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Glossary

ADHB	Auckland District Health Board
BMI	Body Mass Index
CAU	Census Area Unit
CED	Children's Emergency Department
CI	Confidence Interval
cms	Centimetres
CMS	Clinical Management Systems
CRIS	Clinical Record Information System
CSC	Community Services Card
DHB	District Health Board
DOM	Domicile code
Dr	Doctor
DRG	Diagnostic Related Group
ED	Emergency Department
ESOL	English Speaking Other Language
FBC	Full Blood Count
GP	General Practitioner
HRC	Health Research Council
ICD	International Classification of Diseases, Clinical Modification
ISAAC	International Study of Asthma and Allergies in Childhood
MRSA	Methicillin Resistant *Staphylococcus Aureus*
MSSA	Methicillin Susceptible *Staphylococcus Aureus*
NHI	National Health Index
NZ	New Zealand
NZDep	New Zealand Deprivation Index
OR	Odds Ratio

RR	Relative Risk
SA	*Staphylococcal aureus*
SD	Standard Deviation
SES	Socioeconomic status
SPSS	Statistical Package for the Social Sciences
SSH	Starship Children's Hospital
SSTI	Skin and Soft Tissue Infection
USA	United States of America
vs.	Versus
WDHB	Waitemata District Health Board

Chapter 1: Introduction

"Criton, in Thasus, while still on foot, and going about, was seized with a violent pain in the great toe; he took to bed the same day, had rigors and nausea, recovered his heat slightly, at night was delirious. On the second, swelling of the whole foot, and about the ankle erythema, with distension and small bullae (phlyctaenae); acute fever; he became furiously deranged; alvine discharges bilious, unmixed, and rather frequent. He died on the second day from the commencement" *Hippocrates*[1]

Skin and soft-tissue infections (SSTIs) were described several thousand years ago in ancient Chinese, Egyptian, and Greek writings.[1] Whilst the above story of a man affected by cellulitis from Hippocrates is dramatic and rarely seen in modern times, cellulitis remains a significant public health issue in the 20th and 21st centuries.

Cellulitis is a diffuse inflammation of the skin or connective tissue most commonly due to infection with *Staphylococcus aureus* or *Streptococcus pyogenes*. It produces a red, warm and tender area of skin (Figure 1). There may be associated fever, chills and sweats, regional lymph node involvement and proximal red streaking (lymphangitis). Exposed surfaces, particularly legs, are usually most involved, though the distribution may vary by age.[2-4] It may lead to ulceration and abscess and if untreated can lead to complications including death. Medical treatment includes antibiotics and general advice regarding wound care. Whilst most affected individuals can be treated in the community, a proportion develops more serious skin infection which requires hospitalisation for intravenous antibiotics plus or minus surgical drainage.

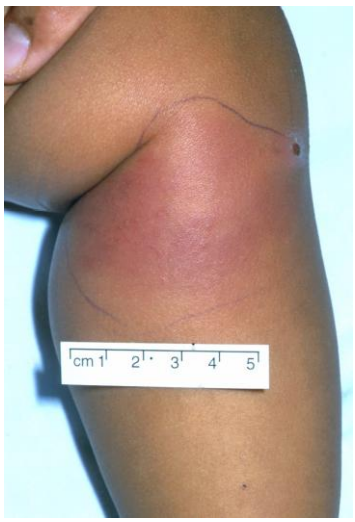

Figure 1: Cellulitis on the leg

Cellulitis occurs across all age groups; however, as a Community Paediatrician interested in the health and wellbeing of children, I have focussed my thesis on cellulitis, or serious skin sepsis, among children.

My thesis describes a journey over ten years: from initial awareness of there being a problem with serious skin sepsis among Auckland children, through a process of exploration and research to reach our current position of increased knowledge. Since many unanswered questions remain, the journey continues.

1.1 Research Journey

Serious skin sepsis was first identified as an issue for Auckland children in 1998 by Donna Neal, Clinical Information Manager, at Starship Children's Hospital.[5] Her 1998 report pulled together data from several different services in Starship Children's Hospital and identified cellulitis as a major cause for admission. It documented a 65% increase in paediatric cellulitis discharges per annum between 1995 and 1998 and identified most children were of Pacific or Māori ethnicity.[5] As a newly employed Community Paediatrician at Starship Hospital, with a recent Masters in Public Health, I was interested in learning more. Why was cellulitis, a supposedly preventable hospitalisation, one of the top three reasons for admission to our children's hospital? And what was it about our children, their environment, and their healthcare that meant it was such a problem in Auckland, when it didn't rank amongst the top 20 reasons for admission to any other children's hospital in Australasia?

What followed was a series of investigations and projects as outlined below:

1.1.1 Epidemiological Investigation

After reading Donna's report, my first step was to examine the available local and international data. This confirmed cellulitis among children had not previously been recognised as a child health problem, either nationally or internationally. Not only was it a common problem in Auckland, but it had significant resource implications with over a million dollars having been spent on cellulitis hospitalisations at Starship Hospital in 1999.[6]

Following identification that this was a child health issue, Grant Close, the General Manager of Starship Children's Hospital, asked the Public Health Protection Unit to comment on the apparent increase in cellulitis cases, determine whether it was a real increase, and recommend next steps. This lead to a more in depth analysis of discharge data undertaken by Carlene Lawes, a public health medicine registrar[7] and confirmed paediatric cellulitis had become a significant public health issue. Cellulitis was the third most common reason for admission to Starship Children's Hospital, and hospital admissions had doubled in the 5 year period between 1994 and 1998.[7] Half

of those children required surgery and more than 40% stayed in hospital for over 2 days. There was a significant ethnic disparity in disease burden with Pacific children 3-4.5 times more likely and Māori children 2-3 times more likely than European children to be admitted to hospital with cellulitis.[7] Children under 5 years of age had hospitalisation rates twice that of the older paediatric age groups. The increase was real and was not artefactual due to changes in coding, admission criteria or population demographics. There was no clear evidence that a change in causative organism was responsible for the increase in cellulitis cases, and it was postulated that the increase was due to a combination of host and environmental factors, and lack of access to primary health care. Carlene concluded further epidemiological research should be undertaken to better define the risk factors (particularly those that are modifiable) for cellulitis, and the risk factors for hospitalisation with cellulitis.

1.1.2 Review of Risk Factor Literature

Whilst skin infections are common in children,[8-10] there was little available information about the risk factors for cellulitis. A literature search undertaken in 1999, revealed only 30 papers on the epidemiology of paediatric cellulitis published since 1966. Of these, most were articles describing case series of children. The study populations were predominately children who were hospitalised, immunocompromised, or those infected with a specific organism.[8,9,11-19] There was little information on populations of children and no information on risk factors for developing cellulitis or hospitalisation with cellulitis. There were also no other reports suggesting a recent increase in the prevalence of the condition or hospitalisation in New Zealand or other countries. At the time, there had been one case-control study among adults looking at the risk factors for hospitalisation with cellulitis.[20] This identified the major role of local risk factors; mainly lymphoedema and disruption of the skin barrier.

1.1.3 Initial Steps

Armed with the information that cellulitis was an issue for our children, and that little was known about risk factors and management, I established a research group to learn more about cellulitis and how we could reduce the impact it was having on our children. We initially gathered more information by organising a community meeting and undertaking a primary care survey. We then developed best practice guidelines for both primary care and public health nurses in schools.

1.1.3.1 Community Meeting

The community meeting (hui) was held in a local hall to explore what the community knew and thought about skin problems in children. Attendees included representatives from the University of Auckland, local primary care organisations, public health nurses, Public Health Protection Unit,

Starship Children's Hospital and members of the local community. Whilst many people had had some experience with skin infections in their children and family, or in their professional roles, most were unaware of the significance of more serious skin sepsis and that it was such as issue for the community. All wanted to learn more.

1.1.3.2 Primary Care Survey

As most skin sepsis and early cellulitis is managed in primary care, we undertook a postal survey of General Practitioners (GPs) in west Auckland. The specific aims were to establish the current management of cellulitis and skin infections in primary care, gather information about GPs beliefs about common predisposing factors, and determine primary care strategies for preventing cellulitis. This project confirmed skin sepsis was a common reason for presentation to primary care with more than 35% of GPs reporting seeing more than 5 children per week with skin sepsis.[21] Almost 10% of GPs were seeing 10-15 affected children per week. Common predisposing factors included insect bites, superficial injury, eczema and scabies. Basic hygiene measures, topical antibiotics and oral antibiotics were the mainstay of primary care management. Sound basic hygiene and early detection and presentation to nurses and/or medical practitioners were key measures in the primary care prevention of skin and soft tissue infections.

1.1.3.3 Best Practice Guidelines

Information from the Primary Care survey in conjunction with a literature review was used to develop best practice guidelines on the management of cellulitis in primary care. This was published in Public Health Advice in October 1999 in combination with a summary of the information from the A+ report.[22] I was also involved in the development of a regional best practice guideline for the management of skin infections in schools. This included a clinical pathway for Public Health Nurses, information for schools, parent information leaflets, and an educational programme for children about skin infections.[23]

1.1.4 Risk Factor Research

We now had a clearly identified need from local data, the literature, the community, and health professionals to learn more about the risk factors for paediatric cellulitis. The next step in our risk factor research was to undertake a prospective case series of children admitted to Starship Children's Hospital with cellulitis. This exploratory study ran from July-October 1999, and generated hypotheses and piloted questions for the subsequent case-control study. We explored the risk factors further via a Health Research Council funded case-control study which ran from June 2001-May 2002. This thesis outlines the design, conduct and findings from both of these cellulitis research studies.

1.2 Research Group

The investigators involved in the design and conduct of the cellulitis risk factor research were Dr Alison Leversha[i] (candidate and lead investigator), Professor Edwin Mitchell[ii], Alistair Stewart[iii], Dr George Aho[iv], and Dr David Holland[v]. Additional staff involved included: Joanne Rowe[vi], and Lynne Hutchison[vii] for the case series, and Natarsha Kruithof[viii] for the case-control study.

1.2.1 Role of Candidate

The candidate was the lead investigator for the primary care survey, the case series, and the case-control study. I was responsible for:

- Leading the cellulitis research group
- Writing the successful funding applications to Starship Foundation and Health Research Council of New Zealand and liaising with these agencies
- Assisting with the development of the study methodology
- Developing and piloting the data collection instruments
- Assisting the study coordinators with the development of the study manual
- Obtaining ethics committee and hospital research board approval for both studies
- Training research coordinators and interviewers
- Supervising research staff
- Undertaking the analyses in this thesis with advice and guidance from Alistair Stewart and Ed Mitchell
- Providing input into subsequent cellulitis clinical pathways and research projects.

[i] Community Paediatrician, Starship Children's Health, and Honorary Senior Lecturer, Department of Paediatrics, University of Auckland
[ii] Professor of Child Health Research, Department of Paediatrics, University of Auckland
[iii] Biostatistician, School of Population Health, University of Auckland
[iv] Medical Officer, Starship Emergency Department, and General Practitioner, Pasifika Fono
[v] Microbiologist, Auckland City Hospital, and Department of Microbiology, University of Auckland
[vi] Surgical Specialty Nurse, Surgical Services, Starship Children's Hospital
[vii] Researcher, Department of Paediatrics, University of Auckland
[viii] Researcher, Department of Paediatrics, University of Auckland

1.3 Funding

This cellulitis research was funded by the Starship Foundation ($22,700 for the case series) and the Health Research Council of New Zealand ($315,433 for the case-control study).

1.4 Thesis Organisation

In this first chapter, cellulitis is described and recognised as an important child health problem for the children of Auckland. I have described the research journey and established the rationale for this thesis.

Chapter 2 provides a focused review of the available literature on cellulitis: its prevalence and risk factors, and outlines the background information that informed the development of the two studies. For ease of reading all figures have been kept within body of the chapters in this volume and all tables are enclosed in the appendices in Volume 2.

Chapter 3 describes the case series and finishes with the hypotheses that arose both from the literature and from our local exploratory research.

Chapter 4 describes the methodology used in the case-control study with particular emphasis on how that may have affected the interpretation of the results.

Chapter 5 describes the characteristics of the study population and includes information about response rates and participation rates. It reports preliminary demographic data about the participants.

Chapter 6 presents the results of the case-control study outlining the risk factors for developing cellulitis. Univariate factors are reported initially, followed by multivariate analyses.

Chapter 7 describes the risk factors for hospitalisation once cellulitis has developed. Again univariate then multivariate factors are reported.

Chapter 8 synthesises the main outcomes of the cellulitis risk factor research. The discussion outlines the findings, compares our findings with the literature, discusses the strengths and weaknesses of the study design and how that may have influenced interpretation of the results, and outlines areas for both current and future work.

Chapter 2: Background

"*The associated or predisposing causes of skin disorders may be hereditary (though less commonly than supposed), or connected with age, sex, temperament, general health, dentition, race, climate, environment and occupation, habits and season"*

Virtues Household Physician 1924[24]

2.1 Introduction

This chapter provides a focused review of the available literature on cellulitis: its prevalence and risk factors, and the background information that informed the development of the cellulitis research studies.

2.2 Definitions

2.2.1 Clinical Definition

Skin and soft tissue infections are a heterogeneous group of conditions with a wide spectrum of clinical disease. The clinical manifestations range from an indolent furuncle (or boil) on the surface of the skin, to cellulitis affecting the superficial layers of the skin and subcutaneous tissue, to a rapidly progressive process affecting deeper layers, such as necrotizing fasciitis, gas gangrene, lymphangitis, or bacteraemia.[25]

Superficial skin infections are common and occur across all age groups. They include conditions such as impetigo, boils, and tinea infections, and comprise one of the most common childhood conditions. At the milder end of the spectrum of skin sepsis, these are often self-limiting or treated within the community.

Serious skin and soft tissue infections (SSTIs) extend more deeply into the soft tissues, require medical or surgical management, and are defined as serious as they require hospital admission. Traditionally serious SSTIs were thought to be accompanied by some element of systemic illness such as fever, tachycardia, or elevated white blood cell count; however, both adult and paediatric literature now suggests a significant proportion of SSTIs requiring hospitalisation lack the clinical features of particularly severe illness (e.g. need for intensive care, bacteraemia, cellulitis requiring surgical debridement or fascial biopsy, and necrotizing fasciitis).[26] Cellulitis and cutaneous abscess constitute the majority of serious skin and soft tissue infections.[27,28]

Cellulitis is an acute spreading infection of the skin, extending to involve the subcutaneous tissues. It is manifested clinically by rapidly spreading areas of swelling, redness, and heat, sometimes accompanied by lymphangitis and inflammation of the regional lymph nodes. Systemic

manifestations are usually mild, but fever, tachycardia, confusion, hypotension, and leucocytosis are sometimes present and may even occur hours before the skin abnormalities appear. Adult literature and that from Northern Europe refer to the term 'erysipelas' as another common form of diffuse, spreading skin and soft tissue infection.[25] The distinction between the terms erysipelas and cellulitis relates to the depth of inflammation: erysipelas affects the upper dermis, including the superficial lymphatics, whereas cellulitis involves the deeper dermis, as well as subcutaneous fat. In clinical practice, however, distinguishing between cellulitis and erysipelas clinically is problematic, and some physicians, especially in northern Europe, use the term 'erysipelas' to describe both infections.[29] In paediatric practice and the countries other than Europe, the term erysipelas is rarely used. In this thesis, the term cellulitis is used as a broad symptom complex describing a red, swollen, warm area of skin and soft tissue infection, and thus includes both cellulitis and erysipelas.

Cutaneous abscesses are collections of pus within the dermis and deeper skin tissues. They are usually painful, tender, and fluctuant red nodules, sometimes tipped by a pustule and usually surrounded by a rim of erythematous swelling.[29] Both cellulitis and cutaneous abscess present as a red, inflamed area of skin and differentiation between the two can be difficult especially in the early stages.

Deep invasive skin and soft tissue infections such as necrotizing fasciitis, myositis and gas gangrene, are associated with systemic toxicity, and have significant complications.[29] They are associated with different clinical conditions, and are rare among children, and are therefore not considered in this thesis.

2.2.2 Epidemiological Definition

The study of skin and soft tissue infections is hampered by a lack of uniform case definitions. Clinicians may group several clinical entities into the term cellulitis, including impetigo, erysipelas, wound infection, and even subcutaneous abscesses and diabetic foot infection. Although cellulitis is a recognisable clinical syndrome, no laboratory gold standard exists for the diagnosis of cellulitis, and confirmation of an infecting microorganism is uncommon.[30] Large epidemiological studies have largely based their findings on hospital international classification of disease (ICD) discharge codes. Different studies have used different definitions, some including abscess, impetigo, and infected wounds in their serious skin infection definition, whereas others have been more exclusive. The lack of a standard definition has meant comparison across different studies looking at incidence and risk factors is difficult. In some instances, the use of ICD coding has been overinclusive with only a proportion of those identified using ICD codes satisfying a clinical definition of cellulitis.[30]

In view of the lack of a consistent and valid case definition, a new epidemiological definition for serious skin infection in children has been developed by Cathryn O'Sullivan and Michael Baker.[28] In their recent analysis they noted the current practice definition using ICD subchapter codes was highly specific, but poorly sensitive in their local population. When comparing the traditional ICD definition to a newly developed extended epidemiological case definition, the traditional definition failed to detect 39% of clinically defined serious skin infection cases. Their suggested new epidemiological definition of serious skin infection is a child 0-14 years admitted to hospital with a principal or additional diagnosis of serious skin infection, with a diagnosis code either within the ICD skin infection subchapter or within the categories of skin infection of an atypical site or skin infection following primary skin disease or external trauma.[28] With the addition of skin infections of atypical anatomical sites, those secondary to either primary skin disease or trauma, and those recorded as additional diagnoses, the sensitivity of the case definition increased from 61.0% to 98.9% with little loss in specificity. Whilst it is useful to have a standard definition to measure the burden of skin sepsis in a hospital setting, it is important the information is presented in a disaggregated format to highlight different coding practices across different hospitals. This definition needs to be validated in other populations and District Health Boards (DHBs) as clinical recording and coding differences will affect the sensitivity and specificity of the definition.

2.3 Etiology

The most common causative agents of cellulitis are part of the skin microbial flora and are thus natural bacterial inhabitants. In healthy individuals the two most commonly isolated organisms in cellulitis are *Staphylococcus aureus* and group A *streptococcus.*[8,29,31-35] Methicillin-resistant *Staphylococcus aureus* (MRSA) has become the predominant *S. aureus* strain causing community-associated skin infections in many places in the world, particularly the United States of America (USA); however, this is not the case in New Zealand (NZ).[7,36-38] A variety of other organisms have been described, particularly in immunocompromised patients,[33,39-43] however, in many instances, pathogens are not able to be isolated.[9,25,35,44,45] Infection typically develops over days with the usual incubation of 4-10 days for staphylococcal, and 1-3 days for streptococcal infections. There is a strong association between cellulitis and foot dermatomycosis (fungal infection of the foot).[20,46-48] It is postulated the fungal infection causes a break in the skin and fosters bacterial overgrowth, thus, facilitating entry of bacteria with a resultant skin infection.[35] More detail about the different microbiological features follows in section 2.8.6.

2.4 Epidemiology

2.4.1 Local Paediatric Incidence

Each year more than 700 children are admitted to Starship Children's Hospital with cellulitis and the number continues to increase.[7,49] Cellulitis has increased from the 6th most common reason for admission in 1995 to the 3rd in 2000 and has remained in that position for the last 12 years. Starship Hospital admission rates for serious skin infection have increased from 2 per 1000 child population in 1990-91 to 4.4 per 1000 in 2006-07.[49] It is now at a level similar to the admission rate for childhood pneumonia, which has remained static during this time period.[49] Whilst there is good information on hospital admission rates for serious skin sepsis, there are no data re the incidence of cellulitis among the child population.

2.4.2 National Paediatric Incidence

Cellulitis is one of the top ambulatory sensitive admissions for children throughout New Zealand,[49] with admissions for cellulitis increasing both locally and nationally. Hospital admissions are defined as ambulatory sensitive if they are potentially preventable though early access to primary care interventions. Admission rates have more than doubled across NZ, with a more rapid increase between 1992 and 2001, and a slower increase since (Figure 2).

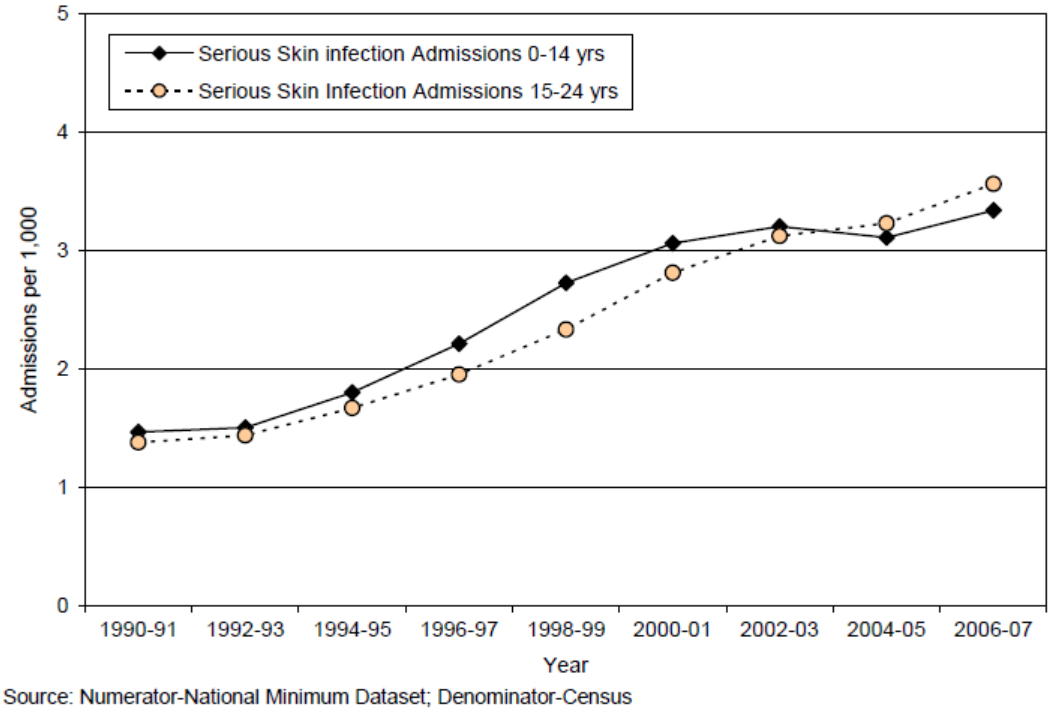

Figure 2: Hospital admissions for serious skin infections in children and young people 0-24 years, New Zealand 1996-2007[49]

There is a clear geographical variation in admission rates with higher rates in the north of the North Island and lower rates in the South Island.[49,50] Tairawhiti DHB has the highest admission rate approaching double the national rate.[50] The greater Auckland region has significantly higher hospital admission rates for serious skin sepsis than the rest of New Zealand.[27] Whilst the region has 34% of the childhood population, it has 43% of all NZ paediatric admissions for serious skin sepsis.[27] As most published data reports admission rates by either ethnicity or deprivation or age, it is unclear whether the higher rates in some geographic areas reflect differences in the ethnic, socioeconomic, and age distribution of their child population, or whether other factors such as ambient temperature, availability of primary care, and crowding are contributing.[7,49,51] In order to address this issue, skin sepsis admission rates in Tairawhiti were examined after adjustment for ethnicity, deprivation, and age.[51] Increased rates compared to the rest of NZ persisted but to a lesser extent, with the population of the region only partly accounting for the difference. This suggests involvement of other as yet undetermined factors.

Hospital admission rates for serious skin infection are 1.5 times higher in children from urban areas compared to children from rural areas.[27,50] Postulated reasons include socioeconomic deprivation, household crowding and a higher frequency of skin contact with other children in more densely populated areas.[50]

Earlier epidemiological analyses used the traditional definition of cellulitis and serious skin infection. This includes hospital discharges with a primary ICD diagnosis of cellulitis, cutaneous abscess/furuncle/carbuncle, impetigo, acute lymphadenitis, pilonidal cyst with abscess and other local infections of the skin and subcutaneous tissue.[7,49]

In view of the concern that this approach missed a significant portion of the disease burden in the hospital, and the true hospitalisation rate for skin sepsis may have been underestimated considerably, the broader epidemiological definition has been used in the most recent epidemiological studies in New Zealand.[27,28,50] Admission rates increased from 3.2 per 1000, to 6.7 /1000 in 2006-7 with the broader definition used by O'Sullivan and Baker.[27] Over an 18-year period the average annual hospitalisation rate for serious skin infections in NZ children almost doubled from 298/100 000 in 1990 to 547/100 000 in 2007 (Figure 3). As illustrated in figure 3, in the first two years there was a largely stable rate around 300/100 000, then from 1992–2002 infection rates steadily rose to over 500/100 000. Rates were relatively static between 2002 and 2005 and while there is an upward swing in rates between 2005 and 2007 it is too early to say whether this is a one off fluctuation or the beginning of an upward trend. When examining the underlying conditions, the increases over time were a direct reflection of changes in the admission rates for serious skin infections of typical sites, with the rates of infections of atypical sites and those secondary to primary skin disease and trauma fairly stable over time.[50]

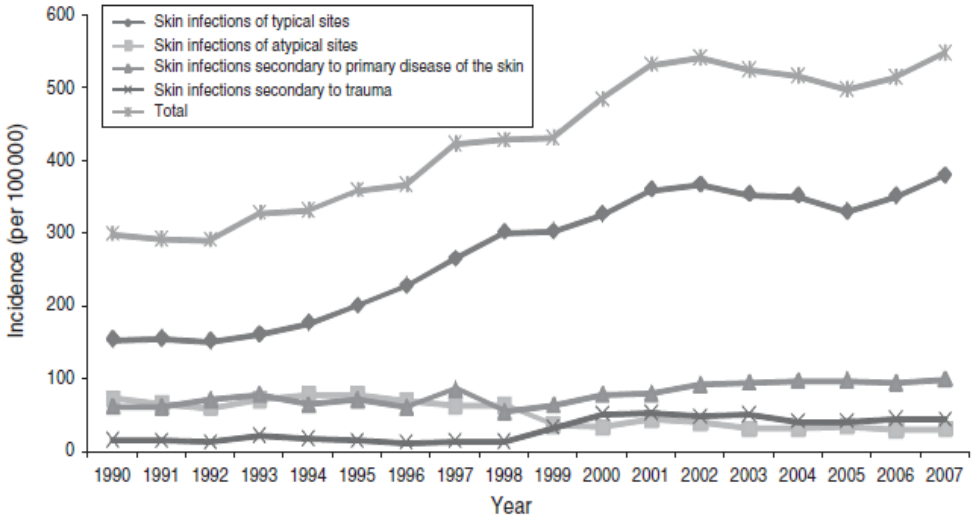

Figure 3: Hospital admissions for serious skin infections in children 0-14 years, New Zealand 1990-2007[50]

There are very little data about how common skin sepsis is in the community thus no true population-based incidence data for serious skin sepsis. However, preliminary findings suggest 14 children are treated for skin sepsis in primary care to every one child requiring hospitalisation.[52]

2.4.3 International Paediatric Incidence

Worldwide, the emphasis on increasing incidence of skin infections has focussed on adults, or on areas where MRSA is prevalent. Comparison between countries is problematic as different countries and health services vary in their definition of skin infections, and the different health systems result in different clinical practice. Furthermore, the increasing incidence means comparisons across different countries need to be made across the same time period. In addition, most data relate to hospital admission rates rather than true community incidence.

Acknowledging this, Hunt compared New Zealand's hospital admission rates for childhood cellulitis with that from other countries using the same definition during an identical time period (2001-3).[37] The NZ rate was double that of the USA and Australia. This is consistent with our finding at the start of our risk factor research, that cellulitis was one of the top 5 reasons for admission to Starship Children's Hospital but was not even one of the top 20 reasons for admission to other Children's Hospitals in Australasia.[6] It is not known if the higher admission

rates in New Zealand reflect a greater community burden of disease, a differing threshold for admission, or whether the skin infections are more severe.

In view of the difficulties stated above, comparisons with the international published literature regarding rates of skin sepsis are almost meaningless with estimates varying considerably. The published studies that contain some information about the incidence of skin sepsis in children have very different case definitions, different data sources, and different populations. The first is a large population-based incidence study of lower leg cellulitis and erysipelas in the Netherlands. Using linked databases of hospital discharge and primary care data for 2001, the hospital admission rate in the 0-15 year age group was <5 per 100 000 population in 2001.[53] Although they report the total population incidence of bacterial cellulitis and erysipelas for inhabitants per year in general practice (179.6 per 100 000), there are no data regarding the primary care rate for specific age groups.

In contrast, another population based study of Mormons in Utah, examined incidence rates for cellulitis from insurance claims over a five year period 1997-2002.[54] Cellulitis was defined using ICD codes which included all cutaneous cellulitis, as well as 'complicated cellulitis' which they defined as cellulitis, lymphangitis, erysipelas and necrotising fasciitis. Paediatric cellulitis incidence rates were 20 per 1000 person years in the 0-4 year age group, 15 per 1000 in the 5-9 year group, and 22 per 1000 in the 10-14 year age group. There were no data regarding hospitalisation rates in the different age groups; however, most of the cases were treated in the community and less than 6% across all ages required hospitalisation. If we assume the admission rate for the younger population is the same as for the broader group (and thus similar to that reported in Tairawhiti), an estimated cellulitis admission rate in the 5-9 year age group would have been approximately 1 per 1000; considerably higher than in the Netherlands. It should also be noted that the Mormon population on the whole is ethnically homogeneous, relatively healthy and has fewer risk factors than the NZ population. Their age-adjusted all-cause mortality is 52% less than that of USA population.[54]

In a nationally representative sample of the USA population, ambulatory care visit rates for skin and soft tissue infections nearly doubled across all ages, and nearly tripled among children from 1997 to 2005.[55] Children and young people had the highest increase over time with ambulatory visits for skin and soft tissue infections among the less than 18 year age group increasing to 27.6 per 1000 in 2005.

2.4.4 National Adult Incidence

Serious skin sepsis has not been identified as an important health issue among adults in New Zealand. There are several possible reasons for this. Firstly, skin sepsis is a broad symptom

complex with a large proportion treated in the community. There is no region-wide or nation-wide consistent data collection in primary care that enables accurate disease surveillance. The community burden of skin sepsis is thus unknown. Secondly, adults hospitalised are admitted under different services within the hospital system, and are more likely to have comorbidities, thus the total hospital burden is probably underestimated. Thirdly, as in most developed countries, rates of chronic disease are rising in New Zealand and the focus for health initiatives among adults has largely centred on obesity, cardiovascular disease, diabetes, and cancer. A recent publication, however, highlighted the importance of serious infectious diseases among the NZ population. In a national epidemiological study of all hospital admissions from 1989-2008, infectious diseases made the largest contribution to hospital admissions of any cause.[56] Their contribution increased from 20.5% of acute admissions in 1989-93 to 26.6% in 2004-08. It also identified significant ethnic and social inequalities in infectious disease risk. Within this analysis, major categories of infectious diseases were tabled providing a total population hospitalisation rate for serious skin infections. The annual age standardised rates of acute hospitalisation for skin and soft tissue infections were 129 per 100 000 in 1989-93 and increased to 292 per 100 000 in 2004-08; an increase of 126%.[56]

2.4.5 International Adult Incidence

As identified in previous sections, there is little international literature about an increasing incidence of cellulitis among children, but an ever expanding literature about the problem among adults. Similar issues with different case definitions, data sources, populations and time periods again complicate direct comparisons. There is, however, evidence of a definite increase in the burden of skin and soft tissue infections across the healthcare continuum. In a nationally representative population study in the United States, ambulatory care visit rates for skin and soft tissue infections nearly doubled across all ages, nearly tripled among children and in the Emergency Departments (EDs), and increased nearly 4-fold among high safety net status EDs from 1997 to 2005.[55] Epidemiological surveys report an incidence that ranges from 0.2 per 1000 person years to 24.6 per 1000 person years depending on the population, and case definition studied.[30,35,54,55,57,58]

In many articles, authors now report cellulitis, abscess, and other infections of the skin and soft tissue to be among the most common infections treated in hospitals.[26,55,57,58] In some institutions, hospitalisations for SSTI are now more common than for community-acquired pneumonia.[26] Skin and soft tissue infections are comparable to that of other medical conditions that frequently require hospitalisation or expenditure of substantial health resources.[30]

2.4.6 Ethnicity

There is a significant ethnic disparity in disease burden with Pacific children 3-4.5 times more likely and Māori children 2-3 times more likely than New Zealand European children to be admitted to Starship Children's Hospital with cellulitis.[7,49] This ethnic disparity is evident whether you examine local, regional or national data (Figure 4).[3,7,28,49,50] Recent epidemiological analysis suggests the disparity is increasing. In 1990–1999 the hospital admission rate was 2·3 times higher in Māori children, and 3·7 times higher in Pacific children, compared to those of other ethnicities. By 2000–2007 that difference had increased to 2·9 times higher in Māori children and 4·5 times higher in Pacific children. The difference in rates over time was statistically significant ($p<0·001$) and postulated to be due to increasing socioeconomic disparities.[50]

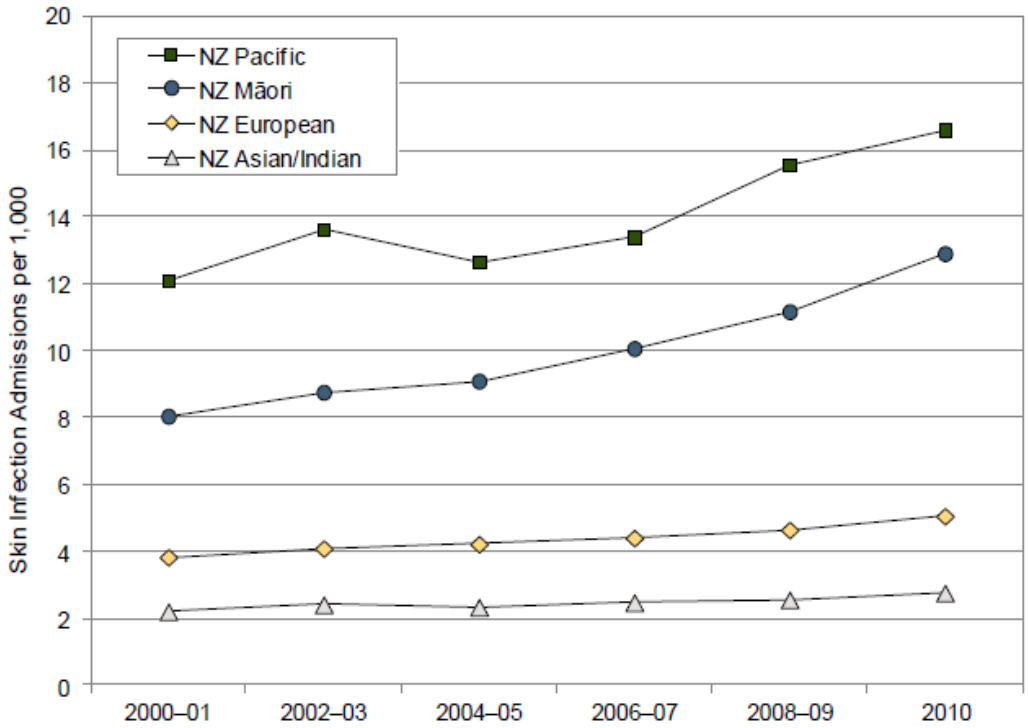

Figure 4: Hospital admissions for serious skin infections in children and young people 0-24 years by ethnicity, New Zealand 2000-2010[27]

Current local and national data are unclear whether Pacific and Māori children have higher community rates of cellulitis, or whether they are more likely to be admitted to hospital with cellulitis due to different disease severity or differing healthcare factors. A preliminary look at these issues in Tairawhiti suggests the ethnic distribution of disease is similar in primary care and hospital, thus the higher admission rates among Māori and Pacific children reflect higher community disease rather than differing admission thresholds.[52] Māori and Pacific children

experience higher rates of infectious diseases in general, particularly childhood pneumonia, invasive staphylococcal disease, meningococcal disease and rheumatic fever.[27,49,56,59-62] The reasons for this are complex and uncertain, however, are likely in part to be due to greater levels of socioeconomic deprivation, crowding, and barriers accessing primary healthcare.[59,63,64] These factors may be interacting with underlying genetically determined disease susceptibilities which to date have not been recognised.[65]

International literature about serious skin sepsis in children is scant with no case-control studies looking at ethnicity as a risk factor. Superficial skin infections have been reported to be endemic in underprivileged populations such as American Indian populations, and Aboriginal Australians.[10,42,66-70] One study followed 150 children prospectively over a three-year period from an American Indian reservation, and documented that 81% of children developed skin infections.[66] Another reported 11% of children in remote villages in Brazil at any point in time had pyoderma.[42] Suggested reasons include household crowding, access to adequate quantities of water, hot weather, humidity, education and personal hygiene.[69] In all these articles regarding common skin diseases, none report information regarding serious skin sepsis requiring hospitalisation, and none specifically examine ethnicity as a risk factor.

Ethnicity has not been routinely or specifically examined in studies of cellulitis among adults. In the only study that examined ethnicity, adults of white ethnicity in Birmingham, United Kingdom, were two times more likely to be admitted with lower leg cellulitis than Asian and Afro-Caribbean ethnic groups.[71] Postulated reasons included differences in skin barrier and function, and different cultural practices. There is a single study reporting trends in infectious disease hospitalisations among American Indian and Alaska Natives.[72] This reported a hospitalisation rate for cellulitis of 253 per 100 000 total population in 1994, but no comparison within the different age groups or comparison with other ethnic groups.

2.4.7 Age

Among children, hospitalisations with serious skin infections are highest in young children and decrease with increasing age (Figure 5).[49,50] There is a second peak in admissions occurring among those in their late teens and early twenties.

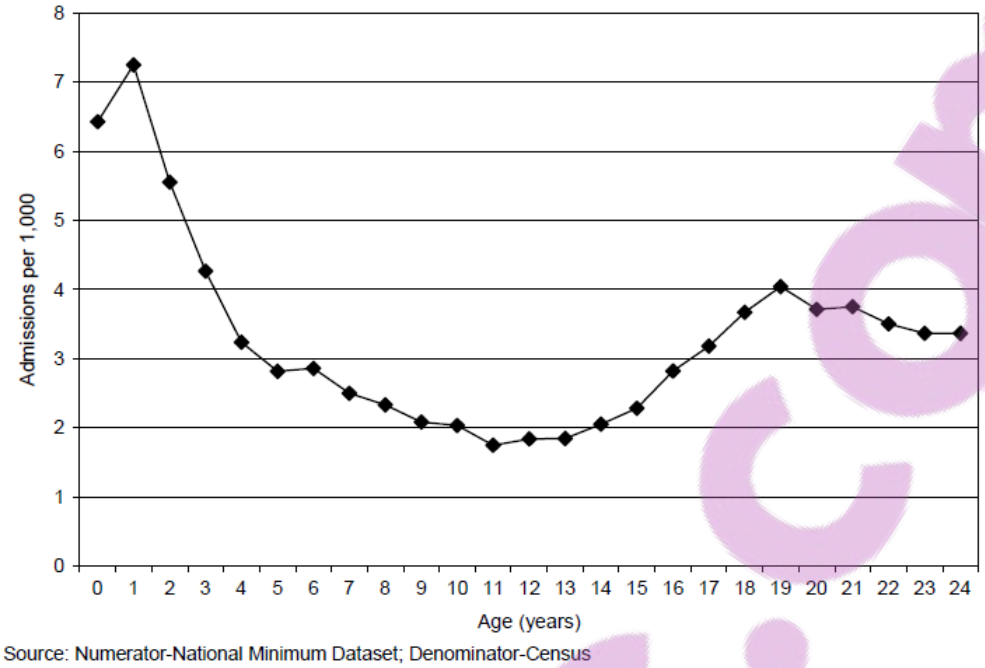

Figure 5: Hospital admissions for serious skin infections in children and young people 0-24 years by age, New Zealand 2003-2007[49]

When exploring the relative risk of admission, children aged 0–4 years have more than double the risk of admission than those aged 5–9 years (RR 2·5 in 2000–2007), and the 10–14 years age group have the lowest rates of infection overall.[50] This, however, combines infants with preschool children, and as illustrated in the graph above, infants under one year of age have approximately twice the hospitalisation rate of children aged four years. The associated risk and protective factors may differ in different age groups. As these studies examine hospitalisation data, it is not clear whether the increased rates reflect a greater risk of developing cellulitis among infants or a greater risk of hospitalisation once cellulitis has developed. An observational study of skin sepsis in primary care sheds some light on this question.[52] Whilst children under 5 years of age accounted for two thirds of hospital admissions, they comprised only 37% of GP cases. Likewise, 15% of hospitalised cases were 5 to 9 years of age but this age group made up 41% of GP cases. This was not what the authors were expecting and was thought to be due to either the small sample size, lower admission thresholds for young children, or more severe disease requiring hospitalisation in a greater proportion of cases.[52]

International literature is scant regarding the effect of age on risk of serious skin sepsis among children. A large population-based study in Utah documented the lowest rates of cellulitis across all age groups in children aged 5-9 years.[54] Another identified children 0-15 years of age as having the lowest incidence across the whole population.[53] The differing results are due to the

age range of the population studied and how the ages are grouped. As different risk and protective factors may be present at different ages, it is important to look closer at factors within the paediatric age group. This will allow us to tease out how much the difference relates to host susceptibility, exposures, behaviour, management and healthcare factors, and will assist with developing appropriate interventions.

International literature among adults identifies age as a significant risk factor for cellulitis[30,53,54] with one large population based study in Minnesota reporting the incidence rate of cellulitis significantly increased with age ($p<0.001$), increasing 3.7% per year increment in age or 43.8% per 10-year increment.[30] Most case-control studies have matched by age thus have been unable to examine the independent effect of age.[20,36,46-48,71,73,74] Serious skin sepsis has not been identified as an issue among adults in New Zealand, however, anecdotally some clinicians do believe this to be the case.[75] As serious skin sepsis is a broad symptom complex, adults are more likely to have comorbidities, and to be admitted under different services within the hospital system. It is likely the disease burden among our adult population is significantly underestimated.

2.4.8 Gender

Paediatric studies identify boys as having a significantly greater risk of hospitalisation with cellulitis than girls.[49,51] In the large New Zealand study of hospital admissions with skin sepsis, boys had a significantly greater risk of infection than girls, with an admission rate of 582/100 000 compared to 454/100 000 (RR 1·28).[50] Data from the same group of authors examining skin sepsis across primary and secondary care identified no difference between the genders in the rates of skin sepsis in primary care. This study, however, involved modest numbers of children both in primary and secondary care, and the previously identified gender disparity in hospitalisation was not confirmed.[52] The reasons why boys are at greater risk of hospitalisation for serious skin sepsis are not clear, but may relate to different types and frequency of exposures, different thresholds for notifying their parents, or different hygiene or host behaviours.

Among adult studies, those that have looked at the gender do not identify any effect.[30,53,54,76] Many studies have matched cases and controls by gender so have been unable to examine this factor independently.[20,36,46-48,71,73,74]

2.4.9 Socioeconomic Status

Local and national data identify socioeconomic status as an important risk factor in hospitalisation with cellulitis.[49,50] Hospitalisation rates for serious skin infections is lowest in areas of least deprivation and increases markedly with rising deprivation levels. During the period 1990–1999, the rate of hospitalisation for skin infection in children from NZDep 9–10 areas (the most deprived

quintile) was 3·6 times greater than for children from NZDep 1–2 areas (179/100 000 and 638/100 000, respectively). By 2000–2007 this difference had increased significantly to 4·3 times higher.[50] This increasing socioeconomic health inequality may be driving the increasing rates of hospitalisation across the country.[50] As these epidemiological studies report univariate analyses, it is not clear how much this socioeconomic gradient is due to conditions relating to socioeconomic factors themselves or how much it relates to different ethnic compositions of the populations. Potential reasons for the socioeconomic inequity include nutrition, household crowding, environmental factors, hygiene, and access to primary care.[27,37,50] To date, none of these have been examined.

Among adults, the literature is less convincing about the impact of socioeconomic status. Most studies do not examine socioeconomic factors specifically.[20,30,46-48,53,54,71,73] Those that do, either show no effect,[77] or have homelessness as the only measure of socioeconomic status.[36,74] Being homeless was a risk factor for serious skin sepsis among US veterans,[74] and in a population based study of non-suppurative cellulitis.[36] In both of these studies the numbers were small, and no other socioeconomic factors were examined.

2.5 Costs

Serious skin infections result in considerable healthcare resource demands and costs.[28] At the time of initiating this research, over a million dollars was spent each year on hospital admissions for cellulitis at Starship Children's Hospital.[6] The direct cost of serious skin infections among children in New Zealand for District Health Boards in 2007 was almost NZ$15 million (based on a 2003 estimate of hospitalisation costs per case of NZ$2180, and an inflation−adjusted cost per case of NZ $2434·21).[50] There are no data regarding the cost of serious skin sepsis among adults in NZ but it is likely to be considerable.

Internationally, there is little data specifically about the healthcare costs associated with serious skin sepsis among children. In an analysis of the expenditure from a Driscoll Children's Health Insurance Plan in South Texas, cellulitis and abscess accounted for increasing percentages of inpatient, outpatient and total expenses of the plan.[78] Seventy percent of the direct health costs from serious skin sepsis were from hospitalisations, and serious skin sepsis accounted for 11% of the inpatient health plan expenses, exceeding the inpatient expenses for asthma.

For adults, most authors report significant healthcare costs but few report actual figures.[20,46,79] Those that do, identify significant costs across the healthcare continuum. In a population based study of lower limb cellulitis in the Netherlands, the average cost per hospitalisation for cellulitis was 5346 euros (~NZ$8839), accumulating to more than 14 million euros in 2001. Although only 7% of the patients were hospitalised, 83% of the total treatment costs, including pharmacy,

hospital and primary care costs, could be attributed to hospitalisation.[53] As recurrences or repeat episodes are common among patients, there can be considerable healthcare costs over several years.[46]

No study has examined the broader societal costs as well as the financial and personal costs to the affected individual and their family.

2.6 Morbidity and Mortality

Superficial skin infections and cellulitis are generally considered relatively benign conditions. In the pre-antibiotic era, the cure rate was 66% and the mortality rate was 11-17%.[80] These have dramatically improved since the advent of antibiotics, but the all-cause mortality for adults requiring hospital admission for cellulitis remains considerable, at 5-7.2%.[57,81] Factors associated with mortality include older age, associated comorbidities, and systemic involvement on admission.[57,79,81]

Very little data exists for morbidity and mortality among children. New Zealand data suggest a case fatality rate of 0.05%.[50] As this includes cases with the expanded case definition of cellulitis,[28] it is unclear how many of these deaths were attributable to the cellulitis itself or whether the children developed cellulitis as a complication of another condition and succumbed from the underlying condition. Two New Zealand children died during the time period 1990-2005 with a primary diagnosis of serious skin infection.[49]

The major complications of cellulitis among adults include prolonged inpatient treatment, recurrent episodes, chronic oedema, ulceration of the leg and rarely invasive infection causing necrotising fasciitis or streptococcal toxic shock syndrome.[82] There are no studies identifying complications among children.

2.7 Postulated Pathway to the Development of Cellulitis

Cellulitis is the end result of a series of events: from an initial breach of skin, to infection, to cellulitis requiring medical treatment, through to cellulitis requiring hospitalisation. This process takes several days to evolve with several factors influencing whether a person subsequently develops a skin infection or requires hospitalisation following the initial event. These include host and environmental factors, microbiological factors, health literacy, access to primary healthcare, and healthcare factors. At present the relative importance and contribution of each of these factors is ill-defined.

The potential influences on the development of cellulitis and events leading to hospitalisation can be considered in the following pathway (Figure 6):

Important influences

Host Susceptibility

Health status
Systemic and local factors
Obesity

Exposures/Breaches of the skin

e.g. insect bites
injury
eczema

Host Behaviours

Hygiene

Past History of Skin Sepsis

Social/Environment

Socioeconomic status
Maternal education
Housing
Crowding

Microbiology

Virulence of organism

Health Literacy/Utilisation

Health literacy/first aid management
Knowledge of when to seek help and where to go

Healthcare Factors

Stage of disease at presentation
Appropriate treatment
Antibiotics given and taken

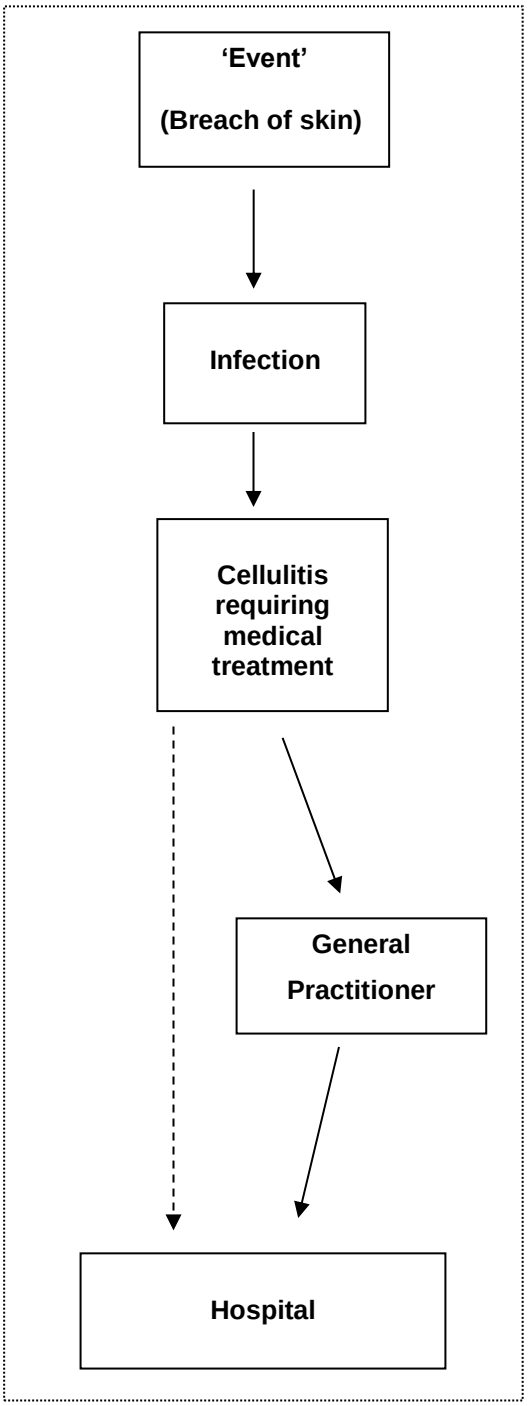

Figure 6: Pathway to Development of Cellulitis (adapted from flow diagram: Paediatric Cellulitis Hospital discharges in the Auckland region)[7]

2.8 Risk Factors

Whilst mild superficial skin infections are common among children,[8-10,52,83] there is little available information about more serious skin and soft tissue infections. In particular there is very little

published literature examining cellulitis in the paediatric population. A literature search undertaken at the beginning of our risk factor research journey, revealed only 30 papers on the epidemiology of paediatric cellulitis published since 1966. Of these, most were articles describing case series of children. The study populations were predominately children who were hospitalised, immunocompromised, or those infected with a specific organism.[8,9,11,12,14-19] There was little information on populations of children and no information on risk factors for developing cellulitis or hospitalisation with cellulitis.

