Pruritus in Pediatric Burn Survivors: Defining the Clinical Course

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Pruritus is a frequent and severe symptom and a significant cause of distress for adult burn patients. Its effects in children are largely unstudied. The aim of this study is to characterize postburn itch in the pediatric population. This is a retrospective review from 2006 to 2013 for pediatric burn survivors who were enrolled in a longitudinal multicenter outcomes study. Demographic data, injury characteristics, associated symptoms (skin-related problems, pain, and sleep), and incidence and intensity (Numerical Rating Scale) of itch were examined. Measures were completed at hospital discharge and at 6, 12, and 24 months after injury. Spearman's correlations were used to examine the correlation between itch intensity and associated symptoms. Multivariate regression analyses examined the impact of associated symptoms on itch intensity. There were 430 pediatric burn survivors with a mean age of 7.8 years and a mean TBSA of 40.8%. Pruritus is present in most children (93%) and is of moderate intensity (5.7 ± 3.1) at discharge. The frequency and intensity of pruritus decreases over time; a majority of children continue to report symptoms at 2 years (63%). Itch was significantly correlated with associated symptoms, Regression analyses showed a correlation between itch intensity and pain at each time point. There was no association between itch intensity and burn etiology, age, gender, or burn size. Pruritus is a frequent complication that lasts for at least 2 years after injury in a majority of pediatric burn survivors. This information will enable better tracking of outcomes and will serve as a baseline for assessing interventions. (J Burn Care Res 2015;36:151-158)

In 1660, the German physician Haffenreffer defined itch as "an unpleasant cutaneous sensation which provokes the desire to scratch." This definition of pruritus

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still remains relevant today.^{1,2} Pruritus in burned adults is common and long-lasting with a reported incidence of 93 and 73% at hospital discharge and 2 years, respectively.³ In a cross-sectional study of adult burn survivors at an average of 17 years postburn injury, 72% reported itching.⁴ Pruritus is a significant cause of distress for burn patients, potentially affecting wound healing, scar formation, sleep, and concentration.^{5–7} Predictors for pruritus in adult burn patients included female gender, burn size and depth, younger age, dry skin, and raised or thick scars.³

Although itch is a frequent and severe symptom in adults in the acute and chronic stages of recovery, its characteristics in the pediatric burn population are largely unstudied. Our current understanding of pediatric pruritus is based on literature that examines itch as a cause of sleep disruption. A preliminary study reported that 70% of pediatric and adolescent burn survivors were "usually" awakened from sleep by itching. Another study indicated that itch

at discharge was a predictor of sleep difficulties at 6-month and 12-month follow-up in children. To date, there have been no studies that examine the prevalence, intensity, and distress related to pruritus for pediatric burn survivors. The aim of this study is to characterize postburn itch and associated factors in the pediatric population.

METHODS

Setting

Funded by the Department of Education's National Institute of Disability and Rehabilitation Research, the Burn Model System (BMS) program maintains a longitudinal database of demographic and outcome information. The BMS database has been in existence since 1994 and currently includes four national centers. The current BMS database enrollment criteria for pediatric patients include

- ≥20% TBSA burn that required surgery for wound closure
- Electrical high-voltage/lightning burn injury that required surgery for wound closure
- Hand, face, or feet burn that required surgery for wound closure

Of note, before August 2009, the first enrollment criterion above was different; pediatric patients with a TBSA of 30% or more who required surgery for wound closure were included. The other two criteria (electrical/lightning injury, critical area injuries) remained constant throughout the study period.

Study data were collected and electronically entered into a centralized BMS database. Subjects were enrolled after providing informed consent. This study was monitored by institutional review boards at each study site. The BMS database design, structure, and collection methods have been reported previously. Data for subjects from 0 to 13 years were obtained from a parent or guardian; data for subjects aged 14 to 18 years were obtained from the survivor.

Study Participants

This study included BMS pediatric patients (aged 18 and under) who were injured from January 2006 to August 2013. Data were collected at hospital discharge and at 6, 12, and 24 months after injury.

