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PREDICTORS OF MODERATE TO SEVERE FATIGUE 12 MONTHS FOLLOWING ADMISSION TO HOSPITAL FOR BURN INJURY: RESULTS FROM THE BURNS REGISTRY OF AUSTRALIA AND NEW ZEALAND (BRANZ) LONG TERM OUTCOMES PROJECT

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Introduction

Fatigue has been identified as an outcome of concern following burn injury but is rarely captured in outcomes studies. We aimed to: i) describe the prevalence, and predictors, of moderate to severe fatigue in the first 12 months following burn injury, and ii) establish the association between fatigue and health-related quality of life and work outcomes.

Methods

Adult burns patients, admitted >24 hours, were recruited from five BRANZ sites. Participants were followed-up at 1-, 6-, and 12-months after injury using the Brief Fatigue Inventory (BFI), 36-item Short Form Health Survey (SF-36) and the Sickness Impact Profile (SIP) – work scale. Moderate to severe fatigue was defined as a global BFI score of 4-10. Multivariable mixed effects regression modelling was used to identify demographic, socioeconomic, burn size and severity predictors of moderate/severe fatigue at follow-up.

Results

The mean±SD age of the 328 participants was 42.1±16.7 years, 70% were male, 47% were flame burns, and the mean±SD %TBSA was 8.7±11.2. The prevalence of moderate/severe fatigue decreased from 37% at 1-month, to 32% at 6-months and 26% at 12-months. The adjusted odds of moderate/severe fatigue were 2.62 (95% CI: 1.27, 5.42) times higher for women compared to men, and 2.64 (95% CI: 1.03, 6.79) in patients with a %TBSA ≥ 20. Compared to patients in major cities, the adjusted odds of reporting moderate/severe fatigue were 2.48 fold higher (95% CI: 1.17, 5.24) for patients residing in inner regional areas, and 3.60 fold (95% CI: 1.43, 9.05) higher for patients living in remote/very remote areas. At each time point, the physical and mental health summary scores, and each sub-scale score, of the SF-36 were significantly lower in patients reporting moderate/severe fatigue. Patients experiencing moderate to severe fatigue reported higher work-related disability on the SIP work scale at each time point after injury.

Discussion and Conclusion

More than a quarter of participants reported moderate to severe fatigue on the BFI at 12-months and fatigue was strongly associated with poorer health-related quality of life and greater work-related disability.

Key Words

Burn registry

Outcomes

Cohort study

Fatigue

Quality of life

INTRODUCTION

Burn injury can have wide ranging impacts on patients' lives including physical and psychosocial issues. Patients have identified fatigue as a debilitating issue after burn injury [1, 2], but is largely omitted from recommendations for measuring burn injury outcomes [3, 4], and not directly captured in existing systems for follow-up of burn patients [5, 6].

Determining the prevalence and severity of fatigue experienced by burn patients is challenging due to differences in the burn populations studied and methods of measuring fatigue, and wide ranging variation in the time post-burn injury at which the prevalence of fatigue was measured. Holavanahalli et al, in their study of 98 adult patients who had experienced a burn of 30% TBSA or greater, reported that 59% had experienced fatigue since the burn and 54% continued to experience fatigue at the point of follow-up, a mean of 17 years after burn injury [7]. Esfahlan et al [8], found that the 66% of 100 hospitalised burns patients in Iran reported fatigue, although the timing of capturing this information was unclear and the method for capturing data about fatigue was not specified. Helm et al, in their secondary report of a 3-year outcome study from a single burn centre in the US, described fatigue as an "almost universal complaint" and a major barrier to return to activities and work [9]. In a longitudinal study of 587 admitted burn patients from a single centre in Western Australia, Toh et al found that levels of fatigue declined over the first 12-months after burn injury, and that fatigue levels were higher in women compared to men, and in major burns compared to minor burns. While Toh et al captured data at multiple time points after injury, the major focus of this study was the validation of an instrument for measuring fatigue in burn patients, and predictors of fatigue were not explored in depth [10]. Other studies have not directly measured fatigue, but have shown disproportionately low aerobic fitness in burn patients when compared to controls [11], and low scores on the 36-item Short Form Health Scale (SF-36) vitality sub-scale following burn injury [12].

Establishing the prevalence of fatigue after burn injury, how this changes over time, and the types of patients who experience fatigue issues, is needed to improve understanding of the burden of burn injury, and to better inform clinical care of burn patients. Therefore, the aims of this study multi-centre study were to describe the prevalence of fatigue in the first 12-months after burn injury, and to establish predictors of experiencing fatigue.

METHODS

Setting

There are 17 burn centres providing specialist burn care to the population of Australia (23.1 million) and New Zealand (4.5 million). Since July 2009, the Burns Registry of Australia and New Zealand (BRANZ), previously called the Bi-National Burns Registry, has collected burn epidemiological and clinical care data for approximately 3000 new inpatient admissions each year where a burn is the principal reason for admission and the admission is within 28 days of injury [13]. Admissions for less than 24 h, and desquamating skin conditions such as Toxic Epidermal Necrolysis (TENS), are excluded.

Participants

Adult (≥ 18 years) burns patients who met the BRANZ inclusion criteria, and survived to hospital discharge, were sequentially recruited from five BRANZ sites to participate in this study.

Ethics statement

The project received Human Research Ethics Committee (HREC) approval from all participating centres and Monash University. Written informed consent was obtained from all participants at the Concord Repatriation General Hospital, Royal Adelaide Hospital, Royal Hobart Hospital, and The Alfred. Royal Perth Hospital received a waiver of consent from their HREC to follow up all survivors to hospital discharge.

Procedures

The project methodology has been described in detail elsewhere [14] and a summary is provided here. Recruitment occurred between October 2009 and December 2010. Participants were predominantly recruited during their inpatient stay, or when discharged prior to invitation to participate, a cover letter, explanatory statement and consent form were mailed to the patient and consent sought by telephone.

