

Randomized controlled trial of three burns dressings for partial thickness burns in children

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Abstract

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

Method: Children (0–15 years) with clean, $\leq 10\%$ total body surface area (TBSA) partial thickness burns who met the inclusion criteria were included in the study. Children received either (1) Acticoat™; (2) Acticoat™ with Mepitel™; or (3) Mepilex Ag™ dressings. Measures of burn re-epithelialization, pain, and distress were recorded at dressing changes every 3–5 days until full re-epithelialization occurred.

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

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

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Introduction

Small to medium sized partial thickness burns are a common occurrence for children in high income countries.¹ Scarring remains the biggest problem for pediatric burn centers, contributing to negative physical and psychosocial outcomes for children.² Therefore the initial care of the burn wound and choice of burn dressing is vital in creating the ideal healing environment to ensure rapid re-epithelialization of the wound and to reduce the possibility of hypertrophic scarring. Currently, $\leq 10\%$ TBSA partial thickness burns in children are predominantly managed in the outpatient setting using specialized dressings which promote moist wound healing and prevent wound infection.³ The standard of care for burns of this size in children has changed in the last 10–15 years. Currently silver-depositing fabric and foam dressings are the most commonly used treatment to manage the bioburden of a wound, with or without a silicone skin interface.⁴

Many trials have been conducted regarding the efficacy of silver dressings for treating burns, using topical silver sulfadiazine applications as the control or comparator dressing. However, the use of silver sulfadiazine as the comparator treatment needs to be reconsidered, as silver fabric dressings have been shown to promote faster wound reepithelialization rates, are associated with lower levels of pain during burn care procedures and do not require daily changes.^{4–6} Despite the large number of silver-impregnated burns dressings now on the market, very few high level trials have been conducted which compare these dressings in pediatric or adult patients.⁵ To date, only one randomized controlled trial has been conducted comparing the use of silver dressings, in a combined adult and pediatric population;⁷ however, none have been conducted specifically in a pediatric population. Therefore there is a need to identify the silver dressing(s) which best meet the current challenges of burn wound management in the pediatric burns population.

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

Methods/design

This study was a prospective, randomized controlled trial. This study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000105741) and was approved by the Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and the University of Queensland Ethics Committee. A protocol paper has been published for this trial; please refer to the article for a more detailed summary of the methods.⁸ This trial was completed as per the published protocol.

Intervention

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

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

Participants

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

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

Primary outcome measures

Days to re-epithelialization

The number of days from the burn date until wound reepithelialization, surface area of the wound and percentage of wound re-epithelialization were calculated via four methods: (1) clinical judgment from the consultant; (2) use of Visitrak™ grids (Smith & Nephew, Hull, UK); (3) 3D camera photographs (3D LifeViz system) and analysis on the Dermapix™ software program (Quantificare, Cedex, France). Visitrak™ and the 3D camera are both reliable and valid methods of calculating wound surface area.⁹ (4) Blinded review of photographs by a panel of three burns surgeons. The surgeons were asked to rate the percentage of wound re-epithelialization at each dressing change. Burn wounds were considered fully re-epithelialised when rated as 95% re-epithelialised or more. The inter-rater reliability was also calculated.

Pain

Pain and distress were assessed by obtaining: (1) the participant's self-report of pain intensity using the Faces Pain Scale-Revised (FPS-R) (if participant was aged 3 years or over);¹⁰ (2) the nurse's observational rating of the participant's pain and distress using the face, legs, activity, cry, consolability (FLACC) scale;¹¹ (3) the



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

participant's self report (if aged over 8 years) or the parent's report of the participant's pain intensity using a Visual Analog Scale-Pain (VAS-P);¹² (4) pulse rate; and (5) respiratory rate of the participant, taken immediately prior to and after dressing changes. Any analgesic and/or sedative medications administered to the participant at each dressing change were also recorded.

Secondary outcome measures

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

Procedures

All participants in the study had their dressings changed every 3–5 days until full re-epithelialization of the wound occurred or grafting of the wound was undertaken.⁸ Demographic information and clinical details were obtained from the caregiver and the patient's chart regarding: mechanism of the burn, the site of the injury, TBSA and first aid the patient received. Burns with a TBSA of <1% are difficult to quantify as a percentage clinically, therefore as a standard rating, all burns <1% were recorded as 0.5% TBSA for this study. Burn depth was categorized by laser Doppler imager (LDI) scan, treating consultant review at the first dressing change (day 3–5) as either 'superficial partial thickness only', 'mixed depth', or 'deep dermal partial thickness only' and blinded photo reviews of burn depth were also performed. Whilst LDI is the gold standard for burn depth analysis, it is technically difficult in the pediatric population and was not possible to complete in all participants, thus burn depth ratings were clinically judged by the treating consultant. At each dressing change appointment, pain and distress measures were taken before and after dressing removal and before and after the re-application of a new dressing. A tracing of the wound using Visitrak™ grids and a 3D photograph were also taken.

