THE UNIVERSITY OF QUEENSLAND

AUSTRALIA

A holistic exploration of paediatric partial thickness burn care in the outpatient setting

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Bachelor of Occupational Therapy (Honours Class I)

A thesis submitted for the degree of Doctor of Philosophy at

The University of Queensland in 2016

School of Medicine

Centre for Children's Burns and Trauma Research

Abstract

Introduction:

Countless children sustain painful burn injuries every year, many requiring hospital treatment. Treatment can involve painful wound care procedures, possible surgical intervention and the risk of lifelong scarring which can have a multi-faceted effect on the child and their family. The current focus of research into paediatric burns lies predominantly with severe burn injuries which generally denote long hospital stays and worse outcomes (functionally, cosmetically and psychosocially). However in high-income countries, the majority of children sustain small partial thickness burns which are treated in the outpatient setting with specialized dressings.

Thesis aim:

The aim of this study was to provide a holistic and comprehensive exploration of pediatric partial thickness burn care. The first phase was to determine the most effective silver dressing for reduced wound re-epithelialization time and pain during dressing changes, establish the reliability of a new wound measurement tool, assess the scar outcome of study participants and complete a cost effective analysis of silver dressings. The second phase was to provide an exploration of parent experiences in the outpatient setting.

Phase 1 Methodology and Results:

RCT: Ninety-six children (0-15 years) with ≤10% total body surface area partial thickness burn injuries were recruited for a randomised controlled trial and received either 1) Acticoat™; 2) Acticoat™ with Mepitel™; or 3) Mepilex Ag™ dressings changed every 3-5 days until full re-epithelialization or skin grafting occurred. When adjusted for burn depth, Acticoat™ significantly increased the expected days to full re-epithelialization by 40% (p < 0.01) and Acticoat™ with Mepitel™ significantly increased days to full re-epithelialization by 33% (p = <0.01) when compared to Mepilex Ag™. Pain scores were also significantly lower at dressing changes in children who received Mepilex Ag and Acticoat with Mepitel compared to Acticoat alone.

3D photography reliability: Burn wound re-epithelialisation was measured at each dressing change using digital planimetry (Visitrak™ system) and stereophotogrammetry (3D photography). Wound surface area measurements were complete for 75 participants at the first dressing change. Level of agreement between wound surface area measurements was excellent (ICC 0.96, 95% CI 0.93, 0.97). Visitrak™ tracings could not be completed in

19 participants with 16 aged less than two years. 3D photography could not be completed for one participant. Barriers to completing Visitrak™ tracings were: excessive movement, pain, young age or wound location.

Cost-analysis: This study was trial based economic evaluation conducted from a healthcare provider perspective. Costs directly related to the management of partial thickness burn injuries ≤10% TBSA were collected from March 2013-July 2014 and for a one year post re-epithelialization time horizon. Incremental cost effectiveness ratios were estimated and dominance probabilities calculated. Costs (dressing, labor, analgesics, scar management) were considerably lower in the Mepilex Ag™ group (median AUD$94.45) compared to the Acticoat™ (median $244.90) and Acticoat™ with Mepitel™ (median $196.66) interventions. There was a 99% and 97% probability that Mepilex Ag™ dominated (cheaper and more effective than) Acticoat™ and Acticoat™ with Mepitel™, respectively.

Scar assessment: An assessment of forty-three children participants' skin appearance was conducted at 3 and 6 months post re-epithelialization for children who presented for follow-ups or sent a photo. Days to re-epithelialization was a significant predictor of skin/scar quality at 3 and 6 months (p<0.01). Patient-rated color and observer-rated vascularity and pigmentation POSAS scores were comparable at 3 months (color vs. vascularity 0.88, p<0.001; color vs. pigmentation 0.64, p<0.001), but patients scored higher than the observer at 6 months (color vs. vascularity 0.57, p<0.05; color vs. pigmentation 0.15, p = 0.60). Burn depth was significantly correlated with skin thickness (r=0.51, p<0.01). Hypopigmentation of the burn site was present in 25.8% of children who re-epithelialized in ≤2 weeks.

Phase 2 Methodology and Results:

This study was a qualitative design using purposive sampling. Ten parents of children aged 0 to 5 years with an acute partial thickness burn injury ≤10% TBSA who were referred for outpatient treatment were interviewed. Semi-structured interviews were conducted on the day of their child's discharge from the service. Interviews were transcribed verbatim and analysed using an inductive thematic analysis method. Themes identified included; going into the unknown, facilitation and resilience.

Discussion:

This body of work has provided a comprehensive and holistic overview of pediatric partial thickness burn care. Outcomes from this study have resulted in the development of a new and more cost-effective dressing protocol for pediatric burn care, which has been implemented Queensland-wide and introduced interstate and in New Zealand. 3D photography is now being utilized as a non-invasive alternative to digital planimetry when completing wound surface area measurements. It has also provided a greater knowledge of challenges and outcomes faced by this population of children and their families, which can be used to inform future clinical practice so that the burn treatment experience includes faster wound re-epithelialization, less pain and reductions in parental stress.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my research higher degree candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Publications during candidature

Peer-reviewed papers

1. Gee Kee, E., Kimble, R. M., Cuttle, L., & Stockton, K. (2013). Comparison of three different dressings for partial thickness burns in children: study protocol for a randomised controlled trial. *Trials, 14*, 403. doi: 10.1186/1745-6215-14-403

2. Gee Kee, E. L., Kimble, R. M., Cuttle, L., Khan, A., & Stockton, K. A. (2015). Randomized controlled trial of three burns dressings for partial thickness burns in children. *Burns*. doi: 10.1016/j.burns.2014.11.005

3. Gee Kee, E. L., Kimble, R. M., & Stockton, K. A. (2015). 3D photography is a reliable burn wound area assessment tool compared to digital planimetry in very young children. *Burns*. doi: 10.1016/j.burns.2015.01.020

4. Gee Kee EL, Kimble RM, Cuttle L, Stockton KA. Scar outcome of children with partial thickness burns: A 3 and 6 month follow-up. *Burns. E-pub ahead-of-print.*

Submitted papers

5. Gee Kee EL, Stockton KA, Kimble RM, Cuttle L, McPhail S. Cost-effectiveness of three silver dressing combinations for pediatric partial thickness burns: an economic evaluation from a randomized controlled trial. *Submitted to Burns Journal (Date:08/03/2016).*

Conference abstracts

1. Gee Kee E, Kimble R, Cuttle L, Stockton K. Scar outcome of children with partial thickness burns: A 3 and 6 month follow-up (*Oral).* Presented: 39th Australian and New Zealand Burn Association Annual Scientific Meeting, Melbourne, October 2015.

2. Gee Kee, E, Kimble R, Cuttle L, Stockton K. Scar outcome of children with partial thickness burns: A 3 and 6 month follow-up (*Oral).* Presented: 16th European Burns Association Congress, Hannover, Germany, September 2015.

3. Simons M*, Gee Kee E, Tyack, Z. Reproducibility of the BT12 Venue 40 MSK ultrasound (GE Healthcare) using scar and normal skin sites in children and adolescents with burn scars (*Poster)*. Presented: 39th Australian and New Zealand Burn Association Annual Scientific Meeting, Melbourne, October, 2015

4. Gee Kee E, Kimble R, Cuttle L, Khan, A, Stockton K. Randomised controlled trial of three burns dressings for partial thickness burns in children (*Oral).* Presented: 17th Congress of International Society for Burn Injuries, Sydney 2014.

5. Gee Kee E, Kimble R, Cuttle L, Stockton K. Randomised controlled trial of three different burns dressings for partial thickness burns in children: study protocol (*Oral poster).* Presented: 38th Australian and New Zealand Burn Association Annual Scientific Meeting, Perth, October 2013.

Publications included in this thesis

Publication 1 – Incorporated as Chapter 2

Gee Kee, E., Kimble, R. M., Cuttle, L., & Stockton, K. (2013). Comparison of three different dressings for partial thickness burns in children: study protocol for a randomised controlled trial. *Trials, 14*, 403. doi: 10.1186/1745-6215-14-403

Contributor	**Statement of contribution**
Emma Gee Kee (Candidate)	Wrote the paper (100%)
Roy Kimble	Designed experiments (30%) Edited paper (15%)
Leila Cuttle	Designed experiments (30%) Edited the paper (35%)
Kellie Stockton	Designed experiments (40%) Edited the paper (50%)

Publication 2 – Incorporated as Chapter 3

Gee Kee, E. L., Kimble, R. M., Cuttle, L., Khan, A., & Stockton, K. A. (2015). Randomized controlled trial of three burns dressings for partial thickness burns in children. *Burns*. doi: 10.1016/j.burns.2014.11.005

Contributor	**Statement of contribution**
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	Statistical analysis of secondary outcomes measures (30%) Edited the paper (50%)

Publication 3 – Incorporated as Chapter 4

Gee Kee, E. L., Kimble, R. M., & Stockton, K. A. (2015). 3D photography is a reliable burn wound area assessment tool compared to digital planimetry in very young children. *Burns*. doi: 10.1016/j.burns.2015.01.020

Contributor	**Statement of contribution**
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Roy Kimble	Designed experiments (20%) Edited the paper (15%)
Kellie Stockton	Designed experiments (60%) Conducted data collection (10%) Conducted statistical analysis (20%) Edited the paper (85%)

Publication 4 – Incorporated as Chapter 5

Gee Kee EL, Stockton KA, Kimble RM, Cuttle L, McPhail S. Cost-effectiveness of three silver dressing combinations for paediatric partial thickness burns. *Submitted to Burns Journal (Date:08/02/2016)*

Contributor	**Statement of contribution**
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Kellie Stockton	Designed experiments (40%) Edited the paper (10%)
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Publication 5 – Incorporated as Chapter 6

Gee Kee EL, Kimble RM, Cuttle L, Stockton KA. Scar outcome of children with partial thickness burns: A 3 and 6 month follow-up. Burns. *Accepted for publication June 26 2015.*

Contributor	**Statement of contribution**
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Roy Kimble	Designed experiments (30%) Edited the paper (10%)
Leila Cuttle	Designed experiments (10%) Edited the paper (20%)
Kellie Stockton	Designed experiments (50%) Conducted data collection (10%) Conducted statistical analysis (20%) Edited the paper (70%)

Contributions by others to the thesis

Dr. Kellie Stockton: project design, assistance with data collection when candidate unavailable or occupied with other participants, assistance with statistical analyses and interpretation, critical revision of thesis (early and final versions)

Prof. Roy Kimble: project design, critical revision of thesis (final version)

Dr. Leila Cuttle: project design, assistance with interpretation of quantitative results, critical revision of thesis (early and final versions)

Dr. Megan Simons: qualitative project design, assistance with data analysis, interpretation and critical revision of qualitative chapter

Dr. Asad Khan: Conducted statistical analysis of primary outcomes measures in randomised controlled trial and assisted candidate to interpret data results

Dr. Steven McPhail: Took a major lead in assisting candidate with statistical analysis for economic evaluation and interpretation of data results, critical revision of cost-analysis chapter

Statement of parts of the thesis submitted to qualify for the award of another degree

None.

Acknowledgements

I feel so thankful to have been given the opportunity to undertake this PhD. I came into the burns world as a relative newcomer but with a passion to make a difference to lives of children who sustain burn injuries. Having spent over 3 years now with the amazing burns and trauma team from RCH/LCCH and CCBTR, it is hard to put into words how much I have learnt from each and every one of you.

To my three supervisors – Kellie, Leila and Roy thank you for putting your trust in me to complete this PhD and for providing invaluable knowledge, advice and support. I wouldn't have made it this far without any of you!

Kellie – your efficiency and multi-tasking skills are second to none! Thank you for educating me in all things clinical research, putting up with my barrage of silly questions, bringing out my inner-stats nerd and providing some humour in my day. You were never short of time to help me out with anything and for that I am very grateful.

Leila – I have learnt so much from you about the important role that lab research plays in understanding burn injuries. Your knowledge of burns is truly amazing and that has brought so much to this project and my own knowledge base. Thank you for your kind words of support when I was frazzled and for encouraging me to keep on going.

Roy – it has been a privilege to have the opportunity to work alongside you. Thank you for bestowing your immense clinical knowledge of burns on me. Your passion for burn care in children and clinical research has instilled in me a love for this field of work and has inspired me to continue to be a part of it. Thank you for being my advocate and for your ever-present enthusiasm.

Special mention to Meg Simons and Steven McPhail who so kindly lent their precious time and expertise to teach me about qualitative and economic research. I am extremely grateful for the time you took out of your busy schedules to assist and guide me through the process!

To the burns unit staff (nurses, doctors and allied health) – thank you for putting up with me holding up the walls in clinic and buzzing around like a bad smell. Your willingness to assist with this research and acceptance of the clinical changes that came with it has been very much appreciated. It has been a pleasure to have been part of such a cohesive and supportive multidisciplinary team.

To my CCBTR and QCMRI colleagues – it has been wonderful meeting so many passionate researchers. I have never been short of a laugh, practical joke, friend to chat about PhD woes with or a delicious morning tea! I have immensely enjoyed being a part of the institute.

To my family and friends, thank you for your support and encouragement throughout these last 3 years, I truly couldn't have done it without you all! Many thanks to Kelly and my mum Jenny for also providing their expert proof-reading skills. To my husband Dan, thank you for being my rock through this period of study – putting up with me doing constant and spontaneous recruitment runs into the hospital, having to deal with my fluctuating stress levels and being a general pillar of support. I'm sure you're glad I'm finally done!

Lastly, thank you to all the children and parents who took the time out of a chaotic point in their lives to take part in this research and tell me about their journey through burn care. Without you all, this research wouldn't have been possible.

Keywords

Paediatrics, burn, silver dressing, wound healing, scar, parent experience, cost-analysis

Australian and New Zealand Standard Research Classifications (ANZSRC)

ANZSRC code: 111403, Paediatrics, 50%

ANZSRC code: 119999, Medical and Health Sciences not elsewhere classified, 50%

Fields of Research (FoR) Classification

FoR code: 1114, Paediatrics and Reproductive Medicine, 50%

FoR code: 1199, Other Medical and Health Sciences, 50%

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Abbreviations

CEA	Cost-effectiveness analysis
CCBTR	Centre for Children's Burns and Trauma Research
CHRC	Children's Health Research Centre
CONSORT	Consolidated Standards of Reporting Trials
FPS-R	Faces Pain Scale-Revised
FLACC	Face, Legs, Activity, Cry, Consolability Scale
FT	Full Thickness
ICC	Intraclass correlation coefficient
ICER	Incremental cost-effectiveness ratio
IRR	Incidence rate ratio
IQR	Interquartile range
LCCH	Lady Cilento Children's Hospital
LDI	Laser doppler imaging
LOA	Level of agreement
NHMRC	National Health and Medical Research Council
PLCBC	Pegg Leditschke Children's Burn Centre
POSAS	Patient and Observer Scar Assessment Scale
PT	Partial thickness
QCMRI	Queensland Children's Medical Research Institute
RCH	Royal Children's Hospital
RCT	Randomised controlled trial
SD	Standard deviation
SPPBC	Stuart Pegg Paediatric Burns Centre
TBSA	Total body surface area
UQ	The University of Queensland
VAS-P	Visual analogue scale – pain

Chapter 1. Introduction

1.1 Background

Childhood injuries are commonplace around the world and for some; the injuries can be more serious and have a multi-faceted impact on the life of the child and their family. Burn injuries are one of the most painful and potentially devastating injury types that a child can experience. According to the World Health Organization [1], burn injuries are globally the fifth most frequent occurrence of non-fatal childhood injuries. Non-fatal burns are also one of the main contributors to hospitalization and disability worldwide with burns under 20% total body surface area (TBSA) in children aged 0-15 years occurring at a rate of 153 per 100,000 population [2].

Burn injuries fall into a spectrum of severity dependent on the level of damage sustained to the skin, ranging from superficial (epidermis only) to deep dermal partial thickness (damage to the epidermis as well as down to the superficial or deep dermis) and full thickness (destruction of all skin layers down to subcutaneous tissue) [3, 4]. Typically only partial and full thickness burns require hospital treatment (with full thickness burns almost always requiring surgical closure). With advances in treatments and reductions in mortality and morbidity, the majority of children with partial thickness burns can now be treated as outpatients.

A study of all burn injuries presenting to the Royal Children's Hospital, Brisbane in 2013 noted that 758 children were treated for a burn. Of the children treated as outpatients, 73.2% had a superficial partial thickness burn and of all presenting children, 97.3% had a burn less than 10% total body surface area [5]. Currently, the focus of research into pediatric burns lies overwhelmingly with large, deep burn injuries >10% total body surface area (TBSA) which generally result in long hospital stays and worse outcomes (functionally, cosmetically and psychosocially). However the fact remains that many children in high-income countries sustain small, but significant partial thickness burns ≤10% TBSA which can be treated in the outpatient setting [2, 6].

There are two main stages of pediatric partial thickness burn care; acute treatment to enable wound closure and longer term wound outcome/scar management. Throughout this continuum of care, the child and parent experience must be taken into account due to its potential impact on care and ultimately the outcome for the child and family. There are

substantial research gaps within each of these components, which need to be addressed in order to improve outcomes for children who sustain partial thickness burn injuries:

1.2 Treatment

Children with partial thickness burns ≤10% TBSA are primarily treated in the outpatient setting with dressing changes occurring up to twice weekly [6]. The choice of burn dressing in this setting is vital to ensure rapid wound re-epithelialization and thus reduce the risk of scarring caused by prolonged re-epithelialization times [7]. The current standard of care in Australasia is silver fabric (Acticoat™) or foam dressings (Mepilex Ag®)), with or without a silicone interface (Mepitel™) (for atraumatic dressing removal), to promote wound re-epithelialization [8, 9]. Hydrofibre and alginate dressings are very rarely used for paediatric patients in Australasia. Multiple research studies [10-15] have shown silver to be effective against a variety of gram positive and negative bacteria. While it is well known that silver can be cytotoxic to healthy keratinocytes, prevention of infection, in particular toxic shock syndrome, even in small burns, is prioritized over promoting wound re-epithelialization for paediatric patients in Australia and New Zealand. As such, it is the standard of care that all children in Australia and New Zealand receive silver dressings as their primary treatment.

A number of studies have been published comparing silver dressings to silver sulfadiazine cream. However silver sulfadiazine cream is a poor comparator as it is no longer used in pediatrics in Australia due to delays in wound re-epithelialization and painful dressing changes [9, 16]. There is a shortage of quantifiable evidence on which silver dressing is most effective, with very few direct comparisons of silver dressings in the literature [17].

In addition there is a need for cost-effective analysis of silver burns dressings. Burns dressings are expensive and with a large number of children treated for burns every year, this is a significant burden on the healthcare system [18]. A systematic review of burn care costs calculated the mean total cost as $3,883 per 1% TBSA burned for burns 0-10% TBSA in high income countries [18]. As a comparison to other morbidities, a study on burn care in Spain reported that the mean annual cost of burn care was $99,773 compared to $13,826 in the first year post-stroke for stroke survivors [19]. Economic evaluations for burn care are scarce, but greatly needed to ensure that new burns treatments that are implemented into the healthcare system are both effective and economical.

1.3 Outcome

Wound re-epithelialization time and risk of hypertrophic scarring from burn injuries are related, with the risk of scarring increasing with delays in re-epithelialization [7]. Partial

thickness burns have been shown in the literature to result in a better scar quality than full thickness burns [20]. However there remains a paucity of research on the longer-term skin appearance or presence of residual scarring in children who sustain partial thickness burns.

1.4 Experience

Finally, while physical/medical treatments and outcomes are often the main focus of burns treatment, the psychosocial impact of a burn injury on families is also significant, with parents often witnessing the accident, accompanying and supporting the child through painful procedures and usually caring for the burn at home [21]. Parents and caregivers have been demonstrated to use negative coping reactions such as blame when caring for a burn-injured child and experience feelings of guilt [22]. Accordingly, research has also shown that a child's psychosocial recovery can be impacted on by parents' responses to the burn event [23]. There is evidence that parent distress levels are not influenced by the size of the burn [24], however the research focus still lies primarily with children who sustain major burn injuries. As a result, the experiences of parents and caregivers of children with partial thickness burns in the outpatient setting are largely unexplored.

Therefore there is a need for a comprehensive overview of treatments and outcomes for partial thickness burns in children and the impact of such injuries on families in order to improve acute care and provide positive long-term results.

1.5 Thesis Aims

The aim of this research was to provide a holistic and comprehensive overview of pediatric partial thickness burn care. The thesis is split into two parts to address the processes involved with burn care and to explore the psychosocial impact of burn injury and care on parents. Part One examines the physical treatments and outcomes and Part Two investigates parent experiences.

1.5.1 Part One Aims

Part One aimed to conduct a clinical trial to determine the most effective silver dressing to use in terms of reduced time to wound re-epithelialization and pain during dressing changes, assess the scar outcome of study participants, complete an economic evaluation of the silver dressing and establish the reliability of 3D photography as a new wound measurement tool.

1.5.2 Part Two Aims

Part Two aimed to provide a qualitative exploration of the lived experiences of parents and caregivers with children who had sustained ≤10% TBSA partial thickness burns.

1.6 Thesis Overview:

This thesis is presented as eight chapters, with chapters 3-6 based on published and submitted manuscripts. Chapter Two is a literature review, exploring and discussing research available regarding pediatric partial thickness burn care. Part One of the thesis will encompass chapters 3-6: Chapter 3 is the methodology of the silver dressing clinical trial (including methodology for assessing scar outcome and cost-analysis), Chapter 4 will present the findings from the clinical trial, Chapter 5 is a reliability study of 3D photography for wound measurement mapping, Chapter 6 will provide an in-depth cost-effective analysis of the silver dressings used in the trial and Chapter 7 discusses the scar outcome of children recruited into the clinical trial and Part Two of the thesis is covered in Chapter 8 which provides an exploratory qualitative investigation into parent experiences in the outpatient setting. Lastly, the final chapter of the thesis, Chapter 9, will provide an in-depth discussion of clinical outcomes from the thesis, limitations and how these can be addressed and future directions from this research.

Chapter 2. Literature Review

2.1 Pediatric burns epidemiology

The burden of pediatric burn injuries worldwide is particularly high, with burn injuries less than 20% total body surface area (TBSA) in children aged 0-15 years, the fifth most common cause of non-fatal childhood injuries worldwide, occurring at a rate of 153 per 100,000 population of children [2]. According to the Australian Institute of Health and Welfare (AIHW) [25], children under the age of four years have the highest rates of hospital admission due to burns in Australia with 12,159 hospitalized (inpatients) with a burn or scald between 1999 and 2004. The majority of burns in this age group were scalds caused by hot beverages, food and cooking oil (50.7%). These burn injury rates have remained consistent across high-income countries in recent years, with American Burn Association data up to 2010 reporting that burns in children aged 1-4 years are the eighth most common cause of non-fatal injuries in the United States [26].

Australian pediatric burn centers report that the majority of children present with partial thickness burns <10% TBSA [5, 27]. As the mortality rates from burn injuries have decreased over time with better treatment options, burns of up to 10% TBSA in children can now be managed in the outpatient setting [6]. Data collected by the Burns Registry of Australia and New Zealand (BRANZ) from seven burns centers over a one year period (2010-2011), stated that the ratio of pediatric outpatient admissions to inpatients was 3.2:1 [28].

The cost of burn care is an undeniably expensive endeavor, with a recent systematic review calculating mean total burn care costs in high-income countries as approximately $3,883 per 1% TBSA burned in injuries 0-10% TBSA [18]. The AIHW [25] estimated the costs to the Australian healthcare system for burn injuries requiring hospitalization (inpatients) as between $37.8 and $40.2 million. The economic burden to the healthcare system of pediatric burn injuries treated as outpatients is likely significant, but difficult to quantify due to limited research and the over-representation of inpatient data such as in the Burns Registry of Australia and New Zealand (BRANZ) which only collects data for patients admitted for longer than 24 hours [28].

2.2 Burn injury classification

Burn injuries are classified according to the level of burn damage to the layers of the skin, with damage ranging from *superficial/erythema only* to *superficial partial* to *full thickness* [3, 4, 29]. (Figure 2-1)

Superficial burns include damage to the epidermis only and do not extend into the dermis. This depth of burn results in redness (erythema) of the affected area, but no blistering (e.g. sunburn) [3, 29].

Superficial partial thickness burns include damage to the epidermis and the papillary dermis resulting in blisters. The underlying skin is wet, pink, painful and, blanches on touch. Re-epithelialization is usually achieved within 10-14 days, with no scarring [3, 29].

Deep partial thickness burns extend through the papillary dermis to the reticular dermis and have a mottled appearance, with slow capillary refill on touch, and have less sensation than more superficial burns. They may take up to 3 weeks or more to re-epithelialize and may require surgical closure in the form of skin grafts. These burns will have variable amounts of scar tissue laid down depending on many factors including skin type, area of body and age [3, 29].

Full thickness burns damage the entire dermis, often continuing through into subcutaneous tissue. These burns are firm, leathery and white with reduced sensation and no blanching on touch, almost always require early excision and grafting to close the wound, and will invariably result in hypertrophic scarring [3, 29].

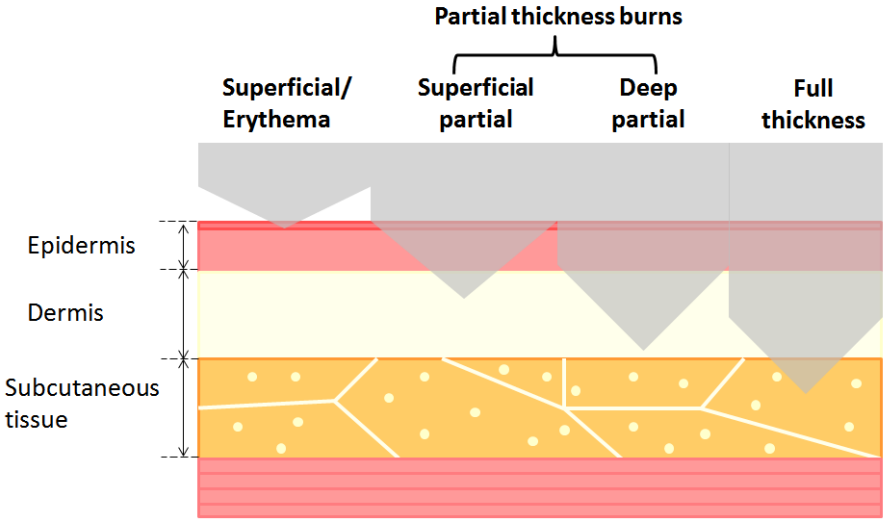

Figure 2-1 Burn depth classification

2.3 Assessing burn depth and healing potential

While clinical assessment of burn depth is most commonly conducted visually, objective measurement is required to provide an accurate measurement of burn depth for clinical and research use. The use of laser Doppler is currently the only objective measure of burn wound healing potential available and is becoming more widely used due to demonstrated inconsistencies between clinicians and inaccuracies when assessing the depth of a burn [30, 31]. The moorLDI2-BI laser Doppler imager (LDI) assesses the blood flow in burn wounds by conducting a 30-second scan which measures the movement of red blood cells within the skin [32] (Figure 2-2). The LDI then provides numerical measures of blood perfusion units, where a higher level of perfusion units indicates a burn with a greater healing potential (i.e. a more superficial burn).

Numerous studies have examined the validity and reliability of this machine in both pediatric and adult burns populations and found laser Doppler to be a reliable measure of burn depth [33-36]. A study by Holland et al [31] assessed 57 pediatric burn wounds and found that 90% of superficial partial thickness burns were correctly predicted by LDI compared to 66% by clinical assessment. However, more research is required to determine if LDI can also be used reliably in children under the age of three years due to challenges with compliance, as children have to remain motionless for 30 seconds with the burn wound exposed.

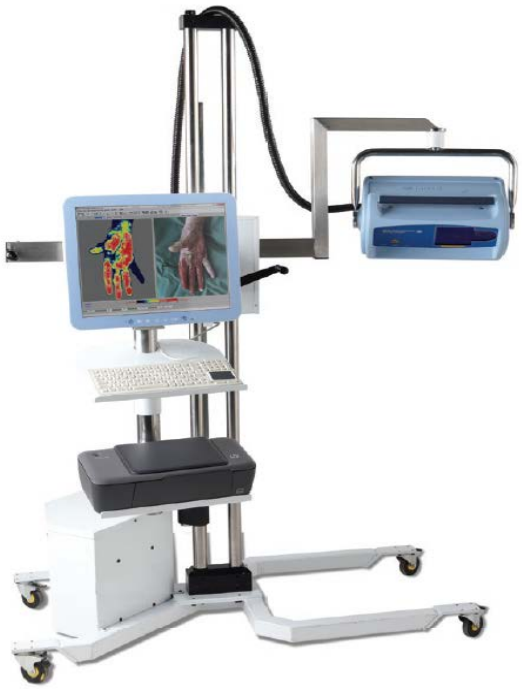

Figure 2-2 moorLDI2-BI laser Doppler imager

2.4 Measurement of progressive wound re-epithelialization

Burn wound re-epithelialization measurement is completed via a process called wound mapping. The wound border is traced and areas of re-epithelialization are measured and recorded as a percentage of the total wound area. This process can be completed serially (i.e. at each dressing change) until full re-epithelialization is recorded.

There is no gold standard for burn wound mapping. Most burn centres use digital planimetry (Visitrak™, Smith and Nephew), as it has been proven to be reliable in the mapping of chronic wounds [37, 38]. Digital planimetry involves placing a plastic grid over the affected area and tracing an outline of the wound and areas of re-epithelialization. The grid is then placed onto the Visitrak device and traced using a digital drawing system (Figure 2-3). Previous studies have found digital planimetry to have good intra- and inter-rater reliability for the measurement of wound surface area [39]; however, it is limited within the pediatric population due to the need for children to remain motionless while the tracing is completed. The plastic grid must also be in contact with the wound bed, which can cause anxiety and discomfort.

3D photography is a non-invasive alternative to digital planimetry (Figure 2-3). Whilst there is evidence on its use in chronic wounds [40], there is limited research on its potential as a burn wound mapping tool in pediatric populations [41]. 3D photography has the potential

advantage over digital planimetry due to its ease of use at the bedside, non-invasive point-and-shoot method, increased accuracy of measurement, and its ability to store wound progression photographs.

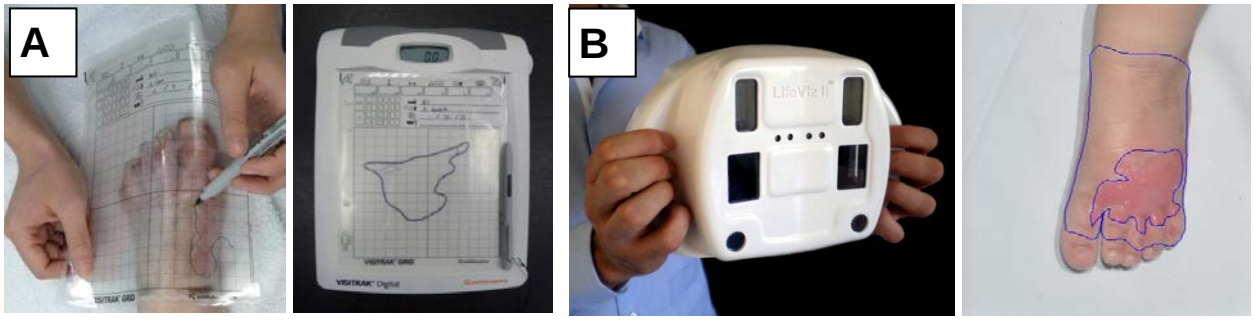

Figure 2-3 Visitrak device (A) and 3D photography example (B)

2.5 Outpatient management of pediatric partial thickness burns

There has been a shift from inpatient management of pediatric partial thickness burns with daily dressings with the majority now managed in the outpatient setting with specialized dressings than can be changed less frequently [6, 16, 42]. By treating these children as outpatients, they are able to return to their normal environment and routine thus reducing the burden on the healthcare system [16, 43, 44].

The main aim of acute pediatric burn care in the outpatient setting is to control infection and maintain an appropriate environment for the wound to re-epithelialize at a rapid rate, in order to minimize the risk and/or presence of scarring and minimize pain and distress where possible [6, 42]. Factors such as infection, wound dressing application, and removal and pain can all affect re-epithelialization rates of the wound and all must be considered during wound treatment decision-making [45, 46].

2.5.1 Pain associated with burn injuries in the pediatric population

While the presence of scarring presents a long-term psychosocial challenge for children with burn injuries, pain and distress during the acute phase of a burn injury can greatly impact upon the child [47, 48]. It has been well-documented that burn wound care procedures are highly traumatic experiences for children, as burn injuries can often be extremely painful due to exposed or damaged nerve endings [48, 49]. Pain and distress during dressing change procedures, particularly in pediatric patients, can affect the healing process of a burn [47, 50]. Stress can be defined as effects of the human body's inability to appropriately respond to threats from their environment (physical or emotional), which can be caused by pain and anxiety and may impact on the cascade of wound healing [51]. In the inflammatory stage of

wound re-epithelialization, stress can induce an increase in glucocorticoids and cortisol levels in the body [52]. These changes in the inflammatory phase can, as a result, delay processes in the proliferation phase of wound re-epithelialization where the recruitment and replication of cells required for tissue generation and capillary growth occurs. In turn, the entire re-epithelialization process can become delayed [45, 46, 52].

2.6 Silver dressings

Silver has been used for centuries in a range of formulations to treat burn injuries due to its antimicrobial properties. Silver sulfadiazine (SSD) was introduced in 1968 as a topical treatment in a cream preparation for all types of burns in pediatric and adult populations [9, 53]. Silvazine^{TM} (Smith and Nephew, Clayton, Australia), a preparation of 1% silver sulfadiazine and 0.2% chlorhexidine digluconate, was formulated for use in Australasia in 1971. Treatment involves daily reapplications after the removal of old cream and the wound is cleaned [9]. Various SSD cream products are used in many countries worldwide as the front-line treatment for burn injuries, given their low cost, availability and anti-microbial properties [10].

A recent systematic review and meta-analysis of non-silver treatments compared to silver sulfadiazine in the treatment of paediatric partial thickness burns [54] found shorter healing times for non-silver treatments and no significant difference in the incidence of wound infection compared to those treated with silver. The majority of studies however, had methodological shortcomings and a high risk of bias, rendering it difficult to accurately draw conclusions from these findings.

Given the potential risk of infection, even in small, clean partial thickness burns, Australasian paediatric burns centres have continued to use silver to treat burns. The paediatric burns centre where this trial was conducted has a 0% toxic shock syndrome (TSS) rate for all burns (outpatient and inpatient). This is in comparison to a survey of UK burns centres demonstrating that in burns centres where incidences of TSS were reported, 2.5% of children admitted showed symptoms of TSS [55]. Numerous research studies have demonstrated challenges with the use of SSD including: delays in burn re-epithelialization (due to cytotoxicity of SSD to keratinocytes); and painful and numerous, resource-intensive dressing changes [9, 16, 43]. Therefore the standard of care in burns dressings for small to medium partial thickness burns has changed in the last 10-15 years in an attempt to resolve these challenges. Currently, silver–impregnated fabric, foam, hydrofibre and alginate dressings are commonly used to manage the bio-burden of a wound in high-income countries. There are many of these dressings currently available on the market [9]. These

dressings are impregnated with different types of silver compounds, which are released in varying amounts from the dressing [10, 56]. A survey of paediatric burns centres in Australia and New Zealand conducted as part of this thesis found that the most commonly used silver dressings are Acticoat™ and Mepilex Ag™. The standard of care in Queensland for paediatric partial thickness burns is Acticoat™ with the addition of Mepitel™ (a silicone interface dressing) (Table 2-1). Due to a lack of rigorous research studies on effective silver dressings, hydrofibre and alginate silver dressings are rarely used in Australia and New Zealand.

Acticoat™ (a three-day dressing) and Acticoat7™ (a seven-day dressing) (Smith and Nephew, Hull, UK) are antimicrobial barrier dressings impregnated with nanocrystalline silver [13]. Acticoat™ consists of three layers: an absorbent middle core of rayon and polyester between two outer layers of nanocrystalline silver-coated, low-adherent polyethylene mesh. Acticoat7™ has one additional absorbent and one silver layer. Acticoat™ dressings are required to be moistened with sterile water to promote the release of silver onto the burn wound.

