sample size was calculated based on an anticipated sensitivity and specificity of 90% for scabies diagnosis, with a confidence interval (CI) of 80–99%. This required enrolment of at least 40 individuals with scabies and 40 without scabies [22]. However, the school principal requested that the study team examine all individuals who provided consent. Therefore, as many participants as feasible were enrolled within the four-day period when all six examiners were available. Eligible participants that could not be examined during this time were examined off-study at a later date.

Sensitivity and specificity were calculated for the diagnosis of scabies and impetigo by comparing the index test to the reference standard. As secondary outcomes, the accuracy in diagnosis of more severe forms of each disease was also calculated. Agreement between the two experts on the diagnosis of scabies and impetigo was calculated using Cohen's kappa coefficient [23]. Inter-rater agreement for the reporting of itch and contact history was calculated using Fleiss's kappa, for all participants where an answer was recorded by all six examiners [24]. Stata 15.1 (Statacorp, College Station, TX, USA) was used for all statistical calculations.

Treatment

All participants diagnosed with scabies by expert examiners, as well as their household contacts, were offered treatment with permethrin 5% cream. Individuals diagnosed with mild

impetigo were provided information on home-based management. Individuals with moderate or severe impetigo, or other conditions requiring treatment, were referred to the local health service.

Results

171 individuals participated, and all were assessed by four non-expert examiners and two experienced doctors, resulting in a paired index and reference test (Fig 1). There were no adverse events. The mean age of the children was 8.8 years (standard deviation 2.3, range 4–14) and 51.5% were female (Table 2).

According to the reference standard, the prevalence of scabies was 55% (95% CI 47.2–62.6), and 67% of these had mild disease (Table 2). The prevalence of impetigo was 45% (95% CI 37.4–52.8), and 83.1% of these had very mild disease (Table 2). Of individuals with scabies, 47 (50.5%) had bacterial superinfection or co-infection (Fig 2).

The prevalence of scabies according to the two individual doctors was 53.2% (95%CI 45.4–60.9) and 49.7% (95%CI 42–57.4) respectively.

Overall, the prevalence of scabies according to the index test (briefly trained nurses) was 34.9% (95% CI 31.4–38.6, Table 3). Prevalence by individual examiner ranged from 22.8% to 40.9% (Fig 3). The prevalence of impetigo according to the index test was 25.2% (95% CI 21.9–28.7, range of individual examiners 18.7% to 32.2%, Table 4).

The sensitivity of the index test compared to the reference standard for scabies diagnosis was 55.3% (95% CI 50.1–60.4, Table 3). Sensitivity for individual non-expert examiners ranged from 41.5% to 64.9% (Table 3). The specificity of the index test was 89.9% (95% CI 86–93.1, range of individual examiners 87.0% to 100%). When considering only the moderate and severe cases of scabies (n = 31), the sensitivity of the index test was 93.5% (95% CI 86.3–97.6,

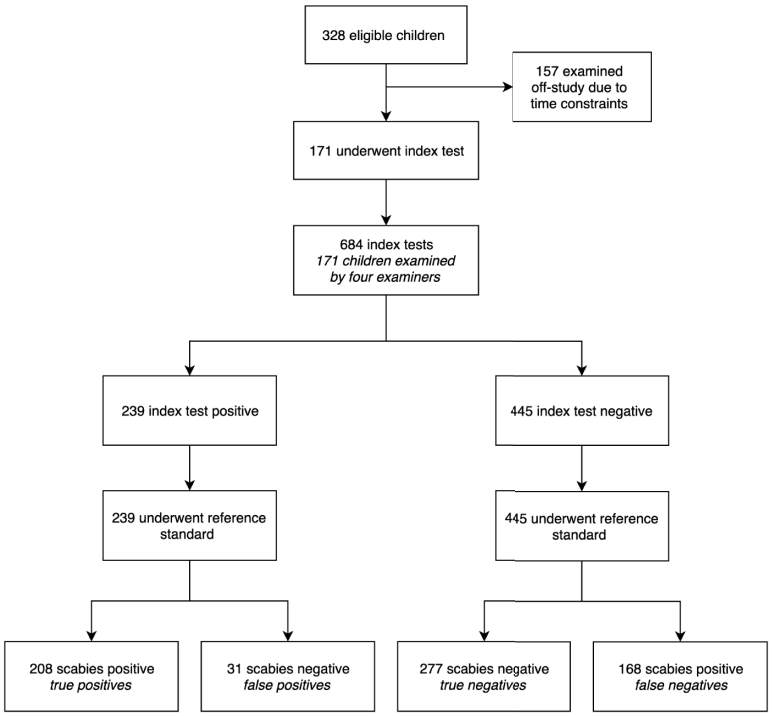


Fig 1. Flow of participants for the diagnosis of scabies.

https://doi.org/10.1371/journal.pntd.0007635.g001

Table 2. Severity of disease and clinical characteristics.

Characteristic	N = 171	%
Scabies	**n = 94**	55.0
Severity		
Mild (1–10 lesions)	63	67.0
Moderate (11–49 lesions)	21	22.3
Severe (≥50 lesions)	10	10.6
IACS Criteria		
Clinical Scabies		
B1: Scabies Burrows*	4	2.3
B3: Typical lesions in a typical distribution with itch and positive contact	65	69.1
Suspected Scabies		
C1: Typical lesions in a typical distribution with itch or positive contact	23	24.5
C2: Atypical lesions or typical distribution with itch and positive contact	6	6.4
Impetigo	**n = 77**	45.0
Severity		
Very mild (1–5 lesions)	64	83.1
Mild (6–10 lesions)	8	10.4
Moderate (11–49 lesions)	2	2.6
Severe (≥50 lesions)	3	3.9

*Individuals with burrows were additionally categorized as either B3, C1, C2

https://doi.org/10.1371/journal.pntd.0007635.t002

range of individual non-expert examiners 87% to 95.7%). The specificity of the index test for moderate and severe scabies was 74.0% (95% CI 70.2–77.5, range of individual non-expert examiners ranged 67.3% to 87.1%, S1 Table).

For impetigo, the sensitivity of the index test was 52.6% (95% CI 46.9–58.3, range of individual non-expert examiners 39.0% to 68.8%), and specificity was 97.8% (95% CI 95.7–99, range of individual non-expert examiners 96.7% to 98.8%, Table 4). If only cases of impetigo with six or more infected lesions were considered (n = 13), then the sensitivity of the non-expert nurses was 84.6% (95% CI 71.9–93.1) and the specificity was 79.8% (95% CI 76.4–82.9).

Repeat assessment was required to define the reference standard for 46 out of 171 (26.9%) cases due to disagreement on presence of scabies or impetigo between the doctors. Agreement between the two experts for scabies was 83.6% (kappa = 0.67) and for moderate to severe scabies was 91.3% (kappa = 0.68). Agreement between the experts for impetigo was 87.1% (kappa = 0.73).

The inter-rater agreement (Fleiss kappa) for the reporting of history by individuals between the six examiners was 0.63 for self-reported itch and 0.52 for any contact history (S2 Table).

The results of the written test completed during training for each non-expert examiner were 76%, 92%, 96% and 96% correct for scabies respectively, and 70%, 76%, 76% and 80% correct for impetigo respectively.

Discussion

We found that briefly trained, non-expert examiners had moderate sensitivity and high specificity in the diagnosis of scabies using the IACS Criteria, compared to reference diagnosis by two expert examiners. The accuracy of examiners is dependent on the effectiveness of training and examination protocols. Our results suggest that modifications to the training protocol are needed to maximize the accuracy and utility for non-expert scabies assessment. More detailed

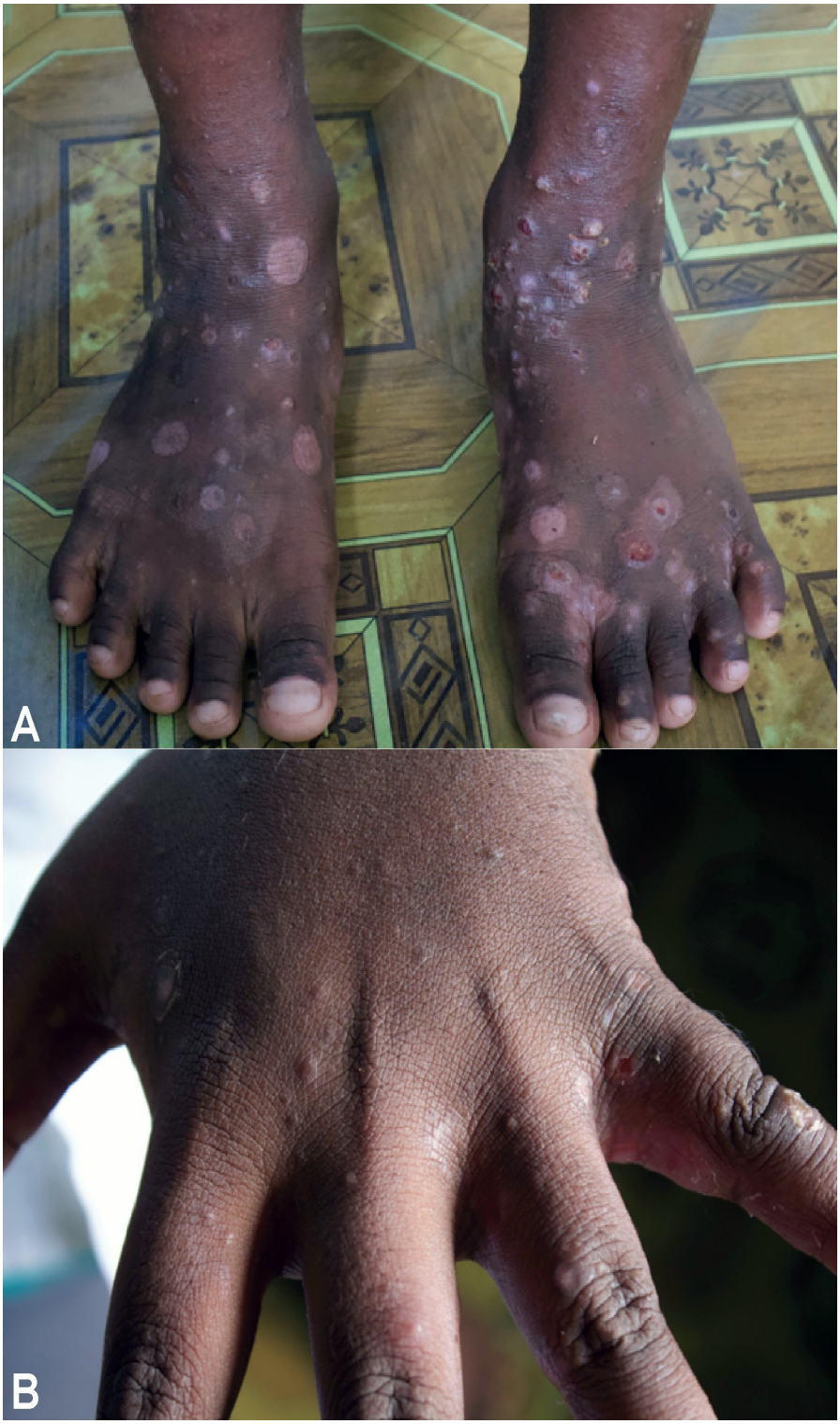


Fig 2. Example appearance of scabies lesions (A. Scabies lesions over feet and ankles with bacterial super-infection, B. Papular scabies lesions over fingers, finger-webs and dorsum of hand).

https://doi.org/10.1371/journal.pntd.0007635.g002

Table 3. Accuracy of scabies diagnosis.

	Participants Screened (n)					Scabies % (95%CI)	Measurement of accuracy (95%CI)				
	TP	FP	FN	TN	Total	Prevalence	Sensitivity	Specificity	PPV	NPV	OR
Nurse A	60	10	34	67	171	40.9 (33.5–48.7)	63.8 (53.3–73.5)	87 (77.4–93.6)	85.7 (73.3–92.9)	66.3 (56.2–75.4)	11.8 (5.4–25.7)
Nurse B	61	6	33	71	171	39.2 (31.8–46.9)	64.9 (54.4–74.5)	92.2 (83.8–97.1)	91 (81.5–96.6)	68.3 (58.4–77.1)	21.9 (8.8–54.3)
Nurse C	39	0	55	77	171	22.8 (16.8–29.8)	41.5 (31.4–52.1)	100 (95.3–100)	100 (91–100)	58.3 (49.4–66.8)	*
Nurse D	48	15	46	62	171	36.8 29.6–44.5)	51.1 (40.5–61.5)	80.5 (69.9–88.7)	76.2 (63.8–86)	57.4 (47.5–66.9)	4.31 (2.2–8.6)
Total	208	31	168	277	684	34.9 (31.4–38.6)	55.3 (50.1–60.4)	89.9 (86–93.1)	87 (82.1–91)	62.2 (57.6–66.8)	11.1 (7.3–16.9)

TP = true positive, FP = false positive, FN = false negative, TN = true negative

*OR could not be calculated due to 0 values

https://doi.org/10.1371/journal.pntd.0007635.t003

information regarding the IACS Criteria, particularly relating to the definition of typical lesions, is expected to be available soon, which will inform components of training [9].

Although a sensitivity of 55% for scabies diagnosis is lower than expected, a sensitivity of 94% for mild to moderate cases is substantial. Our results are similar to a previous study in Fiji, where nurse examiners' diagnosis was compared to a single experienced examiner, with

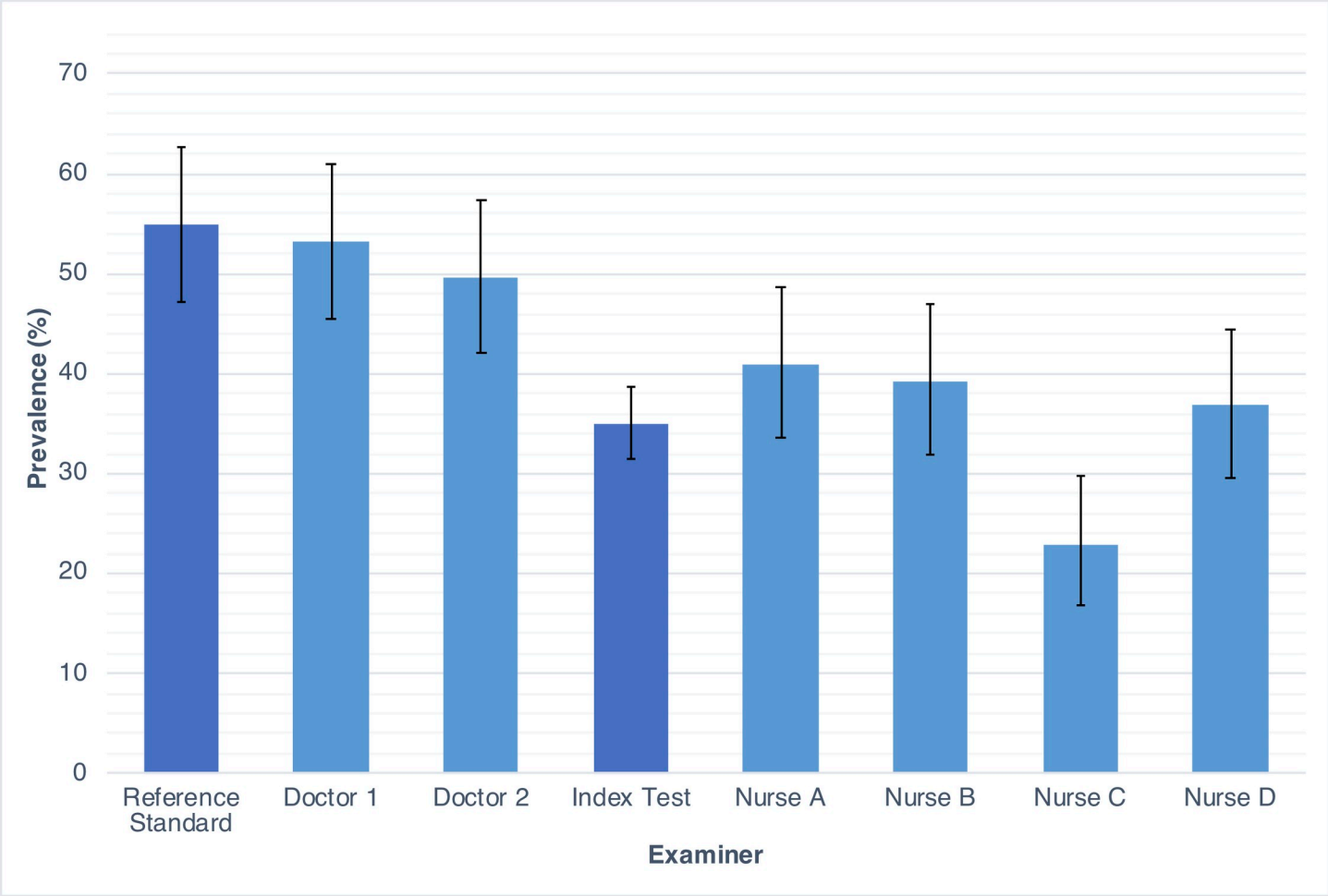


Fig 3. Prevalence of scabies by examiner with 95% confidence intervals.

https://doi.org/10.1371/journal.pntd.0007635.g003

Table 4. Accuracy of impetigo diagnosis.

	Participants Screened (n)					Impetigo % (95%CI)	Measurement of accuracy (95%CI)				
	TP	FP	FN	TN	Total	Prevalence	Sensitivity	Specificity	PPV	NPV	OR
Nurse A	36	1	39	84	160	23.1 (16.8–30.4)	48.0 (36.3–59.8)	98.8 (93.6–100)	97.3 (85.8–99.9)	69.3 (59.3–76.4)	77.5 (12.9-)
Nurse B	42	3	35	89	169	26.6 (20.1–34)	54.5 (42.8–65.9)	96.7 (90.8–99.3)	93.3 (81.7–98.6)	71.8 (63–79.5)	35.6 (10.9–115)
Nurse C	53	2	24	92	171	32.2 (25.2–39.7)	68.8 (57.3–78.9)	97.9 (92.5–99.7)	96.4 (87.5–99.6)	79.3 (70.8–86.3)	102 (25.3-)
Nurse D	30	2	47	92	171	18.7 (13.2–25.4)	39.0 (28.0–50.8)	97.9 (92.5–99.7)	93.8 (79.2–99.2)	66.2 (57.7–74)	29.4 (7.4-)
Total	161	8	145	357	671	25.2 (21.9–28.7)	52.6 (46.9–58.3)	97.8 (95.7–99)	95.3 (90.9–97.9)	71.1 (66.9–75)	49.5 (24.1–102)

TP = true positive, FP = false positive, FN = false negative, TN = true negative

https://doi.org/10.1371/journal.pntd.0007635.t004

diagnosis based on the Integrated Management of Childhood Illness protocol [25]. Nurses in that study had a higher sensitivity (89%) for cases of infected scabies (which may be representative of more severe disease) compared to non-infected scabies (58%). In our study, 66% of scabies cases were mild, similar to the severity found in other studies [17, 20]. We suggest future training incorporate a more specific focus on the diagnosis of mild scabies.

The lower sensitivity in the diagnosis of mild disease may have reflected the normalization of mild cases by nurses, and strict diagnosis by expert examiners. This is supported by the higher prevalence of scabies and impetigo by the reference standard (55% and 45% respectively) compared to the index test (35% for scabies and 25% for impetigo). Scabies and impetigo can be under-recognized by local health care workers at the health clinic level [26], and therefore mapping of scabies and impetigo using non-expert examiners may under-report the true disease prevalence. Improved awareness of scabies in communities and amongst health care workers where it is endemic, as well as the suggested modifications to training, may lead to improvements in accuracy.

Sensitivity for scabies diagnosis varied between the nurse examiners, from 41% to 65%, despite the same training and similar background experience. There were few false positives, reflected by the narrow specificity range among nurses (87–100%). This again highlights that missed mild disease was the major issue encountered. The range in accuracy is as expected and illustrates the inherent variability in proficiency among health care workers at all levels. If examiners were to be employed for mapping exercises, a minimum competency (for example, of $\geq$ 80%) should be achieved for accreditation, similar to methods used in training for trachoma [13] and other diseases.

The written, picture-based test was a valuable component of the training, enabling trainers and nurses to identify areas for further training, prior to commencing supervised practical training. The written test allowed trainers to revisit concepts that individuals may have not grasped adequately, similar to the role of the GTMP slide-assessment [13]. We propose this be used as a hurdle-requirement during training that must be passed to proceed to practical training. Refinements to the written test, such as the inclusion of more mild cases, may ensure that the test is more representative of the clinical disease profile.

This study was the first to implement the IACS Criteria for scabies diagnosis. These criteria were easily adapted for data collection, allowing standardization of diagnosis amongst the examiners. However, the criteria rely on self-reported itch and contact history, which may be less reliable components. Itch was reported more consistently by the participants (Fleiss kappa = 0.63) than contact history (Fleiss kappa = 0.52). Potentially, these self-reported history components may be less reliable in children than in adults.

We found a very high prevalence of scabies (55%) amongst the participants in the study. This is much higher than previous figures reported by the Solomon Islands Ministry of Health.