Outcome Measures

Primary Outcomes

Pruritus. Study subjects reported the intensity of their itching and the level of distress due to their itch. Itch intensity (Numerical Rating Scale [NRS]

Itch Intensity) was measured by the NRS, which is a self-reported, 11-point scale, with 0 representing no itch and 10 representing unbearable, excruciating itch. The NRS Itch Intensity scale has demonstrated validity and reliability in a variety of diagnoses. Subjects also reported the intensity of their distress due to their itch using the NRS (NRS Itch Distress), with 0 representing no distress and 10 representing a lot of distress due to itching. NRS Itch Intensity and NRS Itch Distress were collected at all time points.

Secondary Outcomes

Pain and sleep. Study subjects also reported the intensity of pain (NRS Pain Intensity) and sleeping difficulty (NRS Sleep Intensity). These were reported using an NRS, with 0 representing no pain or sleeping difficulty and 10 representing unbearable or excruciating pain, or being unable to sleep. Subjects also reported their distress due to pain (NRS Pain Distress) and sleeping difficulty (NRS Sleep Distress) on an NRS, with 0 representing no distress or not experiencing the symptom, and 10 representing a lot of distress due to the issue. NRS Pain Intensity, NRS Sleep Intensity, NRS Pain Distress, and NRS Sleep Distress were collected at all time points.

Skin-Related Problems. The presence of skin-related conditions due to the burn injury was recorded as Yes, No, or Unknown. Skin-related problems included dry skin, fragile skin, chronic open wounds, skin tightness that interferes with function, loss of skin sensation, and increased skin sensitivity. Skin-related problem data were collected at all time points.

Demographic and Medical Variables. Demographic data included age, gender, ethnicity, and the language in which the form was administered. Medical data included percent TBSA burn, percent TBSA grafted, and primary etiology of injury. Demographic and medical variables were collected at discharge.

Statistical Analysis

Stata software (version 12) was used for the analyses. Descriptive statistics are used to summarize the demographic and medical data of the study population. Incidence of pruritus, pain, and sleeping difficulty was tabulated as a percentage of subjects with a score of ≥1 on NRS Itch Intensity, NRS Pain Intensity, and NRS Sleep Intensity, respectively. The mean NRS Intensity and NRS Distress scores are calculated as an average of all scores for that particular symptom (pain, itch, and sleep).

Paired t-tests were used to analyze the change in severity between consecutive time points for primary (NRS Itch Intensity and NRS Itch Distress)

and secondary outcomes (NRS Pain Intensity, NRS Sleep Intensity, NRS Pain Distress, and NRS Sleep Distress). Significance was determined by P < .05.

Spearman's correlations were used to examine the correlations between itch intensity (NRS Itch Intensity) and secondary outcomes (NRS Pain Intensity, NRS Sleep Intensity, and skin-related problems) at each time point. A Bonferroni adjustment was used to account for multiple testing. The adjusted significance level was 0.00625.

Univariate linear regression was used to examine associations at each time point between itch intensity (NRS Itch Intensity) and demographic factors, medical factors, and secondary outcomes (pain, sleep, and skin-related problems). Multivariate linear regressions were used at each time point with those variables that were significant ($P \le .05$) in the univariate models to determine significant factors associated with itch intensity.

RESULTS

Patient Demographics

A total of 430 pediatric subjects with a history of burn injury met inclusion criteria. The mean age at the time of injury was 7.8 ± 5.6 years; 289 (67.2%) were male subjects, 271 (63.0%) were Hispanic, and the average burn size (TBSA burn) was $40.8\pm22.4\%$. Table 1 contains the population characteristics.

Primary Outcomes

At discharge, 93% of the population reported itch, with the number decreasing to 87% at 6 months, 78% at 12 months, and 64% at 24 months after injury (Figure 1). The mean NRS Itch Intensity scores were 5.7, 4.3, 3.5, and 2.5 at discharge, 6 months, 12 months, and 24 months, respectively (Figure 2). As evaluated by paired t-tests, NRS Itch Intensity exhibited a significant

