

*Title:* Could an integrated model of health and social care following critical illness reduce socio-economic disparities in outcomes? A Bayesian Analysis

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## **Abstract**

**Background:** There is limited evidence to understand what impact if any, recovery services might have for patients across the socio-economic spectrum following critical illness. We analysed data from a multi-centre critical care recovery programme to understand the impact of this programme across the socio-economic spectrum.

**Methods:** The setting for this pre-planned secondary analysis was a critical care rehabilitation programme- Intensive Care Syndrome: Promoting Independence and Return to Employment. Data were collected from five hospital sites running this programme. We utilised a Bayesian approach to analysis to explore any possible effect of the InS:PIRE intervention on HRQoL across the socio-economic gradient. A Bayesian quantile, non-linear mixed-effects regression model, using a compound symmetry covariance structure, accounting for multiple timepoints was utilised. The Scottish Index of Multiple Deprivation (SIMD) was used to measure socio-economic status and Health Related Quality of Life (HRQoL) was measured via the EQ-5D-5L.

**Results:** In the initial baseline cohort of 182 patients, (55%) patients were male, the median age was 58 (Interquartile Range (IQR): 50-66) years and 129 (79%) had two or more comorbidities at ICU admission. Using the neutral prior, there was an overall probability of intervention benefit of 100% ( $\beta = 0.71$ , 95% CrI: 0.34, 1.09) over 12 months to those in the  $SIMD \leq 3$  cohort, and an 98.6% ( $\beta = -1.38$ , 95% CrI: -2.62, -0.16) probability of greater benefit (i.e., a steeper increase in improvement) at 12 months in the  $SIMD \leq 3$  vs  $SIMD \geq 4$  cohort in the EQ-Visual Analogue Scale.

**Conclusions:** Using multi-centre data, this re-analysis suggests, but does not prove, that an integrated health and social care intervention is likely to improve outcomes across the socio-economic gradient following critical illness, with a potentially greater benefit for those from deprived communities. These findings suggest that future research designed to prospectively analyse how critical care recovery programmes could potentially improve outcomes across the socio-economic gradient is warranted.

## **Introduction**

The number of patients surviving an admission to critical care is increasing<sup>1</sup>. However, this survivorship is often associated with challenges<sup>2</sup>. Following hospital discharge, as many as 60% of survivors can experience physical, social, emotional and cognitive issues, which can impact their ability to return to, or fully re-integrate with activities<sup>3</sup>. These problems can have a profound impact on society and healthcare systems; over 30% of patients require a readmission to hospital within 90 days of hospital discharge and over 50% of those employed before admission, do not return to work in the year following hospital discharge<sup>4,5</sup>.

In response to these issues, a number of initiatives have been tested and implemented internationally<sup>6</sup>. Although there is a lack of empirical data to demonstrate the benefit of these services, recent evidence suggests almost three quarters of hospitals in the UK provide recovery care for survivors of critical illness in the post-hospital discharge period<sup>7,8</sup>.

Socioeconomic differences in outcomes following acute and critical illness are common<sup>9</sup>. Outpatient critical care recovery programmes might narrow these differences by benefiting those most in need by facilitating access to social care providers and support<sup>10</sup>. Alternatively, recovery programmes might exacerbate disparities if individuals with more resources can take greater advantage of what the programmes provide. However, there is limited evidence to understand what impact if any, recovery services might have for patients across the socio-economic spectrum following critical illness.

Given the increasing interest in interventions to correct socioeconomic disparities, we analysed data from a critical care recovery programme to establish the range of credible probabilities that this programme narrowed disparities in outcomes. Specifically, we utilised a Bayesian approach to explore any possible effect of a pre-defined recovery intervention across the socio-economic gradient, with the integration of prior knowledge in relation to critical care outcomes.

## **Methods**

### *Ethical Approval*

This prospective study, which was a pre-planned secondary analysis, was approved by the Liverpool Central Research Ethics Committee (17/NM/0199) (Intensive Care Syndrome: Promoting Independence and Return to Employment (InS:PIRE) a multi-centre study on the 14<sup>th</sup> of February 2017). All procedures were followed in accordance with institutional ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975. All participants provided written informed consent.