Participants were followed-up at 1-, 6-, and 12-months after injury by telephone, self-administration (mail-out), or in-person interview. The mode of administration was kept consistent throughout the study for each individual where possible. Fatigue was measured using the Brief Fatigue Inventory (BFI), which is a generic instrument that measures the severity of fatigue and the impact of fatigue on daily functioning in the past 24 h [15]. It includes nine items measured on an 11-point scale (0 to 10). Health-related quality of life was measured using the 36-item Short Form Health Survey (SF-36) Version 2 (SF-36 v2) which is a generic measure of health status with eight domains; physical functioning, role physical, bodily pain, general health, energy/vitality, social functioning, and general health concepts and mental health. The BFI and SF-36v2 have been validated for use in burn populations [10, 16]. The Sickness Impact Profile (SIP) is a generic health status instrument with 12 scales. The work and recreation scale is validated for use independent of the other scales and includes nine items about return to work and work-related disability with higher scores representing greater work-related disability and a score of zero representing return to work without residual problems [17, 18].

Additional data describing the profile of the participant population were extracted from the BRANZ dataset. Data extracted included demographic details (age and gender), socioeconomic status, geographic remoteness, cause of burn, size and depth of burn, presence of an inhalation injury, surgical management and in-hospital outcomes were obtained from the BRANZ database. The percentage of total body surface area (%TBSA) burned was used to describe the size of the burn and burn depth was classified as superficial only, mid-dermal (with or without superficial areas) and deep-dermal or full thickness (with or without superficial or mid-dermal areas). Postcodes of residence were mapped to the Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) [19], which summarises information about the economic and social conditions of people living in a specific area, and the Accessibility/Remoteness Index of Australia (ARIA) which provides a measure of geographic remoteness (major metropolitan city, inner regional, outer regional, remote, very remote) based on the road distance to centres that provide certain services [20]. For the IRSAD, quintiles were used with one representing the most disadvantaged and five the most advantaged.

Data analysis

Summary statistics were used to describe the overall participant profile. Frequencies and percentages were used for categorical variables. Mean and standard deviation, or median and interquartile range (IQR) were used for continuous variables. Independent t-tests were used to compare fatigue groups at each time point for the SF-36 component summary scales and sub-scales, while Mann-Whitney U-tests were used to compare work disability at different levels of fatigue using the SIP work scale. Pearson's r was used to assess the correlation between the BFI global scale and sub-scales of the SF-36.

The outcome of interest was moderate to severe fatigue, which was defined as a global BFI score of 4 to 10, as recommended by the instrument developers and supported by Toh et al in their validation study of the BFI in burns patients [15,16]. There were missing data for a small number of variables; %TBSA (1.8%), remoteness index (1.2%), IRSAD (0.6%), whether the patient went to theatre (1.8%), whether the patient underwent a grafting procedure (2.4%) and whether the burn depth was recorded (30%). As it was considered reasonable to assume that probability that data were missing did not depend on the unobserved values, conditional on the observed data, the assumption of missing at random (MAR) was made and multiple imputation of these missing values was performed [21, 22]. The missing values were imputed using multiple imputation by chained equations (MICE) which involves iteration through the data imputing one variable at a time conditional on the others, creating multiple imputed datasets [23]. Age, sex, burn cause, %TBSA, burn depth, ARIA, IRSAD, hospital length of stay, whether the patient went to theatre, presence of an inhalation injury, and the burn centre where the patient was managed were all included in the MICE analysis, along with the outcome of interest, although the imputed outcome data were not used in the models. Ten datasets were imputed and the log (odds ratio) estimates from each imputed dataset were combined using Rubin's rules to yield a single robust odds ratio [24]. Summary statistics based on the imputed datasets were used to describe the profile of cases at each time point according to the key outcome of interest.

Random effects logistic regression modelling was used to identify demographic, socioeconomic, burn size and severity predictors of moderate/severe fatigue at follow-up. Models were performed first to establish univariate associations and then for multivariable modelling with variable showing an association ($p<0.20$) on univariate testing entered into the multivariable model. Random effects regression modelling was used to account for the longitudinal nature of the study (i.e. repeated measures from the same participant) and because this modelling approach provides robust estimates when data imbalance (e.g. loss to follow-up) is present. Adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI) were reported for the final model. All analyses were performed using Stata Version 13 (StataCorp, College Station, TX, USA).

RESULTS

Overview of participants

There were 328 participants who completed at least one follow-up in the study; 291 at 1-month, 218 at 6-months and 183 at 12-months. The predictors of loss to follow-up are described elsewhere [14]. Table 1 shows the profile of participants in this study.

<Insert Table 1 here>

Severity of fatigue and degree of interference with activities due to fatigue

The mean level of interference with activities was highest at 1-month for each type of activity and reduced over time (Figure 1). Fatigue interfered least with walking ability and relationships, while fatigue interfered more with normal work, general activity, mood and enjoyment of life (Figure 1).

<Insert Figure 1 here>

The mean (SD) rating of fatigue at the time of interview was 3.9 (2.6) at 1-month and 3.9 (2.7) at 6-months, before reducing to 3.7 (2.5) at 12-months post-injury. When asked their rating of the usual level of fatigue in the 24 hours prior to interview, participant mean (SD) scores were similar: 3.8 (2.5) at 1-month; 3.7 (2.6) at 6-months; and 3.7 (2.5) at 12-months. The participants were also asked to rate their worst level of fatigue in the 24 hours prior to interview and this reduced from 5.3 (2.9) at 1-month to 5.1 (2.9) at 6-months, and 4.8 (2.8) at 12-month post-injury.