Table 1. Patient characteristics

	Population ($N = 430$)
Age at injury, years, mean (SD)	7.8 (5.6)
TBSA burn, %, mean (SD)	40.8 (22.4)
TBSA graft, %, mean (SD)	35.6 (23.8)
Gender	
Male, n (%)	289 (67.2)
Form language, n (%)	
English	215 (50.0)
Spanish	209 (48.6)
Other	1 (0.2)
Ethnicity, n (%)	
Hispanie	. 271 (63.0)
Caucasian ,	106 (24.7)
African American	33 (7.7)
Other (non-Caucasian)	19 (3.2)
Injury etiology, n (%)	
Fire/flame	260 (60.5)
Scald -	100 (23.3)
Electricity	27 (6.3)
Contact with hot object	17 (4.0)
Grease	14 (3.3)
Chemical	2 (0.5)
Flash	2 (0.5)
Other*	4 (0.9)

^{*}Other includes the following etiologies and frequencies: hydrofluoric acid, 1; TENS/Stevens Johnson, 1; abrasions, 1; meningococcemia, 1.

decline at each consecutive time point. Mean NRS Itch Distress scores also/declined significantly at each time point (5.2, 4.4, 3.6, and 2.7 at discharge, 6, 12, and 24 months, respectively). Therefore, subjects experienced similar declines in itch intensity and distress due to itching in the 2 years after their injury (Table 2).

Secondary Outcomes

Pain and sleep characteristics are reported in Table 2. The frequency of pain and sleep difficulty was greatest at discharge and decreased at each subsequent

Table 2. Incidence, intensity, and distress of itch, pain, and sleeping difficulty

	Discharge	6 Months	12 Months	24 Months
Itch incidence (NRS > 0), # (%)	289 (93)	211 (87)	175 (78)	114 (64)
NRS 1tch Intensity, mean (SD)	5.7 (3.1)	4.3 (3.2)**	3.5 (3.2)**	2.5 (2.9)**
NRS itch distress, mean (SD)	5.2 (3.3)	4.4 (3.2)**	3.6 (3.4)**	2.7 (3.1)**
Pain incidence (NRS > 0), n (%)	264 (86)	134 (55)	93 (42)	62 (35)
NRS pain intensity, mean (SD)	4.2 (2.9)	1.7 (2,2)**	1.5 (2.3)	1.2 (2,2)
NRS pain distress, mean (SD)	4.1 (3.0)	2.0 (2.3)**	1.9 (2.5)	1.4(2.3)
Sleep difficulty incidence (NRS > 0), n (%)	227 (73)	125 (52)	101 (45)	52 (29)
NRS sleep intensity, mean (SD)	3.6 (3.3)	2.1 (2.8)**	1.6 (2.5)**	1.0 (2.1)*
NRS sleep distress, mean (SD)	3.4 (3.3)	2.2 (2.9)**	1.8 (2.8)**	1.2 (2.3)

NRS, Numerical rating scale.

 $^{^*}P < .05$ when compared with previous time point.

^{**}P < .001 when compared with previous time point.

time interval (pain incidence: 86, 55, 42, 35; sleep difficulty incidence: 73, 52, 45, 29; Figure 1). Similarly, the intensity of pain and sleep difficulty was most at discharge and decreased at each subsequent time interval (mean NRS Pain Intensity: 4.1, 2.0, 1.9, 1.0; mean NRS Sleep Intensity: 3.6, 2.1, 1.6, 1.0; Figure 2). For NRS Pain Intensity scores, there was a significant decline from discharge to the 6-month time point (4.2 to 1.7, P < .001), but from 6 to 12 months and from 12 to 24 months there was no significant difference in mean NRS Pain Intensity scores. The mean NRS Pain Distress scores also declined from discharge to 6 months after injury, but there was no significant decrease at subsequent time points (Table 2).

Spearman correlations are reported in Table 3 for correlations between itch (NRS Itch Intensity) and secondary outcomes (NRS Pain Intensity, NRS Sleep Intensity, and skin-related problems). There was a moderate positive correlation between itch and pain at 12 and 24 months (r = .46, P < .0001; r = .53, P < .0001). There was also a moderate positive correlation between itch and sleeping difficulty at all time points (discharge: r = .42, P < .0001; 6 months: r = .49, P < .0001; 12 months; r = .42, P < .0001;24 months: r = .46, P < .0001). In terms of skinrelated problems, there was a moderate positive correlation between itch and fragile skin at 24 months (r = .41, P < .0001) and between itch and dry skin at 12 and 24 months (r = .50, P < .0001 and r = .50, P < .0001, respectively) (Table 3).