In comparison, Mepilex Ag™ (Mölnlycke Healthcare, Mikkeli, Finland) is an antimicrobial silver-sulphate-impregnated foam pad with a polyurethane backing film that incorporates Safetac™ silicone technology. Silver particles are released from Mepilex Ag™ when it is moistened from direct contact with wound exudate. Mepilex Ag™ is indicated to be changed every three to seven days.

2.6.1 Silicone interface dressings

Dressings that are adherent to the wound can cause trauma on removal and promote skin stripping which may increase pain and delay re-epithelialization [57]. The use of a low adherent interface such as silicone has advantages, particularly for pediatric patients [58-60]. The Safetac™ technology (Mölnlycke Healthcare) is a new development in dressings and is comprised of soft silicone. It is proposed to adhere to normal, intact skin remaining in situ on the surface of a wound but not adhere to the wound bed, maintaining a moist wound environment while providing a less traumatic and painful removal and subsequently less epidermal damage [8, 61]. This technology may be of great use in the pediatric burn population, where pain during dressing change procedures has been found to be detrimental to the child in terms wound of re-epithelialization [45-47, 62]. Acticoat™ silver dressing can be used in conjunction with non-stick interface dressings such as Mepitel™ (Mölnlycke Healthcare, Mikkeli, Finland) or on its own. Mepitel™ is a silicone-coated nylon grid product

that utilizes non-stick Safetac™ technology to reduce dressing adherence to the wound and subsequent damage to the wound on dressing removal [57].

The majority of evidence available regarding Safetac™ technology is in the form of observational and case studies, with small sample sizes and the presence of bias. A recent study has been conducted in pediatric patients with a variety of burn, traumatic and surgical wounds, investigating the effect of a Safetac™ foam dressing on pain during dressing application and removal and healing [60]. While this study noted that the Safetac technology dressing was associated with lower levels of pain in pediatric patients compared to hydrocolloid, film and foam dressings they were previously being treated with, it was an observational study, non-specific to burns and used a non-silver dressing. Although Safetac™ technology is relatively new and evidence is limited, it shows promise as a dressing property that could improve dressing change procedures in the pediatric population.

2.6.2 Antimicrobial properties of silver dressings

A number of studies have been conducted into the efficacy and antimicrobial properties of Acticoat™ for use in a burns population. Acticoat™ has been found in a number of *in vitro* trials to be effective against a broad spectrum of Gram positive and Gram negative bacteria [10-15]. Furthermore, Acticoat™ when used to treat patients with burn injuries was found to be significantly associated with a lower rate of adverse events (colonizations or infections) than those participants treated with the SSD or other non-silver dressings and applications [11, 12].

A small number of studies have reviewed the evidence regarding the antimicrobial properties of Mepilex Ag on a variety of wound types, including acute wounds such as burns and chronic wounds in adult patients [8, 63, 64]. While they have provided positive evidence regarding the effective antimicrobial action of the silver component in Mepilex Ag™ on a variety of bacteria compared to other fabric and foam silver dressings, these are only case and observational studies. Additionally the results reported in the paper by Chadwick *et.al* [8] may be subject to bias, as the study was funded by Mölnlycke Healthcare and conducted by its employees.

Despite the effective antimicrobial utility of silver products for managing the bio-burden of burn wounds, in-vitro studies have shown silver products to be cytotoxic to healthy keratinocytes in the wound bed which can delay re-epithelialization [14, 15, 65, 66]. SSD was found to be particularly cytotoxic to keratinocytes which result in delayed burn wound

re-epithelialization. Acticoat™ has also been found to be cytotoxic to keratinocytes, albeit not to the extent of SSD, with *in vitro* studies showing that SSD is significantly more cytotoxic than Acticoat™ [66]. A fine balance is needed between managing infections in burn wounds and promoting re-epithelialization of the wound. Although silver-impregnated dressings have been found to be cytotoxic, they remain effective in managing a broad spectrum of bacteria and the sequelae resulting from infection, such as Toxic Shock Syndrome which can be fatal in pediatric patients. For this reason, preventing infection is often prioritized over wound closure [67, 68].

2.6.3 Evidence for the use of silver dressings on acute, pediatric burns

A multi-national survey of burn specialists was conducted by Selig *et.al* [69] in 2012 regarding the ideal properties of a burns dressing. The survey found that 100% of specialists surveyed wanted pain-free dressing changes, 94.2% wanted a dressing that was easy to remove, 87.5% wanted a dressing with a lack of adhesion to the wound bed and 83.5% wanted an antimicrobial dressing. However, the survey also found that 92% of the specialists who responded felt that a dressing which meets all of these criteria did not yet exist on the market, despite the large range available.

The large range of dressings available has also impacted on dressing choices in pediatric burns centers in Australia and New Zealand. A survey completed in 2013 as part of this thesis found that Acticoat™ is used across the majority of centers and the use of Mepilex Ag™ is also quite common. However, across all seven centers, none used the same dressing protocol (Table 2-1). Decision-making regarding burns dressing choice is largely influenced by research studies; however, current evidence does not provide a clear-cut answer as to the most appropriate dressing for pediatric patients.

Table 2-1 Australian and New Zealand pediatric burn center dressing protocols for partial thickness burns

	Dressing choice	**Dressing change frequency**
Royal Children's Hospital, Brisbane	Acticoat™ 3 or 7 with a Mepitel™ interface	Every 3-7 days
Royal Hobart Hospital, Hobart	First 24-48hrs (if silver not required): Hydrofibre, alginate or foam dressings After 48hrs: Foam or hydrocolloid or silver dressings (Acticoat™ 3 or Allevyn Ag Gentle Border)	Wound review at 24-48hrs post-injury Then dressing change every 3-4 days
Princess Margaret Hospital, Perth	Inner face and peri-orbital: Emollient ointment and chlorsig ointment Non-circumferential burns: Acticoat™ with Intrasite Gel interface, DuoDERM® covering Circumferential: Acticoat™ with Intrasite Gel underneath	Face care: Every 4hrs Other burns: Dressing changes after 48hrs
Westmead Children's Hospital, Sydney	Superficial partial thickness: Mepilex™ or Mepilex Ag™ or Comfeel® Mid-dermal: Acticoat™ 7 or Mepilex Ag™ Deep dermal partial thickness: Acticoat™ 7 or Biobrane with Acticoat™ 7 covering	Acticoat™ every 7 days Mepilex Ag™ every 5 days Comfeel® every 3 days
Women's and Children's Hospital, Adelaide	Acticoat™ 3 or 7 or Mepilex Ag™ Intrasite interface under Acticoat™ if particularly dry	Dressings changed as often as clinically indicated
Royal Children's Hospital, Melbourne	Acticoat™ 3 or 7 (up to 3 weeks) Unhealed at 3 weeks change to Mepilex Ag™ or Xeroform	Acticoat™ every 3 or 7 days Mepilex Ag™ every 7 days Xeroform every 3 days
Middlemore Hospital, Auckland, New Zealand	<1% total body surface area: Acticoat™ 3 >1% total body surface area: Biobrane (applied under general anesthetic) Experimental with Mepilex Ag™	Wound reviewed at 48hrs Dressing change every 3 days

A Cochrane review by Wasiak *et.al* [17] reviewed all randomized controlled trials that investigated dressings used for the treatment of superficial and partial thickness burns. The authors included 26 of these studies for analysis in the review on the basis they reported outcome measures including time to wound re-epithelialization, number of dressing changes, dressing cost, pain associated with dressing removal and application, patient satisfaction with the dressing and incidence of infection. Wasiak *et.al* [17] noted that the majority of randomized controlled trials evaluating burns dressings had poor methodology reporting and poor measurement of outcomes; in particular, there was inconsistent and non-objective assessment of burn depth. Only three randomized controlled trials were found to investigate silver-impregnated dressings (Acticoat™ only) [70-72], and all three trials compared Acticoat™ with SSD, despite existing evidence reporting that SSD can delay wound re-epithelialization and is painful to remove and apply. Each of these articles reported that mean re-epithelialization times in the Acticoat™ groups were significantly shorter than SSD groups. Groups treated with Acticoat™ also reported lower levels of pain than SSD treated groups during dressing changes; however, these results were not statistically significant. A systematic review by Aziz, Abu and Chong [73] evaluating trials of silver-containing dressings and topical silver applications for burn injuries also noted that the majority of these trials did not differentiate between pediatric and adult populations and depths of burn injuries, which makes extrapolation to a pediatric population with predominantly partial thickness burn injuries difficult.

Since publication of the above Cochrane review, two studies have been published which compare silver dressings in partial thickness burn injuries [74, 75]. The first investigated the use of Acticoat™ versus the hydrofibre silver dressing Aquacel Ag® in a combined adult and pediatric population with partial thickness burns up to 40% TBSA [74]. The study found that the two dressings resulted in comparable re-epithelialization times, but that Aquacel Ag® was significantly more comfortable for patients and more cost-effective than Acticoat™. This study did not differentiate between adult and pediatric populations and included large TBSA burns which were treated in the inpatient setting. The second study was the only one to compare silver dressings in a purely pediatric population with partial thickness burns ≤ 10% TBSA [75]. The study compared Acticoat™ and Aquacel Ag® and similarly found no statistically significant differences in re-epithelialization between groups at day 10 post-burn, but that Aquacel Ag® required fewer dressing changes.

The evidence regarding the use of Mepilex Ag^{TM} on burn injuries in pediatric or adult populations is relatively limited given its recent development [76-78]. Two randomised, prospective studies investigating the use of Mepilex Ag^{TM} in a burn-specific population have been published [77, 78]. Both studies examined the use of Mepilex Ag^{TM} for combined adult and pediatric burns populations in comparison to the standard care of SSD in terms of pain on application and removal and efficacy with regards to re-epithelialization. Patients treated with Mepilex Ag^{TM} were found to have comparable re-epithelialization rates to those treated with SSD, however, patients treated with Mepilex Ag^{TM} reported lower levels of pain on application and while wearing the dressing compared to SSD. Treatment costs were also significantly lower using Mepilex Ag^{TM} [78] and both studies reported significantly less dressing changes were required for Mepilex Ag™ compared to SSD [77, 78]. These were comprehensive studies, however both were limited given their use of SSD as the comparator dressing and neither objectively measured burn depth. The combined adult and pediatric populations used for each study also makes it difficult to gauge the appropriateness of this dressing for the specific needs of a pediatric population.

The literature on the use of Acticoat™ and Mepilex Ag™ for burn injuries has indicated that there remains a lack of comprehensive research investigating the use of these dressings on partial thickness burns in the pediatric population. Therefore, there is a need to identify which of these dressings is the preferred choice for pediatric patients and which best meet the current challenges of burn wound management in this population.

2.7 Burn scarring and predicting outcome for pediatric partial thickness burns

2.7.1 Evidence around partial thickness burn outcomes

The prevention or management of scarring is of prime importance in the pediatric population, and there is evidence to support the association between burn re-epithelialization time and hypertrophic scarring [7, 79]. A study by Cubison and colleagues [7] on pediatric scald burns in Caucasian children (n=337), reported that for burns which re-epithelialized in 10-14 days, only 2% had a hypertrophic scar compared to 94% of children who had burns which took more than 3 weeks to re-epithelialize. While this research has contributed a significant amount of knowledge to scarring in children it is limited by its inclusion of only children with scald injuries (i.e. other burn mechanisms are excluded). The study was conducted retrospectively and only assessed the presence of hypertrophic scarring and did not comprehensively examine potential confounding variables such as burn characteristics or objectively assess skin pigmentation or skin thickness changes.

Anecdotally there is a wealth of clinical experience with long term burn scar outcome for children; however, there is a lack of long term clinical research on such outcomes, in particular for children who sustain partial thickness burns which re-epithelialize conservatively within 3 weeks. In the literature, deep partial thickness and full thickness burns in children which require skin grafting and/or scar management therapy are the primary focus of research as these burns often require management until a child reaches adulthood and beyond. Partial thickness burns (including superficial and deep partial) are largely under-researched despite this being the most common type of burn injury in children from high-income countries. An observational study by van der Wal [20] compared the outcomes of full thickness and partial thickness burns (in adults and children) and noted the scar maturation patterns were different with regards to the depth of burn, with those sustaining full thickness burns experiencing a worse result. While this has highlighted a difference between these burn types, there is still no comprehensive overview of longer term burn outcomes from partial thickness burns with regards to the resolution of original skin appearance, skin color and return to original color and skin thickness.

Clinical trials of burn dressings are also important in determining if acute dressings impact the scar outcome of the child. Knowledge of longer-term outcomes in addition to acute wound re-epithelialization can assist with treatment decision-making when choosing a dressing. A recent systematic review of the optimal treatment for partial thickness burns [80] noted that of all randomized controlled trials included in the review, only one included a longer term follow-up phase of patients [80]. The follow-up phase of this RCT, however,

only consisted of the review of a small number of children (exact number not stated) at 3 months post re-epithelialization [81]. Furthermore, external to the systematic review, Mabrouk et al. [82] compared Aquacel® Ag to the moist, open dressing MEBO and conducted three and six month follow-ups, however, age range was broad (children and adults), only partial thickness facial burns were included, and follow-up numbers were again not stated. The need remains for a high-level clinical trial comparing silver burns dressings which also includes a longer-term scar outcome follow-up of trial participants.

2.8 Burn scar assessment tools

2.8.1.1 Patient and Observer Scar Assessment Scale

There are a number of burn scar assessments utilized and the Patient and Observer Scar Assessment Scale (POSAS) and the Modified Vancouver Scar Scale (MVSS) are the most commonly used. The inter-rater reliability of the POSAS total scores has been established in burn scars of participants aged 15-73 years between four observers (ICC 0.92) and the inter-rater reliability on individual items of the POSAS is also reasonable [83, 84]. These reliability scores have also been confirmed via Rasch analysis [85] and high inter-reliability is reported to also encapsulate strong test re-test reliability [86], indicating it is appropriate for use longitudinally. [84] While the Modified Vancouver Scar Scale (MVSS) can be considered for use in children aged 2-17 years [87], POSAS has been shown to have a high quality reliability and superior overall performance compared to the MVSS [84]. Furthermore, POSAS is recommended for use when investigating patient opinions of scar in children, despite not being valid for children under 12 years, as the evidence for MVSS is even lower quality and a Rasch analysis has not yet been completed for this scale [87]. The POSAS was also the standard scar assessment scale used in the burns unit at the time of the trial conducted for this thesis and as the majority of children treated are under the age of 3, scar assessment is completed by parents.

The POSAS is a two-part assessment scale (observer scale and patient scale) utilized to assess burn scars [83] (see Appendix 1). Scars are assessed by the observer (occupational therapist or physiotherapist) using visual evaluation and palpation of the scar. The scales assess the scar on six items and an overall opinion score. All items are given a score out of 10, with a score of 10 equal to the ‘worst imaginable scar’:

Observer scale: Vascularity, pigmentation, thickness, pliability, relief and surface area

Patient scale: Itch, pain, thickness, color, stiffness, irregularity

2.8.1.2 Objective burn scar measures

Longitudinal burn scar quantification has made a gradual move from subjective to objective assessment in recent years as new technology has developed and improved. There is an increased interest in quantifiably measuring skin and scar characteristics and examining the changes to the skin as scar tissue matures over time. Two devices which have come to prominence are 3D photography and ultrasound.

2.8.1.3 3D photography

3D photography (or 3D stereophotogrammetry) has been shown to be reliable and valid in the mapping of chronic wounds and some pediatric burn wounds [40, 41].This device also has the ability to measure the height, surface area and volume of burn scars. Previous research has found that 3D stereophotogrammetry is a reliable and valid technique for the measurement scar surface area (ICC 0.99) and volume (ICC 0.99) in burn, keloid and linear scars in combined adult and pediatric populations [88, 89]. Given the non-invasive method of the camera and ease of operation, it is hypothesized that this technique may be suitable for burn scar assessment in the pediatric population where compliance during procedures is challenging.

2.8.1.4 Ultrasound

As clinical evaluation of burn scars is typically completed through visual assessment and palpation of the scar, objective measurement of scar thickness, scar progression over time and the level that scar tissue may extend internally is of interest. Data concerning skin thickness of children at varying ages and by anatomical area is extremely limited. One study of ultrasound measured skin thickness in children aged 2-13 years indicated that skin thickness in children is approximately 1.0-2.0mm which increases with age and can vary depending on the anatomical area of the body (e.g. soles of feet compared to the face) [90] - however, this data has yet to be confirmed via biopsy and/or histological examination.

There is limited research on the use of ultrasound to measure skin and scar thickness and little information regarding the most appropriate device for a pediatric population. Available research on the use of ultrasound for the evaluation of burn scars is primarily focused on the Dermascan C device (Cortex Technology, Denmark). This device is a high frequency 20 MHz echogenic ultrasound which uses a water-filled transducer to produce high resolution soft tissue images at a depth of 15mm [91, 92]. Dermascan C has been found to be a reliable in the measurement of burn scar thickness in adult burn scar populations [91, 92]. The device is, however, clinically reported to have a lengthy and complex set-up process (for

example, the precise application of film over the transducer head) and is cumbersome to transport and use, which may not be logistically appropriate for a pediatric population.

Only one paper has investigated ultrasound assessment of burn scars in children [93]. This study used the GE LOGIQ 500 (GE Healthcare) with a 5-10 MHz transducer head and found that ultrasound measurement of skin thickness correlated with clinical estimation; however, it did not determine if this device was a reliable and valid option for pediatric scar assessment. This study was conducted 15 years ago and new ultrasound devices have since become available that may be more suitable and can scan at a higher frequency.

An appropriate ultrasound device with a high clinical utility for use in pediatric burn scar populations has not yet been identified. The Venue 40 MSK ultrasound (GE Healthcare, Australia) (Figure 2-4) is one of many recently developed ultrasound devices for pediatric burn scar assessment which has simple set-up process, fast scan time and is low profile and easily transportable. This ultrasound device utilizes a higher frequency (compared to the GE LOGIQ 500) 8-18 MHz hockey stick probe and can provide soft tissue images to a penetration depth of 20mm below the surface of the skin. The clinical utility of this device has yet to be established, but will be initially assessed in this thesis.

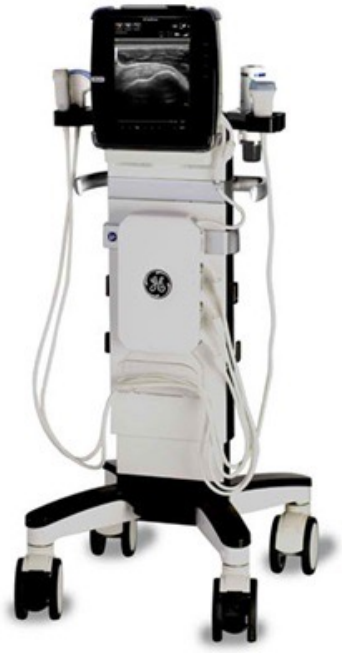

Figure 2-4 Venue 40 MSK Ultrasound (GE Healthcare**)**

2.8.2 Psychosocial impact of partial thickness burn scarring

In comparison to the high risk of hypertrophic scar development in children with severe burns requiring skin grafting, the long term outcome for pediatric partial thickness burns is less complex, with the majority of children discharged at the point of wound re-epithelialization, without requiring scar management therapy. Partial thickness burn sites are clinically reported to return to normal skin appearance and pigmentation within six months post-wound re-epithelialization, but there is very limited research-based evidence to support this.

Changes in skin pigmentation and appearance as a result of partial thickness burns are at the lower end of the spectrum in terms of clinical significance, as many of these changes are assumed to be temporary with resolution in 6-12 months. However, there is the capacity for such appearance changes to negatively impact on the psychosocial functioning of children and their families, particularly for children with darker skin types where pigmentation may take a longer amount of time to return. Studies in children and adolescents with 'visible' burn scars or skin pigmentation conditions such as vitiligo have shown that children and adolescents experience negative psychosocial sequelae such as depression, anxiety, low self-esteem and reductions in health-related quality of life [94-97].

2.9 Parent experience of pediatric outpatient burn care

The child-parent relationship is an important aspect of burn care with many burn patients under the age of five years reliant on parental support and care during treatment. Parents

often witness the burn accident and subsequently accompany the child through painful wound care procedures and assist with managing the burn wound at home, all of which can influence stress levels [21]. The relationship of parent distress and the impact on child distress is well-researched with numerous studies reporting that a child's distress can be influenced by parents' responses to the traumatic event [23, 98, 99]. Studies have found that parent behaviors related to situational distress and anticipation of child distress can influence the child's response and psychological recovery from a burn injury [23, 98, 99].

Parent experiences of pediatric burn care reported in the literature are largely confined to large, severe burns requiring lengthy inpatient hospitalization periods. Qualitative studies of parents found that many reported experiencing negative coping reactions such as guilt, blame and hopelessness during their child's hospitalization. In addition, watching their child in pain or enduring painful procedures was a major stressor [100-102]. While outpatient burn care is a different environment and a more short-lived experience for parents, it remains unexplored in the literature despite evidence that post-traumatic stress symptoms in parents may not be confined to burn injuries at the serious end of the spectrum [24].

2.10 Summary

This review has identified major gaps in the literature for pediatric partial thickness burn care in the outpatient setting; with respect to dressing choice, objective wound and scar assessment tools, partial thickness burn scar outcomes and parent experiences. The aim of this thesis is to therefore provide a holistic and comprehensive overview of pediatric partial thickness burn care to address these discrepancies in the literature.

Part One

Chapter 3. Quantitative Methodology

This chapter is based on a published paper in Trials journal.

Citation: Gee Kee E, Kimble RM, Cuttle L, Stockton K. Comparison of three different dressings for partial thickness burns in children: study protocol for a randomized controlled trial. Trials. 2013;14:403

3.1 Chapter foreword

The dressings applied to acute burn wound injuries in children are a major and vital component of burn care, given the propensity for functional and psychosocial implications associated with delayed wound re-epithelialization time and possible surgical intervention. Specialised burns dressings containing silver for partial thickness burns up to 10% TBSA in children are continually evolving and improving, thus, the requirement for high quality research also increases.

Despite the prevalence of partial thickness burns in children, well-conducted clinical trials of topical applications and dressings for these injuries are lacking [17]. While there is evidence available supporting the use of silver dressings for the management of burn injuries in adults and children, there are significant limitations in the methodologies of many of these studies. Previous systematic reviews have noted that many randomized controlled trials evaluating burns dressings available in the literature contained poor methodology reporting (e.g. trials insufficiently powered to find statistical significance in data, combined adult and pediatric populations, large TBSA ranges) and poor measurement of outcomes (e.g. no formal or objective assessment of burn depth) [17, 80].

As the literature review indicated, a rigorous clinical trial, which also included a follow-up scar assessment phase and economic evaluation, was needed to identify the most effective silver dressing to use for children. This chapter is based on the publication titled *'Comparison of three different dressings for partial thickness burns in children: study protocol for a randomized controlled trial'* and details the methodology for two of the quantitative sections in the thesis. This encompasses a randomized controlled trial of silver dressings in children with partial thickness burns, and a scar assessment of the same group of children. A brief overview of the economic evaluation is presented in this chapter, with a detailed methodology along with results and discussion to follow in Chapter 6. This methodology chapter was developed to address methodological and outcome measurement limitations identified in previous trials and provide a solid base for a clinical trial which would allow for translation of research findings to clinical practice.

3.2 Abstract

3.2.1 Background

In the pediatric population, pain and distress associated with burn injuries during wound care procedures remains a constant challenge. Although silver dressings are the gold standard

for burn care in Australasia, very few high level trials have been conducted which compare silver dressings to determine which will clinically provide the best level of care. Therefore, for pediatric patients in particular, identifying silver dressings that are associated with lower levels of pain and rapid wound re-epithelialization is imperative. This study will determine if there is a difference in time to re-epithelialization and pain and distress experienced during wound care procedures between Acticoat™, Acticoat™ combined with Mepitel™ and Mepilex Ag™ dressings for acute, pediatric partial thickness burns.

3.2.2 Methods/Design

Children aged 0 to 15 years with an acute partial thickness (superficial partial to deep partial thickness inclusive) burn injury and a burn total body surface area of ≤10% will be eligible for the trial. Patients will be randomized to one of the three dressing groups 1) Acticoat™ or 2) Acticoat™ combined with Mepitel™ or 3) Mepilex Ag™. A minimum of 28 participants will be recruited for each treatment group. Primary measures of pain, distress and healing will be repeated at each dressing change until complete wound re-epithelialization occurs or skin grafting is required. Additional data collected will include infection status at each dressing change, physical function, scar outcome and scar management requirements, cost effectiveness of each dressing, and staff perspectives of the dressings.

3.2.3 Discussion

The results of this study will determine the effects of three commonly used silver and silicone burns dressing combinations on the rate of wound re-epithelialization and pain experienced during dressing procedures in acute, pediatric partial thickness burns injuries.

3.3 Trial registration

Australian New Zealand Clinical Trials Registry ACTRN12613000105741.

3.4 Keywords

Child, burn injuries, partial thickness, silver dressings, healing, pain, distress, randomized clinical trial

3.5 Background

The ultimate goal of burn wound healing is to promote early closure, as this has considerable influence on the long term quality and appearance of a hypertrophic scar. It has been demonstrated that even scars considered small in size can contribute to negative psychosocial outcomes for children, hence the importance of effective wound healing techniques [103, 104]. The relationship between scar formation and time taken to re-epithelialize in children is well understood by burns clinicians. According to Cubison *et.al* [7], partial thickness burns that re-epithelialize within the optimal time period of 10-14 days generally do so without scarring, and those taking more than three weeks will invariably scar. Burns re-epithelializing between two and three weeks will have variable amounts of scar tissue laid down depending on many factors including skin type, anatomical location of the burn and age of child [7].

Children whose burn wounds re-epithelialize after the three weeks post-injury are at a high risk of residual or hypertrophic scarring [7]. Scar management therapy facilitated by occupational therapists to manage and prevent hypertrophic scarring currently involves of the use of various types of silicone contact media, pressure garments and splints. Engagement in scar management therapy typically occurs for 18 months or until scars reach maturity. While these scar management techniques are successful for some children in managing scars, there are inevitably children who require ongoing treatment of their scar tissue as they grow older. Scars generally do not grow with the child, and if situated around a joint, can lead to joint contracture and loss of function, resulting in ongoing scar reconstruction to keep up with the child's growing body [105]. Therefore, the initial care of the burn wound and choice of burn dressing is vital in creating the ideal healing environment to ensure rapid re-epithelialization of the wound and to avoid the possibility of hypertrophic scarring.

In the past 30-40 years, children with burns were treated with daily baths, dressing changes and antiseptic or topical silver sulfadiazine-based creams; however, even with appropriate pain relief these procedures were often very distressing and painful for children [106]. It has been well documented that burn wound care procedures are highly traumatic for children and the resultant stress has been shown to interrupt and delay the cascade of wound healing [47]. Decreasing the pain and distress experienced during a dressing change procedure can have positive implications psychosocially for the child as well as encouraging re-epithelialization of the wound within the optimal healing timeframe [50]. Therefore, in the pediatric population, careful attention also needs to be made concerning choosing a

dressing that can be applied and removed with minimal pain and stress to the child. A dressing which requires infrequent reapplication also has obvious benefits by decreasing the number of dressing change procedures the child has to undergo.

Small- to medium-sized partial thickness burns are mainly managed in the outpatient setting using specialized dressings which promote moist wound healing and prevent wound infection [73]. Unfortunately the antibacterial agents in burns dressings are also cytotoxic to keratinocytes: therefore, a fine balance is required between the prevention of a wound infection and the promotion of wound healing [11]. Despite the known cytotoxic effects of antibacterial dressings, they help prevent not only infections (which can delay the rate of re-epithelialization) but also the possibility of toxic shock syndrome (TSS), which is most likely to occur in the first three days post-burn injury and if left untreated can be fatal [65-67].

The standard of care in burns dressings for small to medium partial thickness burns has changed in the last 10-15 years. Currently silver–depositing fabric and foam dressings are the gold standard used to manage the bio-burden of a wound, with or without a silicone skin interface [9]. Acticoat™ (Smith & Nephew, Hull, UK) has been available since the 1990s and is the most widely used silver dressing in the developed world. It is required to be moistened with sterile water to promote the release of silver onto the burn wound and can be left on for 3-4 days. Acticoat™ may be used alone or in combination with a Mepitel™ dressing (Mölnlycke Healthcare, Mikkeli, Finland), which acts as a non-stick interface between Acticoat™ and the burn wound. Mepitel™ is a silicone-coated nylon grid product that utilizes non-stick Safetac™ technology to reduce the pain and trauma experienced by children during dressing changes and the amount of silver in direct contact with the wound. Mepilex Ag™ (Mölnlycke Healthcare, Mikkeli, Finland) has been available since 2007 and is a soft foam, silver-impregnated dressing that absorbs exudate and maintains a moist wound environment [63]. Silver particles are released from Mepilex Ag™ when it is moistened from direct contact with wound exudate. It also has a silicone Safetac™ interface layer incorporated within its design that in a similar way to the Mepitel™, serves to promote easy removal of the dressing and reduce pain and trauma during dressing changes [63].

Many trials have been conducted regarding the efficacy of silver dressings for treating burn injuries, using topical silver sulfadiazine applications as the control or comparator dressing. However, these silver sulfadiazine applications have been shown to delay re-epithelialization and are painful to apply and remove, indicating the possibility of bias in the results of these trials [17]. Additionally, despite the large number of silver-impregnated burns dressings that have become available on the market, very few high level trials have

been conducted which compare these dressings in pediatric or adult patients. For pediatric patients in particular, identifying silver dressings that are associated with lower levels of pain, require fewer reapplications and promote a fast rate of re-epithelialization is vital.

The aim of this study is to then determine whether one of three silver and silicone containing burns dressings—Acticoat™, Acticoat™ combined with Mepitel™ or Mepilex Ag™—will be more effective in terms of pain experienced and the rate of re-epithelialization of acute, partial thickness burns in children.

The following protocol for this study has been reported as per CONSORT guidelines [107].

3.6 Methods

3.6.1 Ethics Approval

This study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee.

3.6.2 Study Design

This study is a prospective, randomized controlled trial. Participants will be randomized to receive one of three commonly used dressings for burn wounds (1) Acticoat™ (2) Acticoat™ and Mepitel™ combined or (3) Mepilex Ag™, in order to determine the effects of the dressings on pain and the rate of re-epithelialization in acute, partial thickness burns in children. It is hypothesized that silver dressings with a silicone interface, compared to no silicone interface, will decrease the time to re-epithelialization of a burn injury and decrease the amount of pain and distress experienced during dressing changes within a pediatric population. The design of data collection is displayed in Figure 3-1.

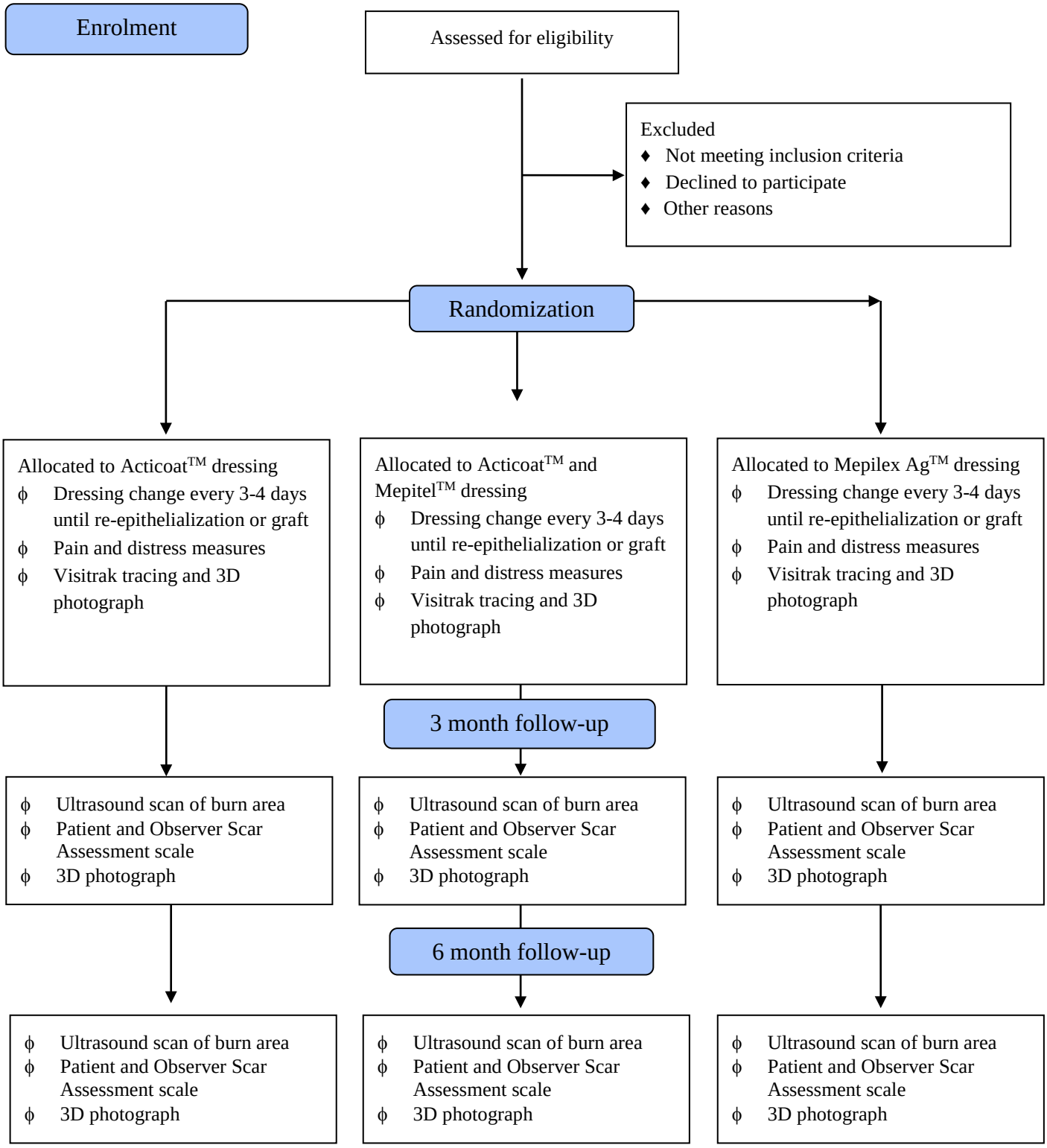

Figure 3-1 Data collection flowchart: The chronological timing and order of data collection within the burn wound care procedure framework

3.6.3 Study setting

Participants for this study will be recruited from the Royal Children's Hospital, Brisbane, Australia**.** Children presenting to the Department of Emergency (DEM) from March 2013 will be screened on presentation by a surgical registrar for eligibility to this study.

3.6.4 Participants

3.6.4.1 Inclusion criteria

Children who are aged 0 to 15 years with an acute partial thickness (superficial partial to deep dermal partial thickness inclusive) burn injury and a burn total body surface area of ≤ 10%, presenting at the DEM within the first 72 hours post-injury will be considered for inclusion in this study.

3.6.4.2 Exclusion criteria

Children will be excluded from this study if they present >72 hours post burn; have received silver dressings prior to presentation at the Royal Children's Hospital; have sustained a superficial (erythema only) or full thickness burn; have sustained a chemical or friction burn; present with cold, flu or viral symptoms (e.g. upper respiratory tract infection); have received inappropriate first aid (e.g. dirty water); have a known reaction to silver products; are non-English speaking; have a cognitive impairment; or are currently involved with Department of Communities (Child Safety).

Additionally, any children who have burn wounds requiring grafting, contract an infection or need to change dressing type during the course of their treatment will only have data collected up until that point in time (as per intention to treat protocol), as these changes in clinical care will void the intervention they have been randomized into for the study.

Apart from the dressings received, children participating in this study will receive the same standard medical care as those children not participating in the study.