Prevalence of moderate to severe fatigue at follow-up

The prevalence of any fatigue was 70% at 1-month, 49% at 6-months, and 51% at 12-months. The prevalence of moderate to severe fatigue decreased from 37% (n=107) at 1-month to 32% (n=70) at 6-months to 26% (n=47) at 12-months. At each time point, the patients reporting moderate to severe fatigue on the BFI reported lower ($p<0.001$) mean SF-36 summary scores for both physical and mental health (Figure 2).

<Insert Figure 2 here>

The mean score for each SF-36 sub-scale was lower ($p<0.001$) for patients reporting moderate to severe fatigue at follow-up at each time point (Figure 3). Physical Role sub-scale scores were notably lower for patients reporting moderate to severe fatigue on the BFI (Figure 3). The global BFI score showed a strong negative linear relationship with the vitality sub-scale of the SF-36 at 1-month ($r=-0.71$) and 6-months ($r=-0.72$), with the vitality sub-scale explaining 50% of the variance in the data when predicting the BFI score. At 12-months, only a moderate negative linear relationship ($r=-0.55$) was present, and the vitality sub-scale explained only 29% of the variance in the data as predictor of the global BFI score.

<Insert Figure 3 here>

Eighty-two percent of participants reported working for income prior to injury. There were no differences in return to work rates between patients without moderate to severe fatigue and those with moderate to severe fatigue at 1-month (62% vs. 49%, p=0.14), 6-months (90% vs. 83%, p=0.36) or 12-months (91% vs. 88%, p=0.63). However, participants reporting moderate to severe fatigue reported higher median SIP work scale scores, indicating greater work-related disability, at 1-month (70.1 vs. 15.5, p=0.008), 6-months (26.5 vs. 0.0, p<0.001) and 12-months (9.7 vs. 0.0, p=0.006).

Predictors of reporting moderate to severe fatigue at follow-up

Table 2 shows the characteristics of participants who did and did not experience moderate to severe fatigue at each time point post-injury. There was no univariate association between reporting moderate to severe fatigue at follow-up and age (p=0.55), level of socioeconomic disadvantage (p=0.27), burn depth (p=0.59), cause of burn (p=0.21), presence of an inhalation injury (p=0.65), whether the patient went to theatre (p=0.61), or their burn was grafted (p=0.33). Only time since injury (p=0.01), %TBSA (p=0.19), gender (p=0.15) and geographic remoteness (p=0.04) were associated with the prevalence of moderate to severe fatigue at follow-up on univariate testing. These variables were entered into the multivariable model (Table 3).

<Insert Table 2 here>

Gender, %TBSA group, geographic remoteness and time since injury were important independent predictors of reporting moderate to severe fatigue at follow-up (Table 3). The adjusted odds of reporting moderate to severe fatigue at 12 months post-injury were 58% lower when compared to 1-month post-injury, while the odds of experiencing moderate to severe fatigue were 2.6 fold higher for women compared to men (Table 3). The adjusted odds of experiencing moderate to severe fatigue were 2.6 fold higher for patients with a %TBSA ≥ 20, and patients residing in rural and remote areas of Australia demonstrated significantly higher risk of reporting moderate to severe fatigue at follow-up when compared to patients living in major cities (Table 3).

<Insert Table 3 here>

DISCUSSION

In this longitudinal, multi-centre study of 328 patients hospitalised for burn injury, fatigue was a commonly reported symptom, interfering most with normal work, general activities, mood and enjoyment of life. At 12-months post-burn injury, 26% continued to experience moderate to severe fatigue, a reduction from 37% at 1-month post-injury. Patients who reported moderate to severe fatigue at follow-up experienced significantly poorer physical and mental health, and greater work disability. The risk of experiencing moderate to severe fatigue increased with %TBSA, while women, and people living in rural and remote areas, were also at greater risk of moderate to severe fatigue.

The prevalence of any fatigue was largely consistent with previous study estimates of 54% [9] and 66% [8], despite differences in the severity of burn injury in the populations studied and variability in the timeframe for follow-up. At 12-months, the mean BFI score for usual, and worst fatigue, levels were 3.8 and 5.3, respectively. These values are higher than previously reported for community-dwelling adults who reported mean BFI scores for usual and worst fatigue of 2.4 and 3.8, respectively [25]. The severity of fatigue experienced by burn patients at 12-months was consistent with cancer patients who reported mean BFI scores for usual and worst fatigue of 3.9 and 5.5, respectively [25]. In contrast, our figures were much lower than the mean BFI scores for usual (5.2) and worst (7.6) fatigue reported by outpatients with clinical depression [25].

Numerous explanations for why burns patients are at risk of fatigue have been proposed in the literature, including a prolonged increase in metabolic rate due to the catabolic response to burn injury, as well as loss of skeletal muscle due to injury, as well as deconditioning due to prolonged hospital length of stay and bed rest [7-9, 11]. Studies showing lower levels of aerobic fitness, and persistent muscle weakness, support these theories [9, 11], and significantly poorer physical health was observed in our study in patients reporting moderate to severe fatigue.

Others have suggested psychological factors contributing to fatigue with Edwards et al observing a strong relationship between the SF-36 vitality scale and the presence of anxiety and depression [12]. In their qualitative study of 12 burn survivors at 6 to 12 months after burn injury, Dahl et al found that fatigue was a major issue for patients and that this impacted their adjustment to life [1]. These authors identified both mental (e.g. apathy) and physical aspects of fatigue in burn patients. Of note, patients reported a loss of strength and difficulty performing tasks which contributed to their fatigue, and that the psychological response to burn injury factored in to fatigue as patients reported processing their burn experience while they slept which left them tired on waking [1]. In our study, both physical and mental health scores were much lower in patients reporting moderate to severe fatigue, supporting the findings of Dahl et al that both physical and psychosocial aspects contribute to fatigue following burn. While we observed a moderate to strong correlation between the BFI and the vitality sub-scale of the SF-36, the vitality scale did not fully explain the BFI and studies interested in measuring the presence and pattern of fatigue may be best served by the inclusion of the more specific BFI.