The investigators in this trial could not be completely blinded to the dressing used for each participant as the Acticoat™ dressing stains the healthy skin around a burn wound brown. Additionally, the primary investigator was present when dressings were applied and removed to obtain pain scores and therefore saw what dressing was used on the child; however, data was coded for analysis.

Discontinuation/adverse events

If an adverse event (e.g. infection, reaction to the dressing) occurred during the trial, participants only had data collected up until that point in time analyzed, as clinical care (including dressing type) was

changed to address the adverse event. If a consultant felt that a particular dressing was not appropriate for a participant's care, they were able to change to a different dressing. If this occurred, data collection for this participant was ceased from that date. All data preceding that date was included for analysis.

Statistical analysis

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

Sample size

Previous data in pediatric burns patients demonstrated re-epithelialization within 15 days (SD = 4) and a minimally clinically important difference is 3 days.¹³ Thus sample size for this trial was calculated at 28 per group at 80% power with an α of 0.05. Allowing for 20% loss to follow up, a total of 100 participants were required. This calculated sample size was also determined to be adequate to find a significant difference in data collected from pain scores.

Primary outcome measures

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

Secondary outcome measures

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

Results

Sample and demographic characteristics

The CONSORT diagram¹⁴ illustrates that a total of 285 children were assessed for eligibility into this trial (see Figure 2). One hundred and three children were randomized into the study and as per intention to treat protocol, 96 children were included for analysis. Groups were similar with respect to baseline variables (age, gender, clinically rated burn depth, mean and minimum wound perfusion units, TBSA, mechanism of burn and anatomical location of the burn) (see Table 1). Participants in all three groups had their dressings changed

