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# Perioperative Research into Memory (PRiMe): Cognitive impairment following a severe burn injury and critical care admission, part 1.

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## **Abstract**

**Introduction:** An investigation into long-term cognitive impairment and Quality of Life (QoL) after severe burns.

**Methods:** A proof of principle, cohort design, prospective, observational clinical study. Patients with severe burns (>15% TBSA) admitted to Burns ICU for invasive ventilation were recruited for psychocognitive assessment with a convenience sample of age and sex-matched controls. Participants completed psychological and QoL questionnaires, the Cogstate® electronic battery, Hopkins Verbal Learning, Verbal Fluency and Trail making tasks.

**Results:** 15 patients (11M, 4F; 41 ±14 years; TBSA 38.4% ±18.5) and comparators (11M, 4F; 40 ±13 years) were recruited. Burns patients reported worse QoL (Neuro-QoL Short Form v2, patient 30.1 ±8.2, control 38.7 ±3.2, p=0.0004) and cognitive function (patient composite z-score 0.01, IQR -0.11 - 0.33, control 0.13, IQR 0.47 - 0.73, p=0.02). Compared to estimated premorbid FSIQ, patients dropped an equivalent of 8 IQ points (p=0.002). Cognitive function negatively correlated with burn severity (rBaux score, p=0.04). QoL strongly correlated with depressive symptoms (Rho=-0.67, p=0.009) but not cognitive function.

**Conclusions:** Severe burns injuries are associated with a significant, global, cognitive deficit. Patients also report worse QoL, depression and post-traumatic stress. Perceived QoL from cognitive impairment was more closely associated with depression than cognitive impairment.

**Keywords:** Severe burns; critical illness; cognitive impairment; mental health; Quality of Life

## 1. Introduction

The survival rates of patients requiring intensive care unit (ICU) admission following severe burns injuries continue to improve with advances in critical care medicine and burns management[1–5]. Admission to ICU is associated with physical, psychological and cognitive sequelae, which are in turn associated with a multi-faceted reduction in Quality of Life (QoL). This spans physical, mental and social domains, with many severe burns patients being unable to return to work within a year of discharge[6–8].

One of the most distressing problems affecting patients following discharge from ICU is that of long-term cognitive impairment (LTCl)[9–17]. This affects up to two thirds of patients[18] and can range in magnitude from subtle to major deficits in executive function and working memory. Cognitive deficits stemming from a wide range of medical conditions are known to have a significant impact on QoL[19–24]. It has been recognised after electrical injury, however there is limited research into ICU LTCl following severe general burns[25–28] and a dearth of research into any effect this may have on QoL. Patients with major burns encounter a markedly greater magnitude of inflammatory and hypermetabolic sequelae than general ICU cohorts[29,30]. In addition to this endogenous biochemical milieu, severe burns necessitate multiple surgeries and accompanying general anaesthetics to treat their injuries, and attract numerous nosocomial infections[31,32]. Anaesthesia[33–37] and pro-inflammatory states[38,39] are also known to be associated with LTCl. As such, severe burns patients admitted to ICU are a unique subgroup of patients that may be at particularly high risk of LTCl.

It is now accepted that the brain mounts an inflammatory response following local and systemic insults[30,40–42]. There is evidence suggesting that inflammatory mediators and the immune system play a significant role in adult hippocampal neurogenesis and memory formation in both health and disease, although the processes involved in immune activated neuroplasticity are not fully understood[43]. With the use of advanced neuroimaging techniques it is possible to identify surrogate markers of neuroinflammation in specific brain regions associated with memory formation in vivo[44,45].

This study has been performed in two parts due to the breadth of data collected. In part one we set out to look for long-term neurocognitive sequelae after a severe burns injury and any resulting impact on QoL. In part two, we look for any corresponding evidence of neuroinflammation with the use of multi-parametric Magnetic Resonance Imaging (MRI), including: diffusion weighted imaging, MR spectroscopy and resting-state fMRI.

## 2. Materials and Methods

This was a proof of principle, cohort design, prospective, observational clinical study. ClinicalTrials.gov ID: NCT03242395

### 2.1. Ethics approval

Ethics approval was granted by the Surrey Borders Research Ethics Committee on the 30th January 2014 (Reference 14/LO/0049). Fully informed written consent was received from all participants in accordance with the UK Good Clinical Practice code of practice.