Our observed findings of greater risk of reporting long-term fatigue issues in women and in larger burns are consistent with Toh et al [10], which was also undertaken in an Australian population. It is likely that the factors that can contribute to fatigue in burn patients such as psychosocial response, greater catabolic response, deconditioning due to prolonged rest, and loss of skeletal muscle mass are more common in larger burns, explaining the presence of this observed risk factor for fatigue. The reasons for women experiencing greater levels of fatigue are not immediately clear. However, multiple studies in injury have shown poorer physical and psychosocial outcomes in women [26-28], potentially due to differences in social roles and responsibilities and psychological impact of injury, or in the willingness to report issues. There is also a growing body of evidence that women also have greater mortality and cancer risk following burn injury [29, 30], suggesting a greater impact of burn injury on women overall.

A previous Australian study has shown differences in the profile of burn patients between urban, rural and remote areas with respect to age, burn size, gender and ethnicity [31]. Despite accounting for many of these differences, we observed higher risk of reporting moderate to severe fatigue observed in patients living in rural, remote and very remote communities. While this observational study cannot determine causation, there may be disparities in the availability of health and support services in regional communities compared to major cities that impact on fatigue outcomes. Factors associated with living in regional and remote communities such as greater travel distances to work and services, and potentially differences in occupations and employment circumstances (e.g. self-employment), may also increase the risk of fatigue further in burn patients, although further exploration of this finding is needed. Similarly, unmeasured confounders such as differences in pre-existing health, including mental health, may explain our findings.

The detailed strengths and weaknesses of this study are described elsewhere [14], but summarised here. The key strengths were the multi-centre approach, and longitudinal design, enabling determination of the prevalence of fatigue over time post-injury. We used validated measures of fatigue and health-related quality of life.

However, only 24% of eligible patients during the recruitment timeframe were recruited to the study, with a bias towards more patients with more severe burns and longer hospital length of stay [14]. Additionally, loss to follow-up was observed and missing data for some variables was also present. For these reasons, we chose analytical approaches best able to provide robust estimates in the presence of loss to follow-up, and valid methods for imputing missing data. Nevertheless, the relatively small sample size, and the low prevalence of larger burns, limited the power to detect all but the largest effects. These limitations need to be considered when interpreting the findings of the studies and comparing to other cohorts.

CONCLUSIONS

Fatigue was a commonly reported symptom in the first 12-months after burn injury and was associated with significantly poorer physical and mental health, and greater work disability. The levels of fatigue experienced by burns patients were consistent with cancer patients but lower than those experienced by patients suffering clinical depression. Further research is needed to better understand the modifiable factors that impact on fatigue, to reduce the overall burden of burn injury.

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REFERENCES

[1] Dahl O, Wickman M, Wengstrom Y. Adapting to life after burn injury - Reflections on care. Journal of Burn Care and Research. 2012;33:595-605.

[2] Johnson R, Taggart S, Gullick J. Emerging from the trauma bubble: Redefining 'normal' after burn injury. Burns. 2016;http://dx/doi.org/10.1016/j.burns.2016.03.016.

[3] Nedelec B, Donelan M, Baryza M, Bhavasar D, Blome-Eberwein S, Carrougher G, et al. Functional outcomes. Journal of Burn Care and Research. 2013;34:376-80.

[4] Palmieri T, Przkora R, Meyer WI, Carrougher G. Measuring burn injury outcomes. Surgical Clinics of North America. 2014;94:909-16.

[5] Klein M, Lezotte D, Fauerbach J, Herndon D, Kowalske K, Carrougher G, et al. The National Institute on Disability and Rehabilitation Research Burn Model System Database: A tool for the multicenter study of the outcome of burn injury. Journal of Burn Care and Research. 2007;28:84-96.

[6] Klein M, Lezotte D, Heltshe S, Fauerbach J, Holavanahalli R, Rivara F, et al. Functional and psychosocial outcomes of older adults after burn injury: Results from a multicenter database of severe burn injury. Journal of Burn Care and Research. 2011;32:66-78.

[7] Holavanahalli R, Helm P, Kowalske K. Long-term outcomes in patients surviving large burns: The musculoskeletal system. Journal of Burn Care and Research. 2015;DOI: 10.1097/BCR.0000000000000257.

[8] Esfahlan A, Lotfi M, Zamanzadeh V, Babapuor J. Burn pain and patients' responses. Burns. 2010;36:1129-33.

[9] Helm P, Herndon D, deLateur B. Restoration of function. Journal of Burn Care and Research. 2007;28:611-4.

[10] Toh C, Li M, Finlay V, Jackson T, Burrows S, Wood F, et al. The Brief Fatigue Inventory is reliable and valid for the burn patient cohort. Burns. 2015;41:990-7.

[11] Ganio M, Pearson J, Schlader Z, Matthew Brothers R, Lucas R, Rivas E, et al. Aerobic fitness is disproportionately low in adult burn survivors years after injury. Journal of Burn Care and Research. 2013;36:513-9.

[12] Edwards R, Smith M, Klick B, Magyar-Russell G, Haythornthwaite J, Holavanahalli R, et al. Symptoms of depression and anxiety as unique predictors of pain-related outcomes following burn injury. Annals of Behavioural Medicine. 2007;34:313-22.

[13] Watterson D, Gabbe B, Cleland H, Edgar D, Cameron P, Committee B-NS. Developing the first Bi-National clinical quality registry for burns—Lessons learned so far. Burns. 2012;38:52-60.

