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Research paper

# Scabies and impetigo in Samoa: A school-based clinical and molecular epidemiological study ☆

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ABSTRACT

*Background:* Common infections of the skin such as impetigo and scabies represent a large burden of disease globally, being particularly prevalent in tropical and resource-limited settings. Efforts to address these infections through mass drug administrations have recently been shown as efficacious and safe. In Samoa, a Pacific Island nation, there is a marked lack of epidemiological data for these neglected tropical diseases, or appreciation of their drivers in this setting.

*Methods:* An observational, cross-sectional survey of children aged between 4 and 15 years attending primary schools in rural areas of Upolu Island, Samoa was carried out to assess the prevalence of impetigo and scabies in schoolchildren residing in rural Samoa, integrated with descriptive epidemiological and microbial genomic data. A phylogenetic assessment of local *Staphylococcus aureus* isolated from Samoan schoolchildren was performed to estimate putative community transmission.

*Findings:* In this survey, the prevalence of impetigo observed in Samoan schoolchildren was one of the highest described globally (57•1%, 95% CI [53•8–60•5%], 476/833). Associations between active impetigo and age and gender were noted, with younger children and males more commonly affected (aOR2•8 [1•8-4•7]and aOR1•8 [1•3-2•5], respectively). The prevalence of scabies was similar to that seen in other South Pacific island countries (14•4%, 95% CI [12•2–17•0%], 120/833). Transmission of *S. aureus* was predicted, primarily between those children attending the same school. Carriage of *S. pyogenes* was notably low, with pharyngeal carriage observed in less than 2% of schoolchildren, consistent with earlier studies from Samoa.

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*Interpretation:* This study describes a considerable burden of disease attributed to impetigo and scabies in Samoa. These findings will be valuable in addressing the public health challenge posed by these conditions, providing baseline prevalence data and highlighting practical strategies to reduce transmission of relevant microbes and parasites in this setting.

*Tala Tomua:* O a'afiaga o le pa'u i fa'ama'i o le po'u (impetigo) ma le utu o le pa'u (scabies), ua tele naua le fanau ua maua ai i le pasefika, ma le lalolagi atoa. O fuafuaga vaai mamao ma polokalame e fofoina ai nei faafitauli, e aofia ai le inumaga o fualaau e tapeina ai nei fa'ama'i, ua aliali mai ai e mafai ona faatamaia nei fa'ama'i. E le o tele ni tusitusiga ma faamaumauga i totonu o Samoa, pe ta'atele nei fa'amai o le pa'u pe leai. Ona o le le faatauaina o nei fa'ama'i, e le o iloa fo'i ni mafuaga ma nisi tulaga e faateleina ai nei fa'ama'i o le pa'u i Samoa.

*Faatinoina o le suesuega:* O le suesuega faasaenisi i le fanau aoga i le va o le 4 ma le 15 tausaga o loo ao'oga i le tulaga lua i nisi o nu'u i tua i Upolu, na faatinoina ai suesuega lea, ia suesueina ai le aotelega ma fainumera o le fanau ua maua i fa'ama'I o le po'u (impetigo) ma le utu o le pa'u (scabies). O lenei foi suesuega, na fia iloa ai fo'i po'o a ituaiga siama eseese o loo maua i luga o pa'u ma tino o le fanau aoga, ina ia iloa ai foi auala ua pipisi ai nei siama mai le isi tamaitiiti i le isi, ona mafua ai lea o nei fa'ama'i o le pa'u.

*Tanuuga o le suesuega:* Ua faailoa mai i le suesuega, le ta'atele o le fa'ama'i o le po'u (impetigo) ua maua ai le fanau aoga (57%), i aoga na faia ai le suesuega. O se fainumera ua maualuga tele i le lalolagi atoa. E toatele atu nisi o le fanau laiti (younger) ma tama (male) e maua i le po'u nai lo isi tamaiti. O le fainumera o le utu o le pa'u (scabies) (14·4%) e tai tutusa lava ma isi motu o le Pasefika. O le feaveaina o le siama faapitoa (staph aureus) ua tupu lea i le fanau ua ao'oga i le aoga e tasi. E le toatele foi nisi o le fanau (2%) na maua i le siama faapitoa o le fa'ai (strep pyogenes) e ona mafua ai le fiva rumatika. O lenei fainumera ua tai tutusa ma suesuega faasaenisi na fai muamua i Samoa.

*Aotelega:* O le aotelega la o lenei suesuega faasaenisi, ua faailoaina mai ai le tele naua o le fa'ama'i o le pa'u, o po'u (impetigo) ma le utu o le pa'u (scabies) i Samoa nei. O nei foi suesuega o le a aoga tele ini polokalame ma ni fuafuaga mamao e fa'afoisia ai nei faafitauli i le soifua maloloina o le fanau i Samoa. O le a avea foi nei fainumera e faamaumauina mo le silafia e le atunuu ma le soifua maloloina, le ta'atele o nei fa'amai o le pa'u, mo le tapenaina o ni fofo talafeagai ise taimi o i luma, ina ia faaitiitina ai le pipisi o nei siami i fanau ao'oga i Samoa.

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Research in context

Evidence before this study

Island nations of the South Pacific are disproportionately burdened by skin infections, including scabies and impetigo. High rates of scabies and impetigo in children likely contribute to a continuing cardiac and renal disease risk via *Streptococcus pyogenes* (group A) infections in this population.

There is a marked gap in our epidemiological understanding of these neglected tropical diseases in many South Pacific island nations. We searched PubMed with no language restrictions for studies published prior to 24th August 2020 relating to scabies and impetigo in the independent state of Samoa, one such island nation, using the terms "scabies" and "impetigo". Of the identified publications, one included data on the prevalence of impetigo and/or scabies in Samoa, and none included data from within the last two decades.

Added value of this study

In this cross-sectional study, we assess the prevalence of scabies and impetigo in schoolchildren residing in rural Samoa; this is integrated with epidemiological and microbial data to better understand the transmission of causative organisms. The prevalence of impetigo observed in Samoan schoolchildren was one of the highest described globally (57•1%, 95% CI [53•8–60•5%]). The prevalence of scabies was similar to that seen in other South Pacific island countries (14•4%, 95% CI [12•2–17•0%]). Transmission of microbes causative of impetigo was inferred, primarily between those children attending the same school.