### 2.2. Recruitment and demographics

All patients admitted to the Chelsea and Westminster Hospital Burns Intensive Care Unit (BICU) between 2004 and 2015 were reviewed and considered for inclusion in this trial. Patients were also recruited through burns charities such as the Katie Piper Foundation. Recruitment ran over a two-year period from April 2014 until April 2016. Collateral information gathered included: age, sex, years of education, employment history, past medical history and the date, mechanism and size of burn. Burn severity and comorbidities were quantified by use of the revised Baux (rBaux) score and the Charlson Comorbidity Index (CCI) respectively[46,47].

A convenience sample of comparators was also recruited. The patients were asked to select a family member of the same sex and similar age for the comparator group. If no suitable kin was available then comparators were recruited via poster advertisements in the burns outpatient waiting room. After initial contact via email or telephone, volunteers were invited to attend the research department. Subsequent to providing written informed consent, participants underwent neurocognitive testing and were individually matched for age, sex and National Adult Reading Test (NART) derived Full-Scale IQ (FSIQ). The closest matches were included in the analysis and went on to have MRI scans in part two of the study.

### 2.3. Inclusion and exclusion criteria

All adult patients admitted to a BICU within the previous ten years (at the time of testing), who had been intubated and ventilated, and with burns greater than or equal to 15% total body surface area (TBSA) were screened for inclusion in this study.

Exclusion criteria included: BICU admission for illnesses other than burns (e.g. Toxic Epidermal Necrolysis Syndrome); evidence of head trauma; known substance misuse or alcohol excess; inability to understand plain verbal or written English; those receiving formal psychiatric treatment; those held under the Mental Health Act, or if their psychological health was deemed to be at risk from inclusion in the study (as assessed by the supervising clinical psychologist). In addition, contraindications to MRI were also contraindications to study inclusion.

### 2.4. Quality of Life

QoL was assessed using the Euro QoL 5 Dimensions (EQ5D) questionnaire, the Instrumental Activities of Daily Living (iADL) scale and the National Institute of Health Neuro-QoL Short Form version 2 (NIH Neuro-QoL SF v2).

### 2.5. Mental health

Three mental health domains were assessed in this study as confounding factors for cognitive impairment and QoL: anxiety, depression and post-traumatic stress. The Patient Health Questionnaire (PHQ-9) and Beck Depression Index II (BDI II) are self-report inventories assessing the presence and severity of symptoms of depression. Higher scores indicate greater depression. In the same manner, the Trauma Screening Questionnaire (TSQ) reports symptoms of post-traumatic stress and the Generalised Anxiety Disorder 7 (GAD- 7) and Beck Anxiety Inventory (BAI) assess symptoms of anxiety. These tests have established validity and reliability[48–56]. Patients with known psychosis were not included in this study, but patients were re-screened during testing through use of the Clinician-Rated Dimensions of Psychosis Symptom Severity scale.

## 2.6. Cognitive assessment

The cognitive domains assessed included: learning (visual and verbal) and memory (working memory, immediate and delayed recall, retention, recognition discrimination), attention and processing speed, executive function, language (semantic and switching fluency). The following validated cognitive tests were used to assess these domains: the Hopkins Verbal Learning Test (HVLT), Trail Making parts A and B (TMA, TMB), semantic and switching verbal fluency (SeF, SwF), as well as the Cogstate® computerised battery: Identification speed (ID), Detection speed (DT), One Card Learning accuracy (OCL), One Back test accuracy (ONB), Two Back test accuracy (TWB), International Shopping List total correct answers (ISL) and Groton Maze Learning total errors (GML)[57]. Premorbid FSIQ was estimated using the NART[58,59]. The NART is a mainstream tool that has been validated in a wide variety of cognitive disorders, from dementia to schizophrenia to traumatic brain injury, and has been shown to remain stable over time[59–62]. All neurocognitive tests were administered in a quiet room with a supervising clinician.

## 2.7. Statistical analysis

According to our power calculations, a sample size of 36 patients was indicated to identify long-term neurocognitive deficits following admission to BICU. However, a target of 10-26 patients for identification of neuroinflammatory changes by using MRI would suffice[44,45,63–65].

Parametric data are presented as means and standard deviations and non-parametric data are presented as medians and interquartile ranges. Continuous parametric data were analysed using the Student t-test (STT) and associations were tested for using the Pearson's correlation coefficient. Non-parametric data were analysed using the Mann Whitney U test (MWUT) and associations were tested for using Spearman's rank correlation coefficient. All p-values presented are one tailed unless otherwise stated and statistical significance is defined as  $p < 0.05$ .

