Evaluating pain in survivors of critical illness: the correlation between the EQ-5D-5L and the Brief Pain Inventory

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ABSTRACT

Introduction Pain is a common and debilitating symptom in survivors of critical illness. The 'Core Outcome Set for Survivors of Acute Respiratory Failure' proposes that the pain and discomfort question of the EuroQol 5 Dimension 5 Level (EQ-5D-5L) could be used to assess pain in this group, however, it was recognised that further research is required to evaluate how this single question compares to other more detailed pain tools. This study aims to evaluate the relationship between the pain and discomfort question of the EQ-5D-5L and the Brief Pain Inventory (BPI) in survivors of critical illness.

Methods This study retrospectively analysed paired EQ-5D-5L and BPI data extracted from a prospective, multicentre study evaluating the impact of a critical care recovery programme. 172 patients who received a complex recovery intervention and 108 patients who did not receive this intervention were included. Data were available for the intervention cohort at multiple time points, namely, baseline, 3 months and 12 months. While, data were available for the usual care cohort at a single time point (12 months). We assessed the correlation between the pain and discomfort question of the EQ-5D-5L and two separate components of the BPI: severity of pain and pain interference.

Results Correlation coefficients comparing the pain and discomfort question of the EQ-5D-5L and the BPI pain severity score ranged between 0.73 (95% CI 0.63 to 0.80) and 0.80 (95% CI 0.72 to 0.86). Correlation coefficients comparing the pain and discomfort question of the EQ-5D-5L and the BPI pain interference score ranged between 0.71 (95% CI 0.62 to 0.79) and 0.83 (95% CI 0.76 to 0.88) across the various time points.

Conclusions The pain and discomfort question of the EQ-5D-5L correlates moderately well with a more detailed pain tool and may help to streamline assessments in survivorship studies. More in-depth tools may be of use where pain is the primary study outcome or a patient-reported concern.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The 'Core Outcome Set for Survivors of Acute Respiratory Failure' proposed that the single pain and discomfort question of the EQ-5D-5L could be used to assess pain.

WHAT THIS STUDY ADDS

⇒ This study found that responses to this single question correlated well with both the pain severity and pain interference components of the Brief Pain Inventory, a more detailed tool for evaluating pain.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The single pain and discomfort question of the EQ-5D-5L may help streamline the assessment of pain in critical illness survivorship studies, however, more detailed tools may be required where pain is the primary study outcome, or a patient-reported concern.

INTRODUCTION

Core outcomes sets (COSs) are an agreed, standardised collection of outcomes which should be measured and reported in trials for a specific clinical area.[1] COSs have been developed in order to facilitate data synthesis with the aim of providing answers to complex questions across multiple studies.[2] COSs have been established in a variety of different areas within the critical care field including recovery and long-term outcomes in survivors of acute respiratory failure (ARF).[3] This COS for survivors of ARF was developed by a modified Delphi consensus process, and identified the Hospital Anxiety and Depression Scale, the Impact of Events Scale-Revised, the EuroQol 5 Dimension 5 Level (EQ-5D-5L) and the 36-item Short Form Health Survey (SF-36) as core outcome measures. During the development process, the assessment of pain was highlighted a key area of importance.[4] While the SF-36 also assesses pain as one of its eight domains, the pain and discomfort question of the EQ-5D-5L was selected for inclusion in this COS to evaluate pain.[3]

Up to 66% of those who survive critical illness will develop chronic pain[5] resulting in wide-ranging functional impact, affecting quality of life, activities of daily living and return to work.[6 7] While the pain and

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discomfort question of the EQ-5D-5L achieved consensus for inclusion as a core outcome measure for pain, it was recognised that the evaluation of pain across the survivorship trajectory is complex and requires further investigation.[3] The properties of this tool have previously been evaluated in patients with chronic pain of other aetiologies validating its internal and external validity for these particular cohorts.[8 9] However, further research is required to specifically assess how the EQ-5D-5L compares to other more detailed, and consequently more time-consuming, measures of pain in survivors of critical illness.[3]

Therefore, using data obtained from a multicentre, prospective, cohort study, we aimed to assess the relationship between the pain and discomfort question in the EQ-5D-5L and the Brief Pain Inventory (BPI) (Short Form) in survivors of critical illness.

METHODS
Study setting
This study is a retrospective analysis of data collected via a multicentre prospective cohort study of patients followed up after discharge from intensive care. Patients in the intervention cohort attended the Intensive care Syndrome: Promoting Independence and Return to Employment (InS:PIRE) programme, a complex integrated health and social care intervention, delivered weekly for 5 weeks, with return visits at 3 and 12 months.[10 11] Patients receive structured reviews from an Intensive Care Unit (ICU) doctor and nurse, a pharmacist and a physiotherapist.[12 13] Clinical neuropsychology input, peer support and input from local community organisations are embedded into the sessions. Patients were recruited between 2016 and 2020 from nine hospitals in Scotland.[10]

Patient and public involvement
Patients who had survived critical illness and their family members were integral to the development of the InS:PIRE programme. They were involved in designing the format of the intervention and the subsequent scaling up of the service. Service user consultation has been fundamental to research design, including prioritisation of the research question, choice of outcome measures and methods of recruitment.[14]

Study design
In this study, we report on data collected from two distinct cohorts: the intervention cohort who attended the InS:PIRE programme and the usual care cohort from the same study, who had been admitted to ICU but had not received the intervention. Full details of these cohorts have been published elsewhere.[10] For the intervention cohort, paired EQ-5D-5L and BPI data were collected at multiple timepoints during the first year of recovery from critical care: baseline data were collected prior to

commencing the InS:PIRE intervention between 4 and 12 weeks following discharge from hospital; 3 months and 12 months data were also collected at each of the return appointments. Data were collected for the usual care cohort at a single time point between 10 months and 16 months following hospital discharge (figure 1).

