

ORIGINAL RESEARCH ARTICLE

Could an integrated model of health and social care after critical illness reduce socioeconomic 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 socioeconomic spectrum after critical illness. We analysed data from a multicentre critical care recovery programme to understand the impact of this programme across the socioeconomic 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 and explore any possible effect of the InS:PIRE intervention on Health-Related Quality of Life (HRQoL) across the socioeconomic 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 socioeconomic status and HRQoL was measured using the EQ-5D-5L.

Results: In the initial baseline cohort of 182 patients, 55% of patients were male, the median age was 58 yr (inter-quartile range: 50–66 yr) and 129 (79%) patients 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% credible interval: 0.34–1.09) over 12 months to those in the $\text{SIMD} \leq 3$ cohort, and an 98.6% ($\beta=-1.38$, 95% credible interval: -2.62 to -0.16) probability of greater benefit (i.e. a steeper increase in improvement) at 12 months in the $\text{SIMD} \leq 3$ vs $\text{SIMD} \geq 4$ cohort in the EQ-visual analogue scale.

Conclusions: Using multicentre data, this re-analysis suggests, but does not prove, that an integrated health and social care intervention is likely to improve outcomes across the socioeconomic gradient after critical illness, with a potentially greater benefit for those from deprived communities. Future research designed to prospectively analyse how critical care recovery programmes could potentially improve outcomes across the socioeconomic gradient is warranted.

Keywords: Bayesian; critical illness; deprivation; quality of life; socioeconomic

Received: 25 August 2023; Accepted: 9 January 2024

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The number of patients surviving an admission to critical care is increasing.¹ However, this survivorship is often associated with challenges.² After 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.³ These problems can have a profound impact on society and healthcare systems; >30% of patients require a readmission to hospital within 90 days of hospital discharge and >50% of those employed before admission do not return to work in the year after hospital discharge.^{4,5}

In response to these issues, a number of initiatives have been tested and implemented internationally.⁶ 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.^{7,8}

Socioeconomic differences in outcomes after acute and critical illness are common.⁹ Outpatient critical care recovery programmes might narrow these differences by benefiting those most in need by facilitating access to social care providers and support.¹⁰ 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 socioeconomic spectrum after 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 predefined recovery intervention across the socioeconomic 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 multicentre study on 14 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.^{11,12} 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 5 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 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 of shared waiting areas and group sessions. Patient and caregiver volunteers further along the recovery trajectory were also in attendance 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, invasive respiratory support, or both), or >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 by inpatient psychiatric services. Data were collected from five hospital sites in Scotland, UK.

Participants' data were collected at three timepoints: initial admission to InS:PIRE (between 4 and 12 weeks after hospital discharge), 3 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.

Socioeconomic status was evaluated with the Scottish Index of Multiple Deprivation (SIMD). The SIMD is a Scottish Government ranking index based on postcode of residence which identifies neighbourhood socioeconomic deprivation.¹³ We undertook two distinct analyses using the SIMD. The first analysis (*dichotomised analysis*) created two study cohorts from the decile classification (predefined classification created by the Scottish Government) of the SIMD; $\text{SIMD} \leq 3$ (*socioeconomically deprived cohort*) and $\text{SIMD} \geq 4$ (*non-socioeconomically 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 socioeconomic disparities in outcomes.¹⁴ The second sensitivity analysis (*quintile analysis*) analysed the predefined quintile SIMD categories (predefined classification created by the Scottish Government) to examine socioeconomic status; quintile one represented the most deprived and quintile five the least. This approach has also been utilised in previous research.¹²

Health-Related Quality of Life (HRQoL) was measured using 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).¹⁵

Statistical analysis

This manuscript was prepared according to the Reporting of Bayes Used in Clinical Studies (ROBUST) guideline (S1 in Supplementary material).¹⁶ We utilised a Bayesian approach to analysis to explore any possible effect of the InS:PIRE intervention across the socioeconomic gradient, with the

Table 1 Application of priors to this analysis, including information on the defining evidence. CrI, credible interval; HUS, health utility score; SD, standard deviation; SIMD, Scottish Index of Multiple Deprivation; VAS, visual analogue scale. *All other priors and adjustors are set to be neutral for all analyses. †All priors followed a normal distribution.