Since the beginning of our research, several paediatric studies have examined some of the epidemiological factors associated with hospitalisation with cellulitis (Volume 2, Table 1: Summary of Descriptive Studies of Cellulitis among Children). These have identified the important risk factors of ethnicity, geographic area, gender, socioeconomic status, and age as mentioned above. Each of these analyses has been univariate analyses only thus the independent contribution of each of these factors is unknown. O'Sullivan undertook some standardisation with age, ethnicity and deprivation to allow comparison of admission rates for skin and soft tissue infections in Tairawhiti with the rest of New Zealand, but did not specifically examine these factors as risk factors.[52]

The only case-control study specifically examining risk factors for cellulitis that includes children is from a US County Hospital and examines factors from 50 cases and 100 controls matched by age, ethnicity and gender.[36] While the age range of cases was 2-83, the average age was 40 years of age and there are no details regarding the actual number of children involved or analysis of risk factors by age. These studies have been summarised in Table 2: Summary of Epidemiological Studies of Risk Factors for Cellulitis among Children. There remains no published study examining the risk factors for cellulitis among children specifically.

At the start of our journey, there was one published case-control study among adults examining the risk factors for hospitalisation with cellulitis.[20] This identified the major role of local risk factors, mainly lymphoedema and disruption of the skin barrier. Since that time, many more articles have been published but almost all have been among adult populations and most specifically exclude children. The published articles fall into two general types; firstly descriptive studies reporting incidence rates and some univariate analyses (Table 3: Summary of Descriptive Studies of Cellulitis among Adults) and secondly specific risk factor studies (Table 4: Summary of Epidemiological Studies of Risk Factors for Cellulitis among Adults). As tabled, there have been 8 published case-control studies examining risk factors for cellulitis among adults.[20,36,46-48,71,73,74] Study sizes have been modest with the number of cases ranging from 47-243 and number of controls from 90-467. All have studied hospital cases thus have only been able to examine the risk factors for hospitalisation with cellulitis and none have examined the risk factors for the

development of cellulitis. Almost all utilised hospital or outpatient controls,[20,36,46-48,71,74] and only one study used community controls.[73] The study populations have been varied including US veterans and patients admitted to dermatology services, thus it is unclear how generalizable their findings are to our paediatric population. In addition, the studies have largely focused on individual host risk factors with very little consideration of social, environmental, and healthcare factors.

The following section summarises the available literature about risk factors for cellulitis. As noted above, there is a scarcity of studies among children so for the most part the risk factors discussed relate to adults. Any available literature relevant to skin sepsis in children is noted at the end of each subsection.

2.8.1 Host Susceptibility

Susceptibility is influenced by health status at a systemic and local skin level, and by behaviours which affect the exposures adults and children come into contact with (e.g. insect bites), and the subsequent development of cellulitis (e.g. level of hygiene, scratching). This section deals with health status factors and subsequent sections address the latter factors.

2.8.1.1 Systemic Factors

Early adult studies identified several systemic factors thought to be associated with the development of serious or rapidly spreading cellulitis.[4,9,20,41,71,81,84,85] These factors included diabetes, being immunocompromised, varicella, chronic steroid use, post-surgery, arterial insufficiency, venous stasis, or other underlying systemic illness. These factors, however, were postulated from case series of adults hospitalised with cellulitis, and subsequent case-control studies have failed to confirm many of these systemic factors as significant risk factors.[20,46-48,71]

Most adults who develop cellulitis are otherwise healthy with no underlying systemic illness. Diabetes was independently associated with development of non-suppurative cellulitis in one case-control study,[36] but not found to be associated with cellulitis in most others.[20,47,71] Obesity appears to be associated with hospitalisation with cellulitis,[20,47,48,74] however, these studies specifically exclude children, have an average age of over 40 years, and utilise hospital cases and controls, thus the information is unlikely to be applicable to our paediatric population.

Although reported in adults, the association between weight and risk of skin infections has not been investigated among children. In a recent New Zealand retrospective chart review of hospital admissions with serious skin infections, 41% of children were greater than or equal to 90th weight percentile.[38] As Māori and Pacific children have higher rates of obesity,[61,62] it is important to

determine if the rates of obesity are different between cases and the general population, and thus whether obesity is contributing to the development of skin sepsis and the ethnic disparity.

2.8.1.2 Local Factors

Almost all published studies have examined risk factors for developing lower limb cellulitis for hospitalised adults. The majority of local factors are therefore conditions that occur among adults. Local factors such as lymphoedema, recent surgery, and breaches of the skin have been found to be more important risk factors for cellulitis than systemic ones.[20,48,71]

For most authors, lymphoedema and lymphatic impairment play a major role in the pathophysiology of cellulitis of the leg.[20,47,48,73,74,82] Other factors implicated include chronic venous insufficiency,[20,48] previous lower leg surgery,[57] ulcers,[47,57] and history of previous deep vein thrombosis.[57,71]

The role of local risk factors among children has not been examined. As children rarely have lymphoedema, preceding surgery and ulcers, other local factors need to be explored.

2.8.2 Exposures/Breaches of the Skin

Disruption of the cutaneous barrier appears to be a consistent risk factor across studies. Whilst a breach of the skin does not per se cause cellulitis, it does impair the defence mechanism of the skin, and provides a portal of entry for potential pathogens. Most studies that systematically examine for a site of entry identify one in more than 80% of cases.[20,35,46-48]

Disruption of the skin barrier has been defined in different ways in different studies; however, all have shown it is a risk factor for hospitalisation with cellulitis. Among adults, disruptions identified include acute injuries such as wounds, and more sub-acute or chronic disruptions such as toe-web intertrigo, ulcers, pressure areas and leg dermatoses.[20,47,71,73] Injuries without a break in the skin have also been implicated.[71] Whilst most studies collate all disruptions into a single group, some have looked at the different risks conferred by different breaches. Toe-web intertrigo is the most common of these and has been explicitly examined in almost all studies amongst adults.[20,35,46,47,71] The focus on intertrigo has occurred after it was identified as a strong risk factor in the first published case-control study, and the authors concluded its detection and treatment could potentially prevent up to 60% of cases of erysipelas/lower limb cellulitis.[20] Since then, other studies have concentrated on the importance of intertrigo, facilitated by the fact they were mostly undertaken by specialist dermatologists.

Although frequent minor skin wounds and prolonged close contact have been implicated in producing outbreaks of staphylococcal skin infection amongst river rafting guides, military

personnel and sportsmen,[86-88] in general, acute wounds such as cuts and scratches have not been associated with the development of cellulitis.[36] Most case-control studies do not examine these as specific risk factors.

Whilst there is a history of trauma breaking the skin in the majority of cases in the adult literature, there are limited data in children on whether breaches of the skin are present prior to the development of cellulitis. Skin injuries among children are common with more than 76% of children nine months and older in one study having at least one recent skin injury, most commonly on the lower limbs.[89] Most injuries were bruises, a smaller proportion abrasions and scratches, and other injuries such as bites occurring in less than 2% of the children examined. There were more injuries in the summer with an increased proportion due to scratches and abrasions. Children five to nine years of age had the greatest frequency and numbers of injuries.[89]

Case series data from New Zealand has identified a preceding injury in 13% to 37% of children hospitalised with cellulitis.[7,37,38] In each of these studies, insect bites were the most common recent injury documented, followed by a cut or accidental fall. These, however, were based on routine documentation in the clinical records (using e-codes or clinical note review) rather than a systematic exploration of parental report of injury or examination of the child's skin. The true frequency of breaches to the skin is likely to be higher. It is not known if children who develop cellulitis do so because they have more frequent breaches of the skin, have different types of breaches which confer different risks, or whether it is different management strategies for common childhood skin injuries that confer the increased risk.

In addition to a preceding acute injury to the skin, children may have an underlying chronic or sub-acute skin condition increasing the likelihood of developing cellulitis.[38] New Zealand has a relatively high prevalence of atopic eczema compared to many countries around the world,[90] and this has been proposed as a risk factor.[37] In disadvantaged populations and the developing world, infestations such as scabies are the most common cause of skin disease in the community,[69] and scabies was identified as an underlying condition in 6% of children admitted to Gisborne Hospital.[38] Chicken pox may also be a contributing factor. Each of these underlying conditions needs to be specifically examined as a potential risk factor.

2.8.3 Host Behaviours

2.8.3.1 Hygiene

Personal and environmental hygiene are important factors in the spread of disease.[91] Skin infections are said to be associated with crowding, poor hygiene, and neglect of minor

trauma.[2,69,92] Factors potentially implicated include hand washing and hygiene measures, sharing of towels and bedding, the mechanism of washing towels and bedding of infected children (hot, cold water, machine washing), and covering or exposing the lesion. Communal linen, towels, wash cloths, and clothing may also be important. Environmental reservoirs of streptococci and staphylococci have been documented in clothing, bedding, fingernail dirt and in school environments.[93-98]

Hand washing practices have not been explicitly examined as a risk factor for skin sepsis; however, there are several reasons why it may be important. The moisture left on hands after washing facilitates transfer of large numbers of bacteria from the hands to other surfaces. Drying hands properly reduces bacteria transmission by up to 99%.[99] Drying hands with clean towels is more efficient at removing bacteria than previously used towels. Sharing towels provides a rich source of bacteria and in situations where other contacts are infected may be a significant risk factor for cross contamination.

Apart from one study, adult studies on the risk factors for cellulitis have not specifically examined the effect of hygiene on the risk of developing cellulitis. Eells in his case-control study examined some health behaviours as a risk for hospitalisation with non-suppurative cellulitis.[36] These included participating in contact sports, re-wearing clothes without washing, wearing someone else's unwashed clothes, sharing a towel, sharing razors, and getting skin cuts, scrapes, and abrasions. None of these were associated with developing cellulitis.

As well as being potentially important as risk factors for the disease, hygiene measures are likely to be important risk factors for hospitalisation once the disease has developed.

2.8.4 Past History

A previous history of cellulitis is reported in 26-50% of adults with cellulitis.[20,30,46,48,57,71,73,79] Early case series of adults hospitalised with lower limb cellulitis report those with a past history of cellulitis were older and more likely to have had previous ipsilateral surgery than those admitted with their first episode.[20,73,79] Adults with recurrent disease are more likely to have systemic factors such as obesity and smoking, and local factors including tinea pedis, venous insufficiency, lymphoedema and acute trauma.[74,79]

More recent case-control studies document an almost 30 times increased risk of hospitalisation with cellulitis for patients with a past history of cellulitis compared to those without.[46,48,71] Most studies identify local factors as the most important risk factors for recurrent cellulitis[35,74] with infection arising from repeated bacterial invasion through breaches in the skin's protective layer.[79] One author suggests an underlying predisposing condition is likely if an infection reoccurs.[53]

Some studies mention recurrences and others a past history of cellulitis, and there is a lack of clarity about whether the episodes are truly recurrences in the same area or whether they are discrete episodes in time and place.

In a population based study of cellulitis presenting to primary care over a 5 year period, 82% of patients had only one episode, 13% had two episodes, 3% had three, and 2% had four or more episodes within the five year period.[54] Importantly, as these data were prospectively collected over a 5 year period, and a past history of cellulitis was not examined, the frequency of repeat episodes in individuals over their lifetime is likely to be much higher.

All of these studies have focussed on host factors and none have examined the effect of behavioural or environmental factors on repeat episodes. It is unclear whether the increased risk associated with a past history is due to host susceptibility, host behaviours, socioeconomic factors, the environment, bacterial exposure, health literacy or a combination of several or all of these factors. No data are available about past history or recurrences of cellulitis among children.

2.8.5 Social and Environmental Factors

2.8.5.1 Socioeconomic Factors

As noted in section 2.4.9, studies among adults have not systematically examined the effect of socioeconomic status on the risk of developing or being hospitalised with cellulitis. There is good evidence from New Zealand regarding the significant effect socioeconomic status has on the risk of being hospitalised with infectious diseases generally and serious skin infections specifically.[56]

Lower socioeconomic status (SES) is consistently associated with poor health, yet little is known about the biological mechanisms underlying this inequality. Potential reasons for the socioeconomic inequity include household crowding, environmental factors, nutrition, hygiene, and access to primary care.[27,37,50,56] To date, none of these factors have been examined in relation to skin sepsis.

2.8.5.2 Household Crowding

Household crowding is associated with increased rates of infectious diseases both nationally and internationally.[60,63] Exposure to infected people and living in crowded housing are both associated with outbreaks of skin infections.[86,100] Prolonged close contact among children who share communal facilities may result in elevated carriage rates of *Staphylococcal aureus*. This could afford increased opportunity for auto-inoculation and cross-contamination of minor skin wounds. Overcrowding, the presence of another infected family member, shared bath facilities, and a large family size could all increase the risk of developing the disease. Although it has been proposed as

a factor in studies of pyoderma and scabies among Aboriginal populations in Northern Australia,[69] to date no studies have specifically examined the effect of crowding on the risk of cellulitis. The only study to consider this, reported housing density was not associated with hospitalisation with cellulitis.[36] This small case-control study of patients admitted with cellulitis had few children in its study population and did not define what they meant by housing density. As Pacific and Māori children in New Zealand are more likely to live in crowded households,[60,62] it is important to examine if this is a risk factor for developing cellulitis and if it is contributing to the ethnic disparities.

2.8.5.3 Environmental Factors

Skin diseases are known to be affected by the physical environment and climate. The direct effects include differing levels of sunshine, heat, cold, and humidity. Indirect effects of the climate are due to altered living circumstances, activities, and parasitic incidence.[101]

A seasonal variation has been noted in all forms of skin sepsis from impetigo through to hospitalisation with serious skin sepsis.[30-32,50,54,66,77,102-104] Most studies identify higher rates in the summer months, however, some also suggest rates are increased in late spring or early autumn. Local data confirm the seasonal variation in admissions with cellulitis: the majority of admissions occurring in the summer months.[7,49,50] Postulated reasons include the increased temperature, more exposed skin, deficiencies in hygiene, greater number of insects, and increased likelihood of minor trauma.[31,32,50,66,89,102] Adult studies have suggested increased minor trauma and increased fungal infections as reasons for the higher incidence in the warmer summer months, however, these have not been specifically examined.[47,79]

A large review of hospital admissions in the United Kingdom identified an increase in late spring and summer which occurred prior to the summer peak in temperature. They thus postulated the seasonal increase in cellulitis was not due to the temperature itself but to other risk factors such as insect bites and skin trauma.[103] Whilst this has not been examined among adults, a study reporting recent skin injuries among 2040 children, in part addresses this.[89] There was a clear seasonal variation, with more injuries, particularly bruises, occurring in the summer. They related this to the temperate climate, with greater outdoor play and less clothing to protect the children from skin trauma from falls and accidental injuries.

In a prospective study of Colombian children, the prevalence of superficial skin infections was highest in the tropics, intermediate in the temperate zones, and lowest in the cool regions.[92] The higher prevalence of skin infections in the hot moist environment was attributed to the greater frequency of insect bites.[92] In addition to providing a breach of skin, insects have been implicated as a vector of streptococci and staphylococci.[32,92] This pattern of higher rates in the warmer

climates and cooler in the colder climates is present in New Zealand but it is unclear if insect bites are associated with risk.[49,50]

2.8.6 Microbiology

The predominant pathogens of skin and soft tissue infections in healthy individuals are the normal skin flora commensals: *Staphylococcus aureus* and group A *streptococcus.*[8,31-35] *S. aureus* is a nasal commensal that can be found in up to 20-30% of the general population, one-third of whom are persistently colonised.[105] Colonisation per se, is not a consistent risk factor for *S. aureus* infection. Despite higher rates of invasive staphylococcal disease among Māori and Pacific Island populations,[49,106,107] *S. aureus* nasal carriage is similar to the rest of the population.[108,109] In these studies, carriage rates were similar irrespective of socioeconomic status, crowding, and previous healthcare contact.[108,109] Similarly, *S. aureus* colonisation rates among African-American and Australian Aboriginal populations are lower than the other population groups despite having higher rates of invasive disease.[108] More recent investigations have suggested nasal colonisation underestimates true colonisation rates, and that colonisation in other body areas including the inguinal region, and oropharynx may be more important risk factors for disease.[110]

S. aureus is the most commonly identified causative agent, accounting for the majority of all SSTIs. *S. aureus* is also a major cause of hospital acquired pneumonia and lower respiratory tract infections, and is now considered the leading cause of invasive bacterial disease.[111] *S. aureus* has become the main focus of attention of research, largely driven by the rapid increase in incidence of skin and soft tissue infections around the world, and the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA). When they first emerged, MRSA infections occurred almost exclusively in hospitalised persons or people who had extensive contact with the health system.[112] Over the last decade, however, there has been increasing emphasis on community-associated *S. aureus* infection. Outbreaks of disease occurred initially among children, rafting guides, prisoners, military personnel, athletes, and other populations who lived in close contact.[113] Community-associated MRSA is now endemic in many countries and is no longer confined to populations with unique exposures or risk factors.

MRSA has not been a significant pathogen in New Zealand, and the majority of *S. aureus* infections in New Zealand are due to methicillin susceptible rather than methicillin resistant strains. At the time of initiation of this research, only 6% of *S. aureus* infections were due to MRSA strains.[114] Whilst this figure has increased since then, it remains relatively low at approximately 10%, but with variation in both resistance and virulence of strains varied around the country.[115] Case series examining the microbiological features of serious skin sepsis among children in New Zealand identify *S. aureus* as the predominant causative organism, with only a

small proportion being MRSA, even in areas where incidence rates are significantly higher than the rest of the country.[3,7,37,38] It is likely therefore, that other factors play a role and researchers are increasingly looking at the interaction between the host and the bacteria for potential reasons for this difference.[109]

S. aureus produces a variety of virulence factors that contribute to its ability to colonise, invade and evade the immune system. One of these is Panton-Valentine leukocidin (PVL) which contributes to tissue necrosis. Initially described as a virulence factor in MRSA infections only, recent local evidence suggests PVL is now a significant cause of methicillin susceptible *S. aureus* infections (MSSA).[105] More than a third of infections in a population–based study of MSSA isolates in Auckland were associated with PVL-positive strains. Those patients with PVL-positive MSSA infection were more likely to be of Pacific ethnicity, be younger in age, have community-onset infection, have SSTI, and need surgical intervention. The underlying reasons for this differential are unclear, and further studies are required to elucidate how much this relates to host, environmental and microbiological factors, or specific interactions between them.

Among adults, there is a strong association between cellulitis and foot dermatomycosis (fungal infection of the foot).[20,46-48] It is postulated the fungal infection causes breaks in the skin and fosters bacterial overgrowth, thus, facilitating entry of bacteria with a resultant skin infection.[35] As fungal infection is uncommon among children, this mechanism is unlikely to be a significant factor in the high rates of cellulitis, and other factors need to be examined.

2.8.7 Health Literacy and Healthcare

2.8.7.1 Health Literacy

Health literacy is the interaction between the skills and knowledge of individuals and the demands of the health system.[116] In New Zealand, good health literacy is defined as 'the capacity to obtain, process and understand health information and services to make informed and appropriate health decisions'.[117] Poor health literacy is a strong predictor of a person's health and affects treatment outcomes and safety of care.[118] It may also be a strong contributor to health inequalities.[118] People with poor health literacy are less likely to use preventative services, less likely to recognise the first signs of medical problems, less likely to communicate concerns to health professionals, more likely to use emergency services, and more likely to be hospitalised with a chronic condition.[117] The Adult Literacy and Life Skills Survey 2006 showed that more than half of New Zealand adults have poor health literacy. Inequities exist with almost 75% of Māori women and 85% of Pacific women having poor health literacy.[117,119]

For skin infections, health literacy encompasses knowledge and expectations about normal skin health, understanding first aid treatment, knowing when, where and how to access the health system, being able to interact confidently with healthcare providers and pharmacists, evaluating and understanding health messages and medications, and acting on the information obtained. None of these factors have been examined. Adult risk factor literature has focussed almost entirely on the host susceptibility with no health literacy or healthcare factors examined.

Further work is needed to explore more of the factors above. Parental awareness of the integrity of their children's skin and their initial management once the skin has been breached are likely to be important factors in the development of cellulitis. Skin infections are said to be associated with neglect of minor trauma,[2] and there is a belief minor breaches and superficial skin infections have been normalised thus ignored among some populations.[120] This has not formally been examined and little is known about how children and their caregivers manage common childhood skin injuries. This relates to mainstream first aid and treatment as well as complementary healthcare practices.[121]

2.8.7.2 Healthcare Utilisation

Hospital admissions for serious skin infections are considered to be ambulatory sensitive thus preventable through early access to primary care.[28] There is no published literature examining the effect of healthcare utilisation on the risk of cellulitis for children or adults.

Primary healthcare in New Zealand is predominantly provided by healthcare professionals, usually a General Practitioner, within a Primary Care Practice. There is a high degree of continuity of care with most people seeing the same health care provider over time, and no difference in continuity across ethnic or socioeconomic groups.[122,123] Māori and Pacific people, however, are more likely to experience barriers in access and use of services across the health system.[117,119] Barriers to access can be a result of a disconnect between patients and providers across the dimensions of affordability, availability, accessibility, acceptability and accommodation.[124]

Affordability relates to the prices of services, and patient perception of worth relative to total cost. Affordability can act as a major barrier to accessing healthcare, particularly for those of lower socio-economic status. Although primary care visits are subsidised by the Government, and free for those less than 6 years of age, families of older children pay a part charge. This is a recognised barrier, particularly for Māori and Pacific families.[117,119,125] Deferring collection of prescription medicines because of cost is disproportionately high among Māori and Pacific people.[125,126]

Availability of doctors both within normal working hours and at other times may act as a barrier to access.

Accessibility factors may act as barriers to access for those who have to travel further to reach a GP, or have difficulty with transportation. Both availability and accessibility influence whether a family visits their primary care provider, an after-hours medical centre or the hospital Emergency Department. These issues play a part more frequently among socioeconomically disadvantaged populations and Māori and Pacific families.[127]

Acceptability is a broad complex that includes the relationship of the patient's attitudes about personal and practice characteristics of doctors, to the actual characteristics of their doctors, as well as to doctor's attitudes about personal characteristics of the patients. Acceptability also encompasses the practice and provider's ability to service customers in a culturally sensitive manner, and whether the philosophical base includes Māori and Pacific approaches to health and disease such as Whare Tapa Wha.[127,128] Language and access to interpreters can be a major barrier to the utilisation of primary healthcare.

Accommodation is the relationship between the manner in which the practices are organised to accept clients (including appointment systems, hours of operation, walk-in facilities, and telephone services) and the clients' ability to accommodate to these factors and the clients' perception of their appropriateness.

Although Pacific and Māori families report they have visited healthcare professional at the same rate as New Zealand Europeans, they are more likely to report unmet need.[62,119] As aspects of most of these dimensions may be modifiable, and affect ethnic groups differently, we need to understand whether any of these factors influenced families of children with cellulitis prior to admission and are contributing to the ethnic discrepancies.

2.8.7.3 Healthcare Factors

As most individuals with skin sepsis are treated within primary care,[53,54] it is important to understand healthcare factors and the health system response.

Primary care management of skin sepsis includes assessment and diagnosis of the condition, appropriate medical management with antibiotics and wound care, investigation of the social and family factors influencing both the development of the condition and affecting the treatment, arranging follow up, and communicating effectively so the skills and knowledge of the family is increased. Little is known about any of these factors in relation to treatment of skin infections and the risk of hospitalisation with cellulitis. Specific areas of interest are the choice of antibiotics, the use of non-steroidal anti-inflammatory medication, and wound care management. Although

several guidelines for the management of skin and soft tissue infections are available in the USA,[29] no primary care guidelines currently exist for New Zealand. It is not known if different antibiotic treatment in the primary care setting alters the risk of hospitalisation. The use of non-steroidal anti-inflammatories has been associated with an increased risk of necrotising streptococcal infection following chicken pox, presumed to be on the basis of altered immune function.[14,19,129] As moisture enhances the ability of *S. aureus* to produce infection, the type of plaster or dressing may influence the subsequent development of the disease.[86]

There is a paucity of evidence based reviews in the international literature which consider effective interventions to reduce serious skin infections at the population level.[27]

2.9 Conclusion

Cellulitis is a significant health issue for New Zealand children. It is a common and increasing problem and is associated with significant ethnic and socioeconomic disparities. While there is a wealth of epidemiological information about serious skin sepsis in New Zealand, all studies have been descriptive, thus the relative importance of these factors has not been determined.

Cellulitis is the end result of a series of events: from an initial breach of skin, to infection, to cellulitis requiring medical treatment, through to cellulitis requiring hospitalisation. This process takes several days to evolve with several factors influencing whether a child subsequently develops a skin infection or requires hospitalisation following the initial event. These include host susceptibility and behaviours, social and environmental factors, microbiological factors, health literacy, and healthcare factors. At present the relative importance and contribution of each of these factors is ill-defined.

Many of these factors have been specifically examined among adults, but no studies have specifically examined risk factors for cellulitis among children. Importantly while adult studies stress the importance of local factors such as lymphoedema and toe web intertrigo, these occur infrequently among children, and their importance in the high rates of paediatric skin sepsis is uncertain. In addition, while most studies among adults have concentrated on host factors, they have largely ignored the potential contributions of social, environmental, health literacy and healthcare factors. As little is known about these potentially modifiable factors, we have been unable to design interventions to reduce both the incidence and impact of cellulitis on our childhood population.

This chapter has outlined the available literature regarding risk factors for cellulitis and raises several questions specifically in relation to children.

Host Susceptibility

Do Māori and Pacific children have higher rates of disease or are they more likely to be admitted with skin sepsis?

Are infants at greater risk of developing cellulitis than older children or are they more likely to be admitted to hospital with the disease?

Are factors such as prematurity, eczema and underlying health conditions associated with the risk of cellulitis?

Are children who have had a previous episode of cellulitis more susceptible to another one?

Exposures

Are local factors important in children?

And if so, what breaches of the skin are associated with the development of cellulitis?

Host Behaviours

What contribution does hygiene have in the development of cellulitis?

Social/Environment

What socioeconomic factors play a role in the development of cellulitis?

Is the ethnic disparity in rates of skin sepsis related to socioeconomic factors or are there other factors at play?

Microbiology

Is there any evidence that microbiological factors are contributing to our high rates of hospitalisation with cellulitis?

Health Literacy/Healthcare Utilisation

How do families manage breaches of the skin?

Do differing first aid management strategies alter the risk of developing cellulitis?

What are the pathways to care once a child develops cellulitis?

Once cellulitis has developed, what factors are associated with hospitalisation?

Do barriers to healthcare affect the risk of hospitalisation?

Healthcare Factors

How does the health system respond and does this influence the risk of being hospitalised?

What follows is a description and the findings of our risk factor research which attempts to address these questions. Chapter 3 summarises the case series; an exploratory study exploring some of these questions and piloting questions and methodology. Chapter 4 outlines the methodology used in the case-control study with particular emphasis on how that may have affected the interpretation of the results. Chapters 5-7 describe in detail the results of our subsequent case-control study which identify and quantify the risk factors for developing cellulitis in children, and the risk factors for subsequent hospitalisation once cellulitis has developed.

Chapter 3: Case Series of Children Admitted to Starship Children's Hospital with Cellulitis

3.1 Introduction

This chapter describes the first part of the risk factor research undertaken to look at potential factors associated with the development of skin sepsis among children admitted to hospital. The case series provided the opportunity to explore pathways to care for children, pilot questions, and generate hypotheses for the case-control study.

3.2 Aims

The specific aims of this study were:

1. To gain a preliminary understanding of some of the potential risk factors for hospitalisation with cellulitis.
2. To explore the pathways of care for children with cellulitis (define the events from initial injury or skin trauma through first-aid management, primary care presentation and ultimately hospital admission).
3. To pilot potential questions and generate hypotheses for the future case-control study.

3.3 Study Design

A prospective case series of 100 children admitted to Starship Children's Hospital with cellulitis was undertaken. At the time of the study, Starship Children's Hospital was the sole provider of general and specialised paediatric and inpatient care for an estimated 160,000 children 0-14 years from the Auckland and Waitemata District Health Boards. This is an urban setting with multiple ethnicities and a temperate climate (latitude 36°52'S).[130]

3.3.1 Rationale for Study Design

A case series was chosen as the initial step in the risk factor research for several reasons. Firstly, at the time of the development of the project, there was little information about risk factors. There were no published studies about the risk factors for cellulitis among children and only one among adults.[20] A report using hospital discharge data had identified several areas of interest,[7] but further information was required prior to a definitive case-control study. Secondly, a case series had the advantage of being relatively low cost with easy access to cases admitted to the only inpatient children's hospital serving a large population. The prospective case series allowed us to capture new cases of cellulitis at the time they were admitted and obtain as much detail as possible on the events leading up to the admission. Thirdly, it allowed us to supplement case note reviews with interviews of caregivers as well as obtain additional information from health

professionals involved in the care of the child. This information would not have been possible if we had undertaken a retrospective chart review as the initial exploratory study. Fourthly, the case series allowed us to pilot study processes and potential questions for use in the subsequent case-control study. The disadvantage of the case series was the lack of a comparison group. Risk factors were therefore not able to be defined. The study did, however, serve to define the hypotheses of cellulitis aetiology more specifically which were then incorporated into the subsequent case-control study.

3.3.2 Case Definition

Cellulitis was defined in the broader context of skin infections: a diffuse expanding area of warm, erythematous skin and soft tissue due to infection. The surrounding area of erythema needed to measure greater than 2cms in diameter. The findings of fever and local pain were not necessary for inclusion. Cases from all body locations were eligible. Cases were selected according to the clinical diagnosis defined by the medical or surgical personnel treating the child. All medical staff involved in the study received instruction from the project manager about the specific case definition, and had a study folder with the definition, explanatory photographs, and study protocols. As cases were identified clinically during the healthcare encounter, use of epidemiological diagnoses and ICD codes was not appropriate.[28]

3.3.3 Selection of Cases

Cases included all eligible children admitted to Starship Children's Hospital with a case definition of cellulitis during the study period. Eligible children were less than 15 years of age living within the catchment area of Starship Children's Hospital. Infants less than 6 weeks of age were excluded in view of the different causative organisms. There were no other exclusion criteria.

All ethnic groups were eligible for the study. Where caregivers indicate multiple ethnicities, ethnicity was assigned using a standard priority system used by Statistics New Zealand:[131]

- Māori - If Māori was one of the ethnic groups reported.
- Pacific Island - If any Pacific island group was reported and Māori was not.
- New Zealand European/Other - All others.

Cases were identified by the hospital co-ordinator after discussion with the nursing staff during daily visits to the medical and surgical wards. A two-stage consent procedure occurred. If a child met the eligibility criteria, their primary nurse approached the family, briefly discussed the study aim and obtained verbal consent for the co-ordinator to discuss the study further (first stage consent). The second stage occurred after discussion with the hospital co-ordinator and the

parent or caregiver gave written consent to being involved in the study (information sheet and consent form, appendix 4).

3.4 Study Period and Sample Size

Cases were collected prospectively during the period of July-October 1999. As this was an exploratory study, data collection stopped once 100 children and their caregivers had been interviewed.

3.5 Data Collection

Qualitative and quantitative information was obtained via:

1. Caregiver Questionnaire (Structured interviews with caregivers),
2. Health Professional Questionnaire (Structured postal questionnaire from the first and subsequent healthcare providers involved in the care of the child during the episode of skin sepsis), and
3. Clinical Information (Clinical record review).

The questionnaires contained questions used in published articles and research from other Department of Paediatrics research instruments as well as from standard instruments. Questions specific to skin sepsis were developed to investigate each of the areas addressed in the background section: exposures, host susceptibility and behaviours, environment, health literacy and utilisation, and healthcare factors. Questions were primarily structured, however, a small number were open ended qualitative questions which were subsequently coded and grouped into related categories. This facilitated the exploratory nature of the research. Usual clinical care was provided with no requirement for additional investigations.

3.5.1 Caregiver Questionnaire

Culturally appropriate people interviewed caregivers using structured questionnaires (Appendix 4). Bilingual interviewers fluent in Māori or one of the Pacific languages were used where the primary caregiver did not speak English, or for instances where the caregiver felt more comfortable speaking in their native language. The interviews occurred in a location of the caregiver's choice with the majority occurring on the ward during the hospital admission (90%).

Socio-demographic data included ethnicity (as specified by the caregiver and defined according to the Principles of Statistics New Zealand),[131] age, and gender. Household composition, car availability, and caregiver ethnicity, age, and education were also documented. Environmental factors included the number of people living in the house, number of bedrooms, and type of

accommodation (rental, owner occupied etc.). A past history of cellulitis, and past history of other skin lesions were recorded.

Pathways of care for children with cellulitis were explored from initial injury or skin trauma through community management, primary care presentation and ultimately hospital admission. The clinical features that brought the lesion to the attention of the caregiver were noted, as were known preceding breaches of skin, and the initial management at home. The duration of symptoms prior to consulting a health professional, types and number of health professionals consulted, and the use of traditional and alternative health care providers and therapy were noted. Difficulties seeing a healthcare professional for the illness were ascertained, and whether the prescribed medication was taken.

3.5.2 Health Professional Questionnaire

Information was collected via a standardised questionnaire sent to the first and subsequent primary care health professionals consulted for the skin sepsis (Appendix 4). Explanatory variables included clinical diagnosis, underlying predisposing conditions, medication prescribed (anti-inflammatories, analgesics, antibiotics, antiseptics), the use of dressings (type and frequency), advice given, and follow up arranged.

3.5.3 Clinical Record Review

Clinical information was extracted from the clinical record using a standardised form (Appendix 4). Explanatory variables included body weight, location of lesion, admitting vital signs, investigations performed, duration of hospital stay, discharge diagnosis, and any surgical intervention. Height was noted if recorded as per standard clinical procedure but was not prospectively collected. Note was made of any microbiology results undertaken in the hospital setting as per standard clinical practice.

3.6 Data Management and Analysis

Data were double entered into an excel spread sheet and tabulated results presented. The simple descriptive analysis was undertaken by the candidate.

3.7 Staff Roles

The study had one study co-ordinator whose role it was to identify eligible children, obtain consent, interview families whose preferred language was English, arrange interviewers for those who preferred another language, liaise with ward staff, enter data, feedback information to the wards, develop protocols, and the study manual.

The candidate designed the study, obtained funding from the Starship Foundation ($22,700), obtained ethics and hospital research office approval, trained and supervised the research staff, and undertook the analysis.

3.8 Ethics Approval

The study protocol was reviewed and approved by the Auckland Ethics Committee and by the ADHB Research Committee.

Written consent was obtained from cases and controls during the face-to-face interviews. Participants were advised they could withdraw from the study at any time or refuse to answer any question without giving a reason. All identifiable information was stored separately and securely from the data forms, with individual identifying information remaining confidential to the researchers only.

3.9 Results

3.9.1 Study Numbers and Response Rate

One hundred cases were enrolled prospectively during the time period. Whilst this was a convenience sample, cross check of enrolled cases with hospital discharge data from the same time period identified we had successfully enrolled 98% of the eligible population. One caregiver declined to be interviewed and no caregivers withdrew part way through. Ninety percent of interviews were completed during the admission and the remainder within a week of discharge.

One hundred and twenty five Health Professional Questionnaires were returned: 72 from the first and 53 from subsequent health professionals.

3.9.2 Demographic Characteristics of Participants

The study population was 61% male and 39% female with a median age of 6.5 years (range 0.2 to 14.1). Pacific (37%) and Māori (25%) children were over-represented in admissions with cellulitis when compared to census data: 19% of children under 15 years in the region were of Pacific origin, 11.5% Māori and 69.5% Other (Appendix 2, Table 5).[130]

3.9.3 Host Factors

Almost all children were reported to be in good health with no underlying medical condition. Twenty-four percent of affected children had a previous episode of cellulitis. Twenty-one percent of children had siblings or parents who had a history of cellulitis.

3.9.4 Socioeconomic Factors

More than half the children were from dual parent households. Thirty-nine percent of care-givers lived in their own homes, 25% in private rental, 27% in Housing New Zealand homes (state owned), and 9% with extended family (Table 6). An average of 5.4 people lived in each household, ranging from 2-12 people in total, and 1-8 children under 15 years of age. The average number of bedrooms was 3.3 (range 2-7).

Families tended to be socioeconomically disadvantaged compared to the general population: 42% of respondents (33 caregivers) reported a gross annual household income of less than NZ$30,000.[130] Sixty-one percent had a Community Service Card (a card which allows subsidised healthcare for low income people). Thirty-three percent of mothers had no formal school qualifications.

Eighty-eight percent of respondents reported they had access to a car and 87% had a telephone connected.

Ninety-two percent of households had an automatic washing machine, and 63% washed the clothes in cold water.

Fifty percent of caregivers reported a problem with insects in their family home: 29% mosquitoes, 23% fleas, and 32% 'other' insects.

3.9.5 Pathways to Care

3.9.5.1 Breaches of Skin

Eighty-five percent of parents identified a preceding lesion; usually an insect bite, cut or scratch that subsequently became infected (Table 7). Other reported skin problems in the preceding two weeks included nappy rash, bruise, splinter, chicken pox, impetigo, and other non-specified skin infections. Twenty-three percent of children had a history of eczema. Sixteen percent of children had a history of scabies, but none reported current infestation.

3.9.5.2 First-Aid Management

Most caregivers administered some first aid including topical cleanser or antibiotic (26%), pain relief (22%), simple dressing (14%), oral antibiotic treatment (9%), or traditional therapy (8%). Approximately one third of caregivers thought no specific attention was required when they first noticed the break in the skin.

3.9.5.3 Initial Symptoms

Redness and swelling were the most common factors first noticed by caregivers (60% and 58% respectively, Table 8). A smaller percentage identified pain (43%), pus (32%), and fever (22%). The most common sites of infection were the lower limbs (49%) and the face, neck and scalp (41%). The trunk and upper limbs were affected less frequently (30% and 17% respectively). Multiple sites were present in 20% of children.

3.9.5.4 Healthcare Utilisation and Healthcare Provision

There was a relatively short time reported between first noticing the lesion to seeking medical attention (mean 1.5 days), and 41% presented within 24 hours. Half the families went to their usual GP or primary care practice with the remaining presenting to another practice or after-hours service. Twenty percent of families reported difficulty seeing a doctor for the illness, including cost (9), lack of transport (4), and the doctor's clinic being closed (3). Twenty-three percent thought the affected area was not bad enough to warrant medical assessment.

The average diameter of the inflamed area at first presentation to a health professional was 4.4 cms (range 0-20 cms). The size was greater for children whose caregivers reported difficulty seeing their doctor for that illness (average 5.9 vs. 3.9 cms, p=0.02). Forty percent of children were admitted to hospital the day of their first medical consultation. The remainder received appropriate treatment in the community, but required admission 1-12 days later. These children were prescribed oral antibiotics (41%), pain relief (24%) or topical antibiotics (12%). One child was prescribed topical antibiotics alone. The majority of families reported picking up the medication within 24 hours and taking the prescribed antibiotics. Four families did not pick up their prescription medication. Reasons given included cost (1), wanted second opinion (1), preferred natural therapies (1) and didn't have time (1). Four children received no intervention at initial presentation.

Ninety-three percent of children presented to health professionals in the community prior to being admitted to hospital. All but one child had a nominated GP. Antibiotics prescribed by primary care were typically broad spectrum due to personal preference, stated concerns about MRSA, previous experience with nonresponse, and poor palatability of the narrow spectrum options.

3.9.6 Clinical Information

Children were admitted to one of 3 services within the hospital depending on the site of the lesion: General Paediatrics (n=30), Orthopaedics (n=35), and Surgery including ENT (n=35). The most common sites of infection were the lower limbs (37%) and the face, neck and scalp (31%). Multiple sites were affected in 20% of children.

Temperature, pulse and respiratory rate on admission were within the normal range for age for almost all children, and only 6 children had a temperature >38.5 degrees. Despite this, 70% had a Full Blood Count, and 53% had blood cultures. The white count was greater than 20 x 10^9 per litre in 12.9% of FBCs. The average haemoglobin (Hb) was 123 gm/l and 11% had a Hb less than 110 gm/l. Two blood cultures were positive; both clinically thought to be contaminants.

Swabs were taken in 61% of children: 18% of swabs were sterile, 57% grew multisensitive *Staphylococcus aureus*, 15% Methicillin resistant *Staphylococcus aureus* (non-multiresistant MRSA), 12.7% *Streptococcus pyogenes*, and small percentages of *moraxella*, *Haemophilus* and *non-haemolytic streptococci* (Table 9). The prevalence of MRSA in this sample was similar to the known community prevalence.[132]

Many affected children were heavy (41% greater than the 90% centile in weight) and only 2% were less than the 10th centile. A greater proportion of Pacific children were obese (50%), compared to Māori (27%) and European (26%). Underlying predisposing conditions were identified in less than 10% of children including varicella (4), eczema (4) and chronic steroid use (1). None had underlying diabetes, infestation with scabies, or were immunocompromised.

The average duration of hospital stay was 3.2 days and median 2.5 days (range 1-15 days). All children received intravenous antibiotics (Flucloxacillin or Amoxicillin/Clavulanic Acid) and thirty-one children required incision and drainage for underlying abscess formation. Rates of surgical intervention were similar across the ethnic groups. No child required joint aspiration and none had a subsequent diagnosis of septic arthritis, or osteomyelitis. No child required a change to another antibiotic for clinical non-response.

3.10 Discussion

This case series of children admitted to hospital with cellulitis showed that breaches to the skin such as insect bites, cuts and scratches commonly precede the development of cellulitis among otherwise healthy children. Previous episodes of skin sepsis were common amongst children admitted to hospital and their families. Although many parents presented to medical attention within 24 hours of first noticing the skin sepsis, 40% of children were admitted to hospital on the day of their first medical consultation suggesting late presentation. Families were more likely to be socioeconomically disadvantaged or report difficulties accessing primary care. Many children had investigations upon presentation to hospital, but these rarely altered management and are thus not routinely indicated. A significant proportion of children admitted with cellulitis required incision and drainage of an underlying abscess.

Community rates of skin sepsis among children are not known in New Zealand but hospitalisation rates are significantly higher than other developed countries. Māori and Pacific children are significantly more likely to be admitted to hospital with skin sepsis than New Zealand European children.[49,133] These children are also more likely to be socioeconomically disadvantaged. Whilst Māori and Pacific children have higher admission rates, it is not known whether they are more likely to develop cellulitis, more likely to be hospitalised once cellulitis has developed, or both. More information is required.

Whilst adult data suggest preceding underlying illness is a risk factor as well as intertrigo, obesity and venous insufficiency,[4,20] almost all children in this study were in good health with no underlying predisposing medical condition. Although the children were documented to be heavy, calculation of BMI was not possible as heights were not routinely recorded on admission to hospital. It is recognised that Pacific and Māori children, have relatively higher weights than their European counterparts,[134] however, the contribution of weight to excess skin sepsis is not known and needs to be further explored.

Among adults, disruption of the skin due to ulcers, wounds, toe-web intertrigo, pressure area and leg dermatoses, are associated with the development of lower leg cellulitis.[4,20] Breaches of skin were common amongst children in this series, particularly insect bites, minor trauma, and eczema. However, it is not known whether breaches of the skin are more common in these children than the general childhood population, or whether they occur at the same frequency but it is the associated environmental factors and subsequent care that increases the risk of infection requiring hospitalisation. As eczema was common factor among children admitted to hospital with cellulitis and postulated to be a risk factor,[27,37] further research needs to include questions relating to the presence, severity and management of eczema as well as a clinical assessment of eczema among both the case and comparison groups.

Previous episodes of skin sepsis and cellulitis were relatively common among children admitted with cellulitis and their families: 24% of affected children had a previous skin infection and a similar percentage had either siblings or parents with a history of cellulitis. We were not able to determine whether these episodes were temporally related to the index case, however, this does highlight the family and environmental loading of skin disease. Whilst it is possible there is an underlying predisposing genetic factor, shared exposures to sociodemographic and environmental risk factors are likely to be the predominant reason for greater family skin disease.[135] Overcrowding, the presence of another infected family member, shared bath facilities, and a large family size could increase the opportunity for auto-inoculation and cross-contamination of minor skin wounds, and thus increase the risk of developing cellulitis.

Skin infections are said to be associated with neglect of minor trauma,[2] thus parental awareness of the integrity of their children's skin and their initial management once the skin has been breached are likely to be important factors in the development of cellulitis. Many parents in this study reported they administered some simple intervention on first noticing the lesion. Although many parents presented to medical attention within the first 24 hours of noticing the skin sepsis, 40% of children were admitted to hospital the same day as their first medical consultation. This suggests either delay in noticing the lesion until the disease is well advanced, or a virulent infection with rapid progression of disease from minor initial symptoms, and/or particularly susceptible hosts. Understanding current health literacy about skin health and skin infections will be important in any health promotion and education intervention.

Ninety-three percent of children presented to health professionals in the community prior to being admitted to hospital and twenty percent reported difficulties accessing primary care for the episode of skin sepsis. Antibiotics prescribed by primary care were appropriate for cellulitis but and were typically broad spectrum. Caregiver reporting of barriers to primary care was associated with a greater size of cellulitis upon presentation suggesting delay in presentation is likely to be a contributing factor. Further research needs to explore this further.

Children were usually systemically well upon presentation to hospital and routine FBC and blood cultures are not indicated. Swabs were frequently taken, particularly if incision and drainage was performed, but the results did not alter management. There was a relatively low incidence of MRSA, usually identified after the child had responded to standard intravenous antibiotics. An unrecognised high prevalence of community acquired MRSA did not appear to account for the high admission rates to hospital with cellulitis. Whilst cellulitis may be the presenting sign of disease states such as septic arthritis, osteomyelitis, or sinusitis, these underlying conditions were not documented in this study population. In contrast, almost one third of children required incision and drainage for underlying abscess formation. These cases, however, were not easily discriminated from the cases not requiring surgical intervention at initial presentation and there were no differences in surgical intervention across the different ethnic groups.

This study adds some important clues into factors associated with skin sepsis requiring admission to hospital and identifies the pathways to care for children from initial breach of the skin to primary care management to hospitalisation. The low rate of underlying illness, the larger size of inflammation at first presentation in caregiver's reporting difficulty accessing primary care, and the presence of multi-sensitive bacteria in most children suggests the high admission rate following initial presentation to primary care may be due to families not recognising the importance of common breaches of the skin and presenting relatively late in the illness. However, the case series design is hindered by a lack of controls and the potential for recall bias. Comparison with

well children in the community and children who are successfully treated in primary care is needed to help determine the risk factors for developing cellulitis and once developed, the risk factors for hospitalisation.

The information obtained from the case series informed the design of the case-control study to examine the risk factors for cellulitis and once developed, the risk factors for hospitalisation. The hypotheses were developed based on the information obtained from the case series as well as review of the literature. The research working group reviewed the questions and results obtained and modified questions and supplemented the questionnaires with additional ones where required. As we were interested in the spectrum of cellulitis, and MRSA comprised only a small proportion of identified cases, we did not pursue microbiological analysis in the case-control study. An article summarising clinical best practice was published in the New Ethicals Journal,[133] a best practice guideline for primary care was developed, and a clinical guideline developed for Starship Clinicians (Appendix 6).[136]

3.11 Conclusion

Data from case series of children admitted with cellulitis, in addition to the information from the literature, allowed us to develop the following hypotheses:

We hypothesised the following factors were related to the development of cellulitis:

Host Susceptibility

Māori and Pacific children have higher rates of developing cellulitis.

Children at different ages have different risk of both developing cellulitis and requiring admission with cellulitis.

Host factors, especially obesity are associated with the disease.

Children who have a past history or a family history of cellulitis are at increased risk of developing cellulitis.

Exposures/Breaches of the Skin

The frequency of breaches of the skin (insect bites, scratches, cuts) differs between children who develop cellulitis and those who do not.

Host Behaviours

Hygiene factors are associated with the development of cellulitis.

Social/Environment

Social factors such as crowding and housing differ between children who develop cellulitis and those that do not.

Health Literacy/Healthcare Utilisation

First aid management of breaches of the skin differs between children who develop cellulitis and those that do not.

Healthcare utilisation differs between cases and controls.

We hypothesised the following factors were related to hospitalisation in those who had developed cellulitis:

Health Literacy/Healthcare Utilisation

First aid management of breaches of the skin differs between children who require hospitalisation with cellulitis and those that do not.

Healthcare utilisation differs between cases and controls.

Healthcare Factors

Primary care management of cellulitis differs between those admitted to hospital than those successfully treated in primary care.

Barriers to healthcare are more frequent among those admitted to hospital than those successfully treated in primary care.

The case-control study research design used to address these hypotheses is discussed in the following chapter.

Chapter 4: Case-Control Study: Research Design

4.1 Introduction

This chapter describes the objectives and hypotheses of the study and the detail about the study design and sampling. At the end of the chapter the reader will have a clear idea about the methodology and how this could have affected the results.

4.2 Aims and Hypotheses

The overall goal of this study was to identify risk factors for cellulitis in childhood. The aim was to identify modifiable risk factors which could lead to prevention and treatment strategies, and result in both reductions in the incidence of the disease and in hospitalisation for those with cellulitis.

4.2.1 Specific Aims

The specific aims of the study were:

1. To identify and quantify the risk factors associated with developing cellulitis.
2. To identify and quantify the risk factors associated with hospitalisation in children who have developed cellulitis.

4.2.2 Hypotheses

The specific hypotheses tested in this study were:

1. The following factors are related to the development of cellulitis:
    a. Ethnicity and age are associated with the disease.
    b. Host factors, especially obesity, are associated with the disease.
    c. The frequency of previous breaches of the skin (insect bites, scratches, cuts, eczema) differs between cases and controls.
    d. Hygiene factors (use of soap, hand washing, separate towels) differ between cases and controls.
    e. Social factors (e.g. overcrowding, poor housing) are associated with the disease.
    f. First aid management of breaches of the skin differs between cases and controls.

2. The following factors are related to hospitalisation in those who have developed cellulitis:
    a. Primary care medical management of cellulitis differs between cases and controls.
    b. Barriers to primary medical care are more frequent in those admitted to hospital.

4.3 Study Design

The aims of the study were to examine the risk factors for cellulitis and the risk factors for hospitalisation once cellulitis had developed. We wanted to explore a range of exposures among affected and non-affected individuals, as well as the interrelationships among these factors.

To achieve this goal and to test the hypotheses we undertook two related case-control studies.