3.6.5 Recruitment

A surgical registrar will be notified of a patient with a burn injury by DEM staff and will then determine patient's eligibility according to study criteria. The potential participants and their parents/caregivers will be notified of their eligibility to participate in this study by the registrar. Parents/caregivers will then be asked if a member of the research team can speak to them about the study. Informed caregiver consent and child assent (for children 6 years and above) will be gained by an investigator on the study after a discussion with the child and their caregiver regarding the information in the Patient Information Sheet. Once consent is gained, the investigator will randomize the patient to one of the three dressing treatment

arms. Randomization will be completed using a computerized random number generator and randomizations will be enclosed in sealed, opaque envelopes by an independent party. All dressings will be carried out by staff experienced in burns dressing application. Baseline measures (pain and behavioral scores from child, nurse and parent, pulse rate and respiratory rate) will be recorded by the primary investigator prior to and after the dressing is applied. The patient will then present at our burns center every 3-4 days for subsequent dressing changes. Any analgesia given to the patient will be recorded.

The first three days post-burn injury often have the highest risk of Toxic Shock Syndrome, which is potentially fatal if left untreated [67, 108].While the incidence rate of Toxic Shock Syndrome at our burns center is extremely low to non-existent, phone calls will be made to each participant by the primary investigator within this period. A set of standardized questions will be used to screen for any Toxic Shock Syndrome symptoms and to assess how the child and their parents or caregivers are managing the dressing and all responses will be recorded.

3.6.6 Intervention

The intervention will be one of either Acticoat™, Acticoat™ combined with Mepitel™ or Mepilex Ag™ dressing arms that the participant is randomized into on presentation. This dressing will then be used to treat the burn wound and will be replaced every 3-4days at each dressing change until re-epithelialization occurs or grafting is required. The dressings will be applied according to manufacturer's instructions.

3.6.7 Data collection

Demographic information and clinical details will be obtained from the caregiver and the patient's chart regarding: mechanism of the burn injury, the site of the injury, total body surface area of the burn and first aid the patient received. Children over the age of 4 years will be given the Ditto™ (virtual reality) device (Diversionary Therapy Technologies, Queensland, Australia) to engage in the "Bobby got a Burn" procedural preparation story at their first dressing change. These children may also engage in a choice of games or stories on the Ditto™ during all dressing changes. At the first dressing change only, each participant will have their burn/s scanned using the LDI2-BI (VR) Laser Doppler Imager (LDI) (Moor Instruments, Axminster, Devon, UK), which measures wound depths (in blood perfusion units) as a percentage of total wound area. The Laser Doppler Imager scan will provide an objective assessment of burn depth to enable a comparison of treatment group demographics [109]. Participants who have burn wounds on different body parts will have separate scans completed for each body part involved. If burn wounds are circumferential

or across curved areas, more than one scan will be taken at frontal, lateral and medial aspects to obtain an accurate scan. In addition, blinded photo reviews of burn depth will be undertaken by a panel of burns specialists (consultants and nursing staff).

At each dressing change appointment, pain, behavior and physiological measures (pulse rate and respiratory rate) will be taken before and after dressing removal and before and after the re-application of a new dressing. The time taken for the dressing removal, cleaning and re-application procedure, the number of nurses required to complete the entire procedure, quantity of dressings used and analgesia given to the participant will be recorded. A tracing of the wound using Visitrak™ grids (Smith & Nephew, Hull, UK) and a photograph using the 3D LifeViz Camera (Quantificare, Cedex, France) will be taken. Nursing staff treating the child will be surveyed on a 5-point Likert-scale regarding the ease of use of the dressing for that particular child. Parents or caregivers and children over the age of 8 years will be surveyed on a 5-point Likert-scale regarding their physical function while wearing the dressing.

All participants in the study will have their dressings changed every 3-4 days at our burns center as a standard measure. This protocol will be followed until full re-epithelialization of the wound occurs or grafting of the wound is required [110]. After full re-epithelialization occurs, participants will be followed-up at 3 months and then 6 months time to assess skin appearance and/or the presence of scarring.

3.6.8 Primary outcome measures

3.6.8.1 Days to re-epithelialization

The number of days from the burn injury date until wound re-epithelialization occurs, surface area of the wound, and percentage of wound re-epithelialization will be calculated by four methods: 1) clinical judgement from the consultant; 2) use of Visitrak™ grids; 3) 3D camera photographs and analysis on specialist computer software; and 4) blinded review of the 3D photographs by a panel of burns specialists (consultants and nursing staff).

3D photographs and Visitrak™ tracings will be taken of a participant's burn wound at every dressing change. A ruler will be included in all 3D photographs for measurement calibration in the associated software package Dermapix™ (Quantificare, Cedex, France). The 3D photographs will be analyzed by the primary investigator on the Dermapix™ software program to calculate burn wound surface area and area of re-epithelialization of the wound from each dressing change. The Visitrak™ will also be used to trace around total burn area

and re-epithelialized areas of the burn wounds at each dressing change, in order to calculate wound surface area and percentage of re-epithelialization.

A blinded review of the 3D photographs will be undertaken by a panel of burn wound specialists (consultants and nursing staff), who will assess the progress of re-epithelialization and appearance of each participant's burn wound after data collection has been completed.

3.6.8.2 Pain

Pain and distress will assessed by obtaining: 1) the participant's self-report of pain intensity using the Faces Pain Scale-Revised (FPS-R) (if participant is aged 3 years or over) [111]; 2) the parent's report of the participant's pain intensity using a Visual Analogue Scale-Pain (VAS-P) (alternatively, if participants are aged 8 years or over they will complete the VAS-P in lieu of the caregiver) [112]; 3) the nurse's observational rating of the participant's pain and distress using the Face, Legs, Activity, Cry, Consolability (FLACC) scale [113]; and 4) pulse and respiratory rates of the participant.. All four of these measures will be taken before and after dressing removal and before and after dressing application. Heart and respiratory rates will be recorded once at each time point to provide an objective measure of pain and distress in participants, as increases in these physiological measures have been shown to be indicative of pain and distress [47, 52]. Heart rate will be measured using a pulse oximeter and respiratory rate will be measured by visually counting the number of breaths taken per minute. Any analgesic and/or sedative medication administered to the participant at each dressing change will also be recorded.

Face scales are particularly useful for obtaining self-report pain scores from younger children as they have been reported to be easier to follow than other types of self-report scales and are well-validated measures [114]. The FPS-R is clinically valid for a pediatric population and was chosen over other faces pain scales due to its psychometrically sound characteristics, including the exclusion of smiling faces or tears, thus eliminating the possible confusion of pain intensity and affect by children [111]. The VAS-P is a valid and reliable self-report measure of acute pain in children over the age of 8 years [112]. The VAS-P is not valid for children under the age of 8, but is valid as a parent-report measure of pain; therefore, parents and caregivers of the children in this study will instead score their child's pain level [112]. The FLACC scale is a valid and reliable behavioral observer-report (nurse or health professional) measure of a child's pain. Self-reports of pain intensity can be difficult to ascertain and inaccurate when a child is receiving sedative and analgesic medications or

is too young to verbalize their pain level, therefore the use of the FLACC scale can be a suitable and accurate alternative [113].

3.6.9 Secondary outcome measures

3.6.9.1 Physical function

A self report of the participants' ease of movement while wearing the dressing will be obtained using a 5-point Likert-scale question from children over the age of 8 years or their caregiver at the first dressing change [78].

3.6.9.2 Grafting

A note will be recorded if a participant's wound requires grafting. Data collection will cease on that date for the participant as different dressings are used for wounds which are grafted, however, all data preceding that point will be included for analysis.

3.6.9.3 Infection

At each dressing change, the wound will be assessed clinically by the consultant. If the consultant deems an infection to be present, a swab will be taken from the wound for confirmation and identification.

3.6.9.4 Cost-effectiveness of dressings

At each dressing change, nursing time to apply the dressing, the amount and size of each dressing used and any other resources required will be recorded and a cost-analysis will then be calculated. Additionally, dressings required for scar management will also be recorded and analyzed.

3.6.9.5 Scar assessment

If further scar management treatment is required after full re-epithelialization of the burn injury occurs, a referral will be made by the treating consultant to the scar management clinic. At 3 months following full re-epithelialization of the burn injury, a face-to-face follow-up will be completed with all participants to conduct a skin and/or scar review in conjunction with Occupational Therapy. An ultrasound scan (BT12 Venue 40 MSK, GE Healthcare) [109] will be taken of the burn area to measure the height of the scar, and digital and 3D photographs will also be taken. The Patient and Observer Scar Assessment Scale will also be completed with the child (if over the age of 6 years) and/or caregiver. All scar management resources used with the participant will be recorded for cost-analysis. At 6 months post-full re-epithelialization, the same measures will be repeated.

3.6.9.6 Burns center staff perspectives on dressings

Nursing staff, consultants and occupational therapists from our burns center will be surveyed regarding their opinions of the three dressings prior to the commencement of data collection. The survey questions will be standardized and consist of Likert scales, tick boxes with a selection of responses and additional space for comments regarding the dressings. Nursing staff will be surveyed again using the same questions after data collection has ceased, to examine any changes in their perceptions of the dressings after using all three for an extended period of time.

3.6.10 Blinding

The dressing used for each participant cannot be completely masked, as the Acticoat™ dressing stains the healthy skin around a burn wound brown. The expert panel of burn wound specialists will be blinded where possible, however, the primary investigator and expert panel may still be able to deduce what dressing a participant received. The primary investigator will also be present when dressings are being applied and removed to obtain pain scores from the participant, caregiver and nursing staff, and will see which dressing is being used on the child. Wherever possible during data collation and analysis, treatment groups will be de-identified.

3.6.11 Discontinuation/adverse events

The infection of the burn wound is a potential adverse effect of any of the burns dressings. Infection rates at our burn center are extremely low, however, if any adverse effects such as infection occur, participants will only have data collected up until that point in time analyzed, as clinical care (including dressing type) may change to address the adverse event. Additionally, if a consultant feels that a particular dressing is not appropriate for a participant's care, they may change to a different dressing. If this occurs, data collection for the participant will cease from this date. All data preceding this date will be included for analysis.

3.6.12 Statistics

3.6.12.1 Sample size

The primary outcome measure will be days until wound re-epithelialization. Previous data in pediatric burns patients demonstrated re-epithelialization within 15 (SD = 4) days and a minimally clinically important difference is 3 days [47]. Thus sample size was calculated at 28 per group at 80% power with an α of 0.05. Allowing for 20% loss to follow up, a total of 100 participants will be required. The burn center treats 800 children per year with burns so recruitment for this study should be achievable within one year. This sample size will also

be adequate to find a significant difference in data collected from pain scores, powered on data from a previous study [47].

3.6.12.2 Data analysis

All statistical analyses will be conducted using SPSS 21 (IBM Corporation, Armonk, NY, USA). Generalized linear models, estimating variance appropriately for repeated measures, will be used to determine whether there are differences between the Acticoat™ group, the Acticoat™ combined with Mepitel™ group and the Mepilex Ag™ group in primary and secondary outcomes. Changes in the intervention effects will be examined with burn depth, burn total body surface area, mechanism of injury, anatomical location of burn, skin type, ease of dressing removal and application, and physical function considered a priori to be of potential interest. All data will be analyzed as intention to treat and on a per protocol basis, with the intention to treat analysis being the primary approach for this trial. Any missing data will be handled using the multiple imputation method. All tests will be two-tailed and only those with a p value <0.05 will be considered statistically significant.

3.6.13 Data storage

Data will be securely stored in a locked filing cabinet in a secure area of Queensland Children's Medical Research Institute, The University of Queensland. Data will be entered into an SPSS spreadsheet and any incomplete data will be coded as missing, unknown or not applicable. The full dataset will be cleaned and checked before being locked for analysis. On completion of the study, data will be kept for a period of 15 years in accordance with NHMRC guidelines.

3.7 Discussion

Pain and distress during dressing change procedures remains a major challenge when treating acute pediatric burn injuries and can have a negative effect on healing [47]. Although silver dressings are the gold standard for burn care in Australasia, very few high level trials have been completed comparing the clinical utilities of these dressings, particularly in relation to pain and rates of re-epithelialization in pediatric burns patients. Additionally, the majority of trials that are available on these dressings only show the benefits of using these silver dressings in comparison with silver sulfadiazine creams for burn injuries, and are not specific to pediatric or adult patients [9, 17, 108]. Therefore, for pediatric patients in particular, identifying silver dressings that are associated with lower levels of pain and rapid wound re-epithelialization is imperative not only for clinical care, but also to facilitate further evidence based practice in this field.

A clear link has been established between the rate of re-epithelialization of a burn wound and the risk of hypertrophic scarring. Partial thickness burn injuries that heal within 10-14 days are at a very low risk of developing hypertrophic scarring, whereas wounds that re-epithelialize within two to three weeks will inevitably produce some scar tissue, and those wounds taking more than three weeks to heal are likely to result in hypertrophic scarring [7]. Given this knowledge, if there is a silver dressing that is associated with a reduced time for a burn injury to re-epithelialize, there is a possibility that partial thickness burns can be healed within the optimal time period of 10-14 days which could subsequently reduce the risk of hypertrophic scarring and the need for reconstructive surgery in pediatric patients with this depth of burn.

The associated pain experienced during dressing removal and re-application by pediatric patients is a significant problem for health professionals. Previous studies have shown that an increase in pain, anxiety and distress during various types of wound care procedures can have a negative effect on the healing cascade [47, 50, 52]. This negative effect on the rate of re-epithelialization in pediatric patients with burn injuries may increase the likelihood of hypertrophic scarring as a result of the injuries not healing in the optimal time period. It is therefore imperative to identify a silver dressing that promotes a fast rate of re-epithelialization and that induces the least amount of pain and discomfort on removal and application for pediatric patients. Dressings that are comfortable, easy to move in, and which require infrequent changes are also beneficial for the pediatric population.

While every precaution possible will be taken for this study, there still may be some limitations involved with data collection. All children recruited into the study will have a Laser Doppler Imager scan taken of their burn wound [109]. Although the scan can be completed for children of any age, children are required to remain still for a period of time with their wound exposed to the air and free of dressings while the scan is being taken. Given that this study is recruiting all children under the age of 16 years, completing these scans may be difficult if not impossible in some circumstances due to the age of the child and associated pain from the exposed wound. Thus, to compensate for this limitation, a blinded photo review of burn depth by a panel of burns specialists will also be undertaken. Additionally, completing Visitrak^{TM} tracings on some children may be a challenge, as they are again required to remain still and may experience pain or discomfort when the Visitrak^{TM} grid is in direct contact with their wound.

3.8 Significance of study

In Australasia, the standard of care in burns dressings for small to medium partial thickness burns has changed over the past 10-15 years. Currently, silver containing dressings are used as the gold standard of burn care to prevent infection and promote healing. However despite the large number of silver burns dressings available on the market, very few high level trials have been conducted in pediatric or adult patients. This study aims to determine the effect of Acticoat™, Acticoat™ combined with Mepitel™ and Mepilex Ag™ burns dressings on the rate of re-epithelialization of partial thickness burn wounds and pain and distress levels during the treatment of these injuries in the pediatric population.

3.9 Trial status

This study commenced recruitment on March 18, 2013. Completion of participant recruitment is planned by December 2013 and data collection is likely to continue to June 2014 (with data collection continuing until six months post re-epithelialization of participant's burns).

3.10 Abbreviations

DEM: Department of Emergency; FLACC: Face, Legs, Activity, Cry, Consolability; FPS-R: Faces Pain Scale-Revised; RCH: Royal Children's Hospital; VAS-P: Visual Analogue Scale-Pain.

3.11 Competing Interests

This clinical trial was partially financially supported by a grant given to the Royal Children's Hospital, Brisbane, by Mölnlycke Healthcare. Despite this financial support, Mölnlycke Healthcare had no part in the study design and data collection of this project, nor will they have any involvement in the analysis or publication of results. The principal researcher has no financial interest in the Acticoat™, Mepitel™ or Mepilex Ag™ dressings or the Mölnlycke Healthcare company and is a student of the University of Queensland.

3.12 Authors' contributions

EGK, RMK, LC and KS all made substantial contributions to the design of this trial. EGK wrote the draft manuscript with substantial input from KS. All authors provided critical review of the article and approved the final manuscript.

3.13 Acknowledgements

The authors would like to thank all the children and families who participate in this study and acknowledge all the staff at the Stuart Pegg Pediatric Burns Center at the Royal Children's Hospital, Brisbane, Australia for their support and assistance throughout data collection.

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3.15 Chapter conclusion

This chapter has described the methodology for the randomized controlled trial and scar assessment follow-up phase in addition to a short summary of the economic evaluation.

In addition to these three sections, a reliability and clinical utility analysis of the 3D LifeViz™ system (3D camera) was also undertaken with wound surface area measurements taken during the randomized controlled trial using the 3D camera and Visitrak™ tools. Previous trials measuring wound surface area have used invasive measures such as the Visitrak™, which involves placing a plastic grid onto the wound to measure the area. However, the 3D camera is a new, non-invasive alternative to Visitrak™ and use of this tool clinically in the acute, pediatric population would be of great benefit. A detailed methodology and presentation of results on this additional section will be provided separately in Chapter 5.

As this methodology was published as a trial protocol, publications included in this thesis will follow the exact scheme of data collection and data analysis as detailed in this chapter for accuracy and consistency. The following chapters will be separated out into the randomized controlled trial, 3D camera and Visitrak™ reliability, scar assessment and economic evaluation respectively. Each chapter will include further elucidation of methodological details where required and detailed results and discussion sections.

Chapter 4. Randomized controlled trial of silver dressings for pediatric partial thickness burns

This chapter is based on a published paper in Burns journal.

Citation: Gee Kee, E. L., Kimble, R. M., Cuttle, L., Khan, A., & Stockton, K. A. (2015). Randomized controlled trial of three burns dressings for partial thickness burns in children. Burns, 41(5), 946-955. doi: 10.1016/j.burns.2014.11.005

4.1 Chapter foreword

A survey of burns surgeons worldwide reported that the essential or desirable features of an 'ideal' burns dressing were; lack of adhesion to the wound bed, pain-free dressing changes, ease of dressing removal, antimicrobial activity of the dressing and twice weekly dressing changes [69]. However, importantly it was noted that a burns dressing which possesses all of these properties has not yet been developed. Therefore treatment choice is reliant on research evidence to discern which dressing/s from those available on the current market best meet ideal dressing characteristics.

Silver dressings are currently the most common dressing used for pediatric partial thickness burns in Australia and New Zealand. The ideal or most effective silver dressing to use for this population though is a point of contention, as high-level research is not currently available for clinicians to assist in treatment decision-making. A survey of pediatric burns units in Australia and New Zealand (Table 2-1) concluded that no two units have the same silver dressing treatment protocol. Many units use Acticoat™ as their primary dressing of choice, based on research purporting its effectiveness over silver sulfadiazine cream. However treatment regimes in some of these centers, for example in Brisbane, have evolved through clinical trial and error, with the use of silicone interface dressings such as Mepitel™ under Acticoat™ to assist with removal. Other burns units use Mepilex Ag™, which combines the benefits of both Acticoat™ and Mepitel™ in a single dressing.

Hence the aim of the clinical trial presented in this chapter was to provide a solid evidence base for clinical treatment decision-making regarding the use of silver dressings and to improve clinical outcomes for children with partial thickness burns. This chapter is based on the publication titled '*Randomized controlled trial of three burns dressings for partial thickness burns in children'* and follows on from the study protocol presented in Chapter 2. Results from the trial will be presented along with a detailed discussion of the trial outcomes and implications for clinical practice.

4.2 Abstract

4.2.1 Background

This study compared the effects of three silver dressing combinations on small to medium size acute partial thickness burns in children, focusing on re-epithelialization time, pain and distress during dressing changes.

4.2.2 Method

Children (0-15 years) with clean, ≤10% Total Body Surface Area (TBSA) partial thickness burn injuries who met the inclusion criteria were included in the study. Children received either 1) Acticoat™; 2) Acticoat™ with Mepitel™; or 3) Mepilex Ag™ dressings. Measures of burn re-epithelialization, pain, and distress were recorded at dressing changes every 3-5 days until full re-epithelialization occurred.

4.2.3 Results

One hundred and three children were recruited with 96 children included for analysis. No infections were detected for the course of the study. When adjusted for burn depth, Acticoat™ significantly increased the expected days to full re-epithelialization by 40% (IRR = 1.40; 95% CI: 1.14-1.73, $p < 0.01$) and Acticoat™ with Mepitel™ significantly increased the expected days to full re-epithelialization by 33% (IRR = 1.33; 95% CI 1.08-1.63, $p < 0.01$) when compared to Mepilex Ag™. Expected FLACC scores in the Mepilex Ag™ group were 32% lower at dressing removal ($p = 0.01$) and 37% lower at new dressing application ($p = 0.04$); and scores in the Acticoat™ with Mepitel™ group were 23% lower at dressing removal ($p = 0.04$) and 40% lower at new dressing application ($p < 0.01$), in comparison to the Acticoat™ group. Expected Visual Analogue Scale-Pain (VAS-P) scores were 25% lower in the Mepilex Ag™ group at dressing removal ($p = 0.04$) and 34% lower in the Acticoat™ with Mepitel™ group ($p = 0.02$) at new dressing application in comparison to the Acticoat™ group. There was no significant difference between the Mepilex Ag™ and the Acticoat™ with Mepitel™ groups at all timepoints and with any pain measure.

4.3 Conclusion

Mepilex Ag™ is an effective silver dressing, in terms of accelerated wound re-epithelialization time (compared to Acticoat™ and Acticoat™ with Mepitel™) and decreased pain during dressing changes (compared to Acticoat™), for clean, <10% TBSA partial thickness burn injuries in children.

4.4 Keywords

Child, burn injury, partial thickness, silver dressing, re-epithelialization, pain

4.5 Introduction

Small to medium sized partial thickness burn injuries are a common occurrence for children in high income countries [42]. Scarring remains the biggest problem for pediatric burn centers, contributing to negative physical and psychosocial outcomes for children [94]. Therefore the initial care of the burn wound and choice of burn dressing is vital in creating the ideal healing environment to ensure rapid re-epithelialization of the wound and to reduce the possibility of hypertrophic scarring. Currently, ≤ 10% TBSA partial thickness burns in children are predominantly managed in the outpatient setting using specialized dressings which promote moist wound healing and prevent wound infection [73]. The standard of care for burns of this size in children has changed in the last 10-15 years. Currently silver–depositing fabric and foam dressings are the most commonly used treatment to manage the bio-burden of a wound, with or without a silicone skin interface [9].

Many trials have been conducted regarding the efficacy of silver dressings for treating burn injuries, using topical silver sulfadiazine applications as the control or comparator dressing. However, the use of silver sulfadiazine as the comparator treatment needs to be reconsidered, as silver fabric dressings have been shown to promote faster wound re-epithelialization rates, are associated with lower levels of pain during burn care procedures and do not require daily changes [9, 17, 115]. Despite the large number of silver-impregnated burns dressings now on the market, very few high level trials have been conducted which compare these dressings in pediatric or adult patients [17]. To date, only one randomized controlled trial has been conducted comparing the use of silver dressings, in a combined adult and pediatric population [74]; however none have been conducted specifically in a pediatric population. Therefore there is a need to identify the silver dressing/s which best meet the current challenges of burn wound management in the pediatric burns population.

The aim of this study was to determine whether one of three silver dressings - Acticoat™, Acticoat™ combined with Mepitel™ or Mepilex Ag™ - would be more effective in terms of reduced pain during change of dressings and the re-epithelialization rate of acute, partial thickness burns in children. Acticoat™, Mepitel™ and Mepilex Ag™ were selected for the trial as all are commonly used within pediatric burn centers in Australia and New Zealand. It was hypothesized that silver dressings with a silicone interface, compared to no silicone interface, would hasten the re-epithelialization of a burn injury and decrease the amount of pain and distress experienced during dressing changes within a pediatric population.

4.6 Methods/Design

This study was a prospective, randomized controlled trial. This study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and was approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee. A protocol paper has been published for this trial; please refer to the article for a more detailed summary of the methods [116]. This trial was completed as per the published protocol.

4.6.1 Intervention

The intervention was randomized to be one of either: Acticoat™; Acticoat™ combined with Mepitel™; or Mepilex Ag™ dressings (See Figure 4-1). Each dressing was replaced every 3-5 days until re-epithelialization occurred or grafting was required.

Acticoat™ was moistened with sterile water and applied over the entire wound, with a nasogastric tube placed on top of the dressing, (with the capped end of the tube left unsecured outside the border of the dressing) before the entire dressing was secured with self-adhesive tape. A dry absorbent pad dressing was then applied over the Acticoat dressing and secured with tape. For the Acticoat™ with Mepitel™ intervention, Mepitel™ was cut to the identical size of the Acticoat™ and was placed onto the wound first, after which Acticoat™ was applied as per the previous protocol. Nasogastric tubes were used to assist in the moistening of the dressing between changes. Depending on the size of the wound, tubes were placed approximately 10cm apart over the Acticoat™, and 1-2ml of sterile water was then inserted via plastic syringe through the tubes 3 times a day by parents at home until the next dressing change. Mepilex Ag™ was applied to the wound and secured with self adhesive tape as per manufacturer instructions.

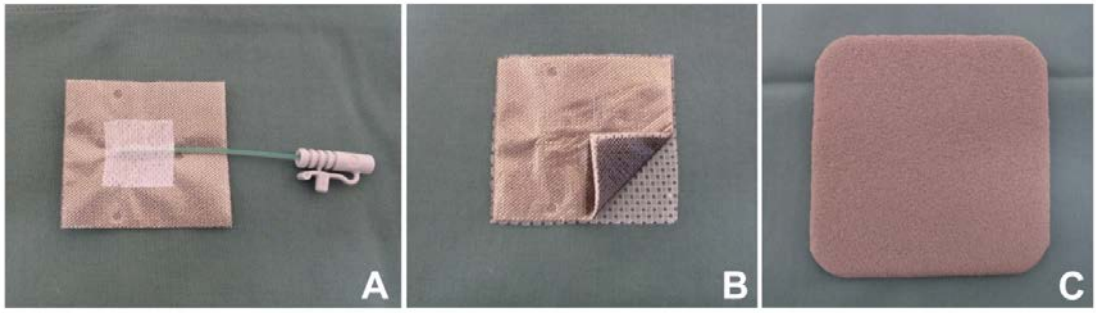

Figure 4-1. Acticoat™ dressing with nasogastric tube attached (A); Mepitel™ dressing in situ beneath Acticoat™ (B); Mepilex Ag™ dressing (C)

4.6.2 Participants

Eligible patients were recruited from the Department of Emergency Medicine and the Stuart Pegg Pediatric Burns Centre (SPPBC) at the Royal Children's Hospital (RCH), Brisbane, Australia between March 2013 and January 2014. Once informed consent was gained, the patient was randomized to one of three dressing treatment arms.

Children aged 0 to 15 years with an acute partial thickness (superficial partial to deep partial thickness inclusive) burn injury and a burn total body surface area (TBSA) of ≤10% who presented within the first 72 hours post-burn injury were considered for inclusion in this study. Children were excluded from the study if they had received silver dressings prior to presentation at RCH; had sustained a superficial (erythema only), full thickness, chemical or friction burn; presented with cold, flu or viral symptoms (e.g. upper respiratory tract infection); had received potentially unclean water as first aid (e.g. non-treated dam or tank water); had a known reaction to silver products; were non-English speaking; had a cognitive impairment; or were currently involved with the Department of Communities, Child Safety and Disability Services.

4.6.3 Primary outcome measures

4.6.3.1 Days to re-epithelialization

The number of days from the burn injury date until wound re-epithelialization, surface area of the wound and percentage of wound re-epithelialization were calculated via four methods: 1) clinical judgment from the consultant; 2) use of Visitrak™ grids (Smith & Nephew, Hull, UK); 3) 3D camera photographs (3D LifeViz system) and analysis on the Dermapix™ software program (Quantificare, Cedex, France). Visitrak™ and the 3D camera are both reliable and valid methods of calculating wound surface area [41]. 4) Blinded review of photographs by a panel of 3 burns surgeons. The surgeons were asked to rate the percentage of wound re-epithelialization at each dressing change. Burn wounds were considered fully re-epithelialized when rated as 95% re-epithelialized or more. The inter-rater reliability was also calculated.

4.6.3.2 Pain

Pain and distress were assessed by obtaining: 1) the participant's self-report of pain intensity using the Faces Pain Scale-Revised (FPS-R) (if participant was aged 3 years or over) [111]; 2) the nurse's observational rating of the participant's pain and distress using the Face, Legs, Activity, Cry, Consolability (FLACC) scale [113]; 3) the participant's self report (if aged over 8 years) or the parent's report of the participant's pain intensity using a Visual Analogue Scale-Pain (VAS-P) [112]; 4) pulse rate; and 5) respiratory rate of the participant, taken

immediately prior to and after dressing changes. Any analgesic and/or sedative medications administered to the participant at each dressing change were also recorded.

4.6.4 Secondary outcome measures

Nursing staff were surveyed on their views of the three dressings using a set of standardized questions and Likert scales. Surveys were completed pre and post data collection. Participants' physical function while wearing the dressing (first dressing change) was obtained on a 5-point Likert scale (1= extremely easy to move; 5= not at all easy to move). The ease of removing and applying the dressing was obtained from the treating nurse on a 5-point Likert scale (1= extremely easy to remove/apply; 5= not at all easy to remove/apply) at each dressing change. At each dressing change, wounds were assessed clinically by the consultant. Nursing time to remove and apply the dressing, amount and size of dressings used and other resources required were also recorded at each dressing change. This data will be utilized in a future paper of dressing cost-analysis.

4.6.5 Procedures

All participants in the study had their dressings changed every 3-5 days until full re-epithelialization of the wound occurred or grafting of the wound was required [116].

Demographic information and clinical details were obtained from the caregiver and the patient's chart regarding: mechanism of the burn injury, the site of the injury, TBSA and first aid the patient received. Burn injuries with a TBSA of <1% are difficult to quantify as a percentage clinically, therefore as a standard rating, all burns <1% were recorded as 0.5% TBSA for this study. Burn depth was categorized by laser Doppler Imager (LDI) scan, treating consultant review at the first dressing change (day 3-5) as either 'superficial partial thickness only', 'mixed depth', or 'deep dermal partial thickness only' and blinded photo reviews of burn depth were also performed. Whilst LDI is the gold standard for burn depth analysis, it is technically difficult in the pediatric population and was not possible to complete in all participants, thus burn depth ratings were clinically judged by the treating consultant. At each dressing change appointment, pain and distress measures were taken before and after dressing removal and before and after the re-application of a new dressing. A tracing of the wound using Visitrak^{TM} grids and a 3D photograph were also taken.

The investigators in this trial could not be completely blinded to the dressing used for each participant as the Acticoat^{TM} dressing stains the healthy skin around a burn wound brown. Additionally, the primary investigator was present when dressings were applied and

removed to obtain pain scores and therefore saw what dressing was used on the child; however data was coded for analysis.

4.6.6 Discontinuation/adverse events

If an adverse event (e.g. infection, reaction to the dressing) occurred during the trial, participants only had data collected up until that point in time analyzed, as clinical care (including dressing type) was changed to address the adverse event. If a consultant felt that a particular dressing was not appropriate for a participant's care, they were able to change to a different dressing. If this occurred, data collection for this participant was ceased from that date. All data preceding that date was included for analysis as per intention to treat protocol.

4.6.7 Statistical Analysis

All statistical analyses were conducted using SPSS 21 (IBM Corporation, Armonk, NY, USA) and Stata 12 (StataCorp LP, College Station, TX, USA). All data was analyzed as intention to treat and on a per protocol basis, with the intention to treat analysis being the primary approach for this trial. All tests were two-tailed and only those with a p-value <0.05 were considered statistically significant. Inter-rater reliability of burn depth and burn re-epithelialization ratings between burn surgeons was calculated using intra class correlation coefficients (ICC 2,1).

4.6.7.1 Sample size

Previous data in pediatric burns patients demonstrated re-epithelialization within 15 (SD = 4) days and a minimally clinically important difference is 3 days [47]. Thus sample size for this trial was calculated at 28 per group at 80% power with an α of 0.05. Allowing for 20% loss to follow up, a total of 100 participants were required. This calculated sample size was also determined to be adequate to find a significant difference in data collected from pain scores.

4.6.8 Primary outcome measures

Days to burn re-epithelialization data was analyzed using a negative binomial regression model, with burn depth, burn total body surface area, mechanism of injury, anatomical location of burn, age and gender considered a priori to be of potential interest. Pain data was analyzed with multilevel generalized linear mixed-effects modeling with a log link function and gamma distribution to determine differences between the treatment groups at timepoints and over time.

4.6.9 Secondary outcome measures

Dressing application and removal time, dressing ease of use and physical function rating data were not normally distributed or were Likert-scale ratings, therefore a non-parametric Kruskal-Wallis test was used to analyze the data from the three groups. If a significant difference between the groups was found, post-hoc analyses were then conducted using the Mann-Whitney U tests to determine which groups were significantly different from each other.

4.7 Results

4.7.1 Sample and demographic characteristics

The CONSORT diagram [107] illustrates that a total of 285 children were assessed for eligibility into this trial (See Figure 4-2). One hundred and three children were randomized into the study and as per intention to treat protocol, 96 children were included for analysis. Groups were similar with respect to baseline variables (age, gender, clinically rated burn depth, mean and minimum wound perfusion units, TBSA, mechanism of burn injury, anatomical location of the burn injury) (Table 4-1). Participants in all three groups had their dressings changed every 3-5 days until re-epithelialization or grafting occurred. At the first dressing change, the median number of days between date of injury and first dressing change was 3 days (IQR 3-4 days) and there was no statistically significant difference between the groups (p = 0.79).

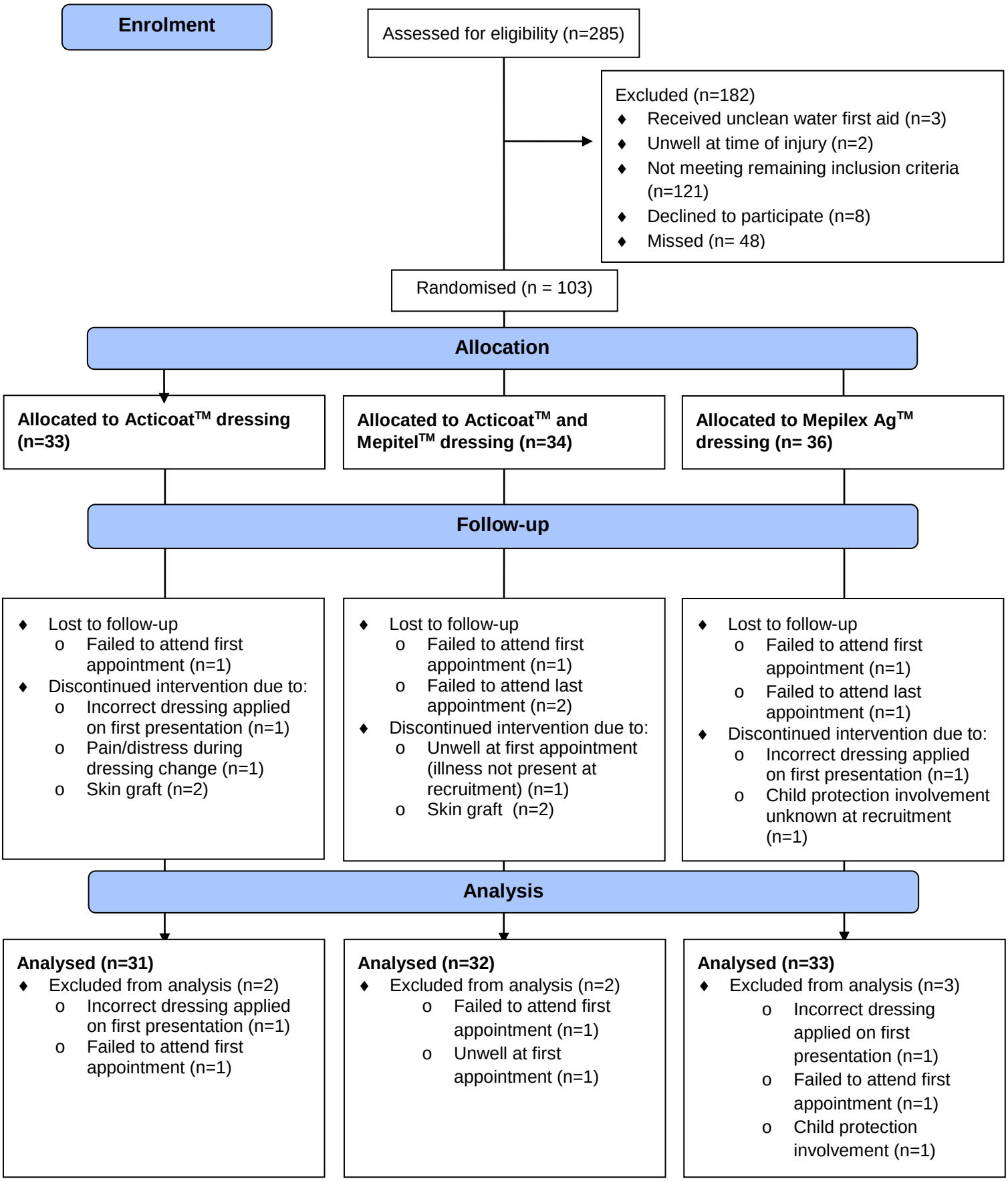

Figure 4-2 CONSORT diagram of study participant

4.7.2 Burn depth classification

LDI scans were successfully completed in 35 out of the 96 participants, with an even number of participants in each group (See Table 4-1). Both the minimum value of perfusion units (deepest part of the burn) and the mean value were recorded for each scan. The majority of scans were abandoned due to high participant pain and distress levels or excessive movement. A number of scans were completed on participants, but were affected by artefacts (blurring of the image) due to movement during the scan, to be utilized for measurements. Of the 61 participants who did not have a successful scan, 75.4% of these were ≤ 2 years of age. Blinded photo review burn depth ratings by three consultants were analyzed using intraclass correlation coefficients (two-way random effects model for absolute agreement). The level of agreement on burn depth between burn consultants was low (ICC 0.34, 95% CI 0.212, 0.47).

