Scar outcomes in children post burn healing with conservative management

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Thesis presented for the degree of

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Preface

This thesis is comprised of three chapters.

Chapter 1 is a synthesized literature review presenting a comprehensive background about burn injuries, the prevalence, management and complications of these, specifically hypertrophic scarring in children.

Chapter 2 is an original retrospective study investigating the outcomes for children sustaining a burn injury that were not grafted and healed in >14 days. This chapter is presented in the form of a manuscript, to be submitted to the journal Burns & Trauma.

Chapter 3 delves deeper into the findings of this thesis and considers the implications for clinical practice. In depth discussion on study limitations and key messages from the retrospective study are reported.

References for Chapter 2 are at the end of the submitted manuscript, while references for Chapters 1 and 3 are presented together after Chapter 3. All references are presented in Oxford SCIMED format as required for the journal Burns & Trauma.

Thesis aims

This thesis aims to build upon current knowledge regarding the prevalence of hypertrophic scarring post burn injury, specifically for conservatively managed children who heal after 14 days.

To achieve this, the objectives of this thesis are to:

- Critically appraise the available literature regarding prevalence, predictors and conservative treatment of hypertrophic scarring in children following burn injury (Chapter 1).

- Describe scar outcomes resulting from routine clinical care at The Children's Hospital at Westmead Burn Unit for conservatively managed burn patients over a 5 year period (Chapter 2).

- Integrate the key findings from the synthesized literature review (Chapter 1) and the original study (Chapter 2) to inform future clinical care and research.

Abstract

This thesis investigates the prevalence and predictors of hypertrophic scarring in children who sustained a burn injury. It builds upon current literature, that increasing days to re-epithelisation is one of the most important factors associated with hypertrophic scar development. Recent literature suggests that wound healing occurring after 14 days may place the child at risk of hypertrophic scar development. Anecdotally, at the Children's Hospital at Westmead, burn therapists have observed a percentage of patients conservatively managed and healing in >14 days develop hypertrophic scarring.

Therefore, a retrospective medical record audit was conducted, surveying the outcomes of 326 children who had sustained a burn injury, were not skin grafted and healed in >14 days. Prevalence of hypertrophic scarring was identified at two time points: 3–6 months for early presence and 12–18 months for persistent hypertrophic scar. Healing times were divided into 14–21, 22–30 and >30 days, in order to identify patients scarring by healing time. Prevalence of hypertrophic scarring at 3–6 months was 56.1% and 16.3% at 12–18 months.

Early hypertrophic scar monitoring, and where indicated initiation of prophylactic scar intervention, may be warranted for all children conservatively managed who heal in >14 days. To provide improved efficacy of individualized prophylactic scar interventions to this patient population, comparison of this intervention to no intervention until hypertrophic scar development or no intervention at all, needs to be conducted. Future research should also focus on defining a hypertrophic scar within a scar scale feasible for clinical use to improve reporting on prevalence and predictors of hypertrophic scarring.

Candidate's Statement

I, Stephanie Ball, certify that the work in this thesis titled 'What are the scar outcomes for children who have had a burn, are not grafted and heal >14 days?' has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree to any other university or institution other than Macquarie University.

I also certify that the thesis is an original piece of research and it has been written by me. Any help and assistance that I have received in my research work and the preparation of the thesis itself have been appropriately acknowledged.

In addition, I certify that all information sources and literature used are indicated in the thesis. The research presented in this thesis was approved by Sydney Children's Hospital Network Human Research Ethics Committee (2020/ETH03201) (Appendix 1) on 9 February 2021.

Stephanie Ball (46096116)

Signed:

Date: 6 May 2022

Supervisor's Statement

As supervisor of Stephanie Ball's Master of Research work, I certify that I consider her thesis 'What are the scar outcomes for children who have had a burn, are not grafted and heal >14 days?' to be suitable for examination.

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To Jess Drysdale, friend and colleague, thank you for always being a huge support through all my work, study and research life. Your support and passion for health knows no bounds.

To my husband, thank you for encouraging me to extend myself and my mind in the field I love, knowing I had to do it, even if it meant I was a little stressed by the end.

To my children, you cannot understand why I needed to do this MRes, but you will when you are older. Thank you for your patience while I worked. I hope you have the opportunities to grow your field and your minds and be supported along the way in the same manner I was. Summer holidays here we come!

List of Abbreviations

BRANZ	Burns Registry of Australia and New Zealand
CHW	Children's Hospital at Westmead
CI	Confidence interval
D/C	Discharge
ECM	Extracellular matrix
ICC	Intraclass correlation coefficient
IQR	Interquartile range
ISBI	International Society of Burn Injuries
HTS	Hypertrophic Scarring
LDI	Laser doppler imaging
mmHg	Millimetre of mercury
mVSS	Modified Vancouver Scar Scale
NHTS	Not hypertrophic scar
NSW	New South Wales
OR	Odds ratio
POSAS	Patient and Observer Scar Scale
RCT	Randomized Control Trial
ROM	Range of movement
SBIS	Severe Burn Injury Service
SD	Standard deviation
%TBSA	Percentage Total Body Surface Area
VSS	Vancouver Scar Scale

Chapter One:

Introduction to Burns and Hypertrophic scarring

1.1 Epidemiology of paediatric burn injury

A burn injury is the fifth most common cause of non-fatal childhood injuries worldwide and is often a preventable occurrence [1]. Burns account for a significant number of Emergency Department visits in Australia [2]. In all age groups, males are more likely to sustain a burn requiring hospital admission compared to females [2]. Children aged 0–4 years are significantly more likely to require a hospital admission due to a burn, than any other age group in Australia [3]. Children aged 7–12 months account for 84% of all children <1 year who are burnt, correlating with increasing development of mobility and curiosity in this age group [3].

Burn mechanism and distribution varies throughout the childhood years. Eighty percent of burns to young children occur within the home, most within the kitchen, with scald injuries ranking as the most common type of burn in children 0–4 years [2, 3]. The distribution of these burns is frequently located on the wrist and hands (25%) followed by the trunk (21%) [3]. As children progress in age, burn distribution more commonly occurs in the trunk and lower limbs from flame and fire. Older children, aged five to nine years, sustain injuries to these areas 27% and 19% of the time respectively, and mirror the pattern of adults (trunk, hips and lower limbs) from the age of ten [3].

In children, the most common burns are minor in size, comprising <10% total body surface area (%TBSA), are partial thickness, and usually do not require inpatient admission for management [4]. In Australia, children that are admitted are statistically more likely to have sustained flame burn, be male, incur an inhalation injury, have deep partial to full thickness depth, and larger %TBSA [5, 6]. The average %TBSA for adults and children treated as outpatients is reported as 1.7% (+/- 2.5) by the Burns Registry of Australia and New Zealand (BRANZ) [6, 7]. The BRANZ study reported all children treated in an outpatient setting as having <10% TBSA, with a rate of 3.2 outpatient encounters for every one inpatient admission [6]. As data is context specific for these two countries, the BRANZ may not be comparable to other clinical contexts globally where the ratio of inpatient management is significantly higher than outpatient [6].

1.2 Burn wound

1.2.1 Burn wound assessment

Burn injuries, as described by Shakespeare, are characterized by depth of injury to the three layers of the skin, being the epidermis, dermis and subcutaneous structures [8]. Burns are therefore described as either being superficial, superficial partial thickness, deep dermal partial thickness or full thickness and involve an increasing number of layers respectively [8].

Assessment of a burn is essential for establishing healing potential and intervention selection. Acute wounds are dynamic and the clinical appearance may change over the first 48 hours, requiring subsequent reassessment [9]. Burns are rarely homogeneous, further complicating the clinical assessment. The most common methods of assessing burn depth are clinical evaluation and laser doppler imaging (LDI). Clinical evaluation of the wound is a subjective assessment that takes into consideration burn mechanism, location, appearance, and quality of blood flow [10, 11]. Although this is the most accessible and clinically used method, its ability to accurately determine depth is only 50–75% when undertaken by experienced burn surgeons [10, 12-16]. LDI is considered the reference standard noninvasive objective measure of determining wound depth. The quality of microvascular circulation is assessed, which is inversely related to burn depth and healing potential. If used 24–72 hours post burn injury, LDI has a positive likelihood ratio of 20.35 for all burn depths [17]. Despite LDI's superiority, its routine use in clinical practice remains limited as a result of high-cost, low ease of use, lack of timely patient presentation and preference of staff to perform the assessment clinically [18].

1.2.2 Burn wound management

Management of acute burn injuries has advanced in recent decades, with the focus shifting from improving survival rates, to promoting optimal functional and cosmetic outcomes associated with the effects of scarring [19]. The development of hypertrophic scarring (HTS) post burn may impair function, contribute to contracture development,

affect cosmetic appearance and increase symptoms of pruritus and pain, all of which may decrease quality of life for patients [20, 21]. Qualitative studies highlight the initial and lingering trauma of children and parents that exists with the daily reminder of the visible scar [22].

Adequate first aid as described by the Australian and New Zealand Burns Association is 'cool running water for 20 minutes within 3 hours of injury' [23]. Studies have reported poor utilization of recommended first aid worldwide, with rates ranging from 6%–71% for children and 35–58% in adults [24-29]. Suboptimal methods such as submersion, wet cloths, or reduced cooling times were readily used [26]. In addition, potentially harmful traditional/home methods such as ice, toothpaste or egg were frequently applied [24, 30]. The likelihood of receiving first aid is reduced in socioeconomically disadvantaged areas and is correlated with poorer outcomes [31, 32]. Administration of adequate first aid immediately post burn injury is hypothesized to halt the burning process, reduce inflammatory mediators, and provide analgesic effects [23, 33]. In reducing the progression of potential damage and maintaining a 'zone of stasis', progression of burn depth is limited, with more favorable outcomes, including reduction in burn severity, time to reepithelization, %TBSA, pain, need for skin grafting, hospital length of stay and HTS development [23-25, 27-29, 34-37].

There remains no single wound dressing that is recommended for all burn wounds [9, 38]. Dressing selection is determined by wound size, depth, anatomical location, product availability and clinician preference [9]. A burn dressing should promote wound healing by providing a moist environment whilst preventing infection [38]. A recent worldwide survey of burn units found that the preferred wound dressing should be non-adherent to the wound bed, enable pain free dressing changes, require fewer dressing changes, prevent infection and absorb wound exudate [39]. Modern dressings such as silver based dressings, are recommended by the International Society for Burn Injuries (ISBI) Burn Care Practice Guidelines as they allow fewer dressing changes, resulting in shorter hospital stays or the ability to manage the injury in an outpatient setting and are subsequently more cost effective compared with conventional dressings [9].

Studies have aimed to identify the most suitable dressings using a variety of patient cohorts with differing study designs. No single conclusion can be drawn, due to the abundance of available dressings and variability of burn wounds making randomization in clinical trials difficult. However, general recommendations can be ascertained from this evidence base [38]. The two most utilized dressing types are those containing silver and bioengineered dressings, both frequently used in Australia. Dressings containing silver, are considered cost effective, safe and decrease the need for grafting and time to re-epithelization [40-42]. A recent systematic review was unable to determine superiority of one silver impregnated dressing to another, however all demonstrate ability to prevent infection [43].

Bioengineered skin substitutes, such as Biobrane®, create optimal wound healing environments and are considered favorable for partial thickness but not full thickness wounds [44]. They are considered superior to silver sulfadiazine, a treatment option still frequently used around the world, in reducing pain, number of dressing changes, number of infections, length of stay and days to heal [38, 44, 45]. Bioengineered skin substitutes are extremely costly, limiting their applicability to all burn patients. Due to a lack of long-term follow up and reporting of HTS within the studies, no recommendation can be made regarding the impact of specific dressings on the development of HTS.

1.3 Post burn hypertrophic scarring

1.3.1 Hypertrophic scar development

A hypertrophic scar presents as highly vascularized, thickened, and raised above the surrounding skin, whilst remaining within the boundaries of the original wound [46-48]. It can be associated with further complications of pruritis, pain, stiffness and contractures [49]. The development of HTS is complex and thought to occur due to disruption in the normal wound healing, commonly arising from a chronic inflammatory process resulting in fibroproliferation [49, 50]. HTS commences with the activation of deep dermal fibroblasts, which proliferate and stimulate fibroblast activity during the inflammatory

phase of wound healing. Fibroblasts produce elastin and collagen; however, the ratio of production is different in scar formation compared with normal skin production [51]. Increased levels of collagen are laid down parallel to the epidermal surface to create a scaffold for wound healing known as the extracellular matrix (ECM). The ECM contains collagen, elastin, proteoglycans and hyaluronic acid which covers the wound and allows for vascular ingrowth [52]. The disruption during this process coupled with lower collagenase production in scar tissue results in less effective remodeling of the collagen produced and a raised and vascular scar develops [51]. As a result, scar tissue is significantly less elastic than normal skin [53]. Non-scarred skin can lengthen up to 60% and recoil to its original state, whereas hypertrophic skin can only lengthen up to 15% [54]. Hypertrophic scar formation is an ongoing and dynamic process, the active phase typically commences one to three months post burn injury and peaks by six months post burn [20, 55]. Following this, the remodeling phase, where the collagen becomes organized, is slower and can last up to two years, during which the scar typically flattens, decreases in size, colour and thickness and resembles surrounding skin [52, 55-57]. To optimize scar outcomes, practice guidelines recommend scar management techniques, with regular reassessment, that should continue until scar maturation, whereby the scar is no longer responsive to therapy [48, 58].

1.3.2 Hypertrophic scar assessment

Numerous subjective assessment scales, with mixed results for validity and reliability have been described in the literature [55, 56, 59-62]. The ability to describe, evaluate and compare scars is essential both clinically and in research. The parameters for subjective scar scales include: vascularity, pigmentation, pliability, and height [63, 64]. There remains a lack of consensus on the utilization of one standard measurement tool or finite value in the scales used to determine the presence or definition of HTS [65]. Objective assessment tools have been developed to combat the challenges of subjective scar scales. Physical characteristics of a scar can be analyzed utilizing objective scar assessment tools to assess colour, stiffness, thickness and transepidermal water loss [66]. Multiple devices are required to encompass all aspects

of HTS, however due to device sizes and high-cost operating times their clinical use is limited [66].

The most common subjective scales include: Vancouver Scar Scale (VSS), Modified Vancouver Scar Scale (mVSS) (See Appendix 2) and the Patient and Observer Scar Assessment Scale (POSAS) (See Appendix 3) [55, 56, 60-62, 67]. The VSS was the first validated scar scale used in research and clinical practice and was developed in 1990 [55]. The scale requires the clinician to rate the scar with regards to its height, pliability, vascularity and pigmentation compared to surrounding skin [55]. The subjectivity of the scale and absence of a universally accepted hypertrophic scar value exposes it to some limitations. The VSS is susceptible to inter-assessor variations [65]. It has low to moderate intraclass correlation coefficients (ICCs) with a single observer (0.69, 95% confidence interval [CI] 0.57–0.79) and moderate to good ICCs (0.90, 95%CI 0.084–0.94) with four observers [67]. Further, in a systematic review, VSS had intermediate evidence for reliability, responsiveness and validity, especially for large and irregular scars [68]. The VSS lacks the ability to document variation within the scar and to detect subtle changes over time [55, 61, 68]. Multiple mVSS's have been developed to make the tool more specific and susceptible to detecting small change [56, 60-62, 69]. Regardless of the changes made in the various mVSS, little advantages exist in their use compared to the original VSS [68]. Results indicate for all mVSS that there is low, intermediate or no evidence supporting reliability or validity [68]. Despite these limitations, both VSS and mVSS remain widely used in clinical practice, due to their simple and easy application.

The POSAS was developed in 2004 and includes both a patient perceived and observer (therapist) rated scar scores and has demonstrated good internal reliability [67, 70]. It also includes additional patient rated aspects of the scar including pain and pruritis. The POSAS is yet to be validated for children <15 years, however a recent study found high test-retest reliability with both adults and children [71]. Its use clinically in the pediatric population remains limited. In particular, the self-reported component (using parents as proxy) requires further investigation to determine its efficacy for young children [67]. In

contrast to VSS, the POSAS has greater single observer reliability with less variability, indicating its applicability to both clinical and research settings [68].

Scars, like burn depths, are rarely homogenous in texture, colour or height, impacting subjective assessment ratings. Objective measuring devices provide a more in-depth picture of these qualities. Burn scars elasticity and stiffness can be measured by a Cutometer which has demonstrated very good reliability (ICC >0.89) [66, 72]. Hypertrophic scars are often drier than surrounding skin and no subjective scale includes this factor. Skin softness and smoothness is relative to its water content and can be determined by transepidermal water loss [73]. Transepidermal water loss is measured by a device such as the Dermalab transepidermal water loss module [73]. Clinically observing the colour of a scar is complex, as changes in pigmentation and vascularity can occur simultaneously and be affected by patient position and temperature [66, 74]. Devices such as Mexameter and DMS II ColorMeter analyse skin colour by utilizing reflection and absorption of light, laser band method or computer analysis of colour [66]. Both have good to excellent reliability when assessing pigmentation and vascularity (ICC 0.94 and 0.72 respectively) [69]. High frequency ultrasound is a reliable (ICC 0.91–0.94) and accurate tool for measuring scar thickness or height and can accurately distinguish between scar and normal tissue [75]. Devices such as the tissue ultrasound palpation system and Dermascan were developed for this particular clinical use [66]. Clinical utilization of these devices is minimal due to high equipment costs of multiple devices, long operating time requirements and size [66].