### *Intervention*

The setting for this analysis was a critical care rehabilitation programme. Details of this programme (InS:PIRE) have been published previously<sup>11,12</sup>. Briefly, InS:PIRE was an integrated health and social care recovery programme, co-designed by patients and caregivers. In the context of this research, Patients took part over five weeks and had access to a health and social care team, with emphasis on welfare support and return to employment advice. This advice was provided by specialists from in-hospital financial inclusion services or external community organisations. Patients received a blend of individual and group sessions. In addition, all patients received individual reviews with an Intensive Care Unit (ICU) nurse and doctor; pharmacist; and physiotherapist. These individual appointments offered a debrief of the ICU stay, an assessment of ongoing problems, goal setting and patient-directed management plans. Occupational therapy, alongside Clinical Psychology services were also available. Peer support was embedded throughout InS:PIRE with the use shared waiting areas and group sessions. Patient and caregiver volunteers further along the recovery trajectory were also in attendance programme and provided peer support. Family members also had access to these services.

Patients were invited between 4 and 12 weeks after hospital discharge. The inclusion criteria were any patient receiving level three care (multiple organ support and/or invasive respiratory support), or more than 7 days of level two care (single organ or postoperative care). Exclusion criteria were those patients who were terminally ill, patients who had suffered a traumatic brain injury or those patients currently being cared for with inpatient psychiatric services. Data was collected from five hospital sites in Scotland, UK.

Participants data was collected at three timepoints: initial admission to InS:PIRE (between four and 12 weeks after hospital discharge), three months post InS:PIRE attendance and at a 12-month follow-up visit.

#### *Data Collection*

In hospital clinical data including severity of illness and ICU course were collected for all patients. This included data on pre-existing health status. Critical care length of stay was taken from the highest level of care during the critical care admission. Multimorbidity was classified as the presence of two or more comorbidities.

Socio-economic status was evaluated via the Scottish Index of Multiple Deprivation (SIMD). The SIMD is a Scottish Government ranking index based on postcode of residence which identifies neighbourhood socio-economic deprivation<sup>13</sup>. We undertook two distinct analyses using the SIMD. The first analysis (*Dichotomised analysis*) created two study cohorts from the decile classification (pre-defined classification created by the Scottish Government) of the SIMD;  $SIMD \leq 3$  (*socio-economically deprived cohort*) and  $SIMD \geq 4$  (*non-socio-economically deprived cohort*), dichotomised by median SIMD. This approach, which has been utilised previously, was chosen in preference to a continuous measure to focus attention on our primary objective—examining socio-economic disparities in outcomes<sup>14</sup>. The second sensitivity analysis (*Quintile analysis*) analysed the pre-defined quintile SIMD

categories (by Scottish Government) to examine socio-economic status; quintile one represented the most deprived and quintile the least. This approach has also been utilised in previous research<sup>12</sup>.

Health Related Quality of Life (HRQoL) was measured via the EQ-5D-5L. This EQ-5D-5L generates two summary measures; the health utility score (EQ-HUS) summarises five health and functional domains with a summary score; the EQ-Visual Analogue Scale (EQ-VAS) records self-rated health using a continuous scale from 0 (worst health) to 100 (best health)<sup>15</sup>.

### *Statistical Analysis*

This manuscript was prepared according to the Reporting of Bayes Used in Clinical Studies (ROBUST) guideline (**S1**)<sup>16</sup>. We utilised a Bayesian approach to analysis to explore any possible effect of the InS:PIRE intervention across the socio-economic gradient, with the integration of prior knowledge in relation to ICU outcomes. This integration of prior knowledge is not possible within a standard frequentist approach. Moreover, the integration of this prior knowledge enables researchers to undertake exploratory analyses seeking to understand outcomes where the sample size was not calculated a priori.