Implications of all the available evidence

This study describes a considerable burden of disease attributed to impetigo and scabies in Samoa. Although recent decades have seen efforts to establish public health strategies for other endemic diseases, the continuing burden of skin disease in the South Pacific is concerning. Further research questions include the efficacy and durability of potential public health interventions, and the acceptability of these interventions to individuals and local communities.

## 1. Introduction

Skin infections such as impetigo and scabies are a major contributor to the global burden of disease, with children having the highest incidence of disease [1,2]. Impetigo is predominantly caused by *Staphylococcus aureus* and *Streptococcus pyogenes* and is estimated to affect 162,000,000 children globally at any one time [3]. Scabies is a parasitic infestation of the dermis caused by *Sarcoptes scabiei* var. *hominis*, presenting as an intense pruritic rash with characteristic anatomical distributions, affecting an estimated 200,000,000 people globally [1,4]. Each of these conditions have an elevated prevalence in tropical and resource-limited countries [1–3,5,6]. Both impetigo and scabies are contagious, with epidemiological risk factors including low socio-economic status and household crowding, especially within sleeping quarters [5-6]. Safe and effective treatments are available for both impetigo and scabies, although population-level strategies for prevention and treatment are challenging to implement in the resource-limited settings in which these diseases have highest prevalence [5–15]. In light of this, scabies and other ectoparasites are now listed as neglected tropical diseases by the World Health Organisation (WHO), with

the further addition of bacterial skin infections being suggested [4–6,16].

Although impetigo and scabies are superficial infections, both conditions can be associated with severe complications. Intense pruritis associated with scabies can lead to scratching and abrasion of affected areas, facilitating secondary bacterial infection [17–20]. A range of serious complications can occur with impetigo, including progression of bacterial infection to subcutaneous tissue and other body sites, causing cellulitis, osteomyelitis and septicaemia [21,22]. In temperate climates, *S. aureus* is the predominant bacterial species causing impetigo, with treatment of complications made increasingly challenging by antimicrobial resistance, especially methicillin-resistant *S. aureus* (MRSA) [23–25]. Observational evidence further suggests a link between *S. pyogenes* impetigo and a range of auto-immune sequelae, including glomerulonephritis, rheumatic fever and rheumatic heart disease [26–37].

Historically, island nations in the South Pacific including Fiji, Vanuatu, and the Solomon Islands have high rates of impetigo and scabies [38–50]. In settings where scabies has a high endemicity, therapies targeting affected individuals and their immediate contacts have had limited success in lowering the overall community prevalence, likely due to high rates of re-infestation [51,52]. This is now being addressed through population-level strategies, including the introduction of mass drug administration (MDA) with compounds such as ivermectin, aimed at decreasing the prevalence of scabies and secondary impetigo. This approach has been shown to decrease the prevalence of both scabies and impetigo in small community-based trials [7,39], and more recently, has been scaled successfully to larger populations, with notable success in a rural population of over 25,000 in the Solomon Islands [8].

Samoa shares many climatic and demographic characteristics with other Pacific Island nations, although there is a paucity of data available on the prevalence of impetigo and scabies in this setting [49,50]. Establishing the burden of disease attributable to impetigo and scabies is a key aspect in developing appropriate population-level treatment and prevention programmes for the management of these conditions. Accordingly, the aims of this study were to: (i) describe the prevalence and epidemiological associations of impetigo and scabies among Samoan schoolchildren, in order to better inform appropriate treatment and prevention strategies at the community level, and (ii) investigate the putative transmission of *S. aureus* and *S. pyogenes* causing impetigo amongst these children, using isolates obtained from the clinical epidemiological study. Collectively, these data provide insights into the prevalence and potential drivers of impetigo and scabies in Samoan schoolchildren.

## 2. Methods

### 2.1. Setting and study population

The Independent State of Samoa is a country comprising the westernmost group of Samoan Islands, located in the Polynesian region of the Pacific Ocean. Samoa was ranked 111th of 189 countries on the United Nations Human Development Index (HDI) in 2019 [53]. Of Samoa's total population of approximately 195,000 people, the majority reside on Upolu island, which includes the main urban area of Apia. The climate is equatorial, with an average annual temperature of 26•5°C (79•7°F) and a rainy season from November to April. Between the 7th and 20th February 2018, inclusive, we conducted an observational, cross-sectional survey of children aged between 4 and 15 years attending primary schools in rural areas of Upolu Island, Samoa (Fig. 1). Each primary school in the administrative district of Falealili in rural Upolu was included, and all children attending school on the day of the survey having prior parental approval were included in the study. Primary school attendance is mandatory for children aged between 5 and 14 years, with total primary school enrolment of 94% in 2018 [54,55].

Assessments of skin infection, sample swabs and accompanying demographic data were collected from the children by senior medical students from the National University of Samoa who were trained in the survey methods and supervised by one of the study authors. Basic demographic data was recorded from each child, including self-reported age, gender, number of occupants in the participants household and their sleeping arrangements. Data were recorded directly onto tablets using a digital questionnaire and uploaded at the end of each day when internet access was available. If scabies and/or active impetigo were identified, authors encouraged families to visit local health centre, with prescriptions provided for children with particularly severe impetigo.

### 2.2. Microbiological sampling and analyses

Each participating child had swabs taken from the nose (anterior nares, assessing *S. aureus* carriage) and throat (oropharynx, assessing *S. pyogenes* carriage). Exposed parts of skin (arms, legs, face and neck) were examined for impetigo, defined as discrete lesions surrounded by erythema with pus or crusts. 'Active' impetigo was defined as discrete sores or lesions with pus or crusts, whilst 'inactive' impetigo was defined as any dry skin sore or lesion. [40] These exposed areas were simultaneously examined for (i) scabies, defined as pruritic inflammatory papules; and (ii) infected scabies as additionally having pus or crusts as per the Fiji Integrated Management for Childhood Illness skin condition algorithm [56,57]. Swabs were taken from the most clinically severe impetigo lesion and/or from an infected scabies lesion if present. To ensure consistency in adherence to study protocols, each infected skin site that was swabbed was also photographed, with the child's face excluded for privacy (Fig. 1). Primary microbiological work was carried out at the Tupua Tamasese Meaole National Hospital laboratory, Apia, Samoa. Swabs were plated onto sheep blood agar, with colonies morphologically resembling *S. pyogenes* or *S. aureus* sent to the Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL), at The University of Melbourne, Australia for further identification and genomic characterisation (Supplementary Methods).