1.3.3 Prevalence of post burn hypertrophic scarring

The ability to draw strong conclusions from current literature of post burn HTS prevalence remains difficult. Studies vary in their definition of HTS, use varied outcome measures, patient populations, wound management techniques, and duration of follow up periods during the scar maturation process. Current HTS prevalence rates for children are reported as 16–69% and adults are reported as 20–77% [36, 47, 48, 76-83]. Table 1.1 shows the HTS prevalence rates for children and adults.

Table 1.1 Prevalence and predictors of post burn hypertrophic scarring

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Deitch et al[76] **1983**	Prospective cohort Study period: 1980– 1981	n=100 Sex not specified 59 children Mean age 3y Mean 14%TBSA 41 adults >14y Mean 21%TBSA 73% Black 27% White Non-grafted patients only	Burn Wound: Inpatient; silver sulfadiazine, daily hydrotherapy Outpatient; Silver sulfadiazine, soap and water cleaning. Burn Scar: Pressure garments used, criteria for use not specified, regime of wear not specified	Clinician evaluation of colour, consistency, and thickness/ elevation Final appointment scar evaluation by clinician used for clinical outcome of HTS presence	9–18 months post burn	38% of cohort 41% for children 34% for adults **HTS distribution–children:** Foot; 50% Perineum & buttocks; 43% Chest; 33% **HTS distribution–Adults:** Foot; 40% Perineum & buttocks; 38% Chest; 33% **Race % HTS:** Cohort; White 16% Black 31%	**Time to heal and HTS prevalence;** **10–14 days to heal;** 14% children 14% adults **14–21 days to heal;** 42% children 28% adults **>21 days to heal;** 70% children 92% adults	Predictors of HTS not analysed

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Spurr and Shakespeare [84] **1990**	Retrospective cohort Study period: 1968, 1984	n=152 Sex not specified Under 5y 5–10%TBSA Included grafted and non-grafted patients Race not specified	Burn Wound: Therapy not described Burn Scar: Pressure garments commenced usage in 1984 patients	Clinician evaluation as present or not, with no note of severity or ultimate quality	Not described	1968 cohort 51% 1984 cohort 63%	Not described	No significant findings between the two time periods were found
Bombaro et al[85] **2003**	Retrospective cohort Study period: 2000	n=89 65% male 13 children (<15y) Mean age 33y (SD ±16y) Mean 20%TBSA 66% White 14% Hispanic 8% Black 5% Asian	Not described	Clinical evaluation, documented as hypertrophic	Not described	**Cohort:** 67% overall 75% non-white 63% white **Children:** 75% white 100% non-white	Not described	No significant results

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Cubinson et al[79] **2006**	Retrospective cohort Study period: 1997– 2003	n=509 58% male Mean age 27m Mean 5.5%TBSA Scald burns only Included grafted and non-grafted patients Race not specified	Not described	Documented as HTS or prescribed scar treatments based on clinician assessment Photographs assessed using VSS	4 months to 5 years post burn	35% for cohort	**Time to heal and HTS prevalence for cohort (%)** **Time to heal;** 0–10d; 0% 10–14d; 8% 15–21d; 20% 22–25d; 40% 26–30d; 68% >30d; 92%	No significant results
Gangemi et al[81] **2008**	Retrospective cohort Study period: 1994– 2006	n=703 63% male Mean age 38y Mean 20%TBSA Included grafted and non-grafted patients Race not specified	Burn Wound: Weekly clinical examination until second month after re-epithelisation Burn Scar: 79% of scar sites were treated with medical and rehabilitative therapy, not described in detail	Pathologic scar or normotrophic[a] scar based on clinical evaluation	Not described	77% Pathologic scar 44% Hypertrophy 28% Hypertrophy + Contracture	**Wound healing time, median (IQR);** **Normotrophic;** 33d (20–60) **HTS;** 40d (27–62) **HTS + Contracture;** 55d (35–87) Medium time for scar healing time; 15m (IQR, 10–23m)	**° Pathologic scar** OR (95% CI); **Burn site lower limb** OR 1.34 (1.03–1.74) **Full thickness burn %TBSA** OR 2.48 (1.8–3.4) **Number of surgical procedures** OR 1.74 (1.43–2.13) **Non-surgical burn healing** OR 0.25 (0.20–0.31)

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
							Active phase 23w, remission phase 40w	**Delayed wound healing time** OR 1.15 (1.02–1.29) **Δ Pathologic scar;** **Burn site neck** OR 3.27 (1.01–10.54) **Older age** OR 0.64 (0.45–0.90)
Van der Wal et al[20] **2012**	Prospective cohort Study period: 2004– 2009	n=474 60% male Mean age 21y (1–46y) Mean 11%TBSA Included grafted and non-grafted patients Race not specified	Burn Wound: Conservative treatment not described. Burn Scar: Silicone and pressure garments prescribed as determined by therapist and burn location.	POSAS* Vascularity: DermaSpectro meter	Assessed at 3,6 and 12 months post burn	Not reported	Not reported	**Δ Higher mean POSAS score** RC (95% CI); **%TBSA** RC 0.02 (0.01–0.04) **Partial thickness depth** RC -1.0 (-1.4–-0.7) **Time to heal** RC -0.05 (-0.1–-0.002) **Age** (p>0.2) and **aetiology** (p=0.8) have no influence on HTS development in **Δ**

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Thompson et al[83] **2013**	Prospective cohort Study period: Not specified	n=300 69% male Median age 39y (18–91) Recruited if at risk of HTS Median 7.1%TBSA Race not specified	Not described	VSS >7 Itch score >4	12 months, one assessment at 1–5 months and at 6–12 months	42%	Not reported	**Δ** Risk **for HTS** OR (CI 95%) American Indian/Alaskan native; 11.97 (1.42–100.82) Facial burns; 9.67 (1.12–83.56) ≥20%TBSA; 1.9 (1.01–3.57)
Hassan et al[86] **2014**	Prospective cohort Study period: 2009– 2011	n= 181 61% male Mean age 24.7y (1m–85y) Mean 2%TBSA Race not specified	Burn Wound: Clinical dressings Burn Scar: Occupational Therapy details not described	VSS Scar height >2mm = HTS	6–19 months	15%	18% took >21d to heal **Time to heal days (SD) by wound depth;** Superficial; 10.2d (5.7) Partial thickness; 14.9d (10.4) Mixed; 19.3d (11.4) Deep dermal; 31.8d (21.0) Full thickness; 47.5d (36)	All who developed HTS had a wound infection No patient healing <21d developed HTS

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Kishikova et al[87] **2014**	Retrospective cohort Study period: 2006, 2009	**2009** n=181 58% male Mean age 4.5 y Mean 2%TBSA **2006** n= 337 57% males Mean age 2.3 y Mean 5.5%TBSA Race not specified	Not described	Described by clinician evaluation as HTS	1 week–47 months	11.6% 2009 35.9% 2006	Time to heal (days); **2009;** 17.9d (range 2–98) **2006;** 22.2d (range 3–271) Significantly faster healing time in 2009 (p<0.01)	No predictors analysed
Sood et al[82] **2015**	Prospective cohort Study period not specified	n=425 70% male Median age 40y Mean 7%TBSA Included grafted and non-grafted patients	Not described	VSS >7 at any point = HTS	3–20 months post burn injury	49%	Not reported	**°VSS score >7** PR (95% CI); Asian race PR 1.54 (1.13–2.10) Black/African American race PR 1.86 (1.42–2.45) Native American race PR 1.87 (1.48–2.35) **MC1R genotype** associated with HTS (p<0.001)

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
		79% White 6% Asian 4% Black 2% Native American						
Gee Kee et al[88] **2016**	Prospective randomized controlled trial Study period: 2013– 2014	n=43 60.5% male Median age 1y Median 1%TBSA Partial thickness burns only	Not described	POSAS	3, 6 months	Not reported	**Time to heal; Median (IQR)** <2w; 31 (72) 2–3w; 7 (16) >3w; 5 (11)	Days to re-epithelization a significant predictor of increased POSAS scores at 3m and 6m (p<0.01)
Wallace et al[47] **2017**	Prospective case control study Study period: 2010– 2015	n=616 65.4% male Mean age 36y Median 2.8%TBSA Race not specified	Burn Scar: management provided; details not specified	mVSS Scar height >1mm = HTS	12 months Assessed at 2, 6 and 12 months	Not reported	28% healed within 14d	**Δ** to **predict SH >1mm** OR (95% CI) **Age 45–60y compared to <30y;** OR 0.2 (0.1–0.4) **Female sex;** OR 2.5 (1.6–3.8) **Fitzpatrick skin type IV–VI;** OR 4.9 (3–8.1) **%TBSA >20% compared to 0–5% TBSA;** OR 8.7 (3.2–23.7)

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
								Hospital stay 30–60 days compared to 0 days; OR 5 (1.3–18.7) **Split skin graft compared to conservative treatment;** OR 5.8 (2.5–5.8)
Wallace et al[78] **2017**	Prospective case controlled Study period: 2011– 2015	n=186 58.1% male Median age 5.3 y Median 3%TBSA Race not specified	Scar management provided; details not specified	mVSS Scar height >1mm = HTS	12 months. Assessed at 3, 6 and 12 months	34.4%	Not reported	°**Younger age on scar height>1mm** (p=0.015) **Δ to predict scar height >1mm** OR (95% CI); **Healing time >14 days** OR 11.6 (3.7–36.2) **Each 1% increase in %TBSA** OR 1.16 (1.0–1.3) **>1 surgical procedure** OR 11.5 (2.0–66.6)
Lonie et al[36] **2017**	Retrospective cohort Study period: 2011– 2015	n=322 Sex not specified 0–17y	Burn Wound: If not full thickness; Acticoat dressing, grafting to areas not healed in 2–3 weeks, details	HTS or never HTS as per clinical evaluation or if documentation of requiring scar therapy, photographs for clinician	Minimum 4 months	16.1% cohort 10.4% conservative wound closure 84% surgical wound closure	Mean number of days to heal 15.4 **Incidence of HTS with time to heal;** **Conservative wound closure;** 15–21d; 7.5%	**Slower to heal burn locations;** Upper limb and trunk (p<0.01) Shoulder (p=0.02)

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
		Outpatients with scald burn only Mean %TBSA not specified Race not specified	per patient not specified Burn Scar: details not specified	evaluation if available			22–30d; 56.5% >30d; 81.3% **Surgical wound closure;** 15–21d; 100% 22–30d; 80% >30d; 85.7% **HTS by location:** Upper limb; 18.3% Lower limb; 12.5% Trunk; 18.8%	
Chipp et al[77] **2017**	Prospective cohort Study period: 2011– 2013	n=383 65% male Mean age 3.28y Mean 2.3%TBSA Conservative management only Race not specified	Burn Wound: Silver based dressings or Biobrane®, details per patient not specified. Burn Scar: details not specified	mVSS HTS = total mVSS score ≥5 and scar height ≥2mm	2 years	17.2%	**HTS rates and healing time;** 8–14d; 6.4% 15–21d; 13.5% >21d; 56%	**Δ** to **predict HS >2mm and total mVSS ³5** OR (95% CI) **Each additional day to heal gives** OR 1.138 (1.1–1.17)
Karlsson et al[89] 2020	Prospective cohort Study period: 2015– 2018	n=38 63% male Mean age 20.5m	Burn Wound: xenograft or silver foam dressing Burn Scar: Pressure garments and	POSAS–observer component only VSS	6 and 12 months	33%		**Δ Days to complete healing as a predictor for HTS OR (95% CI);** Month 6; 1.13 (1.04–1.23 Month 12; 1.18 (1.04–1.32)

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
		Mean 4%TBSA Partial thickness scalds only 68% Fitzpatrick type I–II 31% Fitzpatrick type III–IV 1% Fitzpatrick type V–VI	silicone as prescribed by treating therapist	Photographs for clinician evaluation				**Δ Days to complete healing as predictors of PSOAS;** Month 6; 0.37 (0.22–0.51) Month 12; 0.25 (0.12–0.38)
Thomas et al[80] 2019	Retrospective cohort Study period: 2006– 2016	n=76 53% male Mean age 3.6y Mean 15.5%TBSA Burns to the axilla or in close proximity only 49% Caucasian 10% Aboriginal 12% Asian 12% Arab or African 12% Mixed	Burn Wound: modern dressings, skin grafting where indicated. Burn Scar: silicone, splinting, pressure garments described	mVSS HTS = scar height >1mm	2 years	69%	Mean time to heal; 36d (SD 21.9)	Predictors of HTS not analysed

Study	Study Design	Participants	Therapy provided	Classification of HTS	Follow up period	Results		
						HTS prevalence	Time to heal	Significant predictors of HTS
Thomas et al[90] 2021	Retrospective cohort Study period: 2012– 2016	n=107 64% male Mean age 18m TBSA not reported Palmar burns only Race not specified	Burn Wound: modern dressings, skin grafting where indicated. Burn Scar: silicone, splinting, pressure garments described	mVSS	2 years	22%	Time to heal; < 1m; 51% >1m; 49%	Predictors of HTS not analysed

° Univariate analysis; Δ Multivariate analysis; 95%CI,95% Confidence interval; OR, Odds ratio; RC, Regression coefficients; IQR, Interquartile range; PR, Prevalence ratio; SD, Standard deviation; n, number; d, days; y, years; %TBSA, Percent total body surface area; HTS, Hypertrophic scar; POSAS, Patient and Observer Scar Assessment Scale – Total score ≤6 is considered normal skin, higher scores indicates a more hypertrophic scar; VSS, Vancouver Scar Scale – Score 0 for normal skin, higher scores indicates a more hypertrophic scar; mVSS: Modified Vancouver Scar Scale – Score 0 for normal skin, high scores indicates a more hypertrophic scar; ROM, range of movement; [a]Normotrophic scar, when it assumes characteristics of surrounding skin in terms of pliability, thickness and colour [81]; Fitzpatrick skin types; I–II white/fair skin tones, III–IV medium/olive skin tones, V–VI brown/black skin tones.

1.3.4 Predictors of post burn hypertrophic scarring

The challenge continues for therapists to identify patients at initial presentation who are at risk of hypertrophic scar development and the ability to provide subsequent targeted and timely therapy. It also remains unclear which patients, at baseline, have the potential to respond positively to scar management techniques. A thorough knowledge of HTS risk factors is required to study and evaluate scar management interventions. Table 1.1 shows the studies investigating predictors associated with the development of HTS in children and adults.

The ability to draw robust conclusions from the available literature is difficult due to differing patient populations and methodologies used. Eleven studies addressed risk factors for children only, four considered adults only and three included both age groups (Table 1.1) [20, 36, 47, 50, 76-90]. Differences arose clinically with exclusion of patients based on burn mechanism [36, 79]. Two studies excluded patients who required skin grafting for wound closure, whilst other studies did not exclude for these reasons [20, 47, 76, 77]. The time point of which studies assessed patients as having or not having a HTS varied between three months and five years post injury [79, 82]. Within these studies, treatment regimens were either not described in detail or absent. Initial wound management was described in terms of conservative management with dressings or surgically with split skin grafts. Scar management techniques were not considered in the context of their effect on HTS outcomes, were poorly documented or were not present [36, 47, 76, 77, 82, 83].

Disparities between the definitions of HTS further hinders the ability to draw strong conclusions. Various scar assessment scales were utilized, in addition to retrospective clinical notes, photographs or the presence of prescribed scar management techniques as an indication of HTS presence [36, 79, 81]. To determine the presence of HTS; four studies utilized a subset of the mVSS (i.e. height of the scar compared to surrounding skin), three selected specific scores on mVSS and one subjectively assessed increased thickness or elevation to determine HTS presence [47, 76-78, 80, 82, 90]. Time from post burn injury to time assessed as HTS present, also varied, with most studies either

using any time point throughout the study or only at the completion of the study [36, 47, 76-80, 82, 83, 90].

Despite the differing methodologies and definitions used, consistency in some HTS predictors was identified when considering intrinsic patient characteristics. African American and Asian race were significantly associated with HTS development in one study [82]. In another study, skin types classified as Fitzpatrick skin types IV–VI (brown to black skin type) were significantly associated with HTS development [47]. Two studies described HTS prevalence and the relationship with skin type in children, demonstrating trends of increased scarring with darker skin tones (Fitzpatrick skin type IV–VI), however neither reached significance [77, 78]. Younger age and female sex were considered statistically significant predictors in two studies, whilst three other studies did not find this to be statistically significant [47, 77, 78, 81]. These varied findings are likely a result of differing inclusion and exclusion criteria for patient population, outcome measures and statistical approaches.

In addition to patient specific factors, extrinsic features such as: burn mechanism, severity, larger %TBSA and longer time to heal are associated with HTS development in both adults and children [20, 78, 83]. Deitch et al was the first to establish that burn wounds that healed in under three weeks were at a low risk for HTS development [76]. More recent studies validate this finding, with significantly higher incidences of HTS with increasing healing time after three weeks [20, 47, 77]. Although research supports a lower rate of HTS development if healed under 21 days, for children, it has been found that HTS development can occur in one third of children in which wound re-epithelization occurs between days 14–21 [77]. Chipp et al found an odds ratio of 1.138 of HTS development for each additional day to heal after eight days in children [77]. Predictors of re-epithelization for children have been identified by Brown et al who found that 69% of variability of time to re-epithelization was impacted by burn depth, %TBSA, mechanism of injury, days taken to present to burn center, pain scores and ethnicity [19]. In univariate analysis, children were statistically more likely to develop HTS if there was a greater %TBSA, healing time of longer than 14 days and requirement of multiple

surgeries for wound closure [78]. In multivariate analysis, longer hospital admissions and wound complications, such as infection were significantly associated with HTS development for adults [47]. These findings provide insight into potential scarring predictors and the influence severity of the burn and acute management play in the risk of HTS development.