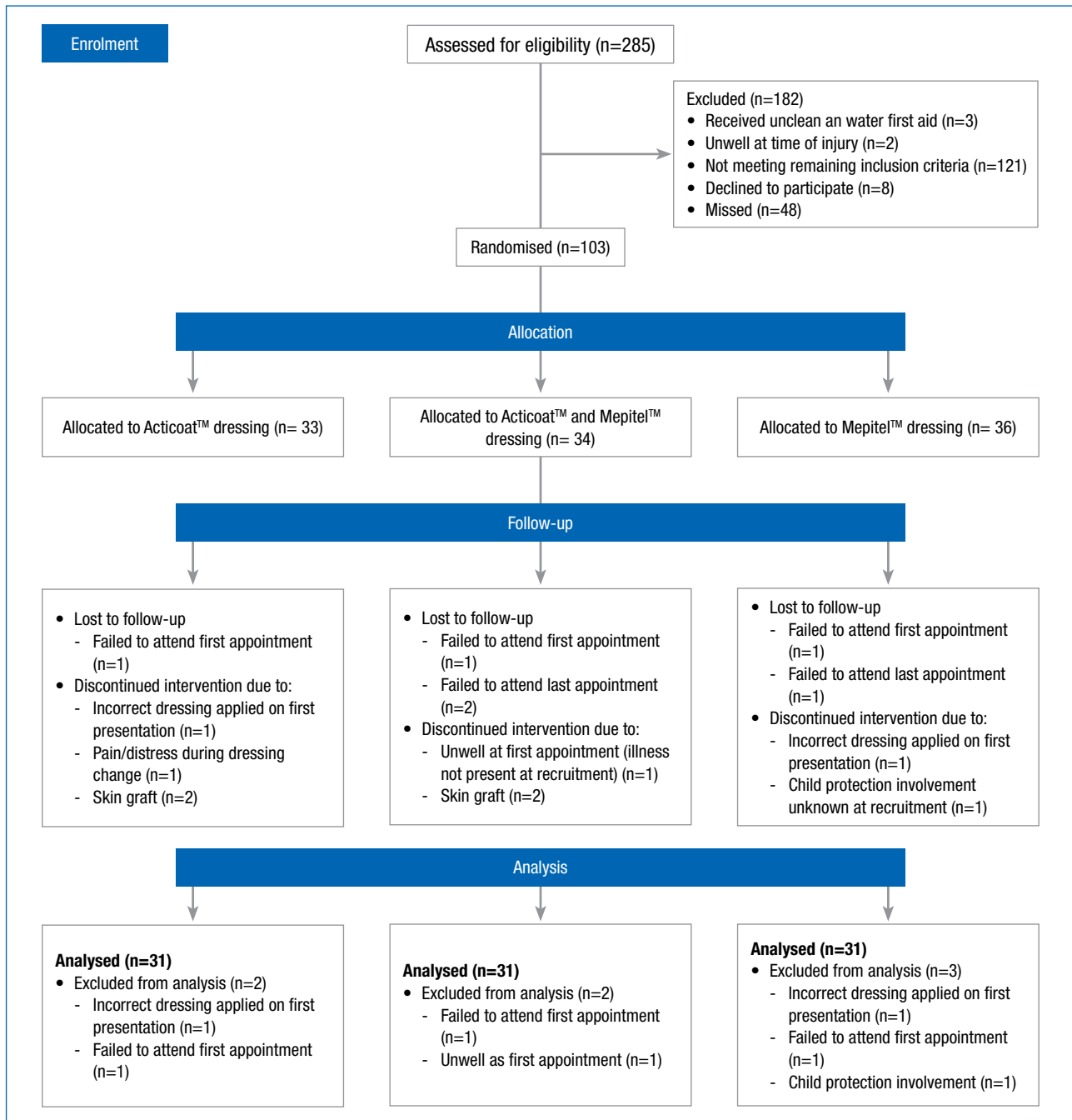


Figure 2: CONSORT diagram of study participants.

every 3–5 days until re-epithelialization or grafting occurred. At the first dressing change, the median number of days between date of injury and first dressing change was 3 days (IQR 3–4 days) and there was no statistically significant difference between the groups ($p = 0.79$).

Burn depth classification

LDI scans were successfully completed in 35 out of the 96 participants, with an even number of participants in each group (see Table 1). Both the minimum value of perfusion units (deepest part of the burn) and the mean value were recorded for each scan. The majority of scans were abandoned due to high participant pain and distress levels or excessive movement. A number of scans were

completed on participants, but were affected by artifacts (blurring of the image) due to movement during the scan, to be utilized for measurements. Of the 61 participants who did not have a successful scan, 75.4% of these were ≤ 2 years of age. Blinded photo review burn depth ratings by three consultants were analyzed using intraclass correlation coefficients (two-way random effects model for absolute agreement). The level of agreement on burn depth between burn consultants was low (ICC 0.34, 95% CI: 0.212, 0.47).

Due to a lack of reliable LDI scans and the low agreement for burn depth consensus, clinical judgment of burn depth by the treating consultant only at day 3–5 after burn was used. Clinical judgment of burn depth encompasses the evaluation of patient health, mechanism of injury and first aid received in addition to reviewing

Table 1: Demographic characteristics.

	Acticoat™ (n = 31) Median (IQR)	Acticoat™ and Mepitel™ (n = 32) Median (IQR)	Mepilex Ag™ (n = 33) Median (IQR)	p-value
Age (years)	1.0 year (1.0–5.0 years)	1.0 year (1.0–4.0 years)	1.0 year (1.0–4.0 years)	0.59
TBSA	1.0% (0.50–3.0%)	1.0% (0.50–3.0%)	0.50% (0.50–2.0%)	0.33
	Acticoat™ n (%)	Acticoat™ and Mepitel™ n (%)	Mepilex Ag™ n (%)	p-value
Gender				
Male	18 (58.1)	21 (65.6)	16 (48.5)	0.38
MOI				
Scald	18 (58.1)	20 (62.5)	18 (54.5)	0.91
Contact	11 (35.5)	11 (34.4)	14 (42.4)	
Flame	1 (3.2)	1 (3.1)	0 (0)	
Electrical	1 (3.2)	0 (0)	1 (3.0)	
Burn site				
Head/neck	3 (9.7)	5 (15.6)	3 (9.1)	0.83
Hand/fingers	9 (29.0)	7 (21.9)	10 (30.3)	
Upper limb	4 (12.9)	6 (18.8)	3 (9.1)	
Foot/toes	6 (19.4)	4 (12.5)	4 (12.1)	
Lower limb	1 (3.2)	4 (12.5)	5 (15.2)	
Torso (front and back)	6 (19.4)	4 (12.5)	7 (21.2)	
Abdomen	2 (6.5)	1 (3.1)	0 (0)	
Perineum	0 (0)	1 (3.1)	1 (3.0)	
Burn depth				
Superficial partial thickness only	24 (77.4)	23 (71.9)	30 (90.9)	0.15
Mixed partial thickness	7 (22.6)	9 (28.1)	3 (9.1)	
	Acticoat™ (n = 12) Mean (SD)	Acticoat™ and Mepitel™ (n = 12) Mean (SD)	Mepilex Ag™ (n = 11) Mean (SD)	p-value
LDI Mean PU	1110.46 (235.70)	1396.05 (457.40)	1161.02 (306.80)	0.12
LDI Min PU	361.42 (191.70)	340.92 (207.80)	279.27 (145.60)	0.55