Due to a lack of reliable LDI scans and the low agreement for burn depth consensus, clinical judgment of burn depth by the treating consultant only at day 3-5 post-burn was used. Clinical judgment of burn depth encompasses the evaluation of patient health, mechanism of injury and first aid received in addition to reviewing the appearance of the wound, therefore it was deemed appropriate to use this classification of burn depth for statistical analyses. The burn depth ratings from clinical judgment for each group were: Acticoat™ ('superficial partial thickness only' n= 24; 'mixed depth' = 7), Acticoat™ with Mepitel™ ('superficial partial thickness only' n= 23; 'mixed depth = 9) and Mepilex Ag™ ('superficial partial thickness only' n= 30; 'mixed depth' n =3). The baseline differences in burn depth between the groups was not statistically significant (p = 0.33).

Table 4-1 Study demographics

		Acticoat™ (n=31) Median (IQR)	Acticoat™ & Mepitel™ (n=32) Median (IQR)	Mepilex Ag™ (n=33) Median (IQR)	*p*-value
Age (years)		1.0 year (1.0-5.0 years)	1.0 year (1.0-4.0 years)	1.0 year (1.0-4.0 years)	0.59
TBSA		1.0% (0.50-3.0%)	1.0% (0.50-3.0%)	0.50% (0.50-2.0%)	0.33
		n (%)	*n* (%)	*n* (%)	
Gender	**Male**	18 (58.1)	21(65.6)	16 (48.5)	0.38
MOI	**Scald**	18 (58.1)	20 (62.5)	18 (54.5)	0.91
	Contact	11 (35.5)	11 (34.4)	14 (42.4)	
	Flame	1 (3.2)	1 (3.1)	0 (0)	
	Electrical	1 (3.2)	0 (0)	1 (3.0)	
Burn Site	**Head/neck**	3 (9.7)	5 (15.6)	3 (9.1)	0.83
	Hand/fingers	9 (29.0)	7 (21.9)	10 (30.3)	
	Upper limb	4 (12.9)	6 (18.8)	3 (9.1)	
	Foot/toes	6 (19.4)	4 (12.5)	4 (12.1)	
	Lower limb	1 (3.2)	4 (12.5)	5 (15.2)	
	Torso (front and back)	6 (19.4)	4 (12.5)	7 (21.2)	
	Abdomen	2 (6.5)	1 (3.1)	0 (0)	
	Perineum	0 (0)	1 (3.1)	1 (3.0)	

Burn depth	**Superficial partial thickness only**	24 (77.4)	23 (71.9)	30 (90.9)	0.15
	Mixed partial thickness	7 (22.6)	9 (28.1)	3 (9.1)	
		(n= 12)	**(n= 12)**	**(n= 11)**	
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	
LDI Mean PU		1110.46 (235.70)	1396.05 (457.40)	1161.02 (306.80)	0.12
LDI Min PU		361.42 (191.70)	340.92 (207.80)	279.27 (145.60)	0.55

SD = standard deviation; TBSA = total body surface area; MOI = mechanism of injury; LDI = laser Doppler image; PU = perfusion units

4.7.3 Primary Outcomes

4.7.3.1 Days to full re-epithelialization

Burn wounds were classified as ≥95% re-epithelialized by the treating consultant, through measurement from 3D photographs and Visitrak™ tracings and by consultants during blind photo reviews. Visitrak™ measurements could not be used as tracings were unable to be completed in 22% of children due to pain and an inability to remain still. However 3D photographs and wound measurements were successfully completed for all participants in the study. The level of agreement between consultants from blinded photo review classification of ≥95% re-epithelialization was excellent, ICC 0.92 (95% CI 0.88, 0.94) and therefore ratings of days to ≥95% re-epithelialization by the treating consultant were used for the analysis. Table 2 shows the raw data for days to ≥95% re-epithelialization between the three dressing groups as classified by the treating consultant.

4.7.3.2 Negative binomial regression

The variance of the days to full re-epithelialization (28.28) was nearly 3 times greater than the corresponding mean (9.66). Given this over-dispersion of the data, a negative binomial regression model was used to compare the differences in the treatment groups, after adjusting for the effects of any potential confounding variables. Four variables (gender, age, burn depth, TBSA) were considered for their potential contribution to the days to re-epithelialization outcome and entered individually into the regression model. Burn depth was the only variable found to have a significant (p <0.05) impact on days to re-epithelialization and was included in the final regression model. Two outliers, one from the Acticoat™ group and one from the Mepilex Ag™ group, were excluded from the final model due to their unusually large residual values (i.e. high number of days to full re-epithelialization compared to the whole cohort). Data was calculated as an incidence rate ratio in the final model.

When adjusted for burn depth, receiving the Acticoat dressing compared to Mepilex Ag™ significantly increased the expected days to full re-epithelialization by 40% (95% CI: 1.14-1.73, p < 0.01; see Table 4-2). Similarly, receiving the Acticoat™ with Mepitel™ dressing compared to Mepilex Ag™ significantly increased the expected days to full re-epithelialization by 33% (95% CI 1.08-1.63, p = 0.01). There was no statistically significant difference between Acticoat™ and Acticoat™ combined with Mepitel™.

Table 4-2 Days to full re-epithelialization between dressing groups

Raw Data	N	Median	IQR
Acticoat™	28	9.50	7.00-14.00
Acticoat™ with Mepitel™	28	10.00	8.00-13.00
Mepilex Ag™	32	7.00	4.00-8.00
Adjusted for Depth	**IRR**	**95% CI**	***p*-value**
Acticoat™ vs. Mepilex Ag™	1.40	1.14, 1.73	<0.01
Acticoat™ with Mepitel™ vs. Mepilex Ag™	1.33	1.08, 1.63	0.01

N = number of participants; IQR = Inter-quartile range; IRR = incidence rate ratio; CI = confidence interval

4.7.3.3 Pain during the dressing change procedure

Multilevel generalized linear mixed-effects modeling with a log link function and gamma distribution was used to analyze the data from each of the 5 pain measures (See Table 4-3).

Four variables (gender, age, burn depth, TBSA) were considered as potential confounders for modeling each of the pain measures (FPS-R, FLACC, VAS-P, pulse rate, respiratory rate). Data were analysed after dressing removal, at new dressing application and overall (all timepoints at all dressing changes). Results were presented as odds ratios and their 95% confidence intervals.

Modeling was not completed for the FPS-R due to a large amount of missing data (the majority of children in the study were too young to use this scale). For respiratory rate, there was no statistically significant difference between the three dressing groups overall, after dressing removal or application. Additionally, at all timepoints and for all pain measures, there was no significant difference between Acticoat™ with Mepitel™ and Mepilex Ag™.

Table 4-3 Multilevel mixed-effects modeling for pain and distress measures

	Pain or distress measure	Dressing comparison	OR	95% CI	*p*-value
After dressing removal	FLACC	Acticoat™ vs. Acticoat™ with Mepitel™	0.77	0.60-0.98	0.04
		Acticoat™ vs. Mepilex Ag™	0.68	0.50-0.91	0.01
	VAS-P	Acticoat™ vs. Acticoat™ with Mepitel™	0.76	0.56-1.02	0.07
		Acticoat™ vs. Mepilex Ag™	0.75	0.56-0.99	0.04
	Pulse rate	Acticoat™ vs. Acticoat™ with Mepitel™	0.92	0.87-0.97	<0.01
		Acticoat™ vs. Mepilex Ag™	0.93	0.89-0.98	0.01
After dressing application	FLACC	Acticoat™ vs. Acticoat™ with Mepitel™	0.60	0.44-0.83	<0.01
		Acticoat™ vs. Mepilex Ag™	0.63	0.41-0.97	0.04
	VAS-P	Acticoat™ vs. Acticoat™ with Mepitel™	0.66	0.46-0.94	0.02
		Acticoat™ vs. Mepilex Ag™	0.70	0.48-1.01	0.06
	Pulse rate	Acticoat™ vs. Acticoat™ with Mepitel™	0.93	0.88-0.99	0.02
		Acticoat™ vs. Mepilex Ag™	0.91	0.84-0.99	0.03
Overall	FLACC	Acticoat™ vs. Acticoat™ with Mepitel™	0.80	0.66, 0.97	0.02
		Acticoat™ vs. Mepilex Ag™	0.78	0.64, 0.95	0.01
	VAS-P	Acticoat™ vs. Acticoat™ with Mepitel™	0.79	0.65-0.95	0.02
		Acticoat™ vs. Mepilex Ag™	0.83	0.68-1.01	0.06
	Pulse rate	Acticoat™ vs. Acticoat™ with Mepitel™	0.92	0.88-0.97	<0.01
		Acticoat™ vs. Mepilex Ag™	0.93	0.89-0.98	<0.01

FLACC = faces, legs, activity, cry, consolability scale; VAS-P = visual analogue scale-pain; OR = odds ratio; CI = confidence interval

4.7.3.4 After dressing removal

Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the expected FLACC score after dressing removal by 23% and 32% compared to receiving the Acticoat™ dressing (p = 0.04; p = 0.01). Receiving the Mepilex Ag™ dressing significantly decreased the expected VAS-P score after dressing removal by 25% (p = 0.04) compared to receiving Acticoat™. There was no statistically significant difference in VAS-P scores between the Acticoat™ and Acticoat™ with Mepitel™. Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the expected pulse rate after dressing removal by 8% and 7% respectively compared to receiving the Acticoat™ dressing (p = <0.01; p = 0.01).

4.7.3.5 After dressing application

Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the expected FLACC score after dressing application by 40% and 37% compared to receiving the Acticoat™ dressing (p = <0.01; p = 0.04). Receiving the Acticoat™ with Mepitel™ dressing significantly decreased the expected VAS-P score after dressing application by 34% compared to receiving the Acticoat™ dressing (p = 0.02). There was no statistically significant difference in VAS-P scores between the Acticoat™ and Mepilex Ag™. Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the expected pulse rate after dressing application by 7% and 9% respectively compared to receiving the Acticoat™ dressing (p = 0.02; p = 0.03).

4.7.3.6 Overall

Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the overall expected FLACC score by 20% and 22% compared to receiving the Acticoat™ dressing (p = 0.02; p = 0.01). Receiving the Acticoat™ with Mepitel™ dressing significantly decreased the overall expected VAS-P score by 21% compared to receiving the Acticoat™ dressing (p = 0.02). There was no statistically significant difference in VAS-P scores between the Acticoat™ and Mepilex Ag™. Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the overall expected pulse rate by 8% and 7% compared to receiving the Acticoat™ dressing (p <0.01; p = <0.01).

4.7.4 Secondary Outcome Measures

4.7.4.1 Analgesia

On the first dressing change, 78% of participants received a narcotic analgesia combination of paracetamol (dosage by body weight, 15mg/kg) and Oxycodone™ (dosage by body weight, 0.1 to 0.2 mg/kg) according to standard practice for the SPPBC. The remainder of

participants received paracetamol only or no analgesic medication as determined by clinical judgment (i.e. burn injury very minor, child too young for Oxycodone™). Three participants in the Acticoat™ group and one participant in the Acticoat™ with Mepitel™ group required a rescue dose of Oxycodone™ (dosage of 0.1mg/kg in addition to the initial paracetamol and Oxycodone™ dose) during their first dressing change procedure. All three participants in the Acticoat™ group who were administered an Oxycodone™ rescue dose also required inhaled Entonox™ (nitrous oxide/oxygen combination) at the first dressing change. One participant in the Acticoat™ group also required Entonox™ (in addition to standard paracetamol/Oxycodone™ dose) for the second and third dressing changes.

4.7.4.2 Dressing removal and application times

Removal and application times were analyzed between the three dressing groups on the first dressing change. Comparison of dressing removal, application and cumulative dressing removal/application time are presented in Figure 4-3. Cumulative dressing removal and application time on the first dressing change was significantly faster in the Mepilex Ag^{TM} group (5:03 minutes, IQR 2:48 – 7:53 minutes) compared to both the Acticoat^{TM} (10:17 minutes; IQR 7:38 – 21:58 minutes; p <0.01) and Acticoat^{TM} combined with Mepitel^{TM} (10:03 minutes; IQR 6:21 – 16:47 minutes; p <0.01) groups.

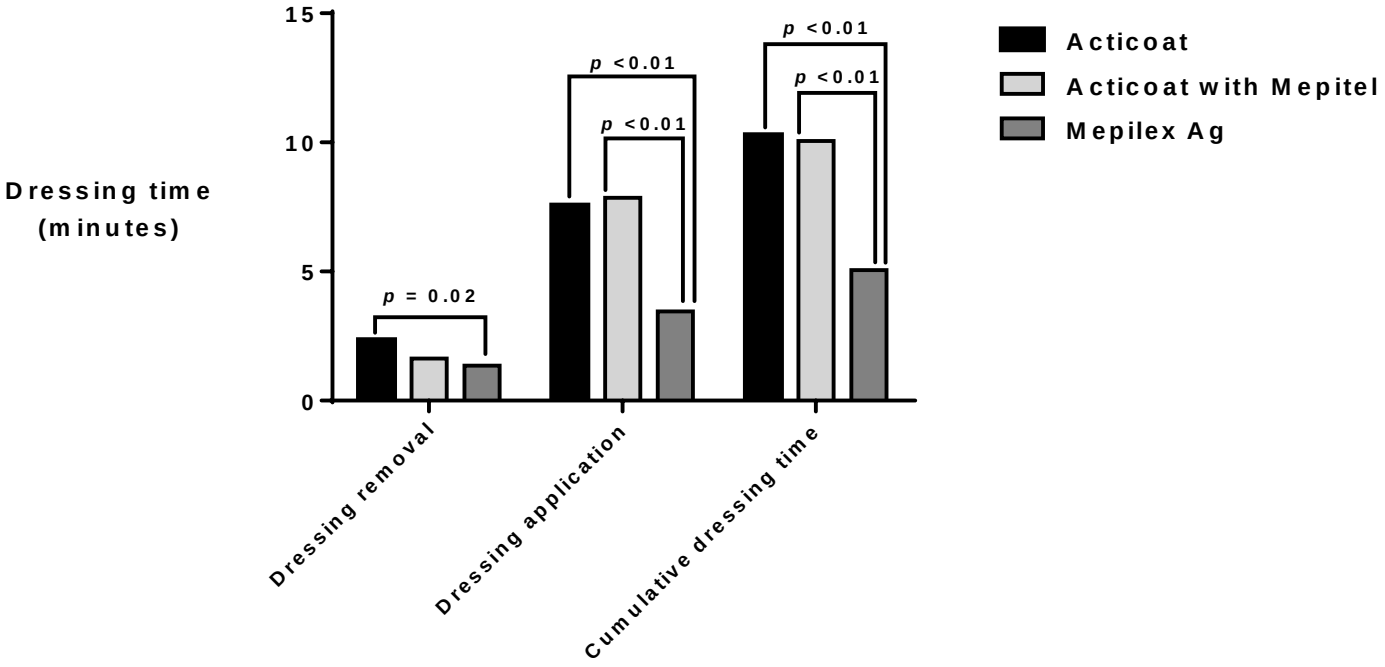

Figure 4-3 Comparison of dressing removal, application and cumulative dressing time at the first dressing change. Removal and application was significantly faster in Mepilex Ag compared to Acticoat ($p < 0.001$) and Acticoat with Mepitel ($p < 0.01$).

4.7.4.3 Dressing ease of removal and application

Dressing ease of removal and application ratings were analysed between the three dressing groups on the first dressing change. Likert scale ratings regarding ease of dressing removal and application are represented in Figure 4-4Aand B.

For dressing removal (Figure 4-4A), the Acticoat™ group was rated as significantly more difficult to remove than both the Mepilex Ag™ group (p <0.01) and the Acticoat™ with Mepitel™ group (p < 0.01). There was no significant difference between Acticoat™ with Mepitel™ and Mepilex Ag™ (p = 0.20).

For dressing application (Figure 4-4B), the Acticoat™ group was rated as significantly more difficult to apply than both the Mepilex Ag™ group (p = 0.03) and the Acticoat™ with Mepitel™ group (p < 0.01). There was no significant difference between Acticoat™ with Mepitel™ and Mepilex Ag™ (p = 0.62).

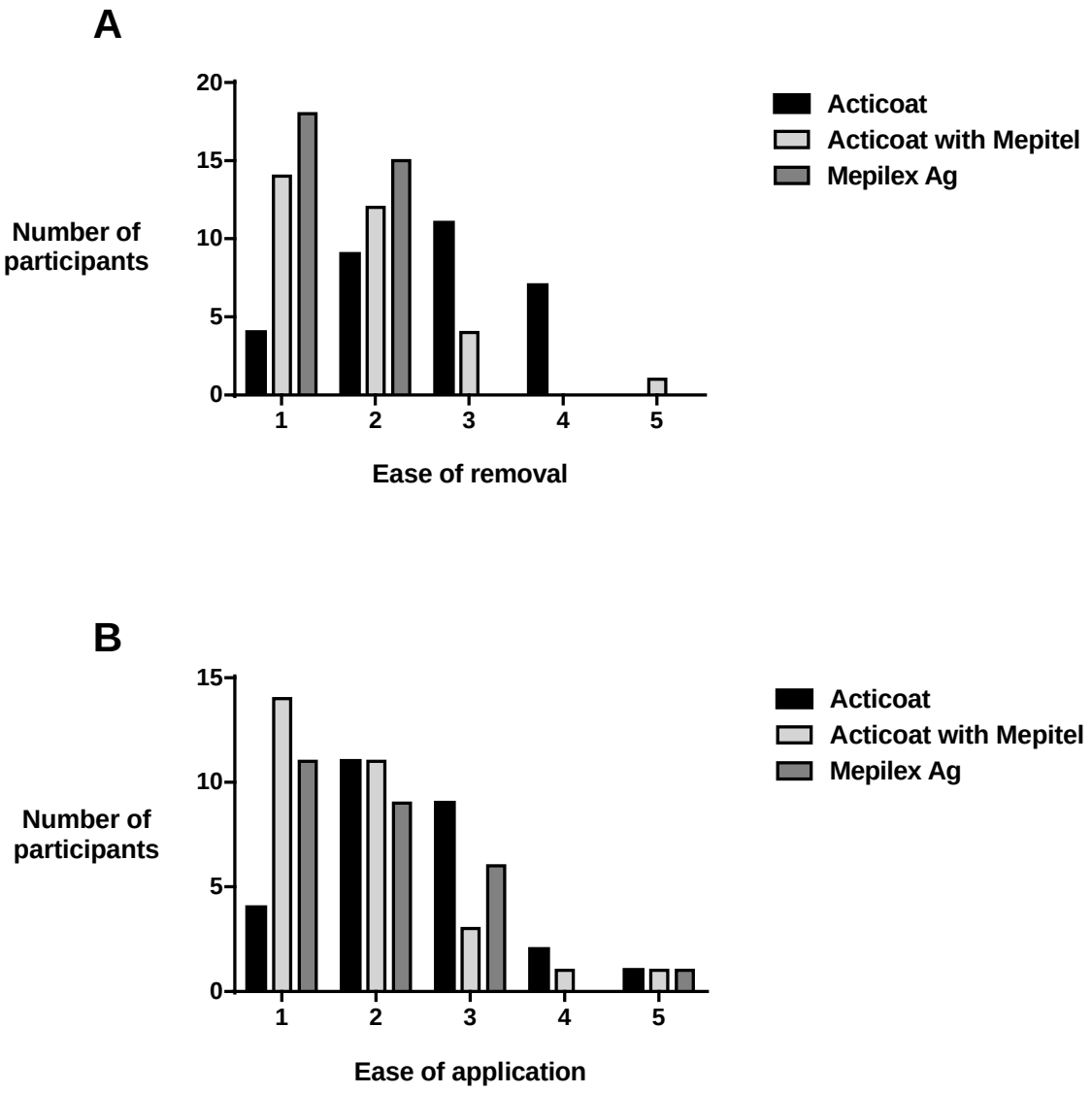

Figure 4-4 Ease of dressing removal at the first dressing change (A) and Ease of dressing application at the first dressing change (B). The treating nurse used a Likert scale where: 1 = extremely easy, 2 = very easy, 3 = somewhat easy, 4 = not very easy, 5 = not at all easy Acticoat was significantly more difficult to remove than Mepilex Ag *(p* < 0.01) and Acticoat with Mepitel (*p* < 0.01). Acticoat was also significantly more difficult to apply than Mepilex Ag (*p*=0.03) and Acticoat with Mepitel (*p*<0.01*).*

4.7.4.4 Nursing staff experience with dressing use

In a pre and post study surveys, nursing staff from the SPPBC rated the three dressings for their perceived or observed ease of removal and application when used on hands or feet and flat surfaces (i.e. chest). Nursing staff rated that Acticoat™ with Mepitel™ and Mepilex Ag™ were the easiest to remove from both hands or feet and flat surfaces. Acticoat™ with Mepitel™ was rated as the easiest to apply to hands or feet and flat surfaces, with Mepilex Ag™ the hardest to apply to hands or feet. Acticoat™ was rated as the hardest to apply to flat surfaces and hardest to remove from all areas. All nursing staff specified that Mepilex Ag™ was the hardest to apply to hands or feet in very young children (under the age of 3 years) as the dressing is the thickest of the three dressings and difficult to conform to very small fingers and toes.

4.7.4.5 Physical function

There was no significant difference between the groups regarding physical function when wearing the dressings.

4.7.5 Adverse events

No infections were recorded for the course of the study in any of the three groups. Nursing staff noted that the Acticoat™ dressing often dried into the wound, despite parents or caregivers being instructed to regularly irrigate the dressing. Additionally, many Acticoat™ dressings were difficult to remove, even after nursing staff soaked the dressing with sterile water, and many children who received this dressing were observed to have bleeding from the wound after the dressing was removed. One child in the Acticoat™ group with a scald burn injury to the face discontinued Acticoat™ use (as per instruction from the treating doctor) due to a high level of pain, distress and bleeding from the wound at dressing changes. The child then received Acticoat™ and Mepitel™ (the standard treatment for the burns unit) for the remainder of their treatment and had an uneventful recovery.

4.8 Discussion

Effective wound healing treatments are vital to diminish the physical and psychosocial challenges children experience after a burn injury, therefore high level evidence is required to identify the most appropriate silver dressing for pediatric burn injuries. Whilst silver fabric dressings demonstrate improved re epithelialization and reduced pain compared to SSD cream [9, 16], there is a lack of high level trials comparing silver dressings to each other in the pediatric burns population [17]. The results of this study demonstrated that clean, <10% TBSA, partial thickness burn injuries in children aged 0-15 years, when dressed with Mepilex

Ag™, re-epithelialized significantly faster than those dressed with Acticoat™ or Acticoat™ with Mepitel™.

The results have shown advantages in using a dressing with a silicone interface (Mepilex Ag™) compared to a dressing without (Acticoat™). Dressings that are silicone or have silicone interfaces, adhere to normal, intact skin and remain in situ on the surface of a wound but don't adhere to it, maintaining a moist wound environment while providing a less traumatic removal and subsequently less epidermal damage [8, 60]. Comparatively, dressings that can adhere to wound beds, such as Acticoat, potentially cause trauma on removal, increase pain and promote skin stripping which has been found to delay wound re-epithelialization [58]. In addition to slower re-epithelialization rates, clinical observations of bleeding from the wound bed dressing removal in participants who received the Acticoat™ dressing further emphasized the benefits of using a dressing with silicone interface for pediatric burn injuries.

Although both dressings had a silicone interface, the difference in re-epithelialization between Mepilex Ag™ and Acticoat™ with Mepitel™ was unexpected and may be due to other factors such as the cytotoxicity or release of silver from the dressings. Silver products are an effective antimicrobial utility for managing the bio-burden of burn wounds and in-vitro studies have shown Acticoat™ can be cytotoxic to healthy keratinocytes which can delay healing [66]. However there has yet to be any published research with respect to the cytotoxicity of the silver used in Mepilex Ag™. In terms of silver release from dressings, an in vitro study by Rigo et al. [10] demonstrated that over a period of 7 days, the silver release from Mepilex Ag™ occurred within the first hour of contact with human serum substitute, whereas Acticoat™ Flex had a sustained silver release over the same 7 days. This difference in silver release rate between the two dressings could account for the difference in re-epithelialization rates, due to the continual release of silver from Acticoat™ over time. Additionally, there could also be an infection risk if Mepilex Ag is left on for 7 days but has released all its silver within the first day of application. It should be noted that the amount of silver released from Acticoat™ with the addition of Mepitel™ has yet to be reported in the literature. Laboratory research would be of major importance to evaluate the cytotoxicity of Mepilex Ag™ in comparison to Acticoat™, the antimicrobial effect of Mepilex Ag™ on dirty wounds and when worn for 7 days or more and the effect of Mepitel on silver release from Acticoat™.

This study also proved that dressings with silicone interfaces were associated with lower pain scores after dressing removal and application and across time in comparison to

Acticoat™ alone. Pulse rate was a significant indicator of pain, however may have little significance clinically due to the relatively small differences found between the groups. Respiratory rate was difficult to record in the children in this study due to excessive movement and crying and the results reflect that it is not a useful indicator of pain or distress in this instance. Given the difference in days to re-epithelialization between the Acticoat™ and Mepilex Ag™ groups and the subsequent difference in pain levels between these two groups, the results from this study sit well within the existing literature. Previous studies in this population have also demonstrated that higher levels of pain during burn care procedures are associated with delays in wound re-epithelialization [45, 47]. The reduced levels of pain associated with Acticoat™ with Mepitel™ and Mepilex Ag™ in this study, in conjunction with significantly faster re-epithelialization in the Mepilex Ag™ group has provided evidence to strongly consider the utilization of dressings with added-on or in-built silicone interfaces to manage acute burn injuries in the pediatric population.

The significant differences noted between the three dressings in this study with regard to re-epithelialization rates and pain levels, have provided sufficient justification to conduct this trial in children with burn injuries >10% TBSA. It would also be of benefit to explore the rate of wound re-epithelialization when changing these dressings at 3 versus 7 days to determine if fewer stressful dressing changes will have an effect on re-epithelialization rates and pain levels in children.

Conducting research in a pediatric population can be difficult and this trial was not without its own difficulties as the majority of children recruited were under the age of three years. Visitrak™ tracings in this study cohort were a challenge due to its invasive nature and many tracings could not be completed, whereas 3D photographs were taken for all children. Stockton et al. [41] noted that 3D photography is a non-invasive and accurate method for calculating wound area for children over the age of 3 years and should be considered for future use in children of this age over other methods such as the Visitrak™. Further research comparing Visitrak™ and 3D photography in children under the age of 3 years is required to extrapolate the results to the population examined in this study.

The most accurate method of burn depth classification for the pediatric population also remains problematic. Completing LDI scans in young children was a challenge in this study with many scans unable to be completed those under the age of 3 years. Challenges associated with LDI scanning in very young children have been documented in the literature with other researchers acknowledging the difficulty of interpreting scans affected by movement artifacts, with some decreasing resolution and scan times to accommodate for

such occurrences [31, 33]. However the fact remains that many studies reporting the success of LDI scan as an accurate, objective measure of burn wound healing potential included children with a mean age of three years or older [34, 36, 117]. Therefore the validity and reliability of LDI use in very young children (under the age of three years) is required for future studies in this population. Alternatively, recently developed Laser Speckle Contrast Imaging has potential as a promising research tool and substitute to LDI scans in the pediatric population, with a scan time of 2 seconds and higher resolution images, however the reliability and validity of this measure has yet to be established in children [118]. In addition to difficulties with LDI scans, the low agreement between medical staff regarding burn depth classification is widely acknowledged in the literature [30] and the similar result from this study was not unexpected. This study has demonstrated that while viewing a photo alone is appropriate for judgment of wound re-epithelialization, it is unsuitable for use in burn depth analysis.

4.9 Conclusion

Mepilex Ag^{TM} has been shown to be an effective silver dressing in regards to wound re-epithelialization time, pain during dressing changes, dressing removal and application time and ease of use in clean, <10% TBSA partial thickness burn injuries in children. The use of dressings with silicone interfaces should be strongly considered for use in the pediatric population to reduce pain and wound trauma during dressing changes.

4.10 Acknowledgements

The authors would look to thank all the children and their families who participated in this study. They would also like to acknowledge all the staff at the Stuart Pegg Pediatric Burns Centre at the Royal Children's Hospital Brisbane for their support and assistance throughout data collection. This clinical trial was partially financially supported by a grant given to the University of Queensland by Mölnlycke Healthcare (grant number: QCMRI50107).

4.11 Chapter conclusion

The randomized controlled trial presented in this chapter has demonstrated that Mepilex Ag™ is a more effective dressing for small to medium partial thickness burns in children than Acticoat™ and Acticoat™ with Mepitel™ in terms of wound re-epithelialization time, dressing time and ease of application and removal. Dressings with silicone interfaces – Mepilex Ag™ and Acticoat™ with Mepitel™ - were associated with significantly lower pain and distress levels during dressing changes compared to Acticoat™. At the time of publication, this study was the only randomised controlled trial available in the literature comparing silver dressings in children with partial thickness burns ≤10% TBSA. Since publication, one other study comparing Aquacel® Ag and Acticoat™ silver dressings has been published in a similar population of children with partial thickness burns [75]. This study demonstrated that while there was no difference between the dressings in terms of wound re-epithelialization rates or adverse events (e.g. infection), Aquacel® Ag required less distressing dressing changes, indicating that it may be more appropriate for a pediatric population compared to Acticoat™. Aquacel® Ag is commonly used in European countries, but rarely used in Australasia, however such results may warrant further research into this dressing in the future.

The results from the trial presented in this chapter enabled a clinical change in practice in December 2014 from the current regime of Acticoat™ with Mepitel™ to Mepilex Ag™ for pediatric partial thickness burns ≤10% TBSA at the Pegg Leditschke Children's Burns Centre (PLCBC) at the Lady Cilento Children's Hospital (LCCH) in Brisbane, Australia. This undertaking has been a major achievement from this body of work. It has seen collaboration from LCCH burns unit medical and nursing staff to provide assistance in developing a new evidence-based burns dressing treatment protocol which has been made available via Queensland Health (See Appendix). As the PLCBC is the main tertiary pediatric burns center in Queensland, the new treatment protocol has been successfully rolled out to all other metropolitan, regional and rural hospitals and medical centers state-wide. Educational seminars and inservices have been provided to all burns unit and emergency department clinicians within LCCH in addition to clinicians in external centers. Results of the trial have also been presented to clinicians at international burns and emergency nursing conferences. A recent and extremely important accomplishment has seen the introduction of the new treatment protocol at the Royal Children's Hospital in Melbourne and Middlemore Hospital in New Zealand. The uptake of this protocol in the remaining Australasian pediatric burns centers in the near future would be an ideal outcome from this research.

Chapter 5. Reliability of 3D photography compared to digital planimetry

This chapter is based on published paper in Burns journal.

Citation: Gee Kee, E. L., Kimble, R. M., & Stockton, K. A. (2015). 3D photography is a reliable burn wound area assessment tool compared to digital planimetry in very young children. Burns, 41(6), 1286-1290. doi: 10.1016/j.burns.2015.01.020

5.1 Chapter foreword

Burn wound re-epithelialization is measured as a percentage of the total wound area, with re-epithelialization >95% taken as being representative of full wound closure. Clinically, wound re-epithelialization is often assessed via visual examination from the treating consultant. Comparatively, in research studies, wound mapping tools are often utilized to provide a quantifiable measure of wound re-epithelialization to ensure the accurate reporting of wound progression [39]. Wound mapping is conducted by measuring the total surface area of the wound (i.e. tracing the wound border), as well as measuring the areas that have re-epithelialized at each timepoint. The gold standard for wound mapping at the commencement of this thesis was digital planimetry using the Visitrak™ device (Smith & Nephew Medical Limited, England). At the commencement of this research however, recently developed technology in the form of stereophotogrammetry (3D photography) became available within the PLCBC using the 3D LifeViz™ System (Quantificare, Sophia Antipolis, France). This new tool was seen as a potential non-invasive alternative to Visitrak™ which could provide an increased ability to obtain objective and accurate measurements of wound re-epithelialization in the pediatric burns population.

While wound mapping is imperative to recording re-epithelialization, completing such measures in the acute, pediatric burn population can be a challenging endeavour. Burn wound care procedures can be painful, distressing and uncomfortable for children and even more so for those too young to comprehend the experience. As a consequence of pain, distress and age, compliance during wound care and assessment procedures is an ongoing struggle, particularly with children under the age of 3 years. This was highlighted in the previous chapter with the low completion rate of laser Doppler imaging to assess burn depth. Therefore there is a need to utilize wound mapping tools which provide not only an accurate measurement of wound re-epithelialization over time but can be used in a non-invasive manner to diminish the trauma experienced by children with burn injuries.

This chapter is based on the publication titled '*3D photography is a reliable burn wound area assessment tool compared to digital planimetry in very young children'.* The chapter will present an analysis of the clinical utility of the 3D camera compared to Visitrak™ based on data collected in the randomized controlled trial. Detailed methods and results will be presented, along with a discussion of clinical implications associated with integrating 3D photography within pediatric burns practice.

5.2 Abstract

5.2.1 Background

Reliability and validity of 3D photography (3D LifeViz™ System) compared to digital planimetry (Visitrak™) has been established in a compliant cohort of children with acute burn injuries. Further research is required to investigate these assessment tools in children representative of the general pediatric burns population, specifically children under the age of three years.

5.2.2 Aim

To determine if 3D photography is a reliable wound assessment tool compared to Visitrak™ in children of all ages with acute burn injuries ≤10% TBSA.

5.2.3 Method

Ninety-six children (median age 1 year 9 months) who presented to the Royal Children's Hospital Brisbane with an acute burn injury ≤10% TBSA were recruited into the study. Wounds were measured at the first dressing change using the Visitrak™ system and 3D photography. All measurements were completed by one investigator and level of agreement between wound surface area measurements was calculated.

5.2.4 Results

Wound surface area measurements were complete (i.e. participants had measurements from both techniques) for 75 participants. Level of agreement between wound surface area measurements calculated using an intra-class correlation coefficient (ICC) was excellent (ICC 0.96, 95% CI 0.93, 0.97). Visitrak™ tracings could not be completed in 19 participants with 16 aged less than two years. 3D photography could not be completed for one participant. Barriers to completing tracings were: excessive movement, pain, young age or wound location (e.g. face or perineum).

5.2.5 Conclusion

This study has confirmed 3D photography as a reliable alternative to digital planimetry in children of all ages with acute burn injuries ≤10% TBSA. In addition, 3D photography is more suitable for very young children given its non-invasive nature.