1.3.5 Conservative scar management

Management of HTS is an unmet challenge for clinicians, despite improvements in burn dressings and literature supporting timely wound closure to optimize or negate HTS development [5, 36, 79]. Commencement of conservative scar management techniques is recommended by the ISBI burn practice guidelines if the burn wound is surgically closed or if conservative treatment takes greater than three weeks [9]. However, no recommendations are present for those healing between 14–21 days. Conservative techniques are readily used by clinicians to prevent and treat the occurrence of HTS, including pressure garments, silicone, exercise, and emollients for children (Table 1.2) [49, 91]. Medical interventions including intralesional corticosteroids, laser, ultrasound, and surgical excision are becoming more readily utilized, however are not included in detail as it is beyond the scope of this literature review [91]. The efficacy of treatments for HTS is often lengthy, incomplete, costly and time consuming for both patients and clinicians [50]. These factors can negatively affect the psychosocial wellbeing of children and their families, and impact upon treatment adherence throughout the rehabilitation phase [22]. The evidence supporting conservative techniques is often empirical with limited published sizable trials, especially for paediatric cohorts. Despite the lack of strong evidence for therapeutic techniques to combat HTS, burn therapists report good outcomes when following the ISBI burns practice guidelines [9].

Table 1.2 Conservative management randomized controlled trials for hypertrophic scar management, only studies which include children

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
Silicone							
Carney et al[92] 1994	RCT Study Period: Not specified Intraindividual	n=42 Mean age 23.2y (2–60y) % male not specified 47 scars 37% limb scars 20% neck scars 13% chest scars Race not specified	Group A: Silasic gel sheet Group B: Cica care Group C: No treatment	24h/day Start time: Not specified	6 months	Clinician assessment of colour, texture, general scar condition Extensibility: Extensometer Photographs used to assess state and colour of scars	**Improved scar per clinician assessment at 2 months;** **Silasic gel sheet;** 86% **Cica care;** 93% **No treatment;** 12% Compared to no treatment; **Colour;** **Silastic gel sheeting;** At 2 months; p=0.005 **Cica Care;** At 2 months; p=0.008 At 6 months; p=0.007 **Texture (softening);** Silastic gel sheeting; At 2 months; p<0.0001 At 6 months; p=0.012 **Cica Care;** At 2 months; p<0.0001 At 6 months; p=0.002 **Great scar extensibility**; Silastic gel sheeting; At 2 months; p<0.0001 At 6 months; p<0.03 **Cica Care;** At 2 months; p<0.001 At 6 months; p<0.04

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
Karagoz et al[93] 2009	RCT Study Period: Not specified Between patient	n=32 Mean age 24y (3–55y) 37% male 45 scars 64% upper limb scars 20% trunk scars Race not specified	Group A: Silicone gel (Scarfade®) Group B: Silicone gel sheet (Epi-derm™) Group C: Onion extract (Contractubex®)	Group A: Applied Twice/day Group B: 24 h/day Group C: Applied Twice/day Started within 6 months of burn injury	6 months	VSS	Lower VSS in total and per subscale using silicone gel or silicone gel sheeting compared to onion extract ($p<0.05$)
Momeni et al[94] 2009	RCT Study period: 2005–2006 Intraindividual	n=34 Median age = 22y (1–60y) 47% male 34 scars 29% upper limb scars 26% face scars 23% lower limb scars Race not specified	Silicone gel sheeting (Cica Care) And Placebo (self-adhesive sheeting)	4h/day with 4h daily increment to 24 h/day Started 2–4 months post burn injury	4 months	mVSS Excluding height Photographs	**1 month:** **Vascularity** significant in favour of silicone ($p<0.05$) Vascularity; 1.59 ± 0.16 **4 months:** All mVSS scar subsets were significantly lower in the silicone group. **Pigmentation**; 0.29 ± 0.08 **Vascularity**; 0.97 ± 0.18 **Pliability**; 0.97 ± 0.13 **Pruritis** reduced in silicone group; 0.41 ± 0.10

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
Pressure Garments							
Engrav et al[95] 2012	RCT Study period: 1995–2007 Intraindividual	n=54 Mean age 36y (7–65y) 85% male 54 scars Forearm burns only Caucasian 69% Non-Caucasian 28%	Normal pressure garment (17–24mmHg) or Low pressure garment (<5mmHg) Allocated to distal or proximal portion of scar	Garments worn 23hr/day Started therapy within 2 weeks of re-epithelisation.	1 year follow up period or earlier if scar stable	Hardness; Rex Durometer Hand Model 1600 Colour; Chromameter Minolta CR-300 Thickness; High resolution ultrasonography Clinical appearance; Photographs	**Normal pressure: Thickness** reduced -0.65mm (95% CI -1.2– -0.13)
Groce et al[96] 2000a	RCT Study period: Not specified Intraindividual	n=58 Mean age 6y (1–17y) Mean TBSA 48.3% Scar number unknown Bilateral extremity burns only Hispanic 57% Black 34% Caucasian 9%	High pressure And Low pressure garment Randomly allocated to left or right limb of the same patient	Garments wear not specified Time to start therapy not specified	6 months	VSS* Photography for clinician assessment	No significant difference

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
Groce et al[97] 2000b	RCT Study period: Not specified Between patient	n=46 Mean age 8y % male not specified Mean TBSA 11.2% Scar number unknown Scar location not specified Caucasian 61% Black 24% Hispanic 15%	Group A: Pressure garments (average 20mmHg) Group B: No pressure	Garment wear not specified Time to start therapy not specified	6 months	VSS* Photography for clinician assessment	**At 6 months;** **Scar height;** Lower for pressure group 95%CI 0.68±0.57 (p<0.05)
Silicone & Pressure Garments							
Li-Tsang et al[98] 2010	RCT Study Period: Not specified Between patient	n=104 Mean age 21.8y (±18y) 60% male Scar number unknown 44% upper limb scars 29% lower limb scars Race not specified	Group A: Pressure garment Group B: Silicone gel sheeting Group C: pressure garment and silicone gel sheeting combined Group D: control Lanolin cream massage 15 minutes daily (all groups told to do this)	Garments to be worn 24hr/day Silicone for as long as tolerated Mean period since injury 14.9m ± 30.8m	6 months	Pliability: VSS* Colour: Spectrocolorimeter Thickness: Tissue Ultrasound Palpation System Pruritis & Pain: Visual Analog Scale	**Thickness** improved (p<0.001); Combined group At month 2 (4.91±1.26) 4 (4.72±1.38) 6 (4.63±1.20) **Thickness** improved p<0.001); Pressure group At month 6 (5.15±2.01) **Colour** improved (p<0.001); At month 6; All groups (p<0.001)

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
							Pliability improved (p=0.002); Combined group At month 2 (2.74±0.85) 4 (2.62±0.71) **Pain** improved (p=0.001); At month 6; Combined (0.46±1.19) Silicone gel sheeting (0.84±1.64)
Massage							
Morien et al[99], 2008	RCT Study period: Not specified Intraindividual	n=8 Mean age 13y (10–17y) 25% male %TBSA not specified Scar number unknown Burn scar location not specified Race not specified	Massage Contralateral limb the control: no massage Massage to areas where grafted only	Massage 20–25 minutes, 1/day for 5 days Therapy started > 2y (2–16y) after burn injury	3–5 days	ROM; Goniometer	ROM increased on massaged tissue side of body (p=0.03)
Patino et al[100] 1999	RCT Study period: Not specified	n=30 Mean age 4y % male not specified	Group A: Massage & pressure garments Group B: Pressure garments alone	Friction massage 10 minutes/day	3 months	mVSS*	No significant differences between groups

Study	Study design	Participants	Therapy Provided	Application of therapy	Therapy Duration	Outcome measure	Significant Results
		%TBSA not specified Scar number unknown Burn scar location not specified Race not specified					

RCT, Randomized controlled trial; Intraindividual, comparison of therapy between two areas of the same patient; Between patient, comparison of therapy between different individuals; n, number; y, years; %TBSA, Percentage total body surface area; VSS, Vancouver scar scale; mVSS, Modified Vancouver scar scale, *Score of 0 is normal skin, higher scores on VSS or mVSS indicates a more hypertrophic scar; Pruritis, itch; 95%CI: 95% Confidence Interval; ROM, Range of Movement

Despite a lack of robust studies, pressure therapy has been considered the mainstay of conservative treatment for HTS. Typically, pressure therapy is worn 23 hours a day, at a pressure of 15–25mmHg, until scar maturation [9]. It is provided through custom pressure garments, tubular stockings or bandaging, depending on the physical location of the scar and healthcare availability [101]. The exact mechanism for how pressure therapy improves scar outcome remains an area requiring ongoing investigation. It is thought that pressure to post burn scars may reduce capillary blood flow to the scar, in turn limiting oxygen and nutrients. This reduction of blood flow aids in controlling excess collagen synthesis and potentially stimulates collagen breakdown, reducing the redness and height of the scar and promoting maturation [102, 103].

Two meta-analyses and systematic reviews have investigated the effectiveness of pressure therapy [102, 104]. The findings of these systematic reviews differed in their conclusions. The more recent review included an additional five RCT's and the authors concluded there was significant evidence supporting the effective use of pressure therapy for prevention and treatment of HTS [102]. While there was no significant difference in vascularity, the authors concluded that with the use of pressure garments (15–25mmHg), HTS showed significant improvement in thickness, pliability, and pigmentation [102]. Inconsistency remains between the studies included in the systematic reviews, with variability in assessment of HTS, time to commencement of pressure therapy, sample sizes and clinical outcomes. There remain ongoing limitations in evidence demonstrating the effects of pressure therapy throughout the full scar maturation phase and the potential of adverse events. Difficulty remains in conducting large objective RCT's for pressure therapy, as it is considered clinically beneficial and withholding it as a treatment may be considered unethical. Two studies of short duration conducted specifically on children, found no difference in scar outcome between high and low pressure, whilst a comparison of pressure to no pressure found only improvement in scar height at six months with the use of pressure [96, 97].

Silicone, in varied forms such as silicone sheets and topical gels, are widely used in clinical practice to reduce the effects of HTS. Studies have attempted to identify the

causal effect of silicone on HTS including pressure, temperature, blood flow, oxygen, hydration by reduction of transepidermal water loss and silicone release, although no clear mechanism of action has been identified [105-107]. It is postulated that with an increase in skin surface temperature at the scar, as little as 1°, may increase collagenase activity and breakdown the excessive collagen deposition at the hypertrophic scar site [106, 108, 109].

Studies demonstrate silicone can significantly reduce vascularity, pliability, pigmentation, pruritis and pain [94, 110-112]. Three studies combined pressure therapy and silicone with favourable results using subjectively rated scar scales [110, 113, 114]. A Cochrane review of silicone use for HTS, found poor study designs and high bias in included studies, limiting their conclusions. However, it remains recommended in ISBI practice guidelines for preventing and managing HTS [9, 115]. Comparability of studies is difficult due to the difference in silicone products used, commencement times from burn injury, regimens (including time periods) and various subjective and objective assessment measures used. Furthermore, the majority of studies are of short duration (two to six months) and therefore do not span the period for complete scar maturation, making it difficult to determine longer term outcomes. Low participant numbers (n=10–104) further reduce the power of the results. No RCT has evaluated the effectiveness of silicone on children only. Therefore, while strong conclusions cannot be drawn, silicone use in children continues to remain a recommendation from ISBI practice guidelines [9].

Other therapeutic techniques commonly used for hypertrophic scar management include massage and hydration. Hydration by emollients (topical lotion e.g. moisturizer) remains a common recommendation for the side effects of transepidermal water loss, however currently has minimal supporting evidence. Of three studies included in a systematic review, all examined different topical lotions, had small sample sizes, and varied intervention time periods [91]. Two of the three studies found improvements in pruritis only, whilst another compared topical silicone to onion extract, with silicone demonstrating a significant improvement in VSS score [93, 116, 117]. A recent systematic review investigating massage therapy for HTS included five adult studies,

two paediatric studies and one rodent study [118]. All studies included were of low to moderate quality and at single centres, therefore limiting their generalisability. Comparison between these studies is further challenged by variations in the methodologies and outcome measures utilized. Massage techniques and dosages varied from 10–30 minutes once per day to three times per week, with often unknown treatment periods documented. Time to intervention commencement varied, in one study after re-epithelisation and in another, two to five years post burn injury [99, 119]. Only short-term conclusions can be drawn from the studies as assessments were made pre and post intervention, with a maximum of three months post intervention. The data demonstrates mixed results to support the use of massage therapy to improve HTS scar pruritis, pain, pliability, vascularity, height and pigmentation, whilst one paper found no improvements in HTS quality [120] and two studies with no improvement in range of motion (ROM) compared to the control [99, 100, 120-124]. Two small, poor quality studies investigated massage with children with no significant findings for the improvement of HTS [99, 100].

1.4 Complications associated with hypertrophic scars

In addition to HTS development, burn injuries may be associated with complications of burn scar contracture, pruritis and neuropathic pain [9]. Development of burn scar contracture is due in part to the replacement of natural pliable skin with that of inextensible scar tissue [53]. A burn injury, if in close proximity or across a joint surface, may result in loss of ROM, leading to deformity and limitations in functional activities [125-127]. Pruritis and neuropathic pain related to HTS appear to be associated with peripheral and central nervous system dysfunction [128-131]. This may affect patients daily, resulting in irritation and impaired sleep [50, 128]. In addition to the altered cosmesis of burn scars, these additional complications often have long-term impacts on function and quality of life post burn injury [22, 50]. Limited research for management of contractures, pruritis or neuropathic pain has been conducted specifically in children.

1.4.1 Contracture development

Burn scar contracture is a well-documented and significant complication post burn injury [125, 127]. A burn adjacent to or crossing a joint is considered at risk of developing a contracture due to the limitation in cutaneous functional units, as impacted by the inelastic nature of scar tissue [53]. Cutaneous functional units are defined as the fields of skin functionally required for ROM [53]. Development of burn scar contracture begins in the acute wound phase with oedema, pain, and tight eschar reducing joint ROM [132, 133]. Eschar is non-viable tissue that covers a wound bed in response to injury and is often thick and hard. It provides an opportunity for infection, prolongs the inflammatory phase of wound healing and physically blocks wound closure [134]. Wound contraction occurs during wound closure, and is often compounded by patients adopting a position of comfort (e.g. commonly flexion and adduction of the joint), which further promotes the development of burn scar contracture [127, 135]. The inelastic nature of scarred skin makes little accommodation for skeletal growth in children, potentially resulting in a delayed development of contracture as they age [54]. For children, prevention of burn scar contracture is therefore imperative to allow for ongoing growth as they develop.

1.4.2 Contracture predictors

Data indicating predictors of contracture development are comparable to HTS development. Variables found to be significantly associated with contracture development in adults were noted to be greater %TBSA, deeper burn, flame burn, grafting and increased surgical procedures [80, 81, 136-140]. Two studies reported that joints of the upper limb and neck were more frequently contracted compared to those of the lower limbs [136, 138]. Specifically for children, longer intensive care admissions and older age groups were identified as variables associated with increased contracture development, while another study identified younger ages and larger %TBSA as associated predictors [137, 141]. A recent study by Thomas et al, found no baseline variable could independently predict contracture development of children sustaining axilla burns [80]. The variability in predictors seen in the literature challenges clinical

decision making to ensure timely and effective treatments are provided to those patients most at risk and responsive to treatment.

1.4.3 Contracture prevalence

Determining burn scar contracture prevalence is difficult due to inconsistent reporting and variations of contracture definition, study designs and populations [81, 132, 136, 137, 139, 140, 142-144]. Time points for determining contracture vary between studies, with four studies measuring contracture at hospital discharge and others measuring throughout the rehabilitation phase at three, six, 12 and 24 months [80, 81, 90, 125, 132, 136, 137, 140, 144]. In adults, reported prevalence rates of contracture at hospital discharge were 38–54% and at 12 months post injury were 9.4–32% [81, 136, 138-140, 144, 145]. Five studies investigated contractures in children only, with a prevalence rate of 0–89% at various time points post injury [80, 81, 90, 125, 139, 146]. Interventions to counteract the development of contracture varied in all studies. Prophylactic splinting, splinting upon loss of ROM and usual care were all named as interventions in different studies, while some studies did not name an intervention. Schouten et al conducted a multi-centre cohort study, including adults and children and identified that patients who did not require skin grafting for wound closure had resolution of their limited ROM secondary to contracture by 6–9 months post injury, while twenty percent of patients who underwent surgery had limited ROM persisting at 12 months [138]. Studies investigating contracture prevalence often do not describe other post burn complications in combination with contracture, for example HTS or pain presence. Further investigations addressing long-term paediatric contracture at skeletal maturity would provide insight into the possible long-term effects complicated by growth and burn injury.

Surgical release of a burn scar contracture may provide insight into contracture prevalence rates. Indication for surgical release is often based on reduced ROM, pain or functional limitations. Four studies reported on prophylactic therapy, including early splinting and scar management, reporting surgical release rates of 0–13% [80, 90, 143,

147]. Conversely, Huang et al reported an incidence of surgical release requirement of 93% for adults who did not use splints or pressure for scar management, compared to 26.3% if splints and pressure garments were worn for any length of time [144]. Differences of inclusion criteria make conclusions difficult as some only selected particular joints, patients with major burns or specifically from inpatient or outpatient settings only [80, 136, 143, 144]. Surgical management for contracture and/or HTS may be indicated despite patients/therapists following best clinical practice interventions.