EQ5D domain data was split into binary outcomes (1 = no reduction in QoL domain, 2 or 3 = reduction in QoL domain) and analysed with the Fisher's Exact test (FET). The Cogstate® tests include population means and standard deviations from which z-scores can be calculated. A composite cognitive score was produced from the median of the z-scores for each participant. This composite score was used to compare the two groups and to test for an association between cognitive function and burn severity.

The comparison group was not successfully matched for premorbid IQ and consequently the patient group was also tested against population data in three ways:

- The proportion of patients scoring Very Poor in at least two tests, a more stringent version of a common methodology used in POCD and similar ITU LTCI studies[33,66–68].
- The cognitive results were categorised according to standardised descriptor outcomes (Very Poor to Superior performance ranges) and parametric distribution was confirmed. The total number of results in the Very Poor (>2SD below the mean) performance range for the patient group was tested against that expected for a normal distribution with a Chi Squared test.

- The difference between premorbid FSIQ z-score and the Cogstate composite z-score was tested to determine if there was a change in IQ after injury.

### 3. Results

#### 3.1. Recruitment and demographics

A total of 15 patients were recruited into the study (see figure 1), including 11 men and 4 women, with a mean age of  $40.5 \pm 13.8$  years and mean estimated premorbid FSIQ of  $108 \pm 12$  (half a standard deviation above the mean). The mean burn size was  $38.4 \pm 18.5\%$  TBSA. Three patients had documented inhalational injuries, resulting in a mean rBaux score of  $79.4 \pm 18$ . No patients experienced a cardiac arrest or head injury as part of the injury, two patients reported transient loss of consciousness. The median interval between injury and neurocognitive assessment was 2.68 years (IQR 2.05-4.55).

None of the patients were willing to provide contacts for the control group. Reasons provided included non-availability or desire for privacy. The 15 age- and sex-matched comparators comprised 11 men and 4 women with a mean age of  $39.9 \pm 12.9$  years and mean estimated premorbid IQ of  $116 \pm 8$ . They had a higher NART FSIQ than the patient group (STT  $p=0.016$ ) but there were no significant differences in age or sex. One control had a recent road traffic accident with ensuing long ICU stay, this was deemed a significant confounding factor and his data was replaced with that of another. There was no significant difference in CCI scores between the groups and both had extremely low levels of comorbidity (patient median 0, IQR 0-0.5, comparator median 0, IQR 0-0, Mann Whitney U test  $p>0.05$ ).

There was a statistically and clinically significant difference in level of education between the groups (patient mean  $14.5 \pm 4$  years, comparator mean  $18 \pm 2$  years, Student t test,  $p=0.024$ ), which is reflected in the premorbid FSIQ scores. Three of the injuries were work-related.

#### 3.2. Quality of Life

The patient group reported a worse QoL on the EQ5D (patient median index value 0.767, IQR: 0.7-1; comparators median 1, IQR 1-1, MWUT  $p=0.007$ ). The patients had worse EQ5D scores in four of the five domains: usual activities (7/15 vs 0/15, FET  $p=0.01$ ), pain/discomfort (10/15 vs 2/15, FET  $p=0.01$ ), mobility (4/15 vs 0/15, FET  $p=0.049$ ), and self-care (4/15 vs 0/15, FET  $p=0.049$ ) (see figure 2). The fifth domain (Anxiety/depression) was not significantly different between the groups (7/15 patients vs 2/15 comparators, FET  $p>0.05$ ). They also reported lower EQ5D visual analogue scale scores (patient mean  $70\% \pm 23.4$ , comparator mean  $84\% \pm 7.37$ , STT  $p=0.04$ ).

A significant drop in cognitive Quality of Life was found on the Neuro-QoL in the burn group (patient mean  $30.1 \pm 8.2$ , comparator mean  $38.7 \pm 3.2$ , STT  $p=0.0004$ ). There was still no correlation between the Neuro-QoL results and either the absolute cognitive score or the relative drop in cognition from baseline. However there was a significant correlation with the BDI-II (Spearman's Rho =  $-0.67$ ,  $p=0.009$ ).

There was no difference in iADL score (all participants scored the maximum score of 6).