It is likely that this high burden of disease has a detrimental impact on schooling and health outcomes, highlighting the need for further epidemiologic mapping and control responses in these settings.

This study has several limitations. First, all evaluations of scabies diagnosis are limited by the lack of an objective reference or "gold" standard for diagnosis. However, agreement between the expert examiners was good (kappa = 0.67 for scabies, kappa = 0.73 for impetigo). Second, the blinding of expert assessment and the requirement of consensus diagnosis between two expert examiners was used for a more rigorous diagnostic process. However, it is possible that the consensus process led to an overly sensitive reference standard, particularly as 27% of individuals required re-assessment and discussion for consensus. Many of these were mild cases with a very small number of lesions, where one examiner had thought the most likely cause to be scabies. The potential overdiagnosis may have reduced the diagnostic accuracy of the index test. Third, we only included clinical assessment of school-aged children, and accuracy may be different in other age groups. However, scabies and impetigo present similarly among older children and adults [27], and the inclusion of a wider age group may not yield vastly different results. Additionally, the inclusion of only four non-expert examiners is a limitation, however, this was a feasible number for training and ensured that training was closely supervised. Finally, due to resources and infrastructure available in the school buildings, particularly a lack of electrical power, and conditions of severe heat and humidity, examiners had suboptimal lighting and examination conditions, which may have influenced the results. Although limiting, this environment may reflect the real-world implementation of the index test in settings such as the Solomon Islands. Conditions for examinations in low resource settings may be optimized by the use of torches or external lighting for examination and by emphasizing the need for appropriate working environments.

The results of this study reflect the training program, the participating examiners and the population and may not be generalizable to other settings, particularly those with a lower prevalence. However, this study is an important step toward standardization of diagnosis of scabies and impetigo for mapping and research in low-resource settings. In order for scabies prevalence mapping to occur, either in isolation, or integrated with other NTD assessments, governments and organizations need to be able to feasibly and confidently train local staff in diagnosis. Further refinements to the training and assessment processes are required and may lead to improvements in diagnostic accuracy.

Supporting information

S1 Table. Accuracy of moderate to severe scabies diagnosis.
(PDF)

S2 Table. Consistency in the reporting of history features.
(PDF)

S3 Table. STARD checklist.
(PDF)

Acknowledgments

We wish to thank the participating nurses, the school principal Nester Thugea and teachers, and the participating children and families for their involvement and support of the study. We would also like to thank Dickson Boara, Sophie Phelan, Michael Marks, John Kaldor, Anneke Grobler, Deanne Seppy, Vivegan Visvalingam and Ender Malasa for their assistance with study design and conduct.

Author Contributions

Conceptualization: Millicent H. Osti, Daniel Engelman.

Data curation: Millicent H. Osti.

Formal analysis: Millicent H. Osti, Daniel Engelman.

Investigation: Margot J. Whitfeld, Daniel Engelman.

Methodology: Millicent H. Osti, Andrew C. Steer, Daniel Engelman.

Supervision: Andrew C. Steer, Daniel Engelman.

Writing – original draft: Millicent H. Osti.

Writing – review & editing: Millicent H. Osti, Oliver Sokana, Christina Gorae, Margot J. Whitfeld, Andrew C. Steer, Daniel Engelman.

References

1. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388(10053):1545–602. https://doi.org/10.1016/S0140-6736(16)31678-6 PMID: 27733282
2. Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Prevalence of scabies and impetigo worldwide: a systematic review. Lancet Infect Dis. 2015; 15(8):960–7. https://doi.org/10.1016/S1473-3099(15)00132-2 PMID: 26088526
3. Engelman D, Kiang K, Chosidow O, McCarthy J, Fuller C, Lammie P, et al. Toward the Global Control of Human Scabies: Introducing the International Alliance for the Control of Scabies. PLoS Neglected Tropical Diseases. 2013; 7 (8) (e2167). https://doi.org/10.1371/journal.pntd.0002167 PMID: 23951369
4. Romani L, Koroivueta J, Steer AC, Kama M, Kaldor JM, Wand H, et al. Scabies and impetigo prevalence and risk factors in Fiji: A national survey. Australasian Journal of Dermatology. 2015;(2):64. https://doi.org/10.1371/journal.pntd.0003452 PMID: 25738499
5. Thornley S, Marshall R, Jarrett P, Sundborn G, Reynolds E, Schofield G. Scabies is strongly associated with acute rheumatic fever in a cohort study of Auckland children. J Paediatr Child Health. 2018; 54 (6):625–32. https://doi.org/10.1111/jpc.13851 PMID: 29442387
6. Report of the tenth meeting of the WHO Strategic and Technical Advisory Group for neglected tropical diseases. Geneva: World Health Organisation; 2017.
7. Thompson MJ, Engelman D, Gholam K, Fuller LC, Steer AC. Systematic review of the diagnosis of scabies in therapeutic trials. Clinical and Experimental Dermatology. 2017; 42(5):481–7. https://doi.org/10.1111/ced.13152 PMID: 28556185
8. Leung V, Miller M. Detection of scabies: A systematic review of diagnostic methods. Canadian Journal of Infectious Diseases and Medical Microbiology. 2011; 22(4):143–6. https://doi.org/10.1155/2011/698494 PMID: 23205026
9. Engelman D, Fuller LC, Steer AC, International Alliance for the Control of Scabies Delphi p. Consensus criteria for the diagnosis of scabies: A Delphi study of international experts. PLoS Negl Trop Dis. 2018; 12(5):e0006549. https://doi.org/10.1371/journal.pntd.0006549 PMID: 29795566
10. Task shifting: rational redistribution of tasks among health workforce teams: global recommendations and guidelines. Geneva World Health Organization 2008.
11. Mahe A, Faye O, N'Diaye HT, Konare H, Coulibaly I, Keita S, et al. Integration of basic dematological care into primary health care services in Mali. Bull World Health Organ. 2005; 83.(12):935–941. https://doi.org/10.1590/S0042-96862005001200016 PMID: 16462986
12. Deribe K, Wanji S, Shafi O, E MT, Umulisa I, Molyneux DH, et al. The feasibility of eliminating podoconiosis. Bull World Health Organ. 2015; 93(10):712–8. https://doi.org/10.2471/BLT.14.150276 PMID: 26600613
13. Solomon AW, Pavluck AL, Courtright P, Aboe A, Adamu L, Alemayehu W, et al. The Global Trachoma Mapping Project: Methodology of a 34-Country Population-Based Study. Ophthalmic Epidemiol. 2015; 22(3):214–25. https://doi.org/10.3109/09286586.2015.1037401 PMID: 26158580

14. Faye O, Hay RJ, Ryan TJ, Keita S, Traore AK, Mahe A. A public health approach for leprosy detection based on a very short term-training of primary health care workers in basic dermatology. Leprosy Review. 2007; 78(1):11–6. PMID: 17518081

15. Provincial Profile of the 2009 Population & Housing Census: Western. Solomon Islands Government; 2009.

16. Solomon Islands Human Development Indices and Indicators: 2018 Statistical Update UNDP; 2018.

17. Mason DS, Marks M, Sokana O, Solomon AW, Mabey DC, Romani L, et al. The Prevalence of Scabies and Impetigo in the Solomon Islands: A Population-Based Survey. PLoS Negl Trop Dis. 2016; 10(6): e0004803. https://doi.org/10.1371/journal.pntd.0004803 PMID: 27348119

18. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015; 351:h5527. https://doi.org/10.1136/bmj.h5527 PMID: 26511519

19. Hay RJ, Steer AC, Engelman D, Walton S. Scabies in the developing world—its prevalence, complications, and management. Clin Micro Infect. 2012; 18(4):313–23.

20. Romani L, Whitfeld MJ, Koroivueta J, Kama M, Wand H, Tikoduadua L, et al. The Epidemiology of Scabies and Impetigo in Relation to Demographic and Residential Characteristics: Basline Findings from the Skin health Intervention Fiji Trial. Am J Trop Med Hyg. 2017; 97(3):845–50. https://doi.org/10.4269/ajtmh.16-0753 PMID: 28722612

21. Steer AC, Jenney AW, Kado J, Batzloff MR, La Vincente S, Waqatakirewa L, et al. High burden of impetigo and scabies in a tropical country. PLoS Negl Trop Dis. 2009; 3(6):e467. https://doi.org/10.1371/journal.pntd.0000467 PMID: 19547749

22. Buderer NM. Statistical Methodology: I. Incorporating the prevalence of Disease into the Sample Size Calculation for Sensitivity and Specificity. Academic Emergency Medicine. 1996;3. PMID: 8870764

23. Cohen J. A Coefficient of Agreement for Nominal Scales. Educational and Psychological Measurement. 1960; 20(1):37–46. https://doi.org/10.1177/001316446002000104

24. Fleiss JL. Measuring nominal scale agreement among many raters. Psychological Bulletin. 1971; 76 (5):378–82.

25. Steer AC, Tikoduadua LV, Manalac EM, Colquhoun S, Carapetis JR, Maclennan C. Validation of an Integrated Management of Childhood Illness algorithm for managing common skin conditions in Fiji. Bull World Health Organ. 2009; 87(3):173–9. https://doi.org/10.2471/BLT.08.052712 PMID: 19377712

26. Yeoh DK, Anderson A, Cleland G, Bowen AC. Are scabies and impetigo "normalised"? A cross-sectional comparative study of hospitalised children in northern Australia assessing clinical recognition and treatment of skin infections. PLoS Neglected Tropical Diseases. 2017; 11 (7) (e0005726). https://doi.org/10.1371/journal.pntd0005726 PMID: 28671945

27. Boralevi F, Diallo A, Miquel J, Guerin-Moreau M, Bessis D, Chiaverini C, et al. Clinical phenotype of scabies by age. Pediatrics. 2014; 133(4):e910–6. https://doi.org/10.1542/peds.2013-2880 PMID: 24685953

3.1 Additional Material

3.1.1 Table of the accuracy of moderate to severe scabies diagnosis (Supplementary table 1)

	Participants Screened (n)					Measurement of accuracy (95%CI)				
	TP	**FP**	**FN**	**TN**	**Total**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**OR**
Nurse A	29	41	2	99	171	93.5 (78.6-99.2)	70.7 (62.4-78.1)	41.4 (29.8-53.8)	98.0 (93-99.8)	35.0 (8.78-)
Nurse B	30	37	1	103	171	96.8 (83.3-99.9)	73.6 (65.5-80.7)	44.8 (32.6-57.4)	99.0 (94.8-100.0)	83.5 (13.8-)
Nurse C	25	14	6	126	171	80.6 (62.5-92.5)	90 (83.8-94.4)	64.1 (47.2-78.8)	95.5 (90.4-98.3)	37.5 (13.4-105)
Nurse D	28	35	3	105	171	90.3 (74.2-98.0)	75.0 (67.0-81.9)	44.4 (31.9-57.5)	97.2 (92.1-99.4)	28 (8.47-91.5)
Total	112	127	12	433	684	90.3 (83.7-94.9)	77.3 (73.6-80.7)	46.9 (40.4-53.4)	97.3 (95.3-98.6)	31.8 (17.1-59.1)

3.1.2 Consistency in the reporting of history features (Supplementary table 2)

	N	Agreement %	Fleiss' Kappa	95% CI
Itch				
Self-reported itch	83	82.8	0.63	0.52-0.75
Contact history				
Household contact with itch	80	81.1	0.60	0.50-0.71
School contact with itch	79	73.8	0.43	0.31-0.55
Household contact with scabies rash	79	82.5	0.59	0.48-0.70
School contact with scabies rash	80	76.8	0.50	0.38-0.61
Any positive contact history*	81	84.0	0.52	0.37-0.67
*Answered yes to any contact history questions				

Chapter 4. Training non-expert health workers in the diagnosis of scabies

This chapter explores and evaluates the training of non-expert health workers in the diagnosis of scabies conducted prior to the diagnostic accuracy study presented in Chapter 3.

4.1 Background

Scabies affects disadvantaged populations where access to health resources and expert personnel are limited.[3] In these settings, specific health-care tasks can be redistributed to less qualified health workers.[127] This process, known as task shifting, is endorsed by the World Health Organization as a way to increase work force capacity and improve access to health services where resources may be stretched or lacking.[128] Task shifting has been utilised for epidemiological mapping and screening for other tropical diseases such as trachoma, Buruli ulcer, leprosy, yaws and rheumatic heart disease.[129-131] For trachoma, the development of standardised training packages for clinical diagnosis has facilitated the implementation of screening in multiple settings.[130]

Clinical diagnosis remains the cornerstone of diagnosis for scabies and impetigo in almost all settings where scabies is endemic.[20, 132] A task shifting approach to scabies diagnosis would expand the workforce capacity to contribute to public health initiatives, such as community prevalence surveys. It may also enable integration of mapping for diseases where task shifting is already utilised, increasing the efficiency of skin programs for neglected tropical diseases (NTDs).[133]

Standardised methods are needed so that diagnostic approaches remain consistent across different regions and locations.[128] Simplified diagnostic algorithms have been used previously

for scabies and other skin disease.[34, 134, 135] A new set of diagnostic criteria for scabies was published in 2018 by the International Alliance for the Control of Scabies (IACS).[33] These criteria were designed to inform a standardised training package for the diagnosis of scabies.

Training non-expert examiners in the diagnosis of scabies and impetigo has been undertaken by several groups in a variety of settings.[62, 70] However, no standardised training package or delivery methodology exists. We aimed to develop such a training package, modelled on the successful Global Trachoma Mapping Project (GTMP) Training protocol.[136] The trachoma protocol consists of: 1) a classroom-based training package; 2) a picture-based inter-grader agreement test; and 3) a live-subject field test.[136] The inclusion of these tests provide a standardised competency hurdle which individuals must pass in order to be involved in the mapping program. Based on this protocol, we developed and delivered a training package for the diagnosis of scabies and impetigo. The aim of this study was to measure the change in knowledge and confidence of the training participants and to evaluate their experience of the training.

4.2 Methods

4.2.1 Setting and Participants

The training was conducted in Gizo, the capital of the Western Province in the Solomon Islands, where the prevalence of scabies was estimated to be 19% in 2014.[8] The study team liaised with the local Ministry of Health staff to identify four local nurses from the Western Province Region based on a desired set of skills and attributes. These reflected those required by GTMP, and included strong communication and teamwork skills, ability to work long hours in the field and capacity to operate handheld technological devices.[136] Training and assessment were completed in August 2018. Informed consent was obtained from the participating nurses.

4.2.2 Training

Training was delivered by two Australians doctors with experience in scabies and other tropical skin conditions. Training materials were based on suggested content from experts in scabies diagnosis, and on material previously delivered in the Solomon Islands and Fiji.[9, 27] The examination and history component of the training was focused on identifying the relevant features required for the diagnosis of scabies and impetigo. Other differential skin diagnoses that were relevant to the setting were also included.

Training consisted of two stages; classroom training at Gizo Hospital and practical training at Gizo Primary School. The classroom training content included background information on the importance of scabies as a public health problem in the Solomon Islands, further context for the study, details on global and local prevalence, complications of the diseases and basic treatment concepts. Training on the diagnosis of scabies was based on the IACS Criteria (Table 2).[33] Diagnosis of impetigo was based on previous definitions used in multiple large studies and defined as papules, pustules or ulcerative lesions with associated erythema, crusting or pustular exudate.[8, 57, 71] Clinical examination was limited to only exposed areas of skin – particularly the arms from the mid-upper arm to the finger tips, and the legs from the mid-upper though to the toes. A brief history component containing questions about itch and contact history was incorporated. Terminology and definitions used in training were consistent with the World Health Organization 2018 training guide, "Recognizing neglected tropical diseases through changes on the skin".[137]

Table 2. The 2018 IACS Criteria subcategories included for training and assessment

	IACS subcategory	Included in assessment
A	**Confirmed scabies**	
A1	Mites, eggs or feces on light microscopy of skin samples	No
A2	Mites, eggs or feces visualised on individual using high powered imaging device	No
A3	Mite visualised on individual using dermoscopy	No
B	**Clinical Scabies**	
B1	Scabies burrows	Yes*
B2	Typical lesions affecting male genitalia	No
B3	Typical lesions in a typical distribution and two history features	Yes
C	**Suspected Scabies**	
C1	Typical lesions in a typical distribution and one history feature	Yes
C2	Atypical lesions or an atypical distribution and two history features	Yes
	History Features	
H1	Itch	
H2	Close contact with an individual who has itch or typical lesions in a typical distribution	

A diagnosis of scabies should only be made if other differential diagnoses are considered less likely than scabies.

* If burrows were identified, individuals were also classified as either B3, C1, or C2, as these were not confirmed with dermoscopy

4.2.3 Education Strategies

The training program was delivered in a small group teaching setting, to encourage group interaction. The goals of the training were outlined early to orientate learning. Active participation was encouraged, with reinforcement and assessment incorporated into the material. Classroom training utilised case-based learning with clinical images, a well-established teaching technique.[138, 139] Case-based learning was used for practice and reinforcement of the data required for the survey.

Practical training incorporated the knowledge gained in classroom training with clinical skills. The training consisted of opportunities to practice the focused skin examinations and brief clinical histories. This was undertaken with school-attending children aged 4 to 15 at the local

primary school, under direct supervision from expert trainers. The school children were examined initially by the trainers while the nurses observed and then the nurses had the opportunity to practice examining. Formative feedback was provided from trainers after each case and at several breaks during the day. All students examined during training had parental consent.

4.2.4 Reference Sheet

A four-page reference sheet was developed, showing typical scabies lesions and typical scabies distribution. The reference sheet also included other helpful images to assist the examiners including images of infected scabies, scabies in infants, crusted scabies and images of common differential diagnoses. A laminated copy was provided to the nurses at the beginning of the training (Figure 19). This sheet was used during history taking to help explain what the scabies rash looks like while asking if the students' lived with or go to school with anyone with a scabies rash. This reference sheet was also utilised in the fieldwork following training to assist with diagnosis and history taking.

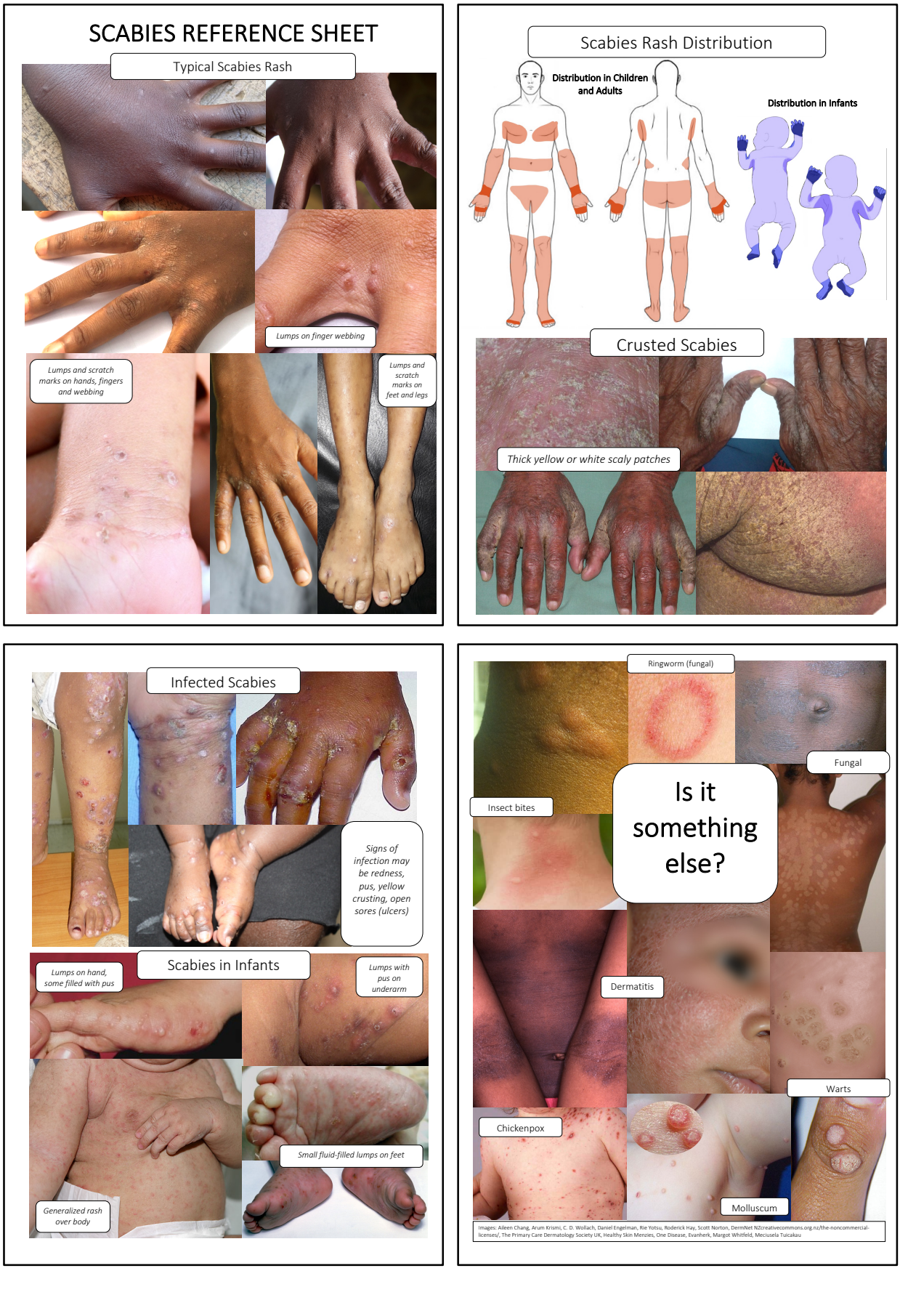


Figure 19. Scabies diagnosis reference sheet

Image represents four pages

4.2.5 Evaluation of Training

Evaluation of the training program was conducted using three different methods: 1) a case-based test; 2) a questionnaire; and 3) semi-structured interviews.