1.4.4 Contracture management

The prevention of contracture is an important goal for burn therapists and patients. Loss of ROM due to contracture can lead to prolonged therapy requirements; including both acute inpatient admissions and rehabilitation, pain and discomfort, decreased independence and, if required, surgical release for contracture correction [135]. Prevention of contracture needs to commence as soon as feasibly possible to oppose the contractile forces that develop during wound healing and scar development [127, 133, 135]. By positioning the scar tissue in an elongated position, with pressure from the splint, collagen bundles are prevented from contracting and thickening in a disorganized manner. The potential development of HTS is reduced, whilst also preventing contracture [50]. The ISBI practice guidelines and a recent expert consensus report recommends the prescription of splinting to patients with deep partial or full thickness burns located within close proximity of a joint, or those crossing a joint [9, 148]. The aim of this intervention is to aid pain and oedema management, protect new grafts and flaps, maintain ROM and to correct joint deformity [9, 148].

Literature to support splinting for contracture management and prevention is limited to five RCTs and several lower quality studies of varying methodologies, including various splint designs and regimes (frequency and duration) [149-153]. A recent systematic review found all but one of five RCTs showed statistically significant ROM improvements associated with the use of orthoses [148]. One practice guideline was able to be drawn from the available evidence, stating that ‘orthotic use should be

considered as a treatment choice for improving ROM or reducing contracture in adults who sustained a burn injury' [148]. No RCT has been conducted with children alone. Despite international recommendations, differences in splint design, joint positioning, regime and time to commencement of intervention are seen throughout clinical practice to manage not only contracture, but also scar management. Splinting to prevent and manage contractures therefore remains an area requiring further research to guide clinical practice guidelines, in particular for children.

It is theorized that additional tension to the healing wound may increase myofibroblast activity, promoting HTS development and in turn increasing the likelihood of contracture development [154, 155]. Conflicting research exists regarding the risk of excessive mechanical tension to scar tissue in association with static splinting [154, 155]. Studies have demonstrated that with increasing mechanical stress, a cells' functional capability is altered through a process called mechanotransduction, resulting in an altered wound healing process and increasing the likelihood of excessive scarring [156-158]. Most studies addressing mechanotransduction have been conducted in non-burn wounds, making it difficult to conclude direct impact upon burn wounds, and subsequently HTS in these populations. With incised wounds, one study demonstrated the development of HTS in the context of the application of mechanical tension to healing wounds [159]. Others have shown a reduction in HTS development with the addition of compression [160]. In literature exploring burn scars only one RCT found no significant difference between active ROM exercise and maintaining joint ROM with static splinting [153]. This indicates that splinting post burn injury is likely not to significantly increase mechanotransduction processes and promote HTS or contractures [142, 148]. There is also a lack of evidence indicating the level in which skin tension is deemed to be excessive [142, 154]. A study investigating mechanical stress in rat models found that younger scars (those less than 14 weeks old) were more reactive to stress remodelling than older scars [161]. This suggests that earlier intervention to address loss of ROM may translate into improved scarring outcomes by preventing contracture before it occurs and thereby excessive mechanical tension forces acting on scar tissue. In the absence of large multicentre studies in children with HTS and contractures, clinical

decision making remains based on local healthcare practices and clinician experience. Future research regarding splint prescription, design and regime is required.

1.4.5 Pruritis

Pruritis associated with HTS is a common and uncomfortable problem for burn survivors. It is recognized that during the rapid scar development phase, histamine production increases as a result of an influx of mast cells resulting in pruritis [162]. However, there are conflicting reports on the development of pruritic symptoms with authors suggesting peripheral and central hyperalgesia [128-131]. Reports document 87–93% of adult and 71–93% of child burn survivors suffer pruritis post burn injury. In paediatrics, it was demonstrated that severity of pruritis declines over time, however at two years post injury, 64% still reported pruritis [162-165]. Currently known predictors for post burn pruritis in adults includes number of surgical procedures, increased %TBSA, female gender, younger age, dry skin and HTS [163, 164]. In children there are conflicting reports of predictors for pruritis with one study finding depth of injury, increased %TBSA, skin grafting and time since burn significant predictors, whilst one paper disagreed with all noted predictors [162, 165]. Further investigations are warranted to definitively determine risk factors to aid treatments and improve long-term outcomes.

1.4.6 Neuropathic pain

Post burn neuropathic pain is a distressing complication for burn survivors. Neuropathic pain is thought to be a peripheral neurological dysfunction, however the exact mechanism for the development post burn pain remains unknown [166, 167]. Symptoms include pins and needles, shooting, stabbing, burning or electric shock sensations [167, 168]. A retrospective study of adult burn patients found pain developed by four months post injury, improved by seven months, with 60% of pain resolving by 13 months [168]. Neuropathic pain has only been studied in adults, with prevalence rates of 7–87% [163,

169-172]. It is associated with increased burn depth, increased surgical procedures, increased %TBSA, longer hospital stays and substance abuse [163, 169-172]. Burn therapists acknowledge children likely suffer neuropathic pain after burn injuries, however it is often poorly reported until adolescent years. Further research is required to understand the prevalence and impact of post burn pain in children.

1.4.7 Pain and pruritis management

Treatment and assessment for pruritis and neuropathic pain remains poorly understood and under researched. Most commonly, a subjective visual analogue scale is used to rate pain or pruritis from 1–10 [173]. Alternatively, the Itch Man Scale has been developed specifically for children post burn injury [174]. Difficulty remains in accurately assessing the largest proportion of paediatric burns patients, those aged 0–4 years. Children of this age are too young to describe or identify their sensations with accuracy. Parental responses are utilized for children under six years; however, accuracy remains variable. Studies recommend antihistamine medication, however symptom relief has been reported in only 29% of children and 20% of adults [162, 175, 176]. Emollients such as moisturizers and lanolin, in conjunction with massage, have also been recommended. Some studies have indicated improved pain and pruritis, with the mechanism likely being the desensitization of the skin [117, 121, 123, 128]. Anecdotally, pressure garments have also had positive effects on reducing pruritis severity, however the evidence base for this is limited, in particular for paediatric populations. Understanding the impact of pruritis and neuropathic pain on daily function and quality of life is critical, in addition to understanding the most effective methods to combat it. The area therefore requires further research to assist clinicians assessing and treating these factors.

1.5 Conclusion

Post burn HTS prevalence remains inclusive for children, a direct result of differing definitions of HTS and various scar scales used within the studies. Inconsistent reports of risk factors for HTS development remain, impacting therapist ability to identify and predict children early for risk of HTS development. Conservative scar management interventions are recommended by ISBI burn care practice guidelines where a burn is surgically closed or heals in >21 days. There are no practice guidelines specific to those healing 14–21 days resulting in management which relies on therapist expertise or institution service availability. Evidence for efficacy of conservative interventions remains inadequate, due to a lack of robust RCTs, however remain widely used in clinical practice both prophylactically and once HTS develops.

Chapter Two:

What are the scar outcomes for children who have had a burn injury, are not grafted and heal >14 days?

This chapter is presented in the format of a manuscript which has been submitted to the journal Burns & Trauma, with the exception of tables and figures embedded throughout the manuscript (rather than in a separate document) for ease of reading. See Appendix 4 for submission guidelines for the journal Burns & Trauma. See Appendix 5 for authorship contribution statement.

Preface

Title

What are the scar outcomes for children who have had a burn injury, are not grafted and heal >14 days?

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Abstract

Background: Hypertrophic scarring is a significant complication post burn injury, especially for children healing after 3 weeks. Burn injuries healing prior to 3 weeks also have the potential to scar, even if prescribed prophylactic conservative scar interventions.

Methods: A retrospective chart audit reviewed 326 burn patients (median age 2 years (range 0–15)) treated at a tertiary hospital from 2014–2019 who did not receive skin grafting for their burn and healed >14 days, for the duration of their follow up. Scar assessment was conducted by experienced burn therapists. A scar was deemed hypertrophic if >1mm in height. To identify early hypertrophic scar prevalence the time period 3–6 months post burn was used, to identify persistent hypertrophic scarring the time period of 12–18 months post burn was used.

Results: Median days to wound closure was 18 (range 14–77 days). Prevalence of hypertrophic scar presence for our cohort at 3–6 months was 56.1% and 16.3% at 12–18 months. At 3–6 months post burn, over half of presenting patients had a hypertrophic scar, of which 56.8% had healed within 14–21 days. Similarly, at 12–18 months, half the presenting patients had a hypertrophic scar, of which 56.6% had healed within 14–21 days. One hundred and thirteen children sustained a burn crossing a joint, no child developed subsequent joint contracture associated with their hypertrophic scar. Seventeen (5.2%) children underwent medical intervention for scar modulation.

Conclusion: Early signs of hypertrophic scarring were seen in just over half the patients presenting to physiotherapy and despite scar intervention, persistent HTS was seen in 16.3%. At both time points, just over half of the children presenting healed between 14–21 days. This study reaffirms that children have the potential to progress to hypertrophic scarring when healing prior to 21 days.

Keywords: Scar, Hypertrophic, Burn, Time to heal, Paediatric, Partial thickness, prevalence

Introduction

Scarring, specifically hypertrophic scarring (HTS) post burn injury is a common and unavoidable sequalae of deep dermal and full thickness burns [1]. Following the trauma of a burn injury, long lasting HTS can impair function, contribute to contracture, affect cosmetic appearance, produce symptoms of pruritus and pain, all of which may decrease quality of life [2]. In children, HTS prevalence rates are reported as 16–69% [3-9]. The wide range in reported prevalence stems from varied study populations and the lack of consensus of one standard measurement tool or finite value in the scar scales used to determine the presence or definition of HTS [10]. Study results are further compounded by the wide-ranging use and availability of burn scar treatment interventions (modern wound dressings, surgical interventions, pressure garments) across healthcare services [11].

Delayed re-epithelization has been correlated as the most prevalent risk factor for HTS development [3, 5, 6, 12]. Deitch et al first reported increasing risk of HTS with re-epithelization after 3 weeks, however specifically for children, re-epithelialization time as low as 8–14 days appears linked to HTS development [5, 6, 12]. In addition, extrinsic factors including burn mechanism (for example, flame burn linked to deeper depth), larger percentage total body surface area (%TBSA), deeper skin depth burned, longer hospital stays and wound complications such as infection or subsequent wound breakdown [8, 10, 12, 13], as well as intrinsic factors including patient characteristics such as ethnicity, younger age and skin type (Fitzpatrick classification IV–VI) can also increase the risk of HTS [6, 13].

Prevention and treatment of HTS remains an ongoing challenge for therapists and patients alike. Pressure therapy, silicone and hydration (emollients) are highly recommended interventions by the International Society for Burns (ISBI) for managing HTS [14]. However, it remains inconclusive as to whether prophylactic action is superior to reactive treatment [11]. Multiple studies have identified the first six months post burn as the most active scarring period, with HTS becoming most apparent during this time, followed by collagen remodelling and reduced vascularity at 12 months [15, 16].

Research suggests targeting scar interventions during the most active phase of scarring, to reduce blood flow to the scar and to aid collagen remodelling [15, 17, 18]. Once a scar is considered mature, little treatment effect is possible in aiding skin to return to normal [19]. What remains unclear, is which patients benefit from intervention to promote collagen remodelling compared to those that may intrinsically improve without intervention.

The Children's Hospital at Westmead (CHW) is the tertiary referral centre for paediatric burn injuries in New South Wales (NSW), providing specialized acute and long-term scar management for all burn injuries. Standard clinical practice is to provide specialist burn wound debridement and assessment by Burn Unit Nurse Practitioner/Medical Practitioner. Silver based dressings are most frequently used and scheduled changes occur predominantly at seven-day intervals. Other dressings may be utilized where clinically indicated. The aim of the Burn Unit is to achieve definitive wound closure within 14 days. Where burn wounds are not healed at 14 days or assessed as not having good healing potential within 21 days, skin grafting of the unhealed areas is considered as soon as possible.

Children who achieve wound closure in >14 days with only conservative management are triaged into a Burn therapist-led outpatient clinic. The burn therapy service is highly specialized comprising of two senior full time equivalent Burn Therapists, each with over 10 years' experience and one junior therapist working under supervision. Children are reviewed by a Burn Therapist within two weeks of wound healing to assess the risk of HTS development. If the risk of HTS is deemed minimal, the child is discharged with education. Where HTS risk is identified, individualized prophylactic scar intervention is commenced and where relevant, prophylactic contracture prevention is initiated. Therefore, the aim of this study is to describe the scar outcomes for children who sustained a burn injury taking >14 days to heal and were managed conservatively within CHW Burn Unit.

Methods

Study design, setting and participants

A retrospective medical record audit was conducted at CHW. To ensure all eligible patients were identified, the NSW Severe Burn Injury Service (SBIS) database and CHW medical records were utilized to capture all patients who sustained a burn and were referred to CHW burn unit between 1 January 2014–28 February 2019. The NSW SBIS coordinates burn care within NSW and CHW is the specialized paediatric component of this state-wide service. For inclusion in this study patients were <18 years, sustained an acute burn that took 14 days or longer to heal and were referred to the burn therapy-led scar clinic. Patients were excluded if their burn healed in <14 days, was closed by skin grafting or primary closure, were discharged at or did not return after initial burn therapy-led scar clinic appointment and those not followed up at CHW as they reside outside NSW. This study was approved by Sydney Children's Hospital Human Research Ethics Committee (2020/STE05504).

Demographic and clinical data collected

The patient's records were reviewed for the duration of burn care management. All nursing, medical and burn therapy appointments were recorded until discharge or loss to follow up.

Participant characteristics

Data was obtained pertaining to the child's age, sex and geographical location (classified as metropolitan or non-metropolitan based on postcode classification from Australian Statistical Geography Standard [20]) at time of burn.

Burn Characteristics

Data was recorded regarding burn mechanism: scald, flame, friction, contact, chemical or electrical; location: bilateral, unilateral or central; worst burn depth described as superficial, partial or full thickness; and size described by %TBSA. Depth and %TBSA are reported by a Burns unit Nurse Practitioner within two appointments at the burn unit.

Acute management

First aid was recorded as optimal, suboptimal, or not reported. First aid was considered optimal if the child received 20 minutes of cool running water within three hours of their burn injury [21]. Hospital admission and length of inpatient stay (days) were recorded. Number of outpatient burn unit appointments were recorded until definitive wound healing. Definitive wound healing was defined as complete reepithelization, no longer requiring dressings and discharged from the burn unit clinic to burn therapy-led clinic. Patients were categorized in groups based on days to heal:14–21 days, 22–30 days and >30 days.

Scar outcomes

Primary scar outcomes

Burn scars were assessed by CHW Burn Therapists using the modified Vancouver Scar Scale mVSS [18]. The mVSS is a therapist reported scale, assessing the scar for vascularity, pliability, pigmentation and height compared to surrounding skin [18]. As CHW therapists do not record the pigmentation component of the mVSS in clinical practice, this has not been reported in this study. A scar was deemed hypertrophic if the patients worst scar height was >1mm, correlating to a subcategory score ≥1 on the mVSS [8, 22]. To identify early prevalence of HTS, the time period of 3–6 months post burn was utilized as this is considered the most active scar development phase post burn [16, 18]. To identify persistent prevalence of HTS, the time period of 12–18 months post burn was used, demonstrating the time in which a scar has progressed through the maturation phase [16, 18].

Secondary scar outcomes

Scar vascularity and pliability was assessed using the mVSS [18]. Wound breakdown was recorded as present, not present, or not reported. Where a scar crossed a joint, range of motion (ROM) was assessed as full, not full, or not reported.

Interventions

Scar management

All patients were prescribed an individualized scar intervention program. Scar interventions were categorized and recorded in four groups: silicone (gel sheeting or creams), pressure (pressure garments, coban, tubigrip, and duoderm), hydration (emollients) and contracture prevention/ROM maintenance (splinting and exercise). Medical interventions to treat scarring were recorded as required or not, the time point post burn injury, procedure performed and quantity of procedures performed.