### 3.3. Mental Health

The patient group had higher depression symptom scores for both the PHQ-9 (patient median: 6, IQR 1.5-13.5, comparator median: 1, IQR 0.5-1.5, MWUT  $p=0.01$ ) and BDI-II (patient median 15, IQR 9.5-23.5; comparator median 3, IQR 1-7.5, MWUT  $p=0.005$ ). They also reported higher traumatic stress symptoms in the TSQ (patient median: 3, IQR 1-6.5, comparator median 0, IQR 0-1.5, MWUT  $p=0.01$ ). There was a non-significant rise in both the BAI (patient median 5, IQR 2-9, comparator median 2, IQR 1.5-3.5, MWUT  $p>0.05$ ) and GAD-7 (patient median 3, IQR 0.5-9.5, comparator median 1, IQR 1-2, MWUT  $p>0.05$ ) (see figure 3).

The Clinician-Rated Dimensions of Psychosis Symptom Severity scale showed a statistically significant difference between the groups (patient median 2, IQR 0.25-4, comparator median 0, IQR 0-1, Mann-Whitney U test  $p=0.001$ ). Participants did not accrue points in any domains except for those of depression and cognitive impairment.

QoL outcomes (EQ5D total score) were strongly associated with each of the mental health questionnaires: PHQ-9 (Spearman's rho 0.78,  $p=0.0007$ ), BDI-II (Spearman's rho 0.71,  $p=0.003$ ) GAD-7 (Spearman's rho 0.80,  $p=0.0004$ ), BAI (Spearman's rho 0.78,  $p=0.0007$ ) and TSQ (Spearman's rho 0.70,  $p=0.004$ ).

### 3.4. Cognitive assessment

The composite z-score for the patients (median 0.01, IQR -0.11 - 0.33) was significantly lower than that of the comparison group (median 0.47, IQR 0.13 - 0.73), MWUT  $p = 0.015$ . A negative correlation was found between the composite z-scores and rBaux score (Spearman's Rho=0.54,  $p=0.039$ ) suggesting that cognitive function was worse with larger burns. The patient group performed worse in all of the tests, reaching statistical significance in six of the seventeen cognitive tests (see table 1). These spanned multiple domains, including working memory (ONB), delayed recall (HVLIT), attention (TMA, ID), executive function (TMB) and language (semantic fluency). Raw scores are provided in table 1 below; statistical tests were performed on age- and education- adjusted conversions where population data was available.

The cognitive test results were categorised into 'Very Poor' to 'Superior'. The categorical results were normally distributed. The patients scored more than two standard deviations below the mean in 23 of the 255 tests performed. This was over three times greater than expected for a normal distribution (observed: 23, expected: 7, Chi squared  $p=0.003$ ) (see figure 4). The comparator group was also normally distributed, albeit with a slight skew toward High Average performance reflecting their NART FSIQ scores. There was no disparity between the number of observed (7) and expected (7) results in the Very Poor performance range for the comparators. Six of the patients (40%) scored more than two standard deviations below the mean [Very Poor] in at least two of the cognitive tests, a threshold for cognitive impairment in many ITU and POCD studies.

Finally, the patients' mean estimated premorbid FSIQ was 108 (0.53 standard deviations above the population mean). This was also half a standard deviation above the Cogstate composite z-score, effectively representing an estimated drop of 7.5 IQ points from their baseline (Student t test  $p=0.017$ ).



## 4. Discussion

This clinical study found that two years after a severe burns injury, patients demonstrated a significant deficit in cognitive function from baseline. Patients also reported an increase in depressive and post-traumatic stress symptoms with an associated reduction in Quality of Life.

### 4.1. Quality of Life

Cognitive impairment after a severe burn injury, as well as its effect on Quality of Life were issues brought to us by our patients and were the primary motivation for this study. We have demonstrated that both cognition and cognitive QoL are worse after a severe burn. As such, the finding of a lack of correlation between these two outcomes was quite unexpected. It is readily understandable that the iADL and EQ5D might not correlate with cognition. These tools measure specific outcomes (e.g.: mobility, self-care, pain/discomfort, mental health) but neither tool includes domains that inquire about cognitive function[69]. Even in populations with severe cognitive impairment, a lack of correlation between cognitive function and EQ5D score has been demonstrated[70].