[14] Gabbe B, Cleland H, Watterson D, Schrale R, McRae S, Parker C, et al. Long term outcomes data for the Burns Registry of Australia and New Zealand: Is it feasible? Burns. 2015;41:1732-40.

[15] Mendoza T, Wang X, Cleeland C, Morrissey M, Johnson B, Wendt J, et al. The rapid assessment of fatigue severity in cancer patients. Cancer. 1998;85:1186-96.

[16] Edgar D, Dawson A, Hankey G, Phillips M, Wood F. Demonstration of the validity of the SF-36 for measurement of the temporal recovery of quality of life outcomes in burns survivors. Burns. 2010;36:1013-20.

[17] Bergner M, Bobbitt R, Carter W, Gilson B. The sickness impact profile: development and final revision of a health status measure. Medical Care. 1981;19:787-805.

[18] De Bruin A, De Witte L, Diederiks J. Sickness Impact Profile: The state of the art of a generic functional status measure. Social Science and Medicine. 1992;35:1003-14.

[19] Australian Bureau of Statistics. Socio-Economic Indexes for Areas (SEIFA) 2011 Available at: http://www.abs.gov.au/ausstats/abs@.nsf/mf/2039.0/.2013.

[20] Department of Health and Aged Care. Measuring Remoteness: Accessibility/Remoteness Index of Australia (ARIA). Commonwealth of Australia; 2001. In: Australia Co, editor. Canberra 2001. Available at: http://www.health.gov.au/internet/main/publishing.nsf/Content/E2EE19FE831F26BFCA257BF0001F3DFA/$File/ocpanew14.pdf.

[21] Sterne J, White I, Carlin J, Spratt M, Royston P, Kenward M, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. British Medical Journal. 2009;338:http://dx.doi.org/10.1136/bmj.b2393.

[22] White I, Royston P, Wood A. Multiple imputation using chained equations: Issues and guidance for practice. Statistics in Medicine. 2011;30:377-99.

[23] Van Burren S. Multiple imputation of discrete and continuous data by fully conditional specifications. Statistics in Medical Research. 2007;16:219-42.

[24] Rubin D. Multiple Imputation for Non-Response Surveys. New York, NY: John Wiley and Sons; 1987.

[25] Anderson K, Getto C, Mendoza T, Palmer S, Wang X, Reyes-Gibby C, et al. Fatigue and sleep disturbance in patient with cancer, patients with clinical depression, and community-dwelling adults. Journal of Pain and Symptom Management. 2003;25:307-18.

[26] Gabbe B, Simpson P, Sutherland A, Wolfe R, Fitzgerald M, Judson R, et al. Improved functional outcomes for major trauma patients in a regionalized, inclusive trauma system. Annals of Surgery. 2012;255:1009-15.

[27] Holbrook T, Hoyt D, Anderson J. The importance of gender on outcomes after major trauma: functional and psychologic outcomes in women versus men. . Journal of Trauma. 2001;50:270-3.

[28] Polinder S, Van Beeck E, Essink-Bolt M, Toet H, Loomen C, Mulder S, et al. Functional outcome at 2.5, 5, 9, and 24 months after injury in the Netherlands. Journal of Trauma. 2007;62:133-41.

[29] Duke J, Rea S, Semmens J, Edgar D, Wood F. Burn and cancer risk: A state-wide longitudinal analysis. Burns. 2011;38:340-7.

[30] Moore E, Pilcher D, Bailey M, Stephens H, Cleland H. The Burns Evaluation and Mortality Study (BEAMS): Predicting deaths in Australian and New Zealand burn patients admitted to intensive care with burns. Journal of Trauma and Acute Surgery. 2013;75:298-303.

[31] Duke J, Rea S, Semmens J, Wood F. Urban compared with rural and remote burn hospitalisations in Western Australia. Burns. 2011;38:591-8.

FIGURE LEGENDS

Figure 1: Mean scores for level of interference on the Brief Fatigue Inventory items in the past 24 hours (0=does not interfere, 10=completely interferes)