Data analysis

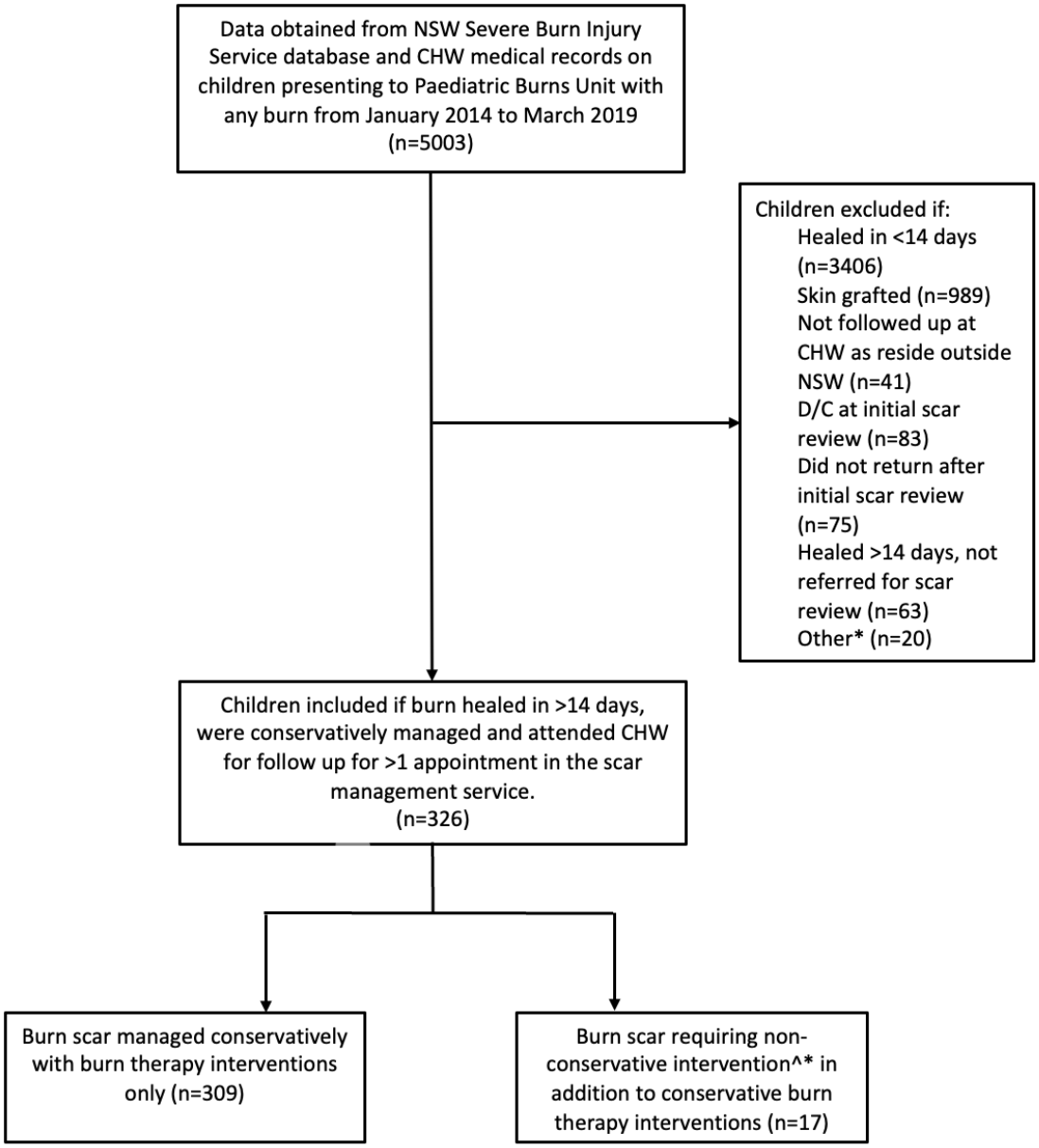
Data was collected and analysed in Microsoft Excel. Data was visually reviewed for normality and standard descriptive statistics were used. Where data was normally distributed, the mean and standard deviation were reported; for non-normally distributed data, the median and range were reported. Descriptive analysis of participant demographics and acute clinical variables were obtained to describe the paediatric population. Scar outcomes and interventions were reported as close to one, 3–6, and 12–18 months post burn.

Results

Demographic and clinical data collected

Three hundred and twenty-six children met the inclusion criteria for this study. Flowchart for patient inclusion is shown in Figure 1.

Figure 1: Flow chart of patient inclusion



Other: primary closure, non-burn wound treated within burn unit; ^ non conservative scar interventions for scar modulation may include microneedling, laser, steroid injection and z-plasty without grafting D/C, discharged; n, number.

Patients

Patient demographics and clinical characteristics are presented in Table 1. The median age at burn was two years (range 0–15 years), with males accounting for just over half (57.7%) of the cohort. The majority of patients (79.7%) were under five years at time of burn. Patients were evenly distributed from metropolitan (52.5%) and non-metropolitan (47.5%) areas. The flow of patients through the treatment period, the presence or absence of HTS and discharge or loss to follow up is shown in Figure 2.

In total, 171 (52.4%) patients completed burn therapy scar treatment until discharge, attending a median number of four burn therapy appointments (range 2–12) for a median of nine months (range 1–53 months). One hundred and forty-five (44.5%) patients were loss to follow up, of these 94 (64.8%) had HTS at their final burn therapy appointment. The remainder of patients (n=10, 3.1%) continued to receive medical intervention for scar management at the end of the study period. Medical intervention was received by a total of 17 (5.2%) patients. Patients requiring medical intervention had a median time to wound closure of 21 days (range 15–43). The patients receiving medical intervention attended a median of eight (range 4–17) burn therapy scar appointments over a median period of 20 months (range 9–45).

There were 31 patients who did not attend within the 3–6 month time period. All patients except one, were either loss to follow up (n=16) or discharged (n=14) prior to three months. At their final burn therapy appointment, 22 patients had not developed HTS and eight had developed HTS. The one patient who attended after six months, had an assessment of HTS and was discharged at eight months.

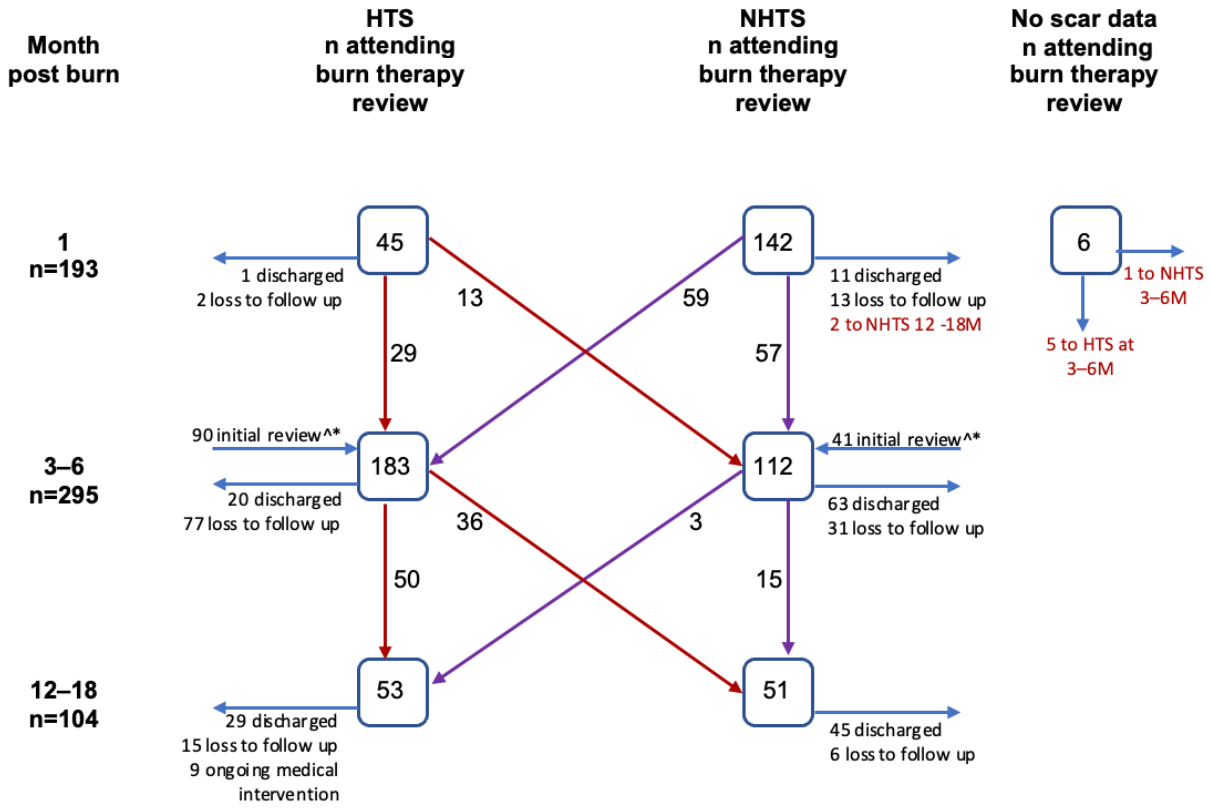
Table 1: Patient demographics and clinical characteristics for cohort and patients presenting for burn therapy at 3–6 and 12–18 months post burn

Categorical variable		Cohort n/326(%)	HTS at 3–6 months n/183(%)	NHTS at 3–6 months n/112(%)	HTS at 12–18 months n/53(%)	NHTS at 12–18 months n/51(%)
Sex	Male	188 (57.7)	103 (56.3)	69 (61.6)	27 (50.9)	30 (58.8)
	Female	138 (42.3)	80 (43.7)	43 (38.4)	26 (49.1)	21 (41.2)
Age (years)	<2	154 (47.3)	91 (49.7)	46 (41.1)	26 (49.1)	28 (54.9)
	2–<5	78 (23.9)	41 (22.4)	28 (25.0)	7 (13.2)	10 (19.6)
	5–<12	72 (22.1)	41 (22.4)	26 (23.2)	16 (30.2)	12 (23.5)
	12–18	22 (6.7)	10 (5.5)	12 (10.7)	4 (7.5)	1 (2.0)
Geographical Location	Metropolitan	171 (52.5)	98 (53.6)	52 (46.4)	28 (52.8)	31 (60.8)
	Non-Metropolitan	155 (47.5)	85 (46.4)	60 (53.6)	25 (47.2)	20 (39.2)
Mechanism	Scald	228 (69.9)	134 (73.2)	77 (68.7)	45 (84.9)	35 (68.6)
	Flame	19 (5.8)	9 (4.9)	10 (8.9)	2 (3.8)	1 (2.0)
	Friction	22 (6.6)	13 (7.1)	4 (3.6)	2 (3.8)	3 (5.9)
	Contact	56 (17.1)	26 (14.2)	20 (17.9)	3 (5.6)	12 (23.5)
	Chemical	2 (0.6)	1 (0.6)	1 (0.9)	1 (1.9)	0 (0.0)
Worst burn depth	Partial thickness	301 (92.3)	165 (90.1)	107 (95.5)	48 (90.6)	45 (88.2)
	Full thickness	25 (7.7)	18 (9.9)	5 (4.5)	5 (9.4)	6 (11.8)
%TBSA affected	<1%	41 (12.6)	26 (14.2)	9 (8.0)	1 (1.9)	8 (15.7)
	1–5%	221 (67.8)	116 (63.4)	85 (75.9)	37 (69.8)	33 (64.7)
	6–10%	43 (13.2)	25 (13.7)	15 (13.4)	8 (15.1)	5 (9.8)
	11–20%	18 (5.5)	13 (7.1)	2 (1.8)	5 (9.4)	5 (9.8)
	>20%	3 (0.9)	3 (1.6)	1 (0.9)	2 (3.8)	0 (0.0)

Categorical variable		Cohort n/326(%)	HTS at 3–6 months n/183(%)	NHTS at 3–6 months n/112(%)	HTS at 12–18 months n/53(%)	NHTS at 12–18 months n/51(%)
Burn Location**	Face/Head	86 (26.3)	55 (30.0)	24 (21.4)	20 (37.7)	15 (29.4)
	Neck	34 (10.4)	18 (9.8)	12 (10.7)	7 (13.2)	5 (9.8)
	Anterior trunk	117 (35.9)	64 (34.9)	37 (33.0)	28 (58.8)	16 (31.4)
	Posterior trunk	20 (6.1)	14 (7.7)	6 (5.4)	6 (11.3)	3 (5.9)
	Upper limb	139 (42.6)	74 (40.4)	55 (49.1)	24 (45.3)	24 (47.0)
	Hand	108 (33.1)	61 (33.3)	31 (27.7)	11 (20.7)	16 (31.4)
	Flank	9 (2.8)	5 (2.7)	4 (3.6)	3 (5.7)	2 (3.9)
	Buttock/genitals	13 (3.9)	7 (3.8)	6 (5.4)	4 (7.5)	1 (2.0)
	Lower limb	85 (26.1)	49 (26.7)	31 (27.7)	21 (39.6)	13 (25.5)
	Foot	37 (11.3)	25 (13.7)	9 (8.0)	6 (11.3)	7 (13.7)
Body distribution^*	Bilateral	57 (17.5)	33 (18.0)	18 (16.1)	17 (32.1)	11 (21.6)
	Unilateral	224 (68.7)	125 (68.3)	84 (75.0)	27 (50.9)	36 (70.6)
	Central	116 (35.6)	65 (35.5)	37 (33.0)	25 (47.2)	14 (27.4)
Burn crossing a Joint space	Yes	113 (34.7)	70 (38.3)	29 (25.9)	17 (32.1)	20 (39.2)
	No	213 (65.3)	113 (61.7)	83 (74.1)	36 (67.9)	31 (60.8)
Joints affected	Fingers^^	50 (15.3)	32 (17.5)	10 (8.9)	3 (5.7)	10 (19.6)
	Wrist	14 (4.3)	8 (4.4)	4 (3.6)	1 (1.9)	4 (7.8)
	Elbow	14 (4.3)	7 (3.8)	6 (5.4)	5 (9.4)	1 (2.0)
	Axilla	4 (1.2)	3 (1.6)	1 (0.9)	1 (1.9)	1 (2.0)
	Neck	5 (1.5)	4 (2.2)	1 (0.9)	3 (5.7)	0 (0.0)
	Knee	8 (2.4)	5 (2.7)	2 (1.8)	2 (3.8)	1 (2.0)
	Ankle	16 (4.9)	10 (5.5)	5 (4.5)	2 (3.8)	2 (3.9)
	Toe	2 (0.6)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

** Burn location is >100% as patients commonly sustained burns in more than one location (157 patients sustained burns to single body locations, 83 patients sustained 2 locations, 54 patients sustained 3 locations, 23 patients sustained 4 locations, 6 patients sustained 5 locations and 3 patients sustained 6 locations); ^* body distribution is >100% as some patients sustained burns in multiple locations, 19 patients had bilateral limb and centrally located burns, 53 patients had unilateral limb and centrally located burns; ^^ includes palmar surface burns; abbreviations; n, number; HTS, hypertrophic scar; NHTS, not hypertrophic scar; %TBSA, percentage total body surface area.

Figure 2. Flow chart depicting patient numbers at burn therapy appointments, hypertrophic and non-hypertrophic scarring at each time point, discharge and loss to follow up



Abbreviations; n, number of patients; HTS, hypertrophic scar; NHTS, non hypertrophic scar; no data, data not documented in medical records; discharged, patient completed treatment and scar deemed mature by burn therapist; loss to follow up, not discharged by burn therapist; medical intervention, surgical intervention for scar modulation may include microneedling, laser, steroid injection and z-plasty without grafting; ^* initial review, first capture within the time points specified, may not be the actual first review by Burn Therapist

Burn Characteristics

Burn characteristics can be seen in Table 1. Median %TBSA for the cohort was 2.3% (range 0.2–40.0%). Scald burns were the most common burn mechanism accounting for 69.9% of all burns. Almost all (92.3%) patients sustained a partial thickness burn. The upper limb and hands accounted for three quarters of all burn areas. One hundred and thirteen (34.7%) patients sustained a burn crossing a joint surface, the most frequent location were the fingers (including the palmar hand surface) (n=50, 44.2%). Upper limb joints accounted for over two thirds of joint locations burned.

Acute management

Optimal first aid was received by 79.1% of patients. One third of patients required hospital admission for initial burn management, staying a median two days (range 1–44) as an inpatient. One patient completed all burn wound healing as an inpatient. The remaining patients required an average of 3.4 outpatient burn unit appointments (SD 1.34) for wound care. The median number of days to definitive wound closure for the cohort was 18 (range 14–77 days). Two hundred and fifteen (65.9%) children healed in 14–21 days, 73 (22.4%) healed in 22–30 days and 38 (11.7%) required >30 days to achieve definitive wound closure.

Scar outcomes

Primary scar outcomes

Table 2 shows patients presenting to burn therapy with HTS categorized by time to heal. At month one, subcategory >30 days to heal does not accurately quantify HTS prevalence, as patients were still undergoing wound healing during this time.

At 3–6 months post burn, 62.0% (183/295) of patients presenting to burn therapy were assessed with early signs of HTS. Considering this as a total percentage of the cohort, the overall prevalence of early HTS was 56.1% (95 CI 50.7%–61.4%). Of these patients, 56.8% healed within 14–21 days, 27.3% within 22–30 days and 15.8% in >30 days.

At 12–18 months, 51.5% (53/103) of patients presenting to burn therapy were assessed with persistent HTS. Considering this as a total percentage of the cohort, the overall prevalence of persistent HTS was 16.3% (95 CI 12.6–20.6%). Of these patients, 56.6% healed within 14–21 days, 22.6% within 22–30 days and 20.7% in >30 days.

Table 2. Patients presenting to burn therapy with hypertrophic scarring categorized by time to heal

Patients presenting with HTS	Days to definitive wound healing		
	14–21	**22–30**	**>30**
	n=215	**n=73**	**n=38**
Month 1	152 (70.1)	38 (52.1)	3 (7.9)
Months 3–6	104 (48.4)	50 (68.5)	29 (76.3)
Months 12–18	30 (13.9)	12 (16.4)	11 (28.9)

n, number of patients; HTS, hypertrophic scar. Month; post burn injury.

Secondary scar outcomes

Data collected for mVSS subcategories of vascularity and pliability can be seen in Table 3. Within the first month post burn, 74.6% of patients, either HTS or no HTS, had scores ≥2 on the subcategory of vascularity. Vascularity persisted at 3–6 months, with 61.8% of patients with HTS and 23.2% patients with no HTS recording scores ≥2. Vascularity scores declined at 12–18 months, with over 85% of patients, assessed as either HTS or no HTS having vascularity scores <2. At all-time points, scar pliability was considered normal or supple (score 0–1) for the majority (>90%) of patients assessed with either HTS or no HTS.