	VAS	HUS	Strength of evidence related to the priors	Distributional parameters [†]	Results
Pessimistic*	<p>SIMD\leq3: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L VAS).</p> <p>SIMD\geq4: over the 12-month recovery trajectory, we believe that this group will have a clinically meaningful improvement (8 points) in the VAS component of the EQ-5D.</p> <p>Evidence: an 8 point change in the VAS component of the EQ-5D-5L has been shown to be clinically meaningful in previous studies.¹⁷</p>	<p>SIMD\leq3: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L HUS).</p> <p>SIMD\geq4: over the 12-month recovery trajectory, we believe that this group will have a clinically meaningful improvement (0.08) in the HUS component of the EQ-5D.</p> <p>Evidence: a 0.08 change in the HUS component of the EQ-5D-5L has been shown to be clinically meaningful in previous studies.¹⁷</p>	<p>Weak/moderate: evidence suggests differences in outcomes across the socioeconomic gradient in those recovering from critical illness.¹⁸ Thus, we hypothesise the intervention could have a smaller effect on those from SIMD\leq3.</p>	<p>VAS: mean=8 SD=8</p> <p>HUS: mean=0.08 SD=0.08</p>	<p>VAS: overall probability of benefit of 99.9% ($\beta=0.60$, 95% CrI: 0.22–0.97)</p> <p>HUS: overall probability of benefit of 96.2% ($\beta=0.004$, 95% CrI: –0.0004 to 0.008)</p>
Neutral*	<p>SIMD\leq3: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L VAS).</p> <p>SIMD\geq4: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L VAS).</p>	<p>SIMD\leq3: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L HUS).</p> <p>SIMD\geq4: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L HUS).</p>	<p>Moderate: a recent Cochrane review demonstrated that ICU recovery programmes show limited benefit to any patient group.⁷ Therefore, we have no prior evidence that this programme would make a meaningful clinical difference.</p>	<p>VAS: mean=0 SD= 8</p> <p>HUS: mean=0 SD=0.08</p>	<p>VAS: overall probability of benefit of 100% ($\beta=0.71$, 95% CrI: 0.34–1.09)</p> <p>HUS: overall probability of benefit of 99.0% ($\beta=0.005$, 95% CrI: 0.00–0.01)</p>
Optimistic*	<p>SIMD\leq3: over the 12-month recovery trajectory, we believe that this group will have a clinically meaningful improvement (8 points) in the VAS component of the EQ-5D-5L.</p> <p>SIMD\geq4: we do not know if the recovery programme makes a clinically meaningful difference on outcome in this group (measured via the EQ-5D-5L VAS).</p>	<p>SIMD\leq3: over the 12 months recovery trajectory, we believe that this group will have a clinically meaningful improvement (0.08) in the HUS component of the EQ-5D-5L.</p> <p>SIMD\geq4: we do not know if the recovery programme makes a clinically meaningful difference on outcomes (measured via the EQ-5D-5L HUS).</p>	<p>Weak/moderate: The programme delivered an integrated model of health and social care, supporting welfare benefit access, return to employment, and mental health.¹⁰ These problems are more prevalent in those from deprived communities, thus the programme might benefit the SIMD\leq3 cohort more.</p>	<p>VAS: mean=–8 SD= 8</p> <p>HUS: mean=–0.08 SD=0.08</p>	<p>VAS: overall probability of benefit of 100% ($\beta=0.83$, 95% CrI: 0.45–1.20)</p> <p>HUS: overall probability of benefit of 99.9% ($\beta=0.006$, 95% CrI: 0.002–0.01)</p>

Table 2 Patient characteristics and demographics across the duration of the intervention. APACHE, Acute and Chronic Health Evaluation; ICU, intensive care unit; IQR, inter-quartile range; LOS, length of stay; RRT, renal replacement therapy; SIMD, Scottish Index of Multiple Deprivation. * Multimorbidity was classified as two or more comorbidities.

Characteristic	Baseline, N=182	3 months, N=134	12 months, N=127
Age (yr), median (IQR)	58 (50–66)	59 (50–67)	59 (51–67)
Gender, n (%)			
Female	82 (45)	59 (44)	56 (44)
Male	100 (55)	75 (56)	71 (56)
ICU LOS (days), median (IQR)	11 (7–18)	11 (7–19)	11 (7–17)
Hospital LOS (days), median (IQR)	30 (16–50)	31 (16–49)	30 (16–48)
Unknown	2	2	1
APACHE II score, median (IQR)	20 (15–25)	20 (15–25)	20 (15–25)
Unknown	2	1	0
Dichotomised SIMD, n (%)			
1–3	100 (55)	68 (51)	66 (52)
4–10	82 (45)	66 (49)	61 (48)
SIMD (quintile), n (%)			
1	76 (42)	51 (38)	44 (35)
2	42 (23)	30 (22)	33 (26)
3	30 (16)	21 (16)	20 (16)
4	19 (10)	16 (12)	14 (11)
5	15 (8.2)	16 (12)	16 (13)
*Multimorbidity, n (%)	129 (71)	91 (68)	80 (63)
Ventilation, n (%)	160 (88)	120 (90)	113 (89)
RRT, n (%)	41 (23)	26 (19)	28 (22)

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 marginal means at 12 months after 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 predefined 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.^{7,10,17,18} 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 <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 (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria) with Stan (CmdStan version 2.33.1, BRMS package) and emmeans (version 1.8.9).