4.2.5.1 Case-based test

The case-based test was administered following the classroom training at the end of day one. The test consisted of 50 dermatological images accompanied by a succinct clinical history. Cases included scabies, impetigo, other common skin diseases (including fungal skin infection and chickenpox), as well as cases with no visible dermatological conditions. Nurses were instructed to determine if scabies and/or impetigo was present or absent. Correct answers were defined as the consensus responses from two experts.

4.2.5.2 Questionnaire

The nurses completed a questionnaire before and after training. Eight questions were asked at both time-points (Table 3), Twenty additional questions were included in the post-training questionnaire (Table 4). Most items were Likert-type questions, scored from 1 to 5. Eight additional free-text questions were included in the post-training questionnaire. Questions covered self-reported outcomes across the domains of knowledge, confidence and training usefulness. Additional questions were asked about logistics and practical components and suggestions for future training.

Table 3. The Likert scale questions for self-reported knowledge and confidence pre- and post- training

How would you describe your knowledge of:		**None**	**Little**			**Lots**
1.	What causes scabies?	1	2	3	4	5
2.	The clinical symptoms and signs of scabies?	1	2	3	4	5
3.	What causes impetigo and skin infection?	1	2	3	4	5
4.	The clinical symptoms and signs of impetigo and skin infection?	1	2	3	4	5
5.	Scabies as a public health problem?					
How confident do you feel in:		**Not at all**		**Neutral**		**Very**
6.	Diagnosing scabies?	1	2	3	4	5
7.	Diagnosing impetigo and infection?	1	2	3	4	5
8.	Completing a data collection form?	1	2	3	4	5

Table 4. Additional post-training questions to assess participant experience

How would you rate the usefulness of:		**Not at all**		**Neutral**		**Very**
1.	The classroom workshop?	1	2	3	4	5
2.	The training at the school?	1	2	3	4	5
3.	The reference sheet?	1	2	3	4	5
How difficult did you find:		**Too easy**		**About right**		**Too Hard**
4.	The classroom workshop?	1	2	3	4	5
5.	The training at the school?	1	2	3	4	5
6.	The slide assessment?	1	2	3	4	5
7.	The Independent examinations and diagnosis at the school?	1	2	3	4	5
How would you rate the quality of:		**Poor**		**Neutral**		**Excellent**
8.	The training?	1	2	3	4	5
9.	The teaching?	1	2	3	4	5
Other		**Not at all**		**Neutral**		**Very**
10.	Did you enjoy the training?	1	2	3	4	5
11.	How prepared do you feel for examinations in the community skin surveys?	1	2	3	4	5
12.	How prepared do you feel for examination for scabies and skin infection of people of other ages (e.g. babies, adults)?	1	2	3	4	5
Free text Questions						
13.	Did you mind travelling to Gizo for the training?					
14.	Where there any aspects of the training that were confusing or not clear to you					
15.	What were the best aspects of the training?					
16.	What were the worst aspects of the training?					
17.	Do you have any suggestions for what could be done differently or better during the classroom workshop?					
18.	Do you have any suggestions for what could be done differently or better during the skin survey?					
19.	In regard to the community skin surveys next year, which aspects of the training do you think are most important to cover during a refresher training course?					
20.	Please comment on if or how this training may impact your practice in your community health centre.					

4.2.5.3 Interviews

One-on-one, semi-structured interviews were undertaken by the study co-ordinator with individual nurses and the local staff involved in training, which included a local doctor and a nurse educator who wished to attend training to upskill. Interviews were guided by the interviewee's responses to the questionnaires and other issues raised during the discussion. Interviews were conducted during the week following training. Discussions focused on the nurses' personal experience and perceptions of the training. Interviews were conducted in English and all of the individuals who were providing feedback were proficient in English.

4.2.6 Analysis

Analysis of Likert-type questions was done by summing the eight individual knowledge and confidence item scores to create a scale. Scores for individual questions were scored out of 5 with overall mean scores calculated for each question. The mean scale score before and after training was compared using a paired t-test.

Thematic analysis was conducted for qualitative data from questionnaires and semi-structured interviews, with key quotes identified. Stata 15.1 (Statacorp, College Station, TX, USA) was used for all statistical calculations.

4.3 Results

The mean results for the four nurses in the case-based test were 90% for scabies and 75.5% for impetigo (Table 5). Individual nurse results varied from 76 to 96% for scabies and from 70 to 80% for impetigo.

Table 5. Case-based test results for scabies and impetigo, by individual nurse

	Scabies correct (N=50)		Impetigo correct (N=50)	
Examiner	n	%	n	%
Nurse 1	46	92	38	76
Nurse 2	48	96	35	70
Nurse 3	48	96	40	80
Nurse 4	38	76	38	76
Overall (mean)	45	90	37.8	75.5

Table 6. Pre and post-training questionnaire for self-reported knowledge and confidence

	Knowledge (mean)		Confidence (mean)	
	Pre	**Post**	**Pre**	**Post**
Nurse 1	2.6	5	3	5
Nurse 2	2.4	4	1.7	4.3
Nurse 3	2.8	4.2	3.3	4.3
Nurse 4	2	4.6	2	4.3
Total	**2.5**	**4.5**	**2.5**	**4.5**

Prior to training, the mean score for both self-reported knowledge and confidence of scabies and impetigo was 2.5 (Table 6). Following the completion of the training program, the mean score for both self-reported knowledge and confidence increased from 2.5 to 4.5 with a mean difference of 2 (95%CI 1.1-2.9, P=0.005). Scores increased for all nurses (Table 6, Figure 20).

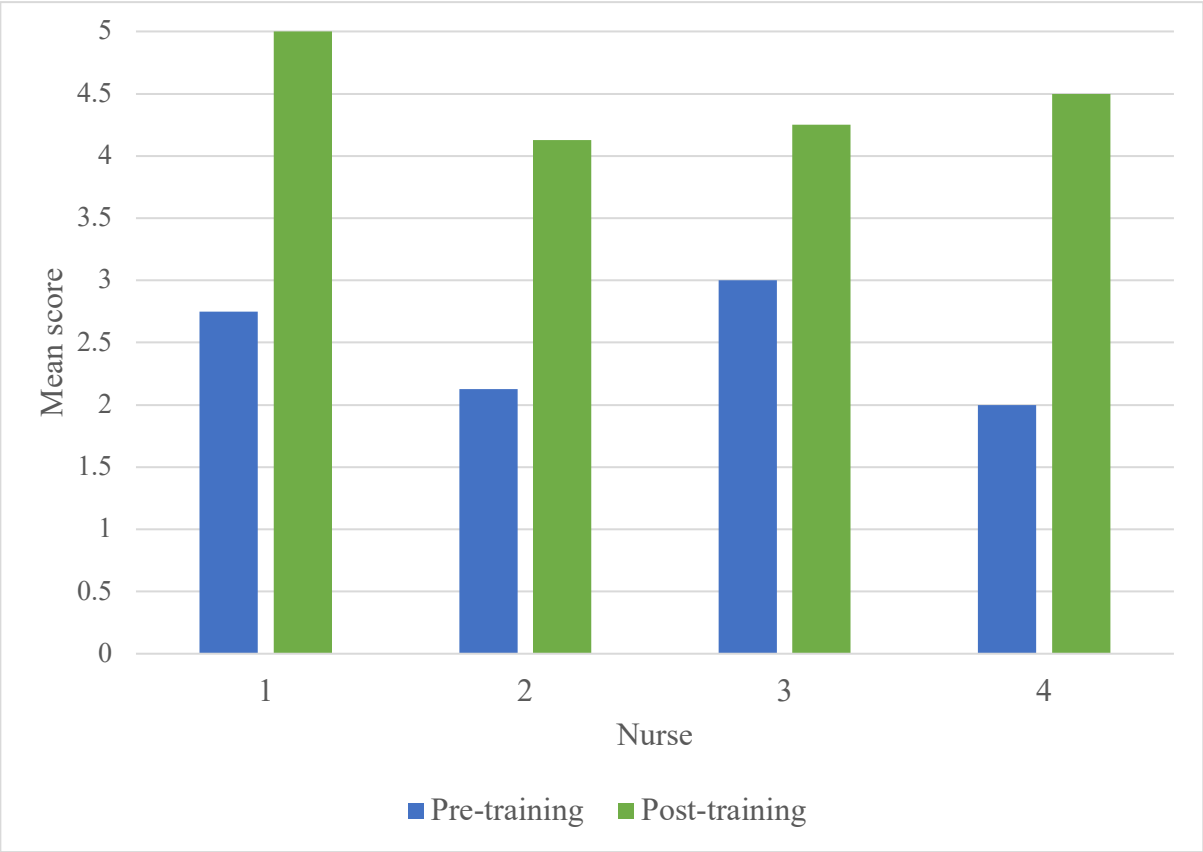


Figure 20. Comparison of pre- and post-test questionnaires for self-reported knowledge and confidence in the diagnosis of scabies and impetigo

Feedback on the training was positive with all nurses stating that both the classroom training (mean score 4.8) and the field training (mean score 4.8) were very useful. Additionally, all nurses reported that the training was very enjoyable (mean score 5).

The reference sheet as an aid for diagnosis and history taking was reported to be very useful (mean score 4.5). One of the nurses also suggested that it may be useful for the community to have access to something similar to the reference sheet in the form of a poster, as a community awareness tool.

Three main themes emerged through the thematic analysis of the qualitative data: the need for improvement in community awareness; the importance of the training setting; and the positive impact of training on ongoing clinical practice.

Nurses reported that there was a lack of awareness of scabies in the community. One nurse stated, *"Parents don't understand the importance of scabies as it is so common, [so] they think it is not serious"*. Although community awareness was not a direct objective of the training program, engagement with the community did occur during the program. This included examination of students at the local school, and providing treatment for families, and so the engagement with the community and the individuals involved in the training was important.

Multiple participants raised the importance the training environment and gave several examples on how this impacted on their training experience and ability to conduct the examinations. Specific concerns were lighting, fans and ventilation, reporting that the *"classroom was dark"*, *"[without] good ventilation"*.

Although the primary aim of training was to train in the diagnostic assessment that can be used in community prevalence surveys, all nurses felt the training would be highly beneficial for their daily routine clinical practice in local hospitals and health centres. One nurse reflected on the experience as *"very good training for me, because scabies has been misdiagnosed and overlooked. Now it will make a difference [when] I go back to my hospital."* Another nurse commented that *"I believe the training impact is very important and useful in my career as mostly scabies is ignored… [The training] is very useful in identifying, diagnosing and [providing] appropriate treatment"*.

4.4 Discussion

We developed and delivered a novel training package for the diagnosis of scabies, based on the IACS criteria. Self-reported knowledge and confidence increased significantly for all nurses following training. The gains in knowledge seen are also reflected in the high scores for the case base test. Training health care workers in the diagnosis of scabies also contributes to

capacity building. The development of new skills and increased confidence may empower individuals to contribute to the health of their community in new ways.

The nurses reported the classroom-based training and field training was highly useful. Our findings suggest that a training model with a classroom and field component, as well as a barrier hurdle examination such as a case-based test is an appropriate method for training in scabies diagnosis. Additionally, for future training, an assessment at the end of training should be considered as an essential component of the training package. This would ideally occur as an objective structured clinical examination (OSCE) in a practical field setting such as a hospital outpatient clinic or in a school. This was not done as part of this study as a fully powered study of diagnostic accuracy was conducted following training (Chapter 3).

When considering the recruitment of individuals (such as school students) to be examined during training, it is important to have sufficient numbers of individuals with the target conditions (scabies and impetigo) with a representative spectrum of disease severity. It is also important to have individuals with common differential diagnoses which may be confused for scabies. Depending on the setting and population prevalence of these conditions, it may be challenging to find suitable participants. Therefore, recruitment of participants for practical training may be required prior to commencement of training.

The International League of Dermatological Societies has identified that consistent terminology is crucial for effective communication and practice of dermatology.[45] In order to develop a training package that can be standardised, terminology and definitions must also be consistent. We used the IACS Criteria as the basis for training in scabies diagnosis with diagnostic terminology was based on the WHO publication, "Recognising neglected tropical diseases through changes on the skin". There are some areas of the criteria which require further characterisation, specifically, definitions of typical scabies lesions and typical

distribution of scabies lesions. When these definitions become available, the standardisation of training is likely to improve.

The results of the case-based test were very good for scabies, although one nurse did not perform as well. Following the test this nurse identified deficiencies in their knowledge and sough further assistance which was provided the following day. The images in the case-based test of scabies mostly depicted moderate to severe scabies, it could be argued that there was not a proportionate representation of mild scabies as was seen during the field training. Therefore, these results in the case-based test may overestimate the true accuracy of the nurses' diagnosis.

The reference sheet was a valuable diagnostic aide. The nurses were able to refer to the sheet as they needed.

Feedback from the nurses highlighted the need for careful consideration of the training location and facilities. It is likely that training in scabies diagnosis will be conducted in low-resource settings, where it may be a challenging to access adequate infrastructure to ensure comfort for trainers and trainees. The nurses identified that good lighting is crucial for examination of skin to diagnose scabies, so access to mobile lighting such as a hand-held torch may be a beneficial teaching and examination aid.

There are several limitations to this study. First, the number of nurses trained was small, and they were drawn from a single setting, so the results may not be generalisable to nurses in other settings with different experience. Second, there was no control group, however due to the resources available this would not have been feasible. Third, self-reporting of knowledge and confidence may have been subject to recall or social desirability bias especially as semi-structured interviews were conducted by a member of the study team. However, as presented

in Chapter 3, the practical skills of the nurses were tested following training using a robust diagnostic accuracy methodology.

Epidemiological mapping of scabies prevalence is required and an effective training program for local health workers in diagnosis of scabies is needed. This study found that brief training in the diagnosis of scabies and impetigo is effective, feasible, enjoyable and empowering for participants. Ongoing work is required to further evaluate our training protocol for the diagnosis of scabies and impetigo. This may include evaluation of training in different settings and collaboration and incorporation with training protocols for the diagnosis of other NTDs.

Chapter 5. Prevalence of scabies and impetigo in the Solomon Islands: a school survey

Osti MH, Sokana O, Phelan S, Marks M, Whitfeld MJ, Gorae C, et al. Prevalence of scabies and impetigo in the Solomon Islands: a school survey. *BMC Infect Dis.* 2019;19(1):803.

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Prevalence of scabies and impetigo in the Solomon Islands: a school survey

Millicent H. Osti[1,2,3], Oliver Sokana[4], Sophie Phelan[5,6], Michael Marks[7], Margot J. Whitfeld[8,9], Christina Gorae[4], John M. Kaldor[5], Andrew C. Steer[1,2,3] and Daniel Engelman[1,2,3*]

Abstract

Background: Scabies, a parasitic disease of the skin, is a major public health problem, largely affecting children. Scabies is often complicated by impetigo which can result in serious complications including invasive infections and immune mediated diseases. Scabies and impetigo are reported to have high prevalence in tropical settings including the Solomon Islands.

Methods: We conducted a cross-sectional prevalence survey at Gizo Primary School in the Western Province of the Solomon Islands in August 2018. The diagnosis of scabies was based on criteria developed by the International Alliance for the Control of Scabies in 2018. Population attributable risk was calculated to determine the effect of scabies on the prevalence of impetigo, and both adjusted and unadjusted risk ratios were calculated to identify differences between sexes and age groups.

Results: A total of 324 students were assessed (47.5% of those enrolled at the school). The prevalence of scabies was 54.3% (95% confidence interval [CI] 48.7–59.8) and most disease was mild (68.8%). The prevalence was higher in males (63.5%; adjusted risk ratio [ARR] 1.4, 95% CI 1.1–1.7), and in those aged 10–12 years (61.4%; ARR 1.8, 95% CI 1.1–2.9 when compared to those aged 4–6 years). The prevalence of impetigo was 32.1%, with males more likely to be affected (41.7%, ARR 1.7, 95% CI 1.2–2.4) but with no significant differences between age groups. 63.5% of those with impetigo had scabies, corresponding to a population attributable risk of 11.8%.

Conclusions: There is a very high burden of scabies and impetigo among primary school students in Gizo. There is a critical need for the development and implementation of control programs in areas where scabies is endemic.

Keywords: Scabies, Impetigo, Diagnostic accuracy, Sarcoptes scabiei, Neglected tropical diseases

Background

Sarcoptes scabiei var. *hominis* is a parasitic mite that burrows into human skin. Infestation with the mite results in an inflammatory reaction producing skin lesions with severe pruritus. Persistent scratching results in broken skin, compromising its barrier function and facilitating secondary bacterial infection with group A *Streptococcus* (GAS; *Streptococcus pyogenes*) or with *Staphylococcus aureus*, presenting as impetigo. Impetigo may progress to severe skin and soft tissue infection, bone and joint infection, sepsis or the immune-mediated complications of GAS infection such as glomerulonephritis and potentially rheumatic fever [1, 2]. Although a range of effective treatment options for scabies exists, the highly contagious nature of the disease makes its public health control challenging.

Scabies is estimated to affect more than 200 million people, especially children [3, 4]. Despite these estimates, a major barrier for global disease control is the scarcity of epidemiologic data [5, 6]. Prevalence surveys using systematic and standardized methods are likely to be a crucial component in determining the global burden of disease and identifying areas where the disease is endemic. The International Alliance for the Control of Scabies (IACS) undertook a Delphi study in order to establish consensus diagnostic criteria for scabies [7]. The 2018 IACS Criteria provide standardized diagnostic

* Correspondence: Daniel.Engelman@rch.org.au
[1]Tropical Diseases Research Group, Murdoch Children's Research Institute, Melbourne, Australia
[2]Department of Paediatrics, University of Melbourne, Melbourne, Australia
Full list of author information is available at the end of the article

methods to enable evaluation and comparison of global prevalence data.

Schools have been a focus for both surveillance and control of neglected tropical diseases (NTDs), including schistosomiasis and soil-transmitted helminthiases [8]. School screening studies conducted in Africa and Asia have investigated the burden of scabies, either in isolation, or in conjunction with other NTDs or skin conditions [9, 10] but there have been no school-based studies from the Solomon Islands. Locally relevant epidemiological evidence of the burden of scabies is required for the design and implementation of community scabies control programs. The primary objective of this study was therefore to determine the prevalence of scabies and impetigo in the population examined using a school screening method. The secondary objectives were to investigate features associated with scabies and impetigo. We also aimed to describe the severity of scabies and impetigo and the distribution of scabies cases using the 2018 IACS Criteria subcategories.

Methods

Study setting and participants

This was a cross-sectional, school-based study that took place in the public primary school in the town of Gizo, the capital of the Western Province of the Solomon Islands. The population in the Gizo region is approximately 7000 [11]. The setting was selected because it is the site of a planned trial. The school was selected as the study site because of the simple facilitation of recruitment of participants within a school setting and its convenient location within the centre of the town.

At the commencement of 2018, the primary school had a school roll of 682 students, consisting of students residing in Gizo town and those who travel by truck or boat from surrounding villages or islands. Students at the primary school are aged 4 to 15 years, with class groupings based on aptitude rather than age.

Study procedures

All students attending Gizo Primary School were eligible for inclusion in the study. All patients underwent a standardized examination for scabies and impetigo.

Clinical assessment was performed by doctors with expertise in scabies diagnosis, and by nurses with clinical experience in scabies diagnosis, supplemented by a training program on the diagnosis of scabies, impetigo and other locally common skin conditions. Scabies was diagnosed using the 2018 IACS Criteria [7]. Although eight subcategories exist in the IACS Criteria, only four were relevant for diagnosis in this study (Table 1). Subcategories of diagnosis that required specialized equipment (including microscopy and dermoscopy) or required examination of the genitals, were not used, as these were not practical for a field survey in this context. Impetigo was diagnosed on the presence of papules, pustules or ulcerative lesions with associated erythema, crusting or pus. Skin examination consisted of assessment of exposed areas: the feet and legs to the thighs, hands to the upper arms, neck, face and scalp. Students were in school uniform which consisted of above-knee shorts and above-elbow shirts or dresses. Shoes were removed prior to examination. A focused history of standardized questions was taken of all participants with skin lesions consisting of information required for the IACS Criteria classification. Questions included whether participants experienced itch. Contact history was assessed by asking if participants lived with someone, or had a friend or classmate with itch, or if they lived with someone, or had a friend or classmate with a rash that looks like scabies. Participants were shown images of people with typical scabies rashes to assist these questions. History was

Table 1 Case definitions for scabies using the 2018 IACS Criteria

Criteria Category		Used in Survey
Confirmed scabies		
A1:	Mites, eggs or feces on light microscopy of skin samples	**No**
A2:	Mites, eggs or feces visualized on individual using high powered imaging device	**No**
A3:	Mite visualized on individual using dermoscopy	**No**
Clinical Scabies		
B1:	Presence of burrows	**Yes***
B2:	Typical lesions affecting male genitalia	**No**
B3:	(Typical lesions) and (typical distribution) and (itch) and (contact history)	**Yes**
Suspected Scabies		
C1:	(Typical lesions) and (typical distribution) and (itch) or (contact history)	**Yes**
C2:	(Atypical lesions) or (atypical distribution) and (itch) and (contact history)	**Yes**

* If burrows were identified, individuals were also classified as either B3, C1, or C2, as these were not confirmed with dermoscopy
A diagnosis of scabies should only be made if other differential diagnoses are considered less likely than scabies.

taken in the local language (Solomon Islands Pijin). Permethrin was supplied for individuals diagnosed with scabies. Permethrin was also supplied for household contacts of diagnosed children, as per local treatment protocol. No treatment was supplied to examined children without scabies. If other conditions were diagnosed, referral was provided to the local health clinic.