In the univariate analyses, a positive linear correlation was found between NRS Itch Intensity and NRS Pain Intensity, NRS Sleep Intensity, NRS Itch Distress, NRS Pain Distress, and NRS Sleep Distress at all time points. No other factors were associated with itch intensity at any of the time points, including ctiology of injury, age, percent TBSA burned, percent TBSA grafted, and gender.

In the multivariate analysis, NRS Itch Intensity was correlated with NRS Pain Intensity and NRS Itch Distress at all time points (P < .05). NRS Itch Intensity was associated with NRS Sleep Intensity at discharge and 6 months (P < .005). At discharge, itch intensity was positively correlated with NRS Pain Distress and NRS Sleep Distress; this correlation was not significant at all the other time points. Factors including etiology, age, TBSA burned, TBSA grafted, and gender were not significant in the univariate analysis and therefore were not included in the multivariate analyses (Table 4).

DISCUSSION

This is the first study to provide a detailed description of the clinical course of pruritus in the pediatric

Table 3. Spearman correlations for NRS Irch Intensity and skin-related conditions, NRS pain intensity, and NRS sleep intensity

	Chronic Open Wounds	Fragile Skin	Dry Skin	Skin Tightness	Loss of Skin Sensation	Increased Skin Sensitivity	NRS Pain Intensity NRS Sleep 'at Same Time Intensity at Same Point Time Point	.NRS Sleep Intensity at Same Time Point
NRS Itch Intensity at discharge 0.11, $P = 0.066$ 0.25, $P = 0.000^*$ 0.25, $P = 0.000^*$ 0.18, $P = 0.003^*$ 0.15, $P = 0.02$ 0.33, $P = 0.000^*$ 0.35, $P = 0.000^*$ 0.08 Itch Intensity at 12 months 0.19, $P = 0.063^*$ 0.24, $P = 0.000^*$ 0.34, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.34, $P = 0.000^*$ 0.35, $P = 0.000^*$ 0.35, $P = 0.000^*$ 0.35, $P = 0.000^*$ 0.37, $P = 0.000^*$ 0.31, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.31, $P = 0.000^*$ 0.32, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.33, $P = 0.000^*$ 0.33, $P = 0.000^*$	0.11, P = 0.06 0.19, P = 0.003* 0.15, P = 0.02 0.11, P = 0.16	0.25, P = 0.000* 0.24, P =0.000* 0.31, P = 0.000* 0.41, P = 0.000*	0.25, P = 0.000** 0.34, P = 0.000* 0.50, P = 0.000* 0.50, P = 0.000*	$P=0.000^{\star} 0.25, P=0.000^{\star} 0.18, P=0.003^{\star} 0.15, P=0.02 0.33, P=0.000^{\star} 0.35, P=0.000^{\star} \\ P=0.000^{\star} 0.34, P=0.000^{\star} 0.18, P=0.005^{\star} 0.07, P=0.29 0.38, P=0.000^{\star} 0.39, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.000^{\star} 0.33, P=0.000^{\star} 0.30, P=0.000^{\star} 0.38, P=0.000^{\star} 0.46, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.000^{\star} 0.31, P=0.000^{\star} 0.21, P=0.009 0.38, P=0.000^{\star} 0.53, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} 0.50, P=0.000^{\star} \\ P=0.000^{\star} 0.50, P=0.0000^{\star}$	0.15, P= 0.02 0.07, P= 0.29 ' 0.30, P= 0.000* 0.21, P= 0.009	0.33, P = 0.000* 0.38, P = 0.000* 0.38, P = 0.000* 0.38, P = 0.000*	0.35, P = 0.000* 0.39, P = 0.000* 0.46, P = 0.000* 0.53, P = 0.000*	0.42, P= 0.000* 0.49, P= 0.000* 0.42, P= 0.000* 0.46, P= 0.000*