A Bayesian median, non-linear mixed-effects regression model, using a compound symmetry covariance structure, accounting for multiple timepoints was utilised. We did not utilise multiple imputation techniques as the mixed effects nature of this modelling approach allows non-balanced designs, including designs with missing data, to be analysed accurately. To generate the probability of the intervention benefit, we calculated the rate of instantaneous change of the outcome by using expected marginalised means at 12 months post hospital discharge. A natural cubic spline was used to ensure a smooth non-linear transition over the three timepoints included. Models were adjusted for: age, gender, Acute Physiology and Chronic Health Evaluation (APACHE) II score and SIMD. All

methodology was similar between the two analyses, except for using the dichotomised SIMD vs the pre-defined quintile categories of the SIMD in the sensitivity analysis.

In keeping with the Bayesian methodology, we considered a range of possible beliefs using optimistic, neutral and pessimistic priors<sup>7,10,17,18</sup>. Details of these priors, evidence that influenced beliefs and distributional parameters are detailed in **Table 1**. Posteriors were summarised with median point estimates and highest posterior density 95% credible intervals (CrI). The proportion of the posterior distribution, with an effect less than 0 ( $\text{Pr}[\beta < 0]$ ), is the probability of benefit. The Bayes Factor estimates the relative change between the prior and posterior distributions, with positive numbers denoting relative change to the alternative hypothesis. To allow for adequate coverage of the Bayes factor analysis, we generated each of the models (pessimistic, optimistic and neutral) using 40,000 iterations. Analyses were conducted using R (v4.3.1) with Stan (CmdStan v2.33.1, BRMS package) and emmeans (v1.8.9).

## **Results**

In total, 253 attended InS:PIRE from the five sites included in this analysis, with 206 patients consenting to participation. We only included patients who had completed both ED-5D-5L (both HUS and VAS) at all three timepoints. As such, 182 patients were included at baseline; 134 (73.6%) completed outcomes measures at 3 months and 127 (69.8%) at 12 months.

In the initial baseline cohort, 100 (55%) patients were male, the median age was 58 (Interquartile Range (IQR): 50-66) years and 129 (79%) had two or more comorbidities at ICU admission. The median APACHE II of the cohort was 20 (IQR:15-25) and the median ICU length of stay was 11 (IQR: 7-18) days. During the critical care stay, 160 (88%) patients required mechanical ventilation and 41(23%) required renal replacement therapy. A detailed breakdown of the entire study cohort is provided in **Table 2**. **Table 3** provides granular data on HRQoL outcomes at each of the three study timepoints included.

### *Dichotomised analysis*

The *Dichotomised analysis* created two study cohorts,  $SIMD \leq 3$  (*socio-economically deprived cohort*) and  $SIMD \geq 4$  (*non-socio-economically deprived cohort*), dichotomised by median SIMD. In total, 100 (55%) patients formed the  $SIMD \leq 3$  cohort and 82 patients formed the  $SIMD \geq 4$ .

Using the neutral prior, there was an overall probability of intervention benefit of 100% ( $\beta = 0.71$ , 95% CrI: 0.34, 1.09) over 12 months to those in the  $SIMD \leq 3$  (*socio-economically deprived*) cohort, and an 98.6% ( $\beta = -1.38$ , 95% CrI: -2.62, -0.16) probability of greater benefit (i.e., a steeper increase in improvement) at 12 months in the  $SIMD \leq 3$  vs  $SIMD \geq 4$  cohort in the EQ-VAS.

Based on the same neutral prior and considering the EQ-HUS, there was an overall probability of intervention benefit of 99.0% ( $\beta = 0.005$ , 95% CrI: 0.00, 0.01) over 12 months to those in  $SIMD \leq 3$  (*socio-economically deprived*) cohort and an 93.1% ( $\beta = -0.01$ , 95% CrI: -0.02, 0.00) probability of greater benefit at 12 months in the  $SIMD \leq 3$  vs  $SIMD \geq 4$  cohort (**Figure 1**). Consistent results were shown for pessimistic and optimistic priors (**Table 1**) (**S2**).

### *Quintile analysis*

The *Quintile analysis* used the five pre-defined SIMD categories to examine the impact of InS:PIRE across the socio-economic gradient; quintile one represented the most deprived geographical areas and quintile five, the least.