5.3 Keywords

Child, burn, reliability, wound area

5.4 Introduction

Measurement of wound area, particularly in burn care, is valuable in clinical and research settings in terms of visually recording wound progression and re-epithelialization [39]. For children with acute burn injuries, the wound care procedure can be a painful and distressing experience. Therefore, while there are many different methods of wound measurement available, consideration must be taken to choose a method that is not only reliable, but limits the amount of distress experienced by the child.

Many types of wound measurement techniques are available with the most commonly used being digital planimetry using a wound measurement system called Visitrak™ (Smith & Nephew Medical Limited, England) (see Figure 1). Visitrak™ is a valid method of wound measurement and is more accurate than the use of a ruler to measure the wound [119]. The Visitrak™ system uses a clear, plastic film grid which is placed on the wound, the wound border is traced and wound surface area can be calculated using the Visitrak™ digital device. Visitrak™ is widely used to measure burn wounds; however is limited by the requirement of direct contact of the grid with the wound bed and for the patient to remain still while the tracing is completed. This can be challenging for a pediatric population thus a less invasive method of wound measurement may be more appropriate and cause less discomfort for children.

Stereophotogammetry has recently emerged as a non-invasive, alternative method to Visitrak™ for wound area measurement. This technique analyzes images and provides a 3D image from which various wound measurements can be calculated [40]. The 3D LifeViz^{TM} system (Quantificare, Sophia Antipolis, France) consists of a high-definition camera with two lenses at slightly different angles (See Figure 5-1). Images taken with the camera are loaded onto a computer and merged to create a 3D figure of the wound. Wound area and volume can be calculated using DermaPix® software (Quantificare, Sophia Antipolis, France).

Preliminary research has found excellent inter-rater reliability in patients with chronic wounds [40]. Additionally, a recent paper by Stockton et al. [120] established the validity and reliability of 3D photography as a measure of acute burn wound surface area in children with acute burn injuries compared to the clinical gold standard digital planimetry (Visitrak™). The study by Stockton et al. [121] included a small, compliant cohort (n=25) of children with a median age of over three years in order to have a group of children who could tolerate both assessment techniques. However further research is required to investigate these two techniques in a larger group of children who represent the general pediatric burns

population, where the age of children is more commonly under the age of three years and compliance during wound care procedures is not always guaranteed. Therefore the aim of this study was to determine if 3D photography was a reliable wound assessment tool compared to Visitrak™ in a large group of children aged 0-15 years with acute burn injuries ≤10% TBSA.

5.5 Method

5.5.1 Participants

Children aged 0 to 15 years with an acute partial thickness (superficial partial to deep partial thickness inclusive) ≤10% TBSA burn injury, who presented to the Royal Children's Hospital, Brisbane within the first 72 hours post-burn injury. Children were excluded from the study if they had a chemical or friction burn; were non-English speaking; had a cognitive impairment; or were currently involved with the Department of Communities, Child Safety and Disability Services.

5.5.2 Ethics

This study was an extension of a randomized controlled trial investigating burns dressings [116]. The trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and was approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee (HREC/12/QRCH/219) and The University of Queensland Ethics Committee.

5.5.3 Recruitment

Eligible patients were recruited into the larger trial from the Department of Emergency Medicine and the Stuart Pegg Pediatric Burns Centre (SPPBC) at the Royal Children's Hospital (RCH), Brisbane, Australia between March 2013 and January 2014. Informed consent and child assent was obtained at first presentation. Recruited children then presented to the SPPBC outpatient clinic for a dressing change at day 3-5 post burn-injury.

5.5.4 Measurement techniques

5.5.4.1 Visitrak™ method

To measure the wound, the plastic Visitrak™ tracing grid was placed over the wound so that the entire wound was included within the grid border, and the perimeter of the wound traced. For larger wounds, two or more grids were joined together in order to encompass the entire wound area. At a later date, the tracing grid was placed on the Visitrak™ analysis pad device. The device stylus was used to the trace around the wound outline on the grid and the device automatically calculated wound surface area.

5.5.4.2 3D photography method

When using the 3D LifeViz System, the camera was held 60cm above the wound until the two lens lights aligned and a photo was taken. A ruler was included in all photos for measurement calibration as per manufacturer instructions. The photo was directly loaded onto the specialist computer software program Dermapix™. The wound outline was manually traced using the software and a 3D image of the wound was generated. Wound surface area was then automatically calculated from the 3D image.

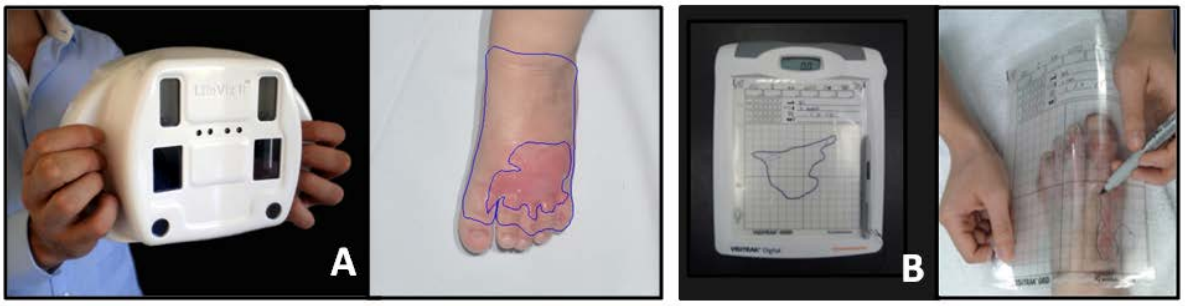

Figure 5-1 The two wound measurement techniques used. (A) The 3D LifeViz™ System (Quantificare, Sophia Antipolis, France), and an example of wound tracing using the DermaPix® software (B) The Visitrak™ analysis pad device (Smith & Nephew Medical Limited, England)

5.5.5 Measurement procedure

At the first dressing change, each child had their burn wound measured using two techniques: Visitrak™ tracing and 3D photography. Measurements were completed after the dressing was removed and the wound was cleaned. There was no specified order in which the measurements were taken. The measurements from each technique were recorded and then analyzed at a later date. Measurements were recorded in cm^2 units. Where a child had multiple wound sites, these were analyzed separately and combined for a total measurement. When circumferential wounds were present, 3D photographs were taken in sections which were then analyzed separately using anatomical landmarks as border markers and individual measurements were combined for a total measurement. Some circumferential wounds also required multiple Visitrak™ grids to be taped together to cover the whole wound. Grids were then analyzed separately and combined for a total measurement.

5.5.6 Statistical analysis

All statistical analyses were conducted using SPSS 21 (IBM Corporation, Armonk, NY, USA) and Graph Pad Prism 6 (Graph Pad Software, La Jolla, CA). Demographic data (age, gender, burn mechanism) are presented as median and interquartile range (IQR) or percentage where appropriate. Level of agreement between wound surface area

measurements from the 3D photography and Visitrak™ methods was calculated using an intra-class correlation coefficient (2,1) and the Bland-Altman method to allow for a visual inspection of the data, bias and level of agreement (LOA) was calculated

5.5.7 Data storage

Data was securely stored in a locked filing cabinet in a secure area of Queensland Children's Medical Research Institute, The University of Queensland. Data was entered into an SPSS spreadsheet and any incomplete data was coded as missing, unknown or not applicable. The full dataset was cleaned and checked before being locked for analysis.

5.6 Results

5.6.1 Demographics

Ninety-six children (55 male/41 female) with a median age of 1 year 9 months (IQR 1 year 3 months – 5 years) who presented to the Royal Children's Hospital with acute burn injuries were recruited into the study. Sixty-eight percent of children were aged three years or younger. Children had partial thickness burns ≤10% TBSA with 57.3% being scald burn injuries and 38.5% being contact burn injuries. The remaining burn injuries were flame burns (2.1%) and electrical burns (2.1%).

5.6.2 Agreement between measurements

Wound surface area ranged from 0.15cm^2 to 246.90cm^2. The wound surface area measurements at the first dressing change were complete (i.e. participants had measurements from both techniques) in 75 cases and were analyzed using an intra-class correlation coefficient (2, 1). The level of agreement between the two methods of wound surface area measurement was excellent (ICC 0.96, 95% CI 0.93, 0.97). Agreement between the two techniques was also visualized by comparing average wound area of the two techniques to the difference in wound area using Bland-Altman plots (See Figure 5-2). The plot demonstrated a heteroscedascity of the data and a greater variability between the two techniques in wounds of larger size, with a bias of 1.86 (LOA -15.86 – 19.58) cm^2. The two outliers above the top LOA line were circumferential wounds where mapping was technically difficult for both techniques and there was a greater difference in measurements.

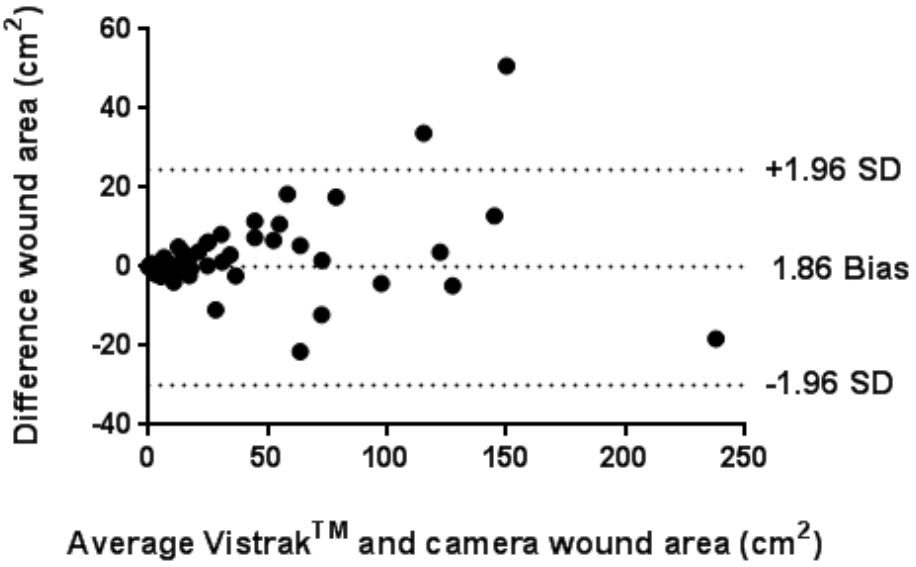

Figure 5-2 Bland-Altman plot comparing average Visitrak™ and camera calculated wound area to difference of Visitrak™ and camera area. Bias 1.86 (LOA -15.86 – 19.58) cm^2.

5.6.3 Missing data

Visitrak™ tracings could not be completed in 19 participants with 16 of those participants aged 2 years or under. Excessive movement in participants, due to pain, young age or wound location (e.g. face), made it difficult to complete tracings or trace accurately, with many tracings completed as quickly as possible to minimize trauma to the child. As wounds were seen acutely at the first dressing change, condensation forming on the Visitrak™ grid also made it difficult to distinguish wound borders. Completing tracings quickly also often meant a rough, inaccurate drawing and in some cases, small sections of the wound were missed. Visitrak™ tracings where only a small section of wound area was missed were still used and extra areas captured by photography were not used in the analysis. One participant (aged 11 years) refused a 3D photograph due to wound location (perineum).

5.7 Discussion

This study has confirmed that 3D photography is a reliable alternative to digital planimetry (Visitrak™) to measure wound surface area in children with burn wounds ≤10% TBSA, with an intra-class correlation coefficient demonstrating excellent agreement between the two techniques. The burn wound care procedure can be a stressful and traumatic time for children, particularly for those under the age of three years and care must be taken to avoid additional distress to the child. Despite excellent wound measurement agreement between

the two techniques, 3D photography was demonstrated to be more appropriate for use in a young, pediatric population than Visitrak™.

While the 3D photography method in this study had a 99% completion rate, Visitrak™ tracings could not be completed for 19 children, with 16 of those under the age of two years. Stockton et al. [41] also compared Visitrak™ and 3D photography in children with acute burn injuries, and recorded a 100% completion rate of tracings. However children in the study were a compliant group with a median age of 3 years 7 months compared to the median age of 1 year 9 months for this study. 3D photography has previously been established to be easier and quicker to use than Visitrak™ at the bedside for children due to its simple point and shoot method and non-invasive technique [120]. Visitrak™ tracings comparatively, involve direct contact of the film with the wound which can cause pain or anxiety and require the child to remain still for a prolonged period of time. Barriers to completing Visitrak™ tracings in this study included high pain and distress levels, excessive movement during the tracing and wound location (e.g. face). Higher levels of pain and distress during wound care procedures in children have been found to be associated with delays in wound re-epithelialization [45]. Thus the use of wound measurement methods that involve direct wound contact or take a prolonged amount of time, such as the Visitrak™ system, should be re-considered for all children, especially those under the age of three years.

Despite its demonstrated clinical utility in the pediatric population, use of 3D photography does present some minor drawbacks. Due to the technological limitations of 3D photography, wounds that extend over curved areas (e.g. ankle, wrist) can be difficult to visualize in 3D and the edges of the image can become distorted, slightly altering the true measurement. In particular, fingers and toes in very young children are especially difficult to map due to the small size of the digits and wounds often extending around the edges of digits. It should also be noted that the angle at which a photo is taken or the angle at which a body part is positioned (e.g. extension vs. flexion) can slightly alter surface area measurements and care should be taken to ensure consistency when photographing a wound over multiple timepoints.

Again, difficulties were experienced mapping large circumferential wounds using both techniques. Four large circumferential wounds required multiple Visitrak™ grids to be joined together and it was challenging applying the stiff film sheets around a leg or arm and to complete an accurate tracing in these children who were in pain or distressed. Similarly, mapping these wounds using the 3D photography software was difficult as serial photographs were taken to capture the entire wound and anatomical landmarks were used

to mark borders on each photograph. To counter this, the software does have the ability to stitch multiple, serial photographs together, but this is technically difficult and has limited clinical utility. While these limitations exist, it should be noted that the majority of children seen in this clinical setting have discrete burn injuries <1% TBSA and large, circumferential burn wounds are an uncommon occurrence [121]. Therefore this study has shown that 3D photography is a reliable measurement technique for smaller, discrete burn wounds and can be utilized clinically for this population.

Photographs produced from the 3D LifeViz™ system are of a high definition and quality. In addition to wound area measurement, photographs taken at multiple timepoints have been utilized successfully for visual judgment of wound re-epithelialization by clinicians. The additional benefits gained from the photographs have strengthened the clinical utility of this system for the acute, pediatric burns population.

5.8 Conclusion

This study has confirmed 3D photography as a reliable alternative to digital planimetry in children of all ages with acute burn injuries ≤10% TBSA. It has also been established that 3D photography is more clinically appropriate to use for young children given its fast and non-invasive nature.

5.9 Acknowledgements

The authors would look to thank all the children and their families who participated in this study. The would also like to acknowledge all the staff at the Stuart Pegg Pediatric Burns Centre at the Royal Children's Hospital Brisbane, Australia for their support and assistance throughout data collection.

5.10 Conflict of Interest Statement

Funding for this study was supplied by a grant given to the Royal Children's Hospital, Brisbane by Mölnlycke Healthcare. Despite this financial support, Mölnlycke Healthcare had no part in the study design and data collection of this project, nor did they have any involvement in the analysis or publication of the results. The chief investigator is a student of the University of Queensland and receives a stipend from this grant.

5.11 Chapter Conclusion

The research study presented in this chapter has shown 3D photography to be a reliable and non-invasive alternative to Visitrak™ for the mapping of wound surface area in children with acute, partial thickness burns. Technological limitations continue to exist in the mapping of larger and also circumferential wounds, but it is hoped that this will become less problematic as technology develops and users of the camera software become more skilled in the complex task of stitching photos together. The 3D LifeViz™ system however remains a device that can be successfully utilized for small to medium size burn wounds in children.

As a result of this study, the 3D LifeViz™ system is now employed as the primary measurement method for burn wound mapping in all research studies conducted at the PLCBC. The camera's quick point and shoot method at the bedside, non-invasive nature and ability to produce high-quality images, along with the capability of the Dermapix™ program to store progressive wound photographs for multiple patients, has rendered it an invaluable tool within the burns unit.

3D photography using this device also has the capacity to measure volume and height of areas on the skin and has been identified as a potential tool for pediatric and adult burn scars and infantile hemangiomas. As a result, I have been extensively involved in research studies external to this thesis, which are currently underway examining the clinical utility and reliability of 3D photography to objectively measure burn scar height and volume and the volume of infantile hemangiomas over time. It is anticipated that results from these studies will demonstrate that the 3D LifeViz™ system is a versatile tool that can provide a multitude of benefits to the pediatric burns and vascular anomalies populations.

Chapter 6. Cost-effectiveness of silver dressings for pediatric partial thickness burns

This chapter is based on a submitted paper ('Cost-effectiveness of silver dressings for pediatric partial thickness burns: an economic evaluation from a randomized controlled trial' in Burns journal (submission date: 08/03/2016).

6.1 Chapter foreword

As previously described in Chapter 4, silver dressings are commonly used to treat pediatric partial thickness burns, however, research evidence regarding the most appropriate dressing to use is lacking. In addition to examining the efficacy of silver dressings, understanding the costs involved is also necessary to determine the burden on the healthcare system. Burn care in the outpatient setting is expensive with children often seen up to twice a week for dressing changes until the wound re-epithelializes, approximately 2-3 weeks later. Scar management therapy and surgery for skin grafting can drastically increase the costs even further. Therefore, care is required to choose a dressing which is not only effective but which also reduces financial burden on the healthcare system.

Despite the expense of burn care in the pediatric setting, very few comprehensive economic evaluations have been conducted for burns dressings in the pediatric outpatient population, with the majority continuing to combine adult and pediatric populations with severe burns requiring inpatient hospitalization. Consequently, there is very little information available to clinicians to allow them to choose a silver dressing which is a cost-effective option to use to treat pediatric partial thickness burns ≤10% TBSA.

Hence, the aim of the economic evaluation presented in this chapter was to provide a detailed cost-effective analysis of the silver dressings included in the RCT presented in Chapter 4, to assist in decision-making for healthcare providers. This chapter is based on the submitted manuscript titled '*Cost-effectiveness of three silver dressings for pediatric partial thickness burns: an economic evaluation from a randomized controlled trial*'. Detailed methodology and results from the economic evaluation will be presented along with a discussion of the implications for clinical practice.

6.2 Abstract

6.2.1 Background

Partial thickness burn injuries of up to 10% total body surface area (TBSA) in children are common injuries primarily treated in the outpatient setting using expensive silver-containing dressings. However, economic evaluations in the pediatric burns population are lacking to assist healthcare providers when choosing which dressing to use. The aim of this study was to conduct a cost-effectiveness analysis of three silver dressings for partial thickness burns ≤10% TBSA in children aged 0-15 years using days to full wound re-epithelialization as the health outcome.

6.2.2 Method

This study was trial based economic evaluation (incremental cost effectiveness) conducted from a healthcare provider perspective. Ninety-six children participated in the trial investigating Acticoat™, Acticoat™ with Mepitel™ or Mepilex Ag™. Costs directly related to the management of partial thickness burn injuries ≤10% TBSA were collected during the trial from March 2013-July 2014 and for a one year post re-epithelialization time horizon. Incremental cost effectiveness ratios were estimated and dominance probabilities calculated from bootstrap resampling trial data. Sensitivity analyses were conducted to examine the potential effect of accounting for infrequent, but high cost, skin grafting surgical procedures.

6.2.3 Results

Costs (dressing, labor, analgesics, scar management) were considerably lower in the Mepilex Ag™ group (median AUD$94.45) compared to the Acticoat™ (median $244.90) and Acticoat™ with Mepitel™ (median $196.66) interventions. There was a 99% and 97% probability that Mepilex Ag™ dominated (cheaper and more effective than) Acticoat™ and Acticoat™ with Mepitel™, respectively. This pattern of dominance was consistent across raw cost and effects, after a-priori adjustments, and sensitivity analyses. There was an 82% probability that Acticoat™ with Mepitel dominated Acticoat™ in the primary analysis, although this probability was sensitive to the effect of skin graft procedures.

6.2.4 Conclusion

This economic evaluation has demonstrated that Mepilex Ag™ was the dominant dressing choice over both Acticoat™ and Acticoat™ with Mepitel™ in this trial-based economic evaluation and is recommended for treatment of pediatric partial thickness burns ≤10% TBSA.

6.3 Keywords

Child, partial thickness burn injury, silver dressings, economic evaluation

6.4 Introduction

In children aged 0-15 years, burn injuries of less than 20% total body surface area (TBSA) are the fifth most common cause of non-fatal childhood injuries worldwide, occurring in 153 per 100,000 population of children [2]. As the mortality rates from burn injuries have decreased over time with better treatment options, burns of up to 10% TBSA in children can now be managed in the outpatient setting and consequently there has been a significant drop in inpatient admissions [42]. According to data collected by the Burns Registry of Australia and New Zealand (BRANZ) from seven burns centers over a one year period (2010-2011), the ratio of pediatric outpatient admissions to inpatients was 3.2:1 [28].

In recent years, burns dressing applications for partial thickness burns ≤10% TBSA in children have changed from daily silver sulfadiazine cream (SSD) applications to the use of silver impregnated dressings which can be changed up to twice weekly in the outpatient setting [9]. The wound re-epithelialization process using dressings can take 2-3 weeks or occasionally more [29]. More than 800 children are typically treated for a burn injury in the city of Brisbane, where the present study was conducted, each year [122]. Outpatient treatment approaches (the majority of cases) are cheaper than admitted cases, but the costs associated with silver dressings utilized, and the health professional labor time consumed during the management of these burn injuries are substantial.

A systematic review of burn care costs calculated the mean total cost as $3,883 per 1% TBSA burned for burns 0-10% TBSA in high income countries [18]. Thus, choosing a silver dressing which can promote a rapid re-epithelialization time (therefore decreasing the need for scar management and surgical intervention), and which is also less costly than other silver dressings on the market, has the potential to greatly reduce the resource consuming burden on the health system from pediatric burn injuries.

Economic evaluations of silver burns dressings are warranted among clinical populations in order to assist decision making for healthcare providers. However, there is a paucity of cost-effective studies among pediatric clinical populations with burn injuries. Notably, despite silver dressings being the treatment of choice for pediatric burns in high-income countries, there has yet to be a rigorous cost-effectiveness study comparing silver burns dressings in a pediatric outpatient population.

A systematic review of the costs of burn care published in 2014 [18] noted that the majority of cost studies available in this area had numerous inconsistencies in study methodology. The majority were combined adult and pediatric populations, there was unreliable

measurement and reporting of TBSA in patients, severe burns requiring inpatient stays were largely the focus of studies and many studies which included direct medical costs often only recorded dressing costs. Cohort studies were most commonly reported (*n* = 107), while a small number were randomized controlled trials (*n* = 24). From the 153 studies included in the review, only three were identified as complete economic evaluations comparing burns dressings using cost effectiveness analyses, the remainder being cost studies only. One study investigated non-standard burns treatments [123] and the remaining two studies included either Aquacel Ag® [124] or Mepilex Ag™ [78] silver dressings however both were compared to SSD which is no longer a standard treatment in high-income countries for children.

Since publication of this systematic review, a comprehensive cost-utility analysis of silver dressings (Mepilex Ag™ and Aquacel Ag®) compared to SSD in partial thickness burns ≤20% TBSA was published [125]. This study among adults with burn injuries incorporated a cost-utility analysis and concluded that silver dressings were cost effective over a wide complication (e.g. infection) range in comparison to SSD among that sample.

The most comprehensive economic evaluation currently in the literature of pediatric burn care is an incremental cost-effective analysis examining the use of a non-pharmacological, procedural preparation and distraction intervention (Ditto™) compared to standard practice in the pediatric burns outpatient setting and the effects on wound re-epithelialization [126]. While this study does not evaluate burn wound treatments, it was conducted from a societal perspective in the same setting as the current study (Royal Children's Hospital, Brisbane) and has provided a detailed overview of cost estimations associated with pediatric burns managed as outpatients.

6.5 Study Objective

The aim of this study was to conduct an economic evaluation (incremental cost-effectiveness analysis) of three silver dressings for partial thickness burns ≤10% TBSA in children aged 0-15 years using a reduction in days to full wound re-epithelialization (days to re-epithelialization saved) as the health outcome.

6.6 Method

6.6.1 Design

A trial based economic evaluation (incremental cost-effectiveness analysis) was conducted from the perspective of a healthcare provider alongside a three-parallel arm randomized controlled trial [127]. This perspective was chosen to inform healthcare decision making for

health service personnel deciding which dressing to use in their service for partial thickness burns (≤10% TBSA) in children aged 0-15 years to minimize days until re-epithelialization. The time horizon for the study included wound and scar management for (up to) one year post-wound re-epithelialization (although most patients with these burns typically complete their wound management regimen in less than 6 months). Therefore, the investigators did not consider discounting for costs or effects to be warranted in this investigation due to the time-frames involved typically being less than 1-year.

6.6.2 Participants and setting

This study examined children aged 0-15 years (*n* = 96) presenting to the former Royal Children's Hospital, Brisbane, Australia from March 2013-January 2014 within 72 hours of sustaining a ≤10% total body surface area (TBSA) partial thickness burn (superficial partial to deep partial inclusive). Children were recruited into a randomized controlled trial investigating silver burns dressings and were randomized to receive one of three silver dressings (Acticoat™, Acticoat™ with Mepitel™ or Mepilex Ag™) until the burn re-epithelialized or skin grafting was required.

This study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee.

6.6.3 Health outcome

Days to re-epithelialization was the health outcome of interest for this evaluation. Prolonged re-epithelialization time for a burn injury can lead to an increased risk in the development of hypertrophic scarring [7]. Burns which re-epithelialize in 14 days or less are at a very low risk of developing residual scarring and children are often discharged upon wound re-epithelialization. Burns which take longer than 14- 21 days to re-epithelialize or those requiring skin grafting generally develop hypertrophic scarring [7]. Hypertrophic scarring can have significant and life-long implications to the physical, psychosocial and emotional functioning of a child [94]. The presence of hypertrophic scarring typically requires long-term scar management therapy to treat and minimize scarring. As scar tissue grows at a slower rate than unaffected skin, this can lead to the need for multiple reconstructive surgeries until the child reaches adulthood. Scar management therapy (including the use of pressure garments and topical silicone), skin grafting and reconstruction are extremely expensive and can increase the cost of treating a burn dramatically in comparison to the cost of a burn treated conservatively and discharged without further follow-up.

6.6.4 Intervention

Use of silver dressings can have a direct impact on the re-epithelialization time of the wound, for example, by prevention of infection (which can prolong time to re-epithelialization). The three silver dressings investigated in the randomized controlled trial were Acticoat™ (Smith and Nephew), Acticoat™ combined with Mepitel™ (Molnlycke Healthcare) and Mepilex Ag™ (Molnlycke Healthcare). All three dressings are presently used in healthcare services to treat pediatric partial thickness burns in Australasia. Both Acticoat™ and Mepilex Ag™ are stand-alone dressings, while Mepitel™ is a silicone interface dressing which is often placed underneath Acticoat™ to assist with dressing removal. A detailed explanation of each dressing has been previously described [127]. Prior to the present trial, the usual standard of care for pediatric burns in Brisbane, Australia was Acticoat™ with Mepitel™. All three dressings were changed every 3-5 days during the trial and this regime continued until burn wound re-epithelialization occurred or skin grafting was required.

6.6.5 Intervention effect (on re-epithelialization)

During the randomized trial, days to wound re-epithelialization was recorded for each participant and analyzed using a negative binomial regression adjusting for burn depth and TBSA [127]. Mepilex Ag™ was found to be the most effective dressing with regard to days to re-epithelialization, and Acticoat™ and Acticoat™ with Mepitel™ found to have a 40% (p <0.01) and 33% (p< 0.01) longer time until re-epithelialization respectively.

6.6.6 Resources and costs

Resource and cost data directly related to the partial thickness burn injury ≤10% TBSA was collected prospectively from March 2013-July 2014 during the trial. In addition, any further resource use relating to scar management and skin grafting requirements after the trial dressing intervention had ceased was collected from patient medical records for the first year post wound re-epithelialization. Costs for this study were applied in (2014) AUD$. (See Appendix 5) for a full breakdown of costs.

6.6.6.1 Resource use

Resource utilization data collected prospectively for each participant during their trial intervention included number of dressing changes required, time taken per dressing change and the nursing staff time (in minutes) required for each dressing change. Nursing time was inclusive of time taken to remove the dressing, clean the wound and apply a new dressing. Dressing type, size and quantity were also recorded at each dressing change. Analgesia administered to the child at each dressing change was also recorded. Amount of analgesic

medication was calculated by weight, with standard of care being Oxycodone (0.1mg/kg) and Paracetamol (15mg/kg).

Labor time for dressing, wound or scar-related management was also recorded for occupational therapists and treating medical or surgical consultants. Labor resource usage was accrued for these professionals as; occupational therapy (30 minutes per scar management therapy appointment), treating medical or surgical consultant (15 minutes per dressing change appointment) for each participant. The investigators considered skin grafting to be an infrequent, but potentially important consideration for resource use. Therefore if participants required a skin grafting procedure and /or scar management therapy, this was also documented.

6.6.6.2 Valuation of costs

Labor time was costed at the appropriate award rates for these respective health professionals working in state-based health facilities and consistent with the participating hospital's wage rates. This included use of three state-based award rates (Nursing [128], Health Practitioner for occupational therapists [129], and Medical [130]). Labor costing for this trial included an additional 25.85% for associated on-costs (e.g. for leave accrual). Costs for dressings and scar management products were obtained from the participating hospitals' Finance and Materials Management Information System consumables pricing list which had prices at market rates. Dressings were individually packaged and price per individual dressing was used. Silicone products for scar management included topical silicone gels and sheets and silicone moulds. Silicone gels were priced per tube prescribed to the patient and silicone sheets as per individual sheet prescribed. Price per silicone mould was calculated from the price of a whole container of putty and then an estimation of number of moulds per container made (from the participating health professionals). Pressure garments for scar management were specifically tailored to each child; therefore price per garment was taken from each child's garment order form. Consistent with the time-horizon for this study, scar management resources were only recorded for the first year post wound re-epithelialization.

The cost of a skin graft was included as the theatre cost and the cost of a negative pressure wound therapy dressing to the graft for 7 days (standard care). Skin grafting theatre cost was estimated from Queensland Health Diagnosis-Related Groups theatre costing where each child was given a DRG procedure code with a corresponding cost [131]. Price for a negative pressure wound therapy dressing encompassed the cost of gauze dressing,

dressing film and the lease of a negative pressure wound therapy canister and machine for a one week period.

6.6.7 Incremental cost effectiveness using randomized trial data

Incremental cost-effectiveness ratios (ICERs) were used to examine the cost per (one less) day to re-epithelialization for each paired comparison of the three intervention arms. The investigators considered it important to investigate each of the three possible between group incremental cost-effectiveness comparisons in order to inform a decision maker choosing between any two of these dressings which may be available to them. This meant that three separate incremental cost effectiveness ratios were estimated for this economic evaluation based on the equations displayed below where Cost was expressed as (2014) AUD$ and Effect as ('days to re-epithelialization'). The three ICER equations represent:

a) Acticoat™ with Mepitel™ versus Acticoat™

$$ICER = \frac{(\text{Cost Acticoat™ group}) - (\text{Cost Acticoat™ with Mepitel™ group})}{(\text{Effect Acticoat™ group}) - (\text{Effect Acticoat™ with Mepitel™ group})}$$

b) Mepilex Ag™ versus Acticoat™

$$ICER = \frac{(\text{Cost Mepilex Ag™ group}) - (\text{Cost Acticoat™ group})}{(\text{Effect Mepilex Ag™ group}) - (\text{Effect Acticoat™ group})}$$

c) Mepilex Ag™ versus Acticoat™ with Mepitel™.

$$ICER = \frac{(\text{Cost Mepilex Ag™ group}) - (\text{Cost Acticoat™ with Mepitel™ group})}{(\text{Effect Mepilex Ag™ group}) - (\text{Effect Acticoat™ with Mepitel™ group})}$$

Potential exclusions and model adjustments for the primary cost-effectiveness analysis were consistent with the primary trial protocol [127]. This principally meant that the small number of patients that required a skin grafting (n=4) were excluded from the primary analysis of both costs and effects to avoid the risk of the findings being unduly influenced by a small number of potential outliers. However, participants who required a skin graft were included in sensitivity analyses to examine their potential impact.

The difference in cost for each paired comparison was estimated from the adjusted regression coefficient derived from a multiple regression that included adjustment for burn depth and TBSA. Similarly, the difference in effect for each paired comparison was

estimated from the regression coefficient derived from a multiple regression that included adjustment for burn depth and TBSA.

Bootstrap resampling (2000 replications of the original sample) was used to calculate 95% confidence intervals (for between group differences in the cost of treatment and days to full re-epithelialization) and 95% confidence ellipses for the ICER estimates (cost per day (less) to full re-epithelialization). The ICER estimates and 95% confidence ellipse were plotted on cost-effectiveness quadrants with lower cost and fewer days to re-epithelialization (dominance) represented in the bottom-right quadrant (Figure 6-1). From these data, the probability that each intervention was less costly and more effective than each of the two respective alternatives was calculated. All statistical analyses for this economic evaluation were completed using Stata 14 (StataCorp, College Station, Texas) and Microsoft Office Excel 2010 (Microsoft Pty Limited, North Ryde, NSW, Australia).

6.6.8 Sensitivity analyses

Sensitivity analyses focused on examining the impact of inclusion of patients with a skin graft on the findings of the economic evaluation. As split skin grafting is seen as 'man-made' wound closure and the day of the grafting procedure in theatre can vary (e.g. three days post-burn to two weeks post-burn) due to factors such as burn depth or theatre availability, it is difficult to obtain a true 'days to re-epithelialization' equivalent time estimate for these patients. As such, two separate sensitivity analyses were conducted using two alternative approaches to assigning a 'days to re-epithelialization' value for the four participants who received a skin graft. The first, and least conservative approach, was to use the day of the skin graft as an artificial proxy of the day of re-epithelialization. The second approach was to use a dummy value of one day longer than the maximum days to re-epithelialization recorded for any non-skin graft participant in the trial. The participant who had the longest time to successful re-epithelialization without skin graft had the same burn depth as those that were grafted. In both sensitivity analyses, the cost of skin grafting and subsequent management of the four skin graft cases was included in the cost component of the equation.

6.7 Results

The demographics and clinical characteristics of the participants in the trial have previously been reported [127]. In summary, participants (n=96) had a mean (standard deviation) age of 3.01 (3.51) years, and 55 (57.3%) were male. Patient outcomes for participants in each of the three groups are summarized in Table 6-1. Overall, participants in the Mepilex Ag group required fewer days to re-epithelialization than the other groups. Four participants (4%) required split skin graft surgery.

6.7.1 Costs

Costs were considerably lower in the Mepilex Ag™ group compared to the Acticoat™ and Acticoat™ with Mepitel™ interventions (Table Table 6-2). The median total cost (excluding skin grafting) for those who received Mepilex Ag™ was $94.45, compared to $196.66 for Acticoat™ with Mepitel™ and $244.90 for Acticoat™. Differences in costs were attributable to both the higher item cost of both Acticoat™ and Mepitel™ (in particular when the two are combined) as well as the additional costs associated with a large number of dressing changes required for Acticoat™ and Acticoat™ with Mepitel™ due to the longer times to re-epithelialization. Two patients in each of the Acticoat™ with Mepitel™ and Acticoat™ groups required grafting that was estimated at $1731 in each case which substantially increased the mean total cost for those groups (Table 6-2). In summary, costs were lowest in the Mepilex Ag™ group with or without consideration of skin graft costs.