Data collection and statistical methods

Demographic information was collected including participant age, sex and school grade.

Scabies diagnosis was classified into one of three IACS Criteria subcategories (Table 1).

Following methods used in previous studies, severity of scabies and impetigo was assessed based on the number of lesions present [12, 13]. Scabies was categorized as: mild, 1 to 10 lesions; moderate, 11 to 49 lesions; or severe, 50 or more lesions. Impetigo was classified as: very mild, 1 to 5 lesions; mild, 6 to 10 lesions; moderate, 11 to 49 lesions; or severe, 50 or more lesions.

Prevalence for scabies and impetigo was calculated for each demographic group. Risk ratios were calculated using generalized linear models, adjusting for age group and sex. Population attributable risk was calculated to further analyze association between scabies and impetigo [14].

Data were collected on forms during the study period and then transcribed and uploaded to a REDCap study database (Research Electronic Data Capture), hosted at Murdoch Children's Research Institute [15]. All statistical analysis was performed using Stata (version 15, StataCorp, College Station, TX, USA).

Ethics statement

Parents were provided with written information regarding the study. A community information night was also held at the school where members of the study team provided further information and answered questions. Written consent was obtained from parents or guardians of all participants and verbal assent from children where possible.

Ethical approval was granted by the Royal Children's Hospital Melbourne Human Research Ethics Committee (reference number 38099A) and the Solomon Islands Health Research and Ethics Review Board (reference number 05/18).

Results

Over 6 days in August 2018, 324 students were recruited and examined (47.5% of those enrolled at the school). All consenting students present at school during study days were examined. Doctors examined 247 participants (76.2%) and the remainder were examined by trained nurse examiners. Of those examined, 51.9% were female and the mean age was 9.6 years (standard deviation 2.3, range 4–15; Table 2).

Scabies and impetigo prevalence

Overall, 176 participants had scabies (prevalence 54.3, 95% confidence interval [CI] 48.7–59.8), and 104 participants had impetigo (prevalence 32.1, 95% CI 27.0–37.5). Most scabies cases were mild (68.8%, $n = 121$) but 14 participants (8%) had severe scabies (Table 3). The majority of those with impetigo had very mild disease ($n = 86$, 82.7%, Table 3). The prevalence of scabies diagnosed by doctor and nurse examiners was similar (52.2, 95% CI 45.8–58.6; vs 61.0, 95% CI 49.2–72.0%).

History features

Itch was reported in 81.8% of individuals with scabies ($n = 144$) and in 18.4% of those without scabies ($n = 21$, missing = 34). A positive contact history was reported in 92.1% ($n = 161$) of those with scabies, and in 52.6% of those without scabies who were asked ($n = 60$, missing = 34). The most common contact history reported was having a friend or classmate with a rash that looks like scabies (75, 95%CI 67.9–81.2, Table 4). Of those with scabies, 26.1% ($n = 46$) reported either a history of itch or a positive contact history and 73.9% ($n = 130$) had both history features. Of those without scabies, 46.5% ($n = 53$) reported either a history of itch or a positive contact history and 12.3% ($n = 14$) had both features.

IACS criteria

The majority of scabies cases ($n = 128$, 72.7%) were classified as Clinical Scabies, subcategory B3, with typical clinical features, itch and contact history according to the IACS Criteria (Table 3). Only four individuals (2.3%) were identified to have clinically visible burrows (B1).

Associations with scabies and impetigo

Scabies was more common in males than females (63.5% vs 45.8%, adjusted risk ratio [ARR] 1.4, 95% CI 1.1–1.7; Table 2) and the most commonly affected age group was children aged 10–12 years (61.4%; ARR 1.8, 95% CI 1.1–2.9, compared to age group 4–6 years; Fig. 1). Prevalence of impetigo was higher in males (41.7% vs 23.2%, ARR 1.7, 95% CI 1.2–2.4) but similar across age groups.

Participants with scabies had a higher prevalence of impetigo than those without scabies (66 of 176, 37.5% vs 38 of 110, 25.7%, ARR 1.5, 95% CI 1.1–2). Overall, 63.5% of those with impetigo had scabies, corresponding to a population attributable risk of 11.8% (95%CI 1.7–21.7, $P = 0.02$). Of the 18 individuals with greater than very mild impetigo, 14 (77.8%) had scabies, and of the individuals with moderate to severe impetigo, all had scabies ($n = 6$, 100%).

Table 2 Participant demographics and prevalence of scabies and impetigo ($N = 324$)

Study Sample		Scabies			Impetigo		
	N (%)	n	% (95%CI)	Adjusted RR (95%CI)	n	% (95%CI)	Adjusted RR (95%CI)
Sex							
Female	168 (51.9)	77	45.8 (38.1-53.7)	Ref	39	23.2 (17.1-30.3)	Ref
Male	156 (48.2)	99	63.5 (55.4-71.0)	1.4 (1.1-1.7)	65	41.7 (33.8-49.8)	1.7 (1.2-2.4)
Age (Years)							
4-6	35 (10.8)	12	34.3 (19.1-52.2)	Ref	14	40.0 (23.9-57.9)	Ref
7-9	121 (37.4)	66	54.5 (45.2-63.6)	1.6 (1.0-2.6)	44	36.4 (27.8-45.6)	1 (0.6-1.5)
10-12	132 (40.7)	81	61.4 (52.5-69.7)	1.8 (1.1-2.9)	35	26.5 (19.2-34.9)	0.7 (0.5-1.2)
13-15	36 (11.1)	17	47.2 (30.4-64.5)	1.4 (0.8-2.5)	11	30.6 (16.3-48.1)	0.8 (0.4-1.5)

Discussion

Our study highlights the very high prevalence of scabies (54%) and impetigo (32%) in school-aged children in Gizo. The prevalence of scabies is higher than a previous study conducted in the same region in 2014 which reported a prevalence of 23% in children aged 5 to 14 [12]. High scabies prevalence has been described in other disadvantaged populations including in children in Fiji (55.7%) [13], rural communities in Nigeria (65%) [16] and amongst asylum seekers in the Netherlands (33.5%) [17].

In our study, males were more likely than females to have scabies, which has been reported previously [18, 19], although this finding is not represented in the Global Burden of Disease Study (2015) estimates [20].

The majority of scabies seen was classified as Clinical Scabies according to the 2018 IACS Criteria (Fig. 2). This was consistent for males and females. Very few scabies cases (4%) had either atypical lesions or an atypical distribution of their rash. We found that the 2018 IACS Criteria for the diagnosis of scabies were easily integrated and implemented into our study design.

Table 3 Details of diagnosis and severity for scabies and impetigo

	Overall ($N = 324$)	Male ($N = 156$)	Female ($N = 168$)	Age Years 4–6 ($N = 35$)	Age Years 7–9 ($N = 121$)	Age Years 10–12 ($N = 132$)	Age Years 13–15 ($N = 36$)
Scabies	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Prevalence	176 (54.3)	99 (63.5)	77 (45.8)	12 (34.3)	66 (54.6)	81 (61.4)	17 (47.2)
Category							
B1: Burrows*	4 (2.3)	2 (2)	2 (2.6)	0 (0)	0 (0)	3 (3.7)	1 (5.9)
B3: Clinical scabies	128 (72.7)	73 (73.7)	55 (71.4)	9 (75)	47 (71.2)	64 (79)	8 (47.1)
C1: Suspected scabies	41 (23.3)	25 (25.2)	16 (20.8)	3 (25)	16 (24.2)	13 (19.7)	9 (52.9)
C2: Suspected scabies	7 (4)	1 (1)	6 (7.8)	0 (0)	3 (4.5)	4 (6.1)	0 (0)
Severity							
Mild (1–10)	121 (68.8)	67 (67.7)	54 (70.1)	8 (66.7)	46 (69.7)	53 (65.4)	14 (82.4)
Moderate (11–49)	41 (23.3)	22 (22.2)	19 (24.7)	4 (33.3)	15 (22.7)	20 (24.7)	2 (11.8)
Severe (≥ 50)	14 (8)	10 (10.1)	4 (5.2)	0 (0)	5 (7.6)	8 (9.9)	1 (5.9)
Impetigo	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Prevalence	104 (32.1)	65 (41.7)	39 (23.2)	14 (40)	44 (36.4)	35 (26.5)	11 (30.6)
Severity							
Very Mild (≥ 5)	86 (82.7)	52 (80.0)	34 (87.2)	12 (85.7)	39 (88.6)	25 (71.4)	10 (90.9)
Mild (6–10)	12 (11.5)	8 (12.3)	4 (10.3)	2 (14.3)	4 (9.1)	6 (17.1)	0 (0)
Moderate (11–49)	3 (2.9)	2 (3.1)	1 (2.6)	0 (0)	0 (0)	2 (5.7)	1 (9.1)
Severe (≥50)	3 (2.9)	3 (4.6)	0 (0)	0 (0)	1 (2.3)	2 (5.7)	0 (0)

*Individuals with burrows were additionally categorized as either B3, C1 or C2

Table 4 Reporting of history features

	Total (*N* = 290)		With scabies (*N* = 176)		Without scabies (*N* = 114)	
Itch	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Itch present	165	56.9 (51–62.7)	144	81.8 (75.3–87.2)	21	18.4 (11.8–26.8)
Contact History						
House contact with itch	97	33.5 (28–39.2)	76	43.2 (35.8–50.8)	21	18.4 (11.8–26.8)
School contact with itch	152	52.4 (46.5–58.3)	117	66.5 (59–73.4)	35	30.7 (22.4–40)
House contact with scabies rash	76	27.2 (22.2–32.8)	65	36.9 (29.8–44.5)	14	12.3 (6.9–19.7)
School contact with scabies rash	177	61 (55.2–66.7)	132	75 (67.9–81.2)	45	39.5 (30.4–49.1)
Contact history positive*	222	76.6 (71.2–81.3)	162	92.1 (87–95.5)	60	52.6 (43.1–62.1)

*Contact history was considered positive if responses to any of the four questions were positive

Implementation of these criteria in other settings would allow comparison across studies and regions.

The high prevalence of impetigo (32%) is consistent with other studies from Pacific Island nations, including in Fiji (26%) and a previous study in the Solomon Islands (33%) [12, 21]. Most of the impetigo (82%) in this study was very mild, consistent with other studies [12, 13]. Impetigo was positively associated with the presence of scabies, although the association was less strong than previously reported [13]. The association between scabies and impetigo in a range of settings warrants further investigation.

Itch was reported by 82% of participants with scabies, which is consistent with other studies (72–100%) [16, 17, 22–26]. A positive contact history was reported in 92% of participants with scabies. In those with scabies, itch was reported to occur in 43% of household members, similar to other studies (50–55%) [22, 24]. However, in our study, more children identified contact with a friend or class member than a household member. Contact between children at school and between friends is likely to be important for disease transmission between children. Contact history questions should be asked in an appropriate way for specific survey settings and participants.

There were several limitations to our study. First, this study only focused on school children and is therefore not generalizable to other age groups. However, as scabies is highly transmissible among household contacts [27] it is likely that there would be a high prevalence amongst the household members of children with scabies. Second, we enrolled 47.5% of students on the school roll, which may have introduced participation bias. The remaining students did not participate because they were away from school or did not provide consent to participate. Those not attending school may have

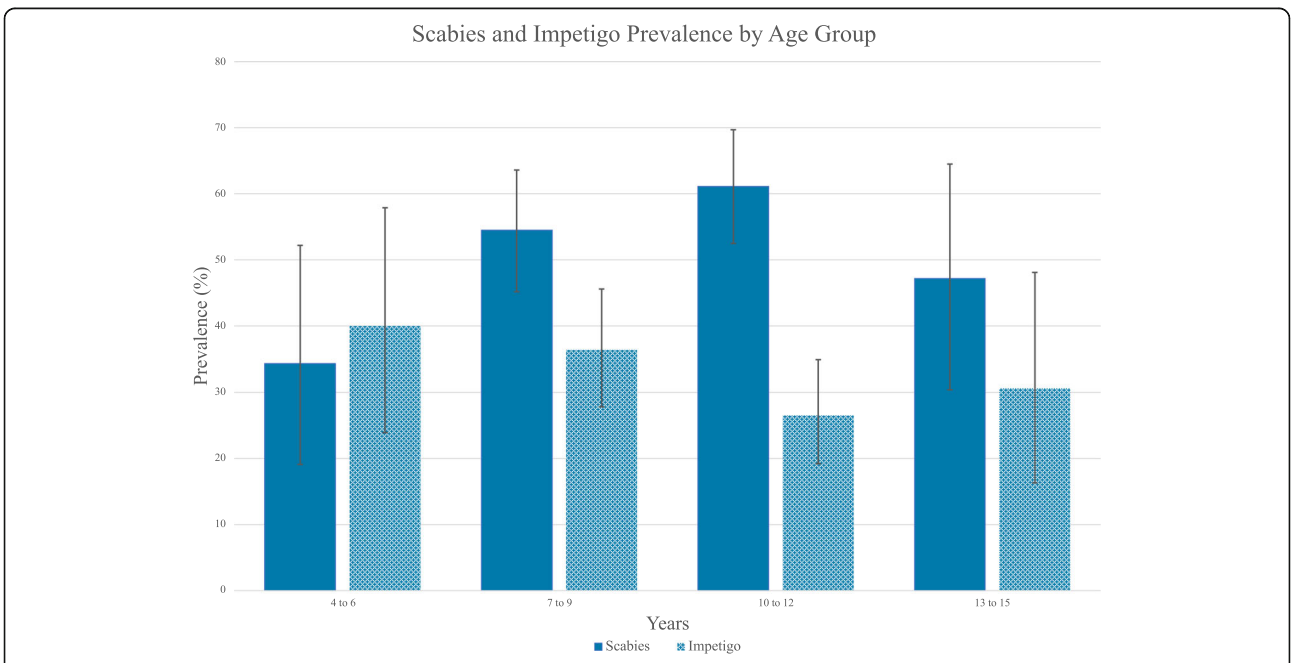


Fig. 1 Prevalence of scabies and impetigo by age group with 95% confidence intervals

Fig. 2 Typical scabies lesions on a child's fingers

been more disadvantaged with an even greater disease burden, possibly leading to an underestimate of the true prevalence. Conversely, it is possible that some families and teachers may have encouraged children with symptoms of scabies or impetigo to participate, which may have led to an overestimate of prevalence. Third, the diagnosis of scabies and impetigo in the study was based on clinical assessment of exposed areas utilizing the IACS Criteria, rather than whole body examination using dermoscopy, microscopy, or skin scrapings. Limited examination may have underestimated the true prevalence, perhaps by up to 10% [28], whereas reliance on clinical signs may have led to some misclassification and overestimate of disease.

Children in low-resource settings are disproportionately affected by scabies and impetigo, predisposing them to significant morbidity and mortality. The high prevalence of scabies in this study supports the ongoing need for prevalence studies and identifying communities where the disease is endemic. The significant burden of disease highlights the need for ongoing health promotion activities for scabies and impetigo. The very high prevalence of scabies also supports the urgent implementation of a population-scale control program in the Solomon Islands. Greater appreciation of scabies as a major global contributor to poor health in children may help to improve awareness and access to treatment in settings where scabies is endemic.

Abbreviations

ARR: Adjusted risk ratio; CI: Confidence interval; GAS: Group A *Streptococcus*; IACS: International Alliance for the Control of Scabies; NTDs-: Neglected Tropical Diseases

Acknowledgements

We wish to thank Gizo Primary School, the students, teachers and wider Gizo community for their generosity and involvement in this study. We would also like to thank Dickson Boara, Nester Thugea, Sana Bisili, Stephen Tiazi, Arthur Keremama, Winter Sino, Deanne Seppy, Ender Malasa, Una Gagahe and Vivegan Visavalingam for their assistance during the study.

Authors' contributions

MHO, ACS and DE conceptualized the study. OS and CG were involved in field-work co-ordination. SP, MM, MJW and DE assisted with data collection. ACS and DE supervised the study. MHO, OS, SP, MM, CG, MJW, JMK, ACS and DE were involved in drafting and revision of the manuscript. All authors have read and approved the final manuscript.

Funding

DE, ACS and JMK are supported by fellowships from the National Health and Medical Research Council of Australia. ACS is also supported by the Heart Foundation of Australia. MHO is supported by an Australian Government Research Training Program (RTP) Scholarship. The funders had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Availability of data and materials

The datasets used and analyzed during the study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was granted by the Royal Children's Hospital Melbourne Human Research Ethics Committee (reference number 38099A) and the Solomon Islands Health Research and Ethics Review Board (reference number 05/18). All participants required written informed consent to participate. For children under 16 years of age, written consent from parents or guardians was obtained.

Consent for publication

Written consent was provided for included material.

Competing interests

MM is an editorial board member for BMC Infectious Diseases. There are no other competing interests to declare.

Author details

[1]Tropical Diseases Research Group, Murdoch Children's Research Institute, Melbourne, Australia. [2]Department of Paediatrics, University of Melbourne, Melbourne, Australia. [3]Melbourne Children's Global Health, Melbourne, Australia. [4]Ministry of Health and Medical Services, Honiara, Solomon Islands. [5]Kirby Institute, University of New South Wales, Sydney, Australia. [6]Research School of Population Health, Australian National University, Canberra, Australia. [7]Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK. [8]St Vincent's Hospital, Sydney, Australia. [9]Department of Medicine, University of New South Wales, Sydney, Australia.

Received: 26 March 2019 Accepted: 15 August 2019
Published online: 13 September 2019

References

1. Lawrence G, Leafasia J, Sheridan J, Hills S, Wate J, Wate C, et al. Control of scabies, skin sores and haematuria in children in the Solomon Islands: another role for ivermectin. Bull World Health Organ. 2005;83(1):34–42.
2. Thornley S, Marshall R, Jarrett P, Sundborn G, Reynolds E, Schofield G. Scabies is strongly associated with acute rheumatic fever in a cohort study of Auckland children. J Paediatr Child Health. 2018;54(6):625–32.
3. Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Prevalence of scabies and impetigo worldwide: a systematic review. Lancet Infect Dis. 2015;15(8):960–7.
4. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1545–602.
5. WHO. Report of the tenth meeting of the WHO Strategic and Technical Advisory Group for neglected tropical diseases. Geneva: WHO; 2017. Available at: https://www.who.int/neglected_diseases/NTD_STAG_report_2017.pdf.
6. Engelman D, Steer AC. Control strategies for scabies. Trop Med Infect Dis. 2018;3(3):98.