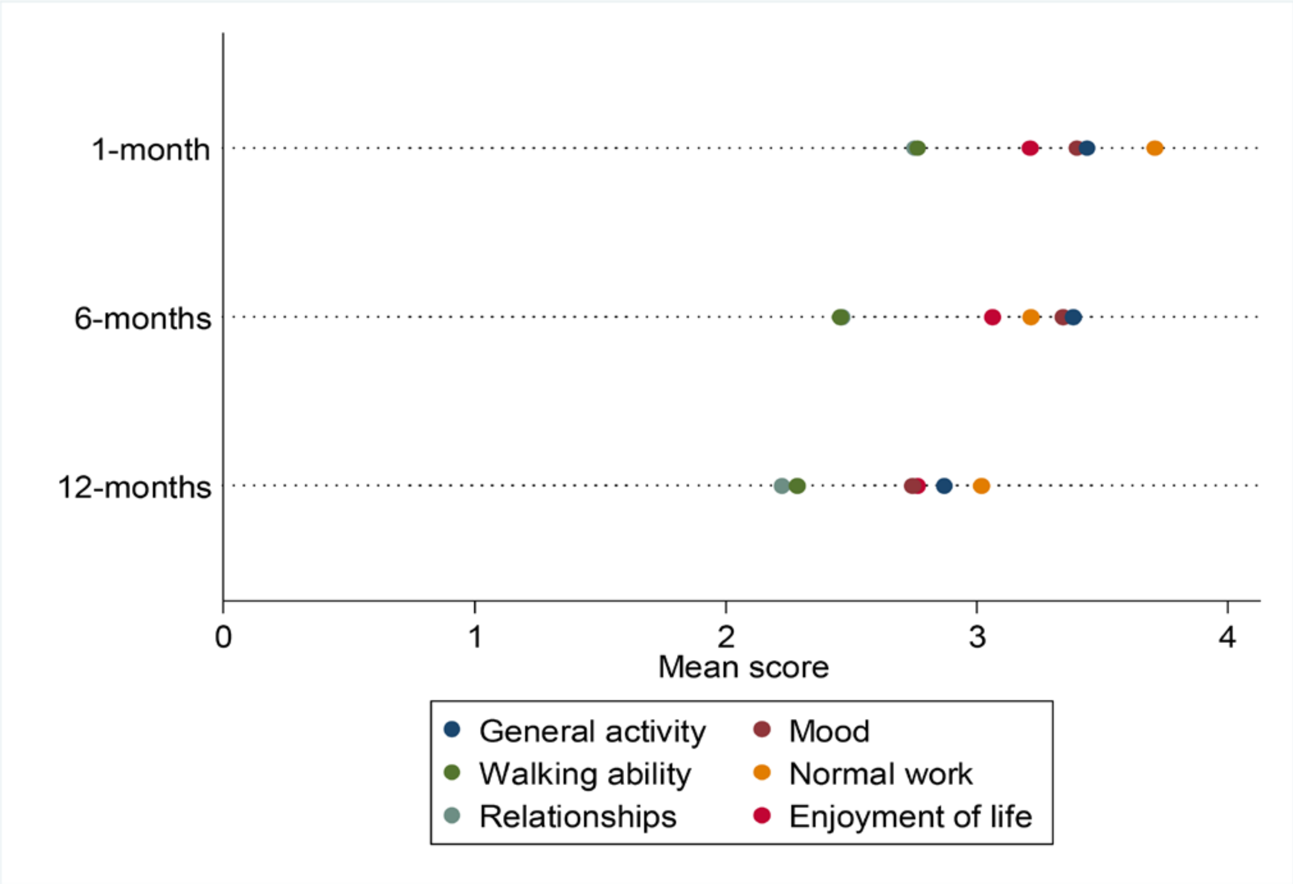

Figure 2: Mean SF-36 summary scores by fatigue group and time following burn (PCS, physical health; MCS, mental health)