### 2.3. Sequencing and microbial genomic analyses

Bacterial isolates collected in this study are listed in the Supplementary Data. DNA extraction and whole genome sequencing (WGS) of study isolates was performed at MDU PHL. Genomic DNA was extracted from a single colony using a QIAsymphony™ DSP DNA Mini Kit (Qiagen) according to manufacturer's instructions, and WGS was performed on an Illumina NextSeq 500 instrument with 150 bp paired-end reads using Illumina libraries and protocols (Illumina, San Diego, California, USA). Phylogenetic and bioinformatic analyses were performed using the *Nullarbor* bioinformatic pipeline (Supplementary Methods). In order to identify putative transmission clusters of *S. aureus*, phylogenetic relatedness was further assessed using hierarchical single linkage clustering, performed on pairwise single nucleotide polymorphism (SNP) distances between isolates. Where a publicly available reference genome was not available for *S. aureus* sequence types (STs), a closed genome was generated using Oxford Nanopore sequencing (Supplementary Methods). Potential transmission of *S. aureus* isolates between individuals was assessed using a pairwise single nucleotide polymorphism (SNP) distance matrix, generated from ST-specific core genome alignments (Supplementary Methods). For inclusion in a cluster, isolates from individuals had to be related to one or more other isolates in the cluster by 10 SNPs or fewer

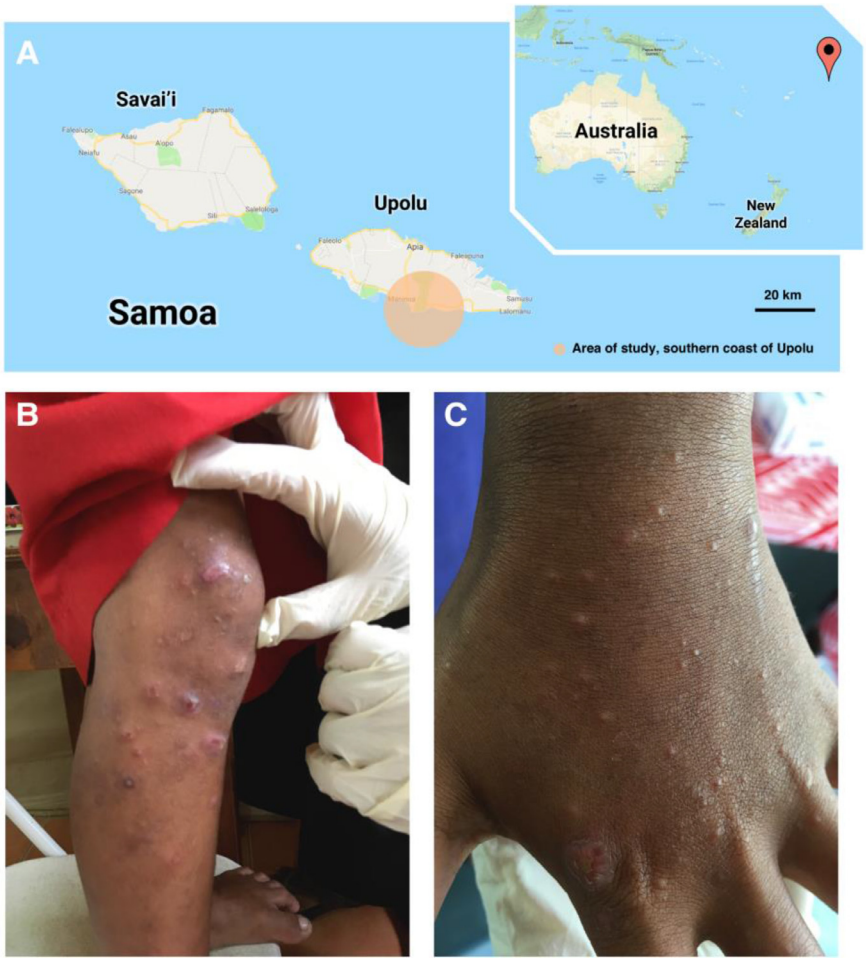



**Fig. 1.** An overview of study location, presentations of impetigo and scabies observed in the study. A) Outline of the study region, on the southern coast of Upolu. Samoa is a country comprising the westernmost group of Samoan Islands, located in the Polynesian region of the Pacific Ocean, shown in the insert. Map data generated from Google Maps, © 2020. B) An example of active impetigo observed in this study. C) An example of scabies infection observed in this study.

(see below). All sequence data generated in this study are publicly available at BioProject PRJNA641487.

### 2.4. Study sampling design

The prevalence of impetigo and scabies in this study population were estimated to be 40-50% and 10-20%, respectively, while pharyngeal carriage of *S. pyogenes* was expected to be lower based on the available literature [50]. An estimated sample size of 785 children was required to estimate the lowest expected prevalence of 5% pharyngeal carriage of *S. pyogenes*, with a precision of +/- 1•5%, based on the low pharyngeal carriage reported in an earlier study in Samoa [50]. This sample size calculation assumes a prevalence ($p$) of 0•05, a confidence level ($cl$) of 0•95, an absolute precision ($d$) of 0•015, a design effect ($DEFF$) of 1•0, a population size of 24,000 (estimated primary school aged children in rural Upolo) corresponding to a finite population correction factor of 0•96733, and does not include non-response inflation. Neighbouring schools sampled on the same day were viewed as closely linked and were grouped accordingly.