7. Engelman D, Fuller LC, Steer AC. International Alliance for the control of scabies Delphi p. Consensus criteria for the diagnosis of scabies: a Delphi study of international experts. PLoS Negl Trop Dis. 2018;12(5):e0006549.
8. WHO. Helminth control in school-age children: a guide for managers of control programmes. Second ed. Geneva: World Health Organization; 2012.
9. Yotsu RR, Kouadio K, Vagamon B, N'Guessan K, Akpa AJ, Yao A, et al. Skin disease prevalence study in schoolchildren in rural cote d'Ivoire: implications for integration of neglected skin diseases (skin NTDs). PLoS Negl Trop Dis. 2018;12(5):e0006489.
10. Korte LM, Bowen AC, Draper ADK, Davis K, Steel A, Teodora I, et al. Scabies and impetigo in Timor-Leste: a school screening study in two districts. PLoS Negl Trop Dis. 2018;12(5):e0006400.
11. Solomon Islands Government. Provincial profile of the 2009 Population & Housing Census: Western. Honiara: Solomon Islands Government; 2009.
12. Mason DS, Marks M, Sokana O, Solomon AW, Mabey DC, Romani L, et al. The prevalence of scabies and impetigo in the Solomon Islands: a population-based survey. PLoS Negl Trop Dis. 2016;10(6):e0004803.
13. Romani L, Whitfeld MJ, Koroivueta J, Kama M, Wand H, Tikoduadua L, et al. The epidemiology of scabies and impetigo in relation to demographic and residential characteristics: Basline findings from the skin health intervention Fiji trial. Am J Trop Med Hyg. 2017;97(3):845–50.
14. Newson RB. Attributable and unattributable risks and fractions and other scenario comparisons. Stata J. 2013;13(4):672–98.
15. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research infomatics support. J Biomed Inform. 2009;42(2):377–81.
16. Ugbomoiko US, Oyedeji SA, Babamale OA, Heukelbach J. Scabies in resource-poor communities in Nasarawa state, Nigeria: epidemiology, clinical features and factors associated with infestation. Trop Med Infect Dis. 2018;3(2):59.
17. Beeres DT, Ravensbergen SJ, Heidema A, Cornish D, Vonk M, Wijnholds LD, et al. Efficacy of ivermectin mass-drug administration to control scabies in asylum seekers in the Netherlands: a retrospective cohort study between January 2014 - march 2016. PLoS Negl Trop Dis. 2018;12(5):e0006401.
18. Anderson KL, Strowd LC. Epidemiology, diagnosis, and treatment of scabies in a dermatology Office. J Am Board of Fam Med. 2017;30(1):78–84.
19. Kouotou EA, Nansseu JR, Kouawa MK, Zoung-Kanyi Bissek AC. Prevalence and drivers of human scabies among children and adolescents living and studying in Cameroonian boarding schools. Parasite Vectors. 2016;9(1):400.
20. Karimkhani C, Colombara DV, Drucker AM, Norton SA, Hay R, Engelman D, et al. The global burden of scabies: a cross-sectional analysis from the global burden of disease study 2015. Lancet Infect Dis. 2017;17(12):1247–54.
21. Steer AC, Jenney AW, Kado J, Batzloff MR, La Vincente S, Waqatakirewa L, et al. High burden of impetigo and scabies in a tropical country. PLoS Negl Trop Dis. 2009;3(6):e467.
22. Dupuy A, Dehen L, Bourrat E, Lacroix C, Benderdouche M, Dubertret L, et al. Accuracy of standard dermoscopy for diagnosing scabies. J Am Acad Dermatol. 2007;56(1):53–62.
23. Jackson A, Heukelbach J, Filho AF, Junior Ede B, Feldmeier H. Clinical features and associated morbidity of scabies in a rural community in Alagoas, Brazil. Tropical Med Int Health. 2007;12(4):493–502.
24. Boralevi F, Diallo A, Miquel J, Guerin-Moreau M, Bessis D, Chiaverini C, et al. Clinical phenotype of scabies by age. Pediatrics. 2014;133(4):e910–6.
25. Nair PA, Vora RV, Jivani NB, Gandhi SS. A study of clinical profile and quality of life in patients with scabies at a rural tertiary care Centre. J Clin Diagn Res. 2016;10(10):WC01–WC5.
26. Worth C, Heukelbach J, Fengler G, Walter B, Liesenfeld O, Feldmeier H. Impaired quality of life in adults and children with scabies from an impoverished community in Brazil. Int J Dermatol. 2012;51(3):275–82.
27. Hay RJ, Steer AC, Engelman D, Walton S. Scabies in the developing world--its prevalence, complications, and management. Clin Microbiol Infect. 2012; 18(4):313–23.
28. Marks M, Engelman D, Romani L, Mason D, Sokana O, Kama M, et al. Exploration of a simplified clinical examination for scabies to support public health decision-making. PLoS Negl Trop Dis. 2018;12(12):e0006996.

Chapter 6. The use of choropleth mapping to display scabies lesion distribution

6.1 Background

The distribution of clinical signs across the skin surfaces of body is an important feature of any disease with dermatological manifestations. In conditions such as scabies, rash distribution may lead to increased clinical suspicion and can inform diagnosis. In settings where microscopy or other diagnostic techniques are not available, the diagnosis of scabies remains dependent on clinical suspicion and the assessment of presenting features.[78] Scabies diagnosis remains challenging, and therefore a better understanding of the distribution of skin lesions may contribute to greater diagnostic accuracy.

Most individuals with scabies exhibit multiple lesions which are often distributed across multiple skin sites.[35, 39, 63] Scabies lesions are commonly found on the fingers, hands, web spaces, wrists, arms, axilla, legs, groin, buttocks, female breast and male genitals.[20, 68, 132] Multiple studies have described body variation in the distribution of scabies lesions among different populations, age groups and sexes.[39, 42, 47] However, these studies have been limited in detail: they reported distribution of scabies over large body regions rather than specific sites. For example, lesions at the legs were reported but they do not distinguish between anterior and posterior or medial and lateral or identify more specific areas such as ankles, knees or feet. Few studies which reported scabies lesion distribution include examination of unexposed areas such as genitals and breasts.

A simplified approach to examination, whereby only exposed areas are examined, has been proposed for public health programs for the diagnosis of scabies. This examination technique

allows rapid examination and reduces the requirements for privacy, both important considerations when examining large populations. A simplified examination has been shown to have a high sensitivity for diagnosis, according to retrospective data.[76]

The reason for the predilection of lesions at certain body sites remains largely unknown. Although exposed areas may be more likely to be sites of contact for initial transmission, distribution does not correlate with initial place of infection in primary infestations, documented as early as the 1940's by Kenneth Mellanby.[140] The scabies mite is known to seek hosts through thermal and host odour stimuli and may be influenced by the lipid composition of tissue.[67, 141] However, the location of mites is not always consistent with lesion location.[142] The itch and lesions associated with initial infection with scabies are typical of a delayed-type hypersensitivity reaction to mites, eggs or faeces.[20] Skin biopsies from individuals with scabies exhibit a cell-mediated immune response with eosinophils, lymphocytes and histocytes.[99] However, the underlying pathophysiology of lesion location in scabies is unknown. Providing a detailed description of the distribution of scabies lesions may assist in developing a greater understanding of the disease.

Choropleth maps are commonly used in geographical mapping. The technique allows representation of variability in numerical data in spatially related regions on a map, by using a colour template to represent different data points or data scales.[143] Colour mapping or heat mapping has been used in the description of rash distribution for skin lesions previously.[47, 72, 144] However, to our knowledge, detailed choropleth maps have not previously been developed for skin lesions.

This study was a pilot study to assess the methods of data collection, analysis and the display of results for a larger study describing detailed lesion distribution in scabies. By piloting the

choropleth mapping technique, we aimed to display the data collected visually, for simple interpretation and clinical correlation.

6.2 Methods

6.2.1 Study design

This study was a prospective, cross-sectional, pilot study of a choropleth approach to mapping scabies lesion body distribution. The study objectives were to collect preliminary data on lesion distribution in scabies, and to assess feasibility of the choropleth technique.

6.2.2 Study participants

The study was conducted in a primary school in Gizo, a town in the Western Province of the Solomon Islands. In 2014, the prevalence of scabies in this region was reported to be 19.2%, with a higher prevalence in school-aged children (22.7%).[8]

All participants were enrolled through convenience sampling during the study period of another research project. As the study aimed to pilot the study methods, the enrolment of a varied sample population was not crucial to the results. All students who provided informed consent and were diagnosed with scabies by a doctor were eligible for enrolment. As participants were children, consent was obtained from parents or guardians.

6.2.3 Clinical assessment and data collection

Participants were examined in a private area of the study location. Assessments were conducted by one of two doctors, an infectious disease physician and a junior doctor both experienced in the diagnosis of scabies. Data collection forms consisted of anterior and posterior diagrams of the body, divided into 98 clinically relevant topographic cutaneous sites (Figure 21 and 22).

Doctors examined the entirety of the body skin surface and recorded the number of scabies lesions at each site. To avoid unnecessary exposure and maintain participant privacy, skin sites were uncovered sequentially so that the participant was never fully exposed. Participants could decline examination of any of the skin sites. Where this occurred, an 'X' was recorded in that site. The number of scabies lesions was recorded using a numerical value in each site, according to what were considered to clinically relevant categories (0, 1, 2, 3, 4, 5, 6-10, 10-20, 20-50, >50). Demographic data (age and sex) were also collected.

Figure 21. Data collection form for the study of scabies lesion distribution

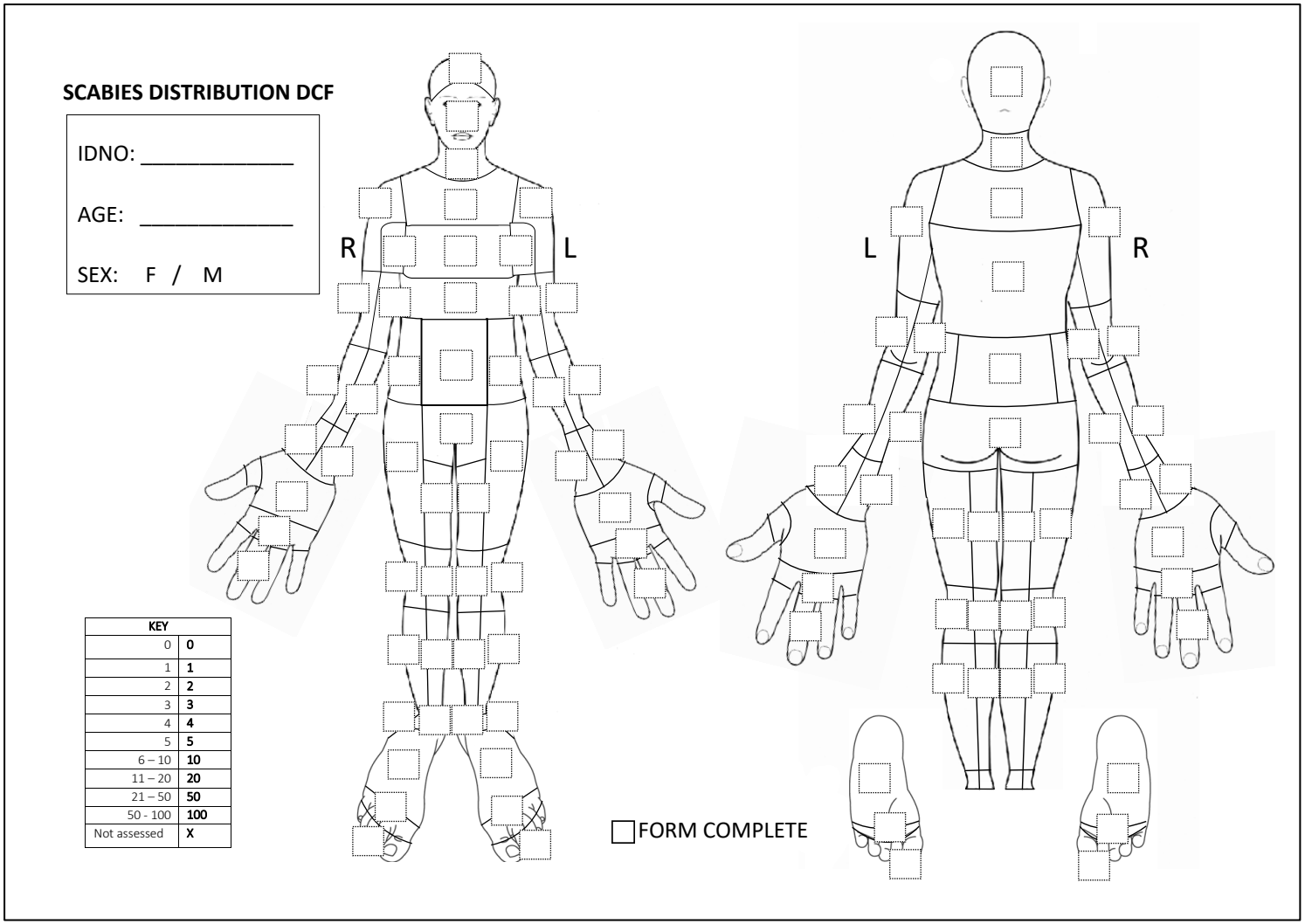
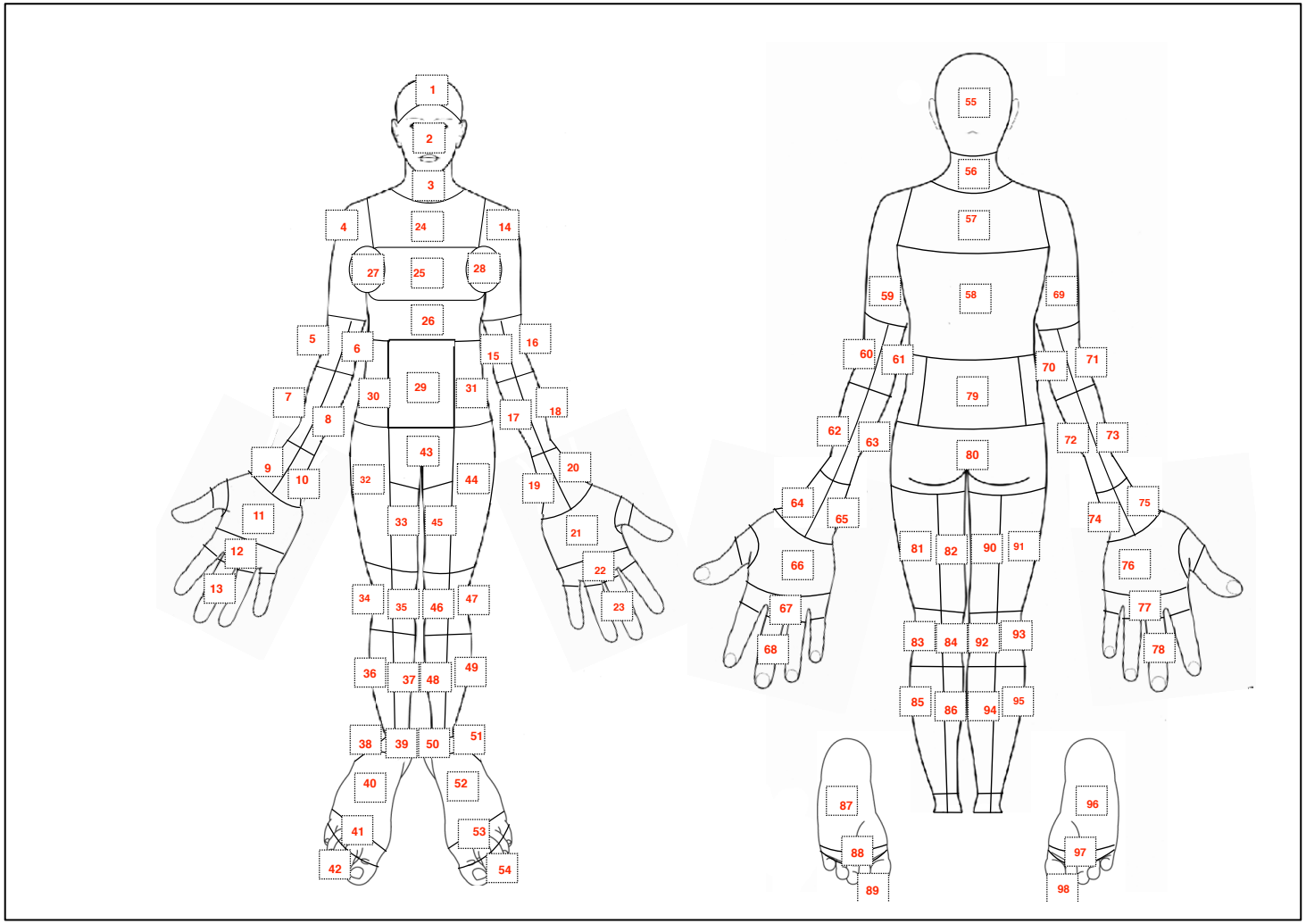


Figure 22. Body distribution sites for data collection and analysis for scabies lesion distrbition, numbered from 1 to 98



6.2.4 Statistical analysis

This was a pilot study, and therefore the sample size did not take into account any statistical calculations. The pilot aimed to examine as many participants as feasible.

Lesion distribution was defined by the proportion of individuals with lesions at each site. This was also determined for males and females. Lesion concentration was defined as the median number of lesions for each site where lesions were present. We analysed groupings of sites by adding up appropriate skin sites to form seven larger grouped regions (Figure 23).

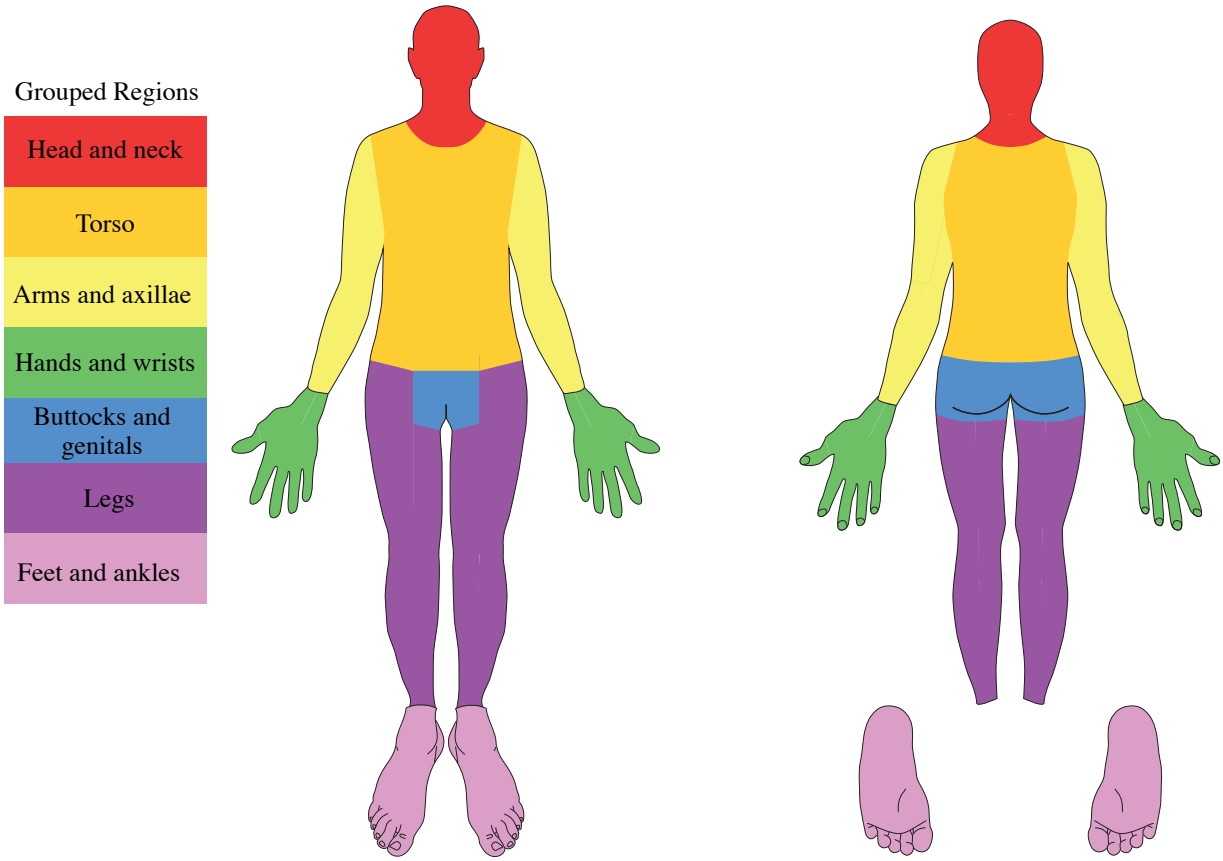


Figure 23. Larger grouped regions for analysis of scabies lesion distribtion

We defined “exposed” and “unexposed” body areas (exposed areas are the arms and hands, the head, and the feet and lower legs, Figure 24) similar to previous studies.[76]

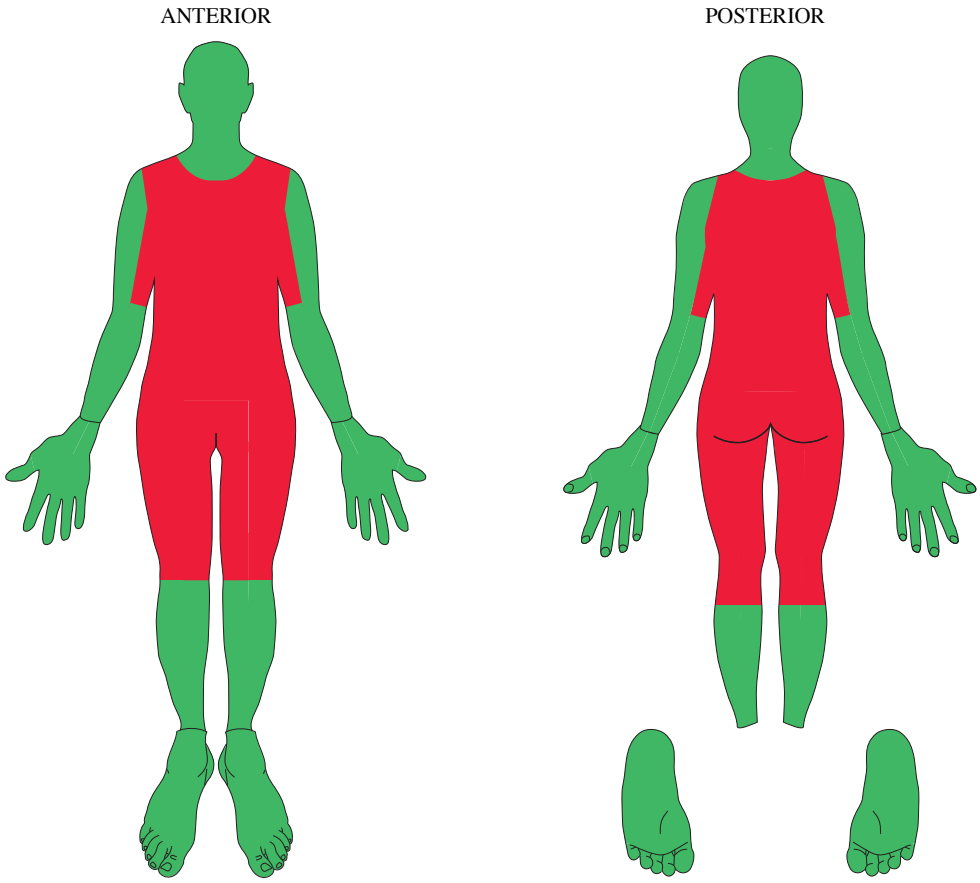


Figure 24. Exposed and unexposed areas of the body

Choropleth maps were produced using a sequential colour palette to visually display data. Each of the 98 individual sites were designated a colour. For lesion distribution, a sequential colour palette was used from light yellow to dark red (Figure 25, colour palette 1). The different colours represented increasing percentage brackets to display the proportion of individuals with lesions in each site. The different colours represented the following bands: 0%, 1-14%, 15-29%, 30-44%, 45-59%, 60-74%, 75-100%. Choropleth maps were created to represent the proportion of participants with scabies lesions at each site. Separate maps were also created for males and females.