Table 6-1 Patient outcomes for each treatment group

Grouping	Acticoat™	Acticoat™ + Mepitel™	Mepilex Ag™
Total number of patients	31	32	33
Healed ≤2 weeks	22	24	29
Healed 2-3 weeks	4	4	2
Healed >3 weeks	2	0	1
Drop outs (failed to attend dressing change)	1	2	1
Split skin graft surgery	2	2	0
Scar management therapy	5	2	1

Table 6-2 Costs accumulated for each treatment group

Grouping	Acticoat™	Acticoat™ + Mepitel™	Mepilex Ag™
Group median (IQR) in AUD$			
Total acute costs (excluding skin grafting)[+]	244.87 (109.22-386.80)	196.66 (134.54-393.87)	94.45 (55.21-137.62)
Dressing costs	69.71 (38.30-183.28)	98.68 (56.70-198.33)	25.20 (16.80-50.45)
Staff labor costs	112.41 (67.85-175.30)	104.99 (72.30-145.53)	67.68 (38.65-74.33)
Analgesia costs	0.40 (0.21-0.63)	0.40 (0.26-0.73)	0.32 (0.20-0.47)
Scar management costs[+]	0 (0,0)	0 (0,0)	0 (0,0)
Group mean (SD) in AUD$			
Total acute costs (excluding skin grafting)[+]	373.30 (428.94)	341.37 (414.16)	116.80 (84.03)
Dressing costs	125.97 (133.17)	164.46 (156.55)	39.05 (34.10)
Staff labor costs	134.06 (92.17)	114.36 (60.36)	76.34 (54.51)
Analgesia costs	0.59 (0.71)	0.54 (0.44)	0.36 (0.27)
Scar management costs[+]	103.46 (282.43)	41.35 (165.35)	2.94 (16.91)
Cost estimate per surgical skin grafting case	17131	17131	Nil cases
Group mean (SD) (including skin grafts)	1478.52 (4499.86)	1412.0.3 (4596.03)	116.80 (84.03)

[+]Total acute costs (excluding skin grafting) = dressings, staff labor, analgesia medication, scar management therapy

Surgical skin grafting costs = surgical cost of a skin graft and cost of negative pressure wound therapy for 1 week

Scar management costs = all scar resources (consumables costs and staff labour)

6.7.2 Incremental cost effectiveness

The primary incremental cost effectiveness ratios (ICERs) for each between-group comparison were calculated and presented graphically (Figure 6-1) with 95% confidence ellipses. There was a 99% and 97% probability that Mepilex Ag™ dominated (was cheaper and more effective) Acticoat™ (Figure 6-1b) and Acticoat™ with Mepitel™ (Figure 6-1c), respectively. After a-priori adjustments, the mean (95% confidence intervals) cost-saving per participant from use of Mepilex Ag™ was $95.19 ($46.67, $142.99) in comparison to Acticoat™ and $74.80 ($30.19, $122.60) in comparison to Acticoat™ with Mepitel™. Similarly, after a-priori adjustments, the mean (95% confidence intervals) fewer days to re-epithelialization per participant from use of Mepilex Ag™ was 2.1 (0.1, 4.1) days in comparison to Acticoat™ and 1.3 (0.22, 2.47) days in comparison to Acticoat™ with Mepitel™. There was an 82% probability that Acticoat™ with Mepitel™ dominated Acticoat™ in the primary analysis. After a-prior adjustments, Acticoat™ with Mepitel™ demonstrated a mean (95% confidence intervals) cost-saving per participant of $107.55 ($-1.57, $239.51) and fewer days to re-epithelialization of 1.1 (-1.25, 3.68) days in comparison to Acticoat™.

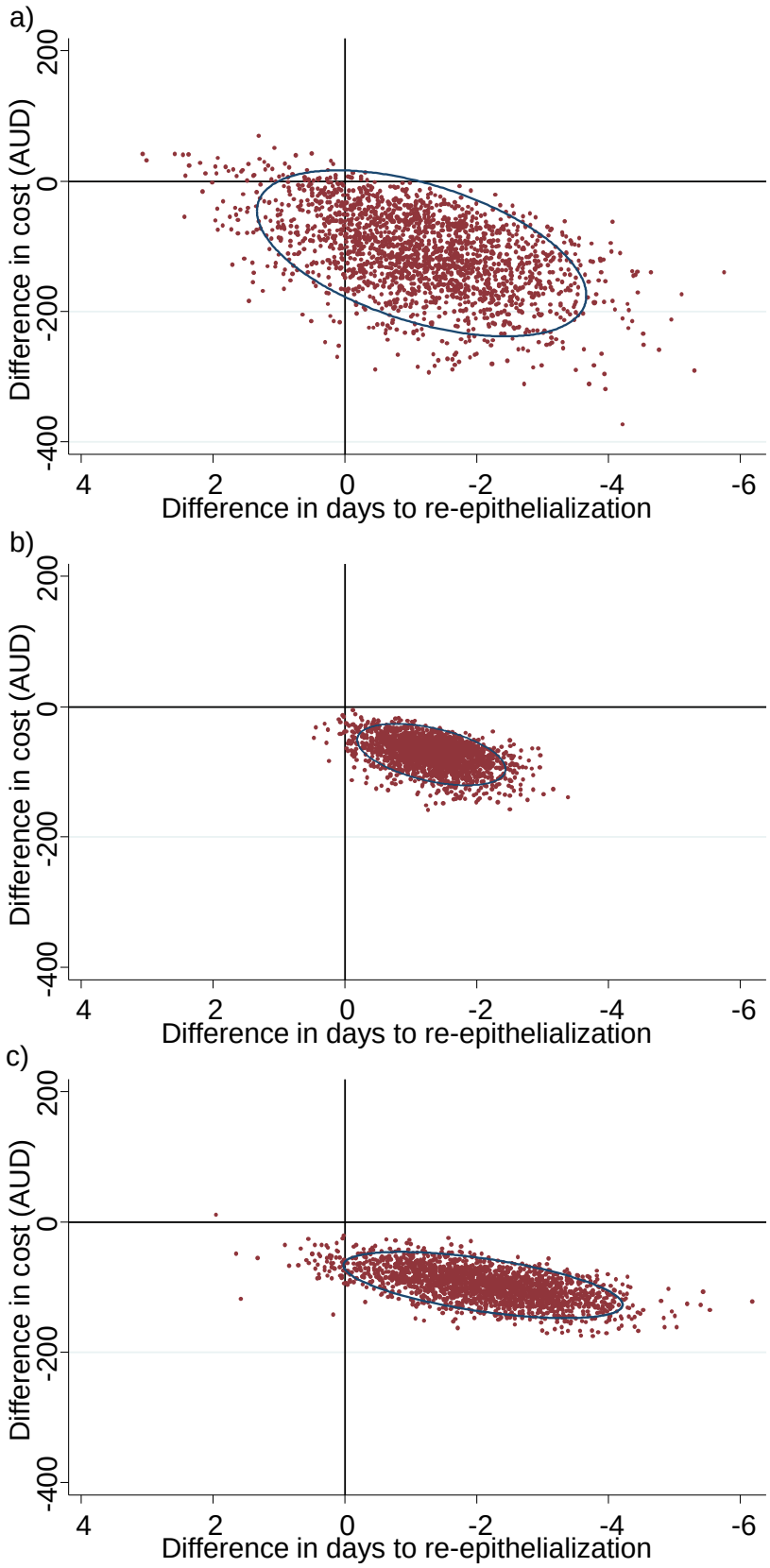

Figure 6-1 Incremental cost-effectiveness (and 95% confidence ellipses) from the primary trial analysis for a) Acticoat™ with Mepitel™ versus Acticoat™ b) Mepilex Ag™ versus Acticoat™ and c) Mepilex Ag™ versus Acticoat™ with Mepitel™

6.7.3 Sensitivity analyses

Both approaches to inclusion of the four participants who required a skin graft (Figure 6-2) yielded similar findings to the primary analysis for the Mepilex Ag comparisons (Figure 6-2c-f), albeit that the scale of cost savings and variance in the data were potentially larger in the direction of effect observed in the primary analysis which was attributable to the substantial costs associated with skin grafts. When the less conservative approach to assigning the 'days to epithelialization' as the day of the surgical split graft was used, there was a 95% and 91% probability that Mepilex Ag™ dominated Acticoat™ and Acticoat™ with Mepitel™, respectively. When an artificial 'time to re-epithelialization' value of one day longer than the longest time to re-epithelialization from conservative management observed in the trial was used, there was a 97% and 94% probability that Mepilex Ag™ dominated Acticoat™ and Acticoat™ with Mepitel™, respectively.

The inclusion of patients who received a graft substantially increased the uncertainty of ICER estimates for the comparison of Acticoat™ to Acticoat™ with Mepitel™, which is demonstrated in the wider confidence ellipse (Figure 6-2a and b in comparison to Figure 6-1). This greater variance in bootstrapped estimates (particularly the cost side of the equation) was directly attributable to the inclusion of a small number of cases with skin grafting that were associated with substantial costs. When the day of surgery was used in the effect estimate, there was a 33% probability that Acticoat™ with Mepitel™ dominated Acticoat™. When the artificial 'time to re-epithelialization' value of one day longer than the longest time to re-epithelialization was used, there was a 52% probability that Acticoat™ with Mepitel™ dominated Acticoat™.

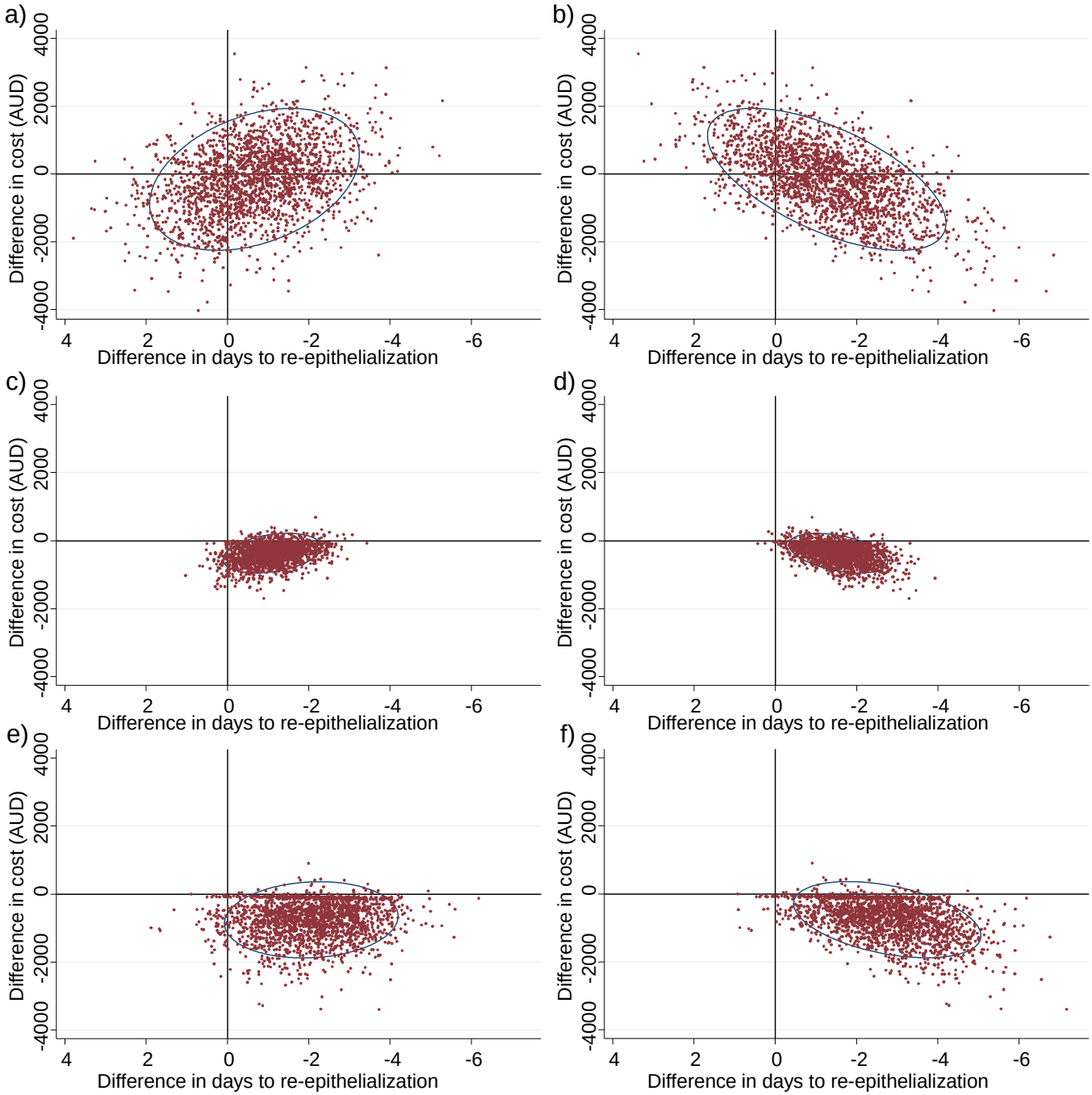

Figure 6-2 Incremental cost-effectiveness (and 95% confidence ellipses) from the sensitivity analyses using date of skin graft (a, c, e) or a dummy value (b, d, f) as a proxy for time to re-epithelization for Acticoat™ with Mepitel™ versus Acticoat™ (a, b) Mepilex™ versus Acticoat™ (c, d) and Mepilex Ag™ versus Acticoat™ with Mepitel™ (e, f).

6.8 Discussion

This study was the first economic evaluation to compare the use of three silver dressings for partial thickness burns ≤10% TBSA in children up to the age of 15 years who were treated in an outpatient setting. Patients who received Mepilex Ag™ required fewer healthcare resources and had significantly shorter re-epithelialization times than those who received Acticoat™ with Mepitel™ or Acticoat™. The Mepilex Ag™ was the dominant intervention (cheaper and more effective) in the primary analysis and both sensitivity analyses. This has lead the authors to conclude that Mepilex Ag™ was more cost-effective than the two other dressings investigated under the conditions of this trial, with this patient sample and with the application of market pricing at the time of the study (2014). The recommendation from this evaluation is that Mepilex Ag™ be the dressing of choice for this population of children who sustain partial thickness burn injuries ≤10% TBSA. While this was a definitive outcome from the present evaluation, and there is a paucity of economic evaluations to support or refute the present finding, there are several caveats that the authors would like to highlight for consideration.

First, the trial on which this economic evaluation was based received some financial support from Molnlycke Healthcare (the company which supplies Mepilex Ag™ and Mepitel™). This company had no input into study design, data collection, analysis or manuscript preparation and no right or opportunity to stop the authors from publishing the findings regardless of how their products performed during the trial. Nonetheless, the authors would encourage further clinical trials and economic evaluations of these dressings (particularly those funded through independent not-for-profit sources) within the same clinical population to confirm or refute the findings observed in this evaluation. It is also noteworthy that this was a single site trial and that variation in clinical practice across facilities within Australia and internationally may influence patient outcomes. Similarly, valuations of labor and non-labor resource use may differ between jurisdictions.

Second, this evaluation was conducted using a healthcare provider perspective and was limited to a time horizon of one year. The authors considered this the most appropriate perspective and time-horizon for this evaluation to inform decision makers choosing which dressing to use for this clinical group. This meant that broader societal impacts (for example, between group differences in productivity losses associated with parents or caregivers accompanying children to burn-related healthcare appointments) were considered beyond the scope of this investigation. Similarly, only resources consumed within one year post re-epithelialization were within the time-horizon for this study. However, given that cost savings

for the Mepilex Ag™ group were (at least in part) attributable to fewer appointments and faster healing, it is likely that a similar patterns of incremental cost-effectiveness estimate ratios would have been observed regardless of the any alternative perspective or time horizon that could have been selected.

A design feature of the present study that may limit comparisons to be made outside the field of wound healing was that no measures of health-related quality of life (HRQoL) were completed for this evaluation. Subsequently, analyses were limited to randomized controlled trial data using the primary outcome of days to re-epithelialization as the health outcome. While this is consistent with prior evaluations in the field [18], the inclusion of a preference based HRQoL measure would have led to a greater understanding of the respective impacts (if any) of earlier healing (and potentially a reduction in the need for scar management or skin grafting). Burn injuries can be a life-changing event for children, young people and their families both physically and psychosocially and the measurement of HRQoL would have been beneficial when determining the cost effectiveness of treatments. Specifically, use of a preference-based measure in future studies would enable the determination of quality adjusted life years gained (or lost). The Child Health Utility 9D Index [132] would seem a worthwhile measure for consideration in future economic evaluations to both understand life impacts from the patients' perspective from a clinical perspective, but also calculate quality adjusted life years for inclusion in cost-utility analyses.

One final point for consideration was the impact of the few cases with the worst outcomes and highest costs. The skewed distribution of resource utilization (and therefore costs) meant that the mean costs were considerably higher than median costs with the mean influenced by a relatively small number of cases with particularly high costs. This was able to be accounted for in the analysis in two ways. First, the bootstrap resampling approach enabled the calculation of non-parametric confidence intervals (for costs and effects) as well as confidence ellipses (for incremental cost effectiveness estimates), to quantify the level of uncertainty and probability of dominance based on the actual distribution of outcomes observed in the trial. Second, the sensitivity analyses examining the potential impact of inclusion of the outlying costs associated with the small number of cases requiring skin grafts further supported the principal finding of the study (dominance of the Mepilex Ag™ intervention). However, the sensitivity analyses demonstrated the potential volatility in cost estimates attributable to the small number cases that may require skin grafts. As skin grafting is primarily used for deep dermal partial thickness and full thickness wounds that will not re-epithelialize in a reasonable amount of time, it is recommended that skin grafting

be considered as an entirely separate, but economically important, type of treatment for burn wounds with its own set of costs and health outcomes.

6.9 Conclusion

This trial-based economic evaluation has demonstrated that Mepilex Ag™ is a dominant (cheaper and more effective) dressing choice over both Acticoat™ and Acticoat™ with Mepitel™ and is recommended for treatment of pediatric partial thickness burns ≤10% TBSA. Acticoat™ with Mepitel™ may also dominate Acticoat™ for the same population based on the primary analysis of this trial; however, there was greater uncertainty in between group differences in cost and effects for these two interventions than for the dominance of Mepilex Ag™ over both of these alternatives.

6.10 Conflict of Interest Statement

This clinical trial was partially financially supported by a grant given to the Royal Children's Hospital, Brisbane by Mölnlycke Healthcare. Despite this financial support, Mölnlycke Healthcare had no part in the study design and data collection of this project, nor did they have any involvement in the analysis or publication of results. The principal researcher has no financial interest in the Acticoat™, Mepitel™ or Mepilex Ag™ dressings or the Mölnlycke Healthcare company and is a student of the University of Queensland. SMM is supported by a National Health and Medical Research Council (of Australia) Fellowship.

6.11 Chapter conclusion

This chapter has demonstrated that Mepilex Ag™ is a cost-effective option over both Acticoat™ and Acticoat™ with Mepite™l. There was a 99% and 97% probability that Mepilex Ag™ was cheaper and more effective Acticoat™ and Acticoat™ with Mepitel™, respectively. The mean cost-savings per participant from use of Mepilex Ag™ was $95.19 in comparison to Acticoat™ and $74.80 in comparison to Acticoat™ with Mepitel™. The use of an effective dressing which is significantly more cost-effective than the usual standard of care will likely reduce the financial burden of such burn injuries to the healthcare system.

The results from this study have indicated that not only is Mepilex Ag™ more effective than Acticoat™ and Acticoat™ with Mepitel™ with respect to wound re-epithelialization time and pain during dressing changes, it is also a less expensive option. As clinical practice for the treatment of pediatric partial thickness burns ≤10% TBSA has already changed within Queensland, these findings will further strengthen the RCT results and further solidify the decision for the change. It is anticipated that the findings of the cost analysis will also strengthen the case for the use of Mepilex Ag™, interstate and in New Zealand, in the treatment of pediatric partial thickness burns in the outpatient setting.

Chapter 7 is a continuation of the RCT presented in Chapter 4. This chapter will discuss and present results from of scar assessments of trial participants, conducted at 3 and 6 months post wound re-epithelialization.

Chapter 7. Long-term scar outcome of pediatric partial thickness burns

This chapter is based on a published paper in Burns journal

Citation: Gee Kee, E. L., Kimble, R. M., Cuttle, L., & Stockton, K. A. (2015). Scar outcome of children with partial thickness burns: A 3 and 6 month follow up. Burns. doi: 10.1016/j.burns.2015.06.019

7.1 Chapter foreword

Hypertrophic scarring from burn injuries with prolonged re-epithelialization times or which require skin grafting can have a potentially devastating effect on a child's physical and psychosocial functioning [94]. They also often necessitate surgical reconstruction to keep up with a child's growing body [42]. In comparison, the longer term outcome for pediatric partial thickness burns is less complex with the majority of children discharged and not requiring scar management therapy post-wound re-epithelialization. Partial thickness burn sites are clinically reported to return to a normal skin appearance and pigmentation within six months post-wound re-epithelialization, but there is very limited research evidence to support this. Education provided to children and their families on longer term outcome from these burn injuries is therefore restricted to clinical knowledge and experience of the treating consultant.

Changes in skin pigmentation and appearance as a result of partial thickness burns are at the lower end of the spectrum in terms of clinical significance, as many of these changes are assumed to be temporary. However there is the capacity for such appearance changes to negatively impact on the psychosocial functioning of children and their families, as has been shown in children and adolescents with 'visible' burn scars or skin conditions such as vitiligo [95-97]. It is therefore vital that information on scar outcome for children with partial thickness burns is thoroughly investigated to ensure appropriate education and advice is provided to children and their parents and to facilitate early identification and management of potential psychosocial concerns prior to discharge from treatment.

This chapter is based on the publication titled '*Scar outcome of children with partial thickness burns: A 3 and 6 month follow-up'.* The chapter will present results from the scar follow-up phase of children recruited into the randomized controlled trial presented in Chapter 3. Detailed methods and results will be presented, along with a discussion of clinical outcomes from this study.

7.2 Abstract

7.2.1 Introduction

There is a paucity of research investigating the scar outcome of children with partial thickness burn injuries**.** The aim of this study was to assess the scar outcome of children with partial thickness burns who received a silver dressing acutely.

7.2.2 Method

Children aged 0 to 15 years with an acute partial thickness burn, ≤10% TBSA were included. Children were originally recruited for an RCT investigating three dressings for partial thickness burns. Children were assessed at 3 and 6 months post re-epithelialization. 3D photographs were taken of the burn site, POSAS was completed and skin thickness was measured using ultrasound imaging.

7.2.3 Results

Forty-three children returned for 3 and 6 month follow-ups or returned a photo. Days to re-epithelialization was a significant predictor of skin/scar quality at 3 and 6 months (p<0.01). Patient-rated color and observer-rated vascularity and pigmentation POSAS scores were comparable at 3 months (color vs. vascularity 0.88, p<0.001; color vs. pigmentation 0.64, p<0.001), but patients scored higher than the observer at 6 months (color vs. vascularity 0.57, p<0.05; color vs. pigmentation 0.15, p = 0.60). Burn depth was significantly correlated with skin thickness (r=0.51, p<0.01). Hypopigmentation of the burn site was present in 25.8% of children who re-epithelialized in ≤2 weeks.

7.2.4 Conclusion

This study has provided information on outcomes for children with partial thickness burns and highlighted a need for further education of this population.

7.3 Keywords

Child, partial thickness burn injury, scar outcome, skin thickness

7.4 Introduction

Small, but significant partial thickness burns in children are common injuries in high-income countries [42]. It is well known that partial thickness burns in children which take longer than two weeks to re-epithelialize are at a greater risk of hypertrophic scarring [7, 79, 133] and that clinically, a normal skin appearance is expected within six months for partial thickness burn injuries which re-epithelialize in two weeks or less., A comprehensive observational study by van der Wal and colleagues [20] compared the long-term scar outcomes in a representative group of children and adults with partial and full thickness burns. Partial thickness wounds were shown to result in a better scar quality than full thickness wound and that in children with scald burns, the scar maturation patterns between partial and full thickness wounds were different. However despite these demonstrated differences in scar maturation and clinical knowledge of partial thickness burn outcome, high-level research solely focusing on the outcomes of children with partial thickness burns is severely lacking.

Partial thickness burns in children are often treated acutely with conservative treatments such as recently developed silver-containing dressings. As acute treatment can have an effect on long-term scar quality, it is essential for comprehensive long-term studies of scar outcome following clinical trials of burn dressings to be completed in order to determine the impact of dressings on scar outcome. A recent systematic review by Vloemans et al. [80] investigating acute dressings and topical treatments for children with partial thickness burns, noted that only one randomized controlled trial (RCT) included a scar follow-up of its participants. The follow-up phase of this RCT however only consisted of the review of a very small number of children (exact number not stated) at 3 months post re-epithelialization [81]. Furthermore, external to the systematic review, Mabrouk et al. [82] compared Aquacel® Ag to the moist, open dressing MEBO and conducted 3 and 6 month follow-ups, however age range was broad (children and adults) only partial thickness facial burns were included and follow-up numbers were again not stated.

Therefore the aim of this study was to assess the scar outcome of children aged 0-15 years with partial thickness burn injuries <10% TBSA who were originally recruited into an RCT comparing silver dressings in the acute phase of treatment [127].

7.5 Method

This study was an extension of the prospective, randomized controlled trial '*Randomized controlled trial of three different dressings for partial thickness burns in children'* [127]. The study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and was approved by the Queensland Children's Health

Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee.

7.5.1 Participants

Children aged 0 to 15 years with an acute partial thickness (superficial partial to deep partial thickness inclusive) burn injury and a burn total body surface area (TBSA) of ≤10%.

7.5.2 Recruitment

Eligible patients were originally recruited from the Stuart Pegg Pediatric Burns Centre (SPPBC) at the Royal Children's Hospital, Brisbane, Australia between March 2013 and January 2014 as part of the RCT. For the RCT, children were randomized to one of three burns dressings (Acticoat™, Acticoat™ with Mepitel™ or Mepilex Ag™) and received this dressing until re-epithelialization or grafting occurred. Children and their families were informed prior to consent that participation in the RCT would require long-term follow-up appointments at 3 and 6 months post wound re-epithelialization.

7.5.3 Procedure

Children who completed the randomized dressing treatment until re-epithelialization of the burn wound or received skin grafting were brought in for follow-up appointments in the burns clinic at 3 and 6 months post burn wound re-epithelialization. Parents were phoned to organize a meeting time and if unable to attend follow-up appointments (e.g. due to living in a regional or rural centre), were given the option of sending in a photo of the child's original burn wound site via email.

At the 3 month appointment, children had a 3D photograph (3D LifeViz™ Camera, Quantificare, Cedex, France) taken of the burn wound site, the Patient and Observer Scar Assessment Scale (POSAS) was completed and an ultrasound scan was taken of the burn site and an unaffected contralateral site. Where a child had multiple sites, this process was completed for each site. This process was then replicated at the 6 month follow-up appointment.

7.5.4 Outcome measures

7.5.4.1 The Patient and Observer Scar Assessment Scale

The Patient and Observer Scar Assessment Scale (POSAS) was completed on participants at both 3 and 6 month follow-ups. The *observer* section was completed by the study investigator and the *patient* section was completed by the child (if over the age of 8) or the caregiver. A total score and overall opinion score were generated from both the patient and

observer assessments. For total scores, a score of 6 is equal to normal skin. For overall opinion scores, a score of 1 is equal to normal skin.

7.5.4.2 3D photography

All children had a 3D photograph taken of their original burn wound site using the 3D LifeViz™ Camera (Quantificare, Cedex, France). The 3D photographs were analyzed by the primary investigator on the Dermapix^{TM} software program (Quantificare, Cedex, France) to calculate scar height (if present). A ruler was included in all 3D photographs for measurement calibration in the associated software package Dermapix^{TM}.

7.5.4.3 Ultrasound

An ultrasound scan using the BT12 Venue 40 MSK with an 8-18 MHz hockey stick probe (GE Healthcare) was taken of the original burn wound site to measure skin thickness. The probe was placed in the center of the original burn site when there was no evidence of scar. If scar tissue was present, the probe was placed on the area originally classified as having the deepest wound depth. An additional measurement was taken of an unaffected contralateral site to the burn. Where a contralateral site was not available (e.g. bilateral burn sites), the closest, unaffected adjacent site was used. Measurements were taken from the top border of the epidermis to the lower border of the dermis (see Figure **7-1**). The direction of the ultrasound probe was recorded at 3 months to ensure consistency for the subsequent 6 month appointment. Five measurements were taken at each site for reliability analysis. To account for differences in scar or burn site location, the mean measurement at each burn site was used to calculate a percentage difference of burn site skin thickness (compared to the normal site) at 3 and 6 months.

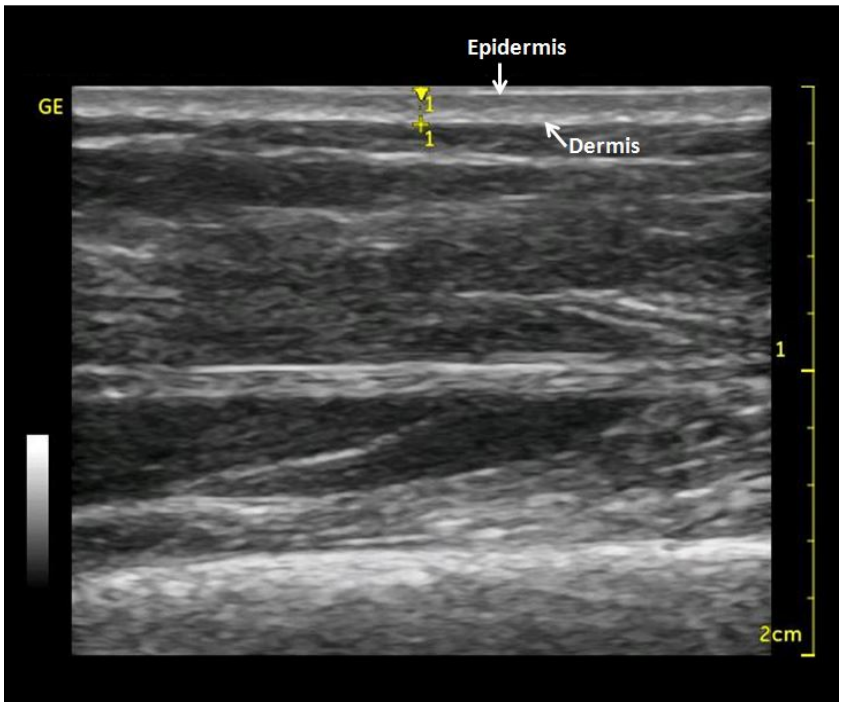

Figure 7-1 Example ultrasound image output indicating epidermal and dermal borders

7.5.5 Statistical Analysis

All statistical analyzes were conducted using SPSS 21 (IBM Corporation, Armonk, NY, USA). Demographic data (age, gender, burn TBSA and burn depth) are presented as median and interquartile range (IQR) or percentage where appropriate. Non-parametric demographic data was calculated using a Kruskal-Wallis test. Correlation of variables was calculated using Pearson correlations or Spearman's rho where necessary. Multiple regression models were used to identify predictors of POSAS scores and Wilcoxon Signed Rank Tests were used to analyze POSAS scores and ultrasound measurements over time. All tests with a p value <0.05 were considered statistically significant.

7.5.6 Data storage

Data is securely stored in a locked filing cabinet in a secure area of the Queensland Children's Medical Research Institute, The University of Queensland. Data were entered into an SPSS spreadsheet and any incomplete data were coded as missing, unknown or not applicable. The full dataset was cleaned and checked before being locked for analysis. Data from this study will be kept for a period of 15 years in accordance with NHMRC guidelines.

7.6 Results

7.6.1 Demographics

7.6.1.1 Follow-up cohort

Ninety-two children from the original RCT who completed the entire course of treatment were contacted for follow-up appointments. From this cohort of 92 children, 43 children (26 male/17 female) with a median age of 1.0 year (IQR 1.0-6.0 years) (See Table 1-1) returned to the hospital for either: 3 and 6 month follow-ups, 3 month follow-up only, 6 month follow-up only, or returned a photo to the primary investigator via email as shown in the participant return flowchart (Figure 7-2). Of the children who returned, 69.8% were classified acutely as having a superficial partial thickness burn. Two out of four children from the original cohort who received a split-skin graft returned for a follow-up at the hospital and one returned a photo (See Table 7-1). From the 3 to 6 month follow-ups, there was a 48% dropout in participants returning to hospital for review and 70% dropout in photo returns.

7.6.1.2 Did not return cohort

Forty-nine children (27 male/ 22 female) with a median age of 1.0 year (IQR 1.0-3.5 years) did not return for any follow-ups (hospital or photos) (See Table 7-1). This group of children were significantly different to the returned cohort in regards to burn depth (p = 0.03), as a larger number of children with deeper burns returned for follow-ups. There was no significant difference between the remaining baseline characteristics of the two groups.

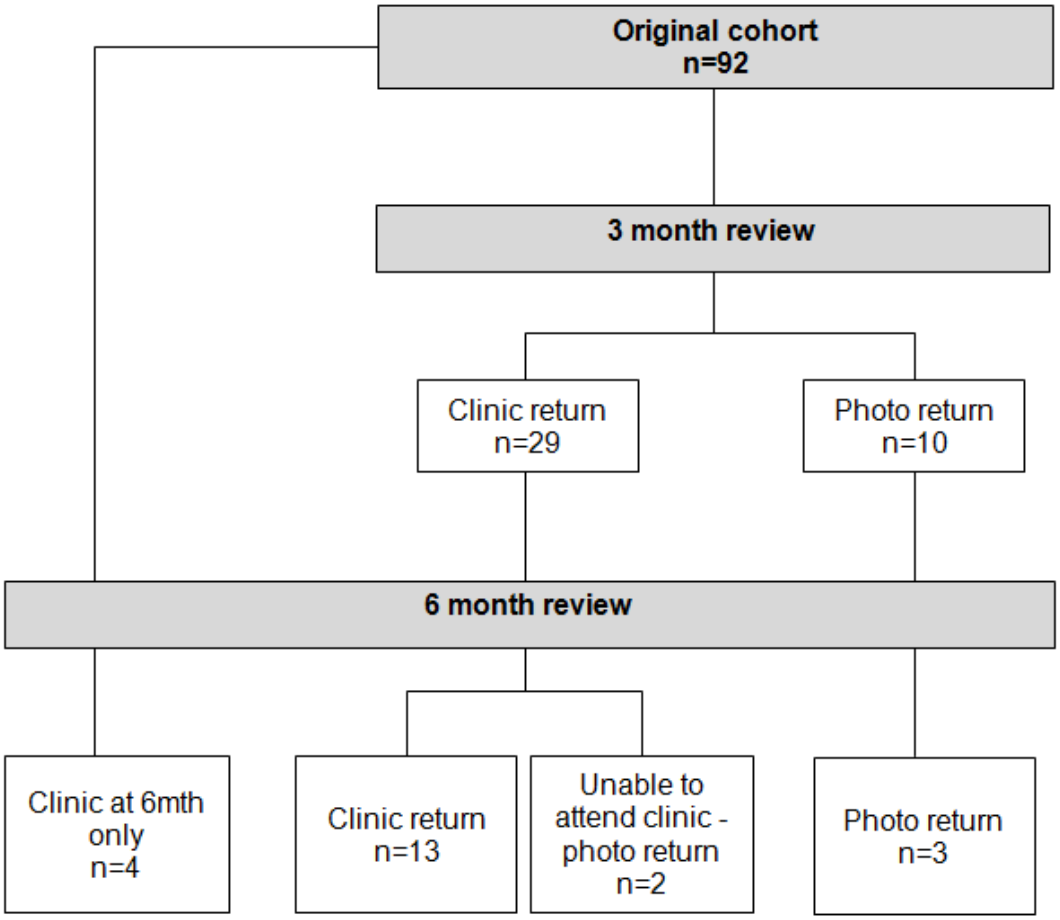

Figure 7-2 Flow chart of participant follow-up numbers

Table 7-1 Demographic characteristics

		Did not return n=49 Median (IQR)	Clinic return n=43 Median (IQR)	*p*-value
Age (years)		1.0 (1.0-3.5)	1.0 (1.0-6.0)	0.13
TBSA (%)		0.5% (0.50-2.50)	1.0% (0.5-2.0%)	0.52
		n (%)	*n* (%)	
Gender	**Male**	27 (55.1)	26 (60.5)	0.60
Burn depth	**Superficial partial only**	43 (87.8)	30 (69.8)	0.03*
	Mixed partial thickness	6 (12.2)	13 (30.2)	
MOI	**Scald**	27 (55.1)	27 (62.8)	0.50
	Contact	20 (40.8)	14 (32.6)	
	Flame	1 (2.0)	1 (2.3)	
	Electrical	1 (2.0)	1 (2.3)	
Residential Postcode	**Metropolitan**	38 (77.6)	38 (88.4)	0.19
	Regional	10 (20.4)	4 (9.3)	
	Different State	1 (2.0)	1 (2.3)	
Wound re-epithelialization time	**<2 weeks**	37 (75.5)	31 (72.1)	0.15
	2-3 weeks	10 (20.4)	7 (16.3)	
	>3 weeks/graft	2 (4.1)	5 (11.6)	
Skin grafts		1	3	

7.6.2 POSAS scores

To account for photo returns where a hospital follow-up was not possible, the POSAS observer section was completed on these photos. To ensure validity of these scores, original burn site photos taken of children who did return for follow-ups were scored on the POSAS observer section again retrospectively. The retrospective observer POSAS scores and original follow-up observer scores were correlated and found to have a high correlation (total scores ICC 0.83, 95% CI: 0.67-0.92; overall opinion scores: ICC 0.87, 95% CI: 0.75-0.94). As a result, observer POSAS scores from the photo returns were included in the overall dataset. Additionally, data from the children who received split skin grafts were identified as outliers and excluded from the analysis.