1. Risk factors associated with developing cellulitis. Patients with cellulitis (General Practitioner (GP) and Hospital cases) were compared with GP patients without cellulitis (controls).
2. Risk factors associated with hospitalisation in children who have developed cellulitis. Patients admitted to Starship Children's Hospital with cellulitis (Hospital cases were thus 'cases') were compared with GP patients with cellulitis who were successfully treated in primary care (GP cases were 'controls').

4.3.1 Rationale for Study Design

A case-control design was chosen as the most appropriate design for addressing the aims of this research for several reasons. Admission to hospital for cellulitis is an infrequent event and is therefore suited to a case-control design. Case-control methodology allows for the investigation of risk factors that are transient or have short induction periods such as recent breaches to the skin. The Auckland and Waitemata District Health Board catchment area has a large number of children and includes all major ethnic groups. Complete Hospital case ascertainment was achievable as inpatient paediatric care for this population was exclusively provided by Starship Children's Hospital.

In this study data from the GP patients with cellulitis were used in two different ways. They were 'cases' for the component examining risk factors for developing cellulitis and 'controls' for the study examining risk factors for hospitalisation. This was an efficient use of resources.

Cohort studies are an alternative design for investigating causality. In cohort studies a sample of the population is followed at intervals and postulated exposures (e.g. insect bites) and outcomes (e.g. cellulitis) are assessed. The design is most suited to investigating exposures that are stable over time but not for short-term exposure associations. As we had a specific interest in recent breaks to the skin this study design was not considered suitable for these study questions. In addition, the outcome of interest (hospitalisation due to cellulitis) has a relatively low occurrence rate and therefore the numbers required for a cohort study and the length of time for follow-up would necessitate a very expensive study.

There are several potential disadvantages to using a case-control design. Biases due to the selection of controls, low response rates, and information biases arising from differential recall of information by cases and controls (recall bias) are the main concerns. Confounding is a potential problem in all observational studies. The approaches used to minimise potential biases in this study are detailed in the following description of the methods. The potential impact of biases is considered in the discussion of the study findings (Discussion, pg.124).

4.3.2 Case Definition

Cellulitis was defined in the broader context of skin infections: a diffuse expanding area of warm, erythematous skin and soft tissue due to infection. The surrounding area of erythema needed to be greater than 2cms in diameter. The findings of fever and local pain were not necessary for inclusion. Cases from all body locations were eligible. Cases were selected according to the clinical diagnosis defined by the medical or surgical personnel treating the child: the GP for the GP cases, and the attending hospital team for the Hospital cases. All medical staff involved in the study, both within the hospital and general practice, received instruction by the project manager regarding the specific case definition, and had a study folder with the definition, explanatory photographs, and study procedures. As cases were identified clinically during the healthcare encounter, use of epidemiological diagnoses and ICD codes was not appropriate.[28]

4.3.3 Sampling Methodology

In order to recruit the GP cases and controls, we utilised a cluster sampling methodology based on the geographic area of the GP practice as the strata, and the GP as the unit of sampling. This allowed an efficient means of identifying GP cases and GP controls so that both cases and controls were representative of the same study population. As such, the socioeconomic characteristics and ethnicity of cases and controls were more similar than if the controls were a representative sample of the whole population. This meant that if we found differences in potential modifiable risk factors, such a hygiene factors, that they would be more likely to be related to the risk of developing cellulitis than to differences in socioeconomic and ethnic factors. This sampling methodology increased our precision for other factors but meant we were less likely to be able to determine the independent effect of socioeconomic status on the risk of both developing cellulitis and requiring hospitalisation with cellulitis.

4.3.4 Sample Frame (Study Base)

4.3.4.1 Source Population

The source population from which all participants were selected was children 0-14 years of age, normally resident in the Auckland District Health Board and Waitemata District Health Board catchment areas (Central Auckland, West Auckland, and North Shore). The area extends north to Waiwera bridge, south to Mangere bridge, Waipuna bridge, and Portage Road, Mt Wellington, and east and west to the coast. During the study period there were an estimated 160,000 children 0-14 years, living in an urban setting, with multiple ethnicities and a temperate climate (latitude 36°52'S).[130] At the time of the study, Starship Children's Hospital was the sole provider of general and specialised paediatric and inpatient care for these children.

4.3.4.2 Eligible Population (subjects meeting the inclusion and exclusion criteria)

There were 3 groups of children:

1. Children with cellulitis who required hospitalisation (Hospital cases).
2. Children with cellulitis successfully treated in primary care (GP cases).
3. Children without cellulitis in the community (Controls).

4.3.4.2.1 Inclusion Criteria

1. Live within the specified geographic area.
2. Have a nominated primary care practitioner who practices within the study area.
3. Aged 6 weeks to 15 years.

4.3.4.2.2 Exclusion Criteria

1. Live out of the specified study area.
2. For whom we were unable to find a nominated primary care practitioner despite reviewing the clinical notes, electronic discharge summaries, and Clinical Management Systems.
3. Infants less than 6 weeks of age in view of the likelihood of different microbiological organisms in this age group.

All ethnic groups were eligible for the study. Where caregivers indicate multiple ethnicities, ethnicity was assigned using a standard priority system used by Statistics New Zealand:[131]

- Māori - If Māori was one of the ethnic groups reported.
- Pacific Island - If any Pacific island group was reported and Māori was not.
- New Zealand European/Other - All others.

4.3.4.2.3 Selection of Hospital Cases

Hospital cases included all eligible children admitted to Starship Children's Hospital with a case definition of cellulitis during the study period. As per the eligibility criteria, for the cases to be comparable to the controls they had to live within the study area, have had a nominated GP who practiced within the study area and be known by that GP. Cases were identified by the hospital co-ordinator after discussion with the nursing staff during daily visits to the medical and surgical wards.

A two-stage consent procedure occurred. If a child met the eligibility criteria, their primary nurse approached the family, briefly discussed the study aim and obtained verbal consent for the coordinator to discuss the study further (first stage consent). The second stage occurred after discussion with the hospital co-ordinator and the parent or caregiver gave written consent to being involved in the study (second stage consent). A suitable time and interviewer was arranged with the majority of the interviews occurring in the ward during the hospital admission. Children who were admitted on more than one occasion were included for their first episode only.

4.3.4.2.4 Selection of GP Cases and Controls

GP cases and GP controls were selected utilising a cluster sampling methodology based on geographic area of GP practice. As GP cases were anticipated to be more prevalent than Hospital cases, recruitment of GP cases and GP controls was done at a rate to correspond to the anticipated rate of hospital cellulitis discharges using data from previous years (1998-1999).

4.3.4.2.5 Selection of GPs as the unit of sampling

1. A central database of GPs within the ADHB and WDHB areas was compiled. As there was no single database available, this was created from a variety of sources (practice databases, the preceding year's hospital discharge data, and the local phone book). General Practitioners were eligible if they lived within the area, saw children in their practice and were part of a primary care practice. Doctors identified as specialists, or who worked solely in after-hours accident and medical centres were excluded.
2. All GPs in the database were listed by the suburb in which they practiced. The study area was broken into census area unit codes and DOM codes and allocated the appropriate code for socioeconomic status as defined by the NZ Deprivation index 2001.[137] The areas were then grouped to 8 larger areas based on geographic alignment, natural groupings of suburbs, and socioeconomic similarity. This was undertaken using a consensus approach of the study investigators. The map of the geographic areas is enclosed in appendix 5.

3. The list of GPs of children hospitalised with cellulitis in 1998-99, the last two years of complete hospitalisation data prior to the study, and the list of number of cases of cellulitis by suburb and geographic area was produced.
4. GPs were randomly selected across the year in proportion to the expected geographic area frequency of the GP taking into account our desired sample size. To aid the development of the sampling frame methodology, a small group of GPs provided an estimate of the number of cases of cellulitis in children they saw each week (approximately five-eight per week).[21] This figure was used to calculate an approximate number of weeks of data collection required to achieve our sample size. Collection weeks were initially of 2 weeks duration, however, due to lower than anticipated identification of GP cases, the sampling methodology was reviewed one month into the project and the collection period was increased to 3 weeks. The project manager visited the identified case or control GP 2-3 weeks prior to the time they were due to start enrolling patients, explained the study and obtained agreement from the GP to be involved (Appendix 5, pg. 240). Information sheets for the family, tracking sheets and a folder with study procedures and definitions remained at the practice.
5. If a GP declined to be involved in the study, a replacement GP from the same geographic area was approached. This GP was allocated the same time period for recruitment as allocated to the previous GP.

4.2.4.2.6 Selection of GP Cases

GP cases were sampled by broader geographic area of GP practice as above identifying the GP as the unit of sampling.

The selected GP was asked to enrol cases of cellulitis for the duration of their collection period. GPs who were allocated 2 or more collection periods within a month of each other, were asked to collect the cases consecutively. Eligible children were all paediatric patients who were between 6 weeks and 15 years on the GPs patient register who lived within the study area and had skin sepsis which met the clinical definition of cellulitis as outlined in the study protocol. Basic demographic data from all eligible children were collected on a tracking sheet irrespective of whether they consented or not. This was faxed to the study centre to enable calculation of consent rates.

A two-stage consent procedure occurred. During the first step, the GP gained consent from the family or caregiver for the primary care co-ordinator to contact the family to discuss the study (first stage consent). This was faxed through to the study centre and contact was then made with the family. The second step occurred after discussion with the co-ordinator and the parent or caregiver gave consent to being involved in the study. A suitable time and interviewer was

arranged. Wherever possible, interviews were performed within a week of enrolment into the study to reduce recall bias. Repeat contact was made for caregivers that did not respond or were not able to be interviewed at the first arranged visit. The family was deemed to have not consented if we were unable to interview them within a month despite several approaches.

GP cases included only those children successfully treated in primary care: i.e. those children whose cellulitis resolved with treatment provided by their primary care practitioner. Those children who required hospitalisation with cellulitis became Hospital cases.

4.2.4.2.7 Selection of GP Controls

GP controls were sampled using the GP as the sampling unit as described above. The selected GP was visited and the controls randomly selected from all paediatric patients who were between 6 weeks and 15 years on the GPs patient register. Children were eligible if they lived within the study area and were on the active list of the practice (i.e. had been seen within the last year). A random number list, generated from an excel spread sheet, was used to select the control child from the list.

A two-stage consent procedure occurred. A standard letter was sent on behalf of the GP advising the family of the study and asking them if they were happy to be contacted by the project manager (first stage). If the GP received no response within a week, they rang the family to discuss first stage consent. This initial consent was faxed through to the study centre and contact was then made with the family. The second step occurred after discussion with the co-ordinator and the parent or caregiver consented to being involved in the study. A suitable time and interviewer was arranged. Wherever possible, interviews were performed within a week of enrolment into the study. Repeat contact was made for caregivers that did not respond or were not able to be interviewed at the first arranged visit. The family was deemed to have not consented if we were unable to interview them within a month despite several approaches.

4.3.4.3 Participant Population

Participants (individuals actually enrolled) therefore fulfilled the following criteria:

- Lived in the specified geographic area
- Had a nominated primary care practitioner who practiced within the geographic area
- Were 6 weeks to 15 years of age
- Were either admitted to Starship Children's Hospital with cellulitis (Hospital case), successfully treated in primary care by a nominated GP (GP case), or were randomly selected from a nominated GP practice register (GP control)

- Consented to be enrolled in the study
- Were successfully interviewed.

Information sheets and consents for both participating GPs and families are enclosed in appendix 5.

4.3.5 Study Period

The study recruitment period was undertaken over a 12 month period extending from June 2001-May 2002.

4.3.6 Sample Size and Power Calculations

Sample size calculations were made with the following assumptions: We assumed 30% of the population was exposed to a risk factor e.g. overcrowding (30%), poor hand washing facilities (20%), obesity (20%). One hundred and seventy five cases and 175 controls would be needed to detect an Odds Ratio (OR) of 2.0 at the 5% level of significance and a power of 90%. This sample size was used by both case-control studies: i.e. 175 cases and 175 controls to examine risk factors for the disease, and 175 Hospital cases and 175 GP cases to examine for risk factors for hospitalisation. Figure 7 shows the magnitude of the main effect ORs able to be detected with this sample size and power of 80% and 90% at the 5% level of significance for differing levels of exposure. This figure shows that the proposed study will be powerful for exposures occurring in between 10-90% of the study population.

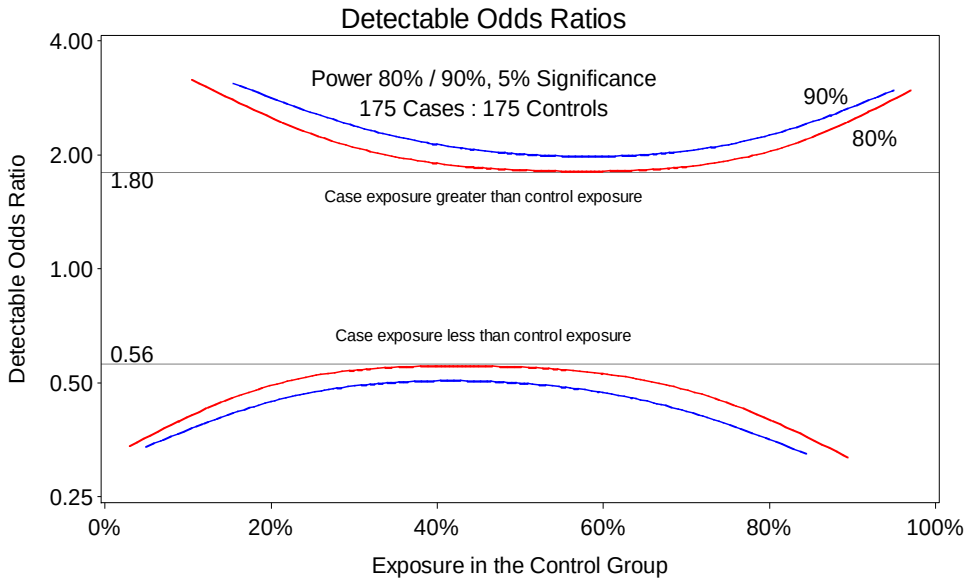

Figure 7: Power Plot

4.4 Study Procedures, and Data Collection

4.4.1 Management and Conduct of the Study

The candidate was the principal investigator for this study and was responsible for overall setup and management of the study. The candidate wrote the successful HRC grant application. The candidate established and led the working group to develop the study design, developed the questionnaires, obtained ethics approval, and monitored the project.

Working group members included:

- Alison Leversha (candidate and Community Paediatrician, Starship Children's Hospital)[i]
- Professor Edwin Mitchell (principal supervisor, Professor of Child Health Research)[ii]
- Alistair Stewart (supervisor, Biostatistician)[iii]
- George Aho (General Practitioner, MOSS, and Pacific Advisor)[iv]
- Natasha Kruitkhoff (Study Co-ordinator)[v]
- David Holland (Microbiologist).[vi]

4.5 Staff Roles and Study Manual

4.5.1 Project Manager/Hospital Co-ordinator

The role of the project manager/hospital co-ordinator was to liaise with the wards, enrol the cases, transcribe clinical information, produce monthly reports, arrange interviewers where required, and perform interviews where appropriate. The co-ordinator was also responsible for data

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iiProfessor of Child Health Research, Department of Paediatrics, University of Auckland

iiiBiostatistician, School of Population Health, University Of Auckland

ivPacific Advisor, Medical Officer, Children's Emergency Department, and General Practitioner, Pasifica Fono

vDepartment of Paediatrics, University of Auckland

viAuckland City Hospital, and Department of Microbiology, University of Auckland

management, maintaining tracking sheets for participants (Hospital cases, GP cases, Controls, GP contacts, interviewers) and assisted with coding prior to data entry.

4.5.2 Primary Care Co-ordinator

The primary care co-ordinator was employed full time for 18 months. Responsibilities included: liaison with GPs and practices, extracting practice data for the sampling, co-ordinating community interviews, arranging culturally appropriate interviewers, performing interviews where appropriate, notifying GPs, faxing surveys, collecting clinical information, arranging Hui, and reviewing practice information. The primary care co-ordinator arranged the interviews for the GP cases and for those Hospital cases that wished their interview to be undertaken in the community.

4.5.3 Interviewers

A group of interviewers who had previously been involved in the cellulitis case series study were employed for the case-control series. They had a broad range of ethnicities appropriate for the families as well as experience in research projects and interviewing. Training was provided during a half day workshop as well as supervision throughout the project.

4.5.4 Study Manual

A study manual was developed containing copies of all questionnaires, explanatory pictures for GPs and medical staff, recruitment procedures, the HRC grant application, the ethics and hospital research office approvals and study protocols. Folders containing all relevant study information were developed for each ward and GP practice enrolled into the study.

4.5.5 Data Collection

Qualitative and quantitative information was obtained via:

1. Caregiver Questionnaire (Structured interviews with caregivers),
2. Health Professional Questionnaire (Structured postal questionnaire from the first General Practitioner involved in the care of the GP or Hospital case during the episode of skin sepsis), and;
3. Clinical Information (Limited physical examination for all children and Clinical record review for Hospital cases).

The questionnaires contained questions from the cellulitis case series (described in Chapter 3.5), used in published articles and research from other Department of Paediatrics research instruments as well as from standard instruments. Questions specific to skin sepsis were developed to investigate each of the areas addressed in the background section: exposures, host

susceptibility and behaviours, environment, health literacy, and healthcare factors. The questionnaire was revised at the end of the case series to incorporate suggested improvements and piloted prior to use in this case-control study. Questions were primarily structured, however, a small number were open ended qualitative questions which were subsequently coded and grouped into related categories.

All children had a core set of data from the caregiver questionnaire and the brief clinical assessment (Appendix 5). Children with cellulitis had supplemental caregiver questions as well as information from the first health professional they saw for their skin sepsis (Health Professional Questionnaire, Appendix 5). The address and DOM code were recorded for each child and subsequently assigned a score from the NZ Deprivation Index (NZDep).[137] The NZDep provides a small area measure of socioeconomic deprivation and is based on nine variables extracted from census data. It is calculated from information regarding individuals with no telephone access, no car access, receipt of a means-tested benefit, unemployment, low household income, single parent families, nil qualifications, non-tenured homes and household crowding. NZDep 1 indicates the least deprivation and 10 indicates the highest deprivation. For the analysis, NZDep scores were divided into quintiles.

4.5.5.1 Caregiver Questionnaire

Culturally appropriate people interviewed caregivers using structured questionnaires. Bilingual interviewers fluent in Māori or one of the Pacific languages were used where the primary caregiver did not speak English, or for instances where the caregiver felt more comfortable speaking in their native language. Primary caregivers were defined as the one or two adults who were most responsible for the care of the child on a daily basis. The interviews occurred in a location of the parent's choice. For Hospital cases, this was usually the hospital, whereas it typically occurred at the child's home or a location of the caregiver's choice for the GP cases and GP controls. Wherever possible, the interviews occurred within the week of presentation to the GP, or hospitalisation to minimise recall bias.

4.5.5.1.1 Core Caregiver Questions

The caregiver questionnaire contained a base set of the same information for Hospital cases, GP cases and controls.

Explanatory variables collected:

Demographic data: Ethnicity (definition according to the Principles of Statistics New Zealand and as defined in section 4.3.4.2.2),[131] date of birth, age (both as identified by caregiver and as calculated from the date of birth and the date of interview), gender.

Parental information (from both mother and father): ethnicity (self-defined as above), age, date of birth, educational achievement (school and post-school qualifications), number of years living in New Zealand, English as a second language (ESOL), current community services card (community card for health subsidies for low income families), smoking, and occupation. Occupation was coded according to the New Zealand Standard Classification of Occupations.[138]

Host susceptibility: Low birth weight as defined as a weight of less than 2500 g (up to and including 2499 g), gestational age, infant feeding practices, and breastfeeding duration and supplementation. Caregivers were also asked whether the child had any specific health problems (if yes, specify) and to give a summary description of their child's health in the 6 months prior to the interview (excellent, very good, good, not very good, or poor).

Exposures/Breaches of Skin: Frequency of breaches to the skin in the previous week including insect bites, cut or scratch, chicken pox, bruise, splinter, animal or human bite, eczema, nappy rash, and other skin problems. Bruise was included as evidence of minor trauma even in the absence of a break of the skin surface in view of literature suggesting it was the most common childhood injury to the skin.[89] Two variables were created: 1. Any breach or injury of the skin (including a bruise) and 2. Any breach of the skin (which excluded bruise but included all other injuries which typically cause a breach of the skin surface). Some exposures had additional questions relating to the severity or type of injury: e.g. number of insect bites, whether the child scratched the bite until it bled or wept, the length and depth of the cut and whether soil was involved in the injury, an estimate of the number of chicken spot lesions, whether any spots were larger than 1 cm diameter, whether the child scratched them until it bled or wept, whether the splinter was completely removed, and the specifics regarding what caused the bite (dog, cat, human, other).

As both eczema and nappy rash were considered more likely to be chronic rather than acute breaches of the skin, caregivers were asked additional questions regarding their usual practice and care of their child's skin. Additional questions for eczema included location on specific areas of the body, how often the eczema had kept the child awake at night in the previous 12 months, whether the child had scratched the eczema until it bled or wept, use of moisturiser and steroid cream, frequency of application both typically and in the week prior to the interview, and use of soap or soap substitute. If the caregiver responded yes to any use of creams or ointment, they were asked to specify what was administered. Additional questions for nappy rash included area the rash covered, use of cloth or disposable nappies, average number of nappy changes per day, washing or wiping at change time, number of hours without nappies per day, and whether the nappy rash bled or wept. Caregivers were also asked whether their child had had any other skin

problem in the previous week or in the preceding year. If they responded yes, then they were asked to specify the type of skin problem.

Host behaviours: Caregivers were asked several questions about their child's hand washing and drying practices at home: temperature of water, running or still water, use of different forms of soap, and what their child usually used to dry their hands. They also responded to questions about the need for reminders to wash hands, and how often their child washed their hands before eating, after eating, after going to the toilet, after handling pets and when visibly dirty. Bathing practices (bath, shower), number of times bathed per week, number of times hair washed per week, number of times child shared bath or bathwater per week, specifics about towel use (personal or shared), and specifics about washing and drying the bath towels.

Past history and family history of cellulitis and skin sepsis: Past history of cellulitis, and past history of other skin problems in the index child, any other child living in the same house, or any other adult living in the same house. If the caregiver responded yes to any of these stem questions, they were asked to specify how long ago the last infection was. They were also asked to report the number of previous episodes of cellulitis for the index child.

Social and environmental factors: Number of people living in the house (adults and children), number of bedrooms, sleeping arrangements for the index child (shared bedroom, shared bed), number of toilets, housing ownership (owner occupied, private rental, Housing NZ rental (state rental), living with extended whānau), household description (couple with children, single parent with children, extended family/whānau/other), dwelling type (house/townhouse/apartment, flat/unit, other), measures of exposure to environmental tobacco smoke (maternal smoking, paternal smoking, number of smokers living in the house), mobility (number of different addresses in previous 12 months), and phone (landline, mobile, nil). Also noted was the presence or absence of household pets, and clothes washing facilities and usual practice (water temperature, and drying options).

Rather than using existing crowding indices, which allow for the social acceptability of sharing bedrooms and beds, we assessed close contact exposure to other household member in terms of the number of occupants per available bedroom.[60] Ages and gender of other household members were not collected thus the equivalised Crowding Index was not calculated.

Health literacy and first aid management: Caregivers were asked if they administered first aid to an identified breach to the skin. Questions included cleaning with soap, water or saline, cleaning with antiseptic, administration of creams including antibiotics, antiseptic and anti-itch ointment, administration of tablets including antihistamine and antibiotics, pain relief, traditional therapy, and whether the breach was covered (and what with). Note was also made of time interval from first

noticing the breach to when first aid was administered. Caregivers were asked if they sought medical advice for the breach when it first happened, and if so, the time interval from when they noticed the breach until the medical attention.

Healthcare utilisation: Caregivers were asked about the usual health care practitioner they used for their child (a single GP or practice, one of several different GPs in different practices, whoever was available, an after-hours service, or other), and an estimate of the number of times they had been to each of these for the index child in the 6 months prior to the interview or episode of skin sepsis. Caregivers were also asked if they had any problems getting to or seeing a doctor or GP for their child's last illness. If caregivers responded yes, they were asked to specify the reason (cost, transport, family too busy, doctors too busy, or other).

4.5.5.1.2 Supplemental Caregiver Questions for GP and Hospital Cases

For those children that developed cellulitis, additional information was obtained relating to first aid management of the redness, healthcare utilisation for the skin sepsis, and questions relating to their interaction with the healthcare system. The same questions were used for the caregivers of both the GP and Hospital cases and were incorporated into the Caregiver Questionnaire.

Health literacy and healthcare utilisation: Questions were asked to assess the caregiver's knowledge of when to seek help and where to go. Specifically they were asked what they did after the redness began, what other symptoms were present at the time they first noticed the redness (fever, swelling, pain/tenderness, crusting/pus/discharge, limp, or other), and what actions they undertook (the same options as for first aid management as above). If the caregiver responded yes to any action, they were asked to specify what was administered and the time interval from when they first identified the redness until the first aid was given. Caregivers were asked if they sought medical advice for the redness when it was first identified, and if so the time interval from noticing the redness until the medical attention. They were asked to specify the types and number of health professionals consulted for the child's redness (family doctor, practice nurse, after-hours service, hospital emergency department or other). Caregivers were asked for their opinion as to the cause of the cellulitis.

Caregivers reported what healthcare was provided as well whether prescriptions were filled and the time interval from receiving the script to picking it up from the pharmacy. They also reported the time from medical assessment until the first dose of medication.

Healthcare factors: Caregivers reported what healthcare was provided including prescriptions for antibiotics, antiseptics, antihistamines, pain relief etc. If the caregiver responded yes to any action, they were asked to specify what was prescribed at what dose, how frequent, and duration

of therapy. Caregivers reported whether their healthcare practitioner provided any other treatment or advice for the cellulitis (specific advice re bites, cuts etc., dressings, local cleaning, or other). Follow up arrangements were recorded as well as consultation with other people for their child's condition (alternative therapist, social worker, traditional healer, community healthworker, friend or other). They were asked to specify the total number of times they saw different health professionals for the child's cellulitis (family doctor, practice nurse, Plunket/public health/school nurse, chemist/pharmacist, after-hours service, or hospital emergency department).

4.5.5.2 Clinical Information

4.5.5.2.1 Core Clinical Information

Explanatory variables collected included weight, height, and a clinical assessment of eczema (as per the research protocol for atopic eczema, defined by Hywell Williams).[139] This reported whether the child had any visible eczema at various sites on the body including around the eyes, around the sides or front of the neck, front of elbows, behind knees, or front of ankles. For children less than four years of age additional record was noted regarding visible signs of eczema on the cheeks, forearms or legs. Weight was measured by the interviewer using electronic scales (SECA 734 Digital scales, Protec Solutions). Height was measured using a stadiometer (Seca 222, Protec Solutions), or for children less than 2 years of age, a measuring mat (Seca 210 mat, Protec Solutions). BMI Z-scores were calculated using WHO Anthro v software for SPSS. Two programs were used: One version for children under 5 years and the other version for children 5-15 years.[140] The core clinical information was collected at the end of the Caregiver Questionnaire.

4.5.5.2.2 Supplemental Clinical Information for GP and Hospital Cases

All cases received care as per usual from their attending clinician. No additional laboratory or microbiological investigations were required as part of the study protocol. Additional clinical information was extracted for the Hospital cases from the clinical records by the project manager or hospital coordinator into a brief standardised clinical information data form. This recorded the admission and discharge dates, and whether surgical intervention was required. The medical records of the cases that were successfully treated in primary care (GP cases) were not reviewed, however, clinical information including presenting complaint, size of area, site etc. were recorded by the assessing health professional. These variables are outlined in the Health Professional Questionnaire section below.

4.5.5.3 Health Professional Questionnaire: GP and Hospital Cases

Information was collected via a standard questionnaire sent to the first health professional the family saw for their child's episode of cellulitis (both GP and Hospital cases). Our experience in the case series of requesting information from all health professionals involved in the care of the child resulted in a significant increase in workload with little additional important information. As we were interested in the severity of the cellulitis when the child first presented to the doctor, we chose to send the health professional questionnaire to the first health professional only. Health professional questionnaires were not collected for control children. Questionnaires were faxed or posted to the General Practitioner, and then faxed back to the study centre. Follow-up phone calls were made 2 weeks later if a response was not received. A non-response was recorded if no information was returned after 2 contacts with the health professional.

Explanatory variables collected included the clinical diagnosis, size of lesion at presentation, maximum size of lesion, medications prescribed, the use of dressings (type and frequency), advice given, follow up arranged, and underlying predisposing conditions. The healthcare professionals were also asked, based on their past experience with the family, to rate the compliance with prescribed therapy and whether they felt there were other factors which contributed to the course of illness in the affected child.

4.5.6 Variables Considered But Not Collected

Several factors were considered but not collected as part of this cellulitis research. Some would have added a significant burden to the participants and thus potentially reduced participation rates, and others were not included due to lack of evidence of their importance at the time we initiated the project. A brief discussion of potential variables is outlined below.

4.5.6.1 Microbiology

The value of microbiological culture in the management of cellulitis is limited. Needle aspirations taken from infected skin areas are positive for bacterial growth in only 10% of cases.[141] Because of the low yield and reproducibility of the microbiological investigations in the infected tissue and in blood, those studies were not considered necessary for the diagnosis, which was based on clinical grounds only. We were also concerned that an invasive investigation would lower the participation rate among the eligible children. This was confirmed during a small pilot of needle aspiration in the setup phase of the study. During this time period, 20 children and caregivers were approached to take part: Three agreed to the questionnaire and aspiration, 8 agreed to the questionnaire but declined the aspiration, and the remainder declined both. In addition, whilst

needle aspiration may have been possible among Hospital cases, it is unlikely we would have been able to undertake this investigation for the GP cases. As a result, this was not pursued.

Microbiology swabs of the lesions were considered for both the GP and Hospital cases. However, as the available evidence suggested virulence of bacteria was not likely to be the cause for the recent change in incidence[7] and the prevalence of MRSA was low in previous laboratory reviews, the case series and from national surveillance,[7,115] specific microbiological factors were not collected in this epidemiological analysis.

Consideration was also given to taking nasal swabs from children; however, without corresponding swabs of the lesions with culture and strain identification, it would have been difficult to determine whether any identified bacteria were the cause of the skin and soft tissue infection or were part of the child's normal skin flora.

4.5.6.2 Toe-web intertrigo

At the time of initiating our research there had been only one published risk factor study.[20] This study among adults identified the importance of toe-web intertrigo. We considered this to be an unlikely risk factor in children and thus did not specifically examine for this. We also used trained research assistants rather than medical professionals and dermatologists. At the time, there was no paediatric dermatologist available for day to day assessments of enrolled children.

4.5.6.3 Nutrient deficiency

As iron deficiency has deleterious effects on the immune response, results in an increased risk of infection, and is particularly prevalent among Pacific and Māori children, consideration was given towards obtaining iron status.[142] This was not furthered, however, due to the following concerns: Iron deficiency was unlikely to have explained the observed changes in prevalence, the requirement for a blood test could reduce compliance, and the difficulties in interpreting iron status during an acute infection. Similarly, low vitamin D levels are more prevalent among Pacific and Māori children and associated with immune problems, however, the same issues apply.[143] We therefore chose not to broaden the scope of the project and potentially reduce participation, and continue with standard clinical practice without imposing any additional investigations.

4.6 Data Management and Analysis

4.6.1 Data Entry and Checking

Completed data forms were checked by the project manager post-interview and coded using the coding dictionary developed in the setup phase. Additional codes were developed for nonstandard responses to open-ended questions and those that asked for the caregivers to specify a response (e.g. specify which pain relief was administered if not paracetemol or ibuprofen).

Several databases were developed for the study using Microsoft Excel. These included databases for tracking GPs, tracking patients, and entering data from each of the questionnaires. Simple descriptives were undertaken to examine the distribution of variables and outliers.

Data were double entered directly from the data forms into the database by an experienced data entry staff member. Weekly team meetings were held with the study team to monitor recruitment and the data entry processes.

4.6.2 Data Analysis

The candidate undertook all analyses presented in this thesis, with the statistical guidance of Alistair Stewart, Biostatistician, and Professor Edwin Mitchell, Professor of Child Health Research. Analyses were performed using Excel and SPSS Complex Sample software. As the GP was the unit of sampling, and the data was stratified by the geographic area of GP practice, the analyses incorporated weighting to account for these differing selection probabilities (SPSS Complex Sample analysis v 19.0.1).

Using complex sampling methodology, sample weights were calculated for the GP cases and Hospital cases to allow us to combine the data from both case groups when undertaking the analysis of risk factors for developing cellulitis. The controls were allocated a weight of 1 as they were considered to be representative of all potential controls. The weights for the GP and Hospital cases were derived by comparing the actual number of cases collected during the study period with the predicted number of cases collected if we had sampled cases across the whole year. For the Hospital cases, the actual number and the predicted number were considered to be identical.

For the GP cases, the actual number of cases was a proportion of the predicted number of cases as we did not sample from all eligible GPs across 52 weeks of the year. Weights were therefore calculated using information about the number of GPs sampled, the number of eligible GPs, the number of actual collection weeks, the number of theoretical collection weeks assuming we

collected for 52 weeks of the year, and the number of GP cases collected. Using the above information we calculated the predicted number of GP cases if we had sampled cases across the whole year. This predicted number was combined with the predicted number of the Hospital cases to estimate the predicted total number of cases of cellulitis if there had been complete sampling. This allowed us to determine the relative contribution of information from the GP cases in relation to the Hospital cases when combining them to determine the risk factors for developing cellulitis. As we used the GPs as the sampling unit within a geographic cluster, the above calculations were undertaken for each of the geographic areas. The spread sheet outlining this weighting is in appendix 5 (pg309).

When performing the analysis of risk factors for hospitalisation with cellulitis, Hospital cases and GP cases were both allocated a weight of 1 as they were considered to be representative of all potential cases.

Exploratory analyses were undertaken to initially investigate the distribution of exposure variables, and potentially important confounders. Frequency tables were used to assess the distribution of categorical variables. Relevant cut-points were used to redefine continuous (e.g. age) and scales as categorical variables. Cut-points were determined by a combination of meaningful boundaries present in the variable, ensuring reasonable numbers in each category, and awareness of categories used by previous researchers. Unadjusted Odds Ratios (OR) were then calculated.

Almost all exposure variables considered in the main analyses of this research had less than 10% missing data. Note was made at the foot of each table re the amount of missing data. Imputations of missing data were not undertaken. Variables with a significant amount of missing data (e.g. paternal education and paternal smoking) were noted and not included in the analyses.

Multivariable unconditional logistic regression analyses were undertaken to estimate the main effects of interest on the risk of either developing cellulitis or being hospitalised with cellulitis, using the least significant difference adjustment for multiple comparisons, independent of the effects of known confounders. Potential confounding variables were assessed by examining the univariate analysis as well as including those that made clinical sense. The multivariate analysis therefore included ethnicity, age and NZ deprivation index.

4.7 Ethics Approval

The study protocol was reviewed and approved by the Auckland Ethics Committee and by the ADHB Research Committee.

Written consent was obtained from cases and controls during the face-to-face interviews. Participants were advised they could withdraw from the study at any time or refuse to answer any question without giving a reason. All identifiable information was stored separately and securely from the data forms, with individual identifying information remaining confidential to the researchers only.

4.8 Conclusion

This chapter describes the objectives and hypotheses of the study and the detail about the study design and sampling. This outlines the methodology and how it may have influenced the interpretation of the results.

Chapter 5: Case-Control Study: Study Base Description

5.1 Introduction

This chapter describes the study base and specifics of the participants and details information re recruitment, response rates, participation rates, and missing data etc. for each of the groups. At the end of the chapter the reader will have a clear idea about the study base and participants for each of the three study groups.

5.2 Study Design

5.2.1 Sampling Methodology

In order to recruit the GP cases and controls, we utilised a cluster sampling methodology based on the geographic area of the GP practice as the strata, and the GP as the unit of sampling (Chapter 4.3.3). This allowed an efficient means of identifying GP cases and GP controls so that both cases and controls were representative of the same study population. As such, the socioeconomic characteristics and ethnicity of cases and controls were more similar than if the controls were a sample of the whole population. This meant that if we found differences in potential modifiable risk factors, such a hygiene factors, that they would be more likely to be related to the risk of developing cellulitis than to differences in socioeconomic and ethnic factors.

5.2.2 Sample Frame (Study Base)

5.2.2.1 Source Population

The source population from which all participants were selected was children 0-14 years of age, normally resident in the Auckland District Health Board and Waitemata District Health Board catchment areas (Central Auckland, West Auckland, and North Shore). The area extends north to Waiwera bridge, south to Mangere bridge, Waipuna bridge, and Portage Road, Mt Wellington, and east and west to the coast.

5.2.2.2 Eligible Population (subjects meeting the inclusion and exclusion criteria)

There were 3 groups of children:

1. Children with cellulitis who required hospitalisation (Hospital cases).
2. Children with cellulitis successfully treated in primary care (GP cases).
3. Children without cellulitis in the community (Controls).

Inclusion Criteria

Children who:

1. Live within the specified geographic area.
2. Have a nominated primary care practitioner who practices within the study area.
3. Aged 6 weeks to 15 years.

Exclusion Criteria

Children who:

1. Live out of the specified study area.
2. For whom we were unable to find a nominated primary care practitioner despite reviewing the clinical notes, electronic discharge summaries, and Clinical Management Systems.
3. Infants less than 6 weeks of age in view of the likelihood of different microbiological organisms in this age group.

5.2.2.3 Participant Population (individuals actually enrolled)

Participants therefore fulfilled the following criteria:

- Lived in the specified geographic area
- Had a nominated primary care practitioner who practiced within the geographic area
- Were 6 weeks to 15 years of age
- Were either admitted to Starship Children's Hospital with cellulitis (Hospital case), successfully treated in primary care by a nominated GP (GP case), or were randomly selected from a nominated GP practice register (GP control)
- Consented to be enrolled in the study
- Were successfully interviewed.

5.2.2.4 Hospital Cases

Hospital cases included all eligible children admitted to Starship Children's Hospital with a case definition of cellulitis during the study period. As per the eligibility criteria, for the cases to be comparable to the controls they had to live within the study area, have had a nominated GP who practiced within the study area and be known by that GP. Cases were identified by the hospital co-ordinator after discussion with the nursing staff during daily visits to the medical and surgical wards.

During the time period, 495 children were identified by the study coordinator on the hospital wards as being potentially eligible for the study. We purposefully asked for names of any child the ward staff thought might be eligible acknowledging there would be a modest high false positive rate, but a corresponding low true negative rate. Three hundred and fifteen of these met all eligibility criteria. Exclusions included not meeting the study definition of cellulitis (46), child not in the study area (120), GP not in the study area (3), incorrect age (1), and duplicate admission (10). All children had a nominated GP.

The eligible population was therefore 315 children. Of these, 286 were asked by their primary nurse about participation in the study and 252 agreed to meet the study coordinator (88% agreement). Two hundred and thirty five agreed to participate in the study (93% agreement). Eight families were unable to be interviewed despite multiple contacts leaving 227 as the participant population (Figure 8). This constituted a response rate of 72% and participation rates of 79% of the eligible approached for the study or 90% of the eligible population who agreed to talk to the study coordinator (gave first stage consent). No family withdrew part way through the interview.

Figure 8: Recruitment of Hospital Cases

5.2.2.5 GP Cases and Controls

GP cases and GP controls were selected utilising a cluster sampling methodology based on geographic area of GP practice. As GP cases were expected to be more prevalent than Hospital cases, recruitment of GP controls and GP cases was done at a rate to correspond to the anticipated rate of hospital cellulitis discharges using data from two previous years (1998-99). GPs were asked to collect cases during specified collection periods assigned during the year designed to achieve recruitment according to the rate as above.

5.2.2.5.1 GP Participation

As there was no single database of eligible GPs, one was created using the methodology outlined in the methods section (Chapter 4.4.3.5). General Practitioners were eligible if they lived within the area, saw children in their practice and were part of a primary care practice. The initial list

contained 854 potentially eligible GPs. Two hundred and eight were excluded as they did not see children, no longer worked at that practice, were on leave (sabbatical or maternity leave), worked solely in an after-hours accident and medical centre, or were identified as medical specialists rather than general practitioners. This left 646 eligible GPs.

As per sampling methodology, 452 eligible GPs were approached to provide the GP cases. Fifty-seven GPs declined, and 397 GPs agreed thus resulting in an 87.4% participation rate for GPs for recruitment of cases. No GP withdrew during their collection period.

Three hundred and sixty-three eligible GPs were approached to provide 693 controls. Twelve GPs declined, and 351 GPs agreed thus resulting in a 96.7% participation rate for GPs for recruitment of controls. Six GPs agreed and provided at least one control but subsequently withdrew before their allocation of controls was complete.

5.2.2.5.2 GP Cases

GP cases were sampled by broad geographic area of GP practice as above identifying the GP as the unit of sampling. The selected GP was asked to identify children with cellulitis seen during their allocated collection period. Eligible children were all paediatric patients who were between 6 weeks and 15 years of age on the GPs patient register who lived within the study area and presented with skin sepsis which met the clinical definition of cellulitis as outlined in the study protocol.

There were 853 collection periods among 397 GPs. Five hundred and twenty-seven GP collection periods resulted in no eligible cases referred, 76 resulted in one case, 30 in two cases, and 15 resulted in more than 2 cases referred. Tracking sheets of the total number of children seen by that GP during that time period were received for 646 collection periods (return rate of 76%). There were limited data regarding ethnicity and DOB of children seen and almost all related to the children referred. A greater number of referral faxes was received (200) than reported number of children seen (155), highlighting the fact that data collection was not complete. GPs anecdotally reported high participation rates; however, there were almost no data available regarding children whose parents did not consent to have contact with the study coordinator. No information was therefore available re the participation and nonparticipation rates in the GP practice, nor whether the participants were representative of the children seen.

During the study enrolment period, 200 children were identified by GPs as being potentially eligible for the study and agreed to contact by the study team (first stage consent). One hundred and eighty two of these met all eligibility criteria. Exclusions included not meeting the study definition of cellulitis (1), requiring hospitalisation thus becoming a hospital case (5), child not in the study area (8), error as child a control case (2), and incorrect age (1).

The eligible population was therefore 182 children. Thirty families were unable to be contacted, thus 152 were approached for second stage consent. Sixteen families declined to be part of the study leaving 136 as the participant population (Figure 9). This constituted a response rate of 75% and a participation rate of 89.5%. Limited data were available regarding the nonparticipants. No family withdrew part way through the interview.

GP cases included only those children successfully treated in primary care: i.e. those children whose cellulitis resolved with treatment provided by their primary care practitioner. Those children who subsequently required hospitalisation with cellulitis became hospital cases. During this time period, 5 cases became Hospital cases: 3.7% overall.

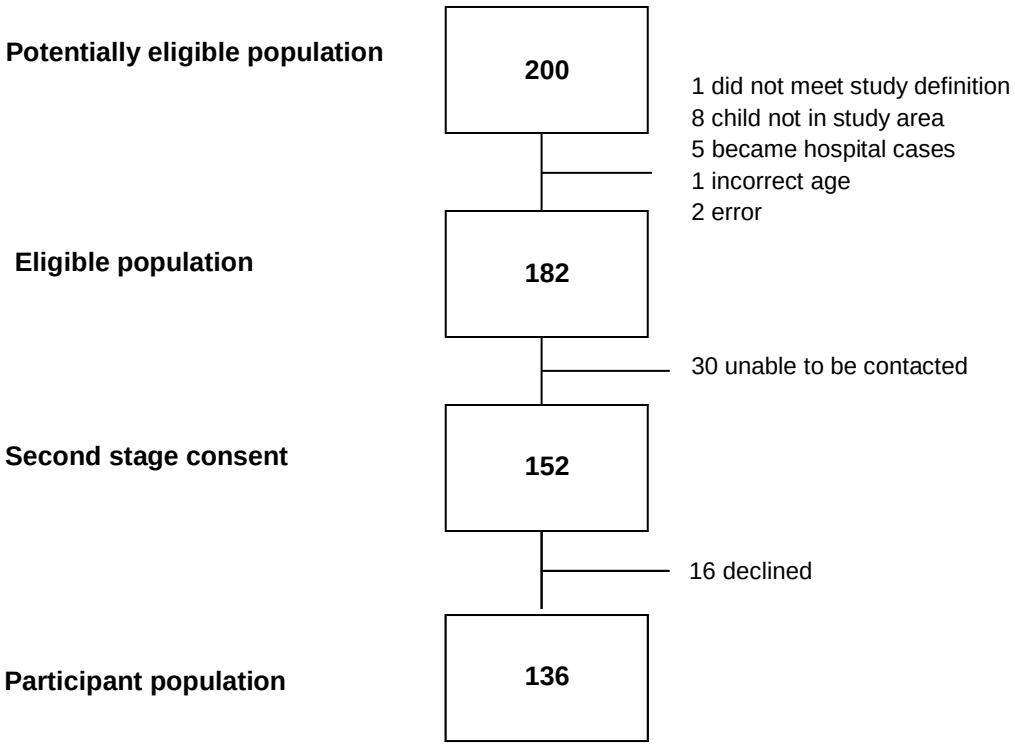

Figure 9: Recruitment of GP Cases

5.2.2.5.3 GP Controls

GP controls were sampled using the GP as the sampling unit as described above. The selected GP was visited and the controls randomly selected from all paediatric patients who were between 6 weeks and 15 years of age on the GPs patient register. Children were eligible if they lived within the study area and were on the active list of the practice (i.e. had been seen within the last year). A random number list, generated from an excel spread sheet, was used to select the control child/children from the list.

There were a total of 693 approaches to 357 GPs for enrolment of controls. Twenty-six approaches were declined (12 GPs) leaving 667 potential controls extracted from recruited GP practices. Families were successfully contacted for 564 children, of which 456 consented to be contacted by the study coordinator (response rate 81%).

During the time period, 456 children were identified by GPs as being potentially eligible for the study. Four hundred and forty two of these met all eligibility criteria. Exclusions included child not in study area (9), duplicate (1), requiring hospitalisation thus becoming a hospital case (1), error as child a GP case (1), error as family had declined 1st stage consent (1), and incorrect age (1).

The eligible population was therefore 442 children. Eighteen families were unable to be contacted thus 424 were approached for second stage consent. Twenty-six families declined to be part of the study leaving 398 as the participant population (

Figure 10). This constituted a response rate of 90% and a participation rate of 94%. No family withdrew part way through the interview.

Because of the sampling process used there were limited data available on those who did not agree to take part and we were unable to compare the participant population with the nonparticipant population

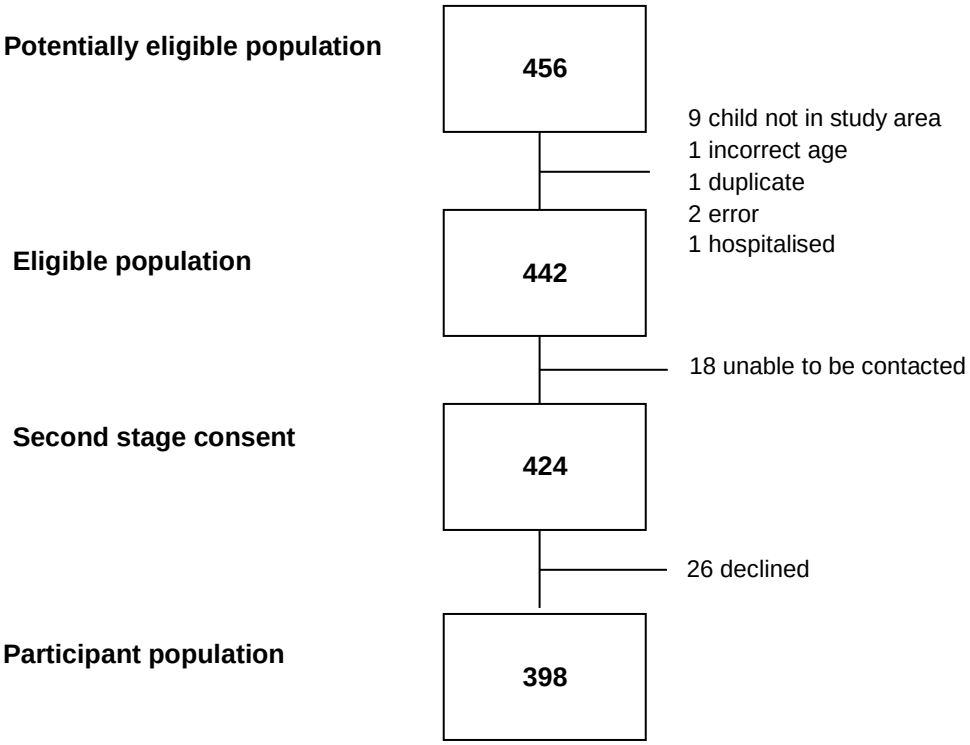

Figure 10: Recruitment of GP Controls

5.2.2.6 Health Professional Questionnaire

The first GP the child saw for their episode of skin sepsis was sent a fax outlining the study and asking them to complete a structured questionnaire of the healthcare provided to the child.

A completed questionnaire was returned to the study centre for 132 of 147 GP cases (91% response rate) and 167 of 227 Hospital cases (74% response rate).

5.2.3 Sampling Modification

The number of GPs required to recruit our desired sample size was estimated using the previous hospital discharge frequency for each geographic area, an estimated number of cases seen in primary care each week (according to a brief survey of GPs prior to study commencement), and an estimated participation rate of 75% from a previous Department of Paediatrics research project with similar recruitment strategy. Initial calculations required 1000 GP control visits and 280 GP case visits.

After 4 weeks of the study, 16 GPs had been allocated collection periods; however, only 1 GP case had been referred through. Potential reasons for the low referral rate included GPs not seeing many cases, forgetting to refer cases through, or a low first stage consent from families. Initial discussions with participating GPs reported high family acceptance of the project, and first stage consent, but low numbers of cases being seen during that time period. The research group considered recruitment strategies and extended the collection period from 2 weeks to 3. As at 1st august, we amended the sampling frame to increase both the number of GPs we sampled and the duration of collection period (calculated 1000 GP controls and 1000 GP cases visits). The final sample thus contained 32 GPs with 2 week collection periods and 819 with 3 week collection periods. This sampling modification was taken into account in the sample weighting.

5.3 Participant Population

The participant population comprised 768 children in total: 227 Hospital cases, 145 GP cases and 395 Controls (Figure 11).