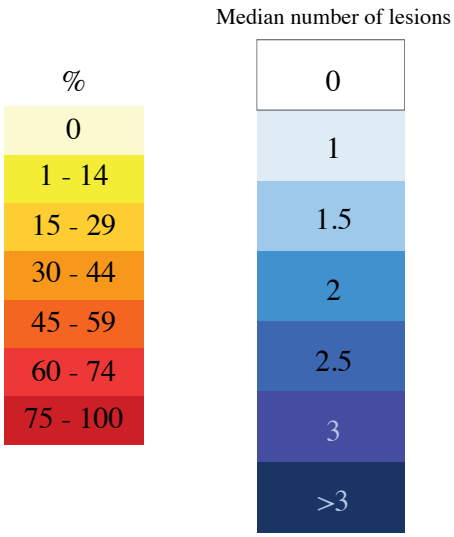


Figure 25. Colour palettes 1 and 2

For lesion concentration, a different colour palette was used, transitioning from light to dark blue (Figure 25, colour palette 2). The lesion concentration map was created to represent the median number of lesions recorded for each site. The colour stops represented the median number of lesions at each site for all participants. The seven colours represented the following numbers: 0, 1, 1.5, 2, 2.5, 3 and >3.

6.2.5 Consent and ethical approvals

Ethics approval was granted by the Royal Children's Hospital Melbourne Human Research Ethics Committee (reference number 38099A), and the Solomon Islands Health Research and Ethics Review Board (reference number 05/18).

6.3 Results

Twenty-five individuals were enrolled. All were children (median 7, range 6-12 years), and there were fewer females (n=9, 36%). Out of 2450 sites, data was missing for 19.

6.3.1 Proportion of individuals with lesions in each site

The most common sites of lesions were the dorsal web spaces (left side 76%, right side 72%), and the dorsal fingers (right 60%, left 56%, Figure 26). The dorsal hand (left 36%, right 48%) and posterior-medial forearms were also common sites of involvement (left 48%, right 40%; Figure 26)

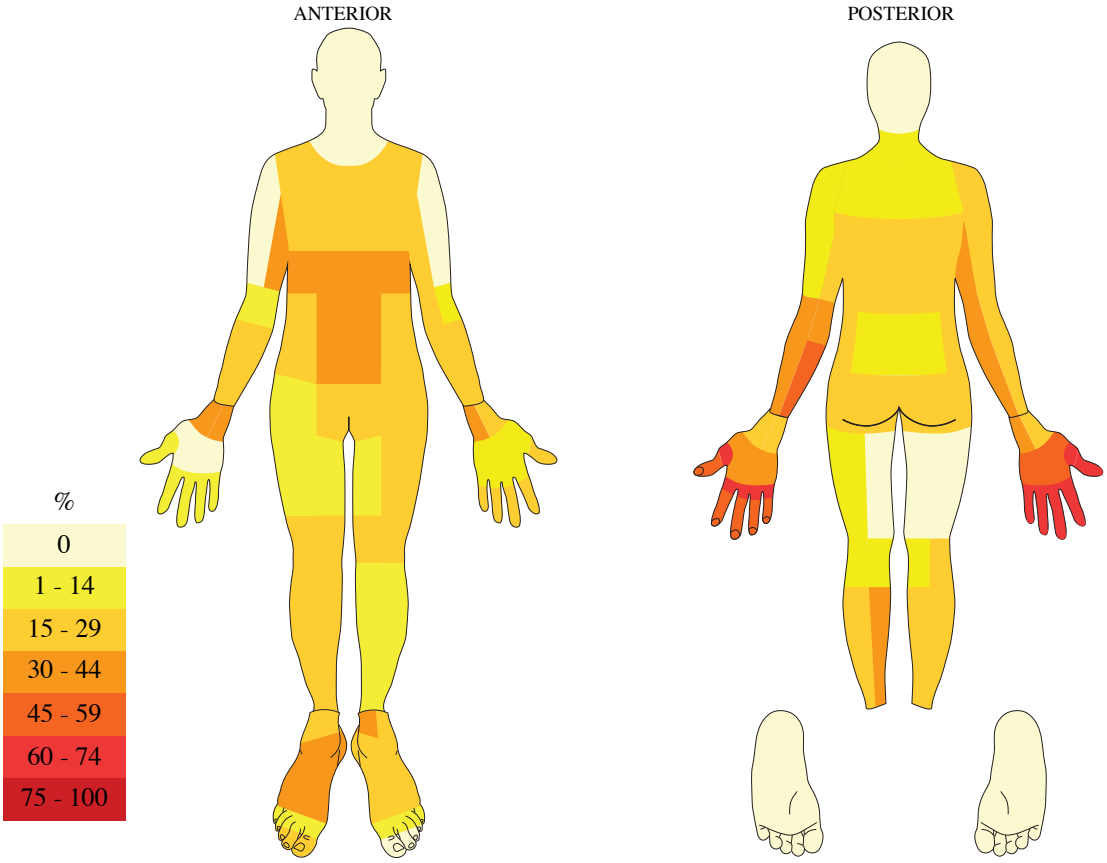


Figure 26. Overall distribution of lesions by proportion of participants with lesions in each site

A high proportion of participants had involvement of the abdomen (44%) and lower anterior chest (36%). On the lower limbs, the most common location was the left posterior medial calf (32%), the left medial ankle (32%) and the right dorsum of the foot (32%). The anterior knees, posterior calves, ankles and dorsum of the feet were generally more common locations for

lesions than other parts of the lower limb (Figure 26). No participant had involvement of the face, neck, anterolateral upper arm or soles of the feet.

6.3.2 Grouped Regions

All participants had involvement of exposed areas. When the sites were grouped (Figure 23) into larger regions the most frequently involved regions were the arms and axilla (100%) and the hands and wrists (96%). The head and neck and the buttocks and genitals were the least frequently involved regions (Figure 27, Table 7).

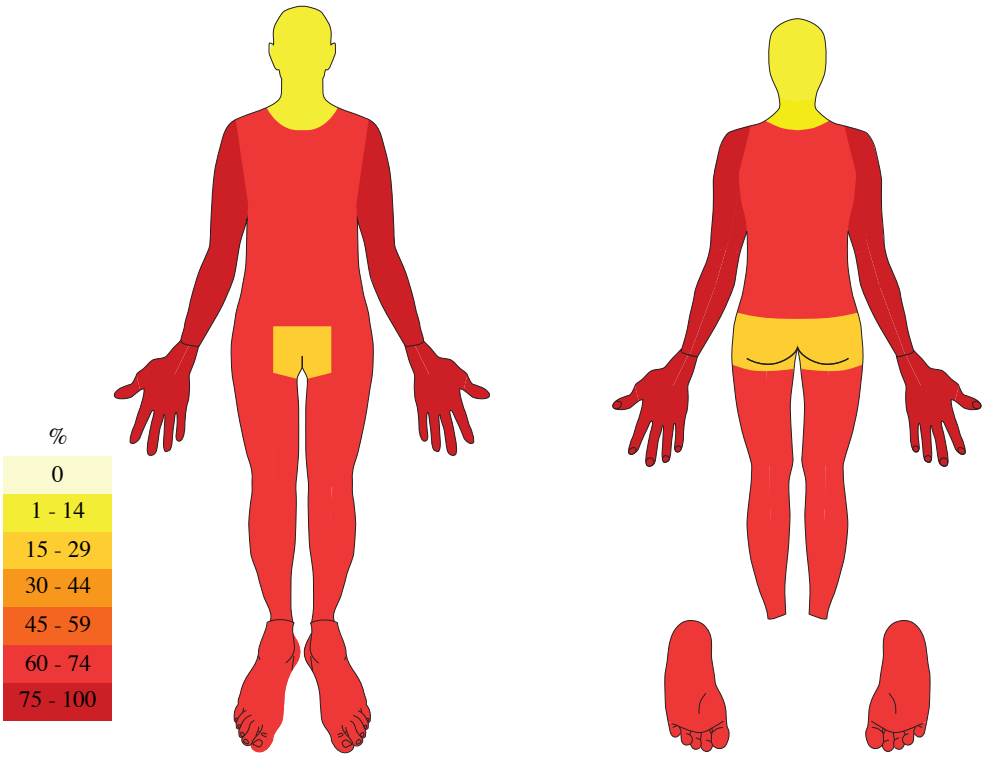


Figure 27. The proportions of individuals with lesions at the grouped regions.

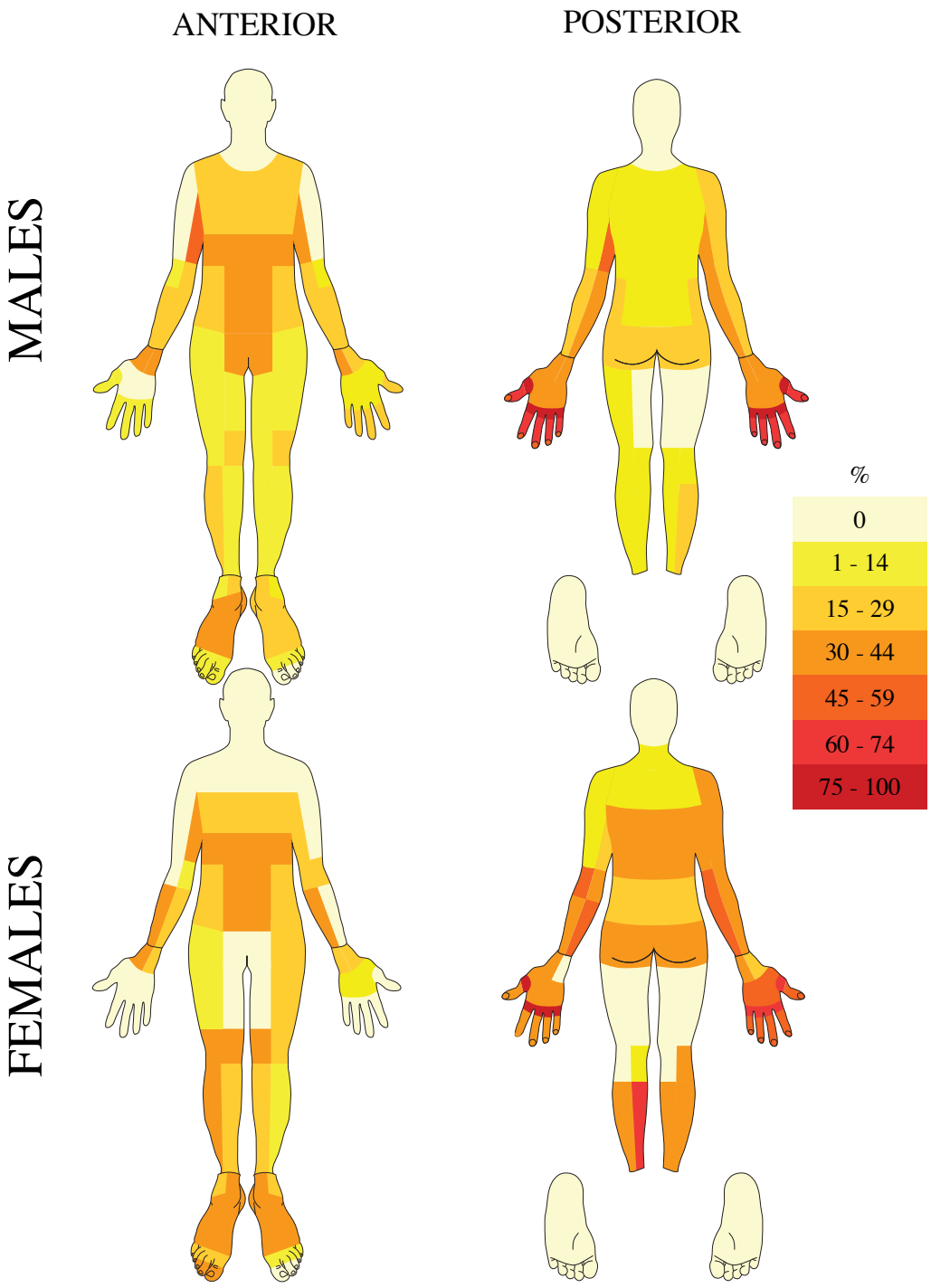
Table 7. The number of individuals with lesions present at each grouped region

Region	Proportion with lesions (%)
Head and neck	4
Torso	68
Arms and axilla	100
Hands and wrists	96
Buttocks and genitals	24
Legs	72
Ankles and feet	68

6.3.3 Proportion of individuals with lesions in each site by sex

The presence of lesions in some sites was similar in both males and females including the dorsal web spaces, the fingers and dorsal hands, the abdomen and the lower anterior chest (Figure 28). The genitals were commonly involved in males (n=6, 37.5%), while no females had genital involvement. The buttocks, back and lower legs were more commonly involved in females.

Figure 28. Distribution of lesions by proportion of participants with lesions in each site by sex



6.3.4 Lesion Concentration

The concentration of lesions was highest on the fingers, web spaces and upper chest (Figure 29). High lesion numbers were also seen at the abdomen, buttocks and axilla. Low lesion

numbers were seen on the back and lower limbs. There were no lesions at the head, face and soles of feet. When comparing the concentration map (Figure 29) to the distribution map (Figure 26) it can be seen that the areas with high lesions numbers are similar to the areas where there are most commonly lesions. However, there are some areas of difference with low number of lesions on the legs and a high number of lesions seen at the upper chest.

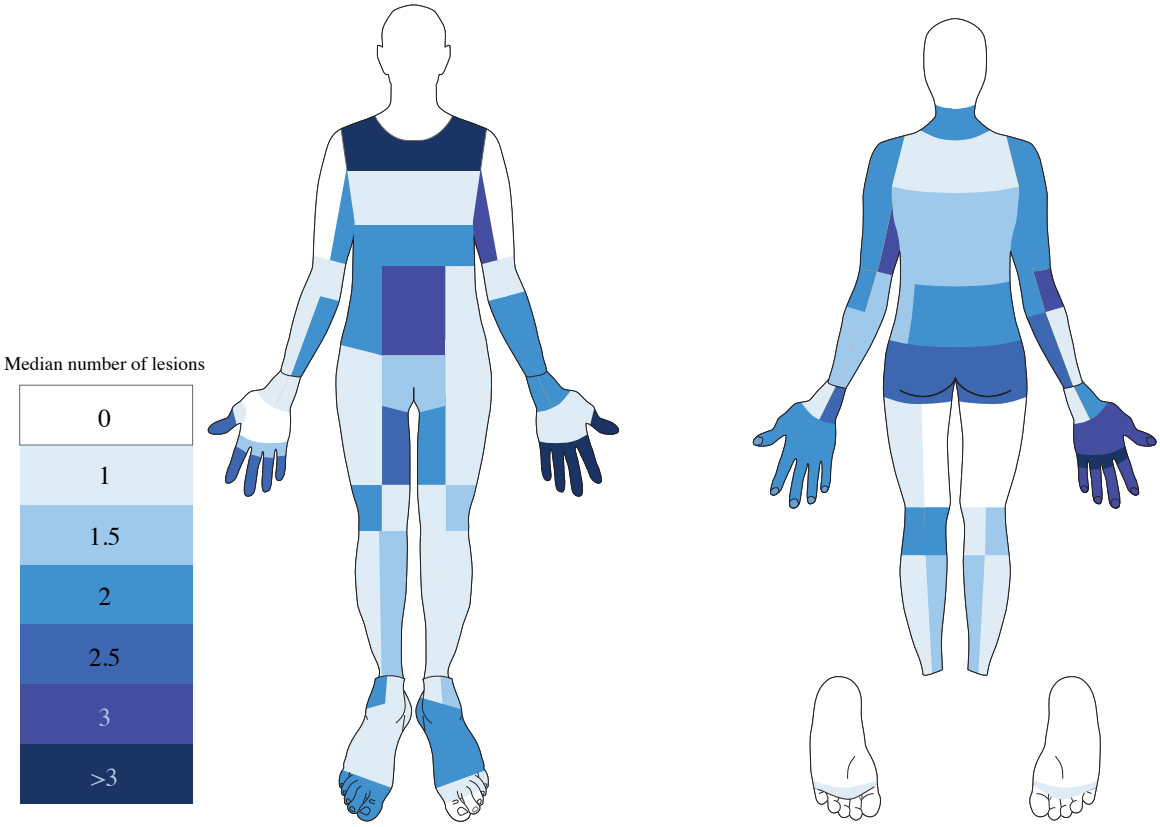


Figure 29. Scabies lesion concentration by mean number of lesions at each site

6.4 Discussion

Our pilot study found that the body distribution of scabies skin lesions can be feasibly performed using the detailed body site examination and recording methods described. This study also showed that choropleth mapping techniques are a useful, novel approach for the display of distribution of skin lesions.

In regard to distribution of scabies lesions, our pilot findings support previous findings in the literature. However, the results provide much greater detail to what has previously been described. Lesions on the web spaces are considered characteristic for scabies and data from other studies support our finding of high rates of involvement at this site.[20, 68 39, 46, 55, 58] However, previous data does not distinguish between the dorsal and palmar web spaces, whereas our results show that involvement of the dorsal aspect is much more common. Similarly, previous studies suggest the arms are a commonly involved site, whereas this study provides more detailed information showing that the medial and posterior aspects of the arms are more commonly involved.[21, 42, 70] Further, the difference in distribution of lesions for males and females is not frequently compared and no studies present data on the comparison of the prevalence of genital lesions between males and females. Our results, if replicated in the larger study, would clearly demonstrate that genital involvement is much more common in males, adding support to the current clinical diagnostic criteria.[33, 145]

All participants had visible scabies lesions in exposed body areas. A previous paper highlighted that only around 10% of cases would be missed if only examining exposed areas, however this used retrospective data.[76] Our data supports those findings, indicating that lesions on visible body areas are common. However, conclusions cannot be drawn as only those with diagnosed scabies following examination of exposed areas were concluded in this study. With replication of this study in a large population and the inclusion of individuals with and without scabies, prospective data on the sensitivity of a simplified examination could be reported. This may provide evidence to support the use of simplified examinations in a public health setting such as epidemiological mapping.

The choropleth map representing the grouped regions (Figure 27) highlights the frequent involvement of the limbs. The map also shows the lack of involvement of the sole of the foot, face or anterior neck, consistent with previous studies.[39, 62, 70] The grouped regions also clearly

identify the dorsum of the hand as much more common location for scabies than the palmar aspect. The graphic representation with a simple colour scheme used in these maps allows simple and intuitive interpretation of the data across a large number of body sites

Choropleth maps have not previously been used to represent dermatological lesion distribution. Visual representation using a heatmap created through a Geographic Information System (GIS) program has previously been used for mapping the distribution of Buruli Ulcer.[144] Although the use of GIS analysis has the advantage of acknowledging or discovering relationships between two variables (i.e. neighbouring areas or skin sites) this method is not appropriate for mapping the distribution of scabies, due to the high number of scabies lesions present.

The study has several limitations. This was a pilot study, with a small sample size from a single location. There was also a limited range of ages included and an overrepresentation of male participants, all of which limit the generalizability of findings to other populations and settings. Additionally, the division of the body surface area into the skin sites, although based on what we considered clinically relevant, may still be considered somewhat arbitrary. In this pilot we only included individuals with scabies, and this initial diagnosis was made by examining at exposed areas. When considering the methodology for a larger study, we will include participants both with, and without, scabies. This will enable the estimation of the proportion of lesions occurring in only unexposed areas, which is helpful when considering the implementation of abbreviated or simplified examinations. It will also be important to recruit participants representative of the community population, including a variety of age groups, which will enable the investigation of lesion distribution by age.