### 2.5. Statistical analyses

Epidemiological data were recorded in an electronic database (REDCap) [58] and analysed using R (version 3•6•1). The prevalence of impetigo, active impetigo and scabies for the study and for sub-groups within the study were calculated using the R packages epitools (v0•5-10) and epiR (v0•9-99), with 95% confidence intervals generated using the 'prop.test' function. Multivariate logistic regression was performed to calculate adjusted odds ratios for various exposures and outcomes using a mixed-effects model with lme4 (v1•1-23). The observation of impetigo, active impetigo, or scabies were independently treated as outcomes. The following a priori specified variables were included in each model as fixed-effects: age, gender, household occupancy. To account for the clustered sampling, school was included in each model as a random-effect to allow for baseline differences in outcome prevalence as a result of attending a given school.

### 2.6. Ethics and permissions

School principals were sent a letter of invitation from Ministry of Education Sports and Culture (MESC) and were visited by their local member of parliament and one of the study investigators to explain the study. Information sheets and consent forms were given to each child's parent or caregiver, and written consent for their child's participation was obtained. All children attending school on the day of data collection whose parents/caregivers had consented, were eligible for inclusion in the study.

Ethics approval was gained from the University of Otago Human Ethics Committee (Health) H17/098, the National University of Samoa Research and Ethics Committee and the Samoan Ministry of Health, Health Research Committee. Approval for the study was

**Table 1**
Characteristics of children participating in the study. Abbreviations: IQR, interquartile range.

| Characteristic | Number (fraction; % of total) |
|---|---|
| **Gender** | |
| Male | 428 (428/825; 51•9%) |
| Female | 397 (397/825; 48•1%) |
| No data | 8 (8/833; 1•0%) |
| **Grouped age** | |
| 4–7 years | 265 (265/833; 31•8%) |
| 8–11 years | 423 (423/833; 50•8%) |
| 12–15 years | 145 (145/833;17•4%) |
| **School** | |
| Schools A and B | 149 (149/833; 17•9%) |
| Schools C and D | 177 (177/833; 21•2%) |
| School E | 138 (138/833; 16•6%) |
| School F | 118 (118/833; 14•2%) |
| Schools G and H | 251 (251/833; 30•1%) |
| **Scabies observed** | |
| All participants | 120 (120/833; 14•4%) |
| Males | 61 (61/428; 14•3%) |
| Females | 59 (59/397; 14•9%) |
| **Impetigo observed*** | |
| All participants | 476 (476/833; 57•1%) |
| Males | 279 (279/428; 65•2%) |
| Females | 193 (193/397; 48•6%) |
| **Active impetigo observed** | |
| All participants | 263 (263/833; 31•6%) |
| Males | 162 (162/428; 37•9%) |
| Females | 99 (99/397; 24•9%) |
| **Inactive impetigo observed** | |
| All participants | 437 (437/833; 52•5%) |
| Males | 252 (252/428; 58•9%) |
| Females | 181 (181/397; 45•6%) |
| **Median age, and IQR** | |
| All participants | 9 years (7–11 years) |
| Males | 9 years (7–11) |
| Females | 9 years (7–11) |
| **Household size, and IQR** | |
| All participants | 8 people (6–10) |
| Males | 7 people (6–10) |
| Females | 8 people (6–10) |
| **Active impetigo severity, of those children affected by impetigo** | |
| Mean of active lesions observed | 1 site |
| Range of active lesions observed | 0–43 sites |
| IQR of active lesions observed | 0–3 sites |
| **Inactive impetigo severity, of those children affected by impetigo** | |
| Mean of inactive lesions observed | 2 sites |
| Range of inactive lesions observed | 0–56 sites |
| IQR of inactive lesions observed | 1–6 sites |

*Impetigo observed is inclusive of active and inactive impetigo visible on exposed parts of skin (arms, legs, face and neck)

granted by MESC, Ministry of Health, and the National Health Services, Samoa.

### 2.7. Role of the Funding Source

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## 3. Results

### 3.1. Characteristics of the study population and prevalence of impetigo and scabies

In total, data and samples were collected for 833 children (428 males, 397 females and 8 not specified) from eight primary schools (Schools A-F), representing 88% (833/948) of children enrolled at these schools. The median age of participants was nine years (range 4 to 15 years), and the median household size was 8 (range 1 to 30 occupants); children frequently reported sharing a bedroom (590/833; 70•8%) and sharing bedmats (681/833; 81•8%), although these variables were not included in our model as discussed below (Table 1).

Overall, the prevalence of impetigo was 57•1% (476/833; 95% confidence interval (CI) [53•8–60•5]), and the prevalence of scabies was 14•4% (120/833; 95% CI [12•1–17•0]) (Table 1). Active impetigo lesions were observed for 31•6% of participants (263/833; 95% CI [28•5–34•8]), inactive impetigo lesions observed in 52•5% of participants (437/833; 95% CI [49•1–55•8]), and 25•6% of participants presented with both active and inactive impetigo lesions (213/833; 95% CI [22•7–28•6]) (Supplementary Data). Within these categories, a range of severities were noted, with some children having >40 active impetigo lesions (range 1 to 43), and others having >50 inactive impetigo lesions (range 1 to 56) (Supplementary Data).

The prevalence of active impetigo was significantly higher in males than females (37•9% compared to 24•9%, aOR 1•8, 95% CI [1•3–2•5]), and was higher in younger children between the ages of four and seven years, compared to those aged twelve to fifteen years (42•3% compared to 20•7%, aOR 2•8, 95% CI [1•8–4•7]) (Table 2). Further, the prevalence of active impetigo varied between schools – the highest prevalence being 45•8% (95% CI 36•6–55•2),