Inclusion criteria
Patients receiving level three care[15] (multiple organ support and/or invasive respiratory support), more than 7 days of level 2 care[15] (single organ support or postoperative patients requiring critical care support) were eligible for enrolment in the InS:PIRE programme. In addition, any patient deemed by clinicians to be at high risk of post intensive care syndrome, taking into account known risk factors such as mental health comorbidity, severity of illness, negative ICU experience and delirium,[16] were also eligible. The following groups of patients were excluded: any patient who was terminally ill; any patient who had suffered a traumatic brain injury; patients who remained an in-patient under psychiatric services and patients currently incarcerated in prison.

Outcomes
The BPI is a tool used to assess the severity of pain and its interference with daily functioning.[17] It also provides information regarding the location of pain, medications used and the effect of these medications. It consists of nine questions with the last question, examining pain interference, separated into seven different domains.[17] The format of the questions is a combination of free text, shading affected areas on a diagram and numeric rating scales from 0 to 10, where 0 represents no pain and 10 represents worst pain. The BPI was initially developed to evaluate pain in patients with malignancy, however, it has since been validated and used to evaluate chronic pain of other aetiologies and also for acute pain in the postsurgical population.[18–20]

In the absence of any 'gold-standard' tool for the assessment of pain in survivors of critical illness, the BPI was selected for use as it is frequently employed to assess pain in this population.[21] It also received positive feedback from patient and public involvement when it was piloted in a previous study conducted by this research group.[5 14]

The EQ-5D-5L is a tool which assesses health-related quality of life (HRQoL) via five domains: mobility; self-care; usual activities; pain and discomfort and anxiety and depression. The patient is asked to assess each domain according to five levels, which are described. The patient also rates their overall health from 0 to 100 on a Visual Analogue Scale.[22] The core outcome measures for clinical research in ARF survivors study recommended that the EQ-5D-5L should be used both as a tool to assess satisfaction with life and personal enjoyment and that the specific pain and discomfort question should be used to measure pain.[3] In the EQ-5D-5L single pain and discomfort question, patients select the response which best
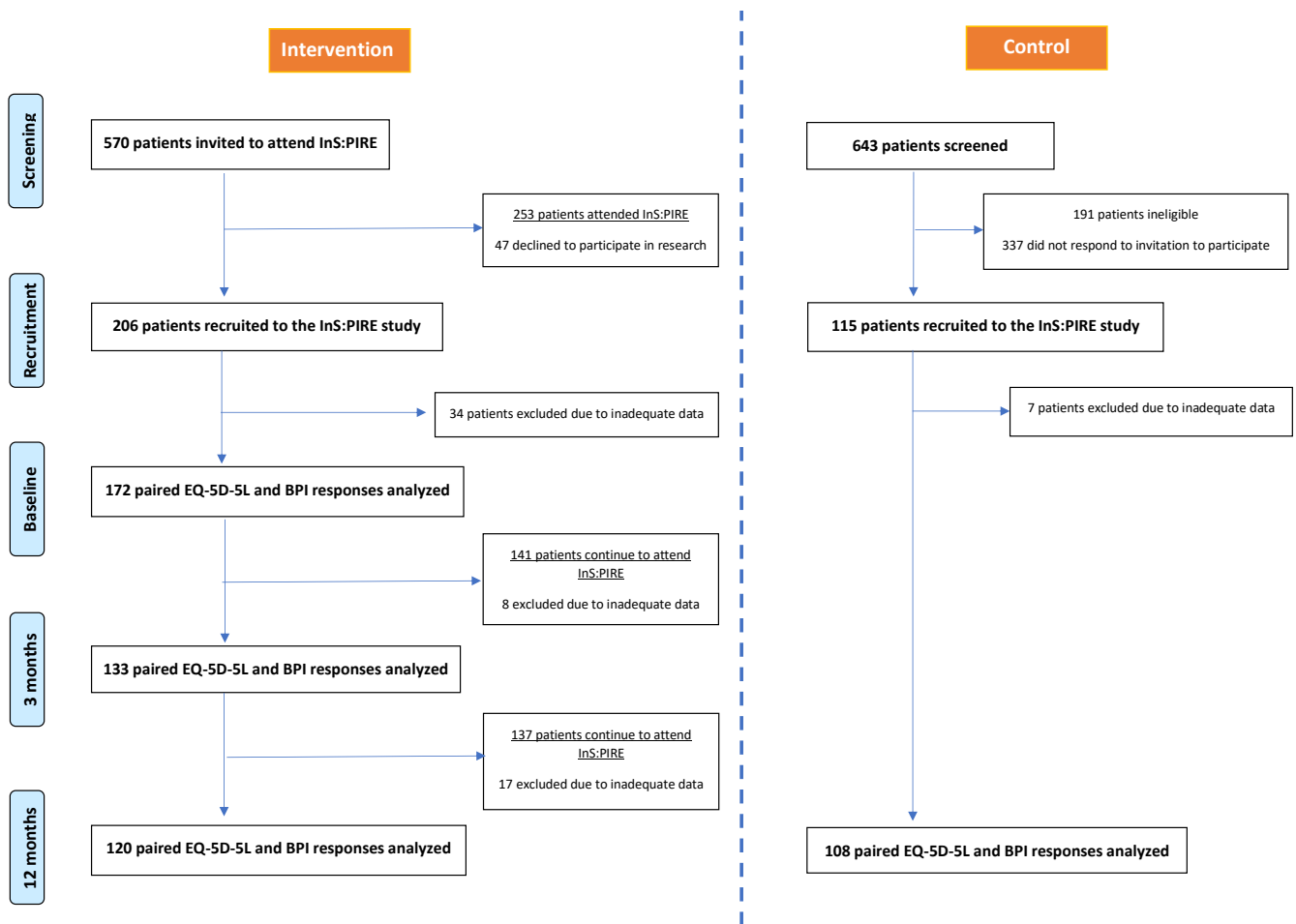
Figure 1 Study participants flow diagram. BPI, Brief Pain Inventory; EQ-5D-5L, EuroQol 5 Dimension 5 Level; InS:PIRE, Intensive care Syndrome: Promoting Independence and Return to Employment.

describes their pain today from the following list: no pain or discomfort; slight pain or discomfort; moderate pain or discomfort; severe pain or discomfort; extreme pain or discomfort. For the purposes of this study the numeric values 1–5 were allocated to the responses respectively (where 1 represents no pain and 5 represents extreme pain).