Results

In total, 253 patients 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 yr (inter-quartile range [IQR]: 50–66 yr) and 129 (79%) patients 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%) patients 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, $\text{SIMD} \leq 3$ (socioeconomically deprived cohort) and $\text{SIMD} \geq 4$ (non-socioeconomically deprived cohort), dichotomised by median SIMD. In total, 100 (55%) patients formed the $\text{SIMD} \leq 3$ cohort and 82 patients formed the $\text{SIMD} \geq 4$.

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 $\text{SIMD} \leq 3$ (socioeconomically deprived)

Table 3 Breakdown of Health-Related Quality of Life (HRQoL) outcomes at each study timepoint, stratified by study cohort. HUS, health utility score; IQR, inter-quartile range; SIMD, Scottish Index of Multiple Deprivation; VAS, visual analogue scale.

Group	Characteristic	Baseline	3 Months	12 Months
SIMD (1–3)	EQ-5D HUS, median (IQR)	0.52 (0.14–0.66)	0.55 (0.29–0.70)	0.63 (0.32–0.76)
	EQ-5D VAS, median (IQR)	50 (35–70)	58 (40–75)	65 (50–84)
SIMD (4–10)	EQ-5D HUS, median (IQR)	0.62 (0.43–0.73)	0.67 (0.55–0.79)	0.67 (0.55–0.84)
	EQ-5D VAS, median (IQR)	62 (49–75)	75 (60–85)	70 (55–90)