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

the appearance of the wound, therefore it was deemed appropriate to use this classification of burn depth for statistical analyses. The burn depth ratings from clinical judgment for each group were: Acticoat™ ('superficial partial thickness only' n = 24; 'mixed depth' n = 7), Acticoat™ with Mepitel™ ('superficial partial thickness only' n = 23;

'mixed depth' n = 9) and Mepilex Ag™ ('superficial partial thickness only' n = 30; 'mixed depth' n = 3). The baseline differences in burn depth between the groups was not statistically significant (p = 0.33).

Primary outcomes

Days to full re-epithelialization

Burn wounds were classified as ≥ 95% re-epithelialised by the treating consultant, through measurement from 3D photographs and Visitrak™ tracings and by consultants during blind photo reviews. Visitrak™ measurements could not be used as tracings were unable to be completed in 22% of children due to pain and an inability to remain still. However, 3D photographs and wound measurements were successfully completed for all participants in the study. The

level of agreement between consultants from blinded photo review classification of ≥ 95% re-epithelialization was excellent, ICC 0.92 (95% CI: 0.88, 0.94) and therefore ratings of days to ≤ 95% re-epithelialization by the treating consultant were used for the analysis. Table 2 shows the raw data for days to ≤ 95% re-epithelialization between the three dressing groups as classified by the treating consultant.

Negative binomial regression

The variance of the days to full re-epithelialization (28.28) was nearly three times greater than the corresponding mean (9.66). Given this overdispersion of the data, a negative binomial regression model was used to compare the differences in the treatment groups, after adjusting for the effects of any potential confounding variables. Four variables (gender, age, burn depth, TBSA) were considered for their potential contribution to the days to reepithelialization outcome and entered individually into the regression model. Burn depth was the only variable found to have a significant (p < 0.05) impact on days to re-epithelialization and was included in the final regression model. Two outliers, one from the Acticoat™ group and one from the

Mepilex Ag™ group, were excluded from the final model due to their unusually large residual values (i.e. high number of days to full re-epithelialization compared to the whole cohort). Data was calculated as an incidence rate ratio in the final model.

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

Table 2: Days to full re-epithelialization between dressing groups.

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

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

Pain during the dressing change procedure

Multilevel generalized linear mixed-effects modeling with a log link function and gamma distribution was used to analyze the data from each of the five pain measures (Table 3). Four variables (gender, age, burn depth and TBSA) were considered as potential confounders for modeling each of the pain measures (FPS-R, FLACC, VAS-P, pulse rate and respiratory rate).

Data were analyzed after dressing removal, at new dressing application and overall (all timepoints at all dressing changes). Results were presented as odds ratios and their 95% confidence intervals. Modeling was not completed for the FPS-R due to a large amount of missing data (the majority of children in the study were too young to use this scale). For respiratory rate, there was no statistically significant difference between the three dressing groups overall, after dressing removal or application. Additionally, at all timepoints and for all pain measures, there was no significant difference between Acticoat™ with Mepitel™ and Mepilex Ag™.

After dressing removal.

Receiving the Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased

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

Acticoat™ with Mepitel™ and Mepilex Ag™ dressings significantly decreased the expected pulse rate after dressing removal by 8% and 7%, respectively, compared to receiving the Acticoat™ dressing ($p \leq 0.01$).