The methods used in this pilot study have been shown to be feasible for implementation in a study with a larger sample size. In undertaking this larger study, we hope to present more detailed information on scabies lesion distribution than has previously been described. The

novel visual representation of the distribution of lesions helps to easily identify lesion distribution patterns and may aid clinical diagnosis.

Chapter 7. Discussion

7.1 The diagnosis of scabies by non-expert examiners: A study of diagnostic accuracy (Chapter 3)

7.1.1 Key findings

This study evaluated the accuracy of non-expert health workers in the diagnosis of scabies after brief training. In a population with very high prevalence of scabies, health workers had a sensitivity of 55% and specificity of 90% for the diagnosis of scabies compared to the consensus diagnosis of two experts. Results were similar for impetigo (sensitivity 53%, specificity 98%). Sensitivity of scabies diagnosis increased when only moderate-severe cases were included in the analysis (sensitivity 94%, specificity of 74%).

7.1.2 Discussion and future research

The diagnosis of scabies and impetigo by non-expert health workers following training was moderate, but improved with increasing disease severity. Improvements in diagnostic accuracy are likely to be seen with modifications**.** These findings provide promise for the role of non-expert examiners in scabies diagnosis, similar to other neglected tropical diseases.[130, 146, 147]

Diagnostic accuracy of non-expert examiners was lowest for mild cases of scabies. Training could address this finding by incorporating a specific focus on these milder clinical presentations. Teaching health workers that scabies may present with only a small number of lesions as well as an emphasis on the importance of careful examination of all areas, may reduce the likelihood of missing mild cases. Additionally, it is important to include images of scabies with mild disease. A focus on the collection of photographs of varied presentations and severity is important as clinical images often feature more obvious, severe disease.

Our results suggested that the majority of scabies cases are mild (with less than 10 lesions). Therefore, if mild cases are missed, then the true prevalence of the disease is likely to be under-reported.

The lower accuracy of the diagnosis of mild cases is similar to findings from other studies. A study conducted in Fiji utilising the International Management of Childhood Illness algorithm identified lower sensitivity for the diagnosis of non-infected scabies over infected scabies, highlighting the difficulty in identifying primary scabies lesions.[134] With modifications to the training program, particularly with an increased emphasis on identification of mild cases, diagnostic accuracy may improve.

With these changes, diagnostic accuracy of non-expert examiners in the clinical diagnosis of scabies may be acceptable for prevalence mapping in low-resource settings. Diagnosis for prevalence mapping should attempt to provide both high sensitivity and high specificity in order to most accurately report true disease prevalence.

Although the IACS criteria are likely to provide greater uniformity to clinical diagnosis, they are yet to be validated, outside of this study. This will be a crucial step to ensure that clinical diagnosis using the criteria accurately represent disease state. The sensitivity and specificity of the criteria should be determined to ensure they provide reliable diagnostic endpoints. Potential methods of validation may compare the IACS criteria for clinical diagnosis to confirmed scabies, where diagnosis is confirmed by mite visualisation. However, as there is no way to determine true negative cases, the accuracy of this method may be hindered. Despite this, attempts should be made to ensure that the criteria are validated using as close to a gold standard as is possible.

Further studies in other settings are needed in order to provide additional support for the use of non-expert examiners to diagnose scabies. In areas where there is a lower prevalence of scabies

and impetigo, the diagnostic accuracy of health workers may be different, due to reduced disease explore. Diagnostic accuracy should also be determined across all age groups. Our study only included children, and there may be differences in other age groups.

Additionally, the development of a simple, cheap and accurate diagnostic test for scabies would have the potential to increase feasibility and accuracy of disease mapping. Although there are research groups working towards the conception of such a test, it is unlikely to be a reality in the near term.[120, 123, 148] Until such tests can be designed and implemented, clinical diagnosis will remain the standard for determining the global burden of scabies, monitoring effectiveness of interventions and as the basis for ongoing surveillance.

7.2 Training non-expert health care workers in the diagnosis of scabies (Chapter 4)

7.2.1 Key findings

Scabies disproportionately affects low-resource communities where diagnosis is usually clinical.[20, 149] In settings where expert clinicians are not available, non-expert health staff can undertake training to diagnose scabies.

This chapter described a training package developed for scabies and impetigo diagnosis and assessed the acquisition of skills and knowledge following its implementation. The study found that the training led to improvements in self-reported knowledge and confidence with the mean score for both increasing from 2.5 to 4.5, with scores increasing for all nurses. Local staff reflected positively on their involvement in the training and acknowledged that the new skills would be useful to them in their daily clinical practice.

7.2.2 Discussion and future research

Training non-expert health workers in low-resource settings in the diagnosis of scabies and impetigo has been undertaken previously[62, 70] However, there is no uniform training protocol or package. This is needed to ensure standardisation of examiners and diagnosis in order to compare data across different studies, settings and across time periods. Our training package for teaching diagnosis of scabies utilised a model with a classroom-based component, a practical component and a hurdle test, and was an effective and enjoyable way to train examiners. Classroom training provides a format for essential theoretical components to be taught and for assessment of this knowledge. Practical experience is essential in establishing good diagnostic skills, requiring individuals with and without the disease to be examined in a supervised and well-supported environment.

Case-based techniques for learning include the use of clinical images and hypothetical situations to present a clinical scenario. This technique has been used previously to assess knowledge following the training of non-expert health workers.[130] In our study, we used clinical images with vignettes to provide an alternative to real life examinations in a controlled classroom environment. This may be considered a helpful component for training to flag any issues (either for individuals or specific components of training) that may require additional focus. It also provides feedback to the trainers on the general comprehension of those undertaking the training.

Additionally, an assessment at the end of training may be considered. This assessment could occur in a practical field setting such as a hospital outpatient clinic or in a school. Although the case-based (picture) assessment may provide valuable feedback and flag specific issues, in our study it did not accurately reflect the results of the diagnostic accuracy study. In the case-based assessment, three out of four examiners performed extremely well. The examiner who

performed less well was not the examiner with the lowest diagnostic accuracy on clinical assessment. However, a sufficiently powered accuracy assessment (where trainees examine hundreds of individuals) is unlikely to be feasible as part of training for mapping in low-resource settings. Therefore, a competency-based assessment with patients or diagnosis under direct supervision is required to ensure a minimum standard competence. A minimum competency will ensure that examiners can be standardised to some degree across difference settings.

While our training package was effective and enjoyable for participants, further development and standardisation is needed. An important modification to training would be a greater focus on mild scabies, as discussed previously.

Additionally, as the IACS criteria suggest, an essential consideration of diagnostic assessment is the absence of a more likely explanation for the skin lesions. This requires examiners to be familiar with geographically and population appropriate differential diagnoses. These will vary considerably across different regions or population groups and need to be considered in the development of a generalised training protocol.

The development of an easily implementable training package may facilitate opportunities for integration with other NTDs. Incorporating scabies diagnosis into other NTD training programs is likely to increase effectiveness and efficiency of programs.[133] Previous research suggests it is feasible to examine for multiple skin diseases concurrently, however integrated training protocols have not been published.[126]

7.3 Prevalence of scabies and impetigo in the Solomon Islands: a school survey (Chapter 5)

7.3.1 Key findings

This study found a very high prevalence of scabies and impetigo in a primary school in Gizo in the Solomon Islands. Of 324 children enrolled, the prevalence of scabies was 54% and the prevalence of impetigo was 32%. Individuals with scabies were more likely to be diagnosed with impetigo resulting in a population attributable risk of 12%.

7.3.2 Discussion and future research

The extremely high prevalence in this school highlights the need for further mapping of scabies in this region. Mapping is required to identify areas of high prevalence which may otherwise remain unknown. Prevalence mapping would also to provide information to develop control strategies and treatment for affected individuals, many who live in hard to reach communities. High scabies prevalence has previously been described in other settings ranging from 34-65%.[49, 62, 72] In order for a true picture of global burden of scabies to be captured, identification of high prevalence populations is crucial.

Conducting a school survey for scabies and impetigo was feasible and efficient. This could provide a methodology for mapping in the future to determine prevalence in other locations. Schools have been used previously as sites for mapping, surveillance or treatment for scabies and other neglected tropical diseases.[70, 126, 150] Schools provide a logistically simple location to examine a cross-section of a community. It is possible that schools may provide an appropriate location to determine a community's prevalence of scabies. In our study we focused on primary school-aged children because of convenience, and because it is known that scabies is often more common in this age-group. Research is needed across a variety of settings to assess if

prevalence mapping conducted using school surveys reflects prevalence in the whole population.

The use of the IACS criteria guided training by focusing on the specific components of examination and history required for diagnosis. Training was provided to address these components which included typical lesions, typical distribution and potential differential diagnoses. Training in how to determine a contact history and a history of itch was also provided. Specific questions were outlined and translations into local languages were determined in order to reduce discrepancies between examiners.

This study also demonstrated that it is possible to incorporate the IACS diagnostic criteria into the study design and data collection. Incorporating the use of the IACS diagnostic criteria into our study provided a framework for standardisation of diagnosis.[33] We found these features simple to incorporate into training. The IACS Criteria also provided the framework for the diagnostic definitions. The incorporation of the IACS diagnostic criteria may allow standardisation and comparison between different research and regions. There may be some minor differences in the delivery of contact and itch questions, as well as potential reporting bias. However, as they are close ended questions (yes or no answers), an attempt has been made to standardise delivery and response as much as possible. Typical lesions and typical distributions of scabies lesions were defined during training to reduce variation between examiners definitions. However, there have not been any universally recognised definitions of these terms which would help to increase standardisation across different regions.

Additionally, the IACS criteria were easily incorporated into the data collection forms used in the studies. However, our forms allowed examiners to complete answers to all components of the clinical assessment as well as determine the IACS subcategory. Analysis of these results showed that the examiners did not always determine the correct IACS subcategory on the forms.

Therefore, we suggest for future studies this is an unnecessary feature of the form, with analysis of the combined clinical features more accurate than the examiners determining the subcategory at the time of form completion. Our experiences suggest that it is likely that if the criteria are used as the basis of diagnosis for other studies, they will allow easier comparison between studies, sites and time points.

7.4 The use of choropleth mapping to display scabies lesion distribution (Chapter 6)

7.4.1 Key findings and discussion

This study developed a protocol for detailed mapping of the body distribution of scabies lesions. Our pilot study found that this protocol is feasible. We developed a novel way of displaying skin lesion distribution data in the form of a choropleth map. This may help to identify distribution patterns in a visually simple way. There are plans for a larger study using this this methodology to provide information on scabies lesion distribution in greater detail than has previously been described.

Clinical diagnosis of scabies relies on identification of clinical features, including typical lesion distribution.[78] This study aims to provide more detailed information on lesion distribution to inform clinical diagnosis of scabies. A greater understanding of the distribution of scabies lesions may leader to greater diagnostic accuracy.

This study also outlined the feasibility of using prospective data to explore the accuracy of simplified examination for scabies, by examining only commonly exposed body areas. The examination of only commonly exposed areas has been used previously in field-work for reasons of modesty and practicality,[70] and there are some retrospective data to suggest that limited examination may acceptable.[76] However, there are no prospective studies to support

this method of examination. The pilot study suggests our methods are appropriate to determine the sensitivity and role of simplified examinations to in epidemiological mapping.

7.5 Conclusion

This thesis has contributed to the existing knowledge of scabies diagnosis in low-resource settings. It provides support for the use of non-expert health workers for scabies diagnosis in prevalence mapping and other public health activities in low resource settings. Implementation of a standardised training protocol for scabies diagnosis is needed. A training model which reflects the one presented in this thesis has been shown to be effective and enjoyable for participants. Support for the implementation of the IACS criteria for scabies within training and diagnostic protocols has been presented. Ongoing improvements to standardisation and diagnostic accuracy of clinical diagnosis for scabies, such as those presented in this thesis, should be investigated and implemented to assist in working towards the global control of scabies.

References

1. Collaborators GBD 2016 Disease and Injury Incidence and Prevalence. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211-59.

2. GBD 2016 DALYS and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390.

3. Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Prevalence of scabies and impetigo worldwide: a systematic review. Lancet Infect Dis. 2015;15(8):960-7.

4. Chung SD, Wang KH, Huang CC, Lin HC. Scabies increased the risk of chronic kidney disease: a 5-year follow-up study. Journal of the European Academy of Dermatology and Venereology : JEADV. 2014;28(3):286-92.

5. Parks T, Smeesters PR, Steer AC. Streptococcal skin infection and rheumatic heart disease. Current Opinion in Infectious Diseases. 2012;25(2).

6. Engelman D, Martin DL, Hay RJ, Chosidow O, McCarthy JS, Fuller LC, et al. Opportunities to investigate the effects of ivermectin mass drug administration on scabies. Parasites and Vectors. 2013;6 (1) (no pagination)(106).

7. Lawrence G, Leafasia J, Sheridan J, Hills S, Wate J, Wate C, et al. Control of scabies, skin sores and haematuria in children in the Solomon Islands: another role for ivermectin. Bulletin of the World Health Organization. 2005;83(1):34-42.

8. Mason DS, Marks M, Sokana O, Solomon AW, Mabey DC, Romani L, et al. The Prevalence of Scabies and Impetigo in the Solomon Islands: A Population-Based Survey. PLoS Negl Trop Dis. 2016;10(6):e0004803.

9. Marks M, Toloka H, Baker C, Kositz C, Asugeni J, Puiahi E, et al. Randomised trial of community treatment with azithromycin and ivermectin mass drug administration for control of scabies and impetigo. Clin Infect Dis. 2018.

10. Romani L, Marks M, Sokana O, Nasi T, Kamoriki B, Cordell B, et al. Efficacy of mass drug administration with ivermectin for control of scabies and impetigo, with coadministration of azithromycin: a single-arm community intervention trial Lancet Infect Dis. 2019;19(5):510-8.

11. 2009 Population and Housing Census National Report, Volume 2. . Honiara, Solomon Islands: Solomon Islands National Statistical Office, Ministry of Finance and Treasury, Solomon Islands Government.

12. Solomon Islands Canberra: The Australian National University 2019 [Available from: https://asiapacific.anu.edu.au/mapsonline/base-maps/solomon-islands-provinces].

13. What is parliament? Honiara, Solomon Islands Research and Information Centre, National Parliament of Solomon Islands [Available from: http://www.parliament.gov.sb/files/project/factsheet1whatisparliament.pdf].

14. Briefing note for countries on the 2018 Statistical Update, Solomon Islands United Nations Development Program 2018.

15. Australian Institute of Health and Welfare. Infant/young child mortality rate Australia: Australian Institute of Health and Welfare; 2018 [Available from: https://www.aihw.gov.au/reports/australias-health/australias-health-2018/contents/indicators-of-australias-health/infant/young-child-mortality-rate].

16. Australia: UNICEF; 2018 [Available from: https://data.unicef.org/country/aus/].

17. Maternal deaths in Australia Australia: Australian Institute of Health and Welfare; 2018 [Available from: https://www.aihw.gov.au/reports/mothers-babies/maternal-deaths-in-australia-2016/contents/report].

18. Hodge N, Slatyer B, Skiller L. Solomon Islands Health System Review. Manila: World Health Organization, Regional Office for the Western Pacifific; 2015.

19. Provincial Profile of the 2009 Population & Housing Census: Western. Solomon Islands Government; 2009.

20. Walton SF, Currie BJ. Problems in diagnosing scabies, a global disease in human and animal populations. Clinical Microbiology Reviews. 2007;20(2):268-79.

21. Worth C, Heukelbach J, Fengler G, Walter B, Liesenfeld O, Feldmeier H. Impaired quality of life in adults and children with scabies from an impoverished community in Brazil. Int J Dermatol. 2012;51(3):275-82.

22. Boralevi F, Diallo A, Miquel J, Guerin-Moreau M, Bessis D, Chiaverini C, et al. Clinical phenotype of scabies by age. Pediatrics. 2014;133(4):e910-e6.

23. Hoy WE, Mathews JD, McCredie DA, Pugsley DJ, Hayhurst BG, Rees M, et al. The multidimensional nature of renal disease: rates and associations of albuminuria in an Australian Aboriginal community. Kidney Int. 1998;54(4):1296-304.

24. Dadabhoy I, Butts JF. Parasitic Skin Infections for Primary Care Physicians. Primary care. 2015;42(4):661-75.

25. Taplin D, Porcelain SL, Meinking TL, Athey RL, Chen JA, Castillero PM, et al. Community control of scabies: a model based on use of permethrin cream. Lancet. 1991;337(8748).

26. Taplin D, Arrue C, Graham Walker J, Roth WI, Rivera A. Eradication of scabies with a single treatment schedule. Journal of the American Academy of Dermatology. 1983;9(4).

27. Romani L, Whitfeld MJ, Koroivueta J, Kama M, Wand H, Tikoduadua L, et al. Mass drug administration for scabies control in a population with endemic disease. New England Journal of Medicine. 2015;373(24):2305-13.

28. Kearns TM, Speare R, Cheng AC, McCarthy J, Carapetis JR, Holt DC, et al. Impact of an Ivermectin Mass Drug Administration on Scabies Prevalence in a Remote Australian Aboriginal Community. PLoS Neglected Tropical Diseases. 2015;9(10):1-13.

29. Engelman D, Steer AC. Control Strategies for Scabies. Trop Med Infect Dis. 2018;3(3).

30. Leung V, Miller M. Detection of scabies: A systematic review of diagnostic methods. Canadian Journal of Infectious Diseases and Medical Microbiology. 2011;22(4):143-6.

31. Thompson MJ, Engelman D, Gholam K, Fuller LC, Steer AC. Systematic review of the diagnosis of scabies in therapeutic trials. Clinical and Experimental Dermatology. 2017;42(5):481-7.

32. Micali G, Lacarrubba F, Verzi AE, Chosidow O, Schwartz RA. Scabies: Advances in Noninvasive Diagnosis. PLoS Neglected Tropical Diseases. 2016;10 (6) (no pagination)(e0004691).

33. Engelman D, Fuller LC, Steer AC, International Alliance for the Control of Scabies Delphi p. Consensus criteria for the diagnosis of scabies: A Delphi study of international experts. PLoS Negl Trop Dis. 2018;12(5):e0006549.

34. Mahe A, Faye O, N'Diaye HT, Ly F, Konare H, Keita S, et al. Definition of an algorithm for the management of common skin diseases at primary health care level in sub-Saharan Africa. Trans R Soc Trop Med Hyg. 2005;99(1):39-47.

35. Worth C, Heukelbach J, Fengler G, Walter B, Liesenfeld O, Hengge U, et al. Acute morbidity associated with scabies and other ectoparasitoses rapidly improves after treatment with ivermectin. Pediatric Dermatology. 2012;29(4):430-6.

36. Shin K, Jin H, You HS, Kim JM, Shim WH, Kim GW, et al. Clinical characteristics of pruritus in scabies. Indian Journal of Dermatology, Venereology and Leprology. 2017;83(4):492-3.

37. Wakhlu I, Thakur S, Govil YC, Rastogi AK. Clinical profile of scabies in north Indian children. Indian pediatrics. 1988;25(11):1050-3.

38. Neri I, Chessa MA, Virdi A, Patrizi A. Nodular scabies in infants: dermoscopic examination may avoid a diagnostic pitfall. Journal of the European Academy of Dermatology and Venereology. 2017;31(12):e530-e1.

39. Jackson A, Heukelbach J, Filho AF, Junior Ede B, Feldmeier H. Clinical features and associated morbidity of scabies in a rural community in Alagoas, Brazil. Trop Med Int Health. 2007;12(4):493-502.

40. Dupuy A, Dehen L, Bourrat E, Lacroix C, Benderdouche M, Dubertret L, et al. Accuracy of standard dermoscopy for diagnosing scabies. J Am Acad Dermatol. 2007;56(1):53-62.

41. Sharma RS, Mishra RS, Dharam P. An epidemiological study of scabies in a rural community in India. Annals of Tropical Medicine and Parasitology. 1984;78(2):157-64.

42. Boralevi F, Diallo A, Miquel J, Guerin-Moreau M, Bessis D, Chiaverini C, et al. Clinical phenotype of scabies by age. Pediatrics. 2014;133(4):e910-6.

43. Yeoh DK, Anderson A, Cleland G, Bowen AC. Are scabies and impetigo "normalised"? A cross-sectional comparative study of hospitalised children in northern Australia assessing clinical recognition and treatment of skin infections. PLoS Neglected Tropical Diseases. 2017;11 (7) (no pagination)(e0005726).

44. Hegazy AA, Darwish NM, Abdel-Hamid IA, Hammad SM. Epidemiology and control of scabies in an Egyptian village. International Journal of Dermatology. 1999;38(4):291-5.

45. Nast A, Griffiths CE, Hay R, Sterry W, Bolognia JL. The 2016 International League of Dermatological Societies' revised glossary for the description of cutaneous lesions. Br J Dermatol. 2016;174(6):1351-8.

46. Kouotou EA, Nansseu JRN, Sieleunou I, Defo D, Bissek ACZK, Ndam ECN. Features of human scabies in resource-limited settings: The Cameroon case. BMC Dermatology. 2015;15 (1) (no pagination)(12).

47. Cassell JA, Middleton J, Nalabanda A, Lanza S, Head MG, Bostock J, et al. Scabies outbreaks in ten care homes for elderly people: a prospective study of clinical features, epidemiology, and treatment outcomes. Lancet Infect Dis. 2018;18(8):894-902.