NRS, Numerical Rating Scale,

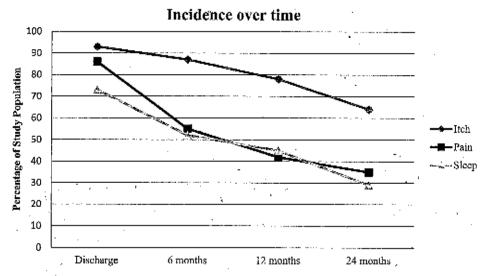


Figure 1. Incidence of itch, sleep problems and pain over time. Incidence of pruritus, pain, and sleeping difficulty was tabulated as a percentage of subjects with a score of ≥1 on the Numerical Rating Scale (NRS) Itch Intensity, NRS Pain Intensity, and NRS Sleep Intensity scales.

burn population. Pruritus is a common symptom in children with burns, present in essentially all children at discharge (93%). The intensity of itch is moderate at time of discharge (5.7 ± 3.1) and decreases over time; however, it is still present in the majority of children at 2 years (63%). Therefore, pruritus is a common problem in both the acute and chronic setting in children with burns.

There is little prior research examining pruritus in the pediatric burn population. In work examining sleep in children with burn injuries, a majority of burn survivors were "usually" awakened from sleep by itching.⁸ Another study of children with

burns reported that itch at discharge was a predictor of sleep difficulties at follow-up. Research examining the psychometric properties of multidimensional outcome instruments for burned children, the Burn Outcomes Questionnaires, reported trends in itch symptoms demonstrating a decline in severity over time. It is a comparison between survivor and parent responses, children rated their itch symptoms as more severe than their parents; interestingly, most all other outcome domains of the instrument demonstrated no difference in ratings between children and their parents. Assessing itch in young children is particularly complicated given the limited verbal

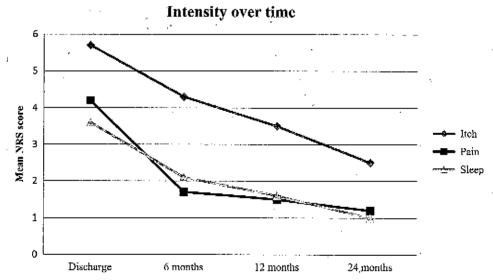


Figure 2. Mean intensity scores over time for itch, sleep, and pain.

Table 4. Multivariate regression analyses examining predictors of NRS 1tch Intensity at discharge and at 6, 12, and 24 months

Time Point and		
Primary Outcome	Coefficient	$\boldsymbol{\mathit{P}}$
Discharge		
NRS pain intensity	0.11	.020*
NRS sleep intensity	0.19	<.001*
NRS itch distress	-0.14	.005*
NRS pain distress	0.85	<.001*
NRS slccp distress	-0.10	035*
6 months	,	,
NRS pain ontensity	0.10	.028*
NRS sleep intensity	0.16	.005*
NRS irch distress	0.77	<.001*
NRS pain distress	-0.05	.325
NRS sleep distress	J 0.0,-	.908
12 months	•	
NRS pain intensity	0.14	.002*
NRS sleep intensity	-0.03	.591
NRS itch distress	0.84	<.001*
NRS pain distress	-0.09	.090
NRS sleep distress	0.10	.144
24 months	•	
NRS pain intensity	0.17	.003*
NRS sleep intensity	0.05	.419
NRS itch distress	0.74	<.001*
NRS pain distress	-0.06	284
NRS sleep distress	0.04	.502

NRS, Numerical Rating Scale.

skills of this age group. Using the parent-administered Burn Outcome Questionnaire for ages 0 to 5, burned children experienced significant itch symptoms; itch symptoms were reported as a combined domain with pain symptoms. Nevertheless, these symptoms recovered gradually over a year from injury but failed to reach the level of unburned agematched children. ¹³ The published literature examining the Burn Outcome Questionnaires did not examine the incidence of pruritus and did not use the NRS to assess symptom severity. ^{11–14} The current study is the first to examine pruritus as the primary outcome and to describe its frequency, severity, and associated symptoms.