Wound break down within the first month post wound healing was noted in 24 patients, with no further breakdown recorded after this time point. In patients with wound breakdown, 12 progressed to present with HTS, ten did not progress to HTS and two were loss to follow up. Burns which crossed a joint surface occurred in 34.7% of the cohort. No patients had restriction to ROM of the affected joint at their final burn therapy appointment.

Table 3. Scar outcomes and burn therapy interventions at months 1, 3–6 and 12–18.

Categorical variable		Month 1		Months 3–6		Months 12–18	
		HTS n/45(%)	NHTS n/142(%)	HTS n/183(%)	NHTS n/112(%)	HTS n/53(%)	NHTS n/51(%)
mVSS vascularity	0- Normal	0 (0.0)	4 (2.8)	17 (9.3)	40 (35.7)	24 (45.3)	37 (72.5)
	1- Pink	12 (27.3)	27 (18.6)	53 (28.9)	46 (41.1)	23 (43.4)	11 (21.6)
	2- Red	25 (56.8)	97 (66.9)	94 (51.4)	23 (20.5)	6 (11.3)	2 (3.9)
	3- Purple	7 (15.9)	15 (10.3)	19 (10.4)	3 (2.7)	0 (0.0)	0 (0.0)
	Not reported	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)
mVSS pliability	0- Normal	15 (34.1)	95 (65.5)	61 (33.3)	102 (91.1)	22(41.5)	42 (82.3)
	1- Supple	28 (63.6)	47 (32.4)	113 (61.7)	9 (8.0)	23 (43.4)	8 (15.7)
	2- Yielding	1 (2.3)	1 (0.7)	8 (4.4)	1 (0.9)	6 (11.3)	0 (0.0)
	3- Firm	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	2 (3.8)	0 (0.0)
	Not reported	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)
Wound/Scar breakdown	Present	4 (9.1)	16 (11.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burn therapy intervention**	Pressure	36 (81.8)	108 (74.5)	155 (84.7)	50 (44.6)	26 (49.0)	11 (21.6)
	Silicone	22 (50.0)	51 (35.2)	130 (71.0)	35 (31.2)	26 (49.0)	7 (13.7)
	Hydration	36 (81.8)	122 (84.1)	117 (63.9)	88 (78.6)	30 (56.6)	35 (68.6)
	ROM/Splint	14 (31.8)	41 (28.3)	38 (20.8)	6 (5.3)	1 (1.9)	3 (5.9)
	Other*^	4 (9.1)	11 (7.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burn therapy recommended interventions per child	0	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	3 (5.7)	11 (21.6)
	1	7 (15.9)	29 (20.0)	30 (16.4)	3 (2.7)	26 (49.0)	29 (56.8)
	2	14 (31.8)	61 (42.1)	63 (34.4)	24 (21.4)	14 (26.4)	6 (11.8)
	3	15 (34.1)	37 (25.5)	67 (36.6)	45 (40.2)	10 (18.9)	5 (9.8)
	4	8 (18.2)	18 (12.4)	23 (12.6)	39 (34.8)	0 (0.0)	0 (0.0)

Abbreviations; mVSS, modified Vancouver Scar Scale; ROM, range of motion; %TBSA, % total body surface area; HTS, hypertrophic scar, NHTS, not hypertrophic scar; Burn therapy interventions; pressure consists of pressure garments, tubigrip, duoderm and coban; silicone interventions includes various silicone based products and brands – gel sheeting, strips, creams: hydration interventions includes all emollients; ROM/splint interventions includes range of motion (ROM) exercises, static/dynamic splinting or serial casting; **burn therapy interventions does not add to 100% as multiple patients received multiple interventions at any one time; *^ other interventions includes wound dressings, corticosteroid cream, sensory desensitisation exercises.

Interventions

Scar management

Table 3. presents scar management interventions utilized at specified time points, number of interventions recommended per burn therapy appointment and whether the patient presented with HTS or not. Silicone, hydration and pressure therapy were the most frequently combined treatment interventions prescribed. Hydration (emollients) was prescribed to more patients within the initial six months than the later follow up period. Within the initial six months, patients with HTS were prescribed a mean 2.5 (SD 0.9) treatments, while patients without HTS were prescribed a mean 3.2 (SD 1.1). At 12–18 months, patients with HTS were prescribed a mean 1.6 (SD 0.9) treatments, while patients without HTS were prescribed a mean 1.1 (SD 0.8) treatments.

Of the 17 patients who required medical intervention for their HTS, all except three began receiving medical interventions after conservative burn therapy scar treatment had finished, at a median 29 months post burn injury (range 4–46). The medical procedures provided were scar laser (29.4%), steroid injections (17.6%), microneedling (11.7%) and z-plasty release without skin graft (11.7%).

Discussion

This is the first study to report early and persistent HTS prevalence rates in conservatively managed children post burn injury. The prevalence of HTS at 3–6 months post burn for children healing within 22–30 days and >30 days was 68.5% and 76.3% respectively and at 12–18 months, was 16.4% and 28.9% respectively. Similar prevalence has been reported in previous studies [23]. Existing literature reports HTS prevalence rates for children as 16–69% while for conservatively treated patients only, the prevalence is 10.4–35.0% [3-9].

A hypertrophic scar is commonly accepted as raised, red and within the margins of the original wound, however no current outcome measure conclusively defines HTS. This study defined a hypertrophic scar as raised >1mm from surrounding skin within 3–6 months to demonstrate the most active scarring period and at 12–18 months post burn for persistent HTS presence [18]. The variability in differing definitions of HTS include utilizing a subset of the mVSS, designation of a specific score on the mVSS, subjectively rating of increased thickness and elevation compared to surrounding skin or documented treatment for a scar [5, 6, 8, 9, 12, 24]. Furthermore, the time point at which a scar is determined hypertrophic varied from ‘any time point within the study’, to 12 months post injury, to the end of the specific study period or up to 5 years [5, 6, 8, 12]. While objective measurement tools provide greater accuracy and reliability in defining HTS, they remain cost prohibitive in the clinical settings.

This data demonstrated that while patients presenting for scar management who had delayed wound healing were more likely to develop HTS, the presence of HTS was also seen in those who healed between 14–21 days. At 3–6 months post burn, over half of presenting patients had HTS, of which 56.8% had healed within 14–21 days. Similarly, at 12–18 months, half the presenting patients had HTS, of which 56.6% had healed within 14–21 days. Considering all children healing between 14–21 days and presenting with HTS, the overall prevalence at 3–6 months was 48.4% and 13.9% at 12–18 months. A variance in HTS presence for early healing of 14–21 days has been reported

from 7.5% to 20.0% [14]. Chipp et al found one third of conservatively managed children healing in <21 days developed HTS [6]. Furthermore, the risk of HTS was multiplied by 1.138 for every additional day to heal after eight days from injury.

Several risk factors have been identified for hypertrophic scar development in children; female sex, younger age, geographical location, anatomical location, depth, %TBSA, multiple operations, skin type (Fitzpatrick classification IV–VI) [5, 8, 12, 15, 25]. In contrast, our data demonstrated even distribution between all age groups, gender, geographical location, anatomical location, %TBSA, and burn mechanism. Data was unable to determine HTS prevalence with accuracy related to skin type, ethnicity and infection rate. It therefore remains inconclusive as to which patients are at risk of HTS development and/or those who may benefit from scar modulation therapies.

While a proportion of children present with early HTS, there remains the potential for improvement to no HTS at 12–18 months. In this study, early signs of HTS at 3–6 months was utilized to encompass the peak scar activity period, whilst 12–18 months demonstrated persisting HTS [16]. Research supports early intervention for burn scars that take longer than three weeks to heal, in particular within the first six months, which may decrease the severity of HTS [27]. While improvements in the prevalence of HTS occurred in the longer follow-up time points, it remains unclear whether this was due to the individualized scar interventions prescribed or the natural course. Treatment adherence was not always documented and therefore, remains unknown in this study. Furthermore, withholding burn and HTS management would be considered unethical to patients who demonstrate all the indicators of progressing to develop HTS.

Scar outcomes are unknown for those lost to follow up. In 55.5% of patients, treatment was completed until burn therapy discharge or requiring ongoing medical intervention at the end of the study period. This is considered consistent for similar cohorts, with two recent studies at the same facility reporting follow up rates of 22.4–53.2% at 2 years [28].

This is the first study to report children requiring non-conservative intervention after receiving only conservative wound and scar intervention. Despite being prescribed prophylactic scar management, 17 (5.2%) patients required medical intervention for scar modulation. This low percentage requiring non-conservative intervention, suggest the prophylactic scar management prescribed may be a useful strategy in minimizing the need for medical/surgical interventions for HTS.

There are limitations to this study. Firstly, while this study was conducted at a single institution, this institution represents the sole tertiary referral centre for paediatric severe burn injuries. However, patients were assessed and managed by burn therapists, highly experienced in burn assessment and treatment. Secondly, while data was limited due to its retrospective nature and with a large loss to follow-up, this study included a large cohort of 326 patients with almost all patients having documented mVSS scores at each appointment. Thirdly, a consequence of the dressing changes not being conducted on the actual day of healing (as seen with the use of seven-day dressings), may over or underestimate wound healing time. However, at CHW the determination of a wound as healed remains a subjective clinical decision by experienced Nursing staff, often in consultation with Burn therapists. Typically, as patients progress toward healing, dressing schedules become more frequent to capture the date of healing. Finally, the continued attendance of patients presenting to burn therapy without HTS throughout the study period was evident, however data available were unable to determine if this was driven by the patient/parent or therapist. Multi-centre, prospective studies, which minimize loss to follow-up and utilize a clinically relevant scar scale incorporating social and emotional factors can improve confidence in findings.

Conclusion

This study demonstrates that children who have a sustained a burn injury, were not grafted, healed in >14 days and received prophylactic scar intervention, still have the potential to present with HTS. Early signs of HTS were seen in just over half the patients presenting to burn therapy and despite scar intervention, persistent HTS was seen in 16.3%. At both time points, just over half of children presenting to the unit healed between 14–21 days. Traditionally, children who have healed within this time frame have been considered not at risk of HTS, however this study reaffirms that children who heal prior to 21 days, have potential to develop HTS. Children with conservatively managed, partial thickness burns may benefit from burn therapist review following wound healing, to ensure timely access to scar management if HTS develops.

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Addendum

Further information pertaining to secondary scar measures can be seen in Table 4. It is recognized that HTS may be associated with pruritis and neuropathic pain. Over 90% of patients did not have documented presence or absence for pruritis and over 98% of patients did not have documented presence or absences for neuropathic pain. Therefore, it was chosen to omit this data from the manuscript due to the lack of useful interpretable data provided. Pruritis and neuropathic pain will be further discussed within Chapter 3.

Table 4. Secondary scar outcomes categorized by month.

	Month post burn	n present	n absent	n not documented
Pruritis	1	17	0	176
	3–6	10	0	285
	12–18	2	0	102
Neuropathic Pain	1	3	0	190
	3–6	1	0	284
	12–18	0	0	104

Abbreviation; n, number.

Chapter 3:

Discussion

This thesis has explored the prevalence of HTS in children presenting post burn injury who were conservatively managed. These children represent the most common presentation to Burn Units within high income countries; scald burn of partial thickness and <10%TBSA [2, 177]. Limited studies have explored long-term outcomes for conservatively managed burn injuries in children, therefore this thesis aimed to explore scarring outcomes in this patient population.

The evidence-base for burn injuries, assessment, wound management, scar outcome measures, interventions and complications have been thoroughly examined and synthesized in Chapter 1. Chapter 2 presents an original research study, ready for submission to the journal Burns & Trauma, titled 'What are the scar outcomes for children who have had a burn injury, are not grafted and heal >14 days?'. This final chapter expands on the findings presented in the paper in Chapter 2. Key findings will be discussed in detail, including clinical and research implications.

The key findings are:

1. A clear definition of hypertrophic scarring is required, that is both important to therapist and child/family.
2. Greater focus on holistic assessment of scar outcomes in clinical care and research would provide a more comprehensive picture of post burn sequalae.
3. Over half of all children who presented for conservative management of burn injuries demonstrated early hypertrophic scarring, reducing to 16.3% of all children with persistent hypertrophic scarring.
4. Healing between 14–21 days places a child at risk of hypertrophic scar development and warrants consideration of prophylactic scar intervention.
5. Individualized prophylactic conservative management may involve multiple interventions throughout scar maturation phase of healing.

Finding 1:
A clear definition of hypertrophic scarring is required, that is both important to therapist and child/family

A hypertrophic scar is commonly accepted as raised, red and within the margins of the original wound, however, there remains significant variation of HTS definitions within research. This is evident (Table 1.1, Chapter 1), where a variety of subjective scar assessments scales were utilized in studies, each with a differing definition of HTS, resulting in a large range for HTS prevalence within the literature. These varied definitions make comparability between the studies difficult, and therefore true HTS prevalence remains unknown. At present, the use of objective measures in routine clinical practice is limited due to high equipment costs of multiple devices, long operating times and size [66]. Scar scales practical for clinical use are subjective in nature and provide therapists the ability to measure scar severity and progression. Research has not determined which scar scale has superior inter or intra-reliability for children and no scale conclusively defines a hypertrophic scar [65]. The need for a consensus on the definition of HTS is necessary to gain a true understanding of prevalence and allow comparison between studies. In addition, a specific score on subjective scar scales designated as 'hypertrophic' would further improve the comparability between studies. The future potential use of objective measures of HTS that are embedded into clinical practice would provide a more in-depth view of a child's entire scar and aid comparability between studies.

In the study presented in Chapter 2, a scar was deemed hypertrophic if the patients worst scar height was >1mm, indicating a subcategory score ≥1 on the mVSS [47, 78]. Scar height >1mm represents a raised scar and has been used in prior research to demonstrate hypertrophy [47, 78, 80]. The subcategory of height was chosen as to not be confounded by vascularity or pigmentation. A consequence of this definition is that the 'worst' aspect, rather than the whole scar surface is captured. A child's scar may be recorded as hypertrophic where the presence is one very minor part of the larger scar area, where the remaining area is soft, supple and flat. This is a well-known limitation of subjectively rated scar scales [55, 61, 66].

Historically, the mVSS is the standard assessment tool used at CHW, the institution within the study in Chapter 2, to clinically assess scarring. The mVSS is widely used in clinical practice due to its simple and easy application, however limitations of this subjective scar scale in both reliability and validity are apparent and are discussed in Chapter 1. The extensive experience and training of the therapists involved in the study and their daily use of the scale, would likely increase consistency with its use at this institution. The study in Chapter 2 identified substantial numbers of returning patients assessed as not hypertrophic throughout the study period. It is unclear from the mVSS data if this is driven by child/parent or therapist. While the mVSS provides an assessment of the physical scar, the introduction of the POSAS into clinical practice, could provide insight into patient perception of their scar [67]. Whilst the POSAS is not yet validated for children under 15 years, a recent study found high reliability for test-retest in children and adults [71]. The holistic nature of the POSAS may be of benefit for comprehensive service delivery to children and families. This may in turn provide a greater understanding of factors contributing to repetitive return of patients with no HTS. Future research into the reliability and validity of the POSAS for younger children is required to determine efficacy in clinical and research settings.

Finding 2:
Greater focus on holistic assessment of scar outcomes in clinical care and research would provide a more comprehensive picture of post burn sequalae

A limitation to the study in Chapter 2 was the inability to collect data on the psychosocial aspects associated with patients/families and the associated burn injury. These factors would provide an understanding of patient experience and potentially provide insight of the high loss to follow up and ongoing return of children without documented HTS. Although the burn injuries in the study in Chapter 2 were predominantly small %TBSA (<10%TBSA) and partial thickness, HTS presence was evident and the complexities of the associated psychosocial functioning for these children and families should not be underestimated. Studies report depression, low self-esteem, poor behaviour, reduced quality of life and anxiety in children post burn injury in particular for those with visible scarring [22, 178]. Incorporating the psychological aspects associated with burn injury and rehabilitation into a holistic and comprehensive health service would be of benefit to these patients.

In addition to HTS, burn injuries may be associated with additional complications such a pruritis, neuropathic pain and contracture [9]. In the study reported in Chapter 2, the documentation of pruritis and neuropathic pain was limited. Pruritis is an uncomfortable problem for burn survivors, particularly within the initial three months post burn due to the rapid influx of mast cells and increased histamine production [162]. Pruritis was only reported in the medical records for 17 children at month one, 10 children at 3–6 months and two children at 12–18 months. There were no reports at any time point confirming no pruritis was present (Table 4, Chapter 2). Anecdotally clinicians at CHW report much higher rates, which align more with the prevalence observed within earlier studies of children (71–93%) [162, 165]. Pruritis is likely underestimated in children, in particular when parents are reporting for young children who cannot express the sensation [67]. In total, three children within the study reported neuropathic pain with one prescribed neuropathic desensitization exercises. Again, this may be a result of the young cohort not being able to express the sensation of neuropathic pain, or a consequence of patients having no pain, or a lack of assessment or documentation by therapists. This is

vastly different from prevalence rates seen in adult populations where the prevalence of pain is reported as 7–87% [163, 169-172]. Currently no study regarding burn scar neuropathic pain has been conducted in children. There were no reports at any time point confirming no neuropathic pain was present within the study (Table 4, Chapter 2). One hundred and thirteen children sustained a burn crossing a joint space. No child had restricted ROM at their final burn therapy appointment. ROM was consistently documented as full or not full by therapists. There is a large variation in reported contracture prevalence for children; 0–89% [80, 90, 139, 146]. Prior studies from CHW report contracture rates for axilla and palmar burns of 0 and 3%, consistent with the study in Chapter 2 [80, 90]. This low prevalence is likely related to the prophylactic splinting practice at CHW, where prevention of contracture involves early prescription and fabrication of an end of range splint to any burn crossing or in close proximity to a joint surface, until apparent risk of contracture has resolved.