After dressing application

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

Overall

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

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

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

FLACC = faces, legs, activity, cry, consolability scale; VAS-P = Visual Analog Scale-Pain; OR = odds ratio; CI = confidence interval

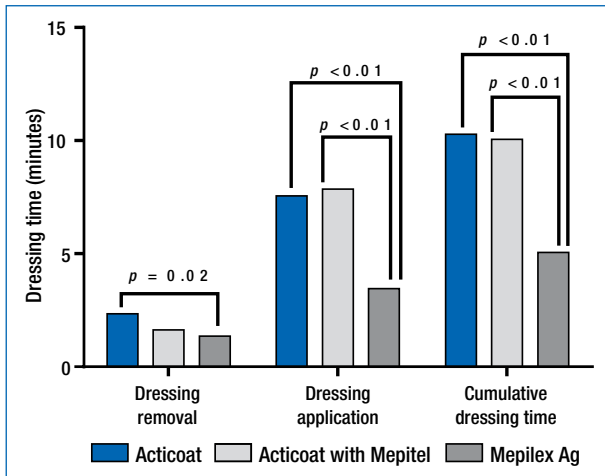


Figure 3: Comparison of dressing removal, application and cumulative dressing time at the first dressing change. Removal and application was significantly faster in Mepilex Ag™ compared to Acticoat™ ($p < 0.001$) and Acticoat™ with Mepitel™ ($p < 0.01$).

and Mepilex Ag™ dressings significantly decreased the overall expected pulse rate by 8% and 7% compared to receiving the Acticoat™ dressing ($p \leq 0.01$).

Secondary outcome measures

Analgesia

On the first dressing change, 78% of participants received a narcotic analgesia combination of paracetamol (dosage by body weight, 15 mg/kg) and Oxycodone™ (dosage by body weight, 0.1–0.2 mg/kg) according to standard practice for the SPPBC. The remainder of participants received paracetamol only or no analgesic medication as determined by clinical judgment (i.e. burn very minor, child too young for Oxycodone™). Three participants in the Acticoat™ group and one participant in the Acticoat™ with Mepitel™ group received a rescue dose of Oxycodone™ (dosage of 0.1 mg/kg in addition to the initial paracetamol and Oxycodone™ dose) during their first dressing change procedure. All three participants in the Acticoat™ group who were administered an Oxycodone™ rescue dose also received inhaled Entonox™ (nitrous oxide/oxygen combination) at the first dressing change. One participant in the Acticoat™ group also received Entonox™ (in addition to standard paracetamol/Oxycodone™ dose) for the second and third dressing changes.

Dressing removal and application times

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

Dressing ease of removal and application

Dressing ease of removal and application ratings were analyzed between the three dressing groups on the first dressing change.

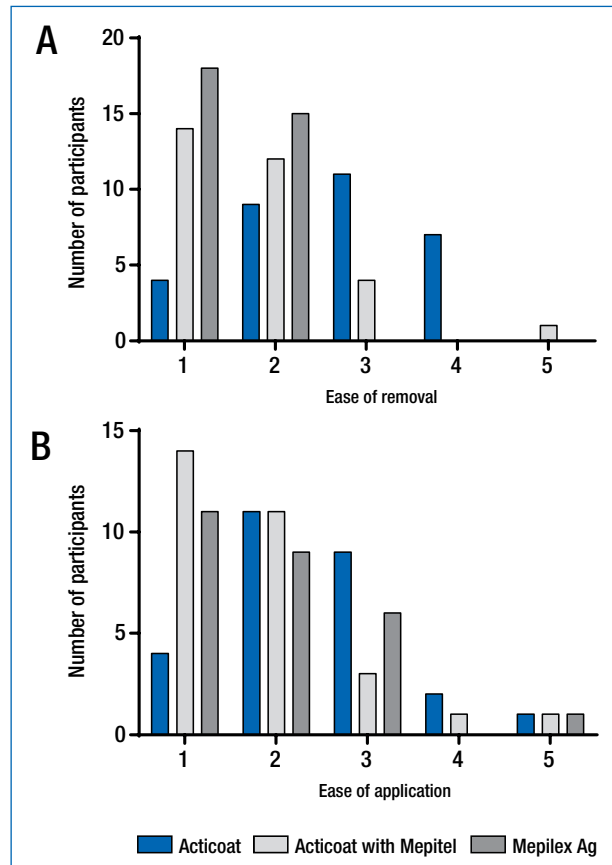


Figure 4: Ease of dressing removal at the first dressing change (A) and ease of dressing application at the first dressing change (B). The treating nurse used a Likert scale where: 1 = extremely easy, 2 = very easy, 3 = somewhat easy, 4 = not very easy, 5 = not at all easy. Acticoat™ was significantly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

Likert scale ratings regarding ease of dressing removal and application are represented in Figure 4A and B. For dressing removal (Figure 4A), the Acticoat™ group was rated as significantly more difficult to remove than both the Mepilex Ag™ group ($p < 0.01$) and the Acticoat™ with Mepitel™ group ($p < 0.01$). There was no significant difference between Acticoat™ with Mepitel™ and Mepilex Ag™ ($p = 0.20$).