Data analysis

The developers of the BPI recommend that pain severity is scored as a mean of the question set relating to pain severity (Q3–6), which asks the patient to rate from 0 to 10 their worst pain, least pain, average pain and pain right now.[23] Similarly, it is recommended pain interference is scored as a mean of the question set relating to pain interference (Q9a–g). The patient is asked to rate from 0 to 10 how pain impacts the following domains: general activity, mood; walking ability; normal work (including both out of the house and housework); relations with other people; sleep; enjoyment of life.[23]

To ensure a comprehensive analysis, the patient must have recorded a response to all of the following to be included in this study: the pain and discomfort question

of the EQ-5D-5L; the pain on average question of the BPI; over 50% of the question set in the BPI regarding pain interference. This is in keeping with the developer's recommendations that if a patient responds to less than 50% of questions relating to pain interference they should be excluded, however, if greater than 50% of this question set were completed then a mean was calculated using only the questions answered.[23]

Question 1 of the BPI is a screening question, which asks if the patient has any pain. If the patient answered no to this question and any of the other questions were unanswered then they were assumed to have also answered 0 to all of the unanswered questions. Other than this, no data were imputed.

The patient's response to the pain and discomfort question of the EQ-5D-5L was assessed for correlation with two separate components of the BPI. First, it was compared with the mean of the patient's responses to the BPI question set relating to pain severity. Second, the response to the pain and discomfort question of the EQ-5D-5L was compared with the mean of the patient's responses to the BPI question set relating to pain interference. This approach to evaluation was chosen to account for both

the severity of pain and pain interference. These are the two major themes of the BPI and are related to quality of life which is the major theme of the EQ-5D-5L.[24] Where there was missing data, the means were calculated using only the questions answered.

The Pearson correlation method was used to generate partial correlation coefficients comparing the pain and discomfort question of the EQ-5D-5L with each of the pain severity score and the pain interference score. All partial correlation coefficients were adjusted for age and the presence of pre-existing chronic pain. Correlation coefficients quantify the strength and direction of linear relationships between two variables.[25] They are expressed as an r value between −1 and 1, where −1 represents a perfect negative linear relationship, 0 represents no discernible relationship and 1 is a perfect positive linear relationship. Interpretation varies within the literature, however, r values above 0.7 are generally accepted to be representative of a strong positive relationship and r values between 0.4 and 0.69 are accepted to be representative of a moderately positive relationship.[25]

In order to determine the discriminatory power of the EQ-5D-5L to detect meaningful change in pain severity, permutation testing was used to calculate the difference in the median BPI pain severity scores associated with each incremental increase in the response to the EQ-5D-5L pain and discomfort question. The Dunn pairwise test (Holm Corrected to account for multiple testing) was used to calculate the pairwise comparisons associated with each increment.

Subgroup analyses

Two subgroup analyses were performed. The first evaluated the correlation between the EQ-5D-5L and the BPI in the cohort of patients who had pre-existing chronic pain prior to ICU admission (further details and results available in online supplemental file 1). The second evaluated these correlations in the cohort of patients who had pre-existing mental health diagnoses prior to ICU admission (further details and results available in online supplemental file 2).

RESULTS
Baseline demographics: intervention cohort

A total of 570 patients were invited to attend the InS:PIRE programme, with 253 of those attending. A total of 206 of those patients consented to participate in research and were recruited to the intervention cohort. A total of 172 patients completed both questionnaires with sufficient detail to be included in this analysis at baseline. At 3 months, 141 patients attended InS:PIRE and 133 of these patients were eligible for this analysis. At 12 months, 137 patients attended InS:PIRE, with 120 patients eligible for analysis (figure 1).

In the intervention cohort 98 (57%) were male. The median age was 58.4 years (IQR 50.6–66.2). The median ICU length of stay (LOS) was 10 days (IQR 6–17) and the

median APACHE II score was 20 (IQR 15–25). Table 1 describes the full demographics of the intervention cohort.

Baseline demographics: usual care cohort

In the usual care cohort, 643 patients were screened and 191 of those found to be ineligible. A total of 452 patients were therefore sent an invitation to participate. A total of 115 patients consented to participate and were recruited to the usual care cohort with data collected at 12 months only. A total of 108 of these patients had completed the questionnaires with sufficient detail to be eligible for inclusion in this secondary analysis (figure 1).

In the usual care cohort 61 (56.5%) were male. The median age was 63.8 years (IQR 49.7–71.4). The median ICU LOS was 5 days (IQR 3–10) and the median APACHE II score was 19 (14.0–24.3). Table 1 describes the full demographics of the usual care cohort.

Pain: intervention cohort

For the intervention cohort at baseline, 3 months and 12 months, the mean responses to the questions assessing severity of pain in the BPI were 3.79/10 (n=172), 3.78/10 (n=133) and 3.59/10 (n=120) respectively. In relation to pain interference measured via the BPI, the mean responses at baseline, 3 months and 12 months were 4.28/10, 3.99/10 and 3.64/10 respectively.