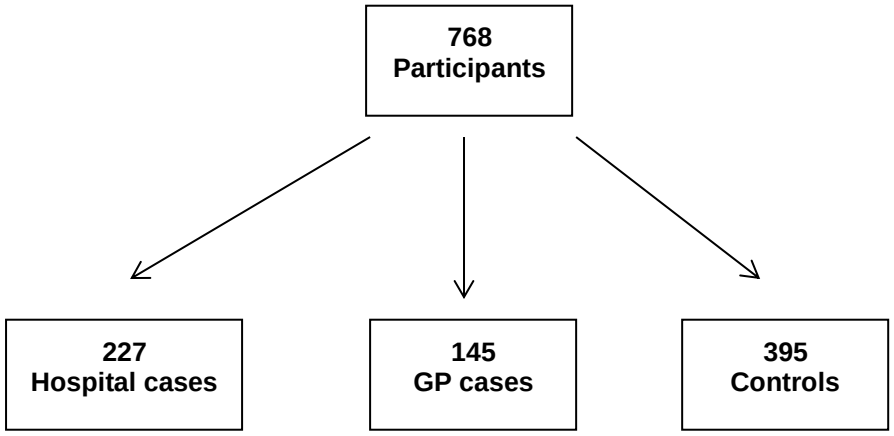

Figure 11: Participant Population

Participants were spread across the eight geographic areas (Table 10).

Ethnicity, age and socioeconomic distributions are outlined for each participant group in Table 11. As the case and control groups are different for the risk factors cellulitis and risk factors for hospitalisation with cellulitis, the case and control groups for each of these analyses are described in more detail at the beginning of the appropriate chapters.

5.3.1 Data Completeness

5.3.1.1 Caregiver Questionnaire

A caregiver questionnaire was completed for all participants. There were no missing data for the key demographic variables (age, gender, ethnicity, and socioeconomic status). There was less than 5% missing data for the remaining variables. The frequency of missing data is outlined at the base of each table.

5.3.1.2 Clinical Information

Clinical information was completed for all participants. We were unable to measure the height or length for some children due to the child's lack of compliance. This is noted as missing data at the base of each table.

5.3.1.3 Health Professional Questionnaire

A completed health professional questionnaire was returned to the study centre for 132 of 147 GP cases (91% response rate) and 167 of 227 Hospital cases (74% response rate). The frequency of missing data is outlined at the base of the each table.

5.4 Conclusion

This chapter describes the characteristics of the study population and includes information about response rates and participation rates. It reports preliminary demographic data about the participants for each of the groups: Hospital cases, GP cases, and GP controls.

Chapter 6: Risk Factors for Developing Cellulitis

6.1 Introduction

This chapter describes the characteristics of the study population and reports the risk factors for developing cellulitis. Findings are presented initially as univariate factors, and followed by multivariate analyses. The chapter finishes with a summary figure of the key findings as they relate to each of the areas examined.

6.2 Characteristics of Study Population

Risk factors for developing cellulitis were explored comparing the cellulitis cases (GP cases n=145, and Hospital cases n=227) with the Controls (n=396). Hospital cases were combined with the GP cases using a weighted sampling methodology described in the methods (section 4.6.2). The numbers presented are therefore weighted counts (N*), and not individually or collectively whole numbers. The frequency of missing data is reported in the footnote of each table.

6.3 Univariate Risk Factors

6.3.1 Demographic Characteristics

Cases and controls were different with respect to demographic composition with cases more likely to be of Māori and Pacific ethnicity ($p<0.001$), and in the school-age group ($p<0.001$) (Table 12). Overall, Māori infants and children were 4.3 times more likely to develop cellulitis than New Zealand European and Other children (2.6-7.2), and Pacific children 6.6 times more likely (3.9-11). Infants less than one year of age were significantly less likely to develop cellulitis than school-age children (OR 0.15, 0.1-0.3). Preschool children were 30% less likely to develop cellulitis than school-age children; however, this did not quite reach statistical significance (OR 0.69, 0.5-1.0). The proportion of males was higher for cases than controls (60.1% vs. 52.3%), but this was not significantly different.

6.3.2 Host Factors/Characteristics

Several host factors were examined but were not found to be associated with risk of developing cellulitis.

6.3.2.1 Perinatal History

Case children were no more likely to be low birth weight than control children (p=0.37). Five percent of case children and 10% of control children were born prematurely (Table 14). Children born prematurely had half the risk of developing cellulitis compared to term infants, however, this did not reach statistical significance (OR 0.5, 0.25-1.02; p=0.058).

Case and control children were equally likely to have been breast fed (p=0.25). There was no difference between cases and controls in the proportion of children who had formula introduced before four months or those with formula introduced after six months (Table 14).

6.3.2.2 Health Status

Almost all children were reported to be in good, very good, or excellent health in the previous six months with no difference between the two groups (Table 15). Children whose health status was reported as 'poor' or 'not very good' were not at increased risk of developing cellulitis (OR 1.5, 0.6-4.0).

Health problems were reported for approximately a third of all study participants: 28% of cases and 35% of controls (Table 15). Children with identified health problems appeared to be at slightly lower risk of developing cellulitis, however, this did not reach statistical significance (OR 0.73, 0.50-1.1). Reported health problems included asthma, eczema, recurrent ear infections/OME, allergies and developmental delay.

6.3.2.3 Clinical Assessment

Infants and children had their height and weight performed and BMI calculated. Cases were less likely than controls to be within the normal weight range (p=0.003). Obese children (BMI z score > 2SD) were twice as likely (OR 2.0, 1.3-3.1) and thin children (BMI z score < -2SD) 2.9 times as likely (0.7-11.6) to develop cellulitis than children of normal weight (Table 16). Clinical signs of eczema were assessed using a standardised eczema assessment tool at the time of the interview.[144] Eczema was identified in similar rates across the cases and controls (12 vs. 13%, p=0.64). Children with clinical signs of eczema were not at increased risk of developing cellulitis (Table 16).

6.3.3 Exposures/Breaches of Skin

6.3.3.1 Frequency

In order to assess whether breaches of the skin were associated with the development of cellulitis, caregivers were asked whether their child had a minor injury or breach to their skin in the week prior to the interview or development of the cellulitis. Such breaches were common among all children. Approximately three quarters of all children had some breach of the skin or minor injury reported in the week prior to being interviewed. The most common injuries were cuts or scratches (34%), insect bites (30%), nappy rash (22% of those who wore nappies), a bruise (22%), other skin problem (15%) and eczema (14%). Splinters (6%), animal or human bites (4%) and chicken pox (0.9%) were less common. Cases and controls had similar overall rates of breaches of the skin, however, the frequency of specific breaches varied between the groups (Table 17).

Children with insect bites in the preceding week were 2.7 times more likely to develop cellulitis than children with no reported insect bites (1.8-4). There was a dose response with the higher the number of bites, the greater the risk of cellulitis (Table 18). Children who scratched their bites until they bled or wept were almost three times more likely to develop cellulitis than those that did not. More than 75% of bites were attributed to mosquitos and a smaller percentage to fleas (Table 19). There was no difference in type of insect bites between the groups.

Children with a cut or scratch were at reduced risk of developing cellulitis ($p=0.008$). Cuts in the cases were longer (19.6 vs. 16.8 mm, $p<0.001$) and deeper (2.2 vs. 1.8 mm, $p<0.001$) than the controls. Twenty-three percent of cuts in cases were contaminated by soil or dirt compared to 28% controls ($p=0.5$).

Bruises were reported to occur less frequently among cases than controls (Table 17, $p=0.02$). As a bruise may not result in a breach of the skin per se, another variable was created looking at any injury that resulted in a breach of the skin (insect bite, cut/scratch/bite, chicken pox, nappy rash, splinter, eczema, other skin problem). Such a breach was not associated with an increased risk of cellulitis.

There was no significant difference in frequency of eczema among cases and controls. Twenty-one percent of cases reported eczema in the last year compared to 28% of controls ($p=0.07$). Thirteen percent of cases reported eczema in the preceding week compared to 16% of controls ($p=0.34$). There was no difference in severity of eczema when measured by how often the baby/child had been kept awake at night by their eczema in the previous 12 months ($p=0.18$). However, when severity was examined by the frequency with which it resulted in the child

scratching until it bled or wept in the week prior to the interview, affected children were three times more likely to develop cellulitis than those that did not (Table 20).

'Other skin problems' reported in the previous week included a mix of conditions such as school sores, boils, coral cut and scabies. Each of these was reported in fewer than 5 children in both the case and control groups.

6.3.3.2 Household Pets

Forty-seven percent of cases had a household pet compared to 67% of controls. Houses with a pet were at lower risk of developing cellulitis than those without one (Table 21, OR 0.44, 0.29-0.65)

6.3.4 Host Behaviours

6.3.4.1 Hand Washing

Parents were asked a series of questions relating to their child's hand washing habits. Seventy-one percent of cases usually washed their hands on their own compared to 61% of controls (p=0.02) (Table 22). Infants and children who were too young to wash their hands without help (either supervised or on their own) were at reduced risk of developing cellulitis.

Among both case and control children who were considered old enough to wash their own hands, there were similar proportions of children who needed frequent reminders (Table 23, p=0.61). Both cases and controls were also similar with the proportion of children that 'always or usually' washed their hands before eating, after eating, after playing outside, after handling a pet, and if visibly dirty. Fewer case children 'always or usually' washed their hands after going to the toilet. Children who 'sometimes, rarely or never washed' their hands after going to the toilet were more than twice as likely to develop cellulitis as children who 'always or usually' washed their hands (Table 24).

Hand washing at home was done under running water and using different forms of soap (Table 24). There were no differences in temperature of water or different types of soap used, although children who used shared family soap were at greater risk of developing cellulitis than those who used liquid soap.

Most children used shared or family hand or bath towels to dry their hands, however, more case children used nothing or their clothes (Table 24, p=0.009). Such children were 6 times more likely to develop cellulitis than those than used a personal towel to dry their hands.

6.3.4.2 Bathing Practices

Similar proportions of children bathed or showered with no association with developing cellulitis (Table 25). Both case and control children bathed an average of six times each week and had their hair washed an average of four times each week. Washing less than daily was not associated with an increased risk of developing cellulitis. Sharing bathwater was not associated with an increased risk of cellulitis (p=0.15). Over three quarters of families reported their child used their own personal bath towel as opposed to sharing a family towel (77% of cases vs. 81% of controls). Forty-two percent of cases reported the towels were washed after a single use compared to 30% of controls. Families who did not wash their towels after every use had a lower risk of developing cellulitis (p=0.01).

6.3.4.3 Clothes Washing Practices

Fewer households among case children had automatic washing machines than controls (Table 26, p=0.006). Living in a house without an automatic washing machine was associated with five times the risk of cellulitis. Approximately two-thirds of families washed their clothes in cold water. The clothes washing temperature did not affect the risk of cellulitis (p=0.08).

6.3.5 Previous Cellulitis and Skin Sepsis

Previous episodes of cellulitis were more common among cases, other children in the household, as well as adults in the household (Table 28). Overall, more than 54% of cases had at least one family member with a past history of cellulitis compared to almost 16% of controls (p<0.001). A previous history of cellulitis in any household member increased the risk of developing cellulitis six fold.

Children with a previous history of cellulitis were nine times more likely to develop cellulitis than those without (OR 9.0, 4.9-16.7). There was a dose response with the greater the number of previous episodes, the greater the risk of cellulitis (Table 29). Children who had cellulitis in the previous 3 months were almost 10 times more likely to develop cellulitis than those who had never had cellulitis (Table 30). An elevated risk remained even if the most recent episode was more distant, with children who had cellulitis more than 3 months prior to the interview having 7 times the risk of cellulitis than those with no prior episode (2.9-16.8).

Eight case children and 2 control children had other children in the household who had cellulitis at the time of the interview. Thirty-four case and 7 control children had other children in the house that had cellulitis at the time of the interview or within the previous month. This increased the risk of developing cellulitis 7 fold (OR 7.5, 2.97-19.02).

Families were asked about previous episodes of other skin infection such as boils or impetigo. Other skin sepsis was more frequent among cases; 37% of cases vs. 22% of controls (Table 31). A history of other skin sepsis increased the risk of cellulitis two fold (OR 2.04, 1.38-3.01). A history of skin sepsis in another child in the house also increased the risk of cellulitis (OR 1.81, 1.23-2.65). No association between other forms of skin sepsis and cellulitis was seen for the adults in the house (p=0.98).

6.3.6 Socioeconomic and Environmental Factors

6.3.6.1 Socioeconomic Status

The effect of socioeconomic status was examined by two different measures: that defined by the social deprivation score of the mesh block (NZDep Index)[137] and that defined by the most recent occupation of the mother and father.[138]

The proportion of cases and controls in each of the social deprivation quintiles is noted in Table 32. There was a different distribution of socioeconomic status with approximately half the cases being in the highest two quintiles (most deprived) compared to 27% of the controls (p<0.001). Children in the most deprived quintiles (4-5) were 2.4 times more likely to develop cellulitis than those in the least deprived quintiles (1-3)(1.6-3.6). There was a dose response for deprivation with the more deprived the household the higher the risk of cellulitis (Table 32).

Questions were asked re the current or last job of both mother and father as per the NZ Standard Classification of Occupations (1999).[138] In view of a significant amount of missing data and uncertainty regarding the responses, this was not a reliable measure of socioeconomic status and was not reported further.

Sixty percent of cases had mothers with a current community services card compared with 27% of controls (Table 32, p<0.001). Children of women with a community services card were 2.8 times more likely to develop cellulitis than those without (1.9-4.2).

6.3.6.2 Maternal Characteristics

Mothers were an average of 36.2 years at the time of the interview, with case mothers slightly younger (35.2 years) compared to control mothers (37.2 years). Children of mothers 35 years or older at interview were less likely to develop cellulitis than those of mothers 20-34 years of age (OR 0.55, 0.36-0.83) (Table 33). Maternal age at the birth of the child was not associated with the risk of developing cellulitis (p=0.18).

There was no difference between cases and controls in the proportion whose mothers were New Zealand born (66% cases and 62% controls, p=0.42) or in those who had immigrated to New Zealand in the last 10 years (14% vs. 12%, p 0.49). A higher proportion of case mothers, however, spoke English as a second language (ESOL) (30% vs. 17%, p=0.003). Children of mothers who spoke a language other than English as their first language were 2.1 times more likely to develop cellulitis than those that did not (1.3-3.4).

Maternal educational attainment varied across the groups with mothers of cases having lower rates of formal educational qualifications than mothers of control children (Table 33, p<0.001). Children of mothers without formal qualifications were more than twice as likely to develop cellulitis as those with such qualifications (OR 2.7, 1.7-4.3).

6.3.6.3 Household Composition

Most children lived in nuclear families; however, there was a greater number of children from single parent or extended families or whānau among children with cellulitis (Table 34, p=0.002). Children living in single parent or extended whānau households were twice as likely to develop cellulitis as those in two parent households.

6.3.6.4 Household Characteristics

Caregivers were asked to specify whether they lived in a house/townhouse, flat/unit, or other type of dwelling. Almost all families lived in houses, townhouses, or apartments with only 5% cases and 4% of controls living in other environments (including flat, unit, caravan, garage, and boarding house) (Table 35, p=0.53). Living in another environment was not associated with an increased risk of cellulitis.

Overall, 67% of families owned their own home, however, significantly fewer cases lived in their own homes than controls (49% vs. 72%, p<0.001). Children living in rental property were at greater risk of developing cellulitis than those in their own homes, with the risk being greater for those in Housing New Zealand rental properties than private rental (Table 35).

Household mobility had no effect on the risk of cellulitis with rates of those that moved in the previous two years the same for both cases (33%) and controls (31%, p=0.69). Neither moving house nor moving two or more times within the last two years were associated with an increased risk of cellulitis.

Almost all families had access to a phone, although cases were more likely to either have no phone or rely on mobile phones compared to controls (6% case vs. 3% controls, p=0.03). Families with no landline were 2.5 times more likely to have a child with cellulitis (1.1-6.0).

6.3.6.5 Household Crowding

The number of people living in the houses varied widely for both cases and controls (range 2-15). There were more people living in the houses of children with cellulitis compared to controls with the average number of household members being 5.1 for cases and 4.5 for controls ($p<0.001$). Thirty-four percent of cases and 17% of controls lived in houses with 6 or more people (Table 36, $p<0.001$). Such households were 2.5 times more likely to develop cellulitis (1.7-3.8). Although the average number of adults in the households were similar (2.5 for cases and 2.4 for controls), there were more children in the houses of cases: 2.7 vs. 2.1 ($p<0.001$).

There was a dose response with the higher number of people in the house the greater the risk of cellulitis (Table 36). The increased risk was attributable to the number of children rather than the number of adults in the house.

There was no difference in the number of bedrooms between cases and controls (3.5 vs. 3.4), however, the higher household occupancy meant there was a significantly higher bedroom occupancy rate ($p<0.001$). Fourteen percent of cases and 4% of controls lived in houses with more than two people per bedroom (Table 37, $p<0.001$). Such children were 3.6 times more likely to develop cellulitis. There was a dose response with higher bedroom occupancy resulting in higher risk of cellulitis. Households with more than five people per toilet were three times more likely to develop cellulitis than those with lower toilet occupancy.

Over half of case children and one third of controls shared a bedroom with another person ($p<0.001$). Sharing a bedroom was associated with a 2.6 times risk of developing cellulitis (1.8-3.7).

Twenty-four percent of cases and 9% of controls were reported to share a bed with another child or person (Table 37, $p<0.001$). Sharing a bed was associated with a 2.4 times greater risk of developing cellulitis (1.5-4.0).

Overall, across a range of different crowding measures, infants and children living in crowded houses were significantly more likely to develop cellulitis than those who did not.

6.3.6.6 Exposure to Household Smoking

Children with cellulitis were more likely to live with smokers. A greater proportion of cases had mothers, fathers or household members who smoked (Table 39). There was a dose response with the greater the number of household smokers, the greater the risk of cellulitis ($p<0.001$).

6.3.7 Health Literacy and Healthcare Utilisation

6.3.7.1 Health Literacy

In order to assess whether the first aid management of breaches of the skin was associated with the development of cellulitis, caregivers were asked questions regarding their initial management of minor injuries or breaches to their child's skin in the week prior to the interview or development of the cellulitis. This informs part of the understanding of health literacy; people's knowledge and expectations about normal skin health, as well as their understanding about when and what first aid treatment to undertake for breaches of the skin.

Insect bites: Slightly more than half the families reported administering some initial first aid management when they first noticed insect bites on their child: most commonly cleaning with water or soapy water, or applying anti-itch cream (Table 40). Use of traditional or alternative therapy was associated with a more than four times increased risk of developing cellulitis. Therapies included homeopathic remedy, ti tree oil, lavender oil, poultice and vinegar but no one therapy predominated. Use of antihistamine tablets and pain relief were also associated with an increased risk of cellulitis, however, these did not reach statistical significance. There was no reported difference between the cases and controls in the timing of how soon the first aid was administered (Table 41).

Cuts and scratches: Approximately 2/3rds of the caregivers reported administering some initial first aid management when they noted a cut or scratch on their child: most commonly cleaning with water or soapy water, or covering it (Table 42). Cleansing occurred more frequently in the controls with an almost 50% reduction in risk of cellulitis, however, did not reach statistical significance. Covering the cut with a Band-Aid or sticking plaster had no effect on the risk of cellulitis. There was no reported difference between the cases and controls in the timing of how soon the first aid was administered (Table 43). Eight percent of cases and 3% of controls sought medical advice for the injury when it first happened (p=0.11).

Eczema: Baseline management of eczema was slightly different between cases and controls (Table 44). While there was no significant difference in whether the caregiver usually used steroid cream or ointment (p=0.26), cases were less likely to usually use moisturiser (0.05). Twenty-one percent of cases used moisturiser 2 or more times a day in the previous week compared to 47% of the controls (p=0.27). Although this is not a statistically significant difference, it is a clinically significant one and has important implications re prevention. In addition, contrary to the controls and the recommended best practice re eczema management, cases used steroid cream more

often than moisturiser. Although it did not reach statistical significance, there was a clinically significant difference in the use of soap substitute (43% of cases vs. 60% controls, p=0.12).

6.3.7.2 Usual Healthcare Utilisation

Most children had a single GP, doctor or practice for the majority of the child's usual healthcare visits (Table 45). Nine percent of cases and 7% of controls reported seeing one of several different GPs in different practices, whoever was available, or after-hours services for usual health care provision for their child. Children who did so were at no greater risk of developing cellulitis than those who saw their usual healthcare provider or practice (OR 1.4, 0.71-2.6).

In the six months prior to the illness or the interview, both cases and controls had similar use of healthcare providers and services (Table 46). The types of healthcare services and the frequency with which they were used were similar for both groups. As the question asked about the number of visits over the preceding six months, it did not differentiate between acute illness, clinical review, or anticipatory guidance visits. Children of caregivers who reported difficulties accessing a doctor on their last visit were more likely to develop cellulitis than those who did not (OR 2.84, 1.51—5.34, Table 47)

6.4 Multivariate Risk Factors

Ethnicity, age and NZ deprivation index score were significant risk factors and were distributed differently across cases and controls. These three factors were therefore used in a multivariate model to examine risk factors for developing cellulitis.

6.4.1 Demographic Characteristics

After adjustment for NZ deprivation score and age, Māori and Pacific children were significantly more likely to develop cellulitis than NZ European/Other children (Table 12). Overall, Māori infants and children were 4 times more likely to develop cellulitis than New Zealand European and Other children (2.3-7.0), and Pacific children 6 times more likely (3.4-10.9).

In view of the persisting effect of ethnicity, further multivariate models were developed to explore whether this could be explained by confounding from other variables such as household crowding, maternal education, a range of socioeconomic factors, and barriers to accessing healthcare (Table 13). As insect bites and a previous history to cellulitis were also strongly associated with cellulitis, a subsequent multivariate model included these factors as well as the socioeconomic and healthcare factors. Whilst reduced slightly, ethnicity remained a significant risk factor after adjusting for age NZDep, sharing bedroom, maternal education, difficulty accessing healthcare, maternal CSC, household smoking, insect bite in the previous week,

previous cellulitis and identified health problems, with Pacific having almost 3.5 times the risk and Māori 2.6 times the risk of developing cellulitis than other New Zealand children (Table 13).

After adjustment for NZ deprivation score and ethnicity, infants less than one year of age were significantly less likely to develop cellulitis than school-age children (aOR 0.13, 0.05-0.33), as were preschool children (aOR 0.53, 0.34-0.82).

Boys were 50% more likely to develop cellulitis than girls (aOR 1.5, 1.0-2.3).

6.4.2 Host Factors/Characteristics

Several host factors were examined in the multivariate model and most were found to not be associated with risk of developing cellulitis. These included perinatal factors such as LBW, prematurity, never being breastfed, and age of introduction of formula as well as current health status, BMI and clinical signs of eczema (Table 14, Table 15, Table 16).

Children with identified health problems were 40% less likely to develop cellulitis than those without (aOR 0.61, 0.39-0.94).

6.4.3 Exposures/Breaches of Skin

With the exception of insect bites, no particular breach of skin in the previous week was associated with the development of cellulitis. Children with insect bites in the preceding week were 2.5 times more likely to develop cellulitis (1.5-3.9). There was a dose response with the higher the number of bites, the greater the risk of cellulitis (Table 18). Children who scratched their bites until they bled or wept were almost three times more likely to develop cellulitis than those that did not.

The presence of eczema and the frequency with which it kept the child awake at night were not associated with cellulitis; however, children who scratched their eczema until it bled were 4 times more likely to develop cellulitis than those who did not (Table 20).

Children with a household pet were at lower risk of developing cellulitis than those without (Table 21, aOR 0.59, 0.37-0.93).

6.4.4 Host Behaviours

Hand washing habits were not associated with a risk of cellulitis (Table 24). There was an association with different hand drying habits with children who used nothing or their clothes to dry their hands at over 3 times the risk of developing cellulitis than those who used their own personal towel (aOR 3.50, 1.14-10.75).

Bathing and clothes washing practices were not associated with a risk of cellulitis. Families who did not wash their towels after every use had a lower risk of developing cellulitis (p=0.03).

As host behaviours could have been modified by previous family history of cellulitis, some variables were examined according to whether any family member had a prior history of cellulitis. For the most part, host behaviours as a risk factor for developing cellulitis did not vary widely whether cellulitis had been reported within the preceding 3 months, greater than or equal to 3 months prior, or never recorded in any family member (Table 27).

6.4.5 Previous Cellulitis and Skin Sepsis

Previous episodes of cellulitis were more common among cases, other children in the household, as well as adults in the household (Table 28). A previous history of cellulitis in any household member increased the risk of developing cellulitis fivefold.

Children with a previous history of cellulitis were almost seven times more likely to develop cellulitis than those without (aOR 6.7, 3.4-13.5). There was a dose response with the greater the number of previous episodes, the greater the risk of cellulitis (Table 29). There was also a dose response with respect to the timing of the previous cellulitis. Children who had cellulitis in the preceding month were nine times more likely to develop cellulitis than those who had never had an episode (Table 30).

6.4.6 Socioeconomic and Environmental Factors

6.4.6.1 Socioeconomic Status

Ethnicity was significantly associated with socioeconomic deprivation. Once ethnicity and age were in the multivariate model, deprivation as defined by the social deprivation score of the mesh block (NZDep Index)[137] was no longer associated with the risk of cellulitis. As our sampling frame was by GP practice this in part matched for socioeconomic status as assessed from the residential address, and thus precludes our examination of socioeconomic status. Children of women with a community services card where 1.6 times more likely to develop cellulitis than those without (1.0-2.6) (Table 32).

6.4.6.2 Maternal Characteristics

Maternal characteristics such as age at birth, being NZ born, a recent immigrant, ESOL, and maternal education were not associated with an increased risk of cellulitis in the multivariate model. Children of mothers 35 years or older at interview continued to be less likely to develop cellulitis than children of mothers 20-34 years of age (aOR 0.5, 0.3-0.8) (Table 33).

6.4.6.3 Household Composition and Characteristics

Although several household factors were associated with cellulitis in the univariate model, household composition, housing ownership and lack of a land line were no longer associated with cellulitis after controlling for ethnicity, age and deprivation (Table 34).

6.4.6.4 Household Crowding

Across a range of different crowding measures, infants and children living in crowded houses were significantly more likely in the univariate analysis to develop cellulitis than those who did not. However, once ethnicity, age and deprivation were in the model, most of these factors lost their effect (Table 37). Children who lived in houses with other children and those who shared a bedroom continued to be at increased risk of developing cellulitis. Sharing a bedroom was associated with a 1.8 times risk of developing cellulitis (1.2-2.7). As the NZDep index has a small area population measure of crowding in it, crowding measures were also examined adjusting for ethnicity and age alone (Table 38). The adjusted ORs remained virtually unchanged.

6.4.6.5 Exposure to Household Smoking

Exposure to cigarette smoking continued to be associated with an increased risk of cellulitis with children living with smokers 1.7 times more likely to develop cellulitis than those who did not (Table 39).

6.4.7 Health Literacy and Healthcare Utilisation

There was no association between health literacy as defined by first aid management of breaches of the skin and the development of cellulitis. The use of several different GPs in different practices, whoever they could get into, or after-hours services rather than a single GP or practice for usual healthcare provision was not associated with an increased risk of cellulitis. Both cases and controls had similar use of healthcare providers and services in the six months prior to the illness or the interview (Table 46). Children of caregivers who reported difficulties accessing a doctor on their last visit were more likely to develop cellulitis than those who did not (aOR 2.39, 1.12—5.11)

6.5 Conclusion

The risk factors for cellulitis include a range of demographic, exposures, socioeconomic, and environmental factors. Health literacy factors do not have an important role in the development of cellulitis; however, children living in families who report difficulties accessing their family doctor are at increased risk of developing cellulitis. Those factors that persist after adjustment for

ethnicity, socioeconomic status, and age have been summarised in the following pathway to development of cellulitis (Figure 12) and summarised in a table in the appendix (Table 48).

Demographic Factors

↑↑ Māori ethnicity
↑↑↑ Pacific ethnicity

↓↓ Infant
↓ Preschool child

↑ Male gender

Host Susceptibility

↓ Identified health problems

Exposures/Breaches of the skin

↑ Insect bites in preceding week

↑ 1-5 insect bites in previous week
↑ 6-9 insect bites
↑↑↑ ≥10 insect bites

Host Behaviours

↑ Scratching insect bites til bled
↑ Scratching eczema til bled
↓ Washing towels less frequently

Past History of Skin Sepsis

↑↑↑ Phx cellulitis index child
↑↑ Phx cellulitis other child
↑ Phx cellulitis adult in household

↑↑ 1 previous episode of cellulitis
↑↑↑ 2 or more previous episodes cellulitis

↑↑↑ Hx cellulitis in previous month in index child
↑↑↑ Hx cellulitis 1-3 months prior in index child
↑↑ Hx cellulitis >3 months prior in index child

Social/Environment

↑ Maternal CSC
↑ # children in the household
↑ Sharing a bedroom
↑ Household smoking

Health Literacy/Healthcare Factors

↑ Difficulties accessing healthcare

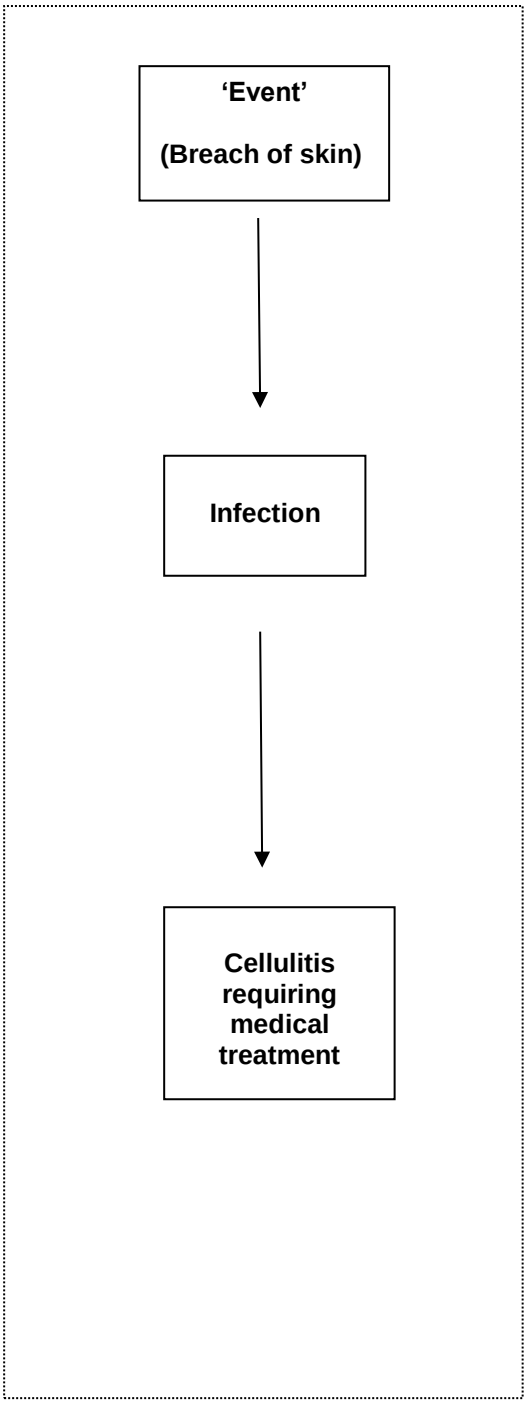

Figure 12: Identified Risk Factors in the Pathway for the Development of Cellulitis

↑=1-3 times increased risk
↑↑=3-6 times increased risk
↑↑↑=6 or more times increased risk
↓=0-30% decreased risk
↓↓=30-60% decreased risk

Chapter 7: Risk Factors for Hospitalisation with Cellulitis

7.1 Introduction

This chapter outlines the risk factors for hospitalisation among those children who have cellulitis. Findings are presented initially as univariate factors, and followed by multivariate analyses.

7.2 Characteristics of Study Population

Risk factors for hospitalisation with cellulitis were explored comparing the children hospitalised with cellulitis (Hospital cases n=227) with the controls (GP cases n=145). The frequency of missing data is reported in the footnote of each table.

7.3 Univariate Risk Factors

7.3.1 Demographic Characteristics

Hospital cases and GP cases were different with respect to their age distribution with Hospital cases more likely to be an infant or preschool child (Table 49, p=0.02). Infants less than one year of age were six times more likely to be hospitalised with cellulitis than school-age children (OR 6.0, 1.36-26.1). Preschool children were almost 60% more likely to be hospitalised with cellulitis than school-age children (OR 1.59, 0.98-2.56). Overall, ethnicity did not contribute to the risk of hospitalisation with both Māori and Pacific infants and children just as likely to be hospitalised once they developed cellulitis compared to New Zealand European and Other children. Gender had no effect on the risk of hospitalisation.

7.3.2 Host Factors/Characteristics

Several host factors were examined but were not found to be associated with risk of being hospitalised with cellulitis.

7.3.2.1 Perinatal History

Hospitalised case children were no more likely to be low birth weight than GP case children (p=0.35). Ten percent of hospitalised children and 5% of GP case children were born prematurely (Table 50). Children born prematurely had twice the risk of being hospitalised with cellulitis compared to term infants, however, this did not reach statistical significance (OR 2.16, 0.94-4.96).

Eighteen percent of hospitalised children and 12% of GP case children had never been breast fed (p=0.11). There was no difference between the groups in the proportion of children who had formula introduced before four months or those with formula introduced after six months.

7.3.2.2 Health Status

Almost all children were reported to be in good, very good, or excellent health in the previous six months (Table 51). Children whose health status was reported as 'poor' or 'not very good' were almost 3 times more likely to be hospitalised with cellulitis, however, this did not reach statistical significance (OR 2.87, 0.95-8.63; p=0.06).

Health problems were reported for approximately a third of all study participants: 34% of Hospital cases and 28% of GP cases (Table 51). Children with identified health problems were not at a higher risk of being hospitalised with cellulitis (p=0.26). Reported health problems included asthma, eczema, recurrent ear infections/OME, allergies, and developmental delay.

7.3.2.3 Clinical Assessment

Underweight and obese children were not at increased risk of hospitalisation with cellulitis compared to children of normal weight (Table 52, p=0.54). Clinical signs of eczema were identified in 21% of Hospital cases and 11% of GP cases (p=0.02). Children with clinical signs of eczema had twice the risk of hospitalisation with cellulitis (OR 2.11, 1.16-3.84).

7.3.3 Exposures/Breaches of Skin

7.3.3.1 Frequency

In order to assess whether breaches of the skin were associated with the development of cellulitis, caregivers were asked whether their child had a minor injury or breach to their skin in the week prior to the development of the cellulitis. Such breaches were common among all children. Eighty percent of children had some breach of the skin or minor injury reported in the week prior to being interviewed. The most common injuries were nappy rash (33% of those who wore nappies), insect bites (32%), cuts or scratches (27%), other skin problem (20%), a bruise (15%), and eczema (15%). Splinters (5%), animal or human bites (3%) and chicken pox (1.9%) were less common.

Hospital and GP cases had similar overall rates of breaches of the skin, however, the frequency of specific breaches varied between the groups (Table 53).

Children with insect bites in the preceding week were half as likely to be admitted to hospital with cellulitis (OR 0.50, 0.31-0.79). There was a dose response with the higher the number of bites, the lower the risk of hospitalisation (Table 54). Children who scratched their bites until they bled or wept were not at increased risk of hospitalisation. More than 50% of bites were attributed to mosquitos and a smaller percentage to fleas (Table 55). There was a difference in type of insect

bites between the groups with a higher proportion of caregivers of Hospital cases being unsure about the type of insect causing the bite (p=0.05)

Nappy rash was more common among the Hospital cases than the GP cases, and was associated with a more than five times risk of hospitalisation (OR 5.45, 1.10-27.04). Other skin problems were also reported more frequently occurring in 25% Hospital cases compared to 12% of GP cases. Other skin problems associated with a 2 fold increase in risk of hospitalisation included school sores, pimples boils.

There was no significant difference in frequency of eczema among Hospital and GP cases (Table 56). Thirty percent of Hospital cases reported eczema in the last year compared to 21% of GP cases. Seventeen percent of Hospital cases reported eczema in the preceding week compared to 12% of GP cases (p=0.27). There was no difference in severity of eczema when measured by how often the baby/child had been kept awake at night by their eczema in the previous 12 months (p=0.38), or by the frequency with which it resulted in the child scratching until it bled or wept (p=0.34).

7.3.4 Host Behaviours

7.3.4.1 Hand Washing

Parents were asked a series of questions relating to their child's hand washing habits. Fifty-six percent of Hospital cases usually washed their hands on their own compared to 71% of GP cases (Table 58, p=0.002). Infants and children who were too young to wash their hands without help (either supervised or on their own) were at increased risk of being hospitalised with cellulitis (OR 2.55, 1.51-4.30).

Among both Hospital and GP cases who were considered old enough to wash their own hands, there were similar proportions of children who needed frequent reminders (Table 59, p=0.16). Fewer Hospital case children 'always or usually' washed their hands before eating or after playing outside. Children who 'sometimes, rarely or never washed' their hands before eating were almost twice as likely to develop cellulitis as children who 'always or usually' washed their hands (Table 60, OR 1.80, 1.15-2.83). A similar proportion of Hospital and GP cases 'always or usually' washed their hands after eating, after going to the toilet, after handling a pet, and if visibly dirty.

Hand washing at home was done under running water and using different forms of soap. Children who washed their hands in warm or hot water were at reduced risk of hospitalisation with cellulitis than those who washed their hands in cold water (OR 0.52, 0.28-0.95). There were no differences in types of soap used.

Most children used shared or family hand or bath towels to dry their hands. Children who did not use a towel but used their clothes or nothing to dry their hands were at no greater risk of being hospitalised with cellulitis than those who used a personal or shared towel (Table 60). Use of a personal towel did not confer a protective effect.

7.3.4.2 Bathing Practices

Similar proportions of children bathed or showered with no association with hospitalisation (Table 61). Both Hospital and GP case children bathed an average of six times each week and had their hair washed an average of four times each week. Washing less than daily was not associated with an increased risk of hospitalisation with cellulitis. Sharing bathwater was not associated with an increased risk of cellulitis (p=0.60), however, a greater proportion of Hospital cases were reported to continue to share bathwater while they had a skin infection (13% vs. 6%).

Fewer Hospital cases families reported their child used their own personal bath towel as opposed to sharing a family towel (15% of Hospital cases vs. 36% of GP cases). Children who shared their bath towel were three times more likely to be hospitalised with cellulitis than those that used their own personal towel (OR 3.10, 1.72-5.59). Thirty-eight percent of Hospital cases reported the towels were washed after a single use compared to 42% of GP cases. Families who did not wash their towels after every use were just as likely to be hospitalised with cellulitis as those who washed their towels after a single use (p=0.53).

7.3.4.3 Clothes Washing Practices

Living in a house without an automatic washing machine was not associated with an increased risk of hospitalisation with cellulitis (Table 62, p=0.62). The majority of families washed their clothes in cold water. The clothes washing temperature did not affect the risk of cellulitis (p=0.39).

7.3.5 Previous Cellulitis and Skin Sepsis

Previous episodes of cellulitis were more common among GP cases, other children in the household, as well as adults in the household (Table 63). Overall, more than 57% of GP cases had at least one family member with a past history of cellulitis compared to 33% of Hospital cases (p<0.001). A previous history of cellulitis in any household member reduced the risk of being hospitalised with cellulitis sixty percent.

Children with a previous history of cellulitis were 50% less likely to be admitted to hospital with cellulitis than those without (OR 0.50, 0.30-0.86). There was a dose response with the greater the number of previous episodes, the lower the risk of hospitalisation (Table 64). The protective effect

of a previous cellulitis in the index child was similar whether the previous episode occurred within the preceding 3 months or more than 3 months prior to the interview (Table 65).

Twelve Hospital case children (5%) and 22 GP case children (15%) had other children in the household who had cellulitis at the time of the interview or within the previous month. This reduced the risk of hospitalisation with cellulitis by almost 70% (OR 0.32, 0.14-0.74). The protective effect of a previous cellulitis in another child in the household was similar whether the previous episode occurred within the preceding 3 months or more than 3 months prior (Table 65).

The protective effect of a previous cellulitis in an adult in the household was similar whether the previous episode occurred within the preceding 3 months, 3 to 12 months prior, or more than 12 months prior to the most recent episode of cellulitis (Table 65, p=0.03).

A history of other skin infections such as boils and impetigo was as frequent among Hospital as GP cases. Similarly, there was no difference in the proportion of other children or adults in the household who had a history of an episode of skin sepsis (Table 66).

7.3.6 Socioeconomic and Environmental Factors

7.3.6.1 Socioeconomic Status

The effect of socioeconomic status was examined by two different measures: that defined by the social deprivation score of the mesh block (NZDep Index)[137] and that defined by the most recent occupation of the mother and father.[138]

The proportion of Hospital and GP cases in each of the social deprivation quintiles is noted in Table 67. The distribution across the quintiles was slightly different; however, there was no evidence of a dose response for deprivation. Children in the most deprived quintiles (4-5) were no more likely to be admitted with cellulitis than those in the least deprived quintiles (1-3) (p=0.19).

Questions were asked about the current or last job of both mother and father as per the NZ standard classification of occupations.[138] In view of a significant amount of missing data and uncertainty regarding the responses, this was not a reliable measure of socioeconomic status and was not reported further.

Just over half of both Hospital and GP cases had mothers with a current community services card (p=0.71). Children of women with a community services card were no more likely to be hospitalised than those without (OR 1.09, 0.69-1.71).

7.3.6.2 Maternal Characteristics

Maternal age at interview and age at the birth of the child were not associated with the risk of hospitalisation with cellulitis (Table 68, p=0.52 and p=0.49). There was no difference between cases and controls in the proportion whose mothers were not New Zealand born (37% Hospital cases vs. 41% GP cases, p=0.41) or in those who had immigrated to New Zealand in the last 10 years (15% vs. 12%, p=0.51). A similar proportion of both Hospital and GP case mothers spoke English as a second language (29% vs. 32%, p=0.49).

Maternal educational attainment did not vary across the groups (p=0.39). Children of mothers without formal qualifications were at no greater risk of hospitalisation than those with mothers with formal qualifications (OR 0.81, 0.50-1.32).

7.3.6.3 Household Composition

Most children lived in nuclear families, with no difference in proportions from single parent or extended families or whānau among children with cellulitis (Table 69, p=0.76). Children living in single parent or extended whānau households were at no greater risk of being hospitalised with cellulitis compared to those in two parent households.

7.3.6.4 Household Characteristics

Caregivers were asked to specify whether they lived in a house/townhouse, flat/unit, or other type of dwelling. Almost all families lived in houses, townhouses, or apartments with only 10% Hospital cases and 5% of GP cases living in other environments (including flat, unit, caravan, garage, and boarding house, Table 70). Living in another environment was associated with 2 times increased risk of hospitalisation with cellulitis; however, this did not reach significance (OR 2.22, 0.95-5.22; p=0.07).

Overall, just under half of families owned their own home. There was no significant difference in risk of hospitalisation between Hospital or GP cases depending on whether they owned their homes, lived in a Housing NZ rental home or lived in a private rental property.

Household mobility had no effect on the risk of hospitalisation with cellulitis with rates of those that moved in the previous two years the same for Hospital cases (35%) and GP cases (33%, p=0.67). Neither moving house nor moving two or more times within the last two years were associated with an increased risk of cellulitis.

Almost all families had access to a phone, although hospitalised cases were more likely to either have no phone or rely on mobile phones compared to GP cases (13% Hospital cases vs. 6% GP

cases, p=0.05). Families with no landline were 2 times more likely to have a child hospitalised with cellulitis (OR 2.2, 1.0-4.91).

7.3.6.5 Household Crowding

The number of people living in the houses varied widely for both Hospital and GP cases (range 2-15). There was no difference in the total number of people living in the houses of hospitalised children with cellulitis compared to GP cases with the average number of household members being 5.4 for Hospital cases and 5.3 for GP cases. Both the average number of adults and children in the households were similar across the two groups. Forty-one percent of Hospital cases and 37% of GP cases lived in houses with 6 or more people (Table 71). Children in such households were at no greater risk of being hospitalised with cellulitis (p=0.47).

In contrast to the risk of developing cellulitis, there was no dose response with the number of people in the house and the risk of hospitalisation with cellulitis (Table 71). The risk did, however, vary with the number of children in the house (p=0.01), with a significant protective effect of having 2-3 children in the house compared to a single child (OR 0.46, 0.23-0.92).

There was no difference in the number of bedrooms or the bedroom occupancy rate between Hospital and GP cases. Twenty-one percent of Hospital cases and 17% of GP cases lived in houses with more than two people per bedroom (p=0.33). However, there was no dose response and higher bedroom occupancy did not result in higher risk of cellulitis (Table 72). Households with more than five people per toilet were no more likely to have a child hospitalised with cellulitis than those with lower toilet occupancy.

Sixty-two percent of Hospital cases and 60% of GP cases shared a bedroom with another person. Sharing a bedroom was not associated with an increased risk of hospitalisation with cellulitis (OR 0.82, 0.51-1.30; p<0.67).

Twenty-three percent of Hospital cases and 26% of GP cases were reported to share a bed with another child or person. Sharing a bed was not associated with an increased risk of hospitalisation with cellulitis (OR 1.09, 0.72-1.65; p<0.39).

Overall, across a range of different crowding measures, infants and children living in crowded houses were not significantly more likely to be hospitalised with cellulitis than those who did not. Living in a house with several children conferred a protective effect on the risk of hospitalisation.

7.3.6.6 Parental Smoking

There was no relationship between maternal smoking, the presence of smokers in the house, or the number of smokers in the household and the risk of hospitalisation with cellulitis (Table 73).

7.3.7 Health Literacy and Healthcare Utilisation

7.3.7.1 Health Literacy

First Aid Management of Breaches

In order to assess whether the first aid management of breaches of the skin had any effect on the risk of hospitalisation with cellulitis, caregivers were asked questions regarding their initial management of minor injuries or breaches to their child's skin in the week prior to the development of the cellulitis. Questions included cleansing with water, soap or saline, cleansing with antiseptic, administration of creams including antibiotics, antiseptic and anti-itch, administration of tablets including antihistamine and antibiotics, pain relief, traditional therapy, and whether the breach was covered (and what with). Note was also made of time interval from first noticing the breach to when first aid was administered and whether medical advice was sought when the breach first occurred.

Insect Bites: Slightly more than half the families reported administering some initial first aid management when they first noticed insect bites on their child: most commonly cleaning with water or soapy water, applying anti-itch cream, or covering them (Table 74). Use of antiseptic or antibiotic cream was associated with a reduced risk of hospitalisation (OR 0.19, 0.05-0.83). No other management strategies were associated with risk of hospitalisation with cellulitis. There was no reported difference between the Hospital and GP cases in the timing of how soon the first aid was administered (Table 75, p=0.38).

Nappy Rash: Comparison of the management across the groups was not possible as there were only two GP cases and 25 Hospital cases with nappy rash. On the whole, the Hospital cases reported using acute management creams, rather than regular barrier creams or ointments.

Eczema: The usual management of eczema was not significantly different between Hospital and GP cases. There was no significant difference in whether the caregiver usually used steroid cream or ointment (p=0.48), or usually used moisturiser (p=0.33). Contrary to the recommended best practice regarding eczema management, both Hospital and GP cases used steroid cream more often than moisturiser (Table 77). Nine percent of Hospital cases used traditional or alternative therapy compared to 17% GP cases (p=0.26). There was no difference in the use of soap substitute (47% of Hospital cases vs. 44% GP cases, p=0.83).

Caregivers were asked a series of questions about their actions once they noticed the area of redness. Questions examined initial symptoms, first aid management, healthcare utilisation and specifics re the healthcare provided.

Initial Symptoms Identified

Caregivers were asked whether they noticed any other problems at the time they first noticed the redness. Almost all reported at least one other symptom with very few caregivers identifying redness alone (0.4% Hospital cases vs. 3.4% GP cases). The majority reported associated pain and tenderness, swelling, fever, and/or pus and discharge (Table 78). The distribution of symptoms was different between Hospital and GP cases. The classic signs of cellulitis with redness, swelling and tenderness were present in 78% of Hospital cases and 66% of GP cases at the time the caregivers first noticed the redness ($p=0.02$). The presence of all three symptoms at first noticing a skin problem almost doubled the risk of hospitalisation with cellulitis (OR 1.84, 1.13-3.01).

First Aid Management of Redness

In order to assess whether the initial management of the redness had any effect on the risk of hospitalisation with cellulitis, caregivers were asked questions about their first aid management once they first noticed the redness. Questions included cleansing with water, soap or saline, cleansing with antiseptic, administration of creams including antibiotics, antiseptic and anti-itch, administration of tablets including antihistamine and antibiotics, pain relief, traditional therapy, and whether the breach was covered (and what with). Note was also made of time interval from first noticing the redness to when first aid was administered and whether medical advice was sought when the redness was first identified.

Important differences between the Hospital and GP cases in first aid management were identified (Table 79). Sixty-five percent of Hospital cases administered some first aid upon first noticing the redness compared to 83% of GP cases ($p<0.001$). Administration of any first aid was associated with a 60% reduction in risk of hospitalisation (OR 0.38, 0.24-0.62). A similar protective effect was seen for almost all forms of first aid including cleansing with water, soap or saline, cleansing with antiseptic, administration of creams including antibiotics, antiseptic and anti-itch, administration of tablets including antihistamine and antibiotics, and whether the redness was covered. The type of plaster cover (plastic or fabric) did not alter the degree of protection. Neither the use of traditional therapy or pain relief had any protective effect.

Among those that received first aid, there was no difference in the timing of administration of first aid with 64% Hospital cases and 61% of GP cases receiving first aid within 3 hours of first noticing the redness (Table 80, $p=0.13$).

In addition to caregivers of Hospital cases being less likely to administer first aid when first noticing the redness, they were also less likely to seek medical advice (54% Hospital cases vs. 70% GP cases, p=0.006). Seeking medical advice when first noticing the redness was associated with a 50% reduction in risk of hospitalisation (OR 0.52, 0.32-0.82). There was a difference in the timing of how soon they sought medical attention after noticing the redness with a greater proportion of Hospital cases seeking medical attention within 24 hours of first noticing the redness (Table 81, 51.6% vs. 39.2%, p=0.02).

As severity of the cellulitis affects whether a child is taken for medical assessment and the risk of admission, the analysis was restricted to those children who were reported by their caregivers to have classic symptoms of cellulitis (redness, pain and swelling) at the time the redness was first noticed. Among this group, 49% of Hospital cases and 42% GP cases sought medical attention within 24 hours of noticing the redness (Table 82, p=0.23).

7.3.7.2 Usual Healthcare Utilisation

Most children had a single GP, doctor or practice for the majority of the child's usual healthcare visits (Table 83). Thirteen percent of Hospital cases and 9% of GP cases reported seeing one of several different GPs in different practices, whoever was available, or after-hours services for usual healthcare provision for their child. Children who did so were at no greater risk of developing cellulitis than those who saw their usual healthcare provider or practice (OR 1.5, 0.76-2.9).