Finding 3:
Over half of all children who presented for conservative management of burn injuries demonstrated early hypertrophic scarring, reducing to 16.3% of all children with persistent hypertrophic scarring

The study presented in Chapter 2 is the first to report both early and persistent HTS prevalence rates in children. Early signs of HTS were described at 3–6 months to encompass the peak scar activity period, whilst persistent HTS was defined at 12–18 when scars typically progress toward the maturation phase [55, 179]. This study had well defined time points in which to measure HTS prevalence and described the clinical course of a paediatric burn population receiving prophylactic individualized scar management throughout a typical treatment period. The data in our study reaffirms earlier studies investigating the maturation pattern of HTS post burn [20, 56]. Hypertrophic scar presence and worst scar quality was evident by six months, with a tendency to improve at 18–24 months [20, 56].

At 3–6 months post burn injury, 56.1% (n=183) of children in the study in Chapter 2 presented with HTS, which is a higher prevalence rate compared with previous literature utilising similar time points for assessment [36, 79, 87, 89]. Lonie et al reported conservatively treated patients prevalence rates of HTS as 10.4%, at the minimum time point for assessment of 4 months [36]. Higher early prevalence rates were seen in the study in Chapter 2, when compared to studies including children who received skin grafting and/or conservative management. These differences may be attributed to varying definition and assessment of HTS; three studies deemed a scar hypertrophic if receiving scar treatment or documented within the medical records as hypertrophic with no objective/subjective measure used, whilst one study used the VSS subcategory of height >1mm similar to the current study presented in Chapter 2 [36, 79, 87, 89]. The assessment of HTS varied in the type and timing of assessment post burn. Given that scar maturation occurs up to 2 years post burn, the previously reported short-term outcomes (one week to six months) are more indicative of early HTS presence and do not provide a clear measure of the long-term persistent HTS results [36, 79, 87-89].

At 12–18 months post burn injury 16.3% (n=53) of children in the study in Chapter 2 presented with persistent HTS, in line with recently documented HTS prevalence (17.2–19.4%) reported in similarly conservatively treated cohorts assessed from 12 months onwards [77, 78]. Both studies shared similar definitions of HTS, utilizing the subcategory of height on the mVSS, with one study using >1mm and the other >2mm in addition to a score ≥5 on mVSS [77, 78]. In contrast, a higher prevalence of 41% as reported by Deitch et al in 1983, subjectively rated the child's scar as thickened compared to surrounding skin at any time from 9 months to 2 years [76]. Further, the population of patients within that study reported greater %TBSA (14%) and a significantly different composition of skin types compared to the study in Chapter 2, where 73% of children had skin documented as black (Fitzpatrick skin type VI) [76]. There was insufficient data to comment on skin type within the study in Chapter 2. Anecdotally the patient cohort presenting to CHW, whilst within a multicultural society includes a range of Fitzpatrick skin types (I–VI).

Chapter 1 identified higher rates of HTS in the research in mixed cohorts with children post burn injury who had received either surgical and/or conservative management for scars and where large time periods for assessment were used (Table 1.1, Chapter 1). It is unclear from these studies as to which patients progressed to develop HTS. In comparison, the study presented in Chapter 2 included predominantly small (median TBSA 2.2%) partial thickness burns. Prior evidence included children with larger %TBSA (mean range 4–15.5%), strict exclusion for burn mechanism or specific anatomical location, resulting in findings which are difficult to compare to the current study [20, 76, 79, 80, 89].

The difference in HTS presence seen within the current study at 3–6 and 12–18 months reaffirms the findings of earlier literature [20, 56]. In the study presented in Chapter 2, peak HTS presence was seen at the 3–6 months post burn, evidenced by the 183 children presenting with a raised scar. In addition to scar height, a high prevalence of other signs of scar activity including >90% of patients with increased vascularity scores and two thirds with increased pliability scores on the mVSS at 3–6 months were noted.

The subsequent reduction in vascularity and pliability reported at 12–18 months demonstrates scars that were continuing to change and mature over time. Maturation of scar tissue involves the reorganization of collagen fibres and commences after the peak phase approximately 6–12 months post burn injury [56, 57]. Earlier work by Van der Wal who investigated the maturation pattern of HTS post burn, demonstrated significant improvements by 12 months in scar vascularization and overall scar quality compared to 3 and 6 month time points [20]. Similarly, Oliveira et al reported in children with large %TBSA (>40%TBSA) burns that worst scar quality was evident by 6 months post burn, with a tendency to improve at 18 and 24 months post burn [56]. A recently published study assessed scars 5–7 years post burn, finding 87% of children's worst scar differed from normal surrounding skin, the predominant difference seen in scar colour [180]. Furthermore, parent reported POSAS scores were higher (mean 2.0–2.6) than observer scores, indicating poorer scar outcome [180]. The vast majority of children within this study were similar to the cohort in the study in Chapter 2, suggesting that counselling children/families regarding long-term skin differences is important during the rehabilitation phase.

The study in Chapter 2 was unable to identify risk factors to aid early prediction of HTS. A consequence of a retrospective chart audit is being limited to the documented contents of patient medical records which prevented the extraction of patient ethnicity, skin type and infection rate, all of which are known to be predictors of HTS. Hypertrophic scar presence in our study was evenly distributed between participants of all age groups, gender, geographical location, anatomical location, %TBSA, and burn mechanism. All of which have previously been identified as risk factors in earlier studies (Table 1.1, Chapter 1). For children specifically, fewer risk factors have been confirmed; two studies identified skin type classified as Fitzpatrick skin type IV–VI, one identified multiple surgical procedures and younger age, and two reported larger %TBSA [20, 77, 78]. Six studies reported increasing days to re-epithelization (>21 days), consistent with the results of our study; with prevalence of HTS at 3–6 months post burn for children healing within 22–30 days and >30 days was 68.5% and 76.3% respectively and persistent HTS at 12–18 months was 16.4% and 28.9% respectively [20, 36, 76-79].

Finding 4:
Healing between 14–21 days places a child at risk of hypertrophic scar development and warrants consideration of prophylactic scar intervention

Hypertrophic scarring post burn injury remains a complicated and unwanted outcome for children and their families, with the potential to impact physical, psychosocial wellbeing and quality of life [22]. Improvements in wound dressings in recent decades has resulted in a reduction of surgical procedures required for skin grafting, however it has not prevented HTS development from occurring [40]. The study presented in Chapter 2 reports on the outcomes of children post burn injury who were conservatively managed and healed in >14 days at a single tertiary institution. It was evident that children with burn injuries who receive prophylactic scar management remain at risk of early and persistent HTS, and that presenting with HTS can occur frequently in children that heal within 14–21 days.

Prior research on scar outcomes for children has largely focused on patients with larger %TBSA, deep dermal or full thickness burns and those requiring surgical intervention. There remains a paucity of research addressing minor (<10%TBSA), partial thickness burns which are conservatively managed, the most common presentation for children within Australia and New Zealand [2]. Data within the study in Chapter 2 found a substantial portion of children healing between 14–21 days presenting with early and persistent HTS. At 3–6 months post burn, 56.8% of children with HTS healed within 14–21 days. Similarly, at 12–18 months, 56.6% of children with HTS healed within 14–21 days. Considering all children healing between 14–21 days and presenting with HTS, the overall prevalence was 48.4% and 13.9% at 3–6 months and 12–18 months respectively. In an earlier study by Cubison et al, data demonstrated that increasing days to re-epithelisation had the greatest impact on HTS presence regardless of whether healing was conservative or surgical [79]. If healing occurred between 14–21 days, whether skin grafted or not, one third of patients developed HTS and if healing occurred >21 days, 78% developed HTS [79]. Assessment for this study occurred any time between 4 months to 5 years post burn injury. Similarly, this is in line with Chipp et

al who found the risk of HTS was multiplied by 1.138 for every additional day to heal after 8 days from injury for conservatively managed children [77].

Finding 5:
Individualized prophylactic conservative management may involve multiple interventions throughout scar maturation phase of healing

Burn Therapists at CHW follow scar management clinical practice guidelines as recommended by the ISBI [9]. ISBI practice guidelines recommend early intervention for burns healing >3 weeks and as mentioned above, ISBI practice guidelines do not specifically recommend management for those healing between 14–21 days [9]. Burn therapists therefore rely on clinical expertise and experience, in conjunction with ISBI guidelines to aid clinical decision making for children healing between 14–21 days. Assessment of patient risk factors for HTS and ensuring early follow up once healed, allows identification of patients at risk of early HTS prior to scar thickening, targeting treatment to those individuals at risk and possibly contributing to lower HTS rates [9]. All children received prophylactic individualized scar management interventions, based upon experienced therapist assessment of risk factors for scarring and ongoing scar assessment as is standard clinical practice at CHW. Due to the retrospective nature of the study in Chapter 2, the therapeutic impact remains unclear as to whether the prescribed interventions altered collagen remodelling during the maturation phase or whether patients may have intrinsically improved without intervention. Further, comparability between our study and previous work is challenging as multiple studies do not detail scar interventions prescribed, with little specification of indication for scar intervention, commencement, or intervention prescribed, whilst others used similar interventions to this study, further contributing to the uncertainty of best evidence-based practice within this patient population [20, 76, 77, 79, 80, 87-90].

Treatments recommended by ISBI are based on the best available evidence, however efficacy is not always conclusively determined due to a lack of robust RCT's. Interventions for HTS management include; pressure, silicone, emollients and splinting for contracture prevention (Table1.2, Chapter 1). As studies involving children are limited, therapists' base treatments on ISBI practice guidelines, experience and service availability. There remains a lack of high-quality evidence to justify a controlled RCT investigating individualized prophylactic scar treatment versus no treatment at CHW. A

percentage of the population not then receiving what is currently considered best practice based on expert consensus, may develop irreversible HTS, which would be considered unethical at CHW without sufficient evidence.

A strength of our paper was a lack of exclusion from the study due to loss to follow up, thus representing a complete clinical cohort and minimizing over or underestimation of results. In 55.8% of patients, treatment was completed until burn therapy discharge or the need for ongoing medical intervention was identified at the end of the study period. Consequently, there was a loss to follow up of one hundred and forty-five (44.2%). Surprisingly, of those loss to follow up, 94 (64.8%) patients were assessed to have HTS at their final burn therapy appointment. Two recent studies also conducted at CHW, report similar follow up rates of 37–53% at 2 years, a similar attrition rate to other burn studies [79, 80, 88, 90].

A considerable number of scar modulation interventions were prescribed throughout the treatment period, with patients frequently prescribed at least two interventions at any time (Table 3, Chapter 2). Scar interventions are often time consuming for patients/families and costly for the health system, which may contribute to the high rate of loss to follow up [50]. An understanding of the burden of care upon the child and/or their family was unable to be collected in the retrospective review in Chapter 2, however it cannot be underestimated. Qualitative studies provide insight into the child and parent experience post burn injury and highlight the initial and lingering trauma that exists with the daily reminder of the visible scar [22]. McGarry et al identified the time point of 3–6 months post burn being considered a ‘turning point’ for parents in terms of accepting the burn injury and the secondary scar [22]. This time point corresponds with the median post burn attendance period for our cohort which was six months, however the range was vast at 0–53 months.

Given the established pattern of HTS presence by six months and maturation from 12 months onwards, the continued prophylactic intervention provided to approximately half the attending patients without an assessed hypertrophic scar, poses the question, when

should prophylactic treatment cease and why do patients with no HTS continue to seek treatment [20, 56]? Based on the data in the study in Chapter 2, there appears a percentage of patients receiving excess intervention and assessments, where it may be deemed unnecessary in the context of treatment of HTS. Taking into consideration a full scar assessment, including risk factors, there is a proportion of children receiving treatment potentially unnecessarily. While the treatments provided are conservative and pose a low risk of harm to patients, the ongoing burden to the healthcare system, and a more focused approach to clinical follow up of individuals with no apparent signs of HTS or other adverse scar outcomes, warrants further consideration.

The vast majority of patients were prescribed emollients throughout the entire study period. This is an important component of treatment, particularly in the early post wound healing phase, due to considerable transepithelial water loss at the scar. Excess moisture loss can trigger scar production [73]. However, data demonstrated patients at 12–18 months were still being prescribed this treatment. Anecdotally, therapists recommend this for general skin care rather than specific scar treatment. However, this may be interpreted by patients/families as more than general skin care, potentially leading to ongoing return to burn therapy due to a belief that children are still receiving active treatment.

Adherence to treatments prescribed is a difficult variable to measure, particularly retrospectively. Patient adherence to treatment protocols was not frequently documented within the medical records in the study in Chapter 2. While patients/families are routinely asked regarding their adherence to treatment modalities, there is reliance on recall and accuracy of the subjective report which cannot be assumed. As a result, the study was unable to quantify the effect of adherence to treatment on HTS outcomes. Interventions for scar management require a consistent approach for optimal outcomes, with the burden of providing care for young children placed on their families [48]. Limited studies have addressed adherence to scar management in paediatric populations. In adults, adherence to pressure garment wear has been documented to be as low as 40% [181]. It is reported that initiating a daily routine improves adherence to scar

management interventions, however negotiating the emotional realities of both the child and family members remains challenging [182].

Clinical implications

Assessment

The use of LDI to determine burn depth and healing potential is of particular use for mixed depth burns, where clinical assessment is challenging [17]. Scald burns, the predominant burn mechanism for young children in Australia, are frequently mixed depth, making clinical examination problematic and the use of LDI appropriate [3]. Introduction of an LDI device into routine clinical practice may be worthwhile, to provide a more comprehensive assessment of burn depth, which relates to healing potential, and the ultimate scar outcome. LDI use may enhance identification of injuries at risk of HTS formation at an earlier time point, to guide early intervention and patient/family education. High-cost, operator dependence, need for timely patient presentation and staff preference currently limit the use of LDI in routine clinical practice [18]. Research has demonstrated the difficulties of use with young children and their inability to remain stationary without anaesthetic/sedation to complete the assessment [183]. This may make clinical use of LDI better suited to older children. In addition, for LDI to be accurate, measurements need to occur approximately 24–72 hours post burn, which at is challenging as patients frequently present to regional service providers prior to attending the tertiary centre where LDI is commonly available [18].

Identification of definitive wound closure is one of the most important aspects of care required for burn injured children. Several studies, including the study in Chapter 2, have demonstrated that delayed healing time increases the risk of HTS [36, 76, 77, 79, 87]. Therefore, once a child is nearing definitive wound closure, more frequent reviews of the wound should occur to ensure an accurate time point is identified for complete wound re-epithelisation. Ensuring those responsible for wound dressing changes have a thorough knowledge of the consequences of delayed re-epithelisation and the importance of accurately identifying this time point would ensure follow up is provided appropriately to those healing from 14 days onwards. In addition, hypertrophic scar education could be provided to patients/families with more certainty when definitive wound closure is identified on the correct day of healing.

The mVSS provides therapists information regarding physical and visible aspects of the scar: vascularity, height, pigment and pliability [61]. However, no further information regarding the patient and their scar can be determined from this single scale. The POSAS, includes both patient and therapist scar assessments, in addition to assessment of pain, pruritis and scar relief [67]. Individual treatment plans can be guided by this scale, with therapist and patient perception of the scar being clear. The POSAS, is currently not validated with children, however a recent study found high test-retest reliability with both adults and children [71]. Limitations in use of the POSAS remains for younger children who require parents as a proxy in reporting their symptoms [67]. It is clear from the limitations within the study in Chapter 2, that a holistic approach to scar assessment is required in clinical practice. If POSAS use was not possible, the addition of measures such as the Itch Man scale, specifically designed for children post burn injury, and a subjective visual analogue scale for pain, may add to the mVSS in providing a measure of the additional symptoms associated with HTS presence [173, 174]. A health-related quality of life measure, such as Brisbane Burn Scar Impact Profile may also warrant introduction into routine clinical care [184]. These assessment tools would ensure timely intervention and referrals occur when appropriate. The limitations seen with the present scar scales mean the complexity of HTS upon a patient/family is not fully appreciated. A scale that puts into perspective the complete scar, and can quantify it, not just the worst component, is required.

Treatment

As there are no current guidelines to inform scar management in patients healing between 14–21 days, the study in Chapter 2, in addition to previous literature, could inform ISBI practice guidelines for patients healing within this time frame [76, 77, 79]. Therefore where resources allow, these children warrant follow up similar to ISBI recommendations for children healing >21 days [9]. Where risk of HTS is low; education in recognizing signs of early hypertrophic scar development and encourage early return to Burn Therapists if signs are identified can be provided. This may prevent significant

or persistent HTS development, reduce the severity if HTS develops, or prevent serious hypertrophic scar complications e.g. contracture requiring surgical release. Where apparent risk of HTS appears high, active prophylactic treatment should commence early. Where resources allow, monitoring should occur until six months, the period in which most hypertrophic scars develop [20, 56]. Ongoing scar management, where indicated, should continue until scars are considered mature, where effectiveness of conservative interventions is limited.