48. Hill TA, Cohen B. Scabies in babies. Pediatric Dermatology. 2017;34(6):690-4.

49. Ugbomoiko US, Oyedeji SA, Babamale OA, Heukelbach J. Scabies in Resource-Poor Communities in Nasarawa State, Nigeria: Epidemiology, Clinical Features and Factors Associated with Infestation. Trop Med Infect Dis. 2018;3(2).

50. Arlian LG, Morgan MS. A review of Sarcoptes scabiei: Past, present and future. Parasites and Vectors. 2017;10 (1) (no pagination)(297).

51. Mahmood W, Viberg LT, Fischer K, Walton SF, Holt DC. An Aspartic Protease of the Scabies Mite Sarcoptes scabiei Is Involved in the Digestion of Host Skin and Blood Macromolecules. PLoS Neglected Tropical Diseases. 2013;7 (11) (no pagination)(e2525).

52. Thomas C, Coates SJ, Engelman D, Chosidow O, Chang A. Part I - Ectoparasites: Scabies. Journal of the American Academy of Dermatology. 2019.

53. Mumcuoglu KY, Gilead L, Ingber A. New insights in pediculosis and scabies. Expert Review of Dermatology. 2009;4(3):285-302.

54. Hewitt KA, Nalabanda A, Cassell JA. Scabies outbreaks in residential care homes: Factors associated with late recognition, burden and impact. A mixed methods study in England. Epidemiology and Infection. 2015;143(7):1542-51.

55. Kouotou EA, Nansseu JRN, Sangare A, Moguieu Bogne LL, Sieleunou I, Adegbidi H, et al. Burden of human scabies in sub-Saharan African prisons: Evidence from the west region of Cameroon. 2018;59(1):e6-e10.

56. Yoshizumi J, Harada T. 'Wake sign': An important clue for the diagnosis of scabies. Clinical and Experimental Dermatology. 2009;34(6):711-4.

57. Romani L, Koroivueta J, Steer AC, Kama M, Kaldor JM, Wand H, et al. Scabies and impetigo prevalence and risk factors in Fiji: A national survey. Australasian Journal of Dermatology. 2015;2):64.

58. Nair PA, Vora RV, Jivani NB, Gandhi SS. A Study of Clinical Profile and Quality of Life in Patients with Scabies at a Rural Tertiary Care Centre. J Clin Diagn Res. 2016;10(10):WC01-WC5.

59. Hewitt KA, Nalabanda A, Cassell JA. Scabies outbreaks in residential care homes: factors associated with late recognition, burden and impact. A mixed methods study in England. Epidemiol Infect. 2015;143(7):1542-51.

60. Kouotou EA, Nansseu JR, Kouawa MK, Zoung-Kanyi Bissek AC. Prevalence and drivers of human scabies among children and adolescents living and studying in Cameroonian boarding schools. Parasite Vectors. 2016;9(1):400.

61. Edison L, Beaudoin A, Goh L, Introcaso CE, Martin D, Dubray C, et al. Scabies and Bacterial Superinfection among American Samoan Children, 2011-2012. Plos One. 2015;10(10).

62. Romani L, Whitfeld MJ, Koroivueta J, Kama M, Wand H, Tikoduadua L, et al. The Epidemiology of Scabies and Impetigo in Relation to Demographic and Residential Characteristics: Basline Findings from the Skin health Intervention Fiji Trial. Am J Trop Med Hyg. 2017;97(3):845-50.

63. Heukelbach J, Wilcke T, Winter B, Feldmeier H. Epidemiology and morbidity of scabies and pediculosis capitis in resource-poor communities in Brazil. British Journal of Dermatology. 2005;153(1):150-6.

64. Fernandez N. Pathologic Findings in Human Scabies. Archives of Dermatology. 1977;113(3).

65. Liu HN, Sheu WJ, Chu TL. Scabietic nodules: A dermatopathologic and immunofluorescent study. Journal of Cutaneous Pathology. 1992;19(2):124-7.

66. Suh KS, Han SH, Lee KH, Park JB, Jung SM, Kim ST, et al. Mites and burrows are frequently found in nodular scabies by dermoscopy and histopathology. Journal of the American Academy of Dermatology. 2014;71(5):1022-3.

67. Arlian LG, Vyszenski-Moher DL. Response of Sarcoptes scabiei var. canis (Acari: Sarcoptidae) to lipids of mammalian skin. J Med Entomol. 1995;32(1):34-41.

68. Chosidow O. Scabies. New England Journal of Medicine. 2006;354(16):1718-27.

69. Flinders DC, De Schweinitz P. Pediculosis and Scabies. American Family Physician. 2004;69(2):341-8+9-50.

70. Korte LM, Bowen AC, Draper ADK, Davis K, Steel A, Teodora I, et al. Scabies and impetigo in Timor-Leste: A school screening study in two districts. PLoS Negl Trop Dis. 2018;12(5):e0006400.

71. Steer AC, Jenney AW, Kado J, Batzloff MR, La Vincente S, Waqatakirewa L, et al. High burden of impetigo and scabies in a tropical country. PLoS Negl Trop Dis. 2009;3(6):e467.

72. Beeres DT, Ravensbergen SJ, Heidema A, Cornish D, Vonk M, Wijnholds LD, et al. Efficacy of ivermectin mass-drug administration to control scabies in asylum seekers in the

Netherlands: A retrospective cohort study between January 2014 - March 2016. PLoS Negl Trop Dis. 2018;12(5):e0006401.

73. Kouotou EA, Nansseu JRN, Sieleunou I, Moguieu Bogne LL, Sangare A, Adegbidi H, et al. Prevalence and drivers of human scabies in Cameroonian prisons. International Journal of Infectious Diseases. 2016;1):368.

74. Hong MY, Lee CC, Chuang MC, Chao SC, Tsai MC, Chi CH. Factors related to missed diagnosis of incidental scabies infestations in patients admitted through the emergency department to inpatient services. Academic Emergency Medicine. 2010;17(9):958-64.

75. Walton SF, Holt DC, Currie BJ, Kemp DJ. Scabies: New future for a neglected disease. Advances in Parasitology. 2004;57:309-76.

76. Marks M, Engelman D, Romani L, Mason D, Sokana O, Kama M, et al. Exploration of a simplified clinical examination for scabies to support public health decision-making. PLoS Negl Trop Dis. 2018;12(12):e0006996.

77. Au TS. A middle-aged man presenting with itchy lesions on his skin. Hong Kong Practitioner. 2005;27(1):31.

78. Hay RJ, Steer AC, Engelman D, Walton S. Scabies in the developing world--its prevalence, complications, and management. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2012;18(4):313-23.

79. Veraldi S, Esposito L, Pontini P, Nazzaro G, Schianchi R. Where to look for the scabies mite. Infectious Diseases. 2017;49(5):427-8.

80. Kaur J, Kalsy J. Study of pruritus vulvae in geriatric age group in tertiary hospital. Indian J Sex Transm Dis. 2017;38(1):15-21.

81. Tempark T, Lekwuttikarn R, Chatproedprai S, Wananukul S. Nail scabies: An unusual presentation often overlooked and mistreated. Journal of Tropical Pediatrics. 2017;63(2):155-9.

82. Witkowski JA, Parish LC. Scabies. Subungual areas harbor mites. Journal of the American Medical Association. 1984;252(10):1318-9.

83. Roberts LJ, Huffam SE, Walton SF, Currie BJ. Crusted scabies: Clinical and immunological findings in seventy-eight patients and a review of the literature. Journal of Infection. 2005;50(5):375-81.

84. Luo DQ, Huang MX, Liu JH, Tang W, Zhao YK, Sarkar R. Case report: Bullous scabies. American Journal of Tropical Medicine and Hygiene. 2016;95(3):689-93.

85. Hengge UR, Currie BJ, Jager G, Lupi O, Schwartz RA. Scabies: a ubiquitous neglected skin disease. Lancet Infectious Diseases. 2006;6(12):769-79.

86. Estrada-Chavez G, Estrada R, Engelman D, Molina J, Chavez-Lopez G. Cushing Syndrome due to Inappropriate Corticosteroid Topical Treatment of Undiagnosed Scabies. Trop Med Infect Dis. 2018;3(3).

87. Karimkhani C, Colombara DV, Drucker AM, Norton SA, Hay R, Engelman D, et al. The global burden of scabies: a cross-sectional analysis from the Global Burden of Disease Study 2015. Lancet Infect Dis. 2017;17(12):1247-54.

88. Amro A, Hamarsheh O. Epidemiology of scabies in the West Bank, Palestinian Territories (Occupied). International Journal of Infectious Diseases. 2012;16(2):e117-e20.

89. Feldmeier H, Jackson A, Ariza L, Lins Calheiros CM, de Lima Soares V, Oliveira FA, et al. The epidemiology of scabies in an impoverished community in rural Brazil: Presence and severity of disease are associated with poor living conditions and illiteracy. Journal of the American Academy of Dermatology. 2009;60(3):436-43.

90. Anderson KL, Strowd LC. Epidemiology, Diagnosis, and Treatment of Scabies in a Dermatology Office. Journal of the American Board of Family Medicine : JABFM. 2017;30(1):78-84.

91. Kouotou EA, Nansseu JRN, Kouawa MK, Zoung-Kanyi Bissek AC. Prevalence and drivers of human scabies among children and adolescents living and studying in Cameroonian boarding schools. Parasites and Vectors. 2016;9 (1) (no pagination)(400).

92. Alsamarai AM. Frequency of scabies in Iraq: Survey in a dermatology clinic. Journal of Infection in Developing Countries. 2009;3(10):789-93.

93. Purnavab S, Ketabchi S, Rowshan V. Chemical composition and antibacterial activity of methanolic extract and essential oil of Iranian Teucrium polium against some of phytobacteria. Natural product research. 2015;29(14):1376-9.

94. Burns BR, Lampe RM, Hansen GH. Neonatal scabies. American Journal of Diseases of Children. 1979;133(10):1031-4.

95. Whitehall J, Kuzulugil D, Sheldrick K, Wood A. Burden of paediatric pyoderma and scabies in North West Queensland. Journal of Paediatrics and Child Health. 2013;49(2):141-3.

96. Kristensen JK. Scabies and pyoderma in Lilongwe, Malawi. Prevalence and seasonal fluctuation. International Journal of Dermatology. 1991;30(10):699-702.

97. Christophersen J. The epidemiology of scabies in denmark, 1900 to 1975. Archives of Dermatology. 1978;114(5):747-50.

98. Tasani M, Tong SYC, Andrews RM, Holt DC, Currie BJ, Carapetis JR, et al. The importance of scabies coinfection in the treatment considerations for impetigo. Pediatric Infectious Disease Journal. 2016;35(4):374-8.

99. Walton SF, Beroukas D, Roberts-Thomson P, Currie BJ. New insights into disease pathogenesis in crusted (Norwegian) scabies: The skin immune response in crusted scabies. British Journal of Dermatology. 2008;158(6):1247-55.

100. Cinotti E, Perrot JL, Labeille B, Cambazard F. Reflectance confocal microscopy for cutaneous infections and infestations. Journal of the European Academy of Dermatology and Venereology : JEADV. 2016;30(5):754-63.

101. Diab HM. Scabies incognito: Diagnostic value of dermoscopy-guided microscopic examination. Journal of the Egyptian Women's Dermatologic Society. 2017;14(1):56-60.

102. Speight EL. Asymmetrical scabies burrows in a hemiplegic patient [5]. British Journal of Dermatology. 1993;128(4):467-8.

103. Wilson MMG, Philpott CD, Breer WA. Atypical presentation of scabies among nursing home residents. Journals of Gerontology - Series A Biological Sciences and Medical Sciences. 2001;56(7):M424-M7.

104. Tsutsumi M, Nishiura H, Kobayashi T. Dementia-specific risks of scabies: Retrospective epidemiologic analysis of an unveiled nosocomial outbreak in Japan from 1989-90. BMC Infectious Diseases. 2005;5 (no pagination)(85).

105. Park JH, Kim CW, Kim SS. The diagnostic accuracy of dermoscopy for scabies. Ann Dermatol. 2012;24(2):194-9.

106. Walter B, Heukelbach J, Fengler G, Worth C, Hengge U, Feldmeier H. Comparison of dermoscopy, skin scraping, and the adhesive tape test for the diagnosis of scabies in a resource-poor setting. Archives of Dermatology. 2011;147(4):468-73.

107. Katsumata K. Simple method of detecting sarcoptes scabiei var hominis mites among bedridden elderly patients suffering from severe scabies infestation using an adhesive-tape. Internal Medicine. 2006;45(14):857-9.

108. Kruesch J. Incident Light Microscopy: Reflections on Microscopy of the Living Skin. International Journal of Dermatology 1992;31(9):618-20.

109. Argenziano G, Fabbrocini G, Delfino M. Epiluminescence microscopy: A new approach to in vivo detection of sarcoptes scabiei. Archives of Dermatology. 1997;133(6):751-3.

110. Lacarrubba F, Musumeci ML, Caltabiano R, Impallomeni R, West DP, Micali G. High-magnification videodermatoscopy: A new noninvasive diagnostic tool for scabies in children. Pediatric Dermatology. 2001;18(5):439-41.

111. Micali G, Lacarrubba F, Verzi AE, Nasca MR. Low-cost equipment for diagnosis and management of endemic scabies outbreaks in underserved populations. Clinical Infectious Diseases. 2015;60(2):327-9.

112. Miller H, Trujillo-Trujillo J, Feldmeier H. In Situ Diagnosis of Scabies Using a Handheld Digital Microscope in Resource-Poor Settings-A Proof-of-Principle Study in the Amazon Lowland of Colombia. Trop Med Infect Dis. 2018;3(4).

113. Lacarrubba F, Verzi AE, Micali G. Detailed analysis of in vivo reflectance confocal microscopy for sarcoptes scabiei hominis. American Journal of the Medical Sciences. 2015;350(5):414.

114. Levi A, Mumcuoglu KY, Ingber A, Enk CD. Assessment of Sarcoptes scabiei viability in vivo by reflectance confocal microscopy. Lasers in Medical Science. 2011;26(3):291-2.

115. Micali G, Lacarrubba F, Tedeschi A. Videodermatoscopy enhances the ability to monitor efficacy of scabies treatment and allows optimal timing of drug application. Journal of the European Academy of Dermatology and Venereology. 2004;18(2):153-4.

116. Banzhaf CA, Themstrup L, Ring HC, Welzel J, Mogensen M, Jemec GBE. In vivo imaging of sarcoptes scabiei infestation using optical coherence tomography. Case Reports in Dermatology. 2013;5(2):156-62.

117. Woodley D, Saurat JH. The Burrow Ink Test and the scabies mite. J Am Acad Dermatol. 1981;4(6):715-22.

118. Wong SSY, Poon RWS, Chau S, Wong SCY, To KKW, Cheng VCC, et al. Development of conventional and real-time quantitative PCR assays for diagnosis and monitoring of scabies. Journal of Clinical Microbiology. 2015;53(7):2095-102.

119. Fukuyama S, Nishimura T, Yotsumoto H, Gushi A, Tsuji M, Kanekura T, et al. Diagnostic usefulness of a nested polymerase chain reaction assay for detecting Sarcoptes scabiei DNA in skin scrapings from clinically suspected scabies. British Journal of Dermatology. 2010;163(4):892-4.

120. Hahm JE, Kim CW, Kim SS. The efficacy of a nested PCR in detecting cytochrome c oxidase subunit 1 gene of Sarcoptes scabiei var. Hominis for diagnosing scabies. Br J Dermatol. 2018.

121. Morgan MS, Rider SD, Arlian LG. Identification of antigenic Sarcoptes scabiei proteins for use in a diagnostic test and of non-antigenic proteins that may be immunomodulatory. PLoS Neglected Tropical Diseases. 2017;11 (6) (no pagination)(e0005669).

122. Walton SF, Slender A, Pizutto S, Mounsey KE, Opresecu F, Thomas WR, et al. Analysis of ige binding patterns to house dust mite allergens in scabies-endemic communities: Insights for both diseases. Clinical and Experimental Allergy. 2015;45(12):1868-72.

123. Arlian LG, Feldmeier H, Morgan MS. The Potential for a Blood Test for Scabies. PLoS Neglected Tropical Diseases. 2015;9 (10) (no pagination)(e0004188).

124. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015;351:h5527.

125. Albrecht J, Bigby M. Testing a test: Critical appraisal of tests for diagnosing scabies. Archives of Dermatology. 2011;147(4):494-7.

126. Yotsu RR, Kouadio K, Vagamon B, N'Guessan K, Akpa AJ, Yao A, et al. Skin disease prevalence study in schoolchildren in rural Cote d'Ivoire: Implications for integration of neglected skin diseases (skin NTDs). PLoS Negl Trop Dis. 2018;12(5):e0006489.

127. Callaghan M, Ford N, Schneider H. A systematic review of task- shifting for HIV treatment and care in Africa. Hum Resour Health. 2010;8:8.

128. Task shifting: rational redistribution of tasks among health workforce teams: global recommendations and guidelines Geneva World Health Organization 2008.

129. Barogui YT, Diez G, Anagonou E, Johnson RC, Gomido IC, Amoukpo H, et al. Integrated approach in the control and management of skin neglected tropical diseases in Lalo, Benin. PLoS Negl Trop Dis. 2018;12(6):e0006584.

130. Solomon AW, Pavluck AL, Courtright P, Aboe A, Adamu L, Alemayehu W, et al. The Global Trachoma Mapping Project: Methodology of a 34-Country Population-Based Study. Ophthalmic Epidemiol. 2015;22(3):214-25.

131. Engelman D, Okello E, Beaton A, Selnow G, Remenyi B, Watson C, et al. Evaluation of Computer-Based Training for Health Workers in Echocardiography for RHD. Glob Heart. 2017;12(1):17-23 e8.

132. Heukelbach J, Feldmeier H. Scabies. Lancet. 2006;367(9524):1767-74.

133. Engelman D, Fuller LC, Solomon AW, McCarthy JS, Hay RJ, Lammie PJ, et al. Opportunities for Integrated Control of Neglected Tropical Diseases That Affect the Skin. Trends Parasitol. 2016;32(11):843-54.

134. Steer AC, Tikoduadua LV, Manalac EM, Colquhoun S, Carapetis JR, Maclennan C. Validation of an Integrated Management of Childhood Illness algorithm for managing common skin conditions in Fiji. Bull World Health Organ. 2009;87(3):173-9.

135. Taal A, Hussaini T, Gayus BA, Dahiru T, Post E. First-line health care provider performance in the management of common skin diseases using an algorithmic approach as a diagnostic tool in Kano State, Nigeria. Research and Reports in Tropical Medicine. 2015.

136. International Coalition for Trachoma Control. Global Trachoma Mapping Project: Training for mapping of trachoma; 3.

137. Recognizing neglected tropical diseases through changes on the skin: a training guide for front-line health workers. Geneva: World Health Organization; 2018.

138. Thistlethwaite JE, Davies D, Ekeocha S, Kidd JM, MacDougall C, Matthews P, et al. The effectiveness of case-based learning in health professional education. A BEME systematic review: BEME Guide No. 23. Med Teach. 2012;34(6):e421-44.

139. Finucane PM, Johnson SM, Prideaux DJ. Problem-based learning: its rationale and efficacy. Medical Journal of Australia. 1998;168.

140. Mellanby K. The development of symptoms, parasitic infection and immunity in human scabies. Parasitology. 1944;35(04):197-206.

141. Arlian LG, Runyan RA, Sorlie LB, Estes SA. Host-seeking behavior of Sarcoptes Scabiei. J Am Acad Dermatol. 1984;11.

142. Jackson R. Scabies by Kenneth Mellanby. Journal of Cutaneous Medicine and Surgery. 2004;8(2):73-6.

143. Brewer CA, Pickle L. Evaluation of Methods for Classifying Epidemiological Data on Choropleth Maps in Series. Annals of the Association of American Geographers. 2002;92(4):662-81.

144. Yerramilli A, Tay EL, Stewardson AJ, Kelley PG, Bishop E, Jenskin GA, et al. The location of Australian Buruli ulcer lesions - Implications for unravelling disease transmission. PLoS Negl Trop Dis. 2017;11(8).

145. Hall A. Scabies. Atlas of Male Genital Dermatology. Cham: Springer International Publishing; 2019. p. 103-6.

146. Faye O, Hay RJ, Ryan TJ, Keita S, Traore AK, Mahe A. A public health approach for leprosy detection based on a very short term-training of primary health care workers in basic dermatology. Leprosy Review. 2007;78(1):11-6.

147. Deribe K, Wanji S, Shafi O, E MT, Umulisa I, Molyneux DH, et al. The feasibility of eliminating podoconiosis. Bull World Health Organ. 2015;93(10):712-8.

148. Engelman D, Cantey PT, Marks M, Solomon AW, Chang A, Chosidow O, et al. The public health control of scabies: priorities for research and action. Lancet. 2019;394(10192):81-92.

149. Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Systematic review of the global prevalence of scabies and impetigo. Australasian Journal of Dermatology. 2015;2):19.

150. World Health Organization. Helminth control in school-age children. France World Health Organization; 2011.