In the six months prior to the skin infection, both groups had similar use of healthcare providers and services (Table 84). There was no difference in the frequency of use of primary healthcare services including community accident and medical centres, however, hospitalised cases had greater use of the hospital Emergency Department. Children who had been to the Emergency Department in the 6 months prior to the infection were over 3 times more likely to be hospitalised with cellulitis than those that had not (OR 3.28, 1.71-6.28).

7.3.7.3 Healthcare Utilisation

Caregivers were asked which healthcare providers they saw for their child's redness. The distribution differed between the Hospital and GP cases (Table 85). Eighty-eight percent of GP cases saw their family doctor for the redness compared to 54% of Hospital cases (p<0.001). Children who consulted their GP for the redness were at significantly lower risk of being hospitalised than those that did not (OR 0.15, 0.09-0.27). Thus, children who did not see their usual GP for their illness were more than six times more likely to be hospitalised with cellulitis (OR 6.5, 3.75-11.21). A greater percentage of Hospital cases saw an afterhours Accident and Medical

Centre (38%) compared to GP cases (18%). Attending an Accident and Medical Centre was associated with an almost three fold risk of hospitalisation (OR 2.79, 1.70-4.58).

Thirty percent of Hospital cases reported difficulties getting to the GP for the episode of skin sepsis compared to 11% of GP cases (Table 86, p=<0.001). Difficulties included cost, transport, families being too busy, not being able to see the doctors as they were too busy etc. Such difficulties were associated with a more than threefold risk of hospitalisation with cellulitis (Table 87, OR 3.35, 1.77-6.33). Cost and transport difficulties were the most significant factors, with children in families reporting difficulties seeing the doctor due to cost being almost five times more likely to be hospitalised with cellulitis (OR 4.80, 2.02-11.40), and those reporting transport difficulties more than 4 times.

7.3.7.4 Healthcare Provided

Caregivers were asked about the healthcare provided by the first healthcare professional they saw for their child's redness. Forty-three percent of Hospital cases were sent straight to the hospital when first seen thus received no further treatment in primary care. The remaining children were prescribed medical therapy but required hospitalisation at a later date. No GP cases were sent to the hospital following the initial assessment and 86% were prescribed medical treatment.

Among the children who remained in the community after their first clinical assessment, healthcare included prescriptions for antibiotics, topical antibiotics and pain relief, as well as dressings and other advice (Table 88). Oral antibiotics were prescribed for 85% Hospital cases and 92% of GP cases (p=0.08). Fewer Hospital cases (15%) were prescribed topical antibiotics compared to GP cases (31%, p=0.01). Children prescribed topical antibiotics were 60% less likely to require hospital admission (OR 0.38, 0.20-0.74). Children who required a prescription for pain relief after their initial medial consultation were three times more likely to be hospitalised than those that did not (OR 3.16, 1.65-6.09). Two hospitalised children and no GP cases were prescribed ibuprofen.

Scripts were reported to be collected in 97% of both Hospital and GP cases (p=0.78). Almost all caregivers collected the prescription from the chemist within 24 hours of getting the prescription and administering the first dose within 3 hours of seeing the doctor (Table 89). There was no difference between the Hospital and GP cases.

Caregivers were asked if their medical practitioner gave them any advice or treatment other than a prescription for medication. Overall, 86% of Hospital cases and 54% of GP cases either could not remember if it was given or reported nil information was given (Table 90, p<0.001). Receiving

or recalling no additional information was associated with a 5 times increased risk of hospitalisation (OR 5.54, 3.30-9.31). As this total number included children who were sent immediately for hospital admission, the analysis was repeated for children who remained in the community after the initial assessment. In this subgroup, 76% of Hospital cases reported receiving no additional information compared to 54% GP cases (p<0.001). Receiving or recalling no additional information was associated with a 3 times increased risk of hospitalisation in children initially treated within primary care (OR 2.74, 1.58-4.75). The remainder received advice about care of bites, cuts etc., dressing, cleaning or other.

Caregivers were asked about the number of times they saw health professionals for the episode of cellulitis. This varied across the Hospital and GP cases (Table 91). Hospital cases were less likely to have seen their family doctor (p<0.001), and more likely to have visited an Accident and Medical Centre (p=0.001). The protective effect of visiting the family doctor was similar whether they were seen once or 2 or more times for the illness.

7.3.7.5 Healthcare Professionals Assessment and Provision

The first healthcare professional the child saw for the illness was asked several questions regarding their involvement. Specific questions related to the clinical assessment, and their opinion about potential contributing factors features. One hundred and thirty five GPs responded for the GP cases and 178 for the Hospital cases, giving response rates of 93% and 78% respectively.

Clinical Assessment

Health professionals were asked about the presenting complaint when the child first presented for medical attention. The majority reported redness, pain and tenderness, swelling, fever, and/or pus and discharge. The presence of swelling, pain and tenderness, or redness were similar across Hospital and GP cases (Table 92). The classic signs of cellulitis with redness, swelling and tenderness were the presenting complaint for 43% of Hospital cases and 41% of GP cases (p=0.70). Fever was more commonly a presenting complaint in the Hospital cases increasing the risk of hospitalisation 13 fold (OR 13.01, 5.50-30.78). The presence of pus or discharge as a presenting complaint was protective and associated with a 50% reduction in of hospitalisation (OR 0.52, 0.30-0.90).

The size of the lesion at the time the child first presented to a doctor with cellulitis ranged from 5-300mm for Hospital cases and 4-150mm for GP cases. The average was estimated at 58.2mm (SE 4.70) for Hospital cases and 39.0mm (SE 2.65) for GP cases (p<0.001). An initial lesion of 50mm or greater was associated with a 3 fold increase in risk of hospitalisation (Table 93, OR 2.80, 1.58-4.95). There was a dose response with the greater the size at first presentation to

medical attention the greater the risk of hospitalisation. Children whose caregiver reported difficulties getting to their GP had significantly more inflammation when they first presented to a health professional than those who did not report difficulties (63.5mm vs. 45mm for the diameter of redness at initial presentation, $p<0.001$).

Sixty percent of Hospital cases (105 children) were considered to be sufficiently severe when first seen in primary care that they were sent straight to the hospital for further assessment and/or admission. The remaining children were prescribed medical therapy but required hospitalisation at a later date. This included 5 children who were initially GP cases but deteriorated and required subsequent hospitalisation (2% of all GP cases initially enrolled). One GP case (0.8%) was sent to the hospital following the initial assessment, however, did not require hospital admission and was successfully treated within primary care.

Potential Contributing Factors

General Practitioners were asked what factors they thought played a role in the child's episode of skin sepsis. Options were provided from data from the health professional information from both the primary care survey and the case series: late presentation, compliance issues, diet, overcrowding, underlying conditions etc. as well as an option to specify other contributing factors. Late presentation was considered a common contributing factor and was identified as an issue for 52% of Hospital cases and 27% of GP cases.

GPs were also asked to rate their thoughts regarding the families' compliance with prescribed therapy based on their past experience. Compliance was generally considered to be good with only 10% of Hospital cases and 11% of GP cases considered to have poor or fair compliance.

7.3.8 Clinical Information

Thirty-nine percent of Hospital cases required incision and drainage during their hospital stay. This did not differ across the different age, ethnic and socioeconomic groups (Table 94). Seventy-one percent of cases were admitted under orthopaedic services, 13.7% general surgical and 15.4% general medical. The average length of stay was 2.59 days with a range of 1-10 days. Eighteen of the 227 children admitted were MRSA positive (8%).

7.4 Multivariate Risk Factors

Age was a significant risk factor for hospitalisation with infants being at almost seven times greater risk of hospitalisation than school-age children. Socioeconomic deprivation and ethnicity did not confer an increased risk for hospitalisation; however, as they were significant factors for the development of cellulitis, these factors, in combination with age, were used in the multivariate model to examine risk factors for hospitalisation once cellulitis had developed.

7.4.1 Demographic Characteristics

After adjustment for NZ deprivation score and ethnicity, the child's age continued to have a significant effect on the risk of hospitalisation with cellulitis. Infants less than one year of age were almost seven times more likely to be hospitalised with cellulitis than school-age children (Table 49, aOR 6.7, 1.45-30.94).

After multivariate adjustment, ethnicity was not associated with the risk of hospitalisation (p=0.83). Socioeconomic status as measured by NZDep was associated with risk of hospitalisation (p=0.05), however, there was no consistent pattern. When the lowest quintiles (1-3) were compared with the highest (4-5), there was no association with hospitalisation (p=0.24).

7.4.2 Host Factors/Characteristics

Several host factors were examined in the multivariate model and were found to not be associated with the risk of hospitalisation with cellulitis. These included perinatal factors such as LBW, prematurity, never being breastfed, age of introduction of formula as well as whether there were any identified health problems (Table 50, Table 51).

Children whose heath was reported to be not good or poor in the preceding 6 months were not at greater risk of hospitalisation with cellulitis. Children who were either underweight or obese were not at increased risk of hospitalisation with cellulitis (Table 52, p=0.61). Children with clinical signs of eczema were at greater risk of hospitalisation (aOR 1.93, 1.04-3.60).

7.4.3 Exposures/Breaches of Skin

Breaches of the skin in the preceding week were as frequent among the Hospital cases as the GP cases. The presence of insect bites reduced the risk, and the presence of nappy rash and other skin problems increased the risk of hospitalisation (Table 53). Children with insect bites in the preceding week were 56% less likely to be hospitalised with cellulitis (aOR 0.44, 0.27-0.72). There was a dose response with the higher the number of bites, the lower the risk of hospitalisation (Table 54). Children who scratched their bites until they bled or wept were at no greater risk of hospitalisation than those that did not (p=0.26). Children with nappy rash were over

six times more likely to be admitted with cellulitis than those without, (aOR 6.50, 1.12-37.74) even after adjusting for age, ethnicity and deprivation. Children with other identified skin problems were twice as likely to be admitted with cellulitis (aOR 2.21, 1.25-3.90), as were children with chicken pox, however, this did not reach significance (aOR 2.37, 0.30-19.07).

The presence of eczema and the frequency with which it kept the child awake at night were not associated with hospitalisation with cellulitis (Table 56). While children who scratched their eczema until it bled were 4 times more likely to develop cellulitis than those who did not, such children appeared to be at lower risk of hospitalisation (aOR 0.28, 0.06-1.24).

7.4.4 Host Behaviours

Infants and children who were too young to wash their hands without help (either supervised or on their own) were at increased risk of being hospitalised with cellulitis (Table 58). Among both Hospital and GP cases who were considered old enough to wash their own hands, there were similar proportions of children who needed frequent reminders (Table 59, p=0.16). Fewer Hospital case children 'always or usually' washed their hands before eating or after playing outside. Children who 'sometimes, rarely or never washed' their hands before eating were almost twice as likely to be hospitalised with cellulitis as children who 'always or usually' washed their hands (Table 60, aOR 1.97, 1.23-3.17). The risk was similar for those children that 'sometimes, rarely or never washed' their hands after playing outside (aOR 1.82, 1.06-3.11). Hospital and GP cases had a similar proportion of children that 'always or usually' washed their hands after eating, after handling a pet, after using the toilet, and if visibly dirty.

Children who washed their hands in warm or hot water were at reduced risk of hospitalisation with cellulitis than those who washed their hands in cold water (aOR 0.52, 0.28-0.96). There were no differences in types of soap used.

There was no association between hand drying habits, bathing practice or clothes washing practices and the risk of hospitalisation (Table 61, Table 62). Children who shared a bath towel were over three times more likely to be hospitalised with cellulitis after multivariate analysis than those that did not (aOR 3.37, 1.83-6.23).

7.4.5 Previous Cellulitis and Skin Sepsis

Previous episodes of cellulitis were more common among GP cases; for each of the index child, other children in the house, as well as adults in the household (Table 63).

Children with a previous history of cellulitis were almost 50% less likely to be admitted to hospital with cellulitis than those without (aOR OR 0.56, 0.32-0.96). There was a dose response with the greater the number of previous episodes, the lower the risk of hospitalisation (Table 64).

A similar but slightly greater protective effect was seen for a past history of cellulitis in another child in the house as well as an adult in the household. The protective effect of a past history of cellulitis in the index child, another child or another adult in the household was similar whether the previous episode occurred within the preceding 3 months or more than 3 months prior to the interview (Table 65). Among the adults it also remained when the episode of cellulitis was more than a year prior to the current episode of cellulitis (p=0.04).

7.4.6 Socioeconomic and Environmental Factors

7.4.6.1 Socioeconomic Status

Deprivation as defined by the social deprivation score of the mesh block (NZDep Index) and maternal community service card ownership were not associated with the risk of hospitalisation in both univariate and multivariate analyses (Table 67).

7.4.6.2 Maternal Characteristics

Maternal characteristics such as age at birth, being NZ born, a recent immigrant, ESOL, and maternal education were not associated with the risk of hospitalisation with cellulitis in the multivariate model (Table 68).

Exposure to cigarette smoking had no effect on the risk of hospitalisation (Table 73).

7.4.6.3 Household Composition and Characteristics

Most household factors were not associated with hospitalisation with cellulitis including household composition, housing ownership and household mobility (Table 69, Table 70). Lack of a land line was associated with hospitalisation in the univariate model, and continued to have a point estimate of 2.22, however, no longer reached significance after controlling for ethnicity, age and deprivation (aOR 2.22, 0.95-5.19; p=0.07).

7.4.6.4 Household Crowding

Children living in a house with more than 1.5 people per bedroom were 75% more likely to be hospitalised than those who lived in houses with lower bedroom occupancy (Table 72, aOR 1.75, 1.03-2.98). There was, however, no dose response for crowding as measured by bedroom occupancy (p=0.52), or the number of people in the house (p=0.19). Living in a house with other children conferred a protective effect on the risk of hospitalisation (p=0.02), however, there was no consistent pattern.

Sharing a bed or a bedroom were not associated with hospitalisation with cellulitis.

7.4.7 Health Literacy and Healthcare Utilisation

7.4.7.1 Health Literacy

First Aid Management of Breaches

Insect bites were more common among GP cases with a difference in the first aid management demonstrated between the groups. Twenty-two percent of GP cases used antiseptic or antibiotic cream for an insect bite compared to 5% of Hospital cases. Use of such a cream reduced the risk of hospitalisation over 85% (aOR 0.12, 0.03-0.51, Table 74). There were no other differences in first aid noted.

Initial Symptoms Identified

Caregivers reporting of another symptom at the time they first noticed the redness was almost universal, and associated with an over nine times greater risk of hospitalisation (Table 78, aOR 9.86, 1.45-67.09). Almost all other associated symptoms with the exception of pain and tenderness and the presence of pus and/or discharge, were associated with an increased risk of hospitalisation. Caregiver reporting the classic signs of cellulitis with redness, swelling and tenderness at the time of first noticing a skin problem doubled the risk of hospitalisation with cellulitis (aOR 2.11, 1.24-3.59). Pus and/or discharge at the time of first identification lowered the risk of hospitalisation (aOR 0.34, 0.20-0.57).

First Aid Management of Redness

Important differences between the Hospital and GP cases in first aid management continued to persist after controlling for age, ethnicity and deprivation (Table 79). Fewer hospital cases administered first aid upon first noticing the redness compared to GP cases (p<0.001). Administration of any first aid was associated with a 60% reduction in risk of hospitalisation (aOR 0.37, 0.22-0.61). A similar protective effect was seen for almost all forms of first aid including cleansing with water, soap or saline, cleansing with antiseptic, administration of creams including

antibiotics, antiseptic and anti-itch, administration of antihistamine and antibiotics, and whether the redness was covered (and what with). Neither use of traditional therapy or pain relief had any effect on the risk.

Among those that received first aid, there was no difference in the timing of administration of first aid (Table 80, p=0.21). Seeking medical advice when first noticing the redness was associated with a 50% reduction in risk of hospitalisation (aOR 0.53, 0.32-0.86). There was a difference in the timing of how soon they sought medical attention after noticing the redness with more of the Hospital cases seeking medical attention within 24 hours of first noticing the redness (Table 81, 61% vs. 48%, p=0.02). When restricted to those children who had the classic symptoms of cellulitis with redness, swelling and tenderness, there was no difference between Hospital and GP cases in the proportion who sought medical attention within the first 24 hours of noticing the redness (Table 82, p=0.23).

7.4.7.2 Usual Healthcare Utilisation

The use of several different GPs in different practices, whoever was available, or after-hours services rather than a single GP or practice for usual healthcare provision was not associated with an increased risk of hospitalisation with cellulitis (Table 83). Both cases and controls had similar use of healthcare providers and services in the six months prior to the illness (Table 84).

7.4.7.3 Healthcare Utilisation

Children who consulted their GP for the redness were at significantly lower risk of being hospitalised than those that did not (Table 85, aOR 0.16, 0.09-0.28). Attending an Accident and Medical Centre increased the risk of hospitalisation more than two fold (aOR 2.51, 1.49-4.20).

Difficulties getting to the GP increased the risk of hospitalisation with cellulitis more than 3 fold (Table 86, aOR 3.50, 1.81-6.80) after adjustment for age, ethnicity and deprivation. Cost and transport difficulties remained significant factors, with children in families reporting difficulties seeing the doctor due to cost being over five times more likely to be hospitalised with cellulitis (aOR 5.38, 2.16-13.41), and those reporting transport difficulties more than 4 times (aOR 4.09, 1.43-11.75). Importantly the doctor being too busy for the family to get an appointment was not related to the risk of hospitalisation (Table 87).

7.4.7.4 Healthcare Provided

Among the children who remained in the community after their first clinical assessment, healthcare included prescriptions for antibiotics, topical antibiotics and pain relief, as well as dressings and other advice (Table 88). Oral antibiotic prescription was not associated with a

reduced hospitalisation rate and neither was prescription for antiseptics. Children prescribed topical antibiotics continued to be at lower risk of hospitalisation than those that were not after adjusting for age, ethnicity and deprivation (aOR 0.36, 0.18-0.74). Children who required a prescription for pain relief after their initial medical consultation were three times more likely to be hospitalised than those that did not (aOR 3.66, 1.85-7.24).

Hospitalisation was not associated with whether all the items were collected from the chemist, whether they were collected within 24 hours, or the time interval from receiving the prescription and the first dose of medication (Table 89).

Caregivers who reported they received no advice or treatment apart from the prescription or could not recall doing so, were 5 times more likely to be hospitalised than those that recalled such information (Table 90, aOR 5.74, 3.33-9.89). The risk remained elevated for those who were not immediately sent to hospital and who remained in the community after the initial assessment (aOR 2.82, 1.58-5.01).

Caregivers were asked about the number of times they saw health professionals for the episode of cellulitis (Table 91). Hospital cases were less likely to have seen their family doctor ($p<0.001$), and more likely to have visited an Accident and Medical Centre ($p=0.001$).

7.4.7.5 Healthcare Professionals Assessment and Provision

Children who presented to their GP with a fever were at increased risk of hospitalisation and those who presented with pus and discharge were at lower risk of hospitalisation (Table 92). The size of the redness at initial presentation was an important predictor of severity with children whose skin sepsis was more than 50mm in diameter at the first presentation to a health professional being at three times the risk of hospitalisation compared to children with a lesion less than 50 mm (aOR 2.90, 1.54-5.49, Table 93).

7.5 Conclusion

The risk factors for hospitalisation with cellulitis include a range of demographic, exposures, socioeconomic, environmental and healthcare factors. Those factors that persist after adjustment for ethnicity, socioeconomic status, and age have been summarised in the following pathway to hospitalisation with cellulitis (Figure 13) and summarised in a table in the appendix (Table 95).

Demographic Factors
↑↑ Infant
↑ Preschool child

Host Susceptibility
↑ Clinical signs eczema

Exposures/Breaches of the skin
↓↓ Insect bite
↓↓ # Insect bites

↑↑↑ Nappy rash
↑ Other skin problem

Host Behaviours
↓↓ Washing hands in warm/hot water
↑ Not washing hands before eating
↑ Not washing hands after playing outside
↑↑ Sharing bath towels

Past History of Skin Sepsis
↓↓ Phx cellulitis index child
↓↓ Phx cellulitis other child
↓↓ Phx cellulitis adult in household
↓↓ 2 or more previous episodes cellulitis

Social/Environment
↑ Incr bedroom occupancy
↓ Other children in the house

Health Literacy/Utilisation
↓↓↓ Antibiotic/antiseptic cream to insect bite
↓↓ Any first aid management to redness
↑↑ Use of ED in the last 6 months
↓↓ Presence of pus as first sign
↑↑ Pain, fever, swelling, other first signs

Healthcare Factors
↑↑ Difficulties accessing healthcare
↑ Use of after-hours clinics
↑↑ Script for pain relief
↓ Script for topical antibiotic
↑↑ No additional healthcare advice given
↑↑↑ Fever at first presentation to GP
↑ Size >50mm at first presentation to GP

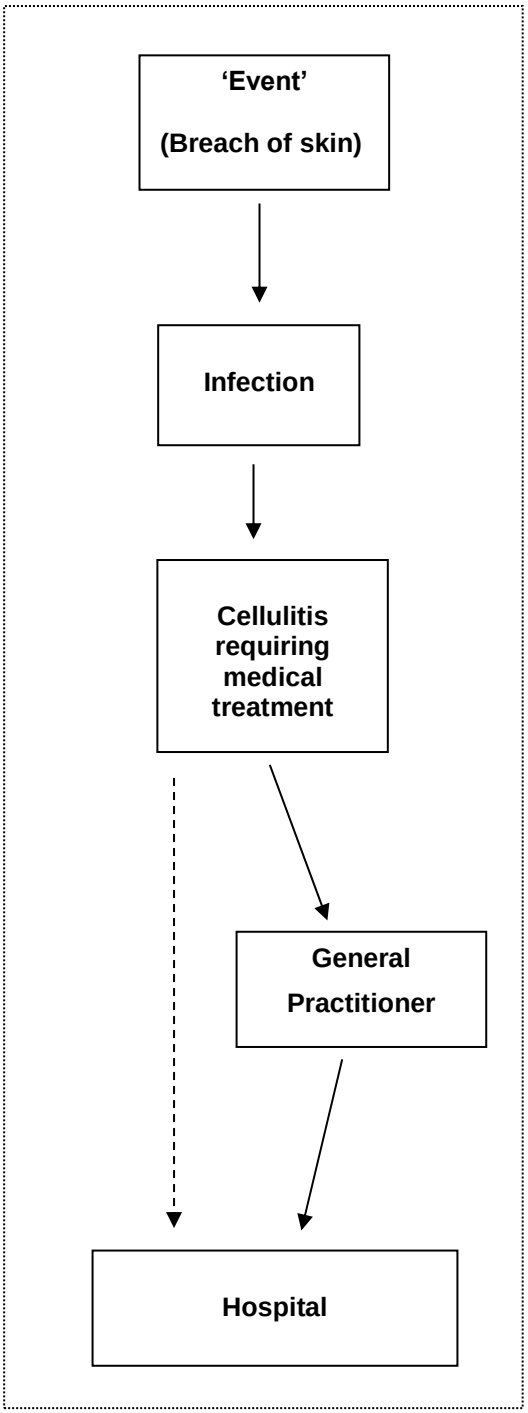

Figure 13: Identified Risk Factors in the Pathway to Hospitalisation with Cellulitis
↑=1-3 times increased risk
↑↑=3-6 times increased risk
↑↑↑=6 or more times increased risk
↓=0-30% decreased risk
↓↓=30-60% decreased risk

Chapter 8: Discussion

8.1 Introduction

"Disease is largely a removable evil. It continues to afflict humanity, not only because of incomplete knowledge of its causes and lack of individual and public hygiene, but also because it is extensively fostered by harsh economic and industrial conditions and by wretched housing in congested communities" *Hermann M. Biggs*[145]

The overall goal of this thesis was to identify risk factors for cellulitis in childhood. The aim was to identify modifiable risk factors which could lead to prevention and treatment strategies, and result in reductions in the incidence of the disease and in hospitalisation for those with the disease. This final chapter starts with an overview of the importance of cellulitis highlighting the gaps in our knowledge. I then revisit our hypotheses and discuss the main findings of our risk factor research in the context of the literature. The strengths and weaknesses of the study methodology are then considered as they relate to study design stage and interpretation of the results. I follow this with a summary of my involvement in projects that have arisen directly out of this research. Finally, remaining unanswered questions and future research needs are briefly outlined.

8.2 Overview

Cellulitis is a significant health issue for New Zealand children. It is a common and increasing problem and is associated with significant ethnic and socioeconomic disparities. While there is a wealth of epidemiological information about serious skin sepsis in New Zealand, all studies have been descriptive, thus the relative importance of these factors has not been determined. Hospital admissions for cellulitis are as common as admissions for pneumonia, but far less is known about the management and even less about the risk factors.

Cellulitis is the end result of a series of events: from an initial breach of skin, to infection, to cellulitis requiring medical treatment, through to cellulitis requiring hospitalisation. This process takes several days to evolve with several factors influencing whether a child subsequently develops a skin infection or requires hospitalisation following the initial event. These include host susceptibility and behaviours, social and environmental factors, microbiological factors, health literacy, and healthcare factors. At present the relative importance and contribution of each of these factors is ill-defined. Many of these factors have been specifically examined among adults, but no studies have specifically examined risk factors for cellulitis among children. Importantly while adult studies stress the importance of local factors such as lymphoedema and toe web intertrigo, these occur infrequently among children, and their importance in the high rates of paediatric skin sepsis is uncertain. In addition, while most studies among adults have

concentrated on host factors, they have largely ignored the potential contributions of social, environmental, health literacy and healthcare factors. As little is known about these potentially modifiable factors, we have been unable to design interventions to reduce both the incidence and impact of cellulitis on our childhood population.

8.3 Aims and Hypotheses

The specific aims of this thesis were to identify and quantify the risk factors associated with developing cellulitis, and to identify and quantify the risk factors associated with hospitalisation in children who have developed cellulitis. Our hypotheses were developed from review of the literature, clinical experience, and the case series, and relate directly to the questions raised at the end of the literature review in Chapter 2.

We hypothesised the following factors were related to the development of cellulitis:

8.3.1 Host Susceptibility

Māori and Pacific children are at increased risk of developing cellulitis.

Children at different ages have different risk of both developing cellulitis and requiring admission with cellulitis.

Host factors, especially obesity and eczema are associated with cellulitis.

Children who have a past history or a family history of cellulitis are at increased risk of developing cellulitis.

8.3.2 Exposures/Breaches of the Skin

The frequency of breaches of the skin (insect bites, scratches, cuts) differs between children who develop cellulitis and those who do not.

8.3.3 Host Behaviours

Hygiene factors are associated with the development of cellulitis.

8.3.4 Social/Environment

Social factors such as housing and crowding differ between children who develop cellulitis and those that do not.

8.3.5 Health Literacy/Healthcare Utilisation

First aid management of breaches of the skin differs between children who develop cellulitis and those that do not.

Healthcare utilisation differs between cases and controls.

We hypothesised the following factors were related to hospitalisation in those who had developed cellulitis:

8.3.6 Health Literacy/Healthcare Utilisation

First aid management of breaches of the skin differs between children who require hospitalisation with cellulitis and those that do not.

Healthcare utilisation differs between children admitted to hospital and those successfully treated in primary care.

8.3.7 Healthcare Factors

Primary care management of cellulitis differs between those admitted to hospital than those successfully treated in primary care.

Barriers to healthcare are more frequent among those admitted to hospital than those successfully treated in primary care.

8.4 Summary of Main Findings

This is the first study to systematically examine risk factors for cellulitis among children. Importantly, while several factors identified among adult studies were confirmed in children, some factors were not contributory, and new factors were identified. The following sections specifically examine the findings for each of our hypotheses.

8.4.1 Host Susceptibility

8.4.1.1 Ethnicity

Māori and Pacific children have higher rates of hospitalisation with cellulitis; however, to date it has been unclear if this reflects higher community rates of disease, or whether they are more likely to be admitted to hospital with cellulitis due to different disease severity or differing healthcare factors.[49,50] As our study design incorporated three comparison groups, we were able to address this gap in the literature. We clearly identified Māori and Pacific children were at

significantly greater risk of developing cellulitis than their New Zealand European counterparts, but were at no greater risk of hospitalisation once cellulitis had developed.

The association between ethnicity and infectious diseases is well recognised but the factors behind the relationship remain unclear. Suggested mechanisms include household crowding, socioeconomic factors, cultural practices, and barriers to primary care.[3,50,56,59,64] In our study, ethnicity was a strong risk factor for developing cellulitis with Pacific children having six times the risk and Māori children four times the risk of developing cellulitis compared to New Zealand European children. Importantly, the effect size persisted despite adjustment for factors thought to be responsible for the difference between ethnicities, including household crowding, maternal education, a range of socioeconomic factors, and barriers to accessing primary care. As insect bites and a previous history to cellulitis were also strongly associated with cellulitis, a subsequent multivariate model included these factors as well as the socioeconomic and healthcare factors. Whilst reduced slightly, ethnicity remained a significant risk factor with Pacific having almost 3.5 times the risk and Māori 2.6 times the risk of cellulitis than other New Zealand children. This suggests there are either unrecognised risk factors, or underlying biological factors.[65] While early reviews suggest the socioeconomic factors interact with currently unknown genetically determined disease susceptibilities,[65] more recent studies suggest there may be some variation in immune responsiveness.[109,146,147]

Ethnicity may affect the risk of cellulitis in any or all of the stages of the infectious process: 1. Frequency or density of colonisation of bacteria, 2. Induction of bacterial toxins and 3. Modulation of the inflammatory response to infection or toxins.[147] Local data has demonstrated no difference in the colonisation rates between Māori, Pacific and New Zealand European children.[108,109] Whilst there was some difference in the strains of *staphylococcus aureus* associated with both colonisation and invasive disease, this did not explain the significant difference in risk. There were also ethnic variations in antibodies to different staphylococcal toxins, with antibody levels being significantly lower in Pacific and Māori compared to New Zealand European adults.[109] Differences in immune responsiveness have been identified in other indigenous groups such as aboriginal Australians and Canadian First Nations children, with documented differences in cytokine gene polymorphisms affecting pro-inflammatory responses.[146,147] Further exploration of differences in innate immune responses and host-bacterial interaction is needed.

Almost all published studies examining ethnicity in relation to cellulitis have used hospital discharge data.[49,50] These identified that Māori and Pacific children have high rates of hospitalisation with skin sepsis, but there has been concern about a possible underestimate of Māori rates due to undercount of ethnicity in hospital coding.[50] As our study used ethnicity as identified by the primary caregiver of the child as opposed to that defined in hospital data, this

concern does not apply to our risk estimates. Interestingly our estimates of more than six times the risk for Pacific and over four times the risk for Māori are higher than the risks reported in other New Zealand studies (approximately 4.5 for Pacific and 2.9 for Māori).[7,27,37,49,50,133] It is unclear whether this reflects different underlying distribution of risk factors, or is related to ethnicity coding, but highlights the significant existing inequity.

Importantly, once cellulitis had developed, our study showed ethnicity was not associated with risk of hospitalisation. This suggests the increased hospitalisation rates for Māori and Pacific children are not due to differential admission criteria, more severe disease, or significant healthcare factors, but due to other factors earlier in the pathway of the development of cellulitis.

Ethnicity has not been routinely or specifically examined in studies of cellulitis among adults. In the only study that examined ethnicity, adults of white ethnicity in Birmingham, United Kingdom, were two times more likely to be admitted with lower leg cellulitis than Asian and Afro-Caribbean ethnic groups.[71] Postulated reasons included differences in skin barrier and function, and different cultural practices. This finding is in contrast to our finding and those of other New Zealand studies which consistently identify a greater risk of cellulitis among non-white ethnic groups. Our research has confirmed the ethnic difference remained after adjusting for skin barrier difficulties such as eczema. We did not examine cultural practices specifically apart from the use of traditional therapies as first aid management.

8.4.1.2 Age

Among children, hospitalisations with serious skin infections are highest in young children and decrease with increasing age.[49,50] Most studies have, however, combined age groups into either children (0-14 years),[27] or preschool children (0-4 years), primary school (5-9 years) and older children (11-14 years).[50] As risk factors may vary across age groups, our finding of a significant difference in risk for infants compared to older children is important. Previous reports also suggest younger children are at increased risk of hospitalisation and imply they are at increased risk of developing cellulitis. One observational study examined the age distribution of skin sepsis in primary care and noted it was different to that occurring in the hospital.[52] They wondered if this was an error due to small sample size or whether it reflected a true pattern due to differing disease severity of admission threshold. In view of the study design incorporating three separate groups of children, we were able to show that infants under one year of age were significantly less likely to develop cellulitis than school-age children but significantly more likely to require hospitalisation once they had developed cellulitis. This may reflect different exposures or risk factors such as breaches to the skin, or the degree of parental supervision, and highlights the

importance of analysing the data in smaller age groups. The higher risk of admission for infants with cellulitis may reflect more severe disease or a lower threshold for admission.

8.4.1.3 Systemic Factors

Most adults who develop cellulitis are otherwise healthy with no underlying systemic illness. This was confirmed among children in our study, with almost all being in good health with no significant underlying illnesses. Importantly, children with reported health problems were at lower risk of developing cellulitis. Pre-existing health problems were therefore protective suggesting the behavioural response to a health problem and potentially the level of parental supervision play an important role in the risk of developing cellulitis.

Obesity appears to be associated with hospitalisation with cellulitis among adults,[20,47,48,74] however, most studies specifically exclude children, have participants with an average age of over 40 years, and utilise hospital cases and controls, thus the information is unlikely to be applicable to our paediatric population. In a recent New Zealand retrospective chart review of hospital admissions with serious skin infections, 41% of children were greater than or equal to 90th weight percentile.[38] As Māori and Pacific children have higher BMIs and higher rates of obesity,[61,62] it was unclear if this was contributing to the ethnic disparity in skin sepsis. Obesity did appear to be a risk factor in our initial univariate analysis; however, subsequent adjustment for ethnicity explained this. Children who were overweight or underweight were not at increased risk of developing cellulitis or subsequent hospitalisation with cellulitis. The increased risk among Māori and Pacific children is therefore not related to higher rates of obesity.

8.4.1.4 Local factors

Disruption of the cutaneous barrier is a consistent risk factor across studies among adults. Most studies that systematically examine for a site of entry identify one in more than 80% of cases.[20,35,46-48] Local factors among adults include recent leg surgery, lymphoedema, and leg ulcers as well as recent breaches to the skin. In general, children in our study had no pre-existing local factors. They did, however, almost uniformly have recent breaches to the skin (section 2.10.2).

In addition to a preceding acute injury to the skin, children may have an underlying chronic or sub-acute skin condition increasing the likelihood of developing cellulitis.[38] New Zealand has a relatively high prevalence of atopic eczema compared to many countries around the world,[90] and this has been proposed as a risk factor.[37] We identified a high frequency of eczema among the children in the case series, but, clinical signs of eczema were just as common among the controls in our case-control study thus eczema was not confirmed as a risk factor for cellulitis. Importantly,

however, differences in the severity and management of eczema were identified, with children who scratched themselves until they bled because of their eczema at significantly greater risk of developing cellulitis.

The presence of eczema and the frequency with which it kept the child awake at night were not associated with hospitalisation with cellulitis. While children who scratched their eczema until it bled were 4 times more likely to develop cellulitis than those who did not, such children appeared to be at lower risk of hospitalisation. While this seems counter-intuitive, it may reflect greater parental awareness of their child's difficulties and subsequent intervention.

8.4.2 Exposures/Breaches of the Skin

Whilst there is a history of trauma breaking the skin in the majority of cases in the adult literature, there are limited data in children on whether breaches of the skin are present prior to the development of cellulitis. Case series data from New Zealand has identified a preceding injury in 13% to 37% of children hospitalised with cellulitis, most commonly insect bites followed by a cut or accidental fall.[7,37,38] These reports were, however, based on routine documentation in the clinical records (using e-codes or clinical note review) rather than a systematic exploration of parental report of injury or examination of the child's skin. With systematic enquiry to all our caregivers, we found, with the exception of insect bites, breaches of the skin were just as common among healthy control children as those children who subsequently develop cellulitis. Parental report of insect bites in the preceding week was, however, a significant risk factor for the development of cellulitis. There was a dose response with the higher the number of bites, the greater the risk of cellulitis. Children who scratched their bites until they bled or wept were almost three times more likely to develop cellulitis than those that did not. This is an important finding and intervention point. The only other risk factor study to specifically examine insect bites did not show any association with cellulitis; however, insect bites were very infrequent and reported in only 1% of adult patients.[71]

Although household pets have been implicated as a risk factor for cellulitis in view of their carriage of fleas and being potential vectors for *staphylococcus aureus,*[94] flea bites were not a commonly reported in our study children. The presence of a household pet was in fact protective against the development of cellulitis and was not associated with risk of hospitalisation once cellulitis had developed. The majority of insect bites were from mosquitos which has important implications for prevention.

Breaches of the skin in the preceding week were as frequent among the Hospital cases as the GP cases. The presence of nappy rash and other skin problems increased the risk of hospitalisation with cellulitis. Children with insect bites in the preceding week were 56% less likely to be

hospitalised with cellulitis. There was a dose response with the higher the number of bites, the lower the risk of hospitalisation. Due to the way the questions were asked and answered we were not able to determine whether the cellulitis developed at the site of the insect bites, or whether they were distant to the site. Irrespective of this, however, insect bites remain a significant factor in whether children develop cellulitis or subsequently require hospitalisation. It is unclear if the bite itself is a factor or whether this is a marker of other environmental or behavioural risk factors.

It is possible there is a degree of information bias in reporting recent breaches of skin. Parents of a child who develops cellulitis or requires hospitalisation with cellulitis may be overtly looking for a reason why their child developed cellulitis and thus potentially be more likely to report recent breaches of the skin. If this was the case, however, one would expect that all breaches of the skin would be more frequent among the cases. This was not the situation, and with the exception of insect bites, all other breaches were as common or less common among the children with cellulitis. This suggests for most children it is not breaches of the skin per se that increase the risk of developing cellulitis but other factors such as management of the breaches and initial redness that are important.

8.4.3 Host Behaviours

Skin infections are said to be associated with poor hygiene, crowding, and neglect of minor trauma.[2,69,92] Factors potentially implicated include hand washing and hygiene measures, sharing of towels and bedding, and the mechanism of washing towels and bedding of infected children (hot, cold water, machine washing).

Our study identified a few specific host behaviours associated with cellulitis. Both scratching insect bites and eczema until it bled were associated with an increased risk of developing cellulitis. This likely reflects a combination of the increased severity of the breach and possible differences in management. Once cellulitis had developed, hand washing practices and sharing towels were important factors associated with subsequent hospitalisation. Neither bathing nor clothes washing practices were identified as risk factors.

Apart from one study, adult studies on the risk factors for cellulitis have not specifically examined the effect of hygiene on the risk of developing cellulitis. Eells in his case-control study examined some health behaviours as a risk for non-suppurative cellulitis.[36] These included participating in contact sports, re-wearing clothes without washing, wearing someone else's unwashed clothes, sharing a towel, sharing razors, and getting skin cuts, scrapes, and abrasions. None of these were associated with developing cellulitis.

8.4.4 Past History and Family History of Skin Sepsis

Whilst adult case series and case-control studies identified a past history of cellulitis in 25-50% of cases,[20,46,48,57,71,73,79] no such studies exist among paediatric populations. Our study has highlighted the importance of a previous history of cellulitis, occurring in 31% of cases and increasing the risk of developing cellulitis nine fold. In addition, we were able to show a dose response relationship with the greater the number of previous episodes the higher the risk of developing cellulitis. This has not previously been reported and provides a key intervention point.

Importantly, while an increased number of episodes increased the risk of developing cellulitis, it decreased the risk of hospitalisation once cellulitis had developed. As all other case-control studies examined the risk factors for hospitalisation with cellulitis, they were not able to see this relationship. Potential reasons for this effect include learned behaviour as a result of previous experience with skin sepsis or development of immune tolerance.

In view of the high frequency of recurrences, some authors suggest cellulitis should be thought of as a recurrent potentially chronic disease rather than as a defined acute illness.[71] This is based on the belief that cellulitis results in long term damage to the lymphatics and subcutaneous tissues and predisposes the patient to recurrent cellulitis.[71] A current Cochrane protocol looking at interventions for the prevention of recurrent cellulitis suggests targeting causative organisms and controlling risk factors that are liable to relapse are key strategies to prevent recurrences.[35] There is a strong focus on local risk factors which potentially overlooks the behavioural, environmental and health literacy factors. Our study highlighting the increased risk associated with other household members suggests it isn't a person-specific disease, but a household disease based on shared environmental, microbiological, genetic, or behavioural factors. Although this has been examined in studies looking at the risk factors for MRSA skin sepsis due to MRSA,[110,148] the importance of skin sepsis in other household members has not been examined in other cellulitis risk factor studies. This has significant implications for development of management and prevention strategies.

We demonstrated the elevated risk of cellulitis from previous skin sepsis in other family members was present to almost the same extent irrespective of the time since the most recent infection. If the increased risk was due to a virulent strain of bacteria, one would have expected the risk to be significantly greater for skin sepsis occurring in the previous month compared to sepsis occurring more than 12 months before. This relationship has not been explored in other studies and suggests environmental or behavioural influences as important factors in the risk of cellulitis.

8.4.5 Social/Environmental

8.4.5.1 Socioeconomic Status

Socioeconomic status is strongly associated with risk of hospitalisation with cellulitis among New Zealand descriptive studies.[27,49-51] However, for the most part these studies reported univariate analyses thus it has been unclear whether this is an independent effect or whether it is an apparent effect due to the strong association with ethnicity. We showed an initial effect of socioeconomic status as measured by the NZDep score; however, once ethnicity was controlled for the effect of socioeconomic deprivation disappeared. Our study design of matching by geographic area effectively partially matched by socioeconomic status and therefore reduced our ability to examine the independent effect of socioeconomic status. It did mean, however, that adjustment for socioeconomic deprivation was incorporated into both the study design and analysis. Subsequent further adjustment by specific socioeconomic factors therefore effectively controlled for residual confounding. The advantage of this study design, whilst reducing our ability to examine the independent effect of socioeconomic factors, increased our ability to identify potentially modifiable risk factors.

8.4.5.2 Housing and Crowding

Apart from homelessness,[36,74] housing has not been specifically examined as a risk factor for either the development of cellulitis or hospitalisation with cellulitis. Several housing factors were associated with both of these outcomes in our study; however, the effects largely disappeared once the effect of ethnicity was taken into account. Sharing a bedroom was associated with an increased risk of developing cellulitis and higher bedroom occupancy was associated with an increased risk of hospitalisation with cellulitis. As socioeconomic status was incorporated into the study design and is strongly associated with crowding, this reduced our ability to show an independent effect of household crowding on the risk of cellulitis.

Crowding increases contact between people who are susceptible and those who are infected or carrying infectious organisms. Crowding has been clearly associated with increased risk of infectious diseases such as meningococcal disease, respiratory syncytial virus, tuberculosis, and rheumatic fever.[60,63,149,150] Crowding has been shown to increase the risk of developing rheumatic fever over and above the effect of socioeconomic status.[60] Crowding may also increase exposure to infectious co-factors, such as exposure to tobacco smoke and is associated with other socioeconomic measures of socioeconomic deprivation including low education level, lower household income, unemployment and fewer material resources such as cars and telephones.[63]

Crowding can be measured by a variety of means using different combinations of the number of adults, children, and bedrooms.[151] Some authors suggest that, because the risk of infection may be greater among children, the number of individuals in susceptible age groups may be more important than the total number of individuals in the household.[151] This effect was shown in our study where living with another child increased the risk of developing cellulitis.

8.4.6 Health Literacy/Healthcare Utilisation

Very little is known about people's understanding of skin hygiene and first aid for breaches of the skin. This is the first study to specifically examine parental first aid management of common childhood injuries. Importantly, first aid management of breaches to the skin was similar for case and controls thus on the whole did not appear to be a factor in the development of cellulitis or subsequent hospitalisation.

Once redness had developed, however, there were important differences in both first aid management and healthcare seeking behaviour. Children whose caregivers noticed the skin sepsis at an earlier stage, either identifying redness alone without corresponding swelling and pain, or who identified it at a smaller initial size, were at lower risk of hospitalisation. Similarly, children whose caregivers administered some form of first aid or sought medical help for the redness were at lower risk of hospitalisation. Although it is intuitive that earlier recognition and management of a skin infection would be beneficial, this study clearly identifies these behaviours as important. Any health literacy intervention must emphasise the importance of early identification and include regular checking of the child's skin particularly if there is a breach of skin or minor redness.

8.4.7 Healthcare Factors

Adult studies have specifically examined individual factors but not healthcare or healthcare utilisation factors. Ours is the first cellulitis risk factor study to do so. Overall, there was no difference in the usual healthcare utilisation for cases and controls. However, there were some important difference in healthcare utilisation and provision among children who developed cellulitis. Children who were seen in an Accident and Medical Centre were at increased risk of being hospitalised with cellulitis. This may reflect several interacting factors including the timing of when parents noticed the skin sepsis, the severity of the cellulitis when it was first identified, the quality of healthcare provided, or the fact that families who attend after-hours centres as opposed to their usual family doctor are different with respect to other unrecognised factors.

Caregivers who reported difficulty accessing a doctor for the illness were at greater risk of being hospitalised. Both cost and transport were clearly identified risk factors. As children under six

receive free healthcare, the effect of adjusting for age should have removed cost as a barrier. The fact it continued to be a significant factor suggests cost is a barrier for the family as a whole and not purely the index child. Very few caregivers reported other barriers to accessing primary care. Whilst another Auckland study reported prescriptions were not taken to the chemist in approximately one-in-five children prescribed antibiotics for pneumonia,[152] almost all the caregivers in our study reported they picked up the prescription and administered the antibiotics promptly.

Healthcare provided by practitioners reflected to some extent the severity of the cellulitis at first presentation to medical care. Sixty percent of Hospital cases were considered to be sufficiently severe when first seen in primary care that they were sent straight to the hospital for further assessment and/or admission. This reflects the severity of illness at first presentation, however, it remains unclear how much was due to rapidly progressive disease, or lack of parental awareness of their child's skin until a severe state. Prescribing practice also reflected the severity at initial presentation with children requiring prescription of pain relief being at greater risk and children prescribed topical antibiotics being at lower risk of hospitalisation with cellulitis. Interestingly, caregivers who reported that their GP gave no advice or treatment apart from a prescription were at greater risk of being hospitalised. Provision of other advice such as care of bites, cuts, dressing, cleaning or hygiene should be an important component to treatment strategies and plays an important role in increasing health literacy.[118] To date, no other studies have specifically examined healthcare factors associated with skin sepsis.

8.5 Strength and Weaknesses of the Study

In this section, the strengths and weaknesses of the study are examined as they relate to the study design, selection issues, information biases, confounding, precision and external validity. Each of these could have had an important impact on the interpretation of the results thus efforts to minimise this during study design, analysis, and interpretation are discussed.

8.5.1 Study Design

A case-control study design was chosen because this is an efficient way to study risk factors for relatively rare outcomes and was the most appropriate design to address the hypotheses proposed in this thesis. Case-control studies are more efficient than cohort studies in terms of resource use and time and can examine multiple etiologic factors for a single disease.[153] Additionally the case-control study design reduces the loss to follow up and enables the measurement of short term or transient exposures or confounders such as breaches to skin in the preceding week. The disadvantages of the case-control study design include participant selection

issues, information bias, and confounding.[154,155] These issues were considered in the initial study design, and efforts made to minimise the impact of these factors wherever possible.

All previous studies compared hospital cases to a control group, whether they were hospital controls or healthy community controls. This provided information about the risk factors for hospitalisation with cellulitis, but not the risk factors for developing cellulitis per se. As a significant proportion of cases with cellulitis are treated in primary care and do not require hospitalisation, we wanted to examine both the risk factors for developing cellulitis and the risk factors for hospitalisation once cellulitis had developed. We therefore utilised three groups: healthy controls, cellulitis cases successfully treated in primary care, and cellulitis cases requiring hospitalisation. In this study data from the GP patients with cellulitis were used in two different ways: They were 'cases' for the component examining risk factors for developing cellulitis and 'controls' for the study examining risk factors for hospitalisation. We combined the GP cases and the Hospital cases when examining the risk factors for developing cellulitis as we wanted to examine factors across the spectrum of disease. Use of GP cases alone as the comparative group would have concentrated on milder disease alone, whilst use of Hospital cases as the comparison, would have examined what the other studies have done: the risk factors for hospitalisation with cellulitis. This strategy, whilst an efficient use of resources, relies on accurate weighting of the contribution of the GP cases relative to the Hospital cases. Our weighting was carefully determined according to the best information at the time, however, as there were some differences in risk factors across the GP cases and the Hospital cases, it is possible a different weighting may have resulted in slightly different point estimates.

8.5.2 Selection Issues

The study eligibility criteria, procedures used to select participants, and the factors that influence participation, can affect the internal validity of the study due to the presence of selection bias, and can affect the generalizability or external validity of the findings. The internal validity depends on cases and controls being derived from the same underlying study population.[153] Bias may arise if the participating cases do not represent the exposure distribution of all cases in the study population, or if the controls do not represent the exposure distribution of the whole study population from which the cases arose.[153,156,157]

The source population was identical for the three study groups: children living in the Waitemata and Auckland DHB areas who were 6 weeks to 15 years of age. This study area was chosen as Starship Children's Hospital was the sole provider of general and specialised inpatient care for these children at the time. The eligibility criteria ensured wherever possible that the cases and controls were from the same pool of potential participants. As we used GPs who practiced within

the study area as the sampling unit for the GP cases and controls, we restricted the eligibility by specifying all Hospital case children had to have a nominated GP who practiced within the study area. Whilst this reduced the number of Hospital cases slightly, it ensured the Hospital cases came from the same population of children as the GP cases and controls.

Hospital Cases: This study attempted to identify all eligible Hospital cases arising from the study base. Case ascertainment is likely to be close to complete because Hospital cases were recruited from the only hospital that provides inpatient treatment to children serving the study area. We used a prospective identification of cases (active case ascertainment strategy) with a clinical case definition of cellulitis. This was intentionally broad; acknowledging we would have a modest false positive rate, but ensured we captured as many eligible cases as possible. The use of a clinical case definition applied at the time of seeing the child and family, ensured the case definition was the same for both the Hospital and GP case populations. We did not recruit in the weekends; however, as we enrolled patients Monday to Friday and the average hospital stay for cellulitis was 2 days, it is unlikely we missed many cases. An alternative case ascertainment strategy for Hospital cases would have been to identify them following discharge using ICD discharge codes. This latter strategy may have provided selection bias as eligibility would have been based on an epidemiological definition,[28] would have resulted in a delay between admission and interview with a potential for increased recall bias, and would likely have reduced participation and increased cost. A strategy based on hospital discharge coding relies on reliable clinical recording and interpretation via the coders, and would not have had a comparable strategy for identification of cases in primary care.