**Table 2**
Prevalence of active impetigo by gender, age, school district and other characteristics.

| Characteristic | Sample (N) | Active Impetigo Observed (n) | Prevalence (95% CI) | OR (95% CI) | Adjusted OR (95% CI) | *p*-value (likelihood ratio test) |
|---|---|---|---|---|---|---|
| **Total** | **833** | **263** | **31•6% (28•4-34•9%)** | - | - | - |
| **Gender** | | | | | | < 0•001 |
| Male | 428 | 162 | 37•9% (33•3-42•7%) | 1•8 (1•36-2•48) | 1•8 (1•33-2•49) | |
| Female | 397 | 99 | 24•9% (20•8-29•6%) | 1•0 | 1•0 | |
| **Grouped Age** | | | | | | < 0•001 |
| 4–7 years | 265 | 112 | 42•3% (36•3-48•5%) | 2•8 (1•77-4•55) | 2•8 (1•76-4•72) | |
| 8–11 years | 423 | 121 | 28•6% (24•4-33•2%) | 1•5 (0•99-2•45) | 1•5 (0•94-2•40) | |
| 12–15 years | 145 | 30 | 20•7% (14•6-28•4%) | 1•0 | 1•0 | |
| **Schools** | | | | | | - |
| Schools A and B | 149 | 55 | 36•9% (29•3-45•2%) | 1•5 (0•98-2•33) | - | |
| Schools C and D | 177 | 49 | 27•7% (21•4-35•0%) | 1•0 (0•64-1•52) | - | |
| School E | 138 | 35 | 25•4% (18•5-33•6%) | 0•9 (0•54-1•40) | - | |
| School F | 118 | 54 | 45•8% (36•6-55•2%) | 2•2 (1•38-3•44) | - | |
| School G and H | 251 | 70 | 27•9% (22•5-33•9%) | 1•0 | - | |
| **Household Size** | | | | | | 0•293 |
| 1–4 people | 88 | 30 | 34•1% (24•5-45•1%) | 1•0 | 1•0 | |
| 5–8 people | 448 | 134 | 29•9% (25•8-34•4%) | 0•8 (0•51-1•35) | 0•8 (0•50-1•38) | |
| 9–12 people | 232 | 78 | 33•6% (27•6-40•1%) | 1•0 (0•59-1•66) | 1•1 (0•66-1•99) | |
| 13–30 people | 65 | 21 | 32•3% (21•5-45•2%) | 0•9 (0•46-1•82) | 1•1 (0•55-2•35) | |
| **Scabies Observed** | | | | | | < 0•001 |
| Observed | 120 | 54 | 45•0% (36•0-54•3%) | 2•0 (1•33-2•92) | 2•1 (1•35-3•13) | |
| Not observed | 713 | 209 | 29•3% (26•0-32•8%) | 1•0 | 1•0 | |

Abbreviations: IQR, interquartile range. Logistic regression was performed with the following *a priori* specified variables in a multivariate model: gender, age, school, household occupants, and scabies status to calculate adjusted odds ratios.

**Table 3**
Prevalence of all impetigo (active and inactive) by gender, age, school district and other characteristics.

| Characteristic | Sample (N) | Impetigo Observed (n) | Prevalence (95% CI) | OR (95% CI) | Adjusted OR (95% CI) | *p*-value (likelihood ratio test) |
|---|---|---|---|---|---|---|
| **Total** | **833** | **476** | **57•1% (53•8-60•5%)** | - | - | - |
| **Gender** | | | | | | < 0•001 |
| Male | 428 | 279 | 65•2% (60•6-69•5%) | 2•0 (1•50-2•62) | 2•0 (1•49-2•68) | |
| Female | 397 | 193 | 48•6% (43•7-53•5%) | 1•0 | 1•0 | |
| **Grouped Age** | | | | | | < 0•001 |
| 4–7 years | 265 | 178 | 67•2% (61•3-72•5%) | 3•6 (2•33-5•46) | 3•6 (2•33-5•67) | |
| 8–11 years | 423 | 245 | 57•9% (53•2-62•5%) | 2•4 (1•62-3•45) | 2•4 (1•59-3•55) | |
| 12–15 years | 145 | 53 | 36•6% (29•2-44•6%) | 1•0 | 1•0 | |
| **Schools** | | | | | | - |
| Schools A and B | 149 | 88 | 59•1% (51•0-66•6%) | 1•4 (0•95-2•16) | - | |
| Schools C and D | 177 | 104 | 58•8% (51•4-65•7%) | 1•4 (0•96-2•09) | - | |
| School E | 138 | 70 | 50•7% (42•5-58•9%) | 1•0 (0•67-1•55) | - | |
| School F | 118 | 88 | 74•6% (66•0-81•2%) | 2•9 (1•81-4•77) | - | |
| School G and H | 251 | 126 | 50•2% (44•1-56•3%) | 1•0 | - | |
| **Household Size** | | | | | | 0•257 |
| 1–4 people | 88 | 52 | 59•1% (48•6-68•8%) | 1•0 | 1•0 | |
| 5–8 people | 448 | 250 | 55•8% (51•2-60•3%) | 0•9 (0•55-1•39) | 0•8 (0•52-1•37) | |
| 9–12 people | 232 | 134 | 57•8% (51•3-63•9%) | 1•0 (0•57-1•55) | 1•1 (0•62-1•80) | |
| 13–30 people | 65 | 40 | 61•5% (49•4-72•4%) | 1•1 (0•58-2•15) | 1•4 (0•69-2•82) | |
| **Scabies Observed** | | | | | | 0•294 |
| Observed | 120 | 74 | 61•7% (52•7-69•9%) | 1•2 (0•84-1•86) | 1•3 (0•82-1•92) | |
| Not observed | 713 | 402 | 56•4% (52•7-60•0%) | 1•0 | 1•0 | |

Abbreviations: IQR, interquartile range. Logistic regression was performed with the following *a priori* specified variables in a multivariate model: gender, age, school, household occupants, and scabies status to calculate adjusted odds ratios.

and the lowest prevalence 25•4% (95% CI 18•5–33•2)(Table 2). These trends held when considering active and inactive impetigo collectively; being observed more commonly in males relative to females (aOR 2•0, 95% CI [1•5–2•7]), more commonly observed in younger children (aOR 3•6, 95% CI [2•3–5•7]), and having a varied prevalence across schools (Table 3).