The clinical course of pruritus in the pediatric burn population is similar to that of adults. Previously reported data in adults using the BMS database are used for comparison.³ Both children (93%) and adults (93%) exhibit a high incidence of pruritus symptoms at discharge. Although the frequency of pruritus decreases over time in both populations, a majority of children (64%) and adults (73%) report

symptoms at 24 months. Similarly, the intensity of pruritus is worst at discharge (5.7; 5.6) and decreases at each subsequent time interval in both populations. In adults, previous studies have identified TBSA burned, TBSA grafted, age, and female gender as predictors of pruritus. 3,16,17 However, none of these predictors were found to be significantly associated with pruritus intensity in the pediatric burn population. A similar pattern of improvement in itch symptoms over time has been shown in other adult burn datasets. In studies of chronic pruritus in other nonburn adult populations, younger age and female gender were associated with chronic pain or pruritus. In

Given the frequency, severity, and duration of pruritus and pruritus' well-documented impact on sleep and overall quality of life, 18,19 there is compelling reason to determine efficacious treatments in this population. Most studies examining treatments for pruritus in burns have focused on the adult population. The following interventions have been examined in the adult burn population with varying levels of evidence; antihistamines (H1 receptor antagonists, both oral and topical); antiepileptics (gabapentin and pregabalin); tricyclic antidepressants (topical doxepin); noninvasive brain stimulation techniques such as transcranial direct current stimulation; and nonmedication interventions such as emollients (aloe vera, lanolin) and massage therapy. 20-24 The only treatments that have been assessed in children include gabapentin, a eutectic mixture of local anesthetics (EMLA), the Unna boot, and loratadine. 20,22,25-27 Researchers demonstrated a significant reduction in itch symptoms within 24 hours of receiving gabapentin in the pediatric burn population.²⁰ EMLA was shown to reduce the number of pruritic episodes on the day in which it was administered.²⁵ EMLA has not been assessed for pruritus relief in the adult burn population; interestingly, EMLA has also been used for pain relief during venipuncture and vaccination in children. 28-30 A pediatric observational study using the Unna boot demonstrated fewer itch symptoms as well as reduced dressing change time, lower cost of dressings, and better appetite, sleep, and play patterns. 22,26 In a pilot study. the administration of loratadine provided subjective relief of itching for all patients.²⁷ Additional research. is needed to assess treatment options for pruritus in the pediatric population.

Existing instruments to assess the severity and quality of pruritus have limitations in the pediatric population. One-dimensional assessments are commonly used and include the NRS, the Visual Analog Scale, and the Verbal Rating Scale. 31-34 These

^{*}P < .05.

scales use an 11-point scale that ranges from 0, representing no itch, to 10, representing the worst itch imaginable. However, numerical scales have demonstrated problems with reliability in small children. ^{35,36} The recently developed 5D itch scale is a more detailed pruritus questionnaire that examines five dimensions of itch (degree, duration, direction, disability, and distribution) with established reliability and validated in children. ^{37,38} The Itch Man Scale is a detailed, child-specific pruritus assessment for burn survivors that was recently developed and validated. ³⁸

LIMITATIONS

The study data are from patient self-reports and parents reporting on their child's health status, introducing potential reporting bias. A recent study demonstrated that children rate their itch as more severe than their parents; however, for essentially all other outcome domains children and parents exhibited similar responses. 15 Additionally, all patients were treated at a major burn center, which may represent selection bias; the BMS database may not be representative of a national sample of burned children. Also, small burns were not included in the dataset (inclusion criteria: TBSA ≥20% or electrical injury or critical area burns); therefore, the findings are not necessarily representative of children with smaller burns. The database does not include data on treatments for pruritus; therefore, investigators cannot control for this variable. The majority of the study population self-identified as Hispanic; this may not be representative of the national pediatric burn population. Nevertheless, in spite of these limitations, this represents an important contribution as the first work to detail the clinical course of pruritus in the pediatric burn population.

CONCLUSION

This investigation provides a description of pruritus in the pediatric burn population and demonstrates that it is a frequent complication that lasts for at least 2 years after injury in a majority of patients. This information will aid patients, families, clinicians, and researchers in better understanding pruritus; furthermore, it will enable better tracking of outcomes and serve as a baseline for assessing interventions. There is a need to demonstrate efficacy of treatments for pruritus in this population.

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