The Hospital case response rate was moderately high (72% of all eligible children participated) as was the participation rate (79% of the eligible cases who were able to be asked about the study participated). The difference relates to families leaving the ward prior to being asked by hospital staff about their interest in the study. The use of a two stage consent process is likely to have increased participation as the families were introduced to the study by their primary nurse rather than a stranger. The use of an experienced researcher in gaining second stage consent also increased participation and both these factors are reflected in the high consent rate with 90% of those families who gave first stage consent (thus agreeing to talk to the researchers) participating in the study. We do not have information as to whether the nonparticipants were systematically different to the participants, however, the relatively small number of nonparticipants means the actual cases are likely to be representative of all Hospital cases.

GP Cases: GP cases for this study were a sample of all GP cases occurring in the study area during that time. GPs were randomly selected in proportion to the geographic areas of admission for cellulitis from two previous years. There was a high participation rate for GPs (87%). The

prospective identification of cases (active case ascertainment strategy) using a clinical definition of cellulitis by experienced clinicians was identical to that for the Hospital cases. Despite attempts at collecting data for nonparticipants, the tracking sheets (with the demographic data of all eligible children) contained very little data thus we were unable to determine whether the cases referred to the study centre were representative of all cases seen. GPs reported they referred all consenting cases to the study and that participation was high with low family decline of involvement. The fact we had a higher number of children referred than were identified in the tracking sheets suggests the nonparticipation rate may have been low. The use of an experienced researcher also increased participation and both these factors are reflected in a high participation rate with 90% of those families who gave first stage consent (thus agreeing to talk to the researchers) participating in the study.

Controls: Our controls were identified using the same sampling process used for identification of the GP cases. At the practice level, children were selected from the practice list using a random number selection strategy. This process and the moderately high first stage consent rate (81%) and subsequent high participation rate (94%) meant the controls were likely to be representative of the whole population.[156,158,159] It also ensured the GP cases and the controls came from the same base population.

Potential alternative sources of controls include family or neighbourhood controls, random digit dialling, and hospital or primary care controls. Use of family members as controls would have been problematic for several reasons. This group would not be representative of the general public, and would have environmental and healthcare utilisation factors in common with the cases which could bias the results. As a proportion of family members will also have had a prior diagnosis of cellulitis, use of this group would obviate the ability to examine differences in family knowledge and behaviour as risk factors for the disease or hospitalisation.

Random digit dialling (RDD) or door knocking would provide random community controls but is timely and expensive. There are also concerns about how representative participants would be of the general public, as response rates are often poor and vary with socioeconomic status.[160] RDD is also now not as effective as it used to be given the increase in use of mobile phones, answer phones, caller identification, and multiple telephone numbers for a given household.[160]

The GP controls were selected using a similar selection process to the GP cases, but occurred using a separate sampling process. Matching GP cases to controls using the same GP would have reduced the ability to examine differences in medical management of cellulitis as a risk factor for hospitalisation.[160,161] Unlike the majority of the adult studies of risk factors for cellulitis,[20,46-48,71,74] we chose not to use hospital controls as we wanted to examine factors

associated with both the development of cellulitis itself, and then once cellulitis had developed, factors associated with hospitalisation. This required examination of factors across three distinct groups: a group of healthy children, a group of children who developed cellulitis but were successfully managed in primary care, and a group of children who required hospitalisation for their episode of skin sepsis. The use of children recruited from hospital outpatient clinics or from hospital admissions as controls would not have been representative of the base population and would have only provided information about risk factors for being hospitalised with cellulitis.

Key strategies suggested in the literature to improve community control response rates include the training, experience and personality of the recruiters, the salience of the research topic, the appearance of the postal material, and in person approaches as opposed to initial telephone contact.[161] In the present study, strategies used to optimise control response rates included the use of interview staff with previous research and interviewing experience, the piloting and testing of the participant information used in the study to ensure its user friendliness, the use of the GP as the person who introduced the study in our approach to GP cases, and a personalised written invitation for controls to participate from their primary healthcare professional with logos from both the Starship Children's Hospital and the University of Auckland. We had a modest use of media in the weeks leading up to the study with an article in the New Zealand Herald, local community papers and a segment on the TV news (Appendix 6). Information boards on cellulitis and the research study were displayed in the Children's Emergency Department and the wards at Starship Children's Hospital for the duration of the study. We found parents willing to be involved as they felt it was going to help the health of their children as well as others with skin sepsis. We provided a small gift as an acknowledgment of the time and effort to take part in the research, however, this was provided to the family at the end of the interview as thanks rather than offered up front as an incentive to increase participation rates.

Because of the sampling process used there were limited data available on those who did not agree to take part and we were unable to compare the participant population with the nonparticipant. However, adjusting for factors known to be associated with poor response, including age and socioeconomic status, should have reduced these biases to some extent. As with all observational studies residual confounding remains a threat to the internal validity of the study. As our participation rates were moderately high, the risk of selection bias would have been low.

All studies suffer from non-participation in some form, whether it is due to missing data, initial non-response or, in longitudinal studies, loss to follow-up or attrition (caused by difficulty locating participants, refusals to continue, or death). Each of these can lead to selection bias.[162] In our study, missing data comprised a small percentage of all data. The key variables, particularly those

that were considered as confounders and thus important for the multivariate model, were complete with no missing data. The few factors with a significant amount of missing data, such as paternal education, were not used as we had other measures which provided similar or more relevant information (e.g. maternal education). Initial response and participation rates were moderately high for all groups and there were no withdrawals from the study. Attrition was modest and largely due to an inability to contact a small number of families. This was in part due to the limited information collected from the family at the time of gaining first stage consent. The researchers only had the child's name and a contact phone number and thus were unable to contact some families. It is likely these families were different in some way to those that participated, however, as the response rates were 72-90% and participation rates 79-94% across the three groups, the potential for selection bias is modest.[161]

8.5.3 Information Biases

Systematic error in a study arises when the information collected from or about study participants is incorrect.[153] Information bias can be an issue for both exposure and outcome variables.

Differential recall of exposure information by cases and controls can result in recall bias.[153] This may have been an issue when comparing the responses from a parent who currently had a child in hospital (as occurred in the majority of Hospital cases), with responses from a parent interviewed at home two weeks after the hospitalisation, or with a healthy control child. Parents of a hospitalised child may be more likely to attribute causality to a particular factor than a parent of a healthy child. This may have been predicted for the questions relating to whether the child had a breach of the skin in the week prior to either the interview for the controls or the episode of skin sepsis for the cases. Our results show, however, that with the exception of insect bites, breaches of the skin were less likely to be reported by case parents than control parents.

Another area where recall bias may have played a role is in the report of a previous history of cellulitis. Cases clearly had a recent or current episode so were aware of what the diagnosis entailed. In contrast, controls may have answered the question differently as they may or may not have been aware of what cellulitis was. We attempted to reduce this discrepancy by talking to the control parents and showing them a picture of cellulitis. If diagnostic transfer occurred, it would have been small as controls reported fewer other skin problems overall in addition to fewer previous cellulitis than the case children with recent or current cellulitis.

Another area of potential differential response relates to the self-report questions re the hygiene, environmental or healthcare practices. It is recognised that exposures that are considered socially undesirable tend to be underestimated.[163] Wherever possible we were careful to say up front that we did not know whether these factors were important or not but wanted to get an understanding

of whether or not they had an impact. There was also the potential for people to not respond to some of the more sensitive questions in a face to face interview. We prefaced the questions with a general comment about trying to understand what was important for our children, were careful to be non-judgemental, and covered the more sensitive questions at the end of the interview.

Like the participants, the interviewers were aware of the outcome status when exposure data were gathered. While the interviewers had been trained to avoid conducting the interviews differently for the cases and controls and the interviews were based on a highly structured questionnaire, it is possible that bias may have been introduced by systematic differences in the way the interviews were conducted. For example, responses may have been different according to whether the interview was undertaken at home or in the hospital, whether it was performed in English or another language, or by different interviewers. Most of the Hospital case interviews were performed by one interviewer in the hospital setting, whilst the GP cases and controls were performed by a selection of different interviewers of different ethnicities. We were careful to match the interviewer and interviewees by ethnicity wherever possible to reduce information bias.[164]

We attempted to minimise bias by ensuring that interviews were based on a structured questionnaire standardising the administration of exposure questions for cases and controls, that interviewers were trained to conduct the interviews in a uniform manner, and that they used a standardised set of relevant prompts. Interviews were undertaken with the primary caregiver for the child and all were face to face. We also ensured the interviewers and caregivers were not aware of the specific hypotheses being investigated as a further means of reducing the risk of systematic measurement error.

All exposure variables considered in the main analysis of this research had less than 10% missing data it is therefore unlikely that effect estimates were substantially affected by missing data. Most relevant or important variables had complete or near complete data and imputation was not considered necessary.

Our primary outcome status was the presence of cellulitis. It is possible this outcome was slightly different in GP cases compared to Hospital cases, however, this was minimised by using a standard clinical definition irrespective of the underlying condition. All participating clinicians had a specific case description with explanatory pictures, and all were experienced clinicians dealing with a clinical condition that is common both in primary care and hospital settings. We considered cellulitis as a broad descriptive outcome and did not divide it into different subgroups. In view of the numbers of cases, the study had insufficient power to detect differences within the subgroups of skin sepsis: e.g. cellulitis associated with abscess requiring incision and drainage compared to non-suppurative cellulitis that responded to antibiotics alone. It remains to be seen if they are

different types of skin sepsis with different risk factors, or whether they are at different points in the spectrum of skin sepsis.

8.5.4 Confounding

With all nonrandomised studies, uncontrolled confounding is the major threat to the validity of the results. Misclassification of confounding variables results in incomplete control of the effect of the confounders; e.g. socioeconomic status and crowding. Incomplete control of confounding occurs due to missing data on the exposures of interest (for most this was low and expected not to be significant), misclassification of potential confounders, and measured and unmeasured factors that may operate as confounding variables. When present, confounding results in a biased estimate of the effect of the risk factor for the development of the disease. The bias can be positive, resulting in the effects of the risk factor being overestimated, or negative, and it can even reverse the apparent direction of the effect.

We undertook both unadjusted and adjusted analyses to help identify and reduce confounding from variables. Factors considered were both those we knew apriori were associated with cellulitis and those shown to be significant during the analyses. As we were aware apriori that socioeconomic status and ethnicity were important risk factors for cellulitis we designed the study to take this into account. We purposefully group matched in a way that would increase the chances of having high numbers of controls with lower socioeconomic status and of Māori and Pacific ethnicity. Whilst this reduced our ability to show an effect regarding these factors, it increased our ability to show the effect of other risk factors which are potentially modifiable. We incorporated this into the study design and statistical programming, and subsequently adjusted further for the effect of residual confounding by socioeconomic status by controlling for deprivation using the NZDep index.

8.5.5 Precision

The study power calculations are discussed in chapter 4.3.5. We based our sampling schema on data from previous admissions, and a GP survey about the number of children seen with skin sepsis per week. As outlined, we overestimated the number of potential primary care cases, and underestimated the amount of time it took to engage primary care, visit practices, and set up the recruitment of both GP cases and controls. Successful contact of caregivers also took more time than anticipated. In order to minimise these factors, we modified the sampling one month into the study, and employed another co-ordinator specifically to engage with the practices.

The final number of participants was sufficiently high for the Hospital cases and controls, but lower than we had hoped for the GP cases. As we combined the two case groups for the analysis

of risk factors for developing cellulitis, the lower than anticipated number of GP cases did not have an impact on the power for this component of the study. It will, however, have reduced our ability to identify effects that were small to modest in size and will have diminished the precision of effect estimates more generally. Some factors had wide confidence intervals, thus a larger study size would have been useful to improve precision of the estimates. A larger sample size would also have provided sufficient power to look at subgroup analyses within different ethnic or age groups, or within different subgroups of skin sepsis.

However, acknowledging this, the number of cases and controls is similar to the sample sizes in many of the adult studies,[20,46-48,71] and larger than the only published study using community controls to determine the risk factors for hospitalisation with cellulitis.[73] This study remains the only case-control study of risk factors for cellulitis among children.

8.5.6 External Validity

The external validity of a study requires that the population being studied adequately represents the population of interest to which you wish to apply the findings. This study was population-based and had few exclusion criteria. The exclusion criteria were specified to ensure the controls and cases were from the same population thus increasing internal validity without significantly compromising external validity. As we effectively oversampled children from lower socioeconomic areas and those of Māori and Pacific ethnicity, our control population will not have been representative of the general child population. Our final analyses did incorporate and adjust for these factors thus it is likely the findings are generalizable. The population we studied were representative of the very populations at greatest risk of cellulitis.

Our inclusion criteria required that children reside within ADHB, and attend a GP within the ADHB area. For Hospital cases, we also specified they had to be admitted to Starship Hospital. A small number of potentially eligible children living in the study area may have been admitted to the children's ward at Middlemore Hospital in South Auckland. Anecdotally the number of such cases is low. We did not include potentially eligible children who attended GPs outside the study area. This would have been important if we were looking for population estimates regarding the prevalence and incidence of skin sepsis among children in the area, however, as this was not what we were trying to determine, it was considered more important to match them by GP suburb.

8.6 Translating the Findings of the Research

This risk factor research has provided some new insights into factors associated with skin sepsis among children. The learnings have been incorporated into several local activities:

1. **Northern Region Child Health Plan**: Skin sepsis is now one of the 5 priority areas for child health for the Northern Region Child Health Plan. I am one of the clinical leaders working with Planning and Funding Managers from the District Health Boards to develop a regional child health plan. This combined plan has specific objectives about skin sepsis and will ensure consistent approaches to prevention, treatment, and management across the four northern DHBs: Auckland DHB, Waitemata DHB, Northland DHB and Counties Manukau DHB. Children living in these four DHBs comprise approximately 50% of the New Zealand hospital admissions for serious skin sepsis.

2. **Primary Care Guidelines:** I am on the advisory group for the development of primary care guidelines under the Greater Auckland Integrated Healthcare Network (GAIHN). These are in their final stage of development and will be incorporated into the primary care practice systems for use by General Practitioners and practice nurses for the northern region. Information from this research has been incorporated into the guidelines specifically regarding the importance of cellulitis being a household disease, socioeconomic factors, and encouraging wound care, and hygiene advice.

3. **School-Based Health Services:** Throat swabbing clinics have been introduced in selected schools in the DHB as part of the Better Public Service Target to reduce Rheumatic fever by two thirds by 2017. As these schools are also the ones with high rates of skin sepsis and principals are concerned that skin problems are contributing to absences and disrupting learning, management of skin infections has been added as a key component to the school-based initiative. Findings from this research have been incorporated into the management with specific focus on health literacy for the school, the children and their families/whānau. Home visits and household assessment and follow-up have been incorporated into the program acknowledging cellulitis is a household disease.

4. **Starship Clinical Guidelines:** Guidelines produced for the management of cellulitis and abscess at presentation to hospital. These are available on the Starship Children's Hospital website and are used by medical staff at Starship and other hospitals around New Zealand. They were initially developed at the beginning of my research journey and have since been updated incorporating relevant findings (Appendix 6).[136]

5. **Kidshealth Fact Sheets:** These fact sheets are available on the internet to provide accurate and reliable information about children's health for New Zealand parents and caregivers, as well as the wider family and whānau who are involved in caring for our children. I have recently reviewed them and am providing a further review of the content.

6. **Health Literacy Project:** I have been on an expert advisory group working with Workbase who have been contracted by the Ministry of Health to undertake research into health literacy about skin sepsis. This project has just finished developing resources that will help families and whānau to understand skin health, assist them with self-care and preventive activities, and guide them to seek healthcare at opportune times. My input has been from the clinical and research perspective, incorporating key findings from this risk factor research.

8.7 Unanswered Questions and Future Research

Cellulitis is a result of a complex interaction between many factors including host, environmental, microbiological and healthcare. Our research has highlighted some important factors, addressed several gaps in the literature, and identified several areas which deserve further attention.

8.7.1 Host Factors

Ethnicity remains a significant risk factor even after adjustment for multiple factors known to be associated with increased risk for skin sepsis. Further work needs to explore if this relates to differences in innate immunity, microbiological exposure, the interaction between the two, or other as yet unrecognised factors.

8.7.2 Environmental Factors

Skin sepsis is a household disease rather than an individual disease. It remains to be determined if this relates to similar susceptibilities, behaviours, bacterial load, exposures, or health literacy.

8.7.3 Past History and Family History of Cellulitis

Cellulitis is a household disease with a strong association with past disease. Future work needs to determine what interventions are appropriate for both the individual and other household members after a first and subsequent episode of skin sepsis.

8.7.4 Microbiology

As MRSA comprised only a small proportion of the cases and preliminary evidence suggested microbiological factors were not significant contributing factors to the recent increase in incidence, we did not examine microbiological characteristics of the children or their families. This would have been another useful contribution to our understanding of cellulitis; however, the decision was based on the best information we had at the time and the concept this was one part of the research journey and was not able to be the definitive study. Since that time, further work has been undertaken, but more is needed. It is important to understand rates of staphylococcal carriage, characteristics of strains that both colonise and infect, and specific virulence factors among specific ethnic groups. It is also important to determine the household carriage rates of staphylococcus for both household occupants and household surfaces, and to explore the complex interactions between bacteria and the host immunological response.

8.7.5 Other Factors

There is a wealth of international literature about the burden of cellulitis and skin sepsis among adults. To date, however, this has not specifically been examined in New Zealand. Given the disproportionately high rates of cellulitis for New Zealand children, and the familial load of disease, the burden of skin sepsis among NZ adults needs to be pursued.

8.7.6 Intervention and Prevention Strategies

There is a paucity of evidence based reviews in the international literature which consider effective interventions to reduce serious skin infections at the population level.[27] The findings of the frequent and recurrent disease in both the index child and other household members are important when designing effective preventive strategies. Treatment and decolonisation strategies that focus on the individual are unlikely to be effective. Similarly, decolonisation without an emphasis on health literacy again is unlikely to be effective. Any strategy must be multipronged addressing the complex issues contributing to the risk and protective factors for skin sepsis.

8.8 Conclusion

The aim of this risk factor research was to understand in children the risk factors for cellulitis and the risk factors for hospitalisation once cellulitis had developed. This research has identified several key factors and addressed many gaps in the literature. Importantly this is the first study to examine the risk factors for cellulitis among children, the first to examine healthcare and health literacy factors, the first to examine the risk factors for developing cellulitis itself as well as the factors that are associated with hospitalisation once cellulitis has developed, and one of the largest risk factor studies of cellulitis among any population.

Cellulitis is a complex disease with overlapping effects of several risk factors. No one factor dominates. Our research has highlighted the persisting effect of ethnicity irrespective of other associated factors. Pacific children are more than 3 times the risk, and Māori children more than twice the risk of developing cellulitis compared to other New Zealand children despite adjustment for all identified risk factors. This is a significant cause of inequity and deserves further exploration into underlying genetic susceptibilities in immune responsiveness.

Cellulitis in children is a recurring household disease due to a combination of factors rather than a recurrent disease of individuals due to local factors. Behavioural and environmental factors are more important than individual factors.

Insect bites are an important factor in both the development of cellulitis and the risk of hospitalisation with cellulitis. This has been under appreciated and needs specific intervention.

Health literacy is key with important factors identified in caregivers' awareness of the integrity of their child's skin as well as differing management of both breaches of skin and the first signs of infection. Key messages must include regular checking of the skin, as well as advice about skin health and first aid management at the first sign of redness.

Healthcare factors play an important role in both the development of and hospitalisation with cellulitis. Access to primary care is key as well as the provision of general advice regarding skin care and health.

It is interesting to consider how little is known about the risk factors and management of cellulitis, particularly when hospital admissions for cellulitis are as frequent as those for pneumonia. The information gained from this risk factor research is an important contribution to our understanding. It has helped inform several local and regional initiatives as well as a new case-control study about to start at Starship Children's Hospital. The journey continues and I look forward to working with others to develop an intervention study to reduce the incidence and impact of cellulitis among children and their families.

Cellulitis in Children

Risk Factors for Developing Cellulitis and

Risk Factors for Hospitalisation with Cellulitis

Volume 2: Appendices

Alison Maree Leversha

A thesis submitted in complete fulfilment of the requirements for the degree of

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Appendix 1: Summary Tables

Table of Descriptive Studies of Cellulitis among Children

Table of Epidemiological Studies of Risk Factors for Cellulitis among Children

Table of Descriptive Studies of Cellulitis among Adults

Table of Epidemiological Studies of Risk Factors for Cellulitis among Adults

Table 1: Summary of Descriptive Studies of Cellulitis among Children

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Lawes, 1998, Auckland, New Zealand, descriptive study[7]	Children 0-14 years.	Children hospitalised with cellulitis.	Starship and Middlemore hospital discharges with a principal diagnosis of cellulitis from 1994-98.	Paediatric hospitalisation rates have doubled over 4 years. Discharge rates 3-4.5 times higher in Pacific children and 2-3 times higher Māori children than European children. Rates 2-3 times higher in children 0-5 years.	Cellulitis has increased. No evidence of a change in causative organism. Likely the increase is due to a combination of host and environmental factors and access to primary care.	• First NZ study identifying skin sepsis was an issue. • Hospital cases thus moderately severe end of spectrum. • Univariate analyses.
Finger, 2004, Auckland, New Zealand, case series[3]	Children 1-14 years.	91 children hospitalised with cellulitis.	Retrospective chart review.	51% abscess, 49% cellulitis. 79% lower limb. Incidence 137.7/100,000 in Polynesian children and 35.4 in European/Other children. Polynesian RR=3.9 (2.3-6.5).	Polynesian children are affected by a high incidence and increased relative risk of skin infections in their limbs. Further research is needed to identify whether genetic predisposition or social and environmental circumstances are involved in this phenomenon.	• Retrospective chart review thus relies on accurate coding and documentation. • Excluded infants under 1 yr of age. • Combined Māori and Pacific into the single ethnic group. • Included abscess and cellulitis. • Used ICD primary diagnosis only.
Hunt, 2004, Wellington, New Zealand, descriptive study[37]	Children 1-14 years.	Children hospitalised with cellulitis.	Wellington region hospital discharges with a principal discharge diagnosis of cellulitis from 1996-2002.	Paediatric hospitalisation rates increased 55% over 7 years. Discharge rates 3 times higher in Pacific children and 2 times higher in Māori children than European children. Rates higher in children living in more deprived areas. Rates 2-3 times higher in children 0-5 years. Cumulative cost >$2 million over 7 years. Rate 2x Australia and USA.	Serious skin infections are a common avoidable cause of hospitalisation with significant ethnic and socioeconomic disparities.	• Good regional overview of the issue. • Univariate analyses only. • Many suggestions re interventions.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Goettsch 2006, Netherlands, population based study[53]	Total population adults and children.	Eligible population =16 million (Netherlands population), 1 million in pharmacy database, 50,000 in GP data base.	Analysis of linked databases; Dutch national hospital data, pharmacy database and subsample of GP data.	179.6 primary care episodes per 100,000 population per year 12.1 admissions/100,000 population. Increased steeply with age. Estimated admissions in 0-15 yr age group <5/100,000. 7% patients with cellulitis were hospitalised. 6.6% of hospitalised patients <24 yrs of age 4-6% of pts had 2 or more episodes during that year. Average cost for hospitalisation 5346 euros. 80% of total costs (13.7 million euros) due to hospital costs.	Bacterial cellulitis and erysipelas of the leg are common and serious infections. Hospitalisation occurs in 1 in 14 patients but contributes more than 80% costs.	• Population based study. • Good data across primary care and hospital. • Useful cost estimates including hospital, pharmacy and GP costs. • Infections of the leg only. • No data re incidence in young ages and children comprised only 7% of the hospital population.
Ellis Simonsen 2006, Utah, USA, population based study[54]	Total population ~27% <15 years.	Population based insurance claims database of Mormons. ~50,000 people. Over 5 year period.	Analysis of insurance database claims.	Cellulitis incidence rate 24.6/1000 person years. Higher incidence among males and individuals 45-64 years. 20/1000 0-4 years. 15/1000 5-9 years. 22.0/1000 10-14 years. 40% in lower leg. 73.8% treated in outpatient setting, 20.5% acute care settings and 5.7% in hospital. 82% had one episode, 12.9% had 2, 2.9% had 3, and 2.2% had 4 or more. Higher numbers in summer.	Cellulitis is fairly common, usually treated in outpatient settings and infrequently complicated. Further research is needed in order to understand how comorbid conditions may predispose individuals to cellulitis infection and recurrence.	• Population based study. Good data across primary care and hospital. • Population=Mormons, who have fewer risk factors than NZ population and age-adjusted all-cause mortality 52% less than that of USA population. • Incidence rates given but no specific data re admission rates for the different age groups. • 27% population <15 years. • Excluded people>65 years thus true population incidence would be higher.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Craig, 2008, New Zealand, population-based study[49]	Children and young people 0-24 years.	National public hospital discharges.	National hospital discharges with a principal or additional discharge diagnosis data from the specific case definition.	Hospital admissions for serious skin infections rose progressively, most rapid rises mid-late 1990s. Bimodal age distribution: highest <5yrs, and then young people in late teens and early 20s. 2006-2007 rate 3.3/1000 in 0-14 yrs, and 3.5/1000 in 15-24 yrs. Pacific RR 4.5x, Māori 2.9x, and Asian 0.9x European. Males 1.1x Females. Deprivation important: NZDep quintile 3-4=1.35x, 5-6=1.7x, 7-8=2.7x, and 9-10=4.3x the least deprived quintile (1-2). Rural 0.5x urban risk.	Hospital admissions for serious skin infections rose progressively, with most rapid rises mid-late 1990s. Admissions in Auckland higher than NZ average. Bimodal age distribution: highest <5yrs, and then young people in late teens and early 20s. Admissions significantly higher Pacific>Māori> European and Asian, males and those in urban or deprived areas. Higher in summer and autumn.	• Univariate analyses only. • Used principal or additional diagnosis code. • First study to examine serious skin sepsis across NZ and look at different ages, ethnicities, and deprivation. • Hospital cases thus moderately severe end of spectrum.
Hersh 2008, USA, population based study[55]	Total population 9% <18 yrs	National population based using a probability sample	National Ambulatory Care Survey and National Hospital Ambulatory Care Survey from 1997-2005	Ambulatory visits for SSTIs incr 65% over the time period. Visit rates increased from 32/1000 population in 1997 to 48/1000 in 2005 (50% increase). Hospital admission rates for SSTIs increased from 0.7/1000 in 1997 to 1.2/1000 in 2005. Ambulatory visits for cellulitis/abscess increased 109%. Visit rates increased from 17.3 per 1000 population in 1997 to 33 per 1000 in 2005 (88% incr). Trends differed among different age groups. Largest increase among <18 yr age group (incr 173%) from 10 to 27.6 per 1000.	Rates of ambulatory visits for cellulitis/abscess have rapidly increased in recent years. From 1997-2005, visit rates nearly doubled overall, nearly tripled among children and in the EDs, and increased nearly 4-fold among high safety net status EDs.	• Nationally representative data over a 9 year time period. • Look across the healthcare continuum: ambulatory care visits, ED visits and hospital admissions. • Examined SSTIs and a subset of cellulitis/abscess. • Some ethnicity data reported but not analysed by ethnicity. • Attendance at a safety net hospital used as a proxy for socioeconomic status but no analysis reported re this. • 9% <18 years.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
O'Sullivan 2011, New Zealand, population-based study[50]	Children 0-14 years.	National public hospital discharges 1990-2007. 64,568 cases.	National hospital discharges with a principal or additional discharge diagnosis data from the specific case definition.	Incidence of serious skin infections almost doubled from 290/100,000 in 1990 to 547/100,000 in 2007. Highest rates observed in boys, preschool children, Māori and Pacific children, those living in deprived neighbourhoods, urban areas, summer and autumn, and northern regions. Over time there were disproportionate increases in infection rates in Māori and Pacific children and children from highly deprived areas.	Skin infections are an increasing problem for NZ children. Worsening ethnic and socioeconomic inequalities may be contributing to increasing rates.	• Good national data examining available hospital discharge data and changes over time. • Hospital cases thus moderately severe end of spectrum. • First study to apply new broader epidemiological case definition of serious skin infection. • Univariate analyses only.
O'Sullivan 2012, Gisborne, New Zealand, case series[38]	Children 0-14 years.	163 children hospitalised with serious skin infection 2006-07.	Retrospective chart review.	38% infections cellulitis. 36% abscesses. Sites of infections: head, face & neck (32%), lower limbs (32%). 34% hx previous skin infection. 12% previous hospitalisation with skin infection. 37% preceding skin injury. 77% saw GP prior to admission. 2.5 days duration of symptoms before seeing GP. 48% staph aureus (nil MRSA). 20% strep pyogenes.	Characteristics of skin infections in the Tairawhiti region are similar to those elsewhere in NZ. Higher rates of preceding skin injury and longer delays before seeing GP may be contributing to the higher rates seen in this area.	• Descriptive study. • Retrospective chart review thus relies on accurate coding and documentation. • Some exploration re other factors reported such as household occupants, preceding injury etc.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
O'Sullivan 2012, Gisborne, New Zealand, case series comparison[52]	Children 0-14 years.	110 cases seen by 9 GPs and 27 hospital discharges during a 10 week period.	Prospective observational analysis using diagnostic coding.	Annual incidence rate 106.7/1000 children. 1 hospital case/14 GP cases. Ethnic distribution the same for both hospital and primary care cases (77% and 78% Māori). No gender predominance. Hospital cases more likely to be under 5 years, and GP cases 5-9 years.	Skin infections common in primary care. Ethnic disparities in admissions reflect ethnic disparity in primary care. Establishment of a sentinel surveillance system in primary care would facilitate further research & monitoring.	• First NZ study to examine primary care cases. • Descriptive study comparing descriptive data from primary care cases to hospital cases. Both obtained via data extraction after identification of cases via coding. • Skin infection was a new diagnosis of bacterial skin infection and included cellulitis, abscess, impetigo, infected eczema. • Standardised rates by age and ethnicity to DHB population • Included infants with older children.

Abbreviations: NZ=New Zealand, GP= General Practitioner, hx=history of, RR=relative risk, yrs=years, MRSA=Methicillin Resistant Staphylococcal Aureus, DHB=district health board, USA=United States of America, NZDep=New Zealand Deprivation score, EDs= Emergency Departments, Incr=increased, SSTIs=skin and soft tissue infections

Table 2: Summary of Epidemiological Studies of Risk Factors for Cellulitis among Children

Study	Population studied	Participants	Study methodology	Identified risk factors	Conclusion	Comments
Eells, 2011, California, USA, case-control study[36]	USA County hospital. Children not excluded but mostly adults.	**Cases: 50** patients admitted with non-suppurative cellulitis. **Controls: 100** hospital controls matched by age, ethnicity, and sex.	Structured interview. Confirmation of dx by dermatologist. Nasal and inguinal swabs.	SA and MRSA colonisation similar between cases and controls with a non-significant aOR for both any SA and MRSA. Diabetes aOR=3.5 (1.4-8.9). Homelessness aOR=6.4 (1.9-20.9)	In contrast to suppurative skin infections, MRSA colonisation is uncommon in non-suppurative cellulitis and similar to controls and the general population.	• Reasonable re response rates. • Hospital cases thus moderately severe end of spectrum. • Unclear re the demographic breakdown of the population. Average age 40 yrs (2-83 yrs). • Unclear re the factors in the multivariate model. • Most risk factors including housing and some behaviours and hygiene measures not associated with development of non-suppurative cellulitis.
O'Sullivan 2012, Gisborne, New Zealand, case series comparison[52]	Children 0-14 years.	**110** cases seen by 9 GPs and **27** hospital discharges during a 10 week period.	Prospective observational analysis using diagnostic coding.	Annual incidence rate 106.7 per 1000 children. 1 hospital case/14 GP cases. Ethnic distribution the same for both hospital and primary care cases (77% and 78% Māori). No gender predominance. Hospital cases more likely to be under 5 years, and GP cases 5-9 years.	Skin infections common in primary care. Ethnic disparities in admissions reflect ethnic disparity in primary care. Establishment of a sentinel surveillance system in primary care would facilitate further research & monitoring.	• First NZ study to examine primary care cases. • Descriptive study comparing descriptive data from primary care cases to hospital cases. Both obtained via data extraction after identification of cases via coding. • Skin infection was a new diagnosis of bacterial skin infection and included cellulitis, abscess, impetigo, infected eczema. • Standardised rates by age and ethnicity to DHB population. • Included infants with older children.

Abbreviations: NZ=New Zealand, GPs= General Practitioners, aOR=adjusted Odds Ratio, dx=diagnosis. yrs=years, DHB=district health board, SA Staphylococcal Aureus, MRSA=Methicillin Resistant Staphylococcal Aureus, USA=United States of America

Table 3: Summary of Descriptive Studies of Cellulitis among Adults

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Koutkia, 1999, Rhode Island, USA, case series[4]	Adults.	**62** patients admitted with lower leg cellulitis.	Structured interview and examination.	Underlying conditions present in most pts. 68% dry skin. 50% diabetes. 48% hx cellulitis. 45% oedema. 40% PVD. 32% trauma and 32% tinea pedis.	Diabetes mellitus, hx of previous episodes of cellulitis, oedema of the lower extremities, and PVD were the most common established underlying conditions.	• Descriptive study. • No risk factor analysis. • Trauma of affected limb not defined.
Pavlotsky, 2004, Israel, retrospective case review[79]	Adults. Children not excluded but only 7 <18 yrs of age.	**574** hospitalised patients with erysipelas.	Retrospective chart review. Compared single and recurrent episodes.	53% first episode of erysipelas. 47% previous history. No multivariate analysis. Univariate factors include overweight, venous insufficiency, lymphoedema, tinea pedis, and previous regional surgical intervention or trauma.	Patients with erysipelas, especially the lower limb, should be instructed to reduce weight, control venous insufficiency and/or lymphoedema and to emphasise prevention and treatment of tinea pedis.	• Retrospective chart review thus relies on accurate coding and documentation. • Compared those with a hx of erysipelas to those without. • Simple comparisons with no multivariate analysis.
Goettsch 2006, Netherlands, population based study[53]	Total population adults and children.	Eligible population =16 million (Netherlands population), 1 million in pharmacy database, 50,000 in GP data base.	Analysis of linked databases; Dutch national hospital data, pharmacy database and subsample of GP data.	179.6 primary care episodes per 100,000 population per year. 12.1 hospital admissions per 100,000 population. Increased steeply with age. Estimated admissions in 0-15 yr age group <5/100,000. 7% patients with cellulitis were hospitalised. 6.6% of hospitalised patients were <24 yrs of age. 4-6% of pts had 2 or more episodes during that year. Average cost for hospitalisation 5346 euros. 80% of total costs (13.7 million euros) due to hospital costs.	Bacterial cellulitis and erysipelas of the leg are common and serious infections. Hospitalisation occurs in 1 in 14 patients but contributes more than 80% costs.	• Population based study. • Good data across primary and hospital. • Useful cost estimates including hospital, pharmacy and GP costs. • Infections of the leg only. • No data re incidence in young ages and children comprised only 7% of the hospital population.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Ellis Simonsen 2006, Utah, USA, population based study[54]	Total population ~27% <15 years.	Population based insurance claims database of Mormons. ~50,000 people. Over 5 year period.	Analysis of insurance database claims.	Cellulitis incidence rate 24.6/1000 person years. Higher incidence among males and individuals 45-64 years. 20/1000 0-4 years. 15/1000 5-9 years. 22.0/1000 10-14 years. 40% in lower leg. 73.8% treated in outpatient setting, 20.5% acute care settings and 5.7% in hospital. 82% had one episode, 12.9% had 2, 2.9% had 3, and 2.2% had 4 or more. Higher numbers in summer.	Cellulitis is fairly common, usually treated in outpatient settings and infrequently complicated. Further research is needed in order to understand how comorbid conditions may predispose individuals to cellulitis infection and recurrence.	• Population based study. • Good data across primary care and hospital. • Population=Mormons, who have fewer risk factors than NZ population and age-adjusted all-cause mortality 52% less than that of US population. • Incidence rates given but no specific data re admission rates for the different age groups. • Excluded people>65 yrs thus true population incidence would be higher.
McNamara 2007, Minnesota, USA, population based study[30]	Adult population Excluded <18 years.	Olmsted County, Minnesota enrolled in the Rochester Epidemiology Project.	Analysis of healthcare database and medical records for 1999.	176 episodes. Incidence 199/100,000 person years. No gender difference. Mean age 58 years. Incidence increased 3.7% per yr increment in age, or 43.5% per 10 yr increment. 22% hospitalised during the year. 22% had a recurrence within 2 years. More cases in late spring and summer.	Incidence of lower extremity cellulitis was high and increased with age. The need for hospitalisation and the prevalence of recurrence added to the burden.	• Narrow case definition: excluded infected wounds, abrasions, secondarily infected eczema, carbuncles, abscesses. • Used medical record review to validate cases identified via ICD coding. Confirmed cases comprised only 15% of those identified by ICD coding.

Study	Population studied	Participants	Study methodology	Findings	Conclusion	Comments
Hersh 2008, USA, population based study[55]	Total population 9% <18 years.	National population based using a probability sample.	National Ambulatory Care Survey and National Hospital Ambulatory Care Survey from 1997-2005.	Ambulatory visits for SSTIs increased 65% over the time period. Visit rates increased from 32/1000 population in 1997 to 48 per 1000 in 2005 (50% increase). Hospital admission rates for SSTIs increased from 0.7 per 1000 population in 1997 to 1.2 per 1000 in 2005. Ambulatory visits for cellulitis/abscess increased 109% over the time period. Visit rates increased from 17.3 per 1000 population in 1997 to 33 per 1000 in 2005 (88% incr). Trends differed among different age groups. Largest increase among <18 yr age group (incr 173%) from 10 to 27.6 per 1000.	Rates of ambulatory visits for cellulitis/abscess have rapidly increased in recent years. From 1997-2005, visit rates nearly doubled overall, nearly tripled among children and in the EDs, and increased nearly 4-fold among high safety net status EDs.	• Nationally representative data over a 9 year time period. • Look across the healthcare continuum: ambulatory care visits, ED visits and hospital admissions. • Examined SSTIs and a subset of cellulitis/abscess. • Some ethnicity data reported but not analysed by ethnicity. • Attendance at a safety net hospital used as a proxy for socioeconomic status but no analysis reported re this. • 9% <18 years.
Edelsberg 2009, USA, population based study[76]	Nationally representative sample of USA hospital admissions All ages.	Stratified random sample of US inpatient data from 2000-04. Healthcare cost and utilization project national inpatient sample.	Analysis of hospital discharge data with primary diagnosis of skin infection.	Age: almost all adult: 5% <15 yrs, ~35% >65 yrs. No gender difference. Estimated number of hospital admissions increased by 29% over 5 years with no change in pneumonia admissions. Increase greatest among superficial infections (cellulitis and abscess).	Total hospital admissions for skin and soft tissue infections increased by 29% during 2000-04. Admissions for pneumonia remained unchanged. Consistent with recent reported increases in CA-MRSA.	• Hospital discharge data. • Broad definition includes superficial, deeper and severe forms (e.g. necrotising fasciitis). • Children comprised 5-6% of the hospitalised population but no comparison to the general population. • Ethnic breakdown provided but no comparison to the general population. • Postulated re CA-MRSA but did not examine microbiology

Abbreviations: hx=history of, phx=past history of, yrs=years, CA-MRSA=community acquired methicillin resistant Staph aureus, pts=patients, PVD=peripheral vascular disease, USA=United States of America, EDs=Emergency Departments, incr=increase, ICD=International Classification of Diseases code

Table 4: Summary of Epidemiological Studies of Risk Factors for Cellulitis among Adults

Study	Population studied	Participants	Study methodology	Identified risk factors	Conclusion	Comments
Dupuy, 1999, 7 centres, France, case-control study[20]	Adults Excluded <15 years.	**Cases: 167** patients admitted with lower leg cellulitis (erysipelas). **Controls: 294** hospitalised patients matched by age, sex and hospital.	Structured interview and examination by dermatologist.	Disruption of cutaneous barrier aOR=23.8 (10.7-52.5). Lymphedema aOR=71.2 (5.6-908) Venous insufficiency aOR=2.9 (1.0-8.7). Overweight aOR=2.0 (1.1-3.7). Adjusted for age, sex, hospital. No association with diabetes, alcohol or smoking. PAR toe-web intertrigo 61%.	Highlights the major role of local risk factors (mainly lymphedema and site of entry). From a public health perspective, detecting and treating toe-web intertrigo should be evaluated in the secondary prevention of erysipelas.	• Limited data re response rates. • Hospital cases thus moderately severe end of spectrum. 7 different centres. • Hospital controls with other conditions. • Disruption of cutaneous barrier included toe-web intertrigo, leg ulcer, wounds and excoriated dermatoses.
Roujeau, 2004, multicentre European (Austria, France, Germany, Iceland), case-control study[48]	Adults.	**Cases: 243** in-patient or outpatient dermatology patients with lower leg cellulitis. **Controls: 467** hospitalised patients matched by age, sex, hospital and admission date (+/-2 months).	Multicentre (30 hospitals from 4 countries). Structured interview and examination by dermatologist at each centre. Mycological samples taken from toes.	Disruption of cutaneous barrier aOR=22 (9.4-51.5). Overweight aOR=2.8 (1.6-5.0). Tinea pedis interdigitalis aOR=3.2 (1.6-6.3). Hx of cellulitis aOR=24(7.1-81.2). Chronic leg oedema aOR=4.5 (1.3-15.6). Adjusted for foot dermatomycosis, overweight, hx cellulitis, hx venous insufficiency, varicose veins, DVT, venous leg surgery, leg ulcer, venous insufficiency, hyperpigmentation, disruption of cutaneous barrier, abolition of peripheral pulse, and chronic leg oedema. PAR obesity 40.7%. PAR tinea pedis 22.5%. PAR disruption of cutaneous barrier 48.5%. PAR hx cellulitis 20.2% .	Tinea pedis and onchomycosis were found to be significant risk factors for acute bacterial cellulitis of the leg that are amenable to treatment with effective pharmacological therapy.	• No data re response rates. • Hospital and outpatient cases under the dermatology services. Unclear re admission criteria or whether this is representative of all cases of cellulitis in these hospitals. • Hospital controls with other conditions. • 30 different hospitals in 4 different countries. • Dermatologist examination with rating scale and mycology of toes. • Unclear if matching variables were incorporated in the analysis. • Disruption of cutaneous barrier included foot dermatomycosis, leg ulcer, and wounds.

Study	Population studied	Participants	Study methodology	Identified risk factors	Conclusion	Comments
Bjornsdottir 2005, Iceland, case-control study[46]	Adults Excluded <18 years.	**Cases: 100** patients admitted with lower leg cellulitis. **Controls: 200** hospitalised patients matched by age, and sex.	Structured interview and examination by dermatologist at each centre. Microbiology and mycology samples taken from toes.	Hx of cellulitis aOR=31.0 (4.1-232.2). SA or Strep in toe webs aOR=29.0 (5.5-153.5). Leg lesions aOR=11.8 (2.5-56.3). Prior saphenectomy aOR= 3.9 (1.3-11.3). Adjusted for BMI≥30, chronic leg oedema, leg lesions, saphenectomy, hx cellulitis, dry skin, staph or strep in toe webs. Second model excluded variable of SA and strep. Toe-web dermatomycosis significant risk factor aOR=3.9 (1.3-11.3).	Risk factors in hospitalised patients include predisposing factors and the presence of sites of pathogen entry on legs and toe-webs. Improved awareness and management of toe-web intertrigo, which may harbour bacterial pathogens, and other skin lesions might reduce the incidence of cellulitis.	• Limited data re response rates. • Hospital cases thus moderately severe end of spectrum. • Hospital controls with other conditions. • Clinical examination with mycology and microbiology. • Leg lesions included erosions, ulcers and wounds.
Mokni, 2006, Tunisia, case-control study[47]	Adults Excluded <15 years.	**Cases: 114** patients admitted with first episode of lower leg cellulitis (erysipelas). **Controls: 208** hospitalised patients matched by age, sex and hospital.	7 hospital centres in Tunisia. Structured interview and examination by dermatologist at each centre.	Disruption of the cutaneous barrier aOR=13.6 (6.3-31). Leg oedema aOR=7.0 (1.3-38). Lymphoedema aOR=19.1 (1.1-331). Adjusted for age, sex, hospital. PAR toe-web intertrigo 44%. PAR traumatic wounds 36%.	Confirmed the major role of local risk factors and the minor role of general risk factors. Detecting and treating toe-web intertrigo and traumatic wounds should be considered in the prevention of erysipelas of the leg.	• No data re response rates. • Replicated Dupuy study. • Hospital cases thus severe end of spectrum. • Hospital controls with other conditions. • Only included first episodes thus excluding approx. half of eligible patients. • Disruption of the cutaneous barrier included toe-web intertrigo, squamous plantar lesions, traumatic wound, excoriated dermatoses, and leg ulcer. • Recruited consecutive patients over a summer period.

Study	Population studied	Participants	Study methodology	Identified risk factors	Conclusion	Comments
Lewis, 2006, Miami, USA, case-control study[74]	Veterans.	**Cases: 47** patients admitted to veterans hospital with lower leg cellulitis and a hx of cellulitis. **Controls: 94** hospitalised patients matched by age, sex and service.	Retrospective chart review.	Risk factors for recurrent cellulitis: Leg oedema aOR=4.4 (1.8-10.8). BMI aOR=1.1 (1.0-1.2). Tobacco use aOR=3.1 (1.2-8.3). Homelessness aOR=3.6 (1.0-12.7). Adjusted for the above variables and venous stasis.	Increased emphasis on weight loss, smoking cessation, and improved foot hygiene in the homeless might decrease recurrences of lower extremity cellulitis.	• Retrospective chart review thus relies on accurate coding and documentation. • Compared those with a hx of recurrent cellulitis to those with no hx cellulitis documented. • Unclear definition of recurrent: a local recurrence or a past history of cellulitis.
Halpern, 2008, Birmingham, United Kingdom, case-control study[71]	Adults Excluded <17 years.	**Cases: 150** patients admitted with lower leg cellulitis. **Controls: 300** hospitalised patients matched by age, and sex.	Structured interview and examination by dermatologist.	Site of entry identified in 87% cases. Systemic factors incl diabetes, alcohol, obesity and smoking not significant. Local factors: phx cellulitis aOR=33.3 (14.2-100) prev surgery aOR=3.13 (1.7-10). preceding injury aOR=10 (5.9-16.7). prev rash aOR=12.5 (4.5-33.3). toe-web disease aOR=3.1 (2.1-4.8). oedema aOR=10 (5.9-16.7). ulceration aOR=20 (8.3-50.0). white ethnicity RR=2.2 cf. all ethnic gps (White, Asian, Black).	Patients of white ethnicity were at increased risk. Local risk factors important. No systemic illnesses were identified as a risk factor.	• No data re response rates. • Hospital cases thus moderately severe end of spectrum. • Hospital controls. • Multivariate analysis reported but nil written re what variables were controlled for. • Unclear if ethnicity as a risk factor was adjusted for and how calculated. • ORs have been converted so they are presented in the same reference groups as the other studies.

Study	Population studied	Participants	Study methodology	Identified risk factors	Conclusion	Comments
Karpellin 2009, Tampere, Finland, case-control study[73]	Adults Excluded <18 years.	**Cases: 90** patients admitted with lower leg cellulitis. **Controls: 90** community controls matched by age, and sex.	Structured interview and examination.	Chronic oedema aOR=11.5 (1.2-114.4). Disruption of the cutaneous barrier aOR=6.2 (1.9-20.2). Obesity aOR=5.2 (1.3-20.9). Adjusted for all factors above plus malignant disease, current smoking. 49% pts had phx cellulitis. Pts with phx were more likely to have had prev surgery and be obese. Pts without were more likely to have had a traumatic wound in the previous month.	Chronic oedema of the extremity, disruption of the cutaneous barrier and obesity are independent risk factors for acute cellulitis leading to hospitalisation. Obesity and a previous ipsilateral surgical procedure were statistically more common in pts with a phx of cellulitis, whereas a recent traumatic wound was more common in pts without a phx of cellulitis.	• Reasonable data re response rates. • Hospital cases thus moderately severe end of spectrum. • First study to use community controls. • Also compared pts with a phx cellulitis to those without. • Disruption of the cutaneous barrier included traumatic wound < 1month, skin disease, toe-web intertrigo, and chronic ulcers.
Eells, 2011, California, USA, case-control study[36]	US County hospital, children not excluded but mostly adults.	**Cases: 50** patients admitted with non-suppurative cellulitis. **Controls: 100** hospital controls matched by age, ethnicity, and sex.	Structured interview. Confirmation of dx by dermatologist. Nasal and inguinal swabs.	SA and MRSA colonisation similar between cases and controls with a non-significant aOR for both any SA and MRSA. Diabetes aOR=3.5 (1.4-8.9). Homelessness aOR=6.4 (1.9-20.9)	In contrast to suppurative skin infections, MRSA colonisation is uncommon in non-suppurative cellulitis and similar to controls and the general population.	• Reasonable data re response rates. • Hospital cases thus moderately severe end of spectrum. • Unclear re the demographic breakdown of the population. Average age 40 years (2-83 years). • Unclear re the factors in the multivariate model. • Most risk factors including housing and some behaviours and hygiene measures not associated with development of non-suppurative cellulitis.