Using the neutral prior, there was an overall probability of intervention benefit of 99.9% ( $\beta = 0.66$ , 95% CrI: 0.28, 1.03) over 12 months to those in the SIMD 1 (*most deprived*) cohort and 99.9% ( $\beta = 1.16$ , 95% CrI: 0.51, 1.83) in those in SIMD 5 (*least deprived*) cohort in the EQ-VAS. There was a 94.2% ( $\beta = -1.48$ , 95% CrI: -3.36, 0.37) probability of greater benefit (i.e., a steeper increase in improvement) at 12 months in the SIMD 1 vs SIMD 5 cohorts, again based on the EQ-VAS.



Based on the same neutral prior and considering the EQ-HUS, there was an overall probability of intervention benefit of 98.1% ( $\beta = -0.00$ , 95% CrI: 0.00, 0.01) over 12 months to those in the SIMD 1 (*most deprived*) cohort and 99.1% ( $\beta = 0.01$ , 95% CrI: 0.00, 0.02) in the SIMD 5 cohort. There was an 86.7% ( $\beta = -0.01$ , 95% CrI: -0.03, 0.01) probability of greater benefit (i.e., a steeper increase in improvement) at 12 months in the SIMD 1 vs SIMD 5 cohorts, based on the EQ-HUS. Consistent results were shown for pessimistic and optimistic priors (**Table 1**) (**S3**). **S3** also provides a full analysis of the intervention benefit across the SIMD quintiles, from both a neutral, optimistic and pessimistic perspective for both the EQ-VAS and the EQ-HUS.

### **Discussion**

Using multi-centre data, this re-analysis suggests, but does not prove, that an integrated health and social care intervention is likely to improve outcomes across the socio-economic gradient following critical illness, with a potentially greater benefit for those from deprived communities. These findings suggest that future research designed to prospectively analyse how critical care recovery programmes could potentially improve outcomes across the socio-economic gradient is warranted.

Patients can experience a wide range of issues following intensive care, these include social and welfare issues such as reduced employment and income and the need for changes to housing and ways of living<sup>19,20</sup>. The intervention delivered in this study specifically targeted some of these issues and supported patients to navigate the sometimes-fractured welfare and social care system. This study did not have a control arm due to data availability, as such It is important to highlight that this study was not intended to provide definitive answers about whether such an intervention is effective in reducing health disparities, instead it provides evidence that the integration of health and social care in the post-ICU discharge period appears feasible with potentially meaningful utility for those in need. Future research should prospectively assess the effectiveness of such an integrated approach.

The findings of this research also demonstrate differences in the recovery trajectory following critical illness for different socio-economic groups. Recent evidence has also suggested that those with multi-morbidity are more likely to benefit from complex interventions following hospital discharge and that there may be different 'responses' to critical care rehabilitation programmes across diverse cohorts<sup>21,22</sup>. There is limited evidence which demonstrates the effectiveness of critical care rehabilitation programmes and follow-up service. This work, alongside other evidence would suggest that a deeper understanding is needed of the potentially different clinical phenotypes of critical illness recovery. These details could be used to design more targeted interventions, including the optimal dose and duration of rehabilitation, for survivors of critical illness.

Although this data represents patients from a single healthcare system, the likelihood is that patients from other healthcare systems, including those which are insurance based, are also likely to benefit from such input. Data from the US has demonstrated that survivors of acute respiratory distress syndrome (ARDS) frequently encounter 'financial toxicity' in the months following hospital discharge, much of which is driven by challenging insurance coverage<sup>23</sup>. Moreover, qualitative data from international COVID-19 recovery settings recognised that the need for social intervention has grown<sup>24</sup>. As such, this type of integrated care in the post hospital discharge period is likely to require adaptation across international settings but should continue to provide potential patient benefit.