Pain: usual care cohort

At 12 months the mean response for the severity of pain question set was 3.41/10 (n=108) in the usual care cohort. In relation to pain interference measured via the BPI, the mean response was 3.61/10.

Correlation between EQ-5D-5L and BPI outcome: severity of pain

In the intervention cohort at baseline, 3 months and 12 months the partial correlation coefficients comparing severity of pain via the BPI with the pain and discomfort question of the EQ-5D-5L were 0.73 (95% CI 0.65 to 0.79), 0.75 (95% CI 0.66 to 0.82) and 0.73 (95% CI 0.63 to 0.80), respectively. For the usual care cohort at 12 months, the correlation coefficient was 0.80 (95% CI 0.72 to 0.86). Correlation coefficients are displayed in table 2. Figure 2 displays the box charts detailing the paired EQ-5D-5L pain and discomfort responses with the BPI severity of pain question set responses at the various time points.

The pairwise comparisons between the responses to the BPI severity of pain question set demonstrated a statistically significant change associated with most increments of the BPI. The pairwise comparisons are detailed in table 3. The number of patients reporting their pain score at each increment of the pain and discomfort question of the EQ-5D-5L is displayed in online supplemental file 3.

Table 1 Demographics of the intervention and usual care cohorts

Characteristic	Intervention cohort (n=172)	Usual care cohort (n=108)	P value
Age	58.4 (50.6–66.2)	63.8 (49.7–71.4)	0.02
Sex (n, %)			0.11
Male	98 (57.0)	61 (56.5)	
Female	74 (43.0)	44 (40.7)	
Unknown	0	3	
SIMD quintile* (n, %)			0.03
1	73 (42.4)	31 (28.7)	
2	37 (21.5)	25 (23.1)	
3	27 (15.7)	12 (11.1)	
4	20 (11.5)	17 (15.7)	
5	15 (8.6)	20 (18.5)	
Unknown	0	3	
Charlson Comorbidity Index†	1 (0–2)	1 (0–2)	0.28
Pre-existing mental health diagnosis (n, %)	55 (32.0)	26 (24.1)	0.20
Pre-existing chronic pain diagnosis (n, %)	39 (22.7)	23 (21.3)	0.90
ICU length of stay (days)	10 (6–17)	5 (3–10)	<0.01
Hospital length of stay (days)	30 (16–50)	19 (12–36)	<0.01
Apache II score‡	20 (15–25)	19 (14–24.3)	0.30
Surgery at admission or within first week of ICU (n,%)	55 (32.0)	47 (43.5)	<0.01
Advanced respiratory support (days)	6 (3–13)	4 (2–9)	0.01
Cardiovascular support (days)	3 (1–5)	2 (1–4)	0.01
Renal replacement therapy (days)	0 (0–0)	0 (0–0)	0.3

Median (IQR) unless otherwise stated.
*SIMD is the Scottish government's standard approach to identifying deprivation. It evaluates deprivation across seven domains: income, employment, education, health, access to services, crime and housing. 1 represents the most deprived and 5 represents the least deprived.
†Charlson Comorbidity Index, unadjusted for age.
‡Acute Physiology and Chronic Health Evaluation II Score.
ICU, Intensive Care Unit; SIMD, Scottish Index of Multiple Deprivation.

Correlation between EQ-5D-5L and BPI outcome: pain interference

In the intervention cohort at baseline, 3 months and 12 months, the partial correlation coefficients exploring pain interference via the BPI with the pain and discomfort question of the EQ-5D-5L were 0.72 (95% CI 0.63 to 0.78), 0.71 (95% CI 0.62 to 0.79) and 0.73 (95% CI 0.63 to 0.80), respectively. For the usual care cohort at 12

Table 2 Unadjusted correlation coefficients comparing EQ-5D-5L and BPI responses

Correlation	Correlation coefficient	95% CI	P value
EQ-5D-5L vs BPI pain severity score			
Intervention cohort baseline	0.73	0.65 to 0.79	<0.01
Intervention cohort 3 months	0.75	0.66 to 0.82	<0.01
Intervention cohort 12 months	0.73	0.63 to 0.80	<0.01
Usual care cohort 12 months	0.8	0.72 to 0.86	<0.01
EQ-5D-5l vs BPI pain interference score			
Intervention cohort baseline	0.72	0.63 to 0.78	<0.01
Intervention cohort 3 months	0.71	0.62 to 0.79	<0.01
Intervention cohort 12 months	0.73	0.63 to 0.80	<0.01
Usual care cohort 12 months	0.83	0.76 to 0.88	<0.01