The prevalence of scabies did not differ significantly between males and females, or between different age groups, although prevalence varied greatly between schools (Table 4). A statistically significant association between scabies and active impetigo was observed (aOR 2•1, 95% CI [1•4–3•1]), although this association is less pronounced when the two classes of impetigo (active and inactive) are considered together (aOR 1•3, 95% CI [0•8–1•9]) (Table 2, Table 4).

### 3.2. Microbiological findings and cluster analysis

In total, *S. pyogenes* was isolated from 65 schoolchildren (7•8%), including 16 oropharyngeal isolates (1•9%), and 50 skin isolates (6•0%), however only 52 of these isolates were viable following shipping, and included in subsequent genomic analyses (Supplementary Data). *S. aureus* was isolated from 288 schoolchildren (34•6%), with 147 oropharyngeal isolates and 202 skin isolates (Supplementary Data). A related species, *Staphylococcus argenteus*, was isolated from four schoolchildren (0•5%). There were 22 examples of co-infection at skin sites between *S. pyogenes* and *S. aureus* in this study.

In total, 349 *S. aureus* isolates and 52 *S. pyogenes* isolates had whole-genome sequence data generated, allowing inference of phylogenetic relatedness and relevant microbial characteristics.

**Table 4**
Prevalence of scabies by gender, age, school district and other characteristics.

| Characteristic | Sample (N) | Scabies Observed (n) | Prevalence (95% CI) | OR (95% CI) | Adjusted OR (95% CI) | *p*-value (likelihood ratio test) |
|---|---|---|---|---|---|---|
| **Total** | **833** | **120** | **14•4% (12•2-17•0%)** | - | - | - |
| **Gender** | | | | | | 0•501 |
| Male | 428 | 61 | 14•3% (11•3-17•9%) | 1•0 (0•65-1•40) | 1•0 (0•65-1•48) | |
| Female | 397 | 59 | 14•9% (11•7-18•7%) | 1•0 | 1•0 | |
| **Grouped Age** | | | | | | 0•700 |
| 4–7 years | 265 | 38 | 14•3% (10•6-19•1%) | 1•1 (0•62-2•04) | 1•2 (0•66-2•34) | |
| 8–11 years | 423 | 63 | 14•9% (11•8-18•6%) | 1•2 (0•68-2•06) | 1•3 (0•72-2•28) | |
| 12–15 years | 145 | 19 | 13•1% (8•6-19•6%) | 1•0 | 1•0 | |
| **Schools** | | | | | | - |
| Schools A and B | 149 | 45 | 30•2% (23•4-38•0%) | 6•0 (2•81-14•17) | - | |
| Schools C and D | 177 | 13 | 7•3% (4•3-12•2%) | 1•1 (0•44-2•83) | - | |
| School E | 138 | 29 | 21•0% (15•0-28•6%) | 3•7 (1•67-8•91) | - | |
| School F | 118 | 8 | 6•8% (3•5-12•8%) | 1•0 | - | |
| School G and H | 251 | 25 | 10•0% (6•8-14•3%) | 1•5 (0•69-3•70) | - | |
| **Household Size** | | | | | | 0•272 |
| 1–4 people | 88 | 14 | 15•9% (9•7-25•0%) | 1•0 | 1•0 | |
| 5–8 people | 448 | 58 | 12•9% (10•2-16•4%) | 0•8 (0•43-1•53) | 0•9 (0•45-1•65) | |
| 9–12 people | 232 | 34 | 14•7% (10•7-19•8%) | 0•9 (0•47-1•84) | 1•0 (0•50-2•04) | |
| 13–30 people | 65 | 14 | 21•5 (13•3-33•0%) | 1•5 (0•63-3•33) | 1•8 (0•74-4.22) | |

Abbreviations: IQR, interquartile range. Logistic regression was performed with the following *a priori* specified variables in a multivariate model: gender, age, school, household occupants, and impetigo status to calculate adjusted odds ratios.

(Supplementary Data). Overall, 26 *S. aureus* MLSTs were identified, with the three most commonly observed STs being ST15 (14•3%), ST779 (8•9%) and ST1 (7•4%) (Supplementary Fig. 1). Samoa has not established national antibiograms for *S. aureus*, relying on those from Australia and New Zealand, although in this study the methicillin-resistance conferring gene *mecA* was identified in 24/349 (6•8%) *S. aureus* isolates, across 7 different sequence types (ST1, ST5, ST8, ST59, ST93, ST97 and ST840, Supplementary Data, Supplementary Figure 1). Other resistance determinants included *ermC* (9/349 of *S. aureus* isolates; 2•6% prevalence), and *dfrG* (8/349 of *S. aureus* isolates; 2•3% prevalence), which are associated with erythromycin and trimethoprim resistance, respectively. A total of 22 *S. pyogenes emm* types were observed, belonging to seven *emm* clusters as determined using *emmtyper* following a previously described scheme (Supplementary Data, Supplementary Fig. 2) [59]. The most commonly observed *emm* types were *emm*101 (7/52; 13•5%), *emm*100 (5/52; 9•6%) and *emm*225 (5/52; 9•6%), and the most commonly observed cluster types were D4 (20/52; 38•5%), E3 (10/52; 19•2%) and E6 (7/52; 13•5%).

Phylogenetic relatedness was further assessed using hierarchical single linkage clustering. To define putative clusters of *S. aureus*, a maximum intra-patient pairwise SNP threshold was chosen — an approach previously applied to *S. aureus* transmission [60]. Of the twenty children for whom intra-host diversity could be assessed (i.e. having *S. aureus* isolates available from different anatomical sites), the median pairwise SNP distance between isolates within a child was 2 SNPs, on a sequence-type specific analysis. The lower bound for intra-host diversity was 0 SNPs, and upper bound was 10 SNPs, the latter chosen as an empirically-defined upper pairwise threshold for clustering.

A total of 36 clusters (defined as two or more children) were detected through ST-specific core genome alignments and a 10 SNP threshold (Fig. 2, Supplementary Data and Supplementary Fig. 3), representing 107/253 (42%) of included *S. aureus* isolates. The median cluster size was 3 children, ranging in size from two to nine children. Of the 36 clusters, 29 (81%) were specific to only one school, and seven clusters (19%) were identified between schools.