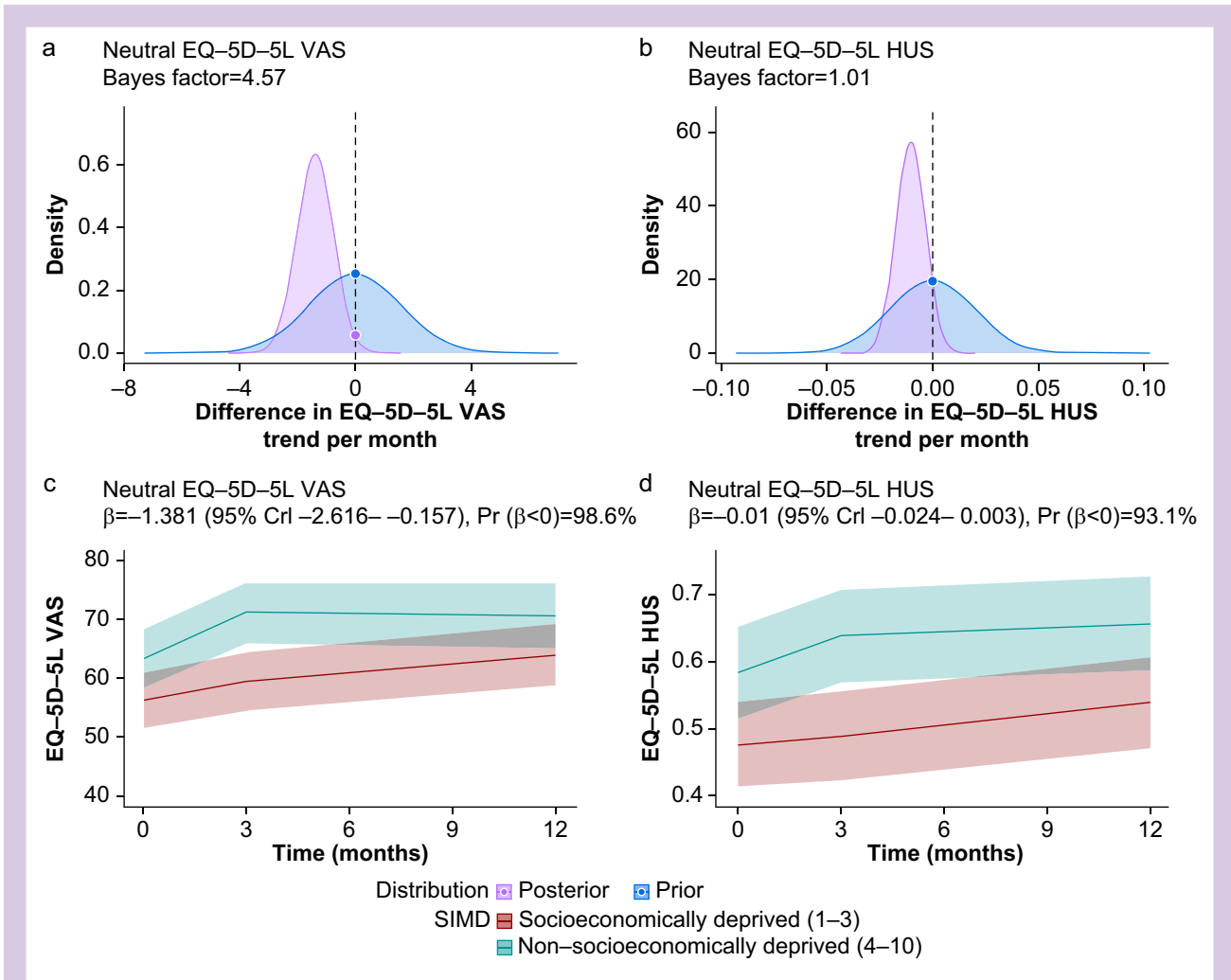


Fig 1. Output of modelling utilising the neutral prior approach. (a) Prior-posterior density plot of EQ-5D-5L VAS trend per month. The neutral prior distribution, which followed a normal distribution with a mean of 0 and standard deviation of 0.08 (the clinically meaningful difference derived from the 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 standard deviation 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. β 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. β 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. CrI, credible interval; HUS, health utility score; SIMD, Scottish Index of Multiple Deprivation; VAS, visual analogue scale.

cohort, and a 98.6% ($\beta = -1.38$, 95% CrI: -2.62 to -0.16) probability of greater benefit (i.e. a steeper increase in improvement) at 12 months in the $\text{SIMD} \leq 3$ vs $\text{SIMD} \geq 4$ 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 $\text{SIMD} \leq 3$ (socioeconomically deprived) cohort and an 93.1% ($\beta = -0.01$, 95% CrI: -0.02 to 0.00) probability of greater benefit at 12 months in the $\text{SIMD} \leq 3$ vs $\text{SIMD} \geq 4$ cohort (Fig 1). Consistent results were shown for pessimistic and optimistic priors (Table 1 and S2 in Supplementary material).

Quintile analysis

The quintile analysis used the five predefined SIMD categories to examine the impact of InS:PIRE across the socioeconomic 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 to 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 to 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 and S3 in Supplementary material). S3 in Supplementary material also provides a full analysis of the intervention benefit across the SIMD quintiles, from a neutral, optimistic, and pessimistic perspective for both the EQ-VAS and the EQ-HUS.

Discussion

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

Patients can experience a wide range of issues after 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.^{19,20} The intervention delivered in this study specifically targeted some of these issues and supported patients to navigate the fractured welfare and social care system. This study did not have a control arm because of 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 after critical illness for different socioeconomic groups. Recent evidence has also suggested that those with multimorbidity are more likely to benefit from complex interventions after hospital discharge and that there may be different 'responses' to critical care rehabilitation programmes across diverse cohorts.^{21,22} There is limited evidence to demonstrate 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 these data represent 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 USA has demonstrated that survivors of acute respiratory distress syndrome (ARDS) frequently encounter 'financial toxicity' in the months after hospital discharge, much of

which is driven by challenging insurance coverage.²³ Moreover, qualitative data from international COVID-19 recovery settings has recognised the need for social intervention in this setting.²⁴ 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 patient benefit.

Strengths of this research include its multicentre approach and its robust integration of prior clinical knowledge and evidence. However, there are limitations. Most notably, this research was not powered to detect differences in socioeconomic outcomes. Moreover, although the take-up of this programme on which the analysis was based is similar to other research in this field, <50% of patients invited to the programme attended, limiting the interpretation of our results.¹¹ 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 presence 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 our 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 from other minoritised 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 socioeconomic 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.

Authors' contributions

Full access to all study data and take responsibility for the integrity of the data analysis: JM, MS
 Conceptualised and designed the study: JM, TIJ, MS
 Contributed to the analysis, interpretation, or both of the data: all authors
 Drafted the original manuscript: JM, MS
 Critically revised the manuscript for important intellectual content: all authors

Declarations of interest

The authors declare that they have no conflicts of interest.

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 jm2565@medschl.cam.ac.uk to gain access.

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).

Funding

An award from the Health Foundation (173544) and a The Healthcare Improvement Studies Institute (University of Cambridge) Fellowship (307748–01/PD-2019-02-16).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bjao.2024.100259>.

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