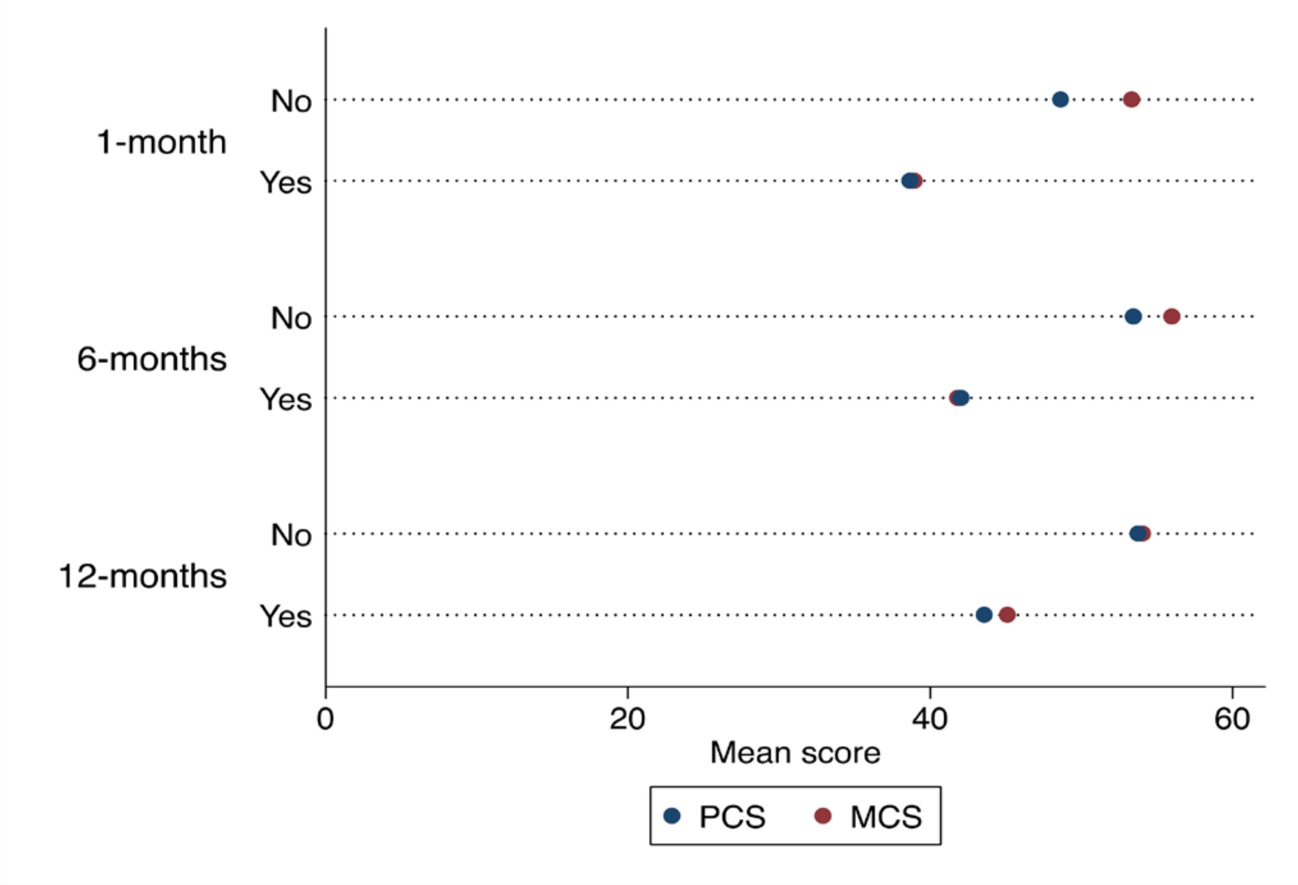

Figure 3: Mean SF-36 sub-scale scores by fatigue group and time following burn

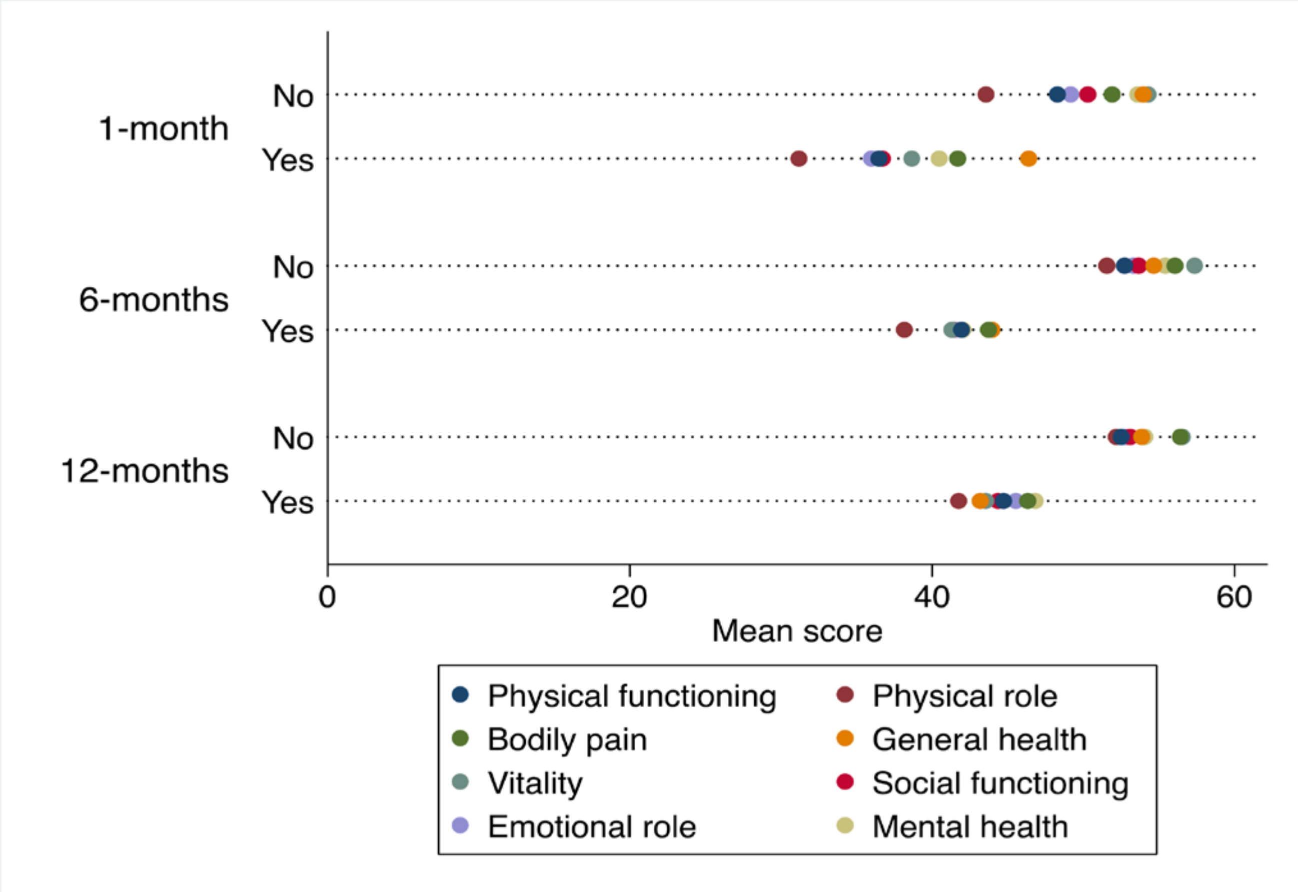

Table 1: Profile of study participants (n=328)

Population descriptor		
Age	Mean (SD) years	42.1 (16.7)
Gender	N (%)	
	Male	228 (69.5)
	Female	100 (30.5)
Level of socioeconomic disadvantage[a]	N (%)	
	1 (Most disadvantaged)	58 (17.8)
	2	55 (16.9)
	3	65 (19.9)
	4	77 (23.6)
	5 (Least disadvantaged)	71 (21.8)
Level of geographic remoteness[b]	N (%)	
	Major city	176 (54.3)
	Inner regional	96 (29.6)
	Outer regional, remote, very remoted	52 (16.1)
Burn cause	N (%)	
	Flame	153 (46.7)
	Scald	87 (26.5)
	Contact	53 (16.2)
	Other	35 (10.7)
Burn Centre	N (%)	
	Centre A	129 (39.5)
	Centre B	80 (24.5)
	Centre C	51 (15.6)
	Centre D	45 (13.7)
	Centre E	23 (7.0)
%TBSA[c]	Mean (SD)	8.7 (11.2)
	N (%)	
	<10%	224 (69.6)
	10-19%	55 (17.1)
	≥ 20%	43 (13.3)
Burn depth[d]	N (%)	
	Superficial	37 (16.1)
	Mid-dermal ± superficial	67 (29.1)
		126 (54.8)

	Deep dermal/Full thickness ± superficial or mid-dermal	
Inhalation injury	N (%)	
	No	312 (95.1)
	Yes	16 (4.9)
Theatre for procedure?[e]	N (%)	
	No	52 (16.1)
	Yes	270 (83.9)
Skin graft?[f]	N (%)	
	No	111 (34.7)
	Yes	209 (65.3)
Hospital length of stay	Median (IQR) days	9.1 (4.7-15.0)