## 4. Discussion

In this study, we demonstrate a significant burden of superficial skin infections amongst children in Samoa. The prevalence of impetigo in children in this setting (57•1%; 476/833) is one of the highest reported globally, and approximately one third of children had active impetigo in this study (31•6%; 263/833). [2, 39-49] A range of clinical severities were observed, with 20 children presenting with ten or more independent active impetigo lesions. Other settings with a similarly high prevalence of impetigo include the Solomon Islands [44] and the Northern Territory of Australia [61,62] (52% and 47–70%, respectively). This study further supports the view that resident Pacific Island and Indigenous children remain one of the most at-risk populations globally for skin and soft tissue infections that may lead to serious complications [2,4].

Previous studies have supported the hypothesis that scabies is an important risk factor for impetigo, however in this study, scabies prevalence was far lower than that of active impetigo (14•4% and 31•6%, respectively). [17-20] Of note, the prevalence of scabies in this study (14•4%, 95% CI [12•1–17•0%]), was higher than that described in a previous study of Samoan schoolchildren conducted in 1999, where the prevalence was estimated at 4•9% (95% CI [3•0–7•0]) [50]. This discrepancy may be partly explained by the widespread use of ivermectin to eradicate filariasis in Samoa at the time of the first study [50]. Moreover, it has been suggested that seasonal variation in scabies prevalence may be linked to lower temperatures and higher relative humidity [63]. The scabies prevalence described in this study, conducted during the local rainy season, could be elevated compared to other times of the year as a result. Further, secondary bacterial infection of scabies was relatively uncommon in this and an earlier study of Samoan schoolchildren [50], suggesting that other factors may be driving impetigo in this setting.

In this study, males were more likely than females to present with active impetigo (aOR 1•8, 95% CI [1•3–2•5]), and children in the youngest age group of four to seven years more likely to present with active impetigo than older children (aOR 2•8, 95% CI [1•8–4.7]). These gender and age associations are well-described in other settings [2,45]. Household size and sharing of bedding have also been reported as drivers of skin infections in other settings, and likely contribute to these infections in Samoa [64]. However, these factors were not included as variables in our model as, following discussions with members of the local community, the majority of children were thought to share a communal sleeping space and communal bedding with other household members, which may not have been recognised as 'sharing a bedroom'.

Previous studies have demonstrated *S. aureus* transmission in community settings in high-income countries, particularly within

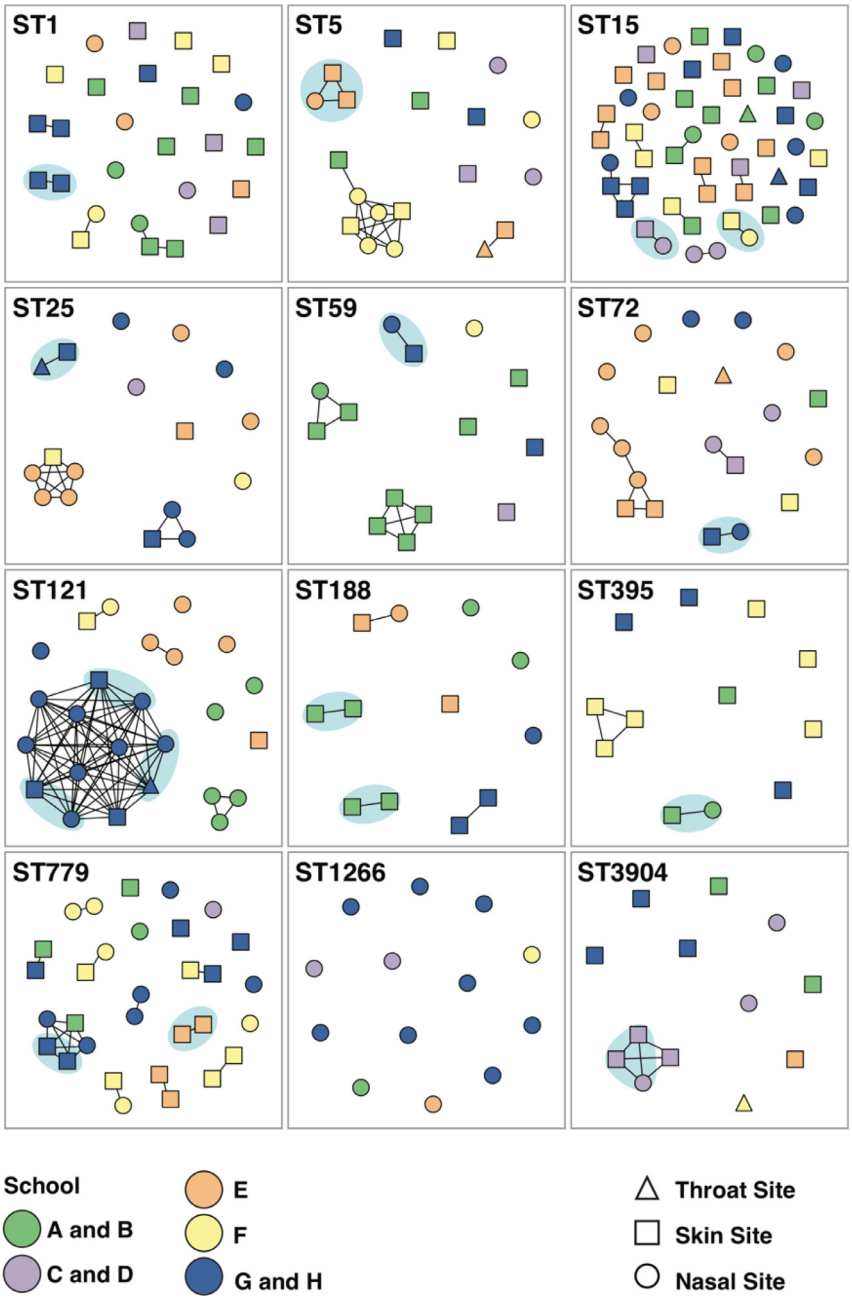



**Fig. 2.** Network plot of *Staphylococcus aureus* isolates belonging to common sequence types in rural Samoa. *S. aureus* isolates (nodes) belonging to one of the twelve most common sequence types have been included in sequence type-specific phylogenetic and clustering analyses each displayed as subpanels. Isolates considered to be shared or putatively transmitted based on being equal to or below a 10 SNP threshold for core genome genetic distance are shown as nodes connected with a line, while those above this threshold are not directly connected with a line. Nodes are colored by the corresponding school in which the isolate was collected, and shaped according to the anatomical site of collection.