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

Nursing staff experience with dressing use

In a pre- and post-study surveys, nursing staff from the SPPBC rated the three dressings for their perceived or observed ease of removal and application when used on hands or feet and flat surfaces (i.e. chest). Nursing staff rated that Acticoat™ with Mepitel™ and Mepilex Ag™ were the easiest to remove from both hands or feet and flat surfaces. Acticoat™ with Mepitel™ was rated as the easiest to apply to hands or feet and flat surfaces, with Mepilex Ag™ the hardest to apply to hands or feet. Acticoat™ was rated as the hardest

to apply to flat surfaces and hardest to remove from all areas. All nursing staff specified that Mepilex Ag™ was the hardest to apply to hands or feet in very young children (under the age of 3 years) as the dressing is the thickest of the three dressings and difficult to conform to very small fingers and toes.

Physical function

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

Adverse events

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

Discussion

Effective wound healing treatments are vital to diminish the physical and psychosocial challenges children experience after a burn, therefore high level evidence is required to identify the most appropriate silver dressing for pediatric burns. Whilst silver fabric dressings demonstrate improved re epithelialization and reduced pain compared to SSD cream,^{4,15} there is a lack of high level trials comparing silver dressings to each other in the pediatric burns population.⁵ The results of this study demonstrated that clean, <10% TBSA, partial thickness burns in children aged 0–15 years, when dressed with Mepilex Ag™, re-epithelialised significantly faster than those dressed with Acticoat™ or Acticoat™ with Mepitel™.

The results have shown advantages in using a dressing with a silicone interface (Mepilex Ag™) compared to a dressing without (Acticoat™). Dressings that are silicone or have silicone interfaces, adhere to normal, intact skin and remain in situ on the surface of a wound but do not adhere to it, maintaining a moist wound environment while providing a less traumatic removal and subsequently less epidermal damage.^{16,17} Comparatively, dressings that can adhere wound beds, such as Acticoat™, potentially cause trauma on removal, increase pain and promote skin stripping which has been found to delay wound re-epithelialization.¹⁸ In addition to slower re-epithelialization rates, clinical observations of bleeding from the wound bed dressing removal in participants who received the Acticoat™ dressing further emphasized the benefits of using a dressing with silicone interface for pediatric burns.

Although both dressings had a silicone interface, the difference in re-epithelialization between Mepilex Ag™ and Acticoat™ with Mepitel™ was unexpected and may be due to other factors such

as the cytotoxicity or release of silver from the dressings. Silver products are an effective antimicrobial utility for managing the bio-burden of burn wounds and in vitro studies have shown Acticoat™ can be cytotoxic to healthy keratinocytes which can delay healing.¹⁹ However, there has yet to be any published research with respect to the cytotoxicity of the silver used in Mepilex Ag™. In terms of silver release from dressings, an in vitro study by Rigo et al.²⁰ demonstrated that over a period of 7 days, the silver release from Mepilex Ag™ occurred within the first hour of contact with human serum substitute, whereas Acticoat™ Flex had a sustained silver release over the same 7 days. This difference in silver release rate between the two dressings could account for the difference in re-epithelialization rates, due to the continual release of silver from Acticoat™ over time. Additionally, there could also be an infection risk if Mepilex Ag is left on for 7 days but has released all its silver within the first day of application. It should be noted that the amount of silver released from Acticoat™ with the addition of mepitel™ has yet to be reported in the literature. Laboratory research would be of major importance to evaluate the cytotoxicity of Mepilex Ag™ in comparison to Acticoat™, the antimicrobial effect of Mepilex Ag™ on dirty wounds and when worn for 7 days or more and the effect of Mepitel on silver release from Acticoat™.