Median total scores at 3 months were patient: 7.00 (IQR 6.00-11.00) vs. observer: 6.00 (IQR 6.00-8.00). At 6 months the median total scores were patient: 8.00 (IQR 6.00-17.75) vs. observer: 6.50 (IQR 6.00-9.00) Total POSAS scores for patient and observer over 3 and 6 months were analyzed using a Wilcoxon Signed Rank Test. There was no significant difference in any score sets between 3 and 6 months.

7.6.2.1 Predictors of POSAS scores

Total scores (patient and observer) and overall opinion scores (patient and observer) at 3 and 6 months were analyzed using separate multiple linear regression models, where each set of scores (e.g. patient total scores at 3 months) were used as the dependent variable for each model. Days to re-epithelialization, burn depth, total burn surface area (TBSA) and dressing type were identified as having a significant contribution to all POSAS score sets and were included in the models. Due to evidence of multicollinearity between days to re-epithelialization, burn depth and dressing type, only days to re-epithelialization was included in the final models. TBSA was included in the models for scores at 3months, but was not included in 6 month models due to low participant numbers.

As shown in Table 7-2, at 3 months, days to re-epithelialization was a significant predictor of all POSAS total scores (total and overall opinion for both patient and observer) – indicating burns which took longer to re-epithelialize were associated with higher POSAS scores (worse scar outcome). Total body surface area was not a significant predictor in any of the models. At 6 months, days to re-epithelialization was again a significant predictor of all POSAS scores except patient total scores (Table 7-2).

Table 7-2. Predictors of total and overall opinion POSAS scores

		B	95% CI	*p*-value
3 month follow-up				
Patient total score	Days to re-epithelialization	0.97	0.51-1.43	<0.01
	TBSA	1.92	0.04-3.80	<0.05
Patient overall opinion score	Days to re-epithelialization	0.23	0.13-0.34	<0.01
	TBSA	0.38	-0.05-0.80	0.08
Observer total score	Days to re-epithelialization	0.73	0.50-0.95	<0.01
	TBSA	0.50	-0.45-1.45	0.29
Observer overall opinion score	Days to re-epithelialization	0.13	0.08-0.18	<0.01
	TBSA	0.19	-0.01-0.38	0.05
6 month follow-up				
Patient total score	Days to re-epithelialization	0.68	-0.15-1.5	0.10
Patient overall opinion score	Days to re-epithelialization	0.20	0.06-0.34	<0.01
Observer total score	Days to re-epithelialization	0.63	0.34-0.92	<0.01
Observer overall opinion score	Days to re-epithelialization	0.15	0.08-0.21	<0.01

7.6.2.2 Agreement of patient and observer POSAS scores

Patient and observer total and opinion scores were correlated using a Pearson Correlation. At 3 months there was a high correlation of total scores between patient and observer (0.84, p <0.001) and overall opinion scores (0.91, p <0.001). However at 6 months, there was a lower correlation for both total (0.62, p=0.01) and overall opinion scores (0.72, p<0.01). POSAS parameters were separated out (e.g. color, thickness etc) and compared between patient and observer. Scores of patient-rated scar or skin color and observer rated vascularity and pigmentation had a high correlation at 3 months (color vs. vascularity 0.88, p<0.001; color vs. pigmentation 0.64, p<0.001), but had a lower correlation at 6 months (color vs. vascularity 0.57, p<0.05; color vs. pigmentation 0.15, p = 0.60).

7.6.3 Ultrasound

As per the analysis for POSAS scores, data from the children who received split skin grafts were identified as outliers and excluded from the analysis. Median skin thickness of burn sites at 3 months was 1.3mm (IQR 1.2-1.6mm) compared to 1.2mm (IQR 1.1-1.5mm) at 6

months. Comparatively, median skin thickness of unaffected sites at 3 months was 1.1mm (IQR 1.0-1.3mm) and 1.1mm (IQR 0.9-1.1mm) at 6 months. Skin thickness of burn sites was found to be significantly lower at 6 months than at 3 months (p<0.02). The percentage difference in skin thickness between burn site and an unaffected site for each participant was calculated at 3 and 6 months. The median percentage difference in skin thickness at 3 months was 15.38% (IQR 0.00-31.82%) compared to 10.03% (IQR 2.18-35.00%) at 6 months. The percentage difference in skin thickness between burn site and unaffected site was significantly lower at 6 months than at 3 months (p<0.02).

Days to re-epithelialization, burn depth and total body surface area of burn were correlated with percentage difference in skin thickness. Burn depth was found to have a moderate and significant correlation with percentage difference in skin thickness at 3 months (0.41, p<0.05), the correlation at 6 months was not significant. The remaining variables did not have significant correlations with percentage difference in skin thickness. Additionally, there was no significant difference between acute dressing type groups (Acticoat™, Acticoat™ with Mepitel™ and Mepilex Ag™) and percentage difference in skin thickness at 3 or 6 months.

Burn site skin thickness measurements and the POSAS observer-rated thickness parameter were also found to have a high correlation at both 3 (0.59, p<0.01) and 6 months (0.62, p<0.05).

7.6.4 Scar height and skin pigmentation

Due to very low numbers of scar areas to map (as the majority of children had no residual scarring at the original burn site) and software limitations mapping scar areas (e.g. circumferential scar areas), scar height was not calculated.

Photos taken of all participants who returned for follow-up were used to visually assess pigmentation changes over time. Photos indicated that a small proportion (n=8, 25.8%) of children with burns that re-epithelialized in two weeks or less had visible hypo-pigmentation at the burn site compared to normal surrounding skin at 3 months. In some instances, hypo-pigmentation was still visible at 6 months post re-epithelialization. Of these 8 participants, six participants originally had a scald burn and two had a contact burn. The most obvious case of hypopigmentation was observed in a child with very dark skin pigmentation at 3 months (Figure 7-3). Ethnic background and skin color were not assessed at recruitment or follow-up and therefore not considered for their contribution to these results; however this should be included in future studies. In terms of acute dressing, four received the Acticoat™

dressing, one received Acticoat™ with Mepitel™ and one received Mepilex Ag™. There were no incidences of hyper-pigmentation in any participants.

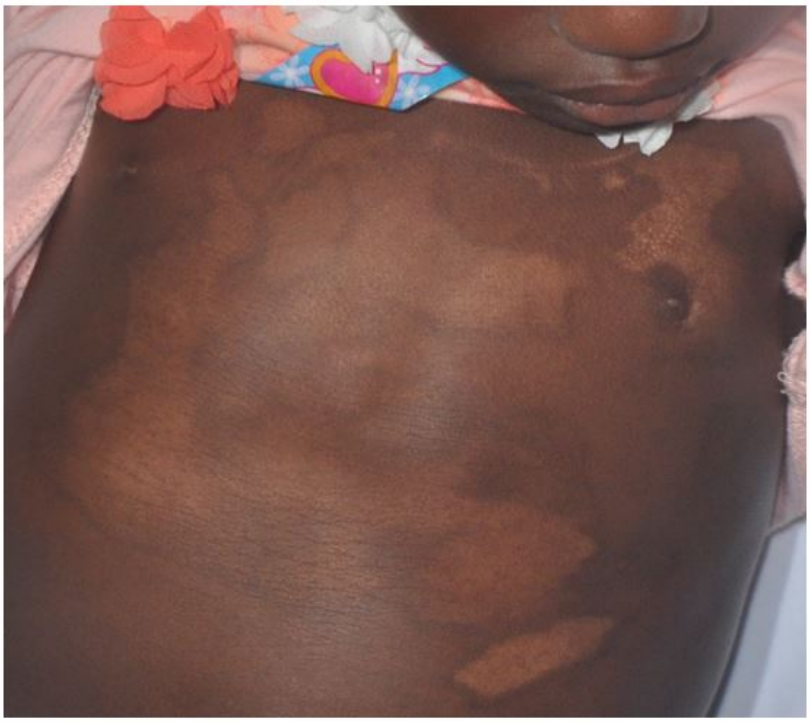

Figure 7-3 Example of burn site hypopigmentation at 3 months in a child with dark skin pigmentation: Scald burn to chest and abdomen which re-epithelialized in 7 days

7.7 Discussion

Small but significant partial thickness burns which re-epithelialize are a common injury for children in high-income countries [42]. While anecdotally there is much known about the scar outcomes of children with partial thickness burns, there is little research available to support such knowledge. The results of this study have demonstrated that time to wound re-epithelialization is predictive of skin or scar quality, while burn depth can impact on skin thickness post-burn injury. Hypo-pigmentation of the burn site can still be present in burn sites up to 6 months, post-injury and patients were found to rate skin appearance as worse than therapists.

While a moderate number of children were able to be followed-up for this study, getting families to return for long-term research post-discharge remains problematic and has been previously highlighted in the literature [20]. For many families in this study, motivation levels to return may have been low as the child was discharged and the burn injury may have been fully resolved (no visible difference). Additionally, arranging time off work was difficult and some families lived regionally or inter-state. These difficulties and large drop-out rates need to be taken into account for future studies. Incidentally, following-up with patients who were

still returning for scar management treatment was more successful and this accounted for the greater number of children with deeper burns returning for a follow-up in this study.

Days to re-epithelialization has been established as a predictor of scar outcome in partial thickness burns at 3 and 6 months post wound re-epithelialization. The relationship between re-epithelialization time and burn scar outcome has previously been reported in the literature [7, 79, 133] and this study has provided current evidence supporting this relationship in children with a range of partial thickness burn injuries. As the majority of children reviewed in this study re-epithelialized in two weeks or less, more in-depth research regarding patients who fall into the grey area of burns which re-epithelialize spontaneously in 2-3 weeks is recommended. Many of these patients go on to receive scar management and are left with residual scarring, while others do not require such therapy. Research into predictors of scar outcome for this cohort would be beneficial and serve to allocate resources and predict treatment needs more effectively.

The BT12 Venue 40 MSK ultrasound (GE Healthcare) has been demonstrated to be simple to use and could be utilized easily and accurately in a busy, hospital environment with small children. Previous research has indicated that ultrasound measured skin thickness (epidermis to dermis) can range from 1.53-1.97mm over a range of body areas in children aged 2-6 years with diabetes and increases with age [134]. The median unaffected skin site thickness in our current study was slightly below this range, however as the majority of children seen were under the age of two years, this fits within the projectory of increasing skin thickness with age. Furthermore, measurements of skin thickness on burn sites had a strong correlation with the POSAS thickness parameter, indicating its potential utility as objective measure of skin thickness in children with burn injuries; however more research is required to validate this. The finding that burn depth is associated with an increase in skin thickness post wound re-epithelialization is consistent with research that there is a greater risk of hypertrophic scar with increasing burn depth [7]. As more robust statistical analyzes could not completed for this current study due to low numbers, further research into the relationship between burn depth and skin thickness with a larger group of children with partial thickness burns would be beneficial to strengthen these results.

It has been demonstrated in this study that hypopigmentation of the burn site can still persist up to or longer than 6 months post re-epithelialization in some children. This finding is despite the general consensus that partial thickness burns in children which re-epithelialize in 2 weeks or less are expected to be resolved by 6 months. Recent research has shown that erythema in donor sites does not fully return to normal until 12 months, indicating that

color changes as a result of partial thickness burns may take longer to resolve in some children than initially thought [135]. Ethnic background and objective skin color measurements was not recorded for this study and such data from future research would further assist in enriching the knowledge of skin pigmentation changes following partial thickness burn injuries in children, particularly those with darker skin pigmentation. This study also noted that parents and patients were scoring higher than therapists on the skin color parameter of the POSAS at 6 months, a finding which is corroborated in previous research [20]. Such findings indicate that clinicians need to be continually aware of patient opinions of skin appearance and that education regarding skin color changes post-burn is imperative, particularly for those who re-epithelialize in 2 weeks or less and do not receive ongoing scar management therapy.

7.8 Conclusion

This study has provided data regarding the long-term scar outcome for children with partial thickness burn injuries and expands the clinical knowledge base for this population. Days to re-epithelialization was identified as a predictor of scar outcome severity. A small proportion (n=8, 25.8%) of children with burns that re-epithelialized in two weeks or less had visible hypo-pigmentation at 3 months and hypopigmentation was still present in some children at 6 months. This study has again demonstrated the discrepancy in opinions of patients and parents and therapists regarding long-term skin appearance and highlighted a further need for education regarding long-term outcomes for patients.

7.9 Acknowledgements

The authors would look to thank all the children and their families who participated in this study. The would also like to acknowledge all the staff at the Stuart Pegg Pediatric Burns Centre at the Royal Children's Hospital Brisbane, Australia for their support and assistance throughout data collection.

7.10 Conflict of Interest Statement

Funding for this study was supplied by a grant given to the Royal Children's Hospital, Brisbane by Mölnlycke Healthcare. Despite this financial support, Mölnlycke Healthcare had no part in the study design and data collection of this project, nor did they have any involvement in the analysis or publication of the results. The chief investigator is a student of The University of Queensland and receives a stipend from this grant.

7.11 Chapter conclusion

The study presented in this chapter has provided an overview of the outcomes of partial thickness burn injuries in children who received a silver dressing acutely.

While the burn injury and changes to skin pigmentation may have resolved completely for some children by six months post wound re-epithelialization, children with darker skin types and burns re-epithelializing in 2-3 weeks may have differing experiences. These children represent a significant proportion of those treated in the outpatient setting. Hence, it is imperative for more research evidence to be obtained for these particular populations of children in order to provide families with accurate education on longer term resolution of such burn injuries.

This study also utilized ultrasound as an objective measure of skin thickness. Traditionally, burn scar thickness is visually and physically assessed using the Patient and Observer Scar Assessment Scale (POSAS). Assessments such as these are widely used but are largely subjective, and ultrasound has the potential to provide an objective quantification of scar thickness. External to this thesis, the clinical utility of the GE Healthcare ultrasound device is currently being assessed in a research study alongside the 3D LifeViz™ system for the objective measurement of burn scars, as stated in the Chapter 5 chapter conclusion. The device is beginning to be utilized clinically in the assessment of burn scars and it is anticipated that the new research study will show ultrasound to be a reliable tool for use in this setting.

While the information obtained from this research has given clinicians some evidence to educate children and their families on longer term outcome post-burn, further research is still required to present a complete picture of pediatric partial thickness burn outcome.

This chapter completes *Part 1* of the thesis. *Part 2* is an exploratory study of the experiences of parents or caregivers supporting a child through burn care in the outpatient setting. This study will be presented as Chapter 8 of this thesis.

Part 2

Chapter 8. Parent experiences of pediatric outpatient burn care

The following chapter is a qualitative exploration of parent experiences of accompanying their child through outpatient burn care. This chapter was not submitted for publication and is presented in this thesis as a stand-alone chapter.

8.1 Introduction

Burn injuries in children are often traumatic involving multiple trips to unfamiliar hospital environments, painful and potentially distressing dressing changes and interactions with numerous staff members as the burn re-epithelializes. Young children and infants who sustain burn injuries are dependent on their parents or caregiver throughout treatment. Parents have the role of supporting the child through wound care procedures and management of the burn at home, but often times also witness the burn accident [21].

Understanding the effect and burden of a child's burn treatment on parent or caregivers is of major importance, given the impact that a parent's experience may have on the child's outcome post-burn injury. For a child who sustains a traumatic, unintentional injury such as a burn, recovery can be affected by both the experience of the parent and child during treatment, as parental stress reactions are known to impact on the child's own reactions to stressful situations [23, 98, 99]. Parents of children who sustain burn injuries have been found to display acute stress reactions related to concerns for their child during the acute treatment phase and longer-term potential psychosocial impacts for the child [136].

Qualitative studies into the experiences of parents of children who sustaining severe burns requiring length hospital stays have shown that many parents experience negative coping reactions such as guilt and blame [22, 102]. Watching their child in pain was particularly distressing and there were reported feelings of hopelessness during hospital stays.

The knowledge of parent experiences of children who sustain severe burns requiring inpatient hospital admission and lengthy rehabilitation has been reported in the literature [22, 102, 137]. However, relatively little is known regarding parents of children who sustain less severe burn injuries which only require outpatient treatment and little to no rehabilitation or scar management therapy. This is despite research evidence demonstrating that post-traumatic stress disorder (PTSD) symptoms in parents may occur as a result of burn injuries of any size and severity [24]. Additionally, research also shows that while many mothers and fathers experience acute stress reactions which can last up to 12 months post-burn but gradually diminish with time, for some parents symptoms can become chronic [138, 139]. As the majority of children in high-income countries sustain burn injuries <10% total body surface area (TBSA) which can be treated in the outpatient setting [6], understanding the burden of minor burn injuries on parents and caregivers can assist in improving the outpatient burn care process.

This study aimed to answer the question: 'What are the experiences of parents accompanying their child through outpatient burn care'? Through answering this question, the study sought to provide healthcare workers with a greater understanding of how to prepare parents for the burn care process and provide appropriate support throughout treatment.

8.2 Methodology

The study was approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee (Approval number: HREC/14/QRCH/8).

8.2.1 Study Design

This was a qualitative study using a phenomological approach which is appropriate for use when a phenomenon is poorly defined [140]. Phenomenology is a person's experience of a phenomenon (i.e. particular situation) and how they make sense of these experiences [134]. A phenomological study therefore aims to examine and analyze people's lived or subjective experiences of the phenomenon [140]. This approach is best suited to small sample sizes (≤10 participants) where larger sample sizes can be difficult to manage.

8.2.2 Participants

Parents and/or caregivers of children aged 0 to 5 years with an acute partial thickness burn injury (re-epithelializing within 2 weeks) and a burn total body surface area (TBSA) of ≤10% were considered for inclusion. Children were required to have been referred to the former Royal Children's Hospital (RCH) or Lady Cilento Children's Hospital (LCCH) burns outpatient unit from the Department of Emergency. The parent must have also been present for all dressing change appointments. Eligible participants were recruited via informed consent between September 2014 and September 2015. Parents and caregivers were excluded if their child had received silver dressings prior to presentation at RCH/LCCH; had sustained a superficial (erythema only), full thickness, chemical or friction burn; had a cognitive impairment; or were currently involved with the Department of Communities, Child Safety and Disability Services. Non-English speaking parents and caregivers were also excluded from the study.

8.2.3 Data collection

Participants were recruited to this study via *purposive sampling*. The aim of purposive or purposeful sampling as defined in Patton [141] is to "select information-rich cases whose study will illuminate the questions under study". Interviews were conducted with parents on the day of their child's discharge from the service, usually the day that the burn wound was

fully re-epithelialized. Semi-structured interviews were conducted using a pre-defined list of prompt questions to ensure a degree of standardization between participants [142] (Table 8-1). Prompting questions were designed to promote open-ended responses to explore participants' experiences and stories and to allow the participant to guide the direction of the interview [142]. Further probing questions were added to the schedule after several interviews were conducted, as data emerged which required further clarification from future participants to determine if a pattern was present.

Interviews were conducted on the outpatient ward either in a private treatment room or available interview room, with a maximum of thirty minutes available for the interview. The timeframe for interviews was set to a maximum of thirty minutes due to: age of children and their patience level after treatment (most parents attended the appointment alone and were without assistance to keep the child occupied during the course of the interview), parent transport restrictions (i.e. hospital parking and cost) and researcher time. All interviews were audio recorded and transcribed verbatim by the principal investigator.

Demographic information was also collected from patients' medical records, including; age of child, burn depth, mechanism of the burn injury, the site of the injury and burn total body surface area.

Table 8-1 Study interview schedule

Interview questions
1. Can you please describe your experience when you first came into emergency?
2. Can you please tell me about your time at the burns outpatients' clinic?
3. Can you please describe your experience of taking part in the first dressing change procedure with your child?
4. What were your thoughts about the dressing and managing it at home?
5. How did you feel about the information you were given while at the clinic?
6. Can you tell me about your experiences in dealing with doctors, nurses and the allied health staff in the burns outpatients' clinic?
7. Parents have mentioned that hearing other children crying or see other children in the waiting room with burn injuries was confronting. How did you feel about this?

8.2.4 Data Analysis

Transcribed interviews were analyzed using an inductive thematic analysis method. The inductive thematic analysis was undertaken according to Braun and Clarke's [143] thematic analysis method: familiarizing self with data, generating initial codes, searching for themes, reviewing themes, defining and naming themes. Coding of interviews was completed by the principal investigator and second rater experienced in qualitative research. Initial line-by-line coding of interviews was completed independently by both raters. Coded data abstracts were compiled under each identified code for each rater and a code definition table was developed which provided a definition for each code. The two raters then came to together and using the definition list, discussed any discrepancies in coding until agreement was reached. Data abstracts were re-compiled (as required where corrections to coding were made) under their relevant codes in a table which was then used to identify themes within the data. All names in data extracts have been replaced with pseudonyms to ensure patient confidentiality. Participant I.D. numbers (e.g. 001) have been used to differentiate between data extracts.

8.3 Results

Data collection and recruitment was ceased when 10 participants were recruited. The aim was to continue recruitment until data saturation of the participant group was reached, however due to time constraints from the principal investigator, recruitment was concluded before it was determined that data saturation was reached. The final sample size is however

acceptable within a phenomological approach to research where small sample sizes of up 10 are most suitable [140].

8.3.1 Demographic characteristics

Ten parents (1 father, 9 mothers) of children with a median age of 1 year (range 1-5 years) participated. Children had superficial partial thickness burns (contact and scald burns) with a median total body surface area (TBSA) of 0.5% (IQR 0.5-2.5%). All burns re-epithelialized within a two week timeframe with a median days to re-epithelialization of 10.5 (IQR 9.75-12.5). Children and parents attended at least two dressing change appointments before discharge.

8.3.2 Themes from the dataset

Analysis of identified codes and data extracts from completed interviews identified three themes and eight subthemes which described the experiences of parents accompanying their child through outpatient burn care treatment (Table 8-2).

Table 8-2 Themes and sub-themes

Theme	Sub-themes
Going into the unknown	Unfamiliarity with hospital environment
	Feeling overwhelmed
	Anticipation of outcome
Facilitation	Familiarity with hospital environment
	Staff support
	Distraction and minimization of pain
Resilience	Guilt and blame
	Short term pain, long term gain

8.3.3 Theme 1: Going into the unknown

The theme ‘going into the unknown’ explained that a major factor in the experiences of parents attending outpatient burn care with their child was not knowing what to expect when it came to burn care or wound healing. Accompanying their child for burn injury treatment was like navigating without a map and triggered feelings of anxiety and fear. This theme comprises of the subthemes: unfamiliarity with the hospital environment, anticipation of outcome and feeling overwhelmed.

8.3.3.1 Unfamiliarity with hospital environment

For many, being unfamiliar with the hospital environment and the process of care in the outpatient burns setting was anxiety-provoking and stressful. One parent described hearing other children crying and she became worried about what her child would experience during the dressing change:

> *Oh I was really scared. Like, yeah how it was going to be ‘cause I could hear all the little ones crying. Like you know, how it was going to come off, I just thought what was it going to look like underneath? Um, yeah just yeah was I wasn’t sure how they were going to get it off and things like that. (004)*

Others parents expressed uncertainty about the length of time a dressing change would take and whether/how they could keep their child occupied for an extended period of time.

> *Um, though I guess coming in as a first time, you don’t know what’s going to happen, you don’t know if there’s toys already in the room or how long you’re going to be waiting or anything like that. (009)*

Parents were also unaware of the processes surrounding pain medication protocols in the outpatient setting and waiting times required for medication to have an effect. This provoked feelings of impatience and the notion that the experience was being unnecessarily prolonged for the child:

> *Erm, last, last time we came they gave him um, painkiller, strong painkiller, and um we were waiting around half an hour, 40 mins. I think it was too much, but no, no I know it’s hospital and they all busy, but nah it just…I thought perhaps too long a wait because he is small and he gets bored or he wants to get out of here. (001)*

8.3.3.2 Anticipation of outcome

The wound healing process and final outcome from a burn injury was particularly concerning for parents. The healing process and what this looks like at each stage was not prior

knowledge for parents and this often meant parents jumped to the worst possible outcome e.g. skin grafting, despite burns being relatively minor.

> *I was more concerned of the fact that, the second time we came in, they were really not happy with his healing process on the shoulder. And they said if this doesn't heal in another week or so, we're going to have to do a skin graft. That actually scared my husband and I. A lot. Because it's like well you have to cut another part of his body, scar that, to fix another part. (007)*

> *I was anxious, I didn't want him to have a skin graft and uh he healed so quickly, so it was great. (003)*

Not knowing what a burn wound looked like as it healed also made it difficult for parents to distinguish progress themselves and this provoked some uncertainty going into dressing changes about whether the burn would be healed or not.

> *It was probably actually harder today, where they were saying they're hoping it's healed, and they took it off and I didn't know if it looked healed or not. (009)*

8.3.3.3 Feeling overwhelmed

Coping with the hospital visits in an unfamiliar environment and sometimes watching their child in pain was particularly difficult for parents. One father described that while he was able to deal with the situation and handle his emotions, his wife had a significantly harder time and was unable to provide support and comfort to her child during treatment as a result:

> *Sarah sort of like can't really, she doesn't really want to go into that side of things, you know? Because you know I know it has to be done, and I can hold it in a little bit and sort of deal with that kind of stuff. But yeah, Sarah just, yeah, as soon she would have to hold her down and watch her bawl her eyes out, she'd be right beside her bawling her eyes out, you know what I mean. (005)*

Another parent described the feeling of having to constantly explain the burn incident and how this negatively affected her ability to stay calm at the time for her child and provide support.

> *The one thing probably, that I did take a little bit to heart, was um when the accident first happened, I think I got asked maybe 10 times what happened. And like, at the time, I was just really upset because I was like, God, I just want to focus on him, I don't want to be, why do I have to keep repeating myself? But afterwards, I understand why they want make sure there's no abuse or whatever there. And I*

understand that. But at the time, I was like, can you just leave me alone? I want to like, just focus on my baby! (007)

8.3.4 Theme 2: Facilitation

The theme 'facilitation' explores aspects of the burn treatment that parents perceived enabled them to cope with the experience and improved their ability to appropriately support their child through the treatment. This theme encapsulates subthemes of: familiarity with the hospital environment, staff support and distraction and minimization of pain.

8.3.4.1 Familiarity with the hospital environment

In contrast to theme 1, parents found that having prior knowledge of the hospital and hospital processes made them feel much more at ease and as a result were less stressed coming in for a dressing change in the burns unit the first time around. Familiarity with the process was represented in various ways. For some, having prior knowledge of hospital processes due to their work background or having other children sustain injuries requiring hospital treatment made the experience easier knowing what was involved. One parent commented:

I guess I've got a pseudo-health background, I've worked around hospitals, so, and I've had kids who've had to come into Emergency before, so I don't think I'm particularly easily ruffled by that kind of thing, so no I didn't find it particularly stressful. (009)

Having friends who had gone through similar experiences also provided background knowledge regarding the outpatient burn care process:

And we did have a friend who is in her music group who did a similar thing two weeks before her, so we had a bit of heads up on what the actual process was. (010)

Knowledge of basic skin physiology also made understanding the burn wound healing process easier for a parent dealing with a chronic skin condition in another child:

I've got one who's got atopic eczema, so, the whole system of the skin, we were right on, aware of that. Like I said, we've spent a lot of time with skin conditions and hospitals and in and out. So yeah. So we've been through it. We go through two different clinics. That for us, hasn't been an issue. (008)

8.3.4.2 Staff support

Support from clinical staff and volunteers was recognized as playing a large part in positively assisting parent coping throughout the treatment phase. Many parents expressed gratitude for the hospital volunteer service which provides staff to help parents navigate the hospital

and to engage with children and their families in the clinic waiting room. Keeping the child occupied and calm with fun activities and engaging with parents helped to alleviate parent anxiety waiting for the appointment:

> *But overall, um, like today there's volunteers out there and they came and played with Zac. And I think that's really nice. It's really nice for um, break up, not break the ice, but something a little bit different for the parents to change their focus, you know. They were quite friendly. (007)*

Parents also described the benefit of the volunteer service for siblings of the child who also had to attend the appointment and could witness treatment and dressing changes. The volunteer service allowed parents to concentrate and focus on the child with the injury without the stress of also supervising siblings:

> *Especially, the um, one thing I really like is the volunteer service here. There was another volunteer here and she helped keep the eldest occupied, with coloring. Part of it is. Um, not just about keeping the um the patient happy, it's about keeping the siblings happy as well. Because they can feel the parents and their siblings pain and worry. So to keep them occupied with toys and volunteers to help them, to play with them, it's just a great service. That took part of the stress away, because the parents could concentrate on Max and that helped a lot. (006)*

Putting trust in the treating clinicians ameliorated feelings of anxiety that parents may have had about what the treatment would entail. Parents acknowledged that witnessing the care provided to their child, and observing improvements that indicated that their child was getting better, reduced stress levels coming into appointments. One parent reported:

> *There was a lot of attention on him, which I think is good. Um, uh and you feel that the doctors and nurses know what they're doing and you can feel their confidence in treating Max. And that made us feel good. (006)*

Another parent commented on staff demeanor towards her child and herself and the positive affect it had on the treatment experience:

> *And the nurse that helped Zac both times, there was two different ones, but we saw them both often. Both of those ladies were really lovely with Zac and really gentle with him and patient. Um, everyone's polite, everyone's not rushing to be rid of you, but at the same time not making you wait too long. I've had a very good experience and I think has Zac has too, because he hasn't cried. (007)*

8.3.4.3 Distraction and minimization of pain

Having a child that was distracted from the burn injury and not in pain was particularly positive for parents as they did not want to see their child in distress during treatment:

> *Um it was ok, because he wasn't bothered by it. You know, it didn't phase him. I think if he was crying or showing agitation or something, I think I would have had to have left the room. (007)*

Many parents described the perceived instantaneous ability of the burns dressings to decrease distress levels and allow the child to return to a pre-burn functioning level. This was seen as an encouraging sign of recovery for the child:

> *So, and no but it was as if nothing had happened to him, so the dressings are great. They cover it up and it's like magic. He didn't even realize it because after they put the dressing on it was as if nothing had had happened to him. He was running around and playing. (001)*

> *Um, he was very distressed a bit, about having to have the dressings changed, that's the bit that distressed him. But once they done it and put it on, he was fine again. (008)*

Parents also reported the benefit of having items such as toys for children to play with during treatment, as this gave the child a sense of normalcy within the process, and a different line of focus away from the burn injury.

> *What great is though, you have toys. Thomas, this case is distracted and has new things to do and is fun for him, and that's great for us. Because it was sometime, we could, we could distract him about his burn no? (001)*

8.3.5 Theme 3: Resilience

The theme 'resilience' explains the impact the burn injury had on reflection of parenting styles and supervision parents provided to their child. It also encompasses parent acceptance of the injury and persevering through feelings of shame for the sake of their child's wellbeing. This theme is comprised of the subthemes: 'guilt and blame' and 'short term pain, long term gain'.

8.3.5.1 Guilt and blame

Parents described disbelief that the accident had occurred and feelings of guilt for not being able to prevent it happening or protect their child. Some parents commented that guilt over the accident (despite the child having a good outcome) would persist indefinitely:

Yeah, you don't think, it, it something like this would happen to you. So, you take all the precautions, still accidents happen. Yes, and part of, I think part of it is feeling really bad that you couldn't protect him from such an accident. Yeah, that guilt will always be there. (006)

*To tell you the truth, I just, I feel like crying now even. I just feel so awful because the cup was right beside me, you know? And I didn't see it *crying*. It was fast. Yeah, you don't want your kids hurt though. You spend so much time trying to protect them all the time and take care of them and I don't know. A few tears, because you know, why does it have to be this way, why does he have to go through that? (007)*

Having to then watch their child in distress while going through treatment further amplified these emotions. One parent described an experience with the burns bath as particularly distressing:

And then the hardest thing for me was having to hold her down in the bath. You know like, you feel like you're letting the kid down, you know when you're sitting there and she's absolutely bawling her eyes out, screaming at you and you can't do anything about it because you know it's the best thing for her cause they're rubbing all the dead skin and all that off. So you have sit there and hold her down in the bath. Not anything I'd wish upon anyone, you know what I mean, having them look at you like that. (005)

8.3.5.2 Short term pain, long term gain

Despite experiencing reactions of guilt over the burn accident, parents spoke of putting on a strong front and pushing their personal feelings aside for the benefit of their child and their recovery:

So yeah like, for me it's, it's not, when I know it's going to benefit her in the long run, I'll do whatever is necessary or whatever they want me to do you know (005)

Parents also commented on acceptance of the injury and not being held back by what may happen and just taking things on as they occurred:

I thought right, we'll just deal with it. If it's worse than what we think it is, we'll just deal with it one step at a time. (008)

Looking back on their experiences of accompanying their child through outpatient burn care gave parents perspective and the realization that things will work out for the best in the long run and that patience and optimism are key:

So, yeah, just that you don't have to stress about it and you can just trust that it will happen even if you have to wait for things to happen. You just don't need to stress about it. (009)

Oh, just be positive and be patient. As well as be confident in what the nurse and that are doing, because in the long run it's always going to be beneficial for your child. You've just got to keep a positive attitude. (005)

8.4 Discussion

This was a pilot study exploring the experiences of parents accompanying their child through burn care treatment in the outpatient setting. The majority of parents identified major stressors related to their experience as being unprepared for the challenges and processes of pediatric outpatient burn care, watching their child in pain or distress and persisting feelings of guilt over the burn accident. Despite this, many also commented on aspects of care, such as support from staff members and prior hospital experiences and knowledge that assisted them to cope and persevere through the treatment phase towards recovery.

Many parents in this study commented on feeling unprepared bringing their child in for outpatient treatment and uncertain of what the process would entail. Associated anxiety regarding the long-term outcome for their child, stemming from a lack of prior knowledge of burn injury severity, was also present for parents. Such concerns were also identified in previous research on the burden of parents from a child's severe burn injury [22, 102] as for many parents with a young child, the burn injury was often the first hospital visit and parents were largely ill-equipped for the stressful hospital environment. The research by Rimmer et.al [102] also identified that educational tools for parents on aspects of acute pediatric burn care may be of benefit to alleviate parent stress and anxiety. In Australia, the Ditto multimodal device provides a procedural preparation story 'Bobby got a burn' for children with burn injuries [47]. Parent experiences from this study would also indicate that the formulation of a parent education tool which can be used in the waiting room prior to the appointment, or an education package given on referral to the burns outpatient clinic would be beneficial in assisting to decrease parent anxiety and increase knowledge of burn care.

Watching their child in pain or distress was identified as a stressor for parents and amplified feelings of guilt over the burn accident. Parents reported feeling overwhelmed during dressing changes, particularly when children had to be physically constrained, which for some affected their ability to appropriately support their child during this time. Similar parental experiences have also been identified in children with severe burns requiring

inpatient hospitalization [22, 102]. Research suggests that effective pain relief for children undergoing dressing changes can consequently help to improve parent distress [144]. A study investigating pediatric pain management for invasive procedures has also found that including parents within the procedure and in distraction of the child may not only improve patient pain levels, but allow parents to feel included and helpful in the process [145]. Such strategies may be of use in the outpatient setting to support the parent and child through dressing changes.