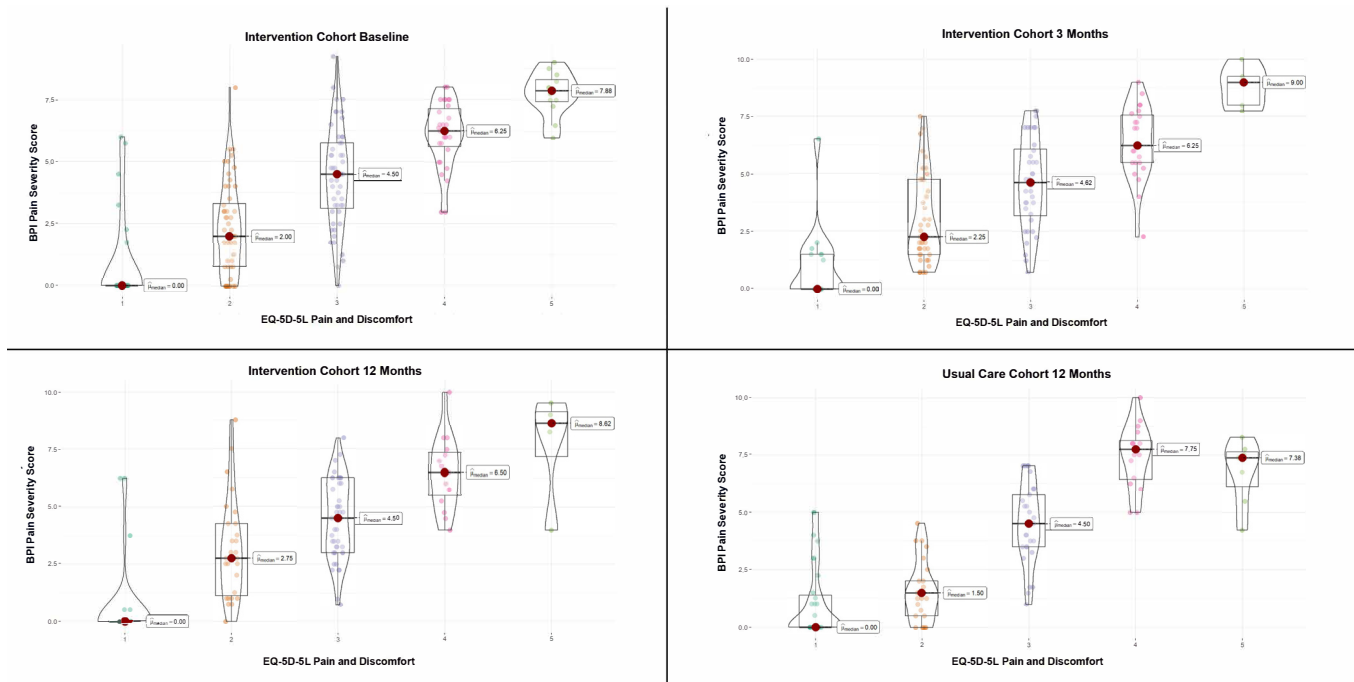BPI, Brief Pain Inventory; EQ-5D-5L, EuroQol 5 Dimension 5 Level.

Figure 2 Paired BPI pain severity scores with EQ-5D-5L responses. Box plots displaying paired BPI pain severity question set responses with EQ-5D-5L pain and discomfort question responses across the intervention cohort at baseline, 3 months and 12 months and the usual care cohort at 12 months. BPI, Brief Pain Inventory; EQ-5D-5L, EuroQol 5 Dimension 5 Level.

months, the correlation coefficient was 0.83 (95% CI 0.76 to 0.88). Correlation coefficients are displayed in table 2. Figure 3 displays the box charts detailing the paired EQ-5D-5L pain and discomfort responses with the BPI pain interference question set responses at the various time points.

Subgroup analyses

The subgroup analyses for the cohorts of patients with pre-existing chronic pain and pre-existing mental health diagnoses consistently demonstrated significant correlations between the EQ-5D-5L pain and discomfort question and each of the BPI pain severity and pain interference scores. Results can be found in online supplemental file 1 and online supplemental file 2, respectively.

DISCUSSION

This study aimed to establish the relationship between the pain and discomfort question of the EQ-5D-5L and components of the BPI in survivors of critical illness. The results demonstrate an important correlation. Of note, this relationship is true both for pain severity and pain interference and was present in those who had, and had not received an ICU follow-up intervention. The results of this study suggest the single question of the EQ-5D-5L may be a useful measurement of pain in survivors of critical illness and could reduce patient and assessor data collection burden.

Consistent with previous research, this study highlights that pain is a prominent issue affecting survivors of critical

illness across the recovery trajectory.[26] At present, there are limited data in this field, with little understanding of potential mechanisms and risk factors for the development of pain in survivors of critical illness. However, given the worrying use of opiates in survivors of critical care, it is clear that this issue has a significant impact on individual recovery and society more widely.[27] Further research is urgently required to establish the mechanisms and identify potential targets to reduce the burden of pain in survivors of critical illness. Of interest, in this study over the first year of recovery from critical illness, while there may be little change in average pain severity scores, there may be an improvement in pain interference. This attests to the difficulties in managing chronic pain but suggests that it may be possible to minimise the interference of pain.

In this multicentre analysis, the EQ-5D-5L pain and discomfort question appears to be a useful indicator of pain problems in survivors of critical illness. It consistently demonstrated at least a moderate correlation with the more detailed BPI, taking into account the confidence intervals and following adjustment for age and the presence of pre-existing chronic pain. This correlation was also demonstrated in subgroup analyses for cohorts of patients with pre-existing chronic pain and mental health diagnoses. However, in the absence of a 'gold-standard' tool for assessing pain in survivors of critical illness this correlation alone may not substantiate that the EQ-5D-5L is an appropriate tool for assessing pain in this group. Other HRQoL instruments also measure pain, such as the SF-36. There may be differences in

Table 3 Change in BPI severity score associated with each increment of EQ-5D-5L

Incremental increase in response to EQ-5D-5L pain and discomfort question	Associated change in median response to BPI pain severity score	Adjusted p value
Baseline intervention		
Increment 1–2	2 (1.75–2.88)	0.06
Increment 2–3	**2.38 (1.25–3.13)**	**<0.01**
Increment 3–4	**1.75 (1.00–2.75)**	**0.01**
Increment 4–5	1.63 (0.88–2.25)	0.1
Intervention 3 months		
Increment 1–2	**2 (1.38–3.00)**	**0.01**
Increment 2–3	**2.5 (1.25–3.63)**	**0.01**
Increment 3–4	**1.88 (0.50–3.25)**	**0.04**
Increment 4–5	2.25 (0.75–3.86)	0.19
Intervention 12 months		
Increment 1–2	**2.75 (1.25–3.75)**	**0.01**
Increment 2–3	1.63 (0.25–2.75)	0.14
Increment 3–4	2 (0.75–3.50)	0.07
Increment 4–5	2.13 (−2.75 to 3.63)	0.66
Usual care cohort 12 months		
Increment 1–2	1.25 (0.25–1.88)	0.49
Increment 2–3	**3.00 (2.13–4.00)**	**<0.01**
Increment 3–4	**3.25 (1.88–4.25)**	**0.02**
Increment 4–5	−0.50 (−2.50 to 0.88)	0.71