households [60,65]. However, to date there has been little assessment of potential *S. aureus* transmission in low-income countries, particularly in the Pacific region. These data demonstrate that approximately 42% of *S. aureus* included in ST-specific analyses are part of putative transmission clusters, and also highlight that public health measures to disrupt ongoing transmission may have potential utility if introduced in schools. These transmission networks identified at the school level may in part represent transmission at the household level, as siblings typically attend the same school, and siblings were not identifiable due to the nature of the study. The predominant sequence types of *S. aureus* observed in this study, namely ST1 and ST121, are known to circulate in the Southwest Pacific, and have been previously identified in Samoa [66]. Similarly, for *S. pyogenes*, common *emm* types (*emm*101 and *emm*100) and *emm* cluster types (D4, E6) observed in this study have been isolated from skin and soft tissue infections in other South Pacific nations, such as New Zealand and Australia [67,68].

Of note, detection of pharyngeal and skin *S. pyogenes* was low in the pharynx (1•9% of children) and skin (6.0% of children), although pharyngeal carriage was comparable to an earlier study of Samoan schoolchildren in which pharyngeal *S. pyogenes* was detected in 2•4% of schoolchildren [50]. Rheumatic heart disease remains a major cause of morbidity and mortality in Samoa, with possible mechanistic links between *S. pyogenes* skin infection and acute rheumatic fever and subsequent rheumatic heart disease [69,70]. Other populations with high rates of acute rheumatic fever have

also reported an unexpected low prevalence of pharyngeal *S. pyogenes* [50].

Although safe and efficacious treatments are available for these common skin infections, prioritisation and introduction of relevant control measures are still needed in many settings where the disease burden is highest [5–15]. For Samoa, our findings suggest a need for several public health measures. These include improved health literacy related to skin infections like scabies and impetigo, including hygiene measures such as washing hands and covering open sores, and placing an emphasis on the need to air and sun bedding. These measures may find greater traction and acceptability following similar messaging for COVID-19. There appears to be an acceptance of these conditions as 'normal' in Samoa, with 224 children self-reporting no impetigo despite having one or more impetigo lesions on observation. Steer *et al.* similarly commented that in Fiji impetigo and scabies may be viewed as 'benign nuisance diseases' belying their personal health, societal, and health system cost [40]. In addition, enhanced community screening may be of benefit for impetigo and scabies, with treatment of cases and contacts where appropriate. This could be integrated into community programmes such as *komiti tumama*, with local women's associations promoting and leading basic public health measures within village communities [71]. More broadly, preventative strategies aimed at alleviating the socio-economic factors which have contributed to the high rates of skin disease in these communities will be of benefit. These include increasing access to first aid supplies such as plasters and dressings to lower the risk of infection, as well as medical care more broadly through initiatives to lower financial barriers to care [72]. Some highlighted socio-economic factors are connected to cultural beliefs and practices, such as communal living and shared bedding, and discussing these potentially sensitive issues as part of programmes such as *komiti tumama* may help develop community-led and grassroots preventative strategies that are culturally appropriate to address these issue.

There are several limitations in this study. First, a subset of the participant data were self-reported including age and household size, by children as young as four years. Second, the observation of scabies was made clinically, without the support of confirmatory microscopy or molecular tests, as these were not practical in the study setting. Scabies may have been under-diagnosed, as only exposed sites were examined in the study, and due to the lower sensitivity in classifying non-infected scabies inherent in the ICMI algorithm applied [56]. Thirdly, the survey included children attending school on the southern coast of Upolu, Samoa, and therefore may not be representative of the broader Samoan community. The microbiological culture in the study likely represents a limited view of the microbial diversity present at the given body sites in the study population, with local isolation, transport and storage practices likely affecting these results. Further, the transmission analyses have inherent limitations relevant to the study, including an inability to infer the direction of transmission, and are based on a subset of collected *S. aureus* isolates which are unlikely to capture the genetic diversity carried by the study population completely. Additionally, given the clustered sampling of the study with transmissible diseases as outcomes, it is likely that the intracluster correlation coefficient (ICC) is greater than zero; an ICC value of 0•001 would correspond to design effects of 1•1 as an example, although an ICC was not included in our original sample size calculation. Despite these limitations, this study provides a contemporary estimate of the burden of superficial skin infections in Samoa, and highlights areas for public health intervention guided by these findings.

In summary, this study describes a considerable burden of impetigo and scabies observed in Samoan schoolchildren. The introduction of community-led control strategies for these conditions in Samoa may be guided by these findings. Importantly, a mass drug administration programme with a triple therapy including ivermectin aimed at the treatment of lymphatic filariasis has been implemented in Samoa following this survey, further highlighting the intersection of public health initiatives in this setting. Ongoing surveillance and management of impetigo and scabies in Samoa is recommended, supporting continued improvements to public health in this setting.

## Contributors

George Taiaroa, Ben Matalavea, Malama Tafunai, Lupeoletalalelei Isaia, Hinauri Leaupepe, Satupaitea Viali, Deborah A. Williamson and Susan Jack conceived and designed the study.

Deborah A. Williamson and Susan Jack supervised the study. George Taiaroa, Jake A. Lacey, and Claire L. Gorrie performed and interpreted genomic analyses. George Taiaroa, David J. Price and Susan Jack performed and interpreted the statistical analyses. All authors were involved in data acquisition and analysis. George Taiaroa, Claire L. Gorrie, Deborah A. Williamson and Susan Jack prepared the manuscript and figures, with contributions from all authors.

## Declaration of Competing Interest

The authors have no known conflicts of interest to declare.

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## Data Availability

Data generated in the study are available on request.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2020.100081.

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