However, despite the Neuro-QoL SF v2 specifically targeting cognitive symptoms, it also demonstrated a lack of correlation with cognitive function. A disconnect between actual and perceived impairment has been noted previously in the literature. Newman et al. found that self-reported post-operative cognitive dysfunction (POCD) was correlated with depressive symptoms but not with objective impairment[71]. Our results mirror this finding with a strong correlation between perceived cognitive function (Neuro-QoL) and depressive symptoms (BDI-II), but not between perceived cognitive function and cognitive ability (Cogstate z-score) or cognitive decline (the discrepancy between premorbid FSIQ z-score and Cogstate z-score).

We speculate that this indicates a measurement issue rather than proof of the null hypothesis. Quality of Life is a human construct and has a particularly nebulous quality. Common HRQL tools seek to define QoL through impact on daily function. We have demonstrated a reduction in actual cognition. The basic abilities that were measured are employed ubiquitously on a daily basis. A priori, there is a reduction in Quality of Life, even if the magnitude is not measurable with the tools used.

However, it would appear that the Neuro-QoL SF v2 was poorly sensitive for cognitive QoL in this cohort and had low discrimination from depressive symptoms. Patients with high levels of depressive symptoms may have an accentuated perception of cognitive impairment when it was present, or potentially false perceptions of impairment in its absence. Irrespective of the cause, the discrepancy between actual and perceived cognitive impairment was overshadowed by the impact of depression in this scenario. Secondly, the Neuro-QoL SF v2 has a limited scope for the impact of cognition on QoL. There were no domains targeting the social and emotional aspects of cognitive impairment, which may have been salient features for the burns cohort.

### 4.2. Mental Health

Our results concur with Logsetty et al., revealing a significant rise in depressive and post-traumatic stress symptoms compared to a comparison group, alongside a non-significant rise in anxiety symptoms[72]. High levels of psychological symptoms are found commonly in burns cohorts, though

this may in part represent low pre-injury mental health. This has been reported in several large studies investigating long-term psychological symptoms after burns injuries[73–75], including BICU populations[76]. High depression and traumatic stress scores correlate strongly with poor QoL.

Participants reported high levels of irritation (PHQ-9, GAD-7, BDI II), agitation (BDI II) and restlessness (GAD-7, PHQ-9). They also reported disturbances in sleep pattern (PHQ 9, BDI II, and TSQ). However, these questions do not differentiate between hyper- and hypo-somnolence. Changes in sleep pattern may be directly attributable to pain and discomfort, rather than their psychological state per se. That said, pain can also affect psychological state and consequently affect sleep indirectly as well. This is difficult to discern, but it is likely that psychological symptoms from burns are over-represented due to a complex relationship with somatic symptoms; further research to explore this is indicated. Sleep disturbance is also pertinent to cognitive impairment as a recognised modulator of neuroplasticity and as a factor that is intrinsically associated with BICU admissions[77].

Although a statistically significant difference was found between the groups in the psychosis tool, the absolute scores were very low and the only domains that accrued points were those of depression and cognitive impairment. As such, the results were not clinically significant. No clinical evidence of psychosis or neurosis was noted in any of the participants throughout the follow up period.

#### 4.3. Cognitive function

This study found evidence of a significant and broad cognitive deficit in the BICU patients when compared to the comparator group and to population data. We did not find any evidence of a domain specific pattern of cognitive dysfunction, thus suggesting a more global deficit spanning working memory, delayed recall, attention, executive function and language. Cognitive impairment after ICU admissions and major surgery is well described in the literature, with deficits in executive function and memory being common findings[10,15–17,78,79]. However, this is the first study to report cognitive impairment in severe burns patients who have been admitted to BICU. Furthermore, the cohort was young and the level of comorbidity was extremely low, demonstrating that the underlying mechanisms of ITU LTCl can occur in absence of premorbid cerebral disease.

The patient group performed worse than the comparators across the cognitive tests. This supports our hypothesis. However, it should be noted that due to the difference in education levels and estimated premorbid FSIQ, the statistical validity of the comparison group is called into question. I.e. one might expect a comparison group to outperform a patient group with a lower estimated premorbid IQ even in the absence of a burns injury.

If one looks beyond the comparison group, population data can be used to assess the burns patients for evidence of cognitive impairment. The estimated premorbid IQ (108) of the patient group was half a standard deviation above the population mean (100) and on the upper border of the Average category (90-110). Indeed, none of the individual patients were scored below the Average category. As such, the null hypothesis would predict that after a severe burn, patients' cognition should still be half a standard deviation above the mean. This was not reflected by the composite z-scores, which dropped by approximately 7.5 IQ points from the baseline.