Change in median BPI responses associated with incremental change in EQ-5D-5L response with pairwise comparisons. Statistically significant changes in median responses are highlighted in bold to demonstrate the discriminatory power of the EQ-5D-5L in detecting differences in pain severity.
BPI, Brief Pain Inventory; EQ-5D-5L, EuroQol 5 Dimension 5 Level.

performance between these tools, however, this was not evaluated in this study as the COS specifically suggested the use of the single pain and discomfort question of the EQ-5D-5L for evaluating pain in survivors of ARF.

The pairwise comparisons evaluating the change in BPI pain severity scores associated with each increment of the EQ-5D-5L, suggests that the increments of the EQ-5D-5L can discriminate between pain severity. The clustering of significant results at the lower end of the pain severity scale is likely related to larger sample sizes in these groups.

Previous research has demonstrated that the EQ-5D-5L can detect clinically meaningful change in pain conditions,[28] which makes it an ideal component of an outcome measurement set. However, the EQ-5D-5L does lack details about the type and location of pain which the patient is suffering. In contrast the BPI provides detailed data about the type of pain and current treatment strategies (ie, medication management).[29] We propose that the pain and discomfort question of the EQ-5D-5L could streamline assessments in survivorship studies where pain is a secondary outcome measure. If pain is the primary

outcome or a patient-reported concern, however, it may be more appropriate to combine the pain and discomfort question of the EQ-5D-5L with the use of a more detailed tool such as the BPI, to ascertain further information about the location of pain, response to analgesia and to aid future care planning.

The strengths of this study are that we have reported on over 500 individual paired data sets from a multicentre cohort. Results include patients who have and have not received an intervention following ICU discharge, with diverse baseline characteristics, across three separate time points. Recruitment, however, was not international and, as such, external validity is limited to survivors in Scotland.

However, our analysis does have limitations, for example, data were only available at multiple time points for one of the two cohorts. Moreover, we have only examined one pain tool in relation to the EQ-5D-5L. Multiple pain assessment tools are available, however, within the context of delivering a complex intervention and following feasibility work, we were only able to collect one additional tool reliably. The BPI was chosen as it did not require an in-person assessment from a member of staff and could be independently completed by patients—an important concept which has been raised in previous COS research.[3] Future research should examine the properties of other pain tools in the context of ICU recovery.

A further limitation of this study is that there may have been barriers to participation for patients experiencing more severe PICS symptoms. First, the procedure for study recruitment may have introduced bias towards patients who were well enough to attend the follow-up programme or respond to a postal questionnaire. It is therefore reasonable to presume that pain may have been less severe in the cohort of patients recruited to this study. Second, the inclusion criteria of this study were consistent with advice from the creators of the BPI that average scores can be calculated where patients have responded to 50% of the items making up the score. It is possible that this impacted the results of the study and also suggests that the tool is perhaps difficult for some patients to complete. Finally, previous research has highlighted that patients with lower mini mental state scores and patients with lower levels of literacy were likely to have incomplete values in the BPI or complete the questionnaire with errors.[30 31] Cognitive impairment is a well-recognised issue in survivors if critical illness and those with lower educational attainment are more likely to have signs and symptoms of PICS in the year following critical illness.[32 33] This may limit the utility of the BPI within this context. The single question assessing pain and discomfort in the EQ-5D-5L is inherently more simple and moreover this tool has been found to be acceptable for use by patients with cognitive impairment due to dementia.[34] Further research in relation to the use of the BPI in the critical care cohort is required.