[a] n=2 missing; [b] n=4 missing; [c] n=6 missing; [d] n=98 missing; [e] n=6 missing; [f] n=8 missing

Table 2: Profile of participants by fatigue group at each time point post-injury

Population characteristic		**1-month**		**6-months**	
		None/mild Fatigue (n=181)	**Moderate/severe Fatigue** (n=107)	**None/mild Fatigue** (n=147)	**Moderate Fatig** (n=7
Age	Mean (95% CI) years	42.1 (39.6, 44.6)	41.9 (38.9, 44.8)	42.8 (40.2, 45.4)	45.8 (41.8
Gender	% (95% CI)				
	Female	27.6 (21.1, 34.2)	39.3 (29.9, 48.6)	28.6 (21.2, 35.9)	34.3 (23.0
	Male	72.4 (65.8, 78.9)	60.7 (51.4, 70.1)	71.4 (64.1, 78.8)	65.7 (54.5
IRSAD quintile	% (95% CI)				
	1 (Most disadvantaged)	16.1 (10.7, 21.5)	19.6 (12.0, 27.2)	17.7 (11.5, 23.9)	20.0 (10.5
	2	17.2 (11.6, 22.7)	19.6 (12.0, 27.2)	17.7 (11.5, 23.9)	18.9 (9.5
	3	21.6 (15.6, 27.7)	13.1 (6.6, 19.5)	17.0 (10.9, 23.2)	13.3 (5.1
	4	23.4 (17.1, 29.6)	26.2 (17.8, 34.6)	24.5 (17.5, 31.5)	29.1 (18.3
	5 (Least disadvantaged)	21.8 (15.7, 27.9)	21.5 (13.6, 29.3)	23.1 (16.3, 30.0)	18.7 (9.4
ARIA classification	% (95% CI)				
	Major city	58.9 (51.6, 66.1)	45.2 (35.6, 54.8)	63.2 (55.3, 71.1)	51.9 (39.9
	Inner regional	27.8 (21.2, 34.4)	37.9 (28.5, 47.2)	23.9 (16.9 (30.8)	27.5 (16.9
	Outer regional/remote	13.3 (8.3, 18.3)	16.9 (9.7, 24.1)	12.9 (7.5, 18.4)	20.6 (10.9
Burn cause	% (95% CI)				
	Flame	44.2 (36.9, 51.5)	51.4 (41.8, 61.0)	49.7 (41.5, 57.8)	48.6, (36.7
	Scald	30.4 (23.6, 37.1)	25.2 (16.9, 33.5)	27.9 (20.6, 35.2)	24.3 (14.1
	Contact	18.8 (13.1, 24.5)	10.3 (4.5, 16.1)	13.6 (8.0, 19.2)	11.4 (3.9
	Other	6.6 (3.0, 10.3)	13.1 (6.6, 19.4)	8.8 (4.2, 13.5)	15.7 (7.1
%TBSA	Mean (95% CI)	7.1 (5.9, 8.3)	10.2 (7.8, 12.5)	9.4 (7.5, 11.2)	10.7 (7.2
	<10%	72.9 (66.3, 79.5)	61.9 (52.5, 71.3)	65.0 (57.1, 72.9)	66.7 (55.4
	10-19%	16.4 (10.8, 21.9)	20.0 (13.3, 27.7)	18.9 (12.4, 25.4)	18.8 (9.5

	≥ 20%	10.7 (6.1, 15.3)	18.1 (10.7, 25.5)	16.1 (10.0, 22.2)	14.5 (6.1
Burn depth	% (95% CI)				
	Superficial	18.7 (11.5, 25.8)	13.7 (5.2, 22.3)	18.4 (11.4, 25.4)	14.6 (4.3
	Mid-dermal	30.9 (23.3, 38.6)	27.6 (18.4, 36.7)	28.5 (20.2, 36.8)	30.6 (17.6
	Deep-dermal/full thickness	50.4 (42.2, 58.6)	58.7 (48.0, 69.3)	53.1 (43.4, 62.8)	54.9 (41.1
Inhalation injury?	% (95% CI)				
	No	96.1 (93.3, 98.9)	94.4 (90.0, 98.8)	92.5 (88.2, 96.8)	95.7 (90.9
	Yes	3.9 (1.0, 6.7)	5.6 (1.2, 10.1)	7.5 (3.2, 11.8)	4.3 (0.0
Theatre for management?	% (95% CI)				
	No	19.5 (13.6, 25.4)	12.4 (6.0, 18.9)	12.9 (7.4, 18.3)	14.7 (6.2
	Yes	80.5 (74.5, 86.4)	87.6 (81.1, 94.0)	87.1 (81.7, 92.6)	85.3 (76.8
Skin graft?	% (95% CI)				
	No	39.6 (32.4, 46.8)	31.4 (22.5, 40.3)	36.1 (28.2, 43.9)	32.0 (20.9
	Yes	60.4 (53.2, 67.6)	68.6 (59.7, 77.5)	63.9 (56.1, 71.8)	68.0 (56.8

Table 3: Predictors of reporting moderate to severe fatigue on the Brief Fatigue Inventory at follow-up (multivariable model)

Predictor		**Adjusted odds ratio (95% CI)**	**p-value**
Time since injury	1-month (reference)	1.00	
	6-months	0.74 (0.44, 1.23)	0.24
	12-months	0.42 (0.43, 0.73)	0.003
%TBSA	<10% (reference)	1.00.	
	10-19%	1.70 (0.74, 3.94)	0.21
	≥ 20%	2.64 (1.03, 6.79)	0.04
Geographic remoteness	Major city (reference)	1.00	
	Inner regional	2.48 (1.17,5.24)	0.02
	Outer regional, remote and very remote	3.60 (1.43, 9.05)	0.007
Gender	Male (reference)	1.00	
	Female	2.62 (1.27, 5.42)	0.009