Abbreviations: hx=history of, phx=past history of, aOR=adjusted Odds Ratio, PAR=population attributable risk, yrs=years, SA=Staph aureus, MRSA= methicillin resistant Staph aureus, DVT=deep vein thrombosis, sig=significant, prev=previous, pts=patients, BMI=body mass index, gps=groups, approx.=approximately, dx=diagnosis

Appendix 2: Case Series: Results

Demographic characteristics of the study population

Characteristics of the study population

Breaches of skin

Initial symptoms noticed by caregiver

Microbiology

Table 5: Demographic Characteristics of Study Population

	% Study Population	% Census*
Age (years)		
<1	17	}37
1-4	27	}
5-10	38	31
11-14	18	32
Ethnicity		
Māori	25	11.5
Pacific	37	19.0
Other	38	69.5
Total	**100**	**100**

* Statistics New Zealand[130]

Table 6: Characteristics of Study Population

	N=%
Household Composition	
Couple with children	56
Solo parent	19
Family/other combination	25
Tenure	
Own home	39
Private rental	25
Housing NZ	27
Extended family/other	9
Community Services Card	61
Annual Household Income	
<NZ$30,000	33
$30-60,000	30
>$60,000	16
Declined	13
Unknown	8
Maternal Education	
No school qualifications	33
School qualifications	42
Post school qualifications	25

Table 7: Breaches of Skin

	N=%
Identified breach of skin	
Insect bite	15
Cut/scratch	25
Other	45
Nil	15
Eczema ever	26

Table 8: Initial Symptoms Noticed by Caregiver

	%
Redness	60
Swelling	58
Pain	53
Pus	32
Fever	22
Other	20

Table 9: Microbiology

	N	%*
Nil growth	11	17.5
SA	36	57
MRSA	10	15
Strep pyogenes	8	12.7
Other	4	6.4
Total	**61**	

*percentages add up to more than 100% as some cultures had growth or more than one bacteria

Appendix 3: Case-Control Study: Results

Study Base Description

Tables of Risk Factors for Developing Cellulitis

Tables of Risk Factors for Hospitalisation with Cellulitis

Results: Study Base Description

Table 10: Geographic Distribution of Participants

Geographic area	Hospital cases	GP cases	Controls
1	31	13	61
2	27	24	37
3	51	31	69
4	16	6	36
5	18	18	47
6	44	38	75
7	23	9	38
8	17	6	33
Total	**227**	**145**	**396**

Table 11: Demographic Characteristics of Participants

	Hospital cases		GP cases		Controls	
	N	%	%	%	N	%
Ethnicity						
Māori	56	24.7	36	24.8	42	10.6
Pacific	78	34.4	56	38.6	42	10.6
NZ Euro/Other	93	41.0	53	36.6	312	78.8
Age						
Infant <1yr	15	6.6	2	1.4	38	9.6
Preschool	86	37.9	43	29.7	140	35.4
School-age child	126	55.5	100	69.0	218	55.1
SES*						
Quintile 1	26	11.5	19	13.1	97	24.5
Quintile 2	47	20.7	15	10.3	106	26.8
Quintile 3	44	19.4	30	20.7	74	18.7
Quintile 4	44	19.4	43	29.7	61	15.4
Quintile 5	66	29.1	38	26.2	58	14.6
Total	**227**		**145**		**396**	

*Socioeconomic status as measured by the NZ deprivation index of the DOM code

Tables of Risk factors for Developing Cellulitis

Risk Factors for Developing Cellulitis

Table 12: Demographic Factors

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Ethnicity										
Māori	42	10.6	87.7	23.5	4.32	2.57-7.24	<0.001	4.04	2.32-7.02	<0.001
Pacific	42	10.6	133.1	35.9	6.59	3.93-11.05		6.11	3.42-10.89	
NZ Euro/Other	312	78.8	150.8	40.5	Ref			Ref		
Age										
Infant <1yr	38	9.6	6.4	1.7	0.15	0.06-0.34	<0.001	0.13	0.05-0.33	<0.001
Preschool	140	35.4	112.4	30.3	0.69	0.45-1.01		0.53	0.34-0.82	
School-age child	218	55.1	252.1	68.0	Ref			Ref		
Gender										
Male	207	52.3	223.6	60.1	1.37	0.93-2.03	0.11	1.53	1.01-2.32	0.04
Total	**396**		**372.3**							

*=weighted count
No missing data
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 13: Ethnicity Effect on the Risk of Developing Cellulitis: Univariate and Multivariate Analyses

	OR	95% CI	p value	aOR[1]	95% CI	p value	aOR[2]	95% CI	p value	aOR[3]	95% CI	p value
Ethnicity												
Maori	4.32	2.57-7.24	<0.001	4.04	2.32-7.02	<0.001	3.18	1.72-5.89	<0.001	2.56	1.34-4.86	<0.001
Pacific	6.59	3.93-11.05		6.11	3.42-10.89		4.47	2.38-8.39		3.42	1.79-6.54	
NZ Euro/Other	Ref			Ref			Ref			Ref		

aOR[1]= adjusted for age and NZ deprivation quintile
aOR[2]= adjusted for age, NZ deprivation quintile, sharing bedroom, maternal education, and difficulty accessing healthcare
aOR[3]= adjusted for age, NZ deprivation quintile, sharing bedroom, maternal education, difficulty accessing healthcare, maternal CSC, household smoking, insect bite in previous week, previous cellulitis and identified health problems

Table 14: Perinatal History

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Low birth weight	24	6.2	15.9	4.4	0.70	0.32-1.52	0.37	0.74	0.31-1.81	0.51
Prematurity	38	9.6	19.0	5.2	0.51	0.25-1.02	0.058	0.58	0.26-1.29	0.18
Never breastfed	38	9.6	47.8	12.9	1.40	0.79-2.47	0.25	0.92	0.53-1.61	0.77
Age formula started										
<4 months	178	50.0	156.0	49.9	1.00	0.61-1.64	1.00	0.85	0.49-1.47	0.82
4-6 months	82	23.0	72.0	23.1	1.00	0.57-1.77		0.83	0.41-1.68	
>6 months	96	27.0	84.3	27.0	Ref			Ref		
Total	396		372.3							

*=weighted count
Missing data: LBW (controls=9, cases=21), Prematurity (controls=2, cases=7), Never breast fed (controls=0, cases=4), Age formula started (controls=40, cases=75)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 15: Health Status

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Gen health in last 6 mo										
Not good/poor	8	2.0	11.0	3.0	1.48	0.55-4.01	0.44	1.22	0.46-3.26	0.69
Health problems	137	34.6	103.8	27.9	0.73	0.50-1.07	0.11	0.61	0.39-0.94	0.02
Total	**396**		**372.3**							

*=weighted count
Missing data: General health (controls=0, cases=1), Health problems (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 16: Clinical Assessment

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
BMI z score										
<-2SD	5	1.3	11.5	3.1	2.85	0.71-11.55	0.003	2.96	0.85-10.38	0.18
-2SD to 2SD	328	84.1	263.4	71.9	Ref			Ref		
>2SD	57	14.6	91.5	25.0	2.0	1.28-3.12		1.23	0.70-2.11	
Clinical signs eczema	52	13.1	43.9	11.8	0.88	0.53-1.49	0.64	0.85	0.45-1.60	0.62
Total	**396**		**372.3**							

*=weighted count
Missing data: BMI z score (controls=6, cases=13), Eczema (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 17: Breaches and Minor Trauma to the Skin

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Any breach/injury	297	75.0	297.2	79.8	1.32	0.85-2.06	0.22	1.85	1.06-3.22	0.03
Any breach	269	67.9	282.1	75.8	1.48	0.93-2.33	0.10	1.61	0.94-2.76	0.08
Insect bite	79	19.9	148.1	39.8	2.65	1.75-4.02	<0.001	2.46	1.54-3.94	<0.001
Cut/scratch	156	39.4	101.1	27.2	0.57	0.38-0.87	0.008	0.68	0.43-1.06	0.09
Bruise	106	26.8	65.0	17.5	0.58	0.36-0.92	0.02	0.72	0.43-1.19	0.20
Nappy rash**	36	32.1	10.5	21.2	0.57	0.22-1.47	0.24	0.50	0.21-1.20	0.12
Other skin problem	67	16.9	49.8	13.4	0.76	0.46-1.24	0.27	0.82	0.48-1.40	0.46
Eczema	63	15.9	47.8	12.9	0.78	0.47-1.30	0.34	0.80	0.42-1.51	0.48
Splinter	28	7.1	19.6	5.3	0.73	0.33-1.63	0.44	0.94	0.42-2.07	0.87
Bite	21	5.3	10.2	2.8	0.51	0.19-1.38	0.81	0.46	0.18-1.24	0.12
Chicken pox	4	1.0	3.1	0.8	0.82	0.17-4.07	0.81	0.47	0.07-3.28	0.45

*=weighted count
**denominator is the number of children who wear nappies not the total number in each group
Missing data nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 18: Characteristics of Insect Bites

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
# insect bites										
nil	317	80.1	222.4	60.2	Ref		<0.001	Ref		0.001
1-5	64	16.2	87.0	13.8	1.92	1.23-3.01		2.09	1.22-3.56	
6-9	11	2.8	30.4	8.2	3.91	1.59-9.61		2.60	1.06-6.36	
≥10	4	1.0	30.6	8.2	10.82	3.23-36.2		6.81	1.79-25.9	
Scratched until bled	22	27.8	78.6	53.1	2.93	1.39-6.18	0.005	2.79	1.23-6.29	0.01
Total	**79**		**148.1**							

*=weighted count
Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 19: Types of Insect Bites

	Controls		GP +Hospital cases		p value
	N	**%**	**N***	**%**	
Mosquito	60	75.9	103.7	70.0	0.37
Flea	5	6.3	12.2	8.2	
Other	1	1.3	10.9	7.4	
Not sure	16	16.5	21.3	14.4	
Total	**79**		**148.1**		

*=weighted count
Missing data: controls=6 and cases=9
Other includes bites attributed to sandfly, white-tailed spider, bee and sealice
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 20: Severity of Eczema

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Eczema in last year	110	27.8	77.3	20.8	0.68	0.45-1.04	0.07	0.64	0.39-1.06	0.08
Eczema in last week	63	15.9	47.8	12.9	0.78	0.47-1.30	0.34	0.80	0.42-1.51	0.48
Kept awake at night										
never	38	58.5	35	70.3	Ref		0.18	Ref		0.19
<1 night per week	9	13.8	9.8	18.4	1.11	0.32-3.84		0.83	0.18-3.78	
≥1 night per week	18	27.7	5.6	11.3	0.34	0.10-1.13		0.32	0.09-1.11	
Scratched until bled	17	26.2	25.1	52.3	3.09	1.22-7.84	0.02	4.07	1.44-11.51	0.009

*=weighted count
Missing data: controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 21: Household Pets

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Household pet	265	66.9	174.5	46.9	0.44	0.29-0.65	<0.001	0.59	0.37-0.93	0.023
Total	**396**		**372.3**							

*=weighted count
Missing data: controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 22: Hand Washing Habits

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Handwashing habits										
Usually on own	243	61.4	261.1	70.5	Ref		0.02	Ref		0.92
Usually needs supervision	51	51.0	50.1	13.5	0.92	0.51-1.64		1.15	0.58-2.28	
Too young	102	25.8	59.3	16.0	0.54	0.35-0.83		1.03	0.51-2.09	
Total	**396**		**372.3**							

*=weighted count
Missing data: (controls=0 and cases=1)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 23: Hand Washing Habits and need for reminders

	Controls		GP + Hospital cases		p value
	N	**%**	**N***	**%**	
Need for reminders					
Not required	102	34.9	111.0	35.9	0.61
Some of the time	134	45.9	121.7	39.4	
Half the time	19	6.5	31.9	10.3	
Most of the time	28	9.6	31.2	10.1	
Always	9	3.1	13.2	4.3	
Total	**294**		**313.0**		

*=weighted count
Includes all children old enough to wash their hands including those that need supervision
Missing data: Need for reminders (controls=2 and cases=5)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 24: Hand Washing Habits among children old enough to wash their own hands

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Wash hands**										
Before eating	162	55.7	184.0	59.1	0.87	0.58-1.31	0.50	0.77	0.48-1.24	0.28
After eating	123	42.3	127.9	41.1	1.05	0.68-1.62	0.83	1.20	0.74-1.96	0.47
After toilet	264	91.3	253.5	81.5	2.39	1.17-4.87	0.02	2.05	1.00-5.19	0.08
After playing outside	105	36.2	108.6	34.9	1.06	0.67-1.68	0.81	1.09	0.65-1.83	0.73
After handling a pet	115	42.4	112.4	39.0	1.15	0.71-1.88	0.57	0.99	0.56-1.76	0.97
If visibly dirty	280	96.2	283.4	91.1	2.48	0.82-7.55	0.11	1.72	0.60-4.92	0.31
Water temp										
Cold	220	75.1	236.0	75.8	Ref			Ref		0.52
Warm/hot	73	24.9	75.3	24.2	0.96	0.58-1.59	0.88	0.85	0.51-1.41	
Soap										
Liquid	170	60.8	148.9	47.8	Ref		0.11	Ref		0.46
Shared bar	108	36.9	145.0	46.6	1.60	1.0-2.59		0.96	0.54-1.71	
Script	4	1.4	8.0	2.2	2.40	0.52-10.90		1.55	0.21-11.56	
Nil soap	3	1.0	9.4	3.0	3.73	0.67-20.7		4.54	0.65-31.67	
Hand drying										
Personal towel	41	13.9	31.1	10.0	Ref		0.009	Ref		0.09
Shared towel	248	84.4	256.9	82.5	1.37	0.72-2.60		1.53	0.71-3.30	
Nothing/clothes	5	1.7	23.2	7.5	6.11	1.92-19.5		3.50	1.14-10.75	
Dry hands after toilet										
Personal towel	45	15.4	35.4	11.4	Ref		0.08	Ref		0.54
Shared towel	237	81.2	251.1	80.7	1.34	0.75-2.42		1.41	0.73-2.74	
Nothing/clothes	10	3.4	24.7	7.9	3.13	1.17-8.37		1.57	0.58-4.21	
Total	**294**		**313.0**							

*=weighted count
** reference group is always or usually wash hands
Includes all children old enough to wash their hands including those that need supervision
Missing data: wash hands (controls=1 and cases=39), hand drying (controls=0 and cases=38) dry hands (controls=2 and cases=38)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 25: Bathing Practices

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Child normally washed in										
Bath	187	47.2	149.7	40.2	Ref		0.16	Ref		0.05
Shower	209	52.8	222.5	59.8	1.33	0.89-1.98		0.60	0.35-1.01	
Washes per week										
<daily	144	36.4	154.2	41.4	1.24	0.82-1.86	0.30	1.33	0.84-2.11	0.22
Daily or more	252	63.6	218.1	58.6	Ref			Ref		
Shared bathwater	157	39.7	117.9	31.8	0.71	0.44-1.13	0.15	0.92	0.56-1.50	0.73
Shared bath towel	90	22.7	70.6	19.0	1.26	0.78-2.02	0.35	0.84	0.49-1.44	0.52
Towel not washed after single use	276	69.9	215.4	58.1	0.60	0.40-0.90	0.01	0.61	0.38-0.96	0.03

*=weighted count
Missing data: Normal washing (nil), sharing bathwater (controls=0, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 26: Clothes Washing Practices

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Automatic washing machine Vs. other	392	99.0	353.5	94.9	Ref 5.22	1.61-16.87	0.006	Ref 2.68	0.56-12.86	0.22
Temp clothes washed in										
Cold	252	63.6	269.8	72.5	3.37	0.91-12.40	0.084	2.64	0.63-11.12	0.41
Warm	125	31.6	96.1	25.8	2.42	0.63-9.21		2.66	0.61-11.62	
Hot	19	4.8	6.0	1.6	Ref			Ref		

*=weighted count
Missing data: controls=6 and cases =9, temperature clothes washed in (controls=0, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 27: Host and Hygiene Behaviours and the Risk of Developing Cellulitis according to time since cellulitis in any household member

	Time since cellulitis in any household member								
	Never (nil fhx)			Within the previous 3 months			≥3 months before		
	aOR	95% CI	p value	aOR	95% CI	p value	aOR	95% CI	p value
Washes per week									
<daily	Ref			ref			Ref		
Daily or more	1.41	0.82-2.41	0.21	1.15	0.29-4.65	0.84	1.43	0.50-4.09	0.51
Share bathwater	1.04	0.58-1.89	0.89	0.89	0.15-5.29	0.89	0.70	0.22-2.18	0.54
Towel not washed after single use	0.69	0.40-1.18	0.17	1.0	0.26-3.9	1.0	0.30	0.11-0.88	0.03

aOR= adjusted for age, ethnicity and NZ deprivation quintile

Table 28: Past History of Cellulitis

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Index child	19	4.8	116.2	31.2	9.01	4.86-16.70	<0.001	6.73	3.37-13.45	<0.001
Other child	25	6.4	105.1	28.6	5.86	3.37-10.19	<0.001	4.81	2.41-9.59	<0.001
Adult	34	8.6	89.9	24.2	3.39	1.88-6.11	<0.001	2.88	1.54-5.38	0.001
Any household member	63	15.9	203.1	54.0	6.35	4.06-9.94	<0.001	4.98	3.09-8.04	<0.001

*=weighted count
Missing data: index child (nil), controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 29: Number of Previous Episodes of Cellulitis

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Index child										
Nil	377	95.2	256.0	68.8	Ref		<0.001	Ref		<0.001
1	11	2.8	49.9	13.4	6.67	3.14-14.18		4.93	2.29-10.61	
2 or more	8	2.0	66.4	17.8	12.22	5.13-29.09		9.35	3.22-27.15	

*=weighted count
Missing data: index child (nil), controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 30: Timing of Previous Cellulitis

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Index child										
<1 month prior	5	1.3	33.8	9.3	9.95	3.29-30.07	<0.001	8.94	2.23-35.92	<0.001
1-3 months prior	4	1.0	26.3	7.2	9.67	3.03-30.89		7.49	2.00-28.06	
>3 months prior	10	2.5	47.3	13.0	6.97	2.90-16.76		5.03	2.15-11.77	
Never	377	95.2	256.0	70.4	Ref			Ref		
Other child										
<1 month prior	7	1.8	44.1	12.1	8.78	3.44-22.44	<0.001	7.41	2.62-20.94	<0.001
1-3 months prior	2	0.5	11.7	3.2	8.18	1.69-39.57		3.42	0.55-21.23	
>3 months prior	14	3.6	45.9	12.6	4.57	2.16-9.71		4.33	1.63-11.51	
Never	365	94.1	261.8	72.0	Ref			Ref		
Adult										
≤3 months prior	2	0.5	15.7	4.2	10.08	1.93-52.63	<0.001	13.24	2.34-78.37	0.001
>3 months prior	28	7.1	70.4	19.1	3.23	1.71-6.10		2.46	1.30-4.70	
Never	363	92.4	282.3	76.6	Ref			Ref		
Adult										
≤3 months prior	2	0.5	15.7	4.3	10.08	1.93-52.63	<0.001	13.14	2.22-77.83	<0.001
3-12 months prior	9	2.3	43.8	11.9	6.24	2.71-14.38		5.16	1.96-13.62	
>12 months	19	4.8	26.6	7.2	1.80	0.61-5.27		1.32	0.54-3.21	
Never	362	92.3	282.3	76.6	Ref			Ref		
Total	**396**		**372.3**							

*=weighted count
Missing data: index child (controls=0 and cases=7), other child (controls=2 and cases=4), adults (controls=2 and cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 31: Past History of Other Skin Problems

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Index child	88	22.2	137.0	36.8	2.04	1.38-3.01	<0.001	1.49	0.95-2.33	0.08
Other child	102	26.2	143.4	39.1	1.81	1.23-2.66	0.002	1.57	1.00-2.46	0.05
Adult	109	27.6	101.1	27.2	0.98	0.63-1.52	0.92	0.72	0.44-1.18	0.19

*=weighted count
Missing data: controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 32: Socioeconomic Status

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Deprivation**										
Lowest deprivation (1-3)	277	69.9	183.7	49.4	Ref		<0.001	Ref		0.23
Highest deprivation (4-5)	119	30.1	188.5	50.6	2.39	1.60-3.57		1.30	0.85-1.99	
Deprivation (quintiles)										
1	97	24.5	56.7	15.2	Ref		<0.001	Ref		0.22
2	106	26.8	44.8	12.0	0.72	0.37-1.40		0.63	0.31-1.30	
3	74	18.7	82.2	22.1	1.90	1.00-3.61		1.30	0.64-2.65	
4	61	15.4	96.3	25.9	2.70	1.43-5.11		1.28	0.64-2.59	
5	58	14.6	92.2	24.8	2.72	1.39-5.31		1.23	0.59-2.54	
Maternal CSC	105	26.9	180.6	50.8	2.80	1.86-4.23	<0.001	1.64	1.04-2.60	0.04

*=weighted count
Missing data: Deprivation (nil), Maternal community services card (controls=6, cases=14)
aOR= adjusted for ethnicity, age and NZ deprivation quintile
**aOR is adjusted for ethnicity and age

Table 33: Maternal Characteristics

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Maternal age at interview										
<20 yrs	2	0.5	0.2	0.1	0.08	0.007-0.88	0.004	0.09	0.006-1.28	0.006
20-34 yrs	133	34.4	170.6	48.9	Ref			Ref		
≥35 yrs	252	65.1	178.2	51.1	0.55	0.36-0.83		0.50	0.30-0.83	
Maternal age at child's birth										
<20 yrs	14	3.6	22.6	6.5	1.75	0.80-3.80	0.18	0.74	0.32-1.73	0.76
20-34 yrs	296	76.7	73.1	78.3	Ref			Ref		
≥35 yrs	76	19.7	53.3	15.3	0.76	0.45-1.29		0.90	0.51-1.61	
Mother not born in NZ	135	34.5	138.6	38.8	1.2	0.77-1.88	0.42	0.75	0.44-1.27	0.28
Recent immigrant	55	14.1	41.4	11.6	0.80	0.43-1.51	0.49	0.99	0.49-2.02	0.99
Maternal ESOL	66	16.9	107.0	29.9	2.10	1.29-3.42	0.003	1.28	0.72-2.28	0.40
Maternal Education										
No formal quals	55	14.2	105.9	30.4	2.65	1.65-4.25	<0.001	1.58	0.91-2.73	0.10
Formal qual	333	85.8	242.4	69.6	Ref			Ref		

*=weighted count
Missing data:
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 34: Household Composition

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Household composition										
Couple	288	72.7	212.2	57.0	Ref		0.002	Ref		0.78
Single parent	45	11.4	66.2	17.8	2.00	1.09-3.67		1.24	0.68-2.27	
Extended whānau/other	63	15.9	93.8	25.2	2.02	1.28-3.18		1.06	0.64-1.76	

*=weighted count
Missing data:
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 35: Household Characteristics

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Dwelling type										
House/townhouse	379	95.7	355.3	95.5	Ref		0.53	Ref		0.54
Flat/unit	16	4.0	16.7	4.5	1.11	0.54-2.28		0.71	0.29-1.73	
Other	1	0.3	0.20	0.1	0.21	0.01-3.46		0.27	0.01-5.71	
Housing ownership										
Private rental	88	22.2	117.5	31.5	2.09	1.29-3.39	<0.001	1.49	0.89-2.50	0.18
HC rental/family	24	6.1	73.4	19.7	4.78	2.75-8.31		1.76	0.85-3.62	
Owned	284	71.7	181.6	48.8	Ref			Ref		
Housing ownership										
Rental	112	28.3	190.7	51.2	2.66	1.78-3.99	<0.001	1.55	0.96-2.51	0.08
Owned	284	71.7	181.6	48.8	Ref			Ref		
Moved in last 2 yrs	122	30.8	121.3	32.6	1.09	0.72-1.64	0.69	0.89	0.57-1.39	0.60
Moved ≥2 in last 2 yrs	29	7.3	26.4	7.1	0.96	0.50-1.84	0.91	0.77	0.41-1.43	0.41
No landline	10	2.5	22.9	6.1	2.53	1.07-5.96	0.03	1.10	0.42-2.85	0.85

*=weighted count
Missing data: Ownership and landline nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 36: Household Occupants

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
# people in house										
≥6	68	17.2	126.7	34.0	2.49	1.65-3.76	<0.001	1.14	0.72-1.83	0.57
# people										
≤3	84	21.2	35.2	9.5	Ref		<0.001	Ref		0.14
4-5	245	61.9	210.3	56.5	2.05	1.14-3.66		1.93	0.98-3.80	
≥6	67	16.9	126.7	34.0	4.51	2.45-8.29		1.96	0.96-4.02	
# children <15										
1	111	28.0	43.9	11.8	Ref		<0.001	Ref		0.008
2-3	254	64.1	261.0	70.1	2.59	1.60-4.20		2.30	1.37-3.88	
≥4	31	7.8	67.3	18.1	5.48	2.95-10.20		1.96	1.01-3.80	
# adults										
1	29	7.3	39.6	10.7	1.75	0.78-3.91	0.07	1.09	0.49-2.40	0.93
2	261	66.1	203.9	55.1	Ref			Ref		
≥3	105	26.6	126.7	34.2	1.54	1.02-2.33		0.94	0.59-1.51	

*=weighted count
Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 37: Household Crowding (with adjustment for NZDep)

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Crowded >1.5/bedroom	101	10.3	151.3	40.7	2.00	1.33-3.02	0.001	1.00	0.63-1.58	0.99
Crowded >2/bedroom	17	4.3	51.18	13.8	3.56	1.85-6.84	<0.001	1.31	0.65-2.62	0.45
Crowded										
≤2/bedroom	379	95.7	320.7	86.2	Ref		<0.001	Ref		0.53
2-3/bedroom	16	4.0	42.9	11.5	3.17	1.57-6.40		1.21	0.59-2.48	
More than 3/bedroom	1	0.3	8.3	2.2	9.74	2.43-39.2		2.87	0.41-20.02	
Toilet occupancy >5/toilet	35	8.8	84.7	22.7	3.04	1.84-5.00	<0.001	1.15	0.64-2.07	0.64
Child shares bedroom	133	33.6	210.9	56.6	2.58	1.81-3.69	<0.001	1.81	1.20-2.73	0.004
Child shares bed	36	9.1	88.6	23.8	2.40	1.46-3.95	<0.001	1.59	0.85-2.98	0.15

*=weighted count
Missing data: Number of bedrooms (controls=nil, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 38: Household Crowding (without NZDep)

	Controls		GP +Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N*	%						
Crowded >1.5/bedroom	101	10.3	151.3	40.7	2.00	1.33-3.02	0.001	1.07	0.66-1.71	0.79
Crowded >2/bedroom	17	4.3	51.18	13.8	3.56	1.85-6.84	<0.001	1.39	0.70-2.78	0.35
Crowded										
≤2/bedroom	379	95.7	320.7	86.2	Ref		<0.001	Ref		0.44
2-3/bedroom	16	4.0	42.9	11.5	3.17	1.57-6.40		1.29	0.62-2.67	
More than 3/bedroom	1	0.3	8.3	2.2	9.74	2.43-39.2		2.93	0.47-18.5	
Toilet occupancy >5/toilet	35	8.8	84.7	22.7	3.04	1.84-5.00	<0.001	1.25	0.69-2.25	0.47
Child shares bedroom	133	33.6	210.9	56.6	2.58	1.81-3.69	<0.001	1.84	1.22-2.77	0.004
Child shares bed	36	9.1	88.6	23.8	2.40	1.46-3.95	<0.001	1.37	0.70-2.67	0.36

aOR= adjusted for ethnicity and age

Table 39: Exposure to Household Smoking

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Maternal smoking	65	16.6	120.4	33.7	2.55	1.61-4.03	<0.001	1.50	0.93-2.41	0.10
Smokers in the house	100	26.1	170.3	50.1	2.84	1.87-4.32	<0.001	1.66	1.04-2.66	0.03
Smokers in the house										
0	283	73.9	169.4	49.9	Ref		<0.001	Ref		0.10
1	62	16.2	96.0	28.3	2.59	1.59-4.21		1.66	1.03-2.68	
≥2	38	9.9	74.2	21.9	3.26	1.86-5.73		1.71	0.50-5.82	

*=weighted count
Missing data:
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 40: Initial Management of Insect Bites

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Any management	43	54.4	96.0	64.8	1.54	0.73-3.28	0.26	1.40	0.62-3.17	0.41
Cleanse: anything	31	39.2	62.7	42.4	1.14	0.53-2.45	0.74	0.82	0.36-1.88	0.64
Cleanse: water/soap	30	38.0	62.1	41.9	1.18	0.55-2.55	0.67	0.89	0.39-2.04	0.78
Cleanse: antiseptic	6	7.7	16.4	11.1	1.50	0.45-4.85	0.51	1.30	0.27-6.26	0.74
Antiseptic/Ab cream	11	13.9	23.7	16.0	1.18	0.47-2.98	0.72	0.84	0.26-2.68	0.77
Anti-itch cream	15	19.0	34.6	23.4	1.30	0.56-3.01	0.53	1.54	0.61-3.89	0.36
Anti-histamine	1	1.3	8.3	5.6	4.65	0.51-42.37	0.17	6.22	0.51-75.81	0.15
Cover	8	10.1	28.3	19.1	2.10	0.72-6.10	0.17	2.35	0.70-7.91	0.17
Pain relief	2	2.5	12.3	8.3	3.48	0.63-19.27	0.15	2.68	0.50-14.32	0.25
Trad/alternative Rx	5	6.3	33.0	22.6	4.32	1.24-15.04	0.02	6.09	1.60-23.18	0.008
Total	**79**		**148.1**							

*=weighted count
Missing data: controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 41: Time until Administration of First Aid for Insect Bites

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
<3 hrs	25	58.1	59.3	63.3	Ref		0.19	Ref		0.17
3-11 hrs	10	9.1	9.1	9.8	0.39	0.11-1.35		0.55	0.09-3.21	
≥12 hrs	8	25.2	25.2	26.9	1.33	0.42-4.23		2.66	0.52-13.61	
Total	**79**		**148.1**							

Missing data: nil (relook at….missing is higher)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 42: Initial Management of Cuts or Scratches

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Any management	110	70.5	58.8	58.2	0.58	0.29-1.17	0.13	0.66	0.29-1.49	0.32
Cleanse: anything	89	57.1	43.1	42.7	0.56	0.29-1.08	0.08	0.53	0.24-1.17	0.12
Cleanse: water/soap	81	51.9	38.4	37.6	0.56	0.28-1.10	0.09	0.59	0.26-1.31	0.19
Cleanse: antiseptic	28	17.9	18.8	18.6	1.04	0.43-2.52	0.92	0.86	0.32-2.37	0.78
Antiseptic/Ab cream	25	16.0	11.4	11.2	0.66	0.25-1.76	0.41	0.65	0.25-1.70	0.38
Cover	54	34.6	34.2	33.9	0.97	0.50-1.87	0.92	0.91	0.41-2.01	0.82
Pain relief	3	1.9	4.1	4.1	2.18	0.38-12.70	0.38	3.01	0.27-34.23	0.37
Trad/alternative Rx	16	10.3	4.1	4.1	0.37	0.09-1.47	0.16	1.05	0.22-4.95	0.95
Total	**156**		**101.1**							

*=weighted count
Missing data: controls=6 and cases =9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 43: Time until Administration of First Aid for Cuts or Scratches

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
<3 hrs	90	87.4	49.2	84.8	Ref		0.90	Ref		0.98
3-11 hrs	12	11.7	8.0	13.8	1.21	0.39-3.85		1.05	0.27-4.10	
≥12 hrs	1	1.0	0.8	1.4	1.46	0.15-13.94		1.41	0.03-74.33	
Total	**156**		**101.1**							

*=weighted count
Missing data: nil (relook at….missing is higher)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 44: Management of Eczema

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Usually use moisturiser	45	69.2	22.8	45.9	0.38	0.14-0.99	0.05	0.43	0.17-1.12	0.07
Usually use steroid	42	64.6	37.6	75.5	1.69	0.67-4.22	0.26	1.37	0.42-4.33	0.60
Moisturiser in last week	37	56.9	19.1	38.5	0.50	0.19-1.32	0.16	0.50	0.16-1.43	0.14
Steroid in last week	32	49.2	25.9	54.0	1.11	0.43-2.90	0.82	1.09	0.35-3.36	0.88
Soap substitute	37	59.7	19.9	31.6	0.46	0.18-1.14	0.09	0.44	0.13-1.43	0.17
Trad/alternative Rx	5	7.7	7.8	15.9	0.26	0.54-9.68	0.26	1.82	0.43-7.81	0.42
Total	**63**		**47.8**							

*=weighted count
Missing data: controls=6 and cases=9
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 45: Healthcare Provider

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Usual healthcare provider										
Single GP/practice	368	92.9	337.4	90.6	Ref		0.35	Ref		0.77
Multiple/whoever/after hrs	28	7.1	34.9	9.4	1.36	0.71-2.58		0.91	0.49-1.69	
Total	**396**		**372.3**							

*=weighted count
Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 46: Healthcare Utilisation in the previous 6 months

	Controls		GP + Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Family Dr/practice										
Nil	67	17.0	80.0	21.6	Ref		0.11	Ref		0.15
1-2 times	191	48.6	144.7	39.1	0.64	0.37-1.08		0.75	0.42-1.35	
3-4	66	16.8	84.8	22.9	1.1	0.59-1.97		1.48	0.78-2.81	
>4	69	17.6	60.5	16.3	0.73	0.38-1.42		0.99	0.47-2.08	
After-hours centre										
Nil	295	74.5	280.0	75.7	Ref		0.78	Ref		0.69
≥ 1 times	101	25.5	89.8	24.3	0.94	0.60-1.47		1.10	0.68-1.79	
Hospital ED										
Nil	353	89.4	332.9	90.0	Ref		0.80	Ref		0.43
≥ 1 times	42	10.6	36.9	10.0	0.93	0.54-1.60		1.26	9.72-2.20	
Total number seen										
Nil	46	11.7	60.4	16.4	Ref		0.13	Ref		0.15
1-2 times	170	43.3	127.8	34.7	0.57	0.32-1.03		0.69	0.35-1.36	
3-4	73	18.6	89.3	24.3	0.93	0.51-1.71		1.41	0.68-2.89	
>4	104	26.5	90.4	24.6	0.66	0.35-1.24		0.90	0.44-1.86	
Total	**396**		**372.3**							

*=weighted count
Missing data: Family practice (controls=3, cases=3), Other practice (controls=0, cases=3), Afterhours (controls=0, cases=4), Hospital ED (controls=1, cases=4)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 47: Difficulties getting to the GP for the last Illness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Difficulties getting to GP	20	5.1	48.6	13.2	2.84	1.51-5.34	0.001	2.39	1.12-5.11	0.02
Total	**396**		**372.3**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 48: Summary Table of Risk Factors for the Development of Cellulitis

Risk Factor	Direction of effect	Magnitude of effect aOR	95% CI
Demographic factors			
Ethnicity			
Māori	↑↑	4.04	2.32-7.02
Pacific	↑↑↑	6.11	3.42-10.89
NZ Euro		Ref	
Age			
Infant	↓↓	0.13	0.05-0.33
Preschool	↓	0.53	0.34-0.82
School		Ref	
Male gender	↑	1.53	1.01-2.32
Host Susceptibility			
Identified health problems	↓	0.61	0.39-0.94
Exposures/Breaches of skin			
Insect bites in previous wk	↑	2.5	1.54-3.94
Number of insect bites			
nil		Ref	
1-5	↑	2.09	1.22-3.56
6-9	↑	2.60	1.06-6.36
≥10	↑↑↑	6.81	1.79-25.9
Host Behaviours			
Scratching insect bites til bled	↑	2.79	1.23-6.29
Scratching eczema til bled	↑↑	4.07	1.44-11.51
Washing towels less freq	↓	0.61	0.38-0.96

Previous Cellulitis			
Previous cellulitis-child	↑↑↑	6.73	3.37-13.45
Previous cellulitis-other child	↑↑	4.81	2.41-9.59
Previous cellulitis-adult	↑	2.88	1.54-5.38
Cellulitis numbers			
Nil		Ref	
1	↑↑	4.93	2.29-10.61
2 or more	↑↑↑	9.35	3.22-27.15
Cellulitis timing-child			
<1 month	↑↑↑	8.94	2.23-35.92
1-3 months	↑↑↑	7.49	2.00-28.06
>3months	↑↑	5.03	2.15-11.77
Never		Ref	
Cellulitis timing-other child			
<1 month	↑↑↑	7.41	2.62-20.94
1-3 months	↑↑	3.42	0.55-21.23
>3months	↑↑	4.33	1.63-11.51
Never		Ref	
Cellulitis timing-adult			
<3 months	↑↑↑	13.14	2.22-77.83
3-12 months	↑↑	5.16	1.96-13.62
> 12 months	↑	1.32	0.54-3.21
Never		Ref	
Social/Environmental			
Maternal CSC	↑	1.64	1.04-2.60
Maternal age at interview			
<20		0.09	0.006-1.28
20-34		Ref	
≥ 35	↓	0.5	0.3-0.8
# Children in house			
1		Ref	1.37-3.88
2-3	↑	2.30	1.01-3.80
≥ 4	↑	1.96	
Sharing a bedroom	↑	1.81	1.20-2.73
Household smoking	↑	1.66	1.04-2.66
Health Literacy/Utilisation			
Difficulties accessing healthcare for last illness	↑	2.39	1.12-5.11

↑=1-3 times increased risk
↑↑=3-6 times increased risk
↑↑↑=6 or more times increased risk
aOR= adjustment for ethnicity, age, and socioeconomic status

Tables of Risk Factors for Hospitalisation with Cellulitis

Risk Factors for Hospitalisation with Cellulitis

Table 49: Demographic Factors

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Ethnicity										
Māori	36	24.8	56	24.7	0.89	0.52-1.52	0.67	0.97	0.53-1.78	0.83
Pacific	56	38.6	78	34.4	0.79	0.48-1.32		0.84	0.48-1.49	
NZ Euro/Other	53	36.6	93	41.0	Ref			Ref		
Age										
Infant <1yr	2	1.4	15	6.6	5.95	1.36-26.12	0.02	6.70	1.45-30.94	0.02
Preschool	43	29.7	86	37.9	1.59	0.98-2.56		1.55	0.95-2.54	
School-age child	100	69.0	126	55.5	Ref			Ref		
Gender										
Male	85	58.6	120	52.9	0.79	0.52-1.21	0.28	0.88	0.57-1.34	0.54
Total	**145**		**227**							

No missing data
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 50: Perinatal History

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Low birth weight	6	4.3	14	6.6	1.59	0.60-4.23	0.35	1.47	0.53-4.07	0.46
Prematurity	7	4.9	22	10.0	2.16	0.94-4.96	0.07	2.09	0.88-4.99	0.10
Never breastfed	17	11.8	41	18.3	1.67	0.90-3.13	0.11	1.78	0.94-3.35	0.08
Age formula started										
<4 months	64	52.5	97	55.4	1.22	0.68-2.19	0.79	1.24	0.68-2.27	0.68
4-6 months	29	23.8	42	24.0	1.17	0.61-2.24		1.32	0.68-2.57	
>6 months	29	23.8	36	20.6	Ref			Ref		

Missing data: LBW (controls=5, cases=16), Prematurity (controls=1, cases=6), Never breast fed (controls=1, cases=3), Age formula started (controls=23, cases=52)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 51: Health Status

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Gen health in last 6 mo										
Not good/poor	4	2.8	17	7.5	2.87	0.95-8.63	0.06	2.74	0.81-9.29	0.11
Health problems	41	28.3	77	33.9	1.30	0.83-2.06	0.26	1.36	0.84-2.20	0.20
Total	**145**		**227**							

Missing data: General health (controls=0, cases=1), Health problems (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 52: Clinical Assessment

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
BMI z score										
<-2SD	4	2.8	3	1.4	0.47	0.11-2.06	0.54	0.45	0.09-2.20	0.61
-2SD to 2SD	102	71.3	162	75.0	Ref			Ref		
>2SD	37	25.9	51	23.5	0.87	0.51-1.47		0.99	0.58-1.68	
Clinical signs eczema	16	11.0	47	20.7	2.11	1.16-3.84	0.02	1.93	1.04-3.60	0.04
Total										

Missing data: Eczema (nil), Weight (controls=x, cases=x), Height (controls=x, cases=x)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 53: Breaches and Minor Trauma to the Skin

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Any breach/injury	114	79.7	182	79.5	1.03	0.62-1.71	0.92	0.89	0.53-1.50	0.66
Any breach	109	76.2	173	75.5	1.00	0.59-1.68	0.99	0.86	0.50-1.46	0.58
Insect bite	60	41.4	59	26.0	0.50	0.31-0.79	0.003	0.44	0.27-0.72	0.001
Cut/scratch	40	28.0	60	26.2	0.94	0.59-1.50	0.80	1.00	0.62-1.62	0.99
Bruise	25	17.2	29	12.8	0.70	0.40-1.24	0.22	0.71	0.39-1.28	0.25
Nappy rash**	2	10.5	25	39.1	5.45	1.10-27.14	0.04	6.50	1.12-37.74	0.04
Other skin problem	18	12.4	56	24.7	2.31	1.33-4.02	0.003	2.21	1.25-3.90	0.007
Eczema	18	12.4	38	16.7	1.42	0.77-2.62	0.26	1.19	0.63-2.22	0.59
Splinter	8	5.5	9	4.0	0.71	0.27-1.85	0.48	0.93	0.35-2.47	0.88
Bite	4	2.8	6	2.6	0.96	0.25-3.62	0.95	1.20	0.31-4.61	0.79
Chicken pox	1	0.7	6	2.6	3.9	0.45-33.7	0.21	2.37	0.30-19.07	0.42

**denominator is the number of children who wear nappies not the total number in each group
Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 54: Characteristics of Insect Bites

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
# insect bites										
nil	85	58.6	168	74.0	Ref		0.001	Ref		0.001
1-5	35	24.1	47	20.7	0.68	0.41-1.13		0.61	0.36-1.04	
6-9	12	8.3	9	4.0	0.38	0.15-0.96		0.31	0.13-0.76	
≥10	13	9.0	3	1.3	0.12	0.04-0.35		0.12	0.04-0.39	
Scratched until bled	31	51.7	24	40.7	0.64	0.32-1.30	0.22	0.64	0.29-1.42	0.26

Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 55: Types of Insect Bites

	Controls GP cases		Hospital cases		p value
	N	**%**	**N**	**%**	
Mosquito	42	70.0	31	52.5	0.05
Flea	6	10.0	5	8.5	
Other	4	6.7	2	3.4	
Not sure	8	13.3	21	35.6	
Total	**60**		**59**		

Missing data: nil
Other includes bites attributed to sandfly, white-tailed spider, and bee
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 56: Severity of Eczema

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Eczema in last year	31	21.4	69	30.4	1.61	0.96-2.70	0.07	1.39	0.81-2.39	0.23
Eczema in last week	18	12.4	38	16.7	1.42	0.77-2.62	0.26	1.19	0.63-2.22	0.59
Kept awake at night										
never	13	72.2	20	52.6	Ref		0.38	Ref		0.59
<1 night per week	3	16.7	8	21.1	1.73	0.42-7.17		1.85	0.37-9.39	
≥1 night per week	2	11.1	10	26.3	3.25	0.55-19.2		2.57	0.33-19.95	
Scratched until bled	9	52.9	15	39.5	0.58	0.19-1.80	0.34	0.28	0.06-1.24	0.09
Total	**18**		**38**							

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 57: Household Pets

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N***	**%**						
Household pet	66	45.5	109	48.0	1.11	0.70-1.74	0.67	1.25	0.77-2.02	0.36

*=weighted count
Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 58: Hand Washing Habits

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Hand washing habits										
Usually on own	102	70.8	127	55.9	Ref		0.002	Ref		0.09
Usually needs supervision	19	13.2	27	11.9	1.14	0.59-2.20		1.35	0.67-2.73	
Too young	23	16.0	73	32.2	2.55	1.51-4.30		2.54	1.11-5.84	
Total	**145**		**227**							

Missing data: controls=1 and cases=0
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 59: Hand Washing Habits and need for reminders

	Controls GP cases		Hospital cases		p value
	N	**%**	**N**	**%**	
Need for reminders					
Not required	43	35.8	70	45.8	0.16
Some of the time	49	40.8	47	30.7	
Half the time	10	8.3	12	7.8	
Most of the time	13	10.8	11	7.2	
Always	5	4.2	13	8.5	
Total	**121**		**154**		

Missing data: Need for reminders (controls=1 and cases=1)
Includes all children old enough to wash their hands including those that need supervision
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 60: Hand Washing Habits among children old enough to wash their own hands

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Need for reminders										
Not required	43	35.8	70	45.8	Ref		0.04	Ref		0.05
Some of the time	72	60.0	70	45.8	0.60	0.37-0.96		0.61	0.37-0.99	
Always	5	4.2	13	8.5	1.60	0.54-4.75		1.74	0.54-5.61	
Wash hands**										
Before eating	73	60.3	70	45.8	1.80	1.15-2.83	0.01	1.97	1.23-3.17	0.005
After eating	54	44.6	54	35.5	1.46	0.87-2.46	0.15	1.51	0.88-2.57	0.13
After toilet	100	82.6	136	89.5	0.56	0.28-1.14	0.11	0.60	0.29-1.23	0.16
After playing outside	45	37.2	39	25.5	1.73	1.01-2.97	0.05	1.82	1.06-3.11	0.03
After handling a pet	46	41.8	49	34.5	1.36	0.78-2.38	0.27	1.46	0.83-2.60	0.19
If visibly dirty	112	92.6	142	92.8	0.96	0.36-2.56	0.94	0.94	0.34-2.56	0.90
Water temp										
Cold	88	72.7	129	83.8	Ref		0.03	Ref		0.04
Warm/hot	33	27.3	25	16.2	0.52	0.28-0.95		0.52	0.28-0.96	
Soap										
Liquid	61	50.4	66	42.9	Ref		0.20	Ref		0.20
Shared bar	58	47.9	79	51.3	1.26	0.74-2.16		1.37	0.76-2.45	
Nil soap	2	1.7	9	5.8	4.16	0.83-20.83		3.98	0.78-20.41	
Hand drying										
Personal towel	12	9.9	14	9.1	Ref		0.75	Ref		0.67
Shared towel	98	81.0	122	79.2	1.07	0.47-2.44		1.12	0.49-2.57	
Nothing/clothes	11	9.1	18	11.7	1.40	0.51-3.83		1.52	0.55-4.26	
Dry hands after toilet										
Personal towel	16	13.2	16	10.4	Ref		0.53	Ref		0.47
Shared towel	95	78.5	120	77.9	1.26	0.62-2.59		1.31	0.62-2.76	
Nothing/clothes	10	8.3	18	11.7	1.80	0.64-5.06		1.91	0.68-5.38	
Total	**121**		**154**							

** reference group is always or usually wash hands

Missing data: Need for reminders (controls=1 and cases=1), wash hands (controls=0 and cases=1), water temp (controls=0, cases=1), soap (controls=0, cases=1), hand drying (nil), dry hands after toilet (controls=0 and cases=11). Includes all children old enough to wash their hands including those that need supervision

aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 61: Bathing Practices

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Child normally washed in										
Bath	55	37.9	102	44.9	Ref		0.22	Ref		0.93
Shower	90	62.1	125	55.1	0.75	0.47-1.19		1.02	0.61-1.72	
Washes per week										
<daily	60	41.4	84	37.0	0.83	0.54-1.29	0.41	0.82	0.51-1.30	0.43
Daily or more	85	58.6	143	63.0	Ref			Ref		
Shared bathwater	45	31.3	162	71.7	0.87	0.51-1.47	0.60	0.74	0.42-1.29	0.29
Shared bathwater if infected	9	6.3	29	12.8	2.21	0.98-4.97	0.06	2.10	0.92-4.81	0.05
Shared bath towel	22	15.2	81	35.7	3.10	1.72-5.59	<0.001	3.37	1.83-6.23	<0.001
Towel not washed after single use	84	58.3	140	61.7	1.15	0.75-1.77	0.53	1.18	0.74-1.88	0.49

Missing data: Normal washing (nil), sharing bathwater (controls=0, cases=2), sharing towels (controls=0, cases=2), Towel not washed (controls=2, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 62: Clothes Washing Practices

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Automatic washing mach vs. other	8	5.5	10	4.4	0.79	0.31-2.02	0.62	0.96	0.35-2.65	0.93
Temp clothes washed in										
Cold	104	71.7	171	76.0	Ref		0.39	Ref		0.37
Warm/hot	41	28.3	54	24.0	0.80	0.48-1.33		0.78	0.46-1.34	

Missing data: controls=6 and cases =9, sharing bathwater (controls=0, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 63: Past History of Cellulitis

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Index child	46	31.7	43	18.9	0.50	0.30-0.86	0.01	0.56	0.32-0.96	0.04
Other child in house	45	31.3	29	13.3	0.34	0.19-0.59	<0.001	0.36	0.20-0.65	0.001
Adult	38	26.2	27	11.9	0.38	0.20-0.71	0.003	0.38	0.20-0.73	0.004
Any household member	83	57.2	75	33.0	0.36	0.23-0.59	<0.001	0.38	0.22-0.64	<0.001

Missing data: index child, other child and adult (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 64: Number of Previous Episodes of Cellulitis

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Index child										
Nil	99	68.3	184	81.1	Ref		0.002	Ref		0.005
1	18	12.4	30	13.2	0.90	0.46-1.74		1.03	0.52-2.05	
2 or more	28	19.3	13	5.7	0.25	0.12-0.54		0.26	0.12-0.59	

Missing data: index child (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 65: Timing of Previous Cellulitis

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Index child										
<1 month prior	14	9.9	11	4.9	0.42		0.07	0.46		0.15
1-3 months prior	12	8.5	10	4.5	0.45	0.16-1.09		0.46	0.17-1.26	
>3 months prior	17	12.0	18	8.1	0.57	0.20-1.02		0.63	0.20-1.09	
Never	99	69.7	184	82.5	Ref	0.28-1.17		Ref	0.30-1.31	
Other child										
<1 month prior	22	15.4	12	5.5	0.29		<0.003	0.31	0.13-0.74	0.01
1-3 months prior	6	4.2	5	2.3	0.44	0.12-0.67		0.59	0.19-1.80	
>3 months prior	16	11.2	11	5.1	0.36	0.15-1.29		0.35	0.15-0.82	
Never	99	69.2	189	87.1	Ref	0.16-0.81		Ref		
Adult										
≤3 months prior	8	5.6	7	3.1	0.47	0.13-1.68	0.01	0.42	0.11-1.60	0.024
>3 months prior	28	19.6	20	8.8	0.38	0.20-0.72		0.41	0.21-0.79	
Never	107	74.8	200	88.1	Ref			Ref		
Adult										
≤3 months prior	8	5.6	7	3.1	0.47	0.13-1.68	0.03	0.42	0.11-1.61	0.04
3-12 months prior	20	14.0	13	5.7	0.35	0.18-0.72		0.36	0.17-0.76	
>12 months	8	5.6	7	3.1	0.47	0.15-1.45		0.55	0.17-1.85	
Never	107	74.8	200	88.1	Ref			Ref		

Missing data: index child (controls=0 and cases=7), other child (nil), adult (controls=2, cases=0)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 66: Past History of Other Skin Problems

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Index child	53	36.6	87	38.3	1.08	0.72-1.63	0.72	1.23	0.81-1.88	0.33
Other child	55	38.2	81	37.2	0.96	0.64-1.43	0.83	0.91	0.60-1.39	0.67
Adult	39	26.9	60	26.4	0.98	0.61-1.57	0.92	1.05	0.65-1.72	0.83

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 67: Socioeconomic Status

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Deprivation**										
Lowest deprivation (1-3)	64	44.1	117	51.5	Ref		0.19	Ref		0.24
Highest deprivation (4-5)	81	55.9	110	48.5	0.74	0.48-1.16		0.74	0.44-1.22	
Deprivation (quintiles)										
1	19	13.1	26	11.5	Ref		0.04	Ref		0.05
2	15	10.3	47	20.7	2.29	1.04-5.04		2.22	1.01-4.86	
3	30	20.7	44	19.4	1.07	0.50-2.32		1.02	0.46-2.26	
4	43	29.7	44	19.4	0.75	0.35-1.60		0.73	0.32-1.64	
5	38	26.2	66	29.1	1.27	0.58-2.80		1.19	0.50-2.85	
Maternal CSC	73	52.9	121	55.0	1.09	0.69-1.71	0.71	1.12	0.69-1.84	0.64