A further limitation of this analysis is that some patients completed questionnaires via postal survey or
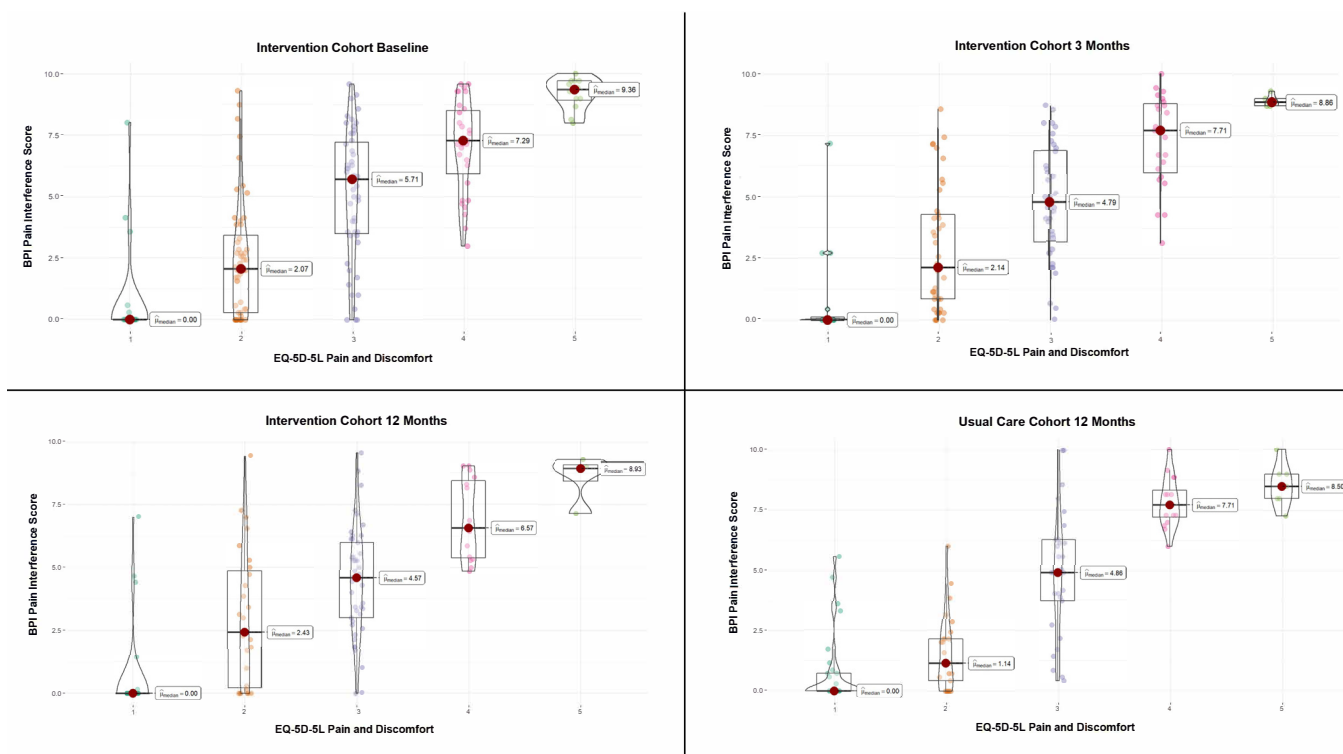
Figure 3 Paired BPI pain interference scores with EQ-5D-5L responses. Box plots displaying paired BPI pain interference question set responses with EQ-5D-5L pain and discomfort question responses across the intervention cohort at baseline, 3 months and 12 months and the usual care cohort at 12 months. BPI, Brief Pain Inventory; EQ-5D-5L, EuroQol 5 Dimension 5 Level.

phone consultation which may have posed a barrier to completing specific questionnaire items such as question 2 of the BPI which asks patients to shade painful areas on a diagram. Although question 2 of the BPI was not relevant to the analysis in this study, results may still have been impacted by the use of phone consultations. Unfortunately, data are not available for which patients completed the questionnaire via phone and as such it is not possible to determine to what extent results were affected by this. Moreover, sample size may have limited results in this study.

Finally, we have used data which were collected as part of an intervention. This intervention may have influenced how patients completed these tools. However, the purpose of this study was not to understand the impact of the intervention on pain, but instead understand how two distinct tools relate to one another. We recognise that the results of this analysis may have been influenced by this.

Conclusion

In conclusion, the EQ-5D-5L pain and discomfort question, which was proposed for inclusion in the COS for survivors of ARF to evaluate pain, appears to correlate well with an established, specific pain measurement tool in two different cohorts of critical care survivors. More research is required to fully understand the extent of pain in survivors of critical illness, alongside interventional research examining potential mechanisms and effective treatment strategies.

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Supplemental material

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SUPPLEMENTAL 1- SUBGROUP ANALYSIS OF PATIENTS WITH CHRONIC PAIN

Methods

A subgroup analysis was performed to calculate the correlation between the EQ-5D pain and
discomfort question and each of the BPI pain severity and pain interference scores for the cohort of
patients who had pre-existing chronic pain prior to ICU admission. As with the overall cohort analyses
the Pearson correlation method was used to calculate partial correlation coefficients. As all the
patients in this cohort had pre-existing chronic pain the correlation coefficients were adjusted for age
only.

Results

Baseline Demographics: Patients with Pre-existing Chronic Pain

In the Intervention cohort at baseline, 3 months and 12 months 39 (22.7%), 26 (19.5%) and 23
(19.2%) patients had a pre-existing chronic pain diagnosis, respectively. In the Usual Care cohort at
12 months 23 (21.3%) patients had a pre-existing chronic pain diagnosis.

Pain Scores: Patients with Pre-existing Chronic Pain

For the subgroup of patients with pre-existing chronic pain in the intervention cohort at baseline, 3
months and 12 months, the mean responses to the questions assessing severity of pain in the BPI were
5.07/10, 4.63/10 and 4.64/10, respectively. In relation to pain interference measured via the BPI, the
mean responses at baseline, 3 months and 12 months were 6.11/10, 4.55/10 and 4.72/10 respectively.

At 12 months the mean response for the severity of pain question set was 3.97/10 for the subgroup of
patients with pre-existing chronic pain in the usual care cohort. In relation to pain interference measured
via the BPI, the mean response was 4.91/10.

**Chronic Pain Subgroup Analysis of the Correlation Between EQ-5D and BPI Outcome: Pain
Severity**

For the subgroup of patients with pre-existing chronic pain prior to ICU admission in the intervention
cohort at baseline, 3 months and 12 months the partial correlation coefficients comparing the pain and
discomfort question of the EQ-5D with the BPI severity of pain score were 0.91 (CI 0.83- 0.95), 0.83
(CI 0.66- 0.92), and 0.85 (CI 0.68- 0.94), respectively. For the subgroup of patients with pre-existing
chronic pain prior to ICU admission in the usual care cohort at 12 months the partial correlation
coefficient was 0.72 (CI 0.44- 0.87). **Table 1** displays the correlation coefficients.