Strengths of this research include its multi-centre approach and its robust integration of prior clinical knowledge and evidence. However, there are notable limitations. Most notably, this research was not powered to detect differences in socio-economic outcomes. Moreover, although the take-up of this programme on which the analysis was based is similar to other research in this field, less than 50% of patients invited to the programme attended, limiting the interpretation of our results<sup>11</sup>. As such, these findings should be interpreted with caution and be used in the context of hypothesis generating. Further, the measured intervention benefit includes both the intervention-specific benefits and those

that may have occurred in the absence of the intervention (e.g. in an untreated arm, had one been available). As such, other factors which we did not account for such as the present of social support and other services, may have contributed to the findings. Moreover, these findings represent data from a single healthcare system. Future investigation is required to understand if similar results are present internationally and in other healthcare systems. Finally, the diversity of cohort is limited, especially from an ethnicity perspective. We have considered inequalities through a social lens, when in reality, inequalities are highly complex. Future research should examine if similar programmes can influence those people other minoritized and disadvantaged groups.

### **Conclusion**

More research is required to optimise outcomes for those recovering from critical illness. Targeting interventions for those residing in areas of deprivation, using an integrated model of health and social care may provide benefit across the socio-economic gradient. More research is required to fully understand the impact of critical care recovery services and how they can be implemented to support all cohorts of patients.

**Author contributions:** JM and MS had full access to all study data and take responsibility for the integrity of the data analysis.

JM, TIJ and MS conceptualized and designed the study.

All authors contributed to the analysis and/or interpretation of the data.

JM and MS drafted the original manuscript. All authors critically revised the manuscript for important intellectual content.

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**Data sharing:** A de-identified dataset and the study protocol may be made available to researchers with a methodologically sound proposal, to achieve the aims described in the approved proposal.

Data will be available upon request following article publication. Requests for data should be directed at [joanne.mcpeake@glasgow.ac.uk](mailto:joanne.mcpeake@glasgow.ac.uk) to gain access.

**Declarations and Conflicts of interest:**

The authors declare no declaration of interests

**Ethics approval and consent to participate:**

All participants provided written informed consent. Ethical approval was granted by the Northwest (Liverpool Central) Research Ethics Committee (reference number: 17/NM/0199).

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### **List of Tables, Figures and Supplementary Materials**

Table 1: Application of Priors to this analysis, including information on the defining evidence

Table 2: Patient demographics

Figure 1: Output of modelling utilising a neutral prior approach (Dichotomised Analysis)

*S1*: Research Checklist

*S2*: Full output of modelling utilising the pessimistic and optimistic priors (Dichotomised Analysis)

*S3*: Full output of modelling utilising the pessimistic and optimistic priors (Quintile Analysis)

## Figure Legend

### Figure 1: Output of modelling utilising a neutral prior approach

(A) Prior-Posterior density plot of EQ-5D-5L VAS trend per month. The neutral prior distribution, which followed a normal distribution with a mean of 0 and SD of 0.08 (the clinically meaningful difference derived from the EQ-5D-5L VAS), is denoted in orange; the posterior distribution is shown in blue. The Bayes factor estimates the relative change between the prior and posterior distributions

(B) Prior-Posterior density plot of EQ-5D-5L HUS trend per month. The neutral prior distribution, which followed a normal distribution with a mean of 0 and SD of 8 (the clinically meaningful difference derived from the EQ-5D-5L HUS), is denoted in orange; the posterior distribution is shown in blue. The Bayes factor estimates the relative change between the prior and posterior distributions

(C) EQ-5D-5L VAS over time in months.  $\beta$  estimate of the difference in EQ-5D-5L VAS trend per month given with 95% credible intervals, and the probability of intervention benefit,  $\Pr(\beta < 0)$ , indicating the likelihood of a significant difference estimate.

(D) EQ-5D-5L HUS over time in months.  $\beta$  estimate of the difference in EQ-5D-5L HUS trend per month given with 95% credible intervals, and the probability of intervention benefit,  $\Pr(\beta < 0)$ , indicating the likelihood of a significant difference estimate



## **List of Abbreviations**

**APACHE:** Acute Physiology and Chronic Health Evaluation

**CrI:** Credible Intervals

**EQ-VAS:** EQ-Visual Analogue Scale

**HUS:** Health Utility Score

**HRQoL:** Health Related Quality of Life

**InS:PIRE:** Intensive Care Syndrome: Promoting Independence and Return to Employment

**IQR:** Inter Quartile Range

**ROBUST:** Reporting of Bayes Used in clinical Studies

**SIMD:** Scottish Index of Multiple Deprivation