Neither the ICD 10 nor DSM-V provide a definition for POCD. The commonly quoted 1995 consensus definition is in specific reference to cardiac surgery, not BICU patients[80,81]. It also specifies that a comparison to baseline performance is essential, which is methodologically implausible for accidental injuries. Due to a lack of definition, the composition of cognitive batteries used in the literature is broad and the statistical limitations of what constitutes abnormal is not standardised[81].

We used a restrictive a priori definition of cognitive impairment, as this had not been determined prior to data collection. Upon reviewing methods described in the literature, we determined that any patient scoring two standard deviations below the mean in at least two tests was the most selective definition that could be applied to our data. This allowed inclusion of all of our data, as the cognitive performance category 'Very Poor' represents an IQ of less than 70 (two standard deviations below 100). The Cogstate®-battery included population z-scores and standard deviations for comparison. According to this definition, six patients had cognitive impairment (40%) at a median interval of 2.7 years post BICU.

The pooled cognitive results for the patient group were of a parametric distribution, which reflects population data. As such, we would expect 2.5% of the test results to be more than two SDs below the mean (6.4 of 255 tests). The patients scored almost four times as many results in the Very Poor performance range than expected, which provides compelling evidence for cognitive impairment after a severe burns injury.

A significant correlation was found between cognitive impairment and our chosen marker of burns severity (rBaux score). However, age is a substantial constituent of the scoring system and is known to correlate negatively with cognitive function. When re-tested with the age element removed from the score there was no correlation between cognitive function and burns severity. This reflects the wider literature, as many papers that have reported evidence of POCD have not found a significant correlation with markers of illness severity such as the APACHE II score [66,82]. Two patients suffered transient loss of consciousness as part of the injury. This was too low to test statistically, but it was noted that they were both in the lowest performing quartile for drop in IQ.

#### 4.4. Limitations and biases

Recruitment was adversely affected by attrition bias. Of the 40 eligible patients, 12 were not contactable and 9 declined to participate in the study. Most patients did not provide a rationale for non-participation but those recorded included: complex community care needs, mental health issues, difficulty with planning, claustrophobia and social anxiety (facial burns). Fewer than half of the eligible patients were able to participate in this study. Patients with significant mental health problems and/or known drug and alcohol misuse issues were excluded from this trial, and those with the most severe cognitive impairment were least likely to attend. We may have recruited a higher-performing subgroup with consequent under-reporting of LTCl incidence and severity. Furthermore, both the patient and the comparator groups had higher than average baseline estimated FSIQs with a significant discrepancy between the two. This calls into question the validity of the comparison and it was necessary to support the hypothesis with population data.

The BAI and BDI-II contained multiple somatic symptoms of anxiety and depression that are common sequelae of burn injuries, e.g. 'tingling in the fingers'. This resulted in uncertainty amongst the patients and possible over-reporting of psychological symptoms. Patients were instructed to respond to this

questionnaire with the understanding that each item was designed to assess the psychological and physical symptoms of anxiety. Similarly, the Neuro-QoL SF v2 appeared to have low discrimination from depression in this cohort, and this requires further investigation

## 5. Conclusions

In summary, patients who experienced an admission to BICU with a severe burns injury demonstrated a reduction in cognitive function when compared to both the comparator groups and to population data. Affected domains included learning and memory, attention and processing speed, executive function and language when tested against an age and sex-matched comparator group. Burns patients also have a reduction in Quality of Life, which was strongly associated with elevated symptoms of depression and post-traumatic stress. This degree of cognitive impairment reflects that of general ITU cohorts, but in a younger and low-comorbidity cohort. No correlation was found between Quality of Life and cognitive impairment. This may be due to the QoL tools used, or the high levels of depressive symptoms affecting patient perception of cognition. Further large, prospective clinical studies are required to confirm these findings.

## 6. Recommendations for future research

More research into long-term cognitive deficits after severe burns injury is needed to validate these cognitive findings in other populations, as well as to profile any changes with time after injury. The use of more sophisticated and ecologically valid cognitive assessments may also be useful in this clinical group to increase sensitivity and specificity across memory and executive function in order to capture cognitive impairments in everyday function. More detailed assessment would also inform our clinical and theoretical understanding of the neurocognitive impact of burns and the development of targeted cognitive rehabilitation interventions. Furthermore, validation of psychology questionnaires in burns patients is indicated to investigate and account for the large crossover of somatic symptoms in this population.

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