Correlation (Subgroup Analysis of Patients with Pre-existing Chronic Pain)	Correlation Coefficient	Confidence Interval	P Value
EQ-5D vs BPI pain severity score			
Intervention cohort baseline	0.91	0.83- 0.95	<0.01
Intervention cohort 3 months	0.83	0.66- 0.92	<0.01
Intervention cohort 12 months	0.85	0.68- 0.94	<0.01
Usual care cohort 12 months	0.72	0.44- 0.87	<0.01
EQ-5D vs BPI pain interference score			
Intervention cohort baseline	0.83	0.69- 0.91	<0.01
Intervention cohort 3 months	0.81	0.61- 0.91	<0.01
Intervention cohort 12 months	0.76	0.51- 0.89	<0.01
Usual care cohort 12 months	0.83	0.63- 0.92	<0.01

Table 1- Correlation coefficients comparing the EQ-5D pain and discomfort question and the BPI pain severity and pain interference scores for the subgroup of patients with pre-existing chronic pain prior to ICU admission

Chronic Pain Subgroup Analysis of the Correlation Between EQ-5D and BPI Outcome: Pain Interference

For the subgroup of patients with pre-existing chronic pain prior to ICU admission in the intervention cohort at baseline, 3 months and 12 months the correlation coefficients comparing the BPI pain interference score with the pain and discomfort question of the EQ-5D were 0.83 (CI 0.69- 0.91), 0.81 (CI 0.61- 0.91), and 0.76 (CI 0.51- 0.89), respectively. For the subgroup of patients with pre-existing chronic pain prior to ICU admission in the usual care cohort at 12 months the correlation coefficient was 0.83 (CI 0.63- 0.92). **Table 1** displays the correlation coefficients.

Supplemental material

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SUPPLEMENTAL 2- SUBGROUP ANALYSIS OF PATIENTS WITH MENTAL HEALTH DIAGNOSES

Methods

A subgroup analysis was performed to calculate the correlation between the EQ-5D pain and discomfort question and each of the BPI pain severity and pain interference scores for the cohort of patients who had pre-existing mental health diagnoses prior to ICU admission. As with the overall cohort analyses the Pearson correlation method was used to calculate partial correlation coefficients, adjusted for age and the presence of pre-existing chronic pain.

Results

Baseline Demographics: Patients with Pre-existing Mental Health Diagnoses

In the Intervention cohort at baseline, 3 months and 12 months 55 (32.0%), 40 (30.1%) and 36 (30.0%) patients had a pre-existing mental health diagnosis. In the Usual Care cohort at 12 months 26 (24.1%) patients had a pre-existing mental health diagnosis.

Pain Scores: Patients with Pre-existing Mental Health Diagnoses

For the subgroup of patients with pre-existing mental health diagnoses in the intervention cohort at baseline, 3 months and 12 months, the mean responses to the questions assessing severity of pain in the BPI were 4.60/10, 4.89/10 and 3.56/10, respectively. In relation to pain interference measured via the BPI, the mean responses at baseline, 3 months and 12 months were 5.34/10, 4.88/10 and 3.66/10 respectively.

At 12 months the mean response for the severity of pain question set was 5.53/10 for the subgroup of patients with pre-existing mental health diagnoses in the usual care cohort. In relation to pain interference measured via the BPI, the mean response was 6.80/10.

Mental Health Subgroup Analysis of the Correlation Between EQ-5D and BPI Outcome: Pain Severity

For the subgroup of patients with pre-existing mental health diagnoses prior to ICU admission in the intervention cohort at baseline, 3 months and 12 months the correlation coefficients comparing severity of pain via the BPI with the pain and discomfort question of the EQ-5D were 0.77 (CI 0.64-0.86), 0.84 (CI 0.72- 0.91), and 0.81 (CI 0.66- 0.90) respectively. For the subgroup of patients with pre-existing mental health diagnoses prior to ICU admission in the usual care cohort at 12 months the correlation coefficient was 0.69 (CI 0.42- 0.85). **Table 1** displays the correlation coefficients.

Correlation *(Subgroup analysis of patients with pre-existing mental health diagnoses)*	Correlation Coefficient	Confidence Interval	P Value
EQ-5D vs BPI pain severity score			
Intervention cohort baseline	0.77	0.64- 0.86	<0.01
Intervention cohort 3 months	0.84	0.72- 0.91	<0.01
Intervention cohort 12 months	0.81	0.66- 0.90	<0.01
Usual care cohort 12 months	0.69	0.42- 0.85	<0.01
EQ-5D vs BPI pain interference score			
Intervention cohort baseline	0.75	0.60- 0.85	<0.01
Intervention cohort 3 months	0.80	0.65- 0.89	<0.01
Intervention cohort 12 months	0.80	0.64- 0.89	<0.01
Usual care cohort 12 months	0.64	0.34- 0.82	<0.01

Table 1- Correlation coefficients comparing the EQ-5D pain and discomfort question and the BPI pain severity and pain interference scores for the subgroup with pre-existing mental health diagnoses

Mental Health Subgroup Analysis of the Correlation Between EQ-5D and BPI Outcome: Pain Interference

For the subgroup of patients with pre-existing mental health diagnoses prior to ICU admission in the intervention cohort at baseline, 3 months and 12 months the correlation coefficients comparing the BPI pain interference score with the pain and discomfort question of the EQ-5D were 0.75 (CI 0.60-0.85), 0.80 (CI 0.65- 0.89), and 0.80 (CI 0.64- 0.90) respectively. For the subgroup of patients with pre-existing mental health diagnoses prior to ICU admission in the usual care cohort at 12 months the correlation coefficient was 0.64 (CI 0.34- 0.82). **Table 1** displays the correlation coefficients.

SUPPLEMENTAL 3

Cohort	EQ-5D increment 1 (no. of patients)	EQ-5D increment 2 (no. of patients)	EQ-5D increment 3 (no. of patients)	EQ-5D increment 4 (no. of patients)	EQ-5D increment 5 (no. of patients)
Intervention Baseline	26	52	51	31	12
Intervention 3 Months	23	45	37	23	5
Intervention 12 Months	29	27	45	15	4
Usual Care 12 Months	31	25	29	16	7

The number of patients reporting their pain score at each increment of the pain and discomfort question of the EQ-5D