Rehabilitation post burn injury can be intensive and long lasting for patients/families. Recent qualitative studies provide insight from the child and parent perspective of scar rehabilitation [22, 182]. A key theme was ensuring both child and parent are provided information and education prior to events occurring, for example, prior to a change of dressing. The aspect of preparing patients/families was not addressed within the study in Chapter 2, however the findings of HTS prevalence provides information which can assist Burn Therapists in targeting patient/family education and preparing their expectations of scar rehabilitation post wound closure. Despite following scar management best practice guidelines, 17 (5.2%) children in the study in Chapter 2 required medical intervention for scar modulation. This is the first study to report children requiring non-conservative intervention after receiving conservative scar intervention. Therefore, clinicians can now inform patient/families that 5.2% of patients required medical intervention after completion of prophylactic scar management.

Research Implications

The synthesized review in Chapter 1 identified an ongoing limited understanding as to the long-term effectiveness of scar management interventions. Further, subjective scar scales remain unable to fully assess the variations of scarring seen within a burned area. Research regarding HTS risk factors, has progressed, however there remains conflicting results with further research required. The study in Chapter 2 was the first to report early and persistent HTS prevalence rates in children conservatively managed, however there was a large loss to follow up and adherence to prescribed interventions was unknown. This study was also the first to describe the prevalence of children requiring medical intervention following conservative scar management. All reported data were clinical based measures due to the retrospective study design.

Assessment

While most aspects of burn care data were available for collection within the medical records, limitations arose in documentation for skin type, ethnicity, and infection, three previously linked factors associated with HTS development. To improve future research, all risk factors should be documented as part of routine practice. A prospectively designed study would ensure data collection of all variables that impact upon wound healing and subsequent scarring be documented.

While the research demonstrates LDI superiority to clinician assessment of burn depth, practices of LDI, in particular for young children is prohibitive due to the time taken to complete the assessment and reduced cooperation of young children [17, 183]. Research to develop devices which are more ‘child friendly’, may increase the uptake of use in clinical practice and enhance accuracy of depth assessment.

While subjective scar scales provide a quick and easy clinical picture of the patient’s scar, a number of objective scar assessment tools are available that can provide a thorough more in-depth view. Such devices include 3D photography, Cutometer for pliability and elasticity, Dermalab for transepidermal water loss, Mexameter for skin

colour and ultrasound for scar thickness and height [66, 73, 75]. The increasing use of these devices in prospective trials is warranted to enhance HTS assessment and guide treatments accordingly. Practically, these are not utilized in clinical practice due to excessive cost in purchasing and use of multiple devices, in addition to the inability of young children to cooperate to ensure accuracy of measurement. Further, these objective measures could investigate the validity and reliability of subjective scar measures. However, without technological advances, progression of these devices beyond research into clinical practice will remain limited.

Children under eight years of age are considered to lack the complex thought processes to describe thoughts and feelings with accuracy [185]. This includes accurately describing pruritis and neuropathic pain, resulting in parents acting as proxy reporters. Difficulty can arise in parental reporting, including difficulty interpreting symptoms, a result compounded by the trauma of the burn injury and subsequent healing process. Collecting proxy measures such as prescription of antihistamine medication may identify the impact of pruritus on children post burn. Development of methods to assess and/or identify neuropathic pain in young children could improve treatment for this complex issue. Given the majority of children presenting to CHW are <5 years, differing methods for identifying nonvisible symptoms is required to ensure they receive the treatment they require.

Prevalence

To fully appreciate and view the extensive maturation phase of HTS, future research should involve prospective longitudinal studies of at least 18–24 months. Optimization of retaining participants to complete the study period is a challenge as seen in multiple studies [79, 80, 88, 90]. Strategies aimed to limit loss to follow up include: obtaining detailed patient contact information, study designs which schedule follow up to coincide with regular follow up visits to minimize excess travel and provide a clear explanation about participant role in research and expectations about personal and future patient benefits from their participation in the research [186]. Further, conducting longitudinal

studies longer than 2 years post injury may demonstrate the impacts of HTS on the growing child, e.g. delayed complications of contracture or need for medical intervention for scar modulation. Utilizing these aspects in future, greater clarity of HTS prevalence rates, both early and persistent HTS may be determined.

Treatment

Interventions impacting HTS prevention and treatment remain complex to investigate within the burn community. Long standing clinical practices within facilities would require conclusive high-quality RCTs to modify practices. At CHW, therapists clinically observe positive results whilst following ISBI practice guidelines prophylactic treatment approach including pressure, hydration, silicone and contracture prevention. It would be considered unethical at this institution to withhold treatment to patients, where assessed risk of HTS is identified. Therefore, a multi-centre prospective study, including a cohort with similar risk factors to CHW who do not prophylactically treat 14–21day healers, could provide insight to the effects of prophylactic intervention. Further, while adherence to treatment was unknown in the study in Chapter 2, future research could document adherence; for example by utilization of diaries, or a mobile application with prompts reminding participants to complete treatment and record completion. A greater understanding of patient adherence would further establish the efficacy of treatments.

The study in Chapter 2 was unable to collect data on the burden of care or psychosocial aspects of burn rehabilitation; large qualitative studies addressing these concerns are required. Research has demonstrated the complexity of a burn injury and associated psychological impact for both children and parents, in particular for hospitalized patients and those with visible scars [22, 182]. To better quantify patient and family burden of care, future research could investigate patients with all burn severities and %TBSA, including both inpatient and outpatient managed patients, specifically relating to long-term scar management interventions. The driving forces of patient/families seeking review with and without an assessed hypertrophic scar could also be explored. This would guide healthcare services and practice provisions, in addition to providing

therapists with insights to prepare their patients/families better through the long rehabilitative phase of scar management.

Seventeen children (5.2%) in the study in Chapter 2 underwent non-conservative medical intervention for their hypertrophic scars. All except three children commenced this treatment after first completing a median of 29 months of conservative scar management. Medical interventions, such as laser or microneedling, for scar modulation have demonstrated promising results in recent years. While limited research exists investigating these treatments in children, they are limited by methodological quality, small sample size, single institutions and short-term follow up periods [195, 196]. Protocols and time to initiate procedures remains variable between studies, with some starting as early as 2 months post wound healing and others 1–2 years post burn [195, 197-199]. While improved scar outcomes, after receiving non-conservative intervention, were seen in children regardless of scar maturity, the most effective time to commence this treatment remains unknown [195, 197-199]. At CHW, non-conservative interventions require general anaesthetic, or intravenous sedation, therefore rigorous multicentre RCTs are warranted to determine efficacy and timing of these treatments.

Conclusion

This thesis has critically reviewed and synthesized the available literature surrounding burn injuries and associated HTS. It has built upon the limited available evidence of conservatively treated burn injuries in children. It has demonstrated that in children who have sustained a burn injury, were not skin grafted, healed in >14 days and received prophylactic scar intervention, there remains potential to present with HTS. Early signs of HTS were seen in just over half the patients presenting to burn therapy and despite scar intervention, persistent HTS was seen in 16.3%.

The original study presented in Chapter 2 demonstrated that while children presenting for scar management who had delayed wound healing were more likely to develop HTS, the presence of HTS was also seen in those who had healed between 14–21 days. Further, while a proportion of children presented with early HTS, there remains the potential for improvement to no HTS at 12–18 months. While the prevalence of HTS is reduced in the longer follow-up time points, the study design employed in Chapter 2 is unable to determine whether this was due to the individualized scar management interventions prescribed or the natural course.

The study in Chapter 2 highlights that children healing conservatively in >14 days may warrant burn therapist review following wound healing, to ascertain risk of HTS and ensure timely access to scar management. Identification of risk factors, in addition to a comprehensive physical scar assessment should guide therapists. Initiation of individualized prophylactic scar intervention should be provided to those deemed at risk with the aim of preventing HTS development or minimizing the extent of such development. Utilization of holistic assessment measures may be of benefit to this population to gain greater understanding as to the patient/family perspective of their scar and the impact of the injury and subsequent treatment upon them.

Future research should focus on clearly defining HTS with a clinically feasible outcome measure to enhance future comparability between studies and to ascertain reliable

prevalence rates between cohorts. Further evidence is required to determine the risk factors of HTS in children, to aid therapists in early identification of children who are more likely to scar, to provide early intervention to those at high risk, and reduce burdening of those at lower or absent risk. Longer term outcomes on scar maturation and efficacy of conservative scar management interventions would provide stronger recommendations to these children, families and therapists.

The findings from this thesis provide valuable information to therapists regarding scarring outcomes in conservatively managed children. Opportunities for future research have also been identified.

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Appendix 1

Sydney Children's Hospital Network ethics approval

The Sydney children's Hospitals Network
care, advocacy, research, education

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9 February 2021

Ms Stephanie Ball
Burns Dept
The Children's Hospital at Westmead

Dear Ms Ball,

HREC Reference: **2020/ETH03201**

Project title: **What is the scar outcome for children who have had a burn injury, are not grafted and heal >14days?**

Sites: **The Children's Hospital at Westmead**

Thank you for submitting the above project for single ethical and scientific review. This project was considered by the Sydney Children's Hospitals Network Human Research Ethics Committee's Executive Committee ("the Committee") at its meeting **7 December 2020**, and subsequently on the **8 February 2021**.

This HREC has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review, and by the National Health and Medical Research Council as a certified committee in the review of multi-centre clinical research projects.

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and *CPMP/ICH Note for Guidance on Good Clinical Practice.*

I am pleased to advise that the Committee has granted ethical approval of this research project. Your approval is valid for five (5) years, effective the date of this letter.

This application has been assessed in accordance with, and meets the requirements of the National Statement on Ethical Conduct in Human Research (2007).

The documents reviewed and approved by the Committee are:

Document Reviewed	*Version*	*Date*
REGIS Project Registration	-	Received 01 Dec 2020
LNR Project plan	V1.1	26 Nov 2020

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Appendix 2

Modified Vancouver Scar Scale

Skin characteristic	Parameter
Pliability	
0	Normal
1	Supple
2	Yielding
3	Firm
4	Banding
5	Contracture
Height	
0	Normal-flat
1	>0 to 1 mm
2	>1 to 2 mm
3	>2 to 4 mm
4	>4 mm
Vascularity	
0	Normal
1	Pink
2	Red
3	Purple
Pigmentation	
0	Normal
1	Hypo-pigmentation
2	Mixed pigmentation
3	Hyper-pigmentation

Appendix 3

Patient and Observer Scar Assessment Scale

Observer Scar Assessment Scale

	normal skin	1	2	3	4	5	6	7	8	9	10	*worst scar imaginable*
Vascularization		○	○	○	○	○	○	○	○	○	○	
Pigmentation		○	○	○	○	○	○	○	○	○	○	Hypo ☐ Mix ☐ Hyper ☐
Thickness		○	○	○	○	○	○	○	○	○	○	
Relief		○	○	○	○	○	○	○	○	○	○	
Pliability		○	○	○	○	○	○	○	○	○	○	

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Total score Observer Scar Scale:

Patient Scar Assessment Scale

	No, no complaints	1	2	3	4	5	6	7	8	9	10	*Yes, worst imaginable*
Is the scar painful ?		○	○	○	○	○	○	○	○	○	○	
Is the scar itching?		○	○	○	○	○	○	○	○	○	○	

	No, as normal skin	1	2	3	4	5	6	7	8	9	10	*Yes, very different*
Is the color of the scar different?		○	○	○	○	○	○	○	○	○	○	
Is the scar more stiff ?		○	○	○	○	○	○	○	○	○	○	
Is the thickness of the scar different?		○	○	○	○	○	○	○	○	○	○	
Is the scar irregular?		○	○	○	○	○	○	○	○	○	○	

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Appendix 4

Burns and Trauma manuscript preparation

Burns and Trauma manuscript preparation available at https://academic.oup.com/burnstrauma/pages/General_Instructions. Accessed 21 March 2022.

Aims and Scope

Burns & Trauma is an open access, peer-reviewed journal publishing the latest developments in basic, clinical and translational research related to burns and traumatic injuries, with a special focus on various aspects of biomaterials, tissue engineering, stem cells, critical care, immunobiology, skin transplantation, prevention and regeneration of burns and trauma injury.

Article Type Guide

The table below indicates requirements for the different article types published in *Burns & Trauma*. Subsequent sections describe in more detail the requirements of different elements, and the definition of each category.

Article type	Title page	Abstract: word count	Abstract structure	Keywords	Required sections	Word count
Research	Yes	350	Structured	3–10	Background, Methods, Results, Discussion, Conclusion	

Article type	Title page	Abstract: word count	Abstract structure	Keywords	Required sections	Word count
Review	Yes	350	Unstructured	3–10	Background, Review, Conclusions	3 –5000 words, >50 references
Guideline	Yes	350	Unstructured	3–10	Use section and sub-section heads with short, informative titles as required.	
Commentary	Yes	n/a	n/a	n/a	Use section and sub-section heads with short, informative titles as required.	
Editorial	Yes	n/a	n/a	n/a	Use section and sub-section	

Article type	Title page	Abstract: word count	Abstract structure	Keywords	Required sections	Word count
					heads with short, informative titles as required.	
Case report	Yes	n/a	Structured	3–10	Use section and sub-section heads with short, informative titles as required.	
Letter to the Editor	Yes	n/a	n/a	n/a	Use section and sub-section heads with short, informative titles as required.	1200 words, up to 10 references
Study protocol	Yes	350	Structured	3–10	Background,	

Article type	Title page	Abstract: word count	Abstract structure	Keywords	Required sections	Word count
					Results, Discussion, Conclusion	
Technical report	Yes	350	Unstructured	3–10	Background, Material and methods, Discussion, Conclusion	

In addition, all submissions require a 'Declarations' section. See instructions below for requirements.

Manuscript Preparation

Manuscript Format, Structure, and Style

LaTeX files	• More information on LaTeX files is available in our guidelines on preparing your manuscript
Language editing pre-submission	• Language editing, particularly if English is not your

	first language, can be used to ensure that the academic content of your paper is fully understood by the journal editors and reviewers • Please note that edited manuscripts will still need to undergo peer review by the journal
Title page	• To facilitate *Burns & Trauma* double-blinded peer review, the main document should consist of a file with no identifying author information. A separate title page should contain authors, affiliations, acknowledgements, and an address for correspondence
Abstract	• See details above • Avoid reference citations and abbreviations
Authors	• Please list all author contributions upon

	submission of the manuscript
Style conventions	• The journal follows Oxford SCIMED style • Please ensure that you refer to these requirements when preparing your manuscript • More information is available on the [Mini Oxford SCIMED style checklist] • UK spelling should be used throughout, except in quotations and references
Abbreviations	• Please define non-standard abbreviations at the first occurrence
Tables & figures	• Figures and text should be submtted in separate files • Should be accompanied by a legend • Please number figures and tables consecutively Figures should use

	a common image format (e.g. pdf, eps, gif, tif, jpg) • Further information on figures can be found in our guidelines about preparing your manuscript
Videos	• This journal accepts videos to be published as part of the article • A still image of the video will appear in the PDF version • Videos should be cited in-text and numbered (Video 1…) like figures • A submission guide can be found in our guidelines about preparing your manuscript
References	• May be formatted in any readable style at submission • Authors are responsible for their accuracy

Acknowledgements/funding details	• These should be included at the end of the text • Please refer to your funding organizations to acknowledge their support • PubMed Central links will require a specific grant number to be referenced
Supplementary data	• Material to be considered as Supplementary Material should be submitted at the same time as the main manuscript • Supplementary material should be referred to in the main manuscript at an appropriate point in the text • Supplementary material will be available online only and will not be copyedited, so ensure that it is clearly and succinctly presented

- The style should conform with the rest of the paper
- The presentation should work on any internet browser
- We recommend that files are no more than 2MB each, although exceptions can be made at the editorial office's discretion

Highlights

- Three to five bullet points that help increase the discoverability of the manuscript via search engines
- Should capture the novel results of your study as well as new methods that were used during the study (if any)
- Highlights sample
- The 'Highlights' file should be clearly named
- The editors may contact the authors for this content after acceptance

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
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Stephanie Ball	Health Sciences, Faculty of Medicine, Health & Human Sciences	Burns & Trauma

2. STUDENTS DECLARATION (if applicable)

Name of HDR thesis author (If the same as corresponding author - write "as above")	Department/Faculty	Thesis title
Stephanie Ball	Department of Health Sciences, Faculty of Medicine, Health & Human Sciences	What are the scar outcomes for children who have had a burn injury, are not grafted and heal in >14 days?
Description of HDR thesis author's contribution to planning, execution, and preparation of the work if there are multiple authors (for example, how much as a percent did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)		
Stephanie Ball; Design of methodology (60%) Completion of ethics application (95%) Design of data collection instrument and collected the data (95%) Data analysis (80%) Interpreting data results (70%) Draft of final manuscript (90%) Critically revised and approved the final version of the manuscript (90%)		
I declare that the above is an accurate description of my contribution to this publication, and the contributions of other authors are as described below.	**Student signature** **Date**	18/4/2022

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Stephanie Ball*	As above
Verity Pacey	Design of methodology, interpreting data analysis, drafting of manuscript, revising manuscript, MRes Supervisor
Kelly Gray	Design of methodology, data analysis, interpreting data analysis, drafting of manuscript, revising manuscript, MRes Supervisort
Stephanie WIcks	Project conceptualisation, interpreting data anlaysis, drafting of manuscript, revising manuscript
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