Parent resilience throughout their child's treatment was a prominent theme. Despite persisting guilt over the burn accident, parents reported accepting the accident and staying strong for the benefit of their child's recovery, which is again consistent with parental reports of severe burn injuries [22, 102]. Preliminary research into the resilience of pediatric burn survivors and resilience in their caregivers concluded that they were correlated, with a child's positive adjustment and well-being post-burn being affected by the psychological responses of the caregiver [146]. This again ties in with the knowledge that parent stress reactions can affect the child's own reactions to a burn or traumatic injury [23, 98, 99].

While the experiences of parents with children who sustain severe burns may be prolonged and involve different hospital procedures compared to children sustaining minor burns, this study has demonstrated that all burn injuries in children are distressing regardless of severity. These study findings highlight the continued need for appropriate support for all parents of children with a burn injury, regardless of burn severity. In this setting, social work and occupational therapy psychosocial support is provided to all families if required. It is possible however, that some families may fall through the cracks or are missed during outpatient appointments. Therefore informing all parents prior to appointments where and how they can request support and counseling may ensure that all families get the assistance they need.

8.4.1 Limitations

While this qualitative exploration has provided a wealth of information regarding the experiences of parents in this setting of burn care, it is considered that data saturation may yet to be reached. The continued collection of interview data until saturation would allow for further exploration of the identified themes or identification of new themes which may be a better fit for the data. In addition to this, re-interviewing participants or discussing study results with a new set of participants would allow investigators to check the accuracy of the data interpretation and determine if the results are representative of the views of the whole parent population within this acute, burn care setting.

The sample of this study was limited due to the inclusion of one father to nine mothers. This may have skewed the sample as in the interview data, a father's view may be different to that of the mother. The father in this study also reflected on gender differences in how he and his wife viewed and reacted to the situation. While the views of fathers are important in this setting, future research would benefit from differentiating between parent gender and how they cope with the hospitalisation of their child post-burn injury.

Interview timing may have been a limiting factor as parents were interviewed on the day of discharge in the hospital environment. As previous research has noted [136], interviewees are likely able to process and understand their experiences more effectively when interviews are timed to occur up to a month post-discharge or completion of treatment. However, given the difficulties experienced with getting discharged participants to return for follow-up in the scar assessment phase of this thesis (Chapter 7), the decision was made to interview parents on day of discharge to ensure a more successful capture rate due to study time constraints.

8.5 Conclusion

This study has provided an understanding and insight into the experiences of parents accompanying their child through acute, outpatient burn care for minor burn injuries. Further data collection and analysis is required to confirm study results, however parent reported experiences of feeling unprepared for treatment, distress and guilt watching a child go through treatment and resilience were consistent with experiences of parents of children who sustain burn injuries of a greater severity. Educational tools and parent psychosocial support may assist in alleviating parent anxiety and stress attending dressing change appointments for the first time.

Chapter 9. Discussion

9.1 Thesis rationale

The aim of this thesis was to provide a holistic and comprehensive overview of pediatric partial thickness burn care in the outpatient setting. There are significant gaps in the research literature pertaining to pediatric partial thickness burns, despite these being the most prevalent types of burns in children. Therefore, this thesis was split into two parts to address the treatment and expected outcomes of partial thickness burn care and to explore the psychosocial impact of burn injury and care on parents.

The research outcomes from this body of work have formed a more complete picture of pediatric partial thickness burn care, informed and changed clinical practice within Queensland and identified area for future research in this field.

9.2 Main findings of thesis

9.2.1 Pediatric partial thickness burn treatment

This thesis included one of the first randomized controlled trial studies comparing silver-impregnated fabric dressings for partial thickness burns ≤10% TBSA in children (age range: 4 months - 15 years). Silver dressings are commonly used to treat pediatric partial thickness burns in Australia and New Zealand. However, previous research in this area has made it difficult to distinguish the most appropriate dressing for use in these children as the majority of studies investigating silver dressings: compared silver-impregnated fabric dressings to silver sulfadiazine cream (SSD); combined adult and pediatric populations; and had flaws in methodology [17, 73].

Due to the paucity of evidence for pediatric dressing treatment protocols, no two pediatric burn centers in Australia and New Zealand utilize the same protocol.

9.2.1.1 Silver dressings

The randomized controlled trial found that children treated with the Acticoat™ dressing, had wound re-epithelialization time extended by 40% ($p < 0.01$) compared to those treated with Mepilex Ag™. Similarly, for those treated with Acticoat™ with Mepitel™, wound re-epithelialization time was extended by 33% ($p<0.01$) compared to Mepilex Ag™.

Pain and distress levels in the study were measured using patient (Faces Pain Scale-Revised and Visual Analogue Scale-Pain), parent (Visual Analogue Scale-Pain) and nurse-report (FLACC) pain scales. The study found that in comparison to those treated with Acticoat, FLACC scores were significantly lower at dressing removal and dressing application for children treated with both Mepilex Ag™ and Acticoat™ with Mepitel™. The VAS-P data showed similar results, with children in the Mepilex Ag™ and Acticoat™ with

Mepitel™ groups recording significantly lower scores at dressing removal and application than those treated with Acticoat™. Data from the Faces Pain Scale were not analyzed in the study due to the limited number of participants who could use this scale (as the majority were under the age of three years).

Acticoat™ alone was shown to be difficult to remove due to adherence to the wound bed, which in some cases caused bleeding on removal. These study results have indicated the importance of using dressings with non-stick interfaces such as silicone for pediatric patients, as they have been demonstrated to reduce pain on dressing removal and application and promote ease of dressing removal.

Overall, this trial found that Mepilex Ag™ is a more effective dressing compared to Acticoat™ and Acticoat™ with Mepitel™ with regards to days to re-epithelialization and pain for partial thickness burns ≤10% TBSA in children aged 0-15 years when dressings are changed twice-weekly. It has however, also highlighted that this dressing in its current form is difficult to apply to the small hands and feet of children under the age of three years. The thickness of the foam renders it a challenge to conform to fingers and toes and results in unnecessary dressing bulk and a potentially lengthy dressing application for a distressed infant. To account for this limitation, the newly developed dressing protocol (see 9.4.1) has included the option of either Mepilex Ag™ or Acticoat™ with Mepitel™ for hands and feet of children less than three years, depending on which is clinically determined by nursing staff to be easier to apply for each individual child. This has clinical implications for these children who may receive Acticoat™ with Mepitel™ as highlighted in Chapter 4 (in terms of re-epithelialization time), but will however limit the possibility of children requiring extra visits to hospital to fix dressings which become loose.

9.2.1.2 Cost-analysis

Identifying effective treatments is necessary in determining which to use, however, cost to the healthcare system is also of prime importance. Cost-analyses of silver dressings in the pediatric population are required to allow healthcare providers to make a well-informed decision. Despite this, true cost-effective analyses in burn care are lacking, with the majority of studies only conducting basic cost comparisons [18] and there is presently with no published study comparing silver dressings in the pediatric outpatient setting. Therefore a cost-effectiveness analysis of the silver dressings: Mepilex Ag™, Acticoat™ and Acticoat™ with Mepitel™ was conducted in conjunction with the RCT.

The economic evaluation completed for this thesis found the cost-saving per participant from use of Mepilex Ag™ was $95.19 (95% CI: $46.67, $142.99) in comparison to Acticoat™ and $74.80 (95% CI: $30.19, $122.60) in comparison to Acticoat™ with Mepitel™. There was a 99% and 97% probability that Mepilex Ag™ dominated (was cheaper and more effective) than Acticoat™ and Acticoat™ with Mepitel™.

The results from this cost-analysis further solidified the findings from the RCT, showing Mepilex Ag™ to be not only a more effective, but also less expensive dressing choice than Acticoat™ and Acticoat™ with Mepitel™. The use of Mepilex Ag™ clinically for pediatric partial thickness burns ≤10% TBSA will improve re-epithelialization times for patients (and decrease the risk of hypertrophic scarring), decrease pain during dressing changes and be a less expensive option than the current standard treatment.

9.2.2 Objective measurement of burn wound characteristics

Objective measurement of burn wound re-epithelialization is imperative for research studies to document progress. Mapping of burn wounds has previously been completed using digital planimetry (Visitrak™ device) which involved placing a plastic grid in contact with an exposed wound and tracing the wound border. While this has been found to be a reliable method of measurement, it can be difficult to utilize in the pediatric burns population, where the majority of children are under the age of three years and compliance is not always guaranteed. A wound measurement device which involves no contact with the wound bed such as stereophotogrammetry (3D photography), would be preferable in the pediatric burns population.

Chapter 4 of this thesis assessed the reliability of 3D photography compared to Visitrak™ for the mapping of burn wounds at the first dressing change for children recruited into the RCT. Wound surface area measurements were able to be completed using both devices for 76 out of 96 participants. The level of agreement between wound surface area measurements calculated using an intra-class correlation coefficient (ICC) was excellent (ICC 0.96, 95% CI 0.93, 0.97), indicating that although the 3D camera was not touching the skin surface, it was still able to give an accurate measure of wound area.

An interesting finding from this study was that Visitrak™ tracings could not be completed in 19 participants, with 16 of those aged less than two years. Barriers to completing Visitrak tracings were identified as: excessive movement from the child, pain, young age and wound location. 3D photography could not be completed for one participant only due to the location of the wound (perineum). These results, along with the lack of laser Doppler scans

completed successfully in the RCT (due to similar patient compliance issues) have emphasized the importance of the use of fast, non-invasive tools in the pediatric burns population. Objective measurements of burn characteristics are vitally important to ensure the collection of accurate and unbiased research data. Research from this thesis has demonstrated that for these to be successful however, care needs to be taken to select appropriate tools and devices which will minimize unnecessary distress to the child.

9.2.3 Partial thickness burn scar outcome

The long-term scar outcome from pediatric partial thickness burns is largely under-researched, with literature on long-term burn scar outcome focused on more severe burns. Clinically, children with partial thickness burns which re-epithelialize in two weeks or less are discharged without scar management, with complete resolution of the burn expected within six months. Research has shown the scar maturation pattern of partial thickness burns to be different to full thickness burns [20], however there is no comprehensive and objective assessment of long term outcome of partial thickness burns in children.

Chapter 6 of this thesis provided insight into the scar outcome for children who sustain partial thickness burns ≤10% TBSA. Results demonstrated that days to re-epithelialization was a significant predictor of scar quality at 3 and 6 months post full re-epithelialization, with burns taking longer to re-epithelialize having a worse outcome. This was finding was as expected, with previous literature stating that prolonged re-epithelialization time increases the risk of hypertrophic scarring [7, 79]. Hypopigmentation of the burn site was present in 25.8% of children with a burn re-epithelializing in 2 weeks or less at 3 months post-burn re-epithelialization. This color difference was most evident in children with darker skin types. It was beyond the realm of this study to determine the exact time for skin color to return post-burn for children with darker skin types, but results suggest it is longer than the 6 month statement commonly used clinically and warrants further investigation. Given this preliminary finding, education provided to patients and parents on discharge regarding the timeframe for skin color changes should be also be reviewed.

Lastly, patients and parents were shown to be rating scars comparably to therapists at 3 months, but at 6 months were rating scars as worse compared to therapists. This was despite many burns assessed by therapists to have returned to a normal skin appearance by this timepoint. Such results indicated that partial thickness burns, although temporary in their appearance, may still have a psychosocial impact even after resolution and that clinicians should be aware of this and provide appropriate education to patients and parents.

9.2.4 Parent experiences of outpatient burn care

The experiences of parents overarch the entire process of pediatric burn care treatment and outcome with many children of a young age and therefore reliant on parent support throughout care. Similarly to the other facets of burn care presented in this thesis, the parent experience of pediatric outpatient burn care (at the lower end of severity) is under-represented in the literature. In the literature, studies relating to parent experiences are restricted to children sustaining severe burns or other traumatic injuries requiring lengthy inpatient hospitalization.

The pilot study presented in this thesis used a phenomological approach to explore the experiences of parents accompanying their child through outpatient burn care. Themes identified in this study appear to be consistent with the experiences of parents with children who sustain severe burn injuries. Parents reported feeling unprepared for the burn care process due to being unfamiliar with the hospital and a lack of prior knowledge of burn injuries. Persistent guilt over the accident and an inability to protect their child was described by parents. However, factors such as staff support and being prepared for the burn care process, facilitated parent's ability to cope and provide support for their child as they recovered.

This study highlighted that burns, regardless of the size or severity are distressing for parents and the burn care process can be a daunting one. These results have also emphasized that psychosocial support for parents of children with partial thickness burns is just as important for those with more severe injuries. As is well documented in the literature, post-traumatic stress disorder (PTSD) in parents does not discriminate across burn size and can occur in parents of children with relatively minor injuries.

Education for parents on the outpatient burn care process and information on basic burn wound healing processes and long-term scar outcome progression is therefore required. Such educational strategies could seek to alleviate stress and prevent the development of PTSD symptoms which may result in longer term mental health issues for parents and children post burn-recovery.

9.3 Research limitations

9.3.1 Objective measurement of burn characteristics

This body of work was not without limitations. A major challenge within this pediatric population is compliance during wound care procedures in children under the age of three years. In this thesis, a number of laser Doppler scans and Visitrak™ measurements were

unable to be completed in many children aged three years or less due to the need for the child to remain still while the wound was exposed. While wound surface area measurement using 3D photography has been shown to be a reliable and non-invasive alternative to Visitrak™, laser Doppler remains the only device for objectively assessing the healing potential of burns. The laser Doppler line scanner is a recent development which has a four second scan time in comparison to the 30 second scan of the laser Doppler used in this study. Using this new device in future studies may improve the total capture rate of objective burn wound healing potential data, reduce the time for the wound to be exposed and subsequent child distress may also be alleviated.

9.3.2 Patient follow-up

This thesis has also highlighted the difficulty following up patients and their families post-discharge, many months after the original injury. Attrition rates in Chapter 6 (scar assessment) of the thesis were close to 50% and this increased at the six month follow-up time point. Due to low numbers of patients returning for follow-ups, rigorous statistical analyses could not be completed. Families participating in this research were often unable to attend follow-up visits due to having to arrange time off school and work, limited transport options or living regionally, rurally or interstate. Appropriate study designs should also be formulated to account for potentially large losses to follow-up, such as increasing sample sizes to account for attrition.

9.3.3 Cost-analysis

The cost-analysis study presented in chapter 5, while presenting favorable results towards Mepilex Ag™, was limited due to no patients in the Mepilex Ag™ group in the RCT having received a skin graft which may have skewed the data. However, sensitivity analyses were included in the analysis, removing skin graft data from the total dataset, with Mepilex Ag™ still shown to be a dominant choice.

9.3.4 Qualitative study design

Lastly, the qualitative chapter 7 presented the experiences of parents accompanying their child through outpatient burn care treatment. Due to time constraints, recruitment for this study was concluded at 10 participants. However after data analysis, it appeared that data saturation may not have been reached. Therefore further interviews with parents may be required to confirm identified themes in the data or the identification of new themes. Furthermore, results from this study were not taken back to the study population to gauge if the conclusions drawn were accurate and representative of the general views of all parents. Completing this step in future research will serve to strengthen and validate the final results.

9.4 Clinical implications and recommendations

9.4.1 Randomized controlled trial and cost-effective analysis

The favorable outcome for Mepilex Ag™ presented from the randomized controlled trial in Chapter 3 and associated cost-analysis in Chapter 5 has resulted in the development of a new treatment protocol for pediatric partial thickness burns (See Appendix 7). The protocol recommends a change from Acticoat™ and Mepitel™ as the standard dressing choice for partial thickness burns ≤10% TBSA to Mepilex Ag™. This new protocol has subsequently altered clinical practice within Lady Cilento Children's Hospital (LCCH), since December 2014. As LCCH is the main tertiary pediatric burns center in Queensland, this change to clinical practice has been state-wide, with the new protocol available online via the Queensland Health QHEPS staff portal and accessible to all clinicians. It has also been made available online to nurses via the International College of Emergency Nurses website. In addition to these changes in Queensland, this research has been presented to clinicians at a national and international burns and emergency nursing conferences and has been taken up in some Australian and New Zealand pediatric centers (Melbourne and Middlemore, NZ).

The randomized controlled trial results have also instigated the development of upcoming statewide (QLD) education sessions on the new protocol to educate staff who may manage patients regionally or treat and refer patients to LCCH. Education sessions will be presented by Pegg Leditschke Children's Burns Centre staff and will be held in major regional hospitals of Queensland (southern, central and far north Queensland) and surrounding regional and rural hospitals will be able to attend via teleconferencing. It is anticipated that these sessions may extend interstate to inform as many clinicians as possible in the near future.

9.4.2 Objective measures

Results from this thesis have also prompted the use of 3D photography instead of Visitrak™ in all clinical trials conducted in the center measuring wound surface area. This change of practice will allow for an increased compliance in assessing of wound area and it has the added benefit of the associated Dermapix™ program allowing the storage of progressive wound photographs to track wound healing over time. The 3D camera is now also used clinically for burn wound mapping and chronic wounds (e.g. pressure areas and ulcerating hemangiomas). As an adjunct to the research completed for this thesis, I have also been extensively involved in establishing the clinical utility of the 3D camera to measure burn scar and infantile hemangioma height and volume and ultrasound to measure scar thickness.

These two devices are now utilized clinically in scar management and vascular anomaly clinics.

9.4.3 Psychosocial support and education

The research presented in Chapters 6 and 7 regarding partial thickness burn outcome and parent experiences has highlighted that patient and parent education on the burn healing process and outpatient care processes is needed. It is recommended as a result of research findings presented in this thesis that an educational tool be developed that could be given to parents new to the burns unit (e.g. on referral or in the waiting room). Such a tool (e.g. procedural preparation video, handout) would cover the outpatient burn care process (e.g. what to expect, what to bring, waiting times etc) and basic information on burn wounds and scarring. Psychosocial support should also be continued to be given to all parents regardless of burn severity as burn care has been shown be distressing for all parents. Given the possibility that some families may not initially appear to require referral for psychosocial support during burn wound care appointments or may not be seen by psychosocial service providers, including information on where to seek support in the educational tool would be of great benefit. Parent experiences already reported in thesis demonstrate that it is likely that such a resource would benefit all parents and potentially alleviate feelings of anxiety and fear when coming to appointments.

9.5 Future directions

This thesis has provided a wealth of information regarding pediatric partial thickness burn care, however more information is still required to completely understand pediatric partial thickness burn care.

9.5.1 Pediatric partial thickness burn research

Further high level research on pediatric, partial thickness burns is required to improve health outcomes for this population of children. As was highlighted in this thesis, research on pediatric partial thickness burns ≤10% TBSA is low in comparison to severe burns despite this being the main type of pediatric burn seen in high-income countries. The replication of research in this thesis in an adult population would also be of interest to compare differences and similarities between the population groups.

9.5.2 Silver dressings

This thesis included one of the first randomized controlled trials to compare silver dressings in the pediatric population. While the dressings used for the trial are commonly used in Australia and New Zealand, there are other silver dressings available which are used in other parts of the world e.g. Aquacel Ag® or Mepilex Ag™ Transfer. It would be extremely

beneficial to continue the comparison of silver dressings by including all currently available dressings to determine if there is a superior dressing for children. Again, research on the efficacy of silver dressings for the adult population is required to determine the best dressing for this population, as the two populations are distinctly different in the challenges they present.

Also of interest is the necessity of silver to treat clean, ≤10% TBSA partial thickness burns in children. Future research into the bacteriology of burn wounds treated with silver dressings compared to non-silver dressings would be important to determine the efficacy of silver treatments. Furthermore, the cytotoxicity and antimicrobial properties of silver dressings (fabric, foam, hydrofibre and alginate) on various gram positive and negative bacteria would be beneficial for clinical decision-making. The Centre for Children's Burns and Trauma Research laboratory team is currently in the process of testing the cytotoxicity of silver dressings compared in this thesis.

There is also a preference from some consultants to prolong time between dressing changes for up to seven days to in order to minimize the disruption to the wound and child. Given that Mepilex Ag™ is indicated to be changed every 5-7 days and Acticoat 7™ can be changed weekly, conducting a similar RCT with less frequent dressing changes would be valuable in determining if longer times between dressing changes affects re-epithelialization time due to less disturbance of the wound. If dressings can be changed once a week compared to twice weekly this may also be a more cost-effective option for the healthcare system as less resources are being utilized. Additionally, it is recommended that future cost-analyses of burns treatments collect health-related quality of life measurements to undertake more rigorous cost-utility analyses and use a societal perspective to take into account the financial burden on families.

9.5.3 Objective measures

As was highlighted in Chapter 4, while 3D photography can reliably measure wound surface area in small, discrete wounds, larger and circumferential wounds require the stitching together of progressive photos and are significantly more technically difficult to measure. Therefore, as technology improves and measurement of these larger wounds becomes more user-friendly, the reliability and validity of the camera to measure such wounds will need to be reassessed to determine if this device is able to be used for all types of burn wounds.

9.5.4 Partial thickness burn outcome

Chapter 6 of this thesis found evidence that skin pigmentation loss was more apparent in children with darker skin types, but the exact timeframe for a return to normal skin appearance is still not known. Further assessment of long-term scar assessment in children who sustain partial thickness burns should include a formal assessment of skin type using the Fitzpatrick skin type scale, objective measurement of burn depth acutely (i.e. laser Doppler imaging) and objective measurement of skin pigmentation. Skin colour and pigmentation was only a minor part of the outcomes measures initially, but resulted in an important finding and therefore slightly more focus was placed on these outcomes in this chapter. Such devices used to measure skin pigmentation (e.g. Colorimeter, Dermalab Combo, Scarbase Duo) were firstly not available for use and secondly not validated for use in burn scars at the time of the trial and thus could not be utilized. The validity of the Dermalab Combo and Scarbase Duo has now been established [147, 148], and validation of the Colorimeter is ongoing. Future use of such devices would certainly be of benefit in obtaining objective measures of pigmentation in burn scars.

The scar outcome of children with partial thickness burns re-epithelializing within 2-3 weeks is still under-represented. A better understanding of the risk factors for scarring is required for better patient management and to provide more information for patients and their families.

9.6 Conclusion

This thesis has provided a comprehensive overview and examination of pediatric partial thickness burn care in the outpatient setting within the facets of treatment, outcome and parent experiences. Partial thickness burns in children are a significant burden on the healthcare system and should not be overlooked or disregarded.

Research presented in this body of work has changed and improved clinical practice in Queensland with the identification of Mepilex Ag™ as a cost-effective alternative to both Acticoat™ and Acticoat™ with Mepitel™ for the treatment of partial thickness burns ≤10% TBSA in children. Additionally, the investigation and introduction of objective and non-invasive burn wound and scar assessment tools (3D photography and ultrasound) has improved the ability to capture objective data and minimize unnecessary distress to children receiving treatment. A wealth of information has been obtained regarding the long term outcome from partial thickness burns, the subjective experiences of parents and the psychosocial implications of burn care.

Findings in this thesis have not only significantly improved clinical knowledge of pediatric partial thickness burns, but have provided clinicians with the tools and recommendations to improve burn care for children who sustain these injuries and their families.

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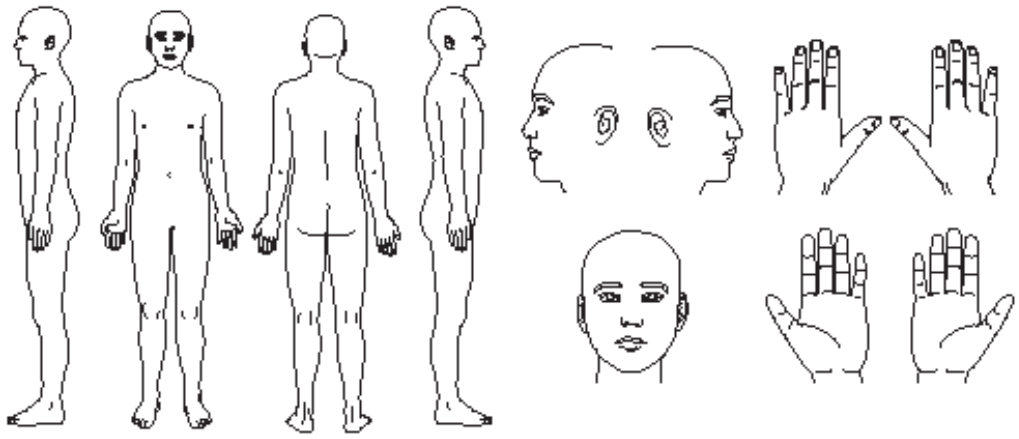
Appendices

Appendix 1: Patient and Observer Scar Assessment Scale

POSAS Observer scale

The Patient and Observer Scar Assessment Scale v 2.0 / EN

Date of examination:	**Name of patient:**
Observer:	
Location:	**Date of birth:**
Research / study:	**Identification number:**



PARAMETER	1 = normal skin	2	3	4	5	6	7	8	9	worst scar imaginable = 10	CATEGORY
VASCULARITY											PALE | PINK | RED | PURPLE | MIX
PIGMENTATION											HYPO | HYPER | MIX
THICKNESS											THICKER | THINNER
RELIEF											MORE | LESS | MIX
PLIABILITY											SUPPLE | STIFF | MIX
SURFACE AREA											EXPANSION | CONTRACTION | MIX
OVERALL OPINION											

Explanation

The observer scale of the POSAS consists of six items (vascularity, pigmentation, thickness, relief, pliability and surface area).
All items are scored on a scale ranging from 1 ('like normal skin') to 10 ('worst scar imaginable').
The sum of the six items results in a total score of the POSAS observer scale. Categories boxes are added for each item. Furthermore, an overall opinion is scored on a scale ranging from 1 to 10.
All parameters should preferably be compared to normal skin on a comparable anatomic location.

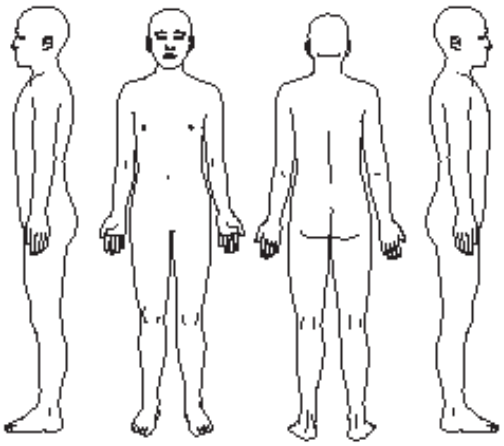
Explanatory notes on the items:

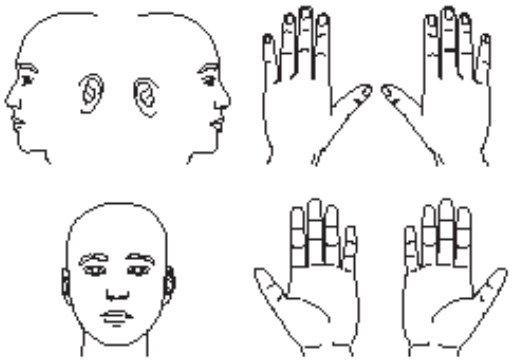
- **VASCULARITY** Presence of vessels in scar tissue assessed by the amount of redness, tested by the amount of blood return after blanching with a piece of Plexiglas
- **PIGMENTATION** Brownish coloration of the scar by pigment (melanin); apply Plexiglas to the skin with moderate pressure to eliminate the effect of vascularity
- **THICKNESS** Average distance between the subcutical-dermal border and the epidermal surface of the scar
- **RELIEF** The extent to which surface irregularities are present (preferably compared with adjacent normal skin)
- **PLIABILITY** Suppleness of the scar tested by wrinkling the scar between the thumb and index finger
- **SURFACE AREA** Surface area of the scar in relation to the original wound area

POSAS Patient scale

The Patient and Observer Scar Assessment Scale v 2.0 / EN

Date of examination:	**Name of patient:**
Observer:	
Location:	**Date of birth:**
Research / study:	**Identification number:**





	1 = no, not at all									yes, very much = 10
	1	2	3	4	5	6	7	8	9	10
HAS THE SCAR BEEN PAINFUL THE PAST FEW WEEKS?	○	○	○	○	○	○	○	○	○	○
HAS THE SCAR BEEN ITCHING THE PAST FEW WEEKS?	○	○	○	○	○	○	○	○	○	○

	1 = no, as normal skin									yes, very different = 10
	1	2	3	4	5	6	7	8	9	10
IS THE SCAR COLOR DIFFERENT FROM THE COLOR OF YOUR NORMAL SKIN AT PRESENT?	○	○	○	○	○	○	○	○	○	○
IS THE STIFFNESS OF THE SCAR DIFFERENT FROM YOUR NORMAL SKIN AT PRESENT?	○	○	○	○	○	○	○	○	○	○
IS THE THICKNESS OF THE SCAR DIFFERENT FROM YOUR NORMAL SKIN AT PRESENT?	○	○	○	○	○	○	○	○	○	○
IS THE SCAR MORE IRREGULAR THAN YOUR NORMAL SKIN AT PRESENT?	○	○	○	○	○	○	○	○	○	○

	1 = as normal skin									very different = 10
	1	2	3	4	5	6	7	8	9	10
WHAT IS YOUR OVERALL OPINION OF THE SCAR COMPARED TO NORMAL SKIN?	○	○	○	○	○	○	○	○	○	○

Appendix 2: Breakdown of cost items (economic evaluation)

Dressing type	Dressing size	Cost per sheet (A$)
Mepilex Ag™	10x10cm	8.40
	10x20cm	20.00
	15x15cm	21.75
	20x20cm	35.00
Acticoat™	5x5cm	10.24
	10x10cm	19.15
	10x20cm	28.75
	20x40cm	100.10
Mepitel™	5x7.5cm	5.20
	7.5x10cm	9.20
	10x18cm	17.80

Scar management resources	Size/Amount	Cost for one (A$)
Kelocote silicone gel	15 g tube	34.75
Mepiform™ silicone sheet	5x7.5cm	9.00
	10x18cm	26.00
Cicacare silicone sheet	6x12cm	40.99
	12x15cm	68.19
Ezemix™ silicone moulds	50 moulds/tub	Per tub: 350.98 Per mould: 7.10
Pressure garments	Custom-made	Range: $298 – 777.40

Analgesia	Amount	Dosage	Cost per bottle (A$)
Oxycodone	250mL	0.1mg/kg	9.76
Paracetamol	20mL	15mg/kg	2.18

Split skin grafting	
DRG code	**Cost (A$)**
Y02B – Skin grafts for other burns w/o catastrophic or severe CC, Emergency	17,131
Negative pressure wound therapy	**Cost (A$)**
Gauze dressing, dressing film and lease of canister and machine for 7 days	408.09

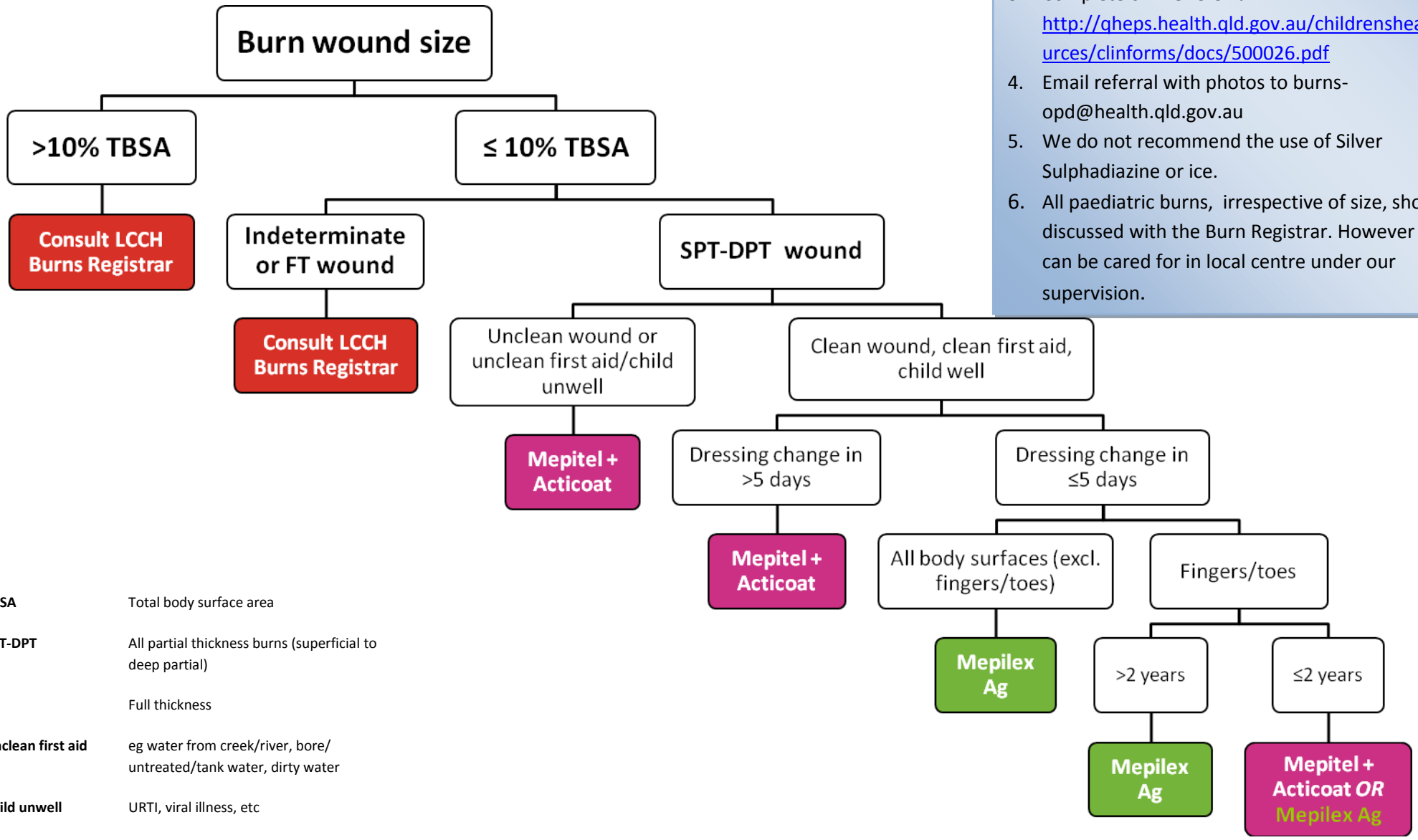
Queensland Health Wage Rates 2014		
Position	**Annual wage plus 25.85% on costs**	**Cost/minute**
L26 (MO2) Consultant	246,290	2.08
Clinical nurse consultant	129,133	1.09
Clinical nurse	105,165	0.89
Registered nurse	77,014	0.65
Occupational therapist (HP3)	75,130	0.63
Occupational therapist (HP4)	121,805	1.03
Occupational therapist (HP5)	138,362	1.17
Occupational therapist (HP6)	158,917	1.34

Appendix 3: New silver dressing treatment protocol

Children's Health Queensland Hospital and Health Service

For all paediatric burns

1. Ensure adequate first aid is provided, 20 mins cool running water up to 3hr post burn
2. Contact the LCCH Burns Registrar (07)30681111 *prior to dressing, or sending referral*
3. Complete online referral http://qheps.health.qld.gov.au/childrenshealth/resources/clinforms/docs/500026.pdf
4. Email referral with photos to burns-opd@health.qld.gov.au
5. We do not recommend the use of Silver Sulphadiazine or ice.
6. All paediatric burns, irrespective of size, should be discussed with the Burn Registrar. However many can be cared for in local centre under our supervision.



TBSA	Total body surface area
SPT-DPT	All partial thickness burns (superficial to deep partial)
FT	Full thickness
Unclean first aid	eg water from creek/river, bore/ untreated/tank water, dirty water
Child unwell	URTI, viral illness, etc

Appendix 4: Burns centre staff perspective of dressings (ease of use Likert scales)

1. **How easy was it to <u>REMOVE</u> this dressing to the child? (please tick)**
    - □ Extremely easy
    - □ Very easy
    - □ Somewhat easy
    - □ Not very easy
    - □ Not at all easy

2. **How easy was it to <u>APPLY</u> this dressing to the child? (please tick)**
    - □ Extremely easy
    - □ Very easy
    - □ Somewhat easy
    - □ Not very easy
    - □ Not at all easy

Appendix 5: Physical function while wearing dressings (Likert scale)

How easy is it move in the dressing?

- □ Extremely easy
- □ Very easy
- □ Somewhat easy
- □ Not very easy
- □ Not at all easy