This study also proved that dressings with silicone interfaces were associated with lower pain scores after dressing removal and application and across time in comparison to Acticoat™ alone. Pulse rate was a significant indicator of pain, however may have little significance clinically due to the relatively small differences found between the groups. Respiratory rate was difficult to record in the children in this study due to excessive movement and crying and the results reflect that it is not a useful indicator of pain or distress in this instance. Given the difference in days to re-epithelialization between the Acticoat™ and Mepilex Ag™ groups and the subsequent difference in pain levels between these two groups, the results from this study sit well within the existing literature. Previous studies in this population have also demonstrated that higher levels of pain during burn care procedures are associated with delays in wound re-epithelialization.^{13,21} The reduced levels of pain associated with Acticoat™ with Mepitel™ and Mepilex Ag™ in this study, in conjunction with significantly faster re-epithelialization in the Mepilex Ag™ group has provided evidence to strongly consider the utilization of dressings with added-on or in-built silicone interfaces to manage acute burns in the pediatric population.

The significant differences noted between the three dressings in this study with regard to re-epithelialization rates and pain levels, have provided sufficient justification to conduct this trial in children with burns >10% TBSA. It would also be of benefit to explore the rate of wound re-epithelialization when changing these dressings at 3 vs. 7 days to determine if fewer stressful dressing changes will have an effect on re-epithelialization rates and pain levels in children. Conducting research in a pediatric population can be difficult and this trial was not without its own difficulties as the majority of children recruited were under the age of 3 years. Visitrak™ tracings in this study cohort were a challenge due to its invasive nature and many tracings could not be completed, whereas 3D photographs were taken for all children. Stockton et al.⁹ noted that 3D photography is

a non-invasive and accurate method for calculating wound area for children over the age of 3 years and should be considered for future use in children of this age over other methods such as the Visitrak™. Further research comparing Visitrak™ and 3D photography in children under the age of 3 years is required to extrapolate the results to the population examined in this study.

The most accurate method of burn depth classification for the pediatric population also remains problematic. Completing LDI scans in young children was a challenge in this study with many scans unable to be completed those under the age of 3 years. Challenges associated with LDI scanning in very young children have been documented in the literature with other researchers acknowledging the difficulty of interpreting scans affected by movement artifacts, with some decreasing resolution and scan times to accommodate for such occurrences.^{22,23} However, the fact remains that many studies reporting the success of LDI scan as an accurate, objective measure of burn wound healing potential included children with a mean age of 3 years or older.^{24–26} Therefore the validity and reliability of LDI use in very young children (under the age of 3 years) is required for future studies in this population. Alternatively, recently developed Laser Speckle Contrast Imaging has potential as a promising research tool and substitute to LDI scans in the pediatric population, with a scan time of 2 s and higher resolution images, however the reliability and validity of this measure has yet to be established in children.²⁷ In addition to difficulties with LDI scans, the low agreement between medical staff regarding burn depth classification is widely acknowledged in the literature²³ and the similar result from this study was not unexpected. This study has demonstrated that while viewing a photo alone is appropriate for judgment of wound re-epithelialization, it is unsuitable for use in burn depth analysis.

Conclusion

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

Conflict of interest

Despite the financial support, Mölnlycke Healthcare had no part in the study design and data collection of this project, nor did they have any involvement in the analysis or publication of the results. The principal researcher has no financial interest in Acticoat™, Mepitel™ or Mepilex Ag™ dressings or the Mölnlycke Healthcare company and is a student of the University of Queensland.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.burns.2014.11.005>.