Missing data: Deprivation (nil), Maternal community services card (controls=7, cases=7)
**aOR is adjusted for ethnicity and age
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 68: Maternal Characteristics

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Maternal age at interview										
19-34 yrs	67	49.3	109	52.9	Ref		0.52	Ref		0.93
≥35 yrs	69	50.7	97	47.1	0.86	0.54-1.39		0.98	0.58-1.64	
Maternal age at child's birth									0.87-4.23	0.20
<20 yrs	9	6.6	21	10.2	1.6	0.73-3.51	0.49	1.92		
20-34 yrs	107	78.7	156	75.7	Ref			Ref	0.43-1.61	
≥35 yrs	20	14.7	29	14.1	1.0	0.53-1.87		0.83		
Mother not born in NZ	57	41.0	80	36.5	0.83	0.53-1.30	0.41	0.85	0.52-1.40	0.53
Recent immigrant	17	12.2	32	14.6	1.23	0.66-2.28	0.51	0.95	0.51-1.77	0.88
Maternal ESOL	45	32.4	63	28.8	0.84	0.51-1.39	0.49	0.87	0.50-1.51	0.62
Maternal Education										
No formal quals	47	35.1	64	30.8	0.81	0.50-1.32	0.39	0.93	0.57-1.52	0.77
Formal qual	87	64.9	144	69.2	Ref			Ref		

Missing data: maternal age (controls=9, cases=21), NZ born (controls=6, cases=8), yrs in NZ (controls=6, cases=8), ESOL (controls=6, cases=7), maternal education (controls=9, cases=21)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 69: Household Composition

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Household composition										
Couple	80	55.2	134	59.0	Ref		0.76	Ref		0.82
Single parent	24	16.6	33	14.5	0.82	0.44-1.54		0.84	0.44-1.63	
Extended whānau/other	41	28.3	60	26.4	0.87	0.54-1.62		0.87	0.49-1.55	

Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 70: Household Characteristics

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Dwelling type										
House/townhouse	138	95.2	204	89.9	Ref		0.07	Ref		0.09
Flat/unit/other	7	4.8	23	10.1	2.22	0.95-5.22		2.12	0.89-5.05	
Housing ownership										
Private rental	47	32.4	66	29.1	1.00	0.57-1.73	0.28	0.94	0.52-1.69	0.06
HC rental/family	30	20.7	65	28.6	1.54	0.88-2.69		1.95	1.03-3.69	
Owned	68	46.9	96	42.3	Ref			Ref		
Housing ownership										
Rental	77	53.1	131	57.7	1.21	0.76-1.91	0.43	1.22	0.72-2.06	0.47
Owned	68	46.9	96	42.3	Ref			Ref		
Moved in last 2 yrs	48	33.1	80	35.2	1.10	0.71-1.70	0.67	1.00	0.64-1.57	0.99
Moved ≥2 in last 2 yrs	12	8.3	22	9.7	1.19	0.54-2.64	0.67	1.08	0.48-2.46	0.85
No landline	9	6.2	29	12.8	2.20	1.00-4.91	0.05	2.22	0.95-5.19	0.07

Missing data: Dwelling type, ownership, moved and landline all nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 71: Household Occupants

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
# people in house										
≥6	54	37.2	93	41.0	1.17	0.77-1.79	0.47	1.40	0.86-2.28	0.18
# people										
≤3	12	8.3	33	14.5	Ref		0.08	Ref		0.19
4-5	79	54.5	101	44.5	0.46	0.23-0.92		0.60	0.28-1.28	
≥6	54	37.2	93	41.0	0.66	0.32-1.23		0.92	0.42-1.99	
# children <15										
1	17	11.7	46	20.3	Ref		0.01	Ref		0.02
2-3	98	67.6	123	54.2	0.46	0.26-0.82		0.55	0.30-1.03	
≥4	30	20.7	58	25.6	0.71	0.35-1.47		1.02	0.47-2.22	
# adults										
1	13	9.0	22	9.7	1.06	0.48-2.32	0.92	1.07	0.46-2.49	0.99
2	78	53.8	125	55.1	Ref			Ref		
≥3	54	37.2	80	35.2	0.92	0.58-1.46		0.99	0.59-1.66	

Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 72: Household Crowding

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Crowded >1.5/bedroom	67	46.2	122	54.2	1.38	0.88-2.17	0.17	1.75	1.03-2.98	0.04
Crowded >2/bedroom	24	16.6	47	20.9	1.33	0.75-2.37	0.33	1.42	0.77-2.61	0.26
Crowded										
≤2/bedroom	121	83.4	178	79.1	Ref		0.62	Ref		0.52
2-3/bedroom	20	13.8	40	17.8	1.36	0.70-2.63		1.49	0.75-2.98	
More than 3/bedroom	4	2.8	7	3.1	1.19	0.34-4.23		1.06	0.33-3.40	
Toilet occupancy										
>5/toilet	36	24.8	64	28.2	1.19	0.75-1.89	0.46	1.43	0.83-2.45	0.20
Child shares bedroom	87	60.0	141	62.1	1.09	0.72-1.65	0.67	1.02	0.64-1.61	0.94
Child shares bed	38	26.2	51	22.5	0.82	0.51-1.30	0.39	0.73	0.43-1.25	0.25

Missing data: Number of bedrooms (controls=nil, cases=2), toilet and sharing (nil)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 73: Exposure to Household Smoking

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Maternal smoking	49	35.3	71	32.3	0.88	0.55-1.40	0.58	0.92	0.56-1.50	0.73
Smokers in the house	68	50.7	110	50.9	1.01	0.66-1.55	0.97	1.09	0.69-1.72	0.71
Smokers in the house										
0	66	49.3	106	49.1	Ref		0.98	Ref		0.85
1	38	28.4	63	29.2	1.03	0.65-1.65		1.15	0.70-1.88	
≥2	30	22.4	47	21.8	0.98	0.55-1.73		1.01	0.55-1.88	

Missing data: maternal smoking (controls=6, cases=7), smokers (controls=11, cases=11)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 74: Initial Management of Insect Bites

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Any management	37	63.3	34	57.6	0.79	0.37-1.70	0.54	0.67	0.29-1.56	0.35
Cleanse: anything	23	38.3	22	37.3	0.96	0.44-2.09	0.91	0.93	0.38-2.27	0.87
Cleanse: water/soap	23	38.3	19	32.2	0.76	0.35-1.65	0.49	0.77	0.31-1.89	0.56
Cleanse: antiseptic	7	11.7	6	10.2	0.86	0.22-3.39	0.82	0.69	0.15-3.08	0.62
Antiseptic/Ab cream	12	21.7	3	5.1	0.19	0.05-0.83	0.03	0.12	0.03-0.51	0.004
Anti-itch cream	15	25.0	9	15.3	0.54	0.21-1.40	0.20	0.45	0.16-1.29	0.14
Anti-histamine	4	6.7	4	6.8	1.02	0.25-4.08	0.98	1.13	0.29-4.37	0.86
Cover	12	20.0	8	13.6	0.63	0.22-1.76	037	0.71	0.23-2.21	0.31
Pain relief	5	8.3	8	13.8	1.76	0.47-6.54	0.40	2.05	0.50-8.44	0.31
Trad/alternative Rx	11	18.6	5	8.6	0.41	0.12-1.38	0.15	0.21	0.05-0.84	0.03
Sought medical advice	4	6.7	8	14.0	2.29	0.63-8.36	0.21	1.93	0.51-7.30	0.33
Total	**60**		**59**							

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 75: Time until Administration of First Aid for Insect Bites

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
<3 hrs	24	63.2	17	54.8	Ref			Ref		
3-11 hrs	4	10.5	7	22.7	2.47	0.61-10.00	0.38	1.64	0.32-8.32	0.57
≥12 hrs	10	26.3	7	22.6	0.99	0.32-3.06		0.64	0.17-2.39	
Total	**60**		**59**							

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 76: Initial Management of Cuts and Scratches

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Any management	23	57.5	37	61.7	1.19	0.50-2.84	0.69	1.24	0.49-3.12	0.65
Cleanse: anything	16	40.0	28	46.7	1.31	0.61-2.84	0.49	1.50	0.66-3.44	0.33
Cleanse: water/soap	14	35.0	22	36.7	1.08	0.48-2.43	0.86	1.20	0.51-2.82	0.68
Cleanse: antiseptic	8	20.0	10	16.7	0.80	0.27-2.39	0.69	0.76	0.25-2.35	0.64
Antiseptic/Ab cream	5	12.5	3	5.0	0.37	0.08-1.77	0.21	0.34	0.06-1.88	0.21
Cover	15	37.5	16	26.7	0.61	0.24-1.52	0.28	0.60	0.23-1.52	0.28
Pain relief	2	5.0	2	3.3	0.66	0.08-5.12	0.68	0.23	0.02-2.60	0.23
Trad/alternative Rx	2	5.0	3	5.0	1.0	0.15-6.87	1.0	0.92	0.10-8.40	0.94
Sought medical advice	3	7.5	4	6.7	0.88	0.18-4.37	0.88	0.63	0.11-3.60	0.60
Total	**40**		**60**							

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 77: Management of Eczema

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Usually use moisturiser	8	44.4	22	57.9	1.72	0.57-5.23	0.33	1.17	0.30-4.58	0.82
Usually use steroid	13	72.2	24	63.2	0.66	0.20-2.13	0.48	0.56	0.10-2.97	0.48
Moisturiser in last week	6	33.3	22	57.9	2.75	0.87-8.9	0.08	2.21	0.54-9.02	0.26
Steroid in last week	9	50.0	21	55.3	1.24	0.40-3.82	0.71	0.83	0.15-4.72	0.83
Soap substitute	8	44.4	18	47.4	1.13	0.37-3.38	0.83	0.70	0.18-2.67	0.59
Trad/alternative Rx	3	16.7	3	8.6	0.47	0.08-2.82	0.40	0.62	0.11-3.63	0.59
Sought medical advice	8	44.4	13	34.2	0.65	0.21-2.02	0.45	0.50	0.08-3.02	0.44
Total	**18**		**38**							

Missing data: nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 78: Symptoms First Noticed by Caregivers

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Fever	42	29.0	130	57.5	3.32	1.96-5.62	<0.001	3.81	2.17-6.66	<0.001
Swelling	104	71.7	201	89.3	3.30	1.83-5.96	<0.001	3.92	2.09-7.35	<0.001
Pain and tenderness	117	80.7	195	86.3	1.51	0.85-2.66	0.16	1.63	0.91-2.92	0.01
Pus/discharge	84	57.9	72	31.9	0.34	0.21-0.55	<0.001	0.34	0.20-0.57	<0.001
Limp	45	31.0	101	44.9	1.81	1.11-2.96	0.19	2.08	1.25-3.45	0.005
Other	16	11.0	69	30.5	3.54	1.92-6.63	<0.001	3.15	1.67-5.92	<0.001
Classic triad cellulitis	95	65.5	175	77.8	1.84	1.13-3.01	0.02	2.11	1.24-3.59	0.006
Something else	5	3.4	1	0.4	8.04	0.89-72.56	0.06	9.86	1.45-67.09	0.02

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 79: First Aid Management of Redness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Any management	120	82.8	147	64.8	0.38	0.24-0.62	<0.001	0.37	0.22-0.61	<0.001
Cleanse: water/soap	78	54.2	7	34.8	0.45	0.29-0.71	<0.001	0.43	0.27-0.68	<0.001
Cleanse: antiseptic	45	31.3	33	14.5	0.37	0.23-0.61	<0.001	0.40	0.24-0.66	<0.001
Antiseptic/Ab cream	47	32.9	24	10.6	0.24	0.14-0.42	<0.001	0.23	0.13-0.41	<0.001
Anti-itch	23	16.0	16	7.0	0.40	0.21-0.76	0.005	0.39	0.20-0.76	0.006
Antihistamine	7	4.9	3	1.3	0.26	0.06-1.06	0.06	0.25	0.07-0.95	0.04
Cover	63	44.4	54	23.9	0.39	0.26-0.60	<0.001	0.36	0.23-0.57	<0.001
Pain relief	50	34.7	89	39.4	1.22	0.82-1.82	0.32	1.29	0.85-1.97	0.23
Trad/alternative Rx	17	11.9	31	13.8	1.18	0.58-2.43	0.64	1.19	0.58-2.45	0.64
Sought medical advice	101	69.7	123	54.2	0.52	0.32-0.82	0.006	0.53	0.32-0.86	0.01
Total	**144**		**227**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 80: Time until Administration of First Aid for Redness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
<3 hrs	72	60.5	87	64.0	Ref		0.13	Ref		0.29
3-11 hrs	21	17.6	32	23.5	1.26	0.66-2.42		0.90	0.40-2.03	
≥12 hrs	26	21.8	17	12.5	0.54	0.28-1.06		0.62	0.35-1.12	
Total	**145**		**227**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 81: Time until Seeking Medical Attention for Redness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
<3 hrs	20	14.0	47	20.9	Ref		0.12	Ref		0.12
3-11 hrs	17	11.9	34	15.1	0.88	0.39-1.86		0.88	0.39-1.99	
≥12 hrs	106	74.1	144	64.0	0.58	0.32-1.03		0.58		
<3 hrs	20	14.0	47	20.9	Ref		0.11	Ref		0.14
3-11 hrs	17	11.9	34	15.1	0.85	0.39-1.86		0.88	0.39-1.98	
12-23	19	13.3	35	15.6	0.78	0.37-1.66		0.76	0.35-1.62	
≥24 hrs	87	60.8	109	48.4	0.53	0.30-0.96		0.53	0.29-0.98	
≥24 hrs	87	60.8	109	48.4	0.61	0.40-0.91	0.02	0.61	0.40-0.93	0.02
Total	**145**		**227**							

Missing data: controls=2 and cases=2
Includes all cases: those who responded no the seeking medical attention initially have been coded as seeking medical attention ≥24 hrs.
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 82: Time until Seeking Medical Attention for the Classic Signs of Cellulitis

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
<3 hrs	12	12.9	35	20.1	Ref		0.37	Ref		0.31
3-11 hrs	14	15.1	25	14.4	0.61	0.24-1.59		0.57	0.21-1.51	
≥12 hrs	67	72.0	114	65.5	0.58	0.28-1.23		0.55	0.26-1.18	
≥24 hrs	54	58.1	88	50.6	0.74	0.45-1.21	0.23	0.74	0.44-1.22	0.23
Total	**93**		**174**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile
Classic signs of cellulitis = pain, redness and swelling

Table 83: Usual Healthcare Provider

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Usual healthcare provider										
Single GP/practice	132	91.0	198	87.2	Ref		0.25	Ref		0.22
Multiple/whoever/after hrs	13	9.0	29	12.8	1.49	0.76-2.92		1.56	0.77-3.15	
Total	**145**		**227**							

Missing data: Nil
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 84: Healthcare Utilisation in the previous 6 months

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Family Dr/practice										
Nil	30	20.8	52	23.1	Ref		0.33	Ref		0.14
1-2 times	54	37.5	102	45.3	1.09	0.60-1.98		0.89	0.47-1.68	
3-4	34	23.6	41	18.2	0.70	0.36-1.35		0.57	0.27-1.20	
>4	26	18.1	30	13.3	0.70	0.32-1.38		0.44	0.19-1.01	
After-hours centre										
Nil	108	75.0	176	78.6	Ref		0.46	Ref		0.36
≥ 1 times	36	25.0	48	21.4	0.82	0.48-1.40		0.77	0.43-1.36	
Hospital ED										
Nil	131	91.0	169	75.4	Ref		<0.001	Ref		<0.001
≥ 1 times	13	9.0	55	24.6	3.28	1.71-6.28		3.65	1.82-7.30	
Total number seen										
Nil	23	16.1	43	19.2	Ref		0.47	Ref		0.20
1-2 times	46	32.2	80	35.7	0.93	0.48-1.79		0.77	0.39-1.50	
3-4	35	24.5	56	25.0	0.86	0.45-1.64		0.70	0.34-1.44	
>4	39	27.3	45	20.1	0.62	0.31-1.24		0.44	0.20-0.96	
Total	**145**		**227**							

Missing data: Family practice (controls=1, cases=2), Other practice (controls=0, cases=3), Afterhours (controls=1, cases=3), Hospital ED (controls=1, cases=3), Total (controls=2, cases=3)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 85: Healthcare Utilisation at Onset of Cellulitis

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Family doctor	128	88.3	122	53.7	0.15	0.09-0.27	<0.001	0.16	0.09-0.28	<0.001
Practice nurse	15	10.3	15	6.6	0.61	0.29-1.29	0.20	0.65	0.30-1.43	0.28
After-hours clinic	26	17.9	86	37.9	2.79	1.70-4.58	<0.001	2.51	1.49-4.20	0.001
Other med practitioner	4	2.8	15	6.6	2.49	0.80-7.78	0.12	2.86	0.74-11.03	0.13
Total	**145**		**227**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 86: Difficulties getting to the GP for this Illness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Difficulties getting to GP	16	11.1	67	29.5	3.35	1.77-6.33	<0.001	3.50	1.81-6.80	<0.001
Total	**145**		**227**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 87: Reasons for Difficulties getting to GP for this Illness

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Cost	8	5.6	50	22.0	4.80	2.02-11.40	<0.001	5.38	2.16-13.41	<0.001
Transport	5	3.5	29	12.8	4.07	1.48-11.19	0.007	4.09	1.43-11.75	0.009
Too busy	3	2.1	1	0.4	0.21	0.02-2.11	0.18	0.20	0.03-1.53	0.12
Doctors too busy	2	1.4	5	2.2	1.60	0.30-8.48	0.58	1.11	0.20-6.18	0.91
Other	5	3.5	5	2.2	0.63	0.16-2.45	0.50	0.59	0.18-2.00	0.40
Total	**145**		**227**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 88: Healthcare Provided*

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Topical antibiotics	44	30.8	17	14.5	0.38	0.20-0.74	0.01	0.36	0.18-0.74	0.005
Oral antibiotics	132	92.3	99	84.6	0.46	0.19-1.08	0.08	0.46	0.18-1.17	0.10
Pain relief	17	11.9	35	29.9	3.16	1.65-6.09	0.001	3.66	1.85-7.24	<0.001
Antiseptic	6	4.2	4	3.4	0.81	0.20-3.20	0.76	1.17	0.29-4.67	0.83
Other	18	12.6	10	8.5	0.65	0.27-1.59	0.34	0.60	0.24-1.49	0.27
Total	**143**		**117**							

*Excludes the hospital cases who were sent straight to hospital
Missing 142/214
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 89: Collection of Prescription Items

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
All items collected	134	97.1	109	96.5	0.81	0.19-3.43	0.78	0.68	0.17-2.69	0.58
Collected within 24 hrs	137	99.3	108	98.2	0.39	0.03-4.89	0.47	0.32	0.03-3.08	0.32
Time until first dose										
≤3hrs	123	91.1	91	92.9	Ref		0.74			
4-12hrs	10	7.4	5	5.1	0.68	0.22-2.09		0.93	0.30-2.90	0.73
>12hrs	2	1.5	2	2.0	1.35	0.19-9.77		2.22	0.30-16.56	
Total	**138**		**113**							

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 90: Healthcare Advice Provided

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	**%**	**N**	**%**						
Nil advice	76	53.5	185	86.4	5.54	3.30-9.31	<0.001	5.74	3.33-9.89	<0.001
Nil advice*	76	53.9	77	76.2	2.74	1.58-4.75	<0.001	2.82	1.58-5.01	<0.001
Total	**143**		**117**							

*Excludes the hospital cases who were sent straight to hospital
N=142/214
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 91: Healthcare Utilisation for Duration of Cellulitis Episode

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Family doctor										
0	12	8.3	99	43.8	Ref		<0.001	Ref		<0.001
1	70	48.3	75	33.2	0.13	0.06-0.27		0.14	0.07-0.28	
≥2	63	43.4	52	23.0	0.10	0.05-2.0		0.10	0.05-0.21	
Practice nurse										
0	127	87.6	215	95.1	Ref		0.05	Ref		0.03
1	9	6.2	5	2.2	0.33	0.10-1.06		0.30	0.10-0.91	
≥2	9	6.2	6	2.7	0.39	0.14-1.09		0.38		
PHN, school nurse										
0	137	94.5	213	94.2	Ref		0.96	Ref		0.99
1	2	1.4	4	1.8	1.29	0.23-7.31		1.12	0.18-7.08	
≥2	6	4.1	9	4.0	0.97	0.34-2.78		1.05	0.35-3.18	
Chemist										
0	113	77.9	196	86.7	Ref		0.06	Ref		0.11
1	26	17.9	27	11.9	0.60	0.34-1.10		0.60	0.33-1.10	
≥2	6	4.1	3	1.3	0.29	0.07-2.78		0.34	0.07-1.56	
After-hours clinic										
0	115	79.3	135	59.7	Ref		0.001	Ref		0.004
1	18	12.4	61	27.0	2.89	1.64-5.09		2.63	1.44-4.79	
≥2	12	8.3	30	13.3	2.13	1.05-4.34		1.92	0.91-4.03	

Missing data: controls=0 and cases=1
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Health Professional Responses

Table 92: Presenting Complaint at First Healthcare Presentation

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
Redness	100	76.9	120	68.2	0.64	0.35-1.20	0.16	0.62	0.31-1.26	0.19
Swelling	79	60.8	117	66.5	1.28	0.78-2.10	0.32	1.15	0.62-2.14	0.65
Pain and tenderness	80	61.5	118	67.0	1.27	0.79-2.05	0.32	1.02	0.56-1.83	0.96
Cellulitis triad	53	40.8	76	43.2	1.10	0.67-1.82	0.70	0.78	0.41-1.47	0.44
Pus/discharge	45	34.6	38	21.6	0.52	0.30-0.90	0.02	0.43	0.21-0.86	0.02
Fever	6	4.6	68	38.6	13.01	5.50-30.78	<0.001	6.66	2.62-16.94	<0.001
Other	11	8.5	24	13.6	1.71	0.79-3.68	0.17	1.85	0.74-4.63	0.19
Total	**132**		**178**							

Missing: all variables (controls=2, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 93: Size of Lesion at First Healthcare Presentation

	Controls GP cases		Hospital cases		OR	95% CI	p value	aOR	95% CI	p value
	N	%	N	%						
≥50mm	30	30.3	51	54.8	2.79	1.58-4.95	0.001	2.90	1.54-5.49	0.001
Size										
<50	69	69.7	42	45.2	Ref		0.001	Ref		0.001
50-100	24	24.2	32	34.4	2.20	1.16-4.13		2.16	1.08-4.32	
≥100	6	6.1	19	20.4	5.20	1.93-14.02		6.49	2.37-17.81	

Missing: all variables (controls=2, cases=2)
aOR= adjusted for ethnicity, age and NZ deprivation quintile

Table 94: Demographic Characteristics of Hospital Cases who Required Incision and Drainage

	Controls No drainage		Hospital cases Req drainage		p value
	N	**%**	**N**	**%**	
Ethnicity					
Māori	29	51.8	27	48.2	0.23
Pacific	49	62.8	29	37.2	
NZ Euro/Other	61	65.6	32	34.3	
Age					
Infant	9	60.0	6	40.0	0.64
Preschool	56	65.1	30	34.9	
School-age	74	58.7	52	41.3	
NZDep quintile					
1 (least deprived)	17	65.4	9	34.6	0.58
2	16	66.0	16	34.0	
3	21	52.3	21	47.7	
4	25	56.8	19	43.2	
5 (most deprived)	23	65.2	23	34.8	
Total	**139**		**88**		

Missing: nil

Table 95: Summary Table of Risk Factors for Hospitalisation with Cellulitis

Risk factor	Direction of effect	Magnitude of effect aOR	95% CI
Demographic Factors			
Age			
Infant	↑↑↑	6.70	1.45-30.94
Preschool	↑	1.55	0.95-2.54
School		Ref	
Host Susceptibility			
Clinical signs eczema	↑	1.93	1.04-3.60
Previous cellulitis-child	↓	0.56	0.32-0.96
Previous cellulitis-other child	↓	0.36	0.20-0.65
Previous cellulitis-adult	↓	0.38	0.20-0.73
Cellulitis numbers			
nil		Ref	
1		1.03	0.52-2.05
2 or more	↓↓	0.26	0.12-0.59
Exposures/Breaches of skin			
Insect bites in previous wk	↓	0.44	0.27-0.72
Number of insect bites			
Nil		Ref	
1-5	↓	0.61	0.36-1.04
6-9	↓	0.31	0.13-0.76
>=10	↓↓	0.12	0.04-0.39
Host Behaviours			
Not washing hands before eating	↑	1.97	1.23-3.17
Not washing hands after playing outside	↑	1.82	1.06-3.11
Washing hands in warm/hot water	↓	0.52	0.28-0.96
Shared bath towel	↑↑	3.37	1.83-6.23
Social/Environmental			
Crowded >1.5/ bedroom	↑	1.75	1.03-2.98
Health Literacy/Utilisation			
Use of hospital ED	↑↑	3.65	1.82-7.30
Symptoms noticed			
Cellulitis triad	↑	2.11	1.24-3.59
First aid management for redness	↓	0.37	0.22-0.61
Sought medical advice for redness	↓	0.53	0.32-0.86
Difficulties getting to GP			
Any	↑↑	3.50	1.81-6.80
Cost	↑↑	5.38	2.16-13.41
Transport	↑↑	4.09	1.43-11.75

Healthcare Factors			
Size of lesion at presentation > 50mm	↑	2.90	1.54-5.49
Nil other advice given	↑	2.82	1.58-5.01

↑=1-3 times increased risk
↑↑=3-6 times increased risk
↑↑↑=6 or more times increased risk
aOR= adjustment for ethnicity, age, and socioeconomic status

Appendix 4: Case Series: Supporting Information

Information sheet

Consent form

Caregiver questionnaire

Health Professional questionnaire

Clinical Information

Info sheet 1

Info sheet 2

Consent 1

Consent 2

Cellulitis
Caregiver Questionnaire

ID No

Interviewers name _____ Date of interview_____

Child's name: _____ Child's NHI: _____

Caregiver's relationship to child:_____

1 When did you first notice the skin infection?

Date | | | |
|---|---|---|
| *dd* | *mm* | *yy* |

2 What was it that you first noticed?

Spont	*Prompt*	
		Fever
		Redness
		Swelling
		Pain/tenderness
		Crusting/pus/discharge
		Other: specify_____

3 Where was it?

	Face		Shoulder		Hip
	Neck		Arm		Leg
	Scalp		Hand		Foot
	Trunk		Finger		Toe
	Bottom				
	Other (specify)	_____			

4 Was there anything else you noticed?

	No
	Yes (specify)

5 What do you think might have caused the skin problem?

Before the skin problem started, did baby/child have:

6 An insect bite on the area?

- ☐ Don't know
- ☐ No
- ☐ Yes (specify)

7 Did the baby/child have a cut or scratch?

- ☐ Don't know
- ☐ No
- ☐ Yes (specify)

8 Did the baby/child have anything else where the skin problem started?

- ☐ Don't know
- ☐ No
- ☐ Yes (specify)

9 What did you do when it first began?

- ☐ Nothing
- ☐ Local cleaning/antiseptic/topical antibiotic (specify)
- ☐ Dressing (specify)
- ☐ Traditional therapy (specify)
- ☐ Pain relief (specify)
- ☐ Oral antibiotics (specify)
  - Name of antibiotic _____
  - ☐ Dose (mg)
  - ☐ Times per day
  - ☐ Length of course (days)
  - Source (eg GP, cupboard) _____
- ☐ Other (specify)

10 Who, in your household, gave advice about treating your child?

11 What advice was given?

12 Did you seek help from outside your household when it first began?

☐ No. **If not, why not?**

☐ Yes. **If yes, from whom?**

Spont.	*prompt*	
		Family doctor/GP
		GPs practice nurse
		Plunket nurse/district nurse/public health nurse/school nurse
		Chemist/pharmacist
		Doctors in after hours clinic (e.g. WestCare)
		Starship emergency department
		Alternative therapist e.g. naturopath, homeopath
		Social worker/counsellor
		Traditional healer such as tohunga, rongoa
		Community Healthworker
		Relative or friend
		Other (specify) _____

13 What was it about the skin problem that made you ask for help?

14 Did you see any doctors before you came to hospital?

☐ No
☐ Yes

If yes, whom did you see and how many times?

Tick if seen	*No. times seen*	
		Own family doctor
		Another doctor in the same practice
		Another doctor
		After hours care
		Children's emergency department
		Other (specify) _____

15 How many days was it from when you first noticed the skin problem to when your child first saw a doctor?

☐ Days

16 How many days was it from when you first noticed the skin problem to when your child was admitted to hospital?

☐ Days

17 What was the reason you came to hospital?

☐ Referred by doctor
☐ Someone else advised them to come (specify who) _____
☐ Child was getting worse
☐ Wanted another opinion
☐ Other (specify) _____

18 Why do you think the skin problem got worse?

We are now wanting to find out what happened each time you went to a doctor for the skin problem. We will begin with the first doctor's visit and then ask about the others one at a time.
**

19 Who was the first doctor you saw?

- ☐ Own family doctor
- ☐ Another doctor in the same practice
- ☐ Another doctor
- ☐ After hours care doctor
- ☐ Children's Emergency Department doctor
- ☐ Other (specify)

20 Date seen: ☐☐ ☐☐ ☐☐
dd *mm* *yy*

21 Name: _____

22 Practice: _____

23 What was the reason you went to see this doctor?

24 What did the doctor tell you was the name for the skin problem?

- ☐ Cellulitis
- ☐ Boil
- ☐ Infected bite
- ☐ Skin sores
- ☐ Don't know / don't remember
- ☐ Other (specify) _____

25 Were you given a prescription for some medicine or ointment?

- ☐ No *(go to Q. 30)*
- ☐ No, but sent to hospital *(go to Q. 30)*
- ☐ Local antibiotics (specify): _____
- ☐ Oral antibiotics (specify name)_____
  - ☐ Dose (mg)
  - ☐ Times per day
  - ☐ Length of course (days)
- ☐
- ☐ Pain relief (specify) _____
- ☐ Don't know / don't remember
- ☐ Other (specify) _____

26 Were all the items of the prescription collected from the chemist?

☐ Don't know / don't remember
☐ No
☐ Yes

27 When were the items collected from the chemist?

☐ Within 24 hours of getting the prescription
☐ Between 1-2 days
☐ More than 2 days

28 What were the reasons for not taking the prescription to the chemist, the delay in getting the medicine, or not collecting all of the items?

1. (first mention)

2. Other

People often forget to take all the medicine according to the instructions, but I need to know as accurate an answer to this question as you can give me.

29 How many days did your child take the medicine according to the instructions?

☐ days

30 What other treatment or advice did the doctor give you?

☐ None
☐ Local cleaning/antiseptic (specify)_____

☐ Dressing (specify) _____

☐ Traditional therapy (specify) _____

☐ Specific advice re care of bites, cuts etc.
☐ Other (specify) _____

31 Did you see the same doctor or any other doctor for your child's skin problem before they ended up admitted to hospital?

☐ No. Move to next section and q 32
☐ Yes.

**

If yes: Now some questions about the second time you went to a doctor for your child's skin problem…*[repeat all questions from ** to ** (q 19-q 31) on supplementary sheet.]*

I would now like to ask some other questions about your child's skin and whether they have ever had this before

32 Has your child ever had this skin problem before?

☐ Don't know
☐ No
☐ Yes ☐ (*If yes)* How many times?

33 If yes, how long ago was the last time your child had the skin problem?

☐ weeks

34 Has your child ever had eczema?

☐ Don't know
☐ No
☐ Yes ☐ (*If yes)* How long ago was it last a problem? (weeks)

35 Has your child ever had scabies?

☐ Don't know
☐ No
☐ Yes ☐ (*If yes)* How long ago was it last a problem? (weeks)

36 Has your child ever had any other skin problems?

☐ No
☐ Yes (specify)

37 Have any of your other children had the same cellulitis problem?

☐ Not applicable (only child)
☐ No
☐ Yes ☐ (*If yes)* How long ago? (weeks)

38 Do you think that children can catch cellulitis off each other?

☐ Don't know
☐ No
☐ Yes. If yes, what did you do to stop the others from getting it?

39 **Some people have difficulties getting to or seeing a doctor or GP when they need to. Did you have any problems getting to or seeing a family doctor or GP for your baby/child with this illness? By doctor I mean any GP, family doctor, or doctor in a medical clinic or centre rather than a hospital.**

- ☐ No
- ☐ Yes

40 **If yes**
What were the things that made it difficult for your child to see a doctor or GP?
1. (first mention)

2. other

I would now like to ask some questions about your family and the home situation

41 **How many people (including children and babies) are there in your household?**

☐

42 **How many children under 15 years are there in your household?**

☐

43 **Which one of the statements best describes this household?**

- ☐ Solo parent with children
- ☐ Couple with children
- ☐ Extended family/Whanau
- ☐ Family/other combination
- ☐ Other (specify)

44 **How many different houses have you lived in over the last 2 years?**

☐

45 **What type of house or home do you live in?**

- ☐ House/townhouse
- ☐ Flat/unit
- ☐ Garage
- ☐ Caravan, cabin or tent
- ☐ Other (specify)

46 **Is this rented or owned?**

- ☐ Rented privately
- ☐ Rented (housing corp.)
- ☐ Owned
- ☐ Living with relatives
- ☐ Other (specify)

47 **Is there a telephone that is connected?**

- ☐ No
- ☐ Yes

48 How many bedrooms are there in this house, including rooms furnished as bedrooms and any sleep-out or caravan that is used as a bedroom?

☐

49 What sort of facilities does your house have to wash your child?

☐	Bath	☐	How many times per week?
☐	Shower	☐	How many times per week?
☐	Tub / sink	☐	How many times per week?
☐	Other (specify)	☐	How many times per week?

50 What sort of facilities does your house have to wash your family's clothes?

☐ Automatic washing machine
☐ Wringer washing machine
☐ Hand washing in a tub
☐ Local laundromat
☐ Other (specify)

51 What temperature do you wash your clothes/towels in?

☐ Cold
☐ Warm
☐ Hot

Some people have problems with insects in their house. Do you have a problem with:

52 Mosquitoes?

☐ No
☐ Yes

53 Fleas?

☐ No
☐ Yes

54 Other insects?

☐ No
☐ Yes (specify) _____

55 If yes to the above insect problem questions,
What have you done to try to get rid of the insect problem and has it worked?

Now some last few questions about you

56 Do you have access to a car, during the day?

- [ ] No
- [ ] Yes

57 During the night?

- [ ] No
- [ ] Yes

58 Do you have a Community services card?

- [ ] No
- [ ] Yes

59 Have you received any of these types of income support in the past 12 months?

- [ ] National super
- [ ] Unemployment benefit
- [ ] Youth or student allowance
- [ ] DPB
- [ ] Family support
- [ ] Sickness benefit
- [ ] Invalids benefit
- [ ] ACC weekly payments
- [ ] Other government benefit
- [ ] None of these

60 What is the total gross household income from all income earners and all other income before taxes?

- [ ] Less than $20,000 per year
- [ ] Between $20-30,000
- [ ] Between $30-40,000
- [ ] Between $40-60,000
- [ ] More than $60,000 per year
- [ ] Declined
- [ ] Don't know

61 What was the last level you completed in your formal education?

- [ ] Primary school
- [ ] Secondary school/no school cert.
- [ ] School cert.
- [ ] UE/6th form cert./bursary
- [ ] Technical or trade certificate
- [ ] Tertiary
- [ ] Other

62 How old are you?

- [ ] years

63 How many years have you lived in New Zealand?

- [ ] years

Thank you for your time. I have two last questions to finish and we are very interested in your thoughts.

64 Skin infection leading to hospital admission is becoming more common. Why do you think that may be?

65 Do you have any ideas as to what we can do to help the problem?

Thank you for your time and co-operation. We will send you a copy of our results. If you have any questions about the study please feel free to contact Lynne Hutchison, the study co-ordinator on 3737-599 ext 3701.

Cellulitis
Health Professional Questionnaire

ID No

Child's NHI:
Child's name:
GP name:
Practice

Because you may have seen this child more than once for the current infection, the boxes in the questions below are numbered 1 to 3 (1=1st consultation, 2=2nd consultation etc. Add more boxes if necessary)

1 Date of presentation

1 (1st consult'n)	2 (2nd consult'n)	3 (3rd consult'n)

2 Presenting complaint? ***(tick box)***

	1	2	3
Fever			
Redness			
Swelling			
Pain/tenderness			
Crusting/pus/discharge			
Booked follow-up			
Other (specify)			

3 Site? ***(tick box)***

Face		Shoulder		Hip	
Neck		Arm		Leg	
Scalp		Hand		Foot	
Trunk		Finger		Toe	
Bottom					

Other (specify) _____

4 What was the approximate size of the lesion? ***(maximum diameter in cms)***

1	2	3

5 Was there joint involvement?

		1	2	3
	No			
	Yes, specify joint			

6 What was your diagnosis? ***(tick box– specify where necessary)***

	1	2	3
Cellulitis			
Carbuncle/boil			
Impetigo			
Acute lymphadenitis			
Abscess			
Other (specify)			

7 What do you think was the underlying etiology? ***(tick box – specify where necessary)***

Insect bite/sting (specify type)	
Other animal	
Sharp object (specify type)	
Struck an object	
Accidental fall	
Motor vehicle or cyclist accident	
Complication of surgical procedure	
Sports injury	
Other (specify)	

8 What advice/treatment was given? ***(tick box – specify where necessary)***

	1	**2**	**3**
None			
Local cleaning/antiseptic specify)			
Dressing (specify)			
Traditional therapy (specify)			
Pain relief (specify)			
Local antibiotics: Specify name			
- dose			
- length of course			
Oral antibiotics: Specify name			
- dose			
- length of course			
General advice re preventive measures for the future			
Other (specify)			

9 What follow up was arranged? ***(tick box)***

	1	**2**	**3**
GP			
Hospital ED			
Hospital admission			
Other (specify)			

10 Were there any predisposing factors contributing to the child's infection? ***(tick box)***

- ☐ None
- ☐ Diabetes
- ☐ Chronic steroid use
- ☐ Immunocompromised (specify) _____

- ☐ Varicella
- ☐ Post surgery
- ☐ Underlying systemic illness (specify) _____

- ☐ Malnutrition
- ☐ Past history of cellulitis (specify details) _____

- ☐ Other (specify)

11 Are there any other health or social factors you feel could have influenced this child's illness?

Thank you for your time and co-operation. We will send you a copy of our results. If you have any questions about the study please feel free to contact Lynne Hutchison, the study co-ordinator on 3737-599 ext. 3701.

Please fax this questionnaire back to Lynne at fax no. 373 7486

Cellulitis
Clinical Information

ID No

NHI
Name

DOB

Age
Address

Ethnicity

- ☐ NZ Maori
- ☐ European
- ☐ Asian
- ☐ Other (specify)
- ☐ Samoan
- ☐ Tongan
- ☐ Niuean
- ☐ Cook Island Maori
- ☐ Tokelauan
- ☐ Fijian

Gender

- ☐ Male
- ☐ Female

Family doctor

Date of admission:
Date of discharge:

Admission recordings

- ☐ Weight
- ☐ Length/height
- ☐ Temperature deg C
- ☐ Heart rate
- ☐ Respiratory rate
- ☐ Centile
- ☐ Centile

Service admitted under

- ☐ General Paediatrics
- ☐ Orthopaedics
- ☐ Surgical
- ☐ ENT
- ☐ Other (specify)

Admitting diagnosis

- ☐ Lymphadenitis
- ☐ Impetigo
- ☐ Cellulitis
- ☐ Local skin infection
- ☐ Abrasion, insect bite, foreign body
- ☐ Abscess
- ☐ Other (specify)

Site?

- ☐ Face
- ☐ Neck
- ☐ Scalp
- ☐ Trunk
- ☐ Bottom
- ☐ Shoulder
- ☐ Arm
- ☐ Hand
- ☐ Finger
- ☐ Other (specify)
- ☐ Hip
- ☐ Leg
- ☐ Foot
- ☐ Toe

Event code

☐ Insect bite/sting (specify type) _____
☐ Other animal
☐ Sharp object (specify type) _____
☐ Struck an object
☐ Accidental fall
☐ Motor vehicle or cyclist accident
☐ Complication of surgical procedure
☐ Sports injury
☐ Other (specify) _____

Admitting treatment

☐ Local cleaning/antiseptic (specify) _____

☐ Dressing (specify) _____

☐ Traditional therapy (specify) _____

☐ Pain relief _____

☐ Local antibiotics (specify) _____

☐ IV antibiotics (specify) –name
-dose
-length of course

☐ Oral antibiotics (specify) –name
-dose
-length of course

☐ Other (specify) _____

Inpatient treatment

☐ Local cleaning/antiseptic (specify) _____

☐ Dressing (specify) _____

☐ Traditional therapy (specify) _____

☐ Pain relief _____

☐ Local antibiotics (specify) _____

☐ IV antibiotics (specify) –name
-dose
-length of course

☐ Oral antibiotics (specify) –name
-dose
-length of course

☐ Other (specify) _____

Discharge treatment

☐ Local cleaning/antiseptic (specify) _____

☐ Dressing (specify) _____

☐ Traditional therapy (specify) _____

☐ Pain relief _____

☐ Local antibiotics (specify) _____

☐ Oral antibiotics (specify) –name
-dose
-length of course

☐ Other (specify) _____

Operation

☐ Incision and Drainage Date_____ Time_____

☐ Joint aspiration Date_____ Time_____

☐ Other (specify)

Microbiology/Investigations

☐ Swab taken: Site_____ Growth_____

Sens: _____

☐ Blood culture: Growth _____ sens _____

☐ FBC Hb=
MCV=
White count=
ESR=

☐ Xray

☐ Bone scan

☐ Other e.g. MRI, CT scan, Ultrasound

Predisposing factors

☐ None

☐ Diabetes

☐ Chronic steroid use

☐ Immunocompromised (specify) _____

☐ Varicella

☐ Post surgery

☐ Underlying systemic illness (specify) _____

☐ Malnutrition

☐ Past history of cellulitis (specify details) _____

☐ Other (specify)

Appendix 5: Case-Control Study: Supporting Information

Map of the Eight Geographic Study Areas

Information Sheets and Consent Forms

- **GP- Information Sheet**
- **GP- Consent Form**
- **Hospital Case- Information Sheet**
- **Hospital Case- Consent Form**
- **GP Case- Information Sheet**
- **GP Case- Consent Form**
- **GP Control- Information Sheet**
- **GP Control- Consent Form**
- **GP Case and GP Control- Consent Form to researcher contact**
- **Child Friendly Information Sheet**

Questionnaires

- **Hospital and GP case- Caregiver Questionnaire**
- **Hospital and GP case- Health Professional Questionnaire**
- **Child Severity Assessment**
- **GP Control Caregiver Questionnaire**

Weighting Calculation

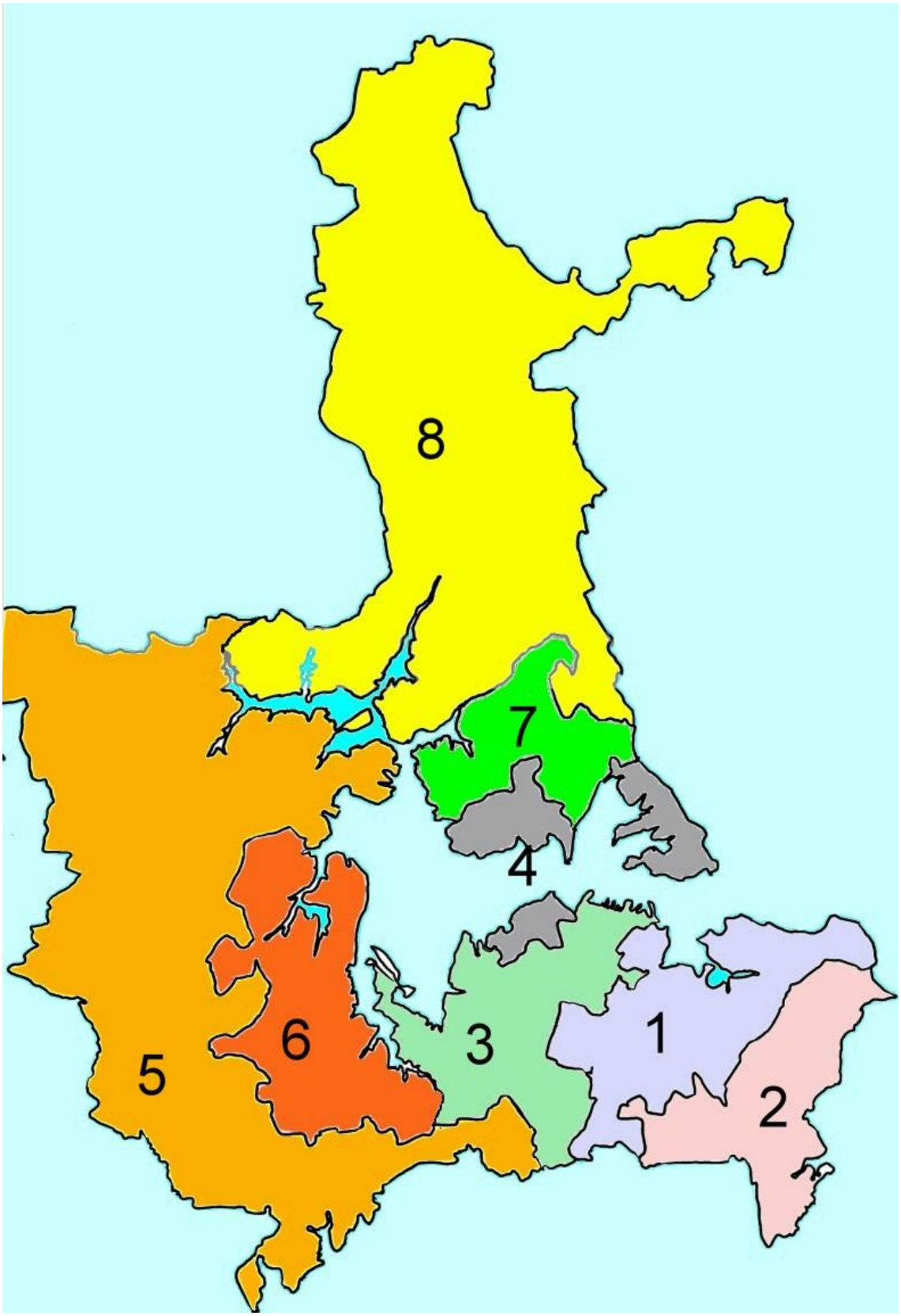

Figure 14: Map of the 8 Geographic Study Areas

Info sheet and consent forms x 14 pages

Questionnaires x 49 pages

Area	GP's	Total GP-weeks	#GP with 2 weeks of observation	#GP with 3 weeks of observation	Actual GP-weeks collected	% actual of Total		#GP Cases	#Hosp Cases	Predicted # GP cases	Predicted # hosp & GP cases		GP case weights	Hosp case weights	double check	double check	
1	110	5720	5	102	316	6%	18.1	10	32	181	213	5.07	3.8034	0.2101	44.76	18.1	6%
2	48	2496	2	99	301	12%	8.3	23	27	190.9	217.9	4.36	1.7441	0.2101	45.79	8.3	12%
3	95	4940	7	187	575	12%	8.6	28	54	240.8	294.8	3.60	1.8072	0.2101	61.95	8.6	12%
4	48	2496	4	62	194	8%	12.9	6	14	77.4	91.4	4.57	2.7107	0.2101	19.21	12.9	8%
5	51	2652	4	84	260	10%	10.2	18	18	183.6	201.6	5.60	2.1434	0.2101	42.36	10.2	10%
6	98	5096	7	176	542	11%	9.4	38	45	357.2	402.2	4.85	1.9753	0.2101	84.52	9.4	11%
7	55	2860	0	60	180	6%	15.9	9	22	143.1	165.1	5.33	3.3411	0.2101	34.69	15.9	6%
8	84	4368	3	49	153	4%	28.5	5	18	142.5	160.5	6.98	5.9888	0.2101	33.73	28.5	4%
Total	**589**	**30628**	**32**	**819**	**2521**		**111.9**	**137**	**230**		**1746.5**				**367**		

Table 96: Calculation of weighting used for combining the GP cases and Hospital cases

Case weights are normalised weights based on the assumption all hospital cases were collected and the calculated number of GP cases that would have been collected if GP collection had occurred for 52 weeks across the year

Appendix 6: Additional Information

Newspaper Clips

Starship Clinical Guideline

New Zealand herald article

Skin infection rate quadruple for Maori, Pacific Islanders

HEALTH: Further research needed to explore genetic, environmental factors

by Rebecca Walsh
health reporter

Pacific Island and Maori children are nearly four times more likely to suffer skin infections than their European counterparts, an Auckland study has found.

The study, published in the *New Zealand Medical Journal* today, looked at patient admissions to Middlemore Hospital in 2000.

It identified 91 children, aged 1 to 14, with either skin abscesses or cellulitis, a skin infection that penetrates below the surface and often requires surgical treatment.

Severe forms of skin infections can be limb- or life-threatening.

Of the 91 children identified, 73 were Polynesian, and 38 of those were Maori.

The researchers estimated that the incidence of skin infection among the Polynesian population was 137.7 per 100,000, compared with 35.4 per 100,000 among European children.

But they said further research was needed to identify whether genetic or social and environmental factors were involved.

Dr Alison Leversha, a community paediatrician at Starship children's hospital, where cellulitis is one of the leading causes of admission, said the results did not surprise her. Earlier studies had revealed similar figures.

Skin infections were more common among disadvantaged families, where overcrowding was more likely, she said.

Infections could easily spread through shared bedding, clothing and towels.

Children low in iron or other nutrients were also more prone.

But she said Pacific people also had higher rates of other types of infection.

"I would hesitate to say it was totally socio-economic. At the moment we don't believe there's any genetic involvement, but we don't know."

Dr Leversha said cellulitis, which could start with a cut or mosquito bite, should be preventable through good hygiene. Any scratch or insect bite should be washed frequently and antiseptic used.

Anyone with an infection should not share towels or bedding.

Last year the Auckland District Health Board started a campaign to reduce cellulitis in Glen Innes, which has one of the worst rates in the city.

Preliminary results show that the number of people hospitalised with cellulitis in the area has dropped.

Between July and December, 30 to 40 cellulitis patients from Glen Innes were hospitalised, compared with 50 to 60 for the same period in 2002.

>> Skin infections

- Infection rate in Polynesian population was 137.7 per 100,000, compared with 35.4 per 100,000 among European children.
- Some infections, such as abscesses or cellulitis, can require surgical treatment.
- Cellulitis is one of the leading causes of admission to Starship children's hospital.

The New Zealand Herald ★ Friday, April 23, 2004

SSH guideline 1

SSH guideline 2

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