References

- Lee JO, Herndon DN. Special considerations of age: the pediatric burned patient. In: Herndon DN, editor. *Total burn care*. 4th ed. Saunders; 2012. p. p405–14.
- Maskell J, Newcombe P, Martin G, Kimble R. Psychological and psychosocial functioning of children with burn scarring using cosmetic camouflage: a multi-centre prospective randomised controlled trial. *Burns* 2014;40:135–49.
- Aziz Z, Abu SF, Chong NJ. A systematic review of silver containing dressings and topical silver agents (used with dressings) for burn wounds. *Burns* 2012;38:307–18.
- Cuttle L, Naidu S, Mill J, Hoskins W, Das K, Kimble RM. A retrospective cohort study of Acticoat versus Silvazine in a paediatric population. *Burns* 2007;33:701–7.
- Wasiak J, Cleland H, Campbell F. Dressings for superficial and partial thickness burns. *Cochrane Database Syst Rev* 2013;3:1–62.
- Kumar RJ, Kimble RM, Boots R, Pegg SP. Treatment of partial-thickness burns: a prospective, randomized trial using Transcyte. *ANZ J Surg* 2004;74:622–6.
- Verbelen J, Hoeksema H, Heyneman A, Pirayesh A, Monstrey S. Aquacel1 Ag dressing versus Acticoat dressing in partial thickness burns: a prospective, randomized, controlled study in 100 patients. Part 1: burn wound healing. *Burns* 2014;40:416–27.
- Gee Kee E, Kimble RM, Cuttle L, Stockton K. Comparison of three different dressings for partial thickness burns in children: study protocol for a randomised controlled trial. *Trials* 2013;14:403.
- Stockton KA, McMillan CM, Storey KJ, David MC, Kimble RM. 3D photography is as accurate as digital planimetry tracing in determining burn wound area. *Burns* 2014. <http://dx.doi.org/10.1016/j.burns.2014.04.022>.
- Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain* 2001;93:173–83.
- Merkel S, Voepel-Lewis T, Malviya S. Pain assessment in infants and young children: the FLACC scale. *Am J Nurs* 2002;102:55–8.
- Wilson GAM, Doyle E. Validation of three paediatric pain scores for use by parents. *Anaesthesia* 1996;51:1005–7.
- Miller K, Rodger S, Kipping B, Kimble RM. A novel technology approach to pain management in children with burns: a prospective randomized controlled trial. *Burns* 2011;37:395–405.
- Schulz K, Altman D, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Trials* 2010;11:32.
- Peters DA, Verchere C. Healing at home: comparing cohorts of children with medium-sized burns treated as outpatients with in-hospital applied Acticoat to those children treated as inpatients with silver sulfadiazine. *J Burn Care Res* 2006;27:198–201.
- Morris C, Emsley P, Marland E, Meuleneire F, White R. Use of wound dressings with soft silicone adhesive technology. *Paediatr Nurs* 2009;21:38–43.
- Chadwick P, Taherinejad F, Hamberg K, Waring M. Clinical and scientific data on a silver-containing soft-silicone foam dressing: an overview. *J Wound Care* 2009;18:483–90.
- Matsumura H, Imai R, Ahmatjan N, Ida Y, Gondo M, Shibata D, et al. Removal of adhesive wound dressing and its effects on the stratum corneum of the skin: comparison of eight different adhesive wound dressings. *Int Wound J* 2012;11:50–4.
- Kempf M, Kimble RM, Cuttle L. Cytotoxicity testing of burn wound dressings, ointments and creams: a method using polycarbonate cell culture inserts on a cell culture system. *Burns* 2011;37:994–1000.
- Rigo C, Roman M, Munivrana I, Vindigni V, Azzena B, Barbante C, et al. Characterization and evaluation of silver release from four different dressings used in burns care. *Burns* 2012;38:1131–42.
- Brown NJ, Kimble RM, Rodger S, Ware RS, Cuttle L. Play and heal: randomized controlled trial of Ditto intervention efficacy on improving re-epithelialization in pediatric burns. *Burns* 2014;40:204–13.
- Cho JK, Moon DJ, Kim SG, Lee HG, Chung SP, Yoon CJ. Relationship between healing time and mean perfusion units of laser Doppler imaging (LDI) in pediatric burns. *Burns* 2009;35:818–23.
- Holland AJA, Martin HCO, Cass DT. Laser Doppler imaging prediction of burn wound outcome in children. *Burns* 2002;28:11–7.
- Mill J, Cuttle L, Harkin DG, Kravchuk O, Kimble RM. Laser Doppler imaging in a paediatric burns population. *Burns* 2009;35:824–31.
- Stewart TL, Ball B, Schembri PJ, Hori K, Ding J, Shankowsky HA, et al. The use of laser Doppler imaging as a predictor of burn depth and hypertrophic scar postburn injury. *J Burn Care Res* 2012;33:764–71.
- Hoeksema H, Van de Sijpe K, Tondt T, Hamdi M, Van Landuyt K, Blondeel P, et al. Accuracy of early burn depth assessment by laser Doppler imaging on different days postburn. *Burns* 2009;35:36–45.
- Lindahl F, Tesselar E, Sjöberg F. Assessing paediatric scald injuries using laser speckle contrast imaging. *Burns* 2013;39:662–6.
- Monstrey S, Hoeksema H, Verbelen J, Pirayesh A, Blondeel P. Assessment of burn depth and burn wound healing potential. *Burns* 2008;34:761–9.