BMJ

RESEARCH

# The PRaCTICaL study of nurse led, intensive care follow-up programmes for improving long term outcomes from critical illness: a pragmatic randomised controlled trial

B H Cuthbertson, chief of critical care medicine and professor of anaesthesia,[1] J Rattray, senior lecturer,[2] M K Campbell, director and professor,[3] M Gager, intensive care follow-up nurse,[4] S Roughton, intensive care follow-up nurse,[3,5] A Smith, intensive care follow-up nurse,[2] A Hull, consultant pyschiatrist,[6] S Breeman, trial manager,[3] J Norrie, professor of biomedical statistics,[7] D Jenkinson, statistician,[3] R Hernández, health psychologist,[3,8] M Johnston, professor of health psychology,[9] E Wilson, consultant in anaesthesia and intensive care ,[10] C Waldmann, consultant in anaesthesia and intensive care[4] on behalf of the PRaCTICaL study group

[1]Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, Toronto
[2]School of Nursing and Midwifery, University of Dundee, Dundee
[3]Health Services Research Unit, University of Aberdeen, Aberdeen AB32
[4]Intensive Care Unit, Royal Berkshire and Battle Hospital, Reading
[5]Intensive Care Unit, Aberdeen Royal Infirmary, Aberdeen
[6]Department of Mental Health, Murray Royal Hospital, Perth
[7]Robertson Centre for Biostatistics, University of Glasgow, Glasgow
[8]Health Economics Research Unit, University of Aberdeen
[9]Health Psychology Unit, University of Aberdeen
[10]Department of Anaesthesia and Intensive Care Medicine, Ninewells Hospital and Medical School, Dundee

**Correspondence to:** B H Cuthbertson
brian.cuthbertson@sunnybrook.ca

Cite this as: *BMJ* 2009;339:b3723
doi:10.1136/bmj.b3723

## ABSTRACT

**Objectives** To test the hypothesis that nurse led follow-up programmes are effective and cost effective in improving quality of life after discharge from intensive care.

**Design** A pragmatic, non-blinded, multicentre, randomised controlled trial.

**Setting** Three UK hospitals (two teaching hospitals and one district general hospital).

**Participants** 286 patients aged ≥18 years were recruited after discharge from intensive care between September 2006 and October 2007.

**Intervention** Nurse led intensive care follow-up programmes versus standard care.

**Main outcome measure(s)** Health related quality of life (measured with the SF-36 questionnaire) at 12 months after randomisation. A cost effectiveness analysis was also performed.

**Results** 286 patients were recruited and 192 completed one year follow-up. At 12 months, there was no evidence of a difference in the SF-36 physical component score (mean 42.0 (SD 10.6) *v* 40.8 (SD 11.9), effect size 1.1 (95% CI −1.9 to 4.2), P=0.46) or the SF-36 mental component score (effect size 0.4 (−3.0 to 3.7), P=0.83). There were no statistically significant differences in secondary outcomes or subgroup analyses. Follow-up programmes were significantly more costly than standard care and are unlikely to be considered cost effective.

**Conclusions** A nurse led intensive care follow-up programme showed no evidence of being effective or cost effective in improving patients' quality of life in the year after discharge from intensive care. Further work should focus on the roles of early physical rehabilitation, delirium, cognitive dysfunction, and relatives in recovery from critical illness. Intensive care units should review their follow-up programmes in light of these results.

**Trial registration** ISRCTN 24294750

## INTRODUCTION

More than 140 000 patients are admitted to intensive care units in the United Kingdom each year, of whom more than 50 000 die within a year of admission.[1 2] These patients have an excess long term risk of death compared with the general population matched for age and sex,[3 4] and a substantial percentage continue to experience both physical and psychological problems after discharge.[5-11] Studies assessing health related quality of life after intensive care suggest that it improves over time but that people do not return to the same level of health that they had before they fell ill and their health related quality of life is lower than the general population norms for at least the first year.[1 2 12-18] The reported prevalence of anxiety, depression, and post-traumatic stress disorder is also high and may endure for many years.[7 8 10 17 18] Patients' perceptions of their intensive care experience are also associated with subsequent distress.[19-22] These continuing problems have implications for patients and families and carers, and impose a continuing financial burden on primary and secondary health services.

A follow-up programme after intensive care has been suggested as a potential means of addressing these issues, but there is little evidence to suggest that such an intervention is effective. Despite this lack of evidence, at least 80 hospitals across the UK have now developed such follow-up services in an attempt to improve outcomes after discharge.[23] Despite UK guidelines, the nature of these programmes varies markedly between centres, and no optimal model has been identified.[23 24] Given the widespread proliferation of these programmes, it is crucial that their effectiveness is established without delay. We formally tested the hypothesis that nurse led follow-up programmes are effective at improving physical and psychological health related quality of life in the year after discharge from intensive care.

## METHODS

### Participants and treatment allocation

Patients were recruited from three UK hospitals (two teaching hospitals and one district general hospital) from September 2006 until October 2007. All patients receiving level 3 dependency (intensive care unit) care at any time during their hospital stay and who survived until hospital discharge were eligible for inclusion in the trial.[24] Patients less than 18 years old, not expected to survive to leave hospital, unable to complete questionnaires or attend clinics, and who did not consent to participate were excluded. Patients were approached in the period after discharge from intensive care when they were able to give informed consent. Before the participants' randomisation, we recorded their baseline measurements, quality of life (with the SF-36 (short form 36) and EuroQol EQ-5D questionnaires), intensive care experience (ICE score), and mood disorder (HADS (hospital anxiety and depression scale) score).[9 25-27] Patients were randomised to intervention or control in a non-blinded fashion using a computerised telephone randomisation service which incorporated minimisation by age, sex, HADS score, severity of disease (APACHE II (acute physiology, age, and chronic health evaluation) score), ICE score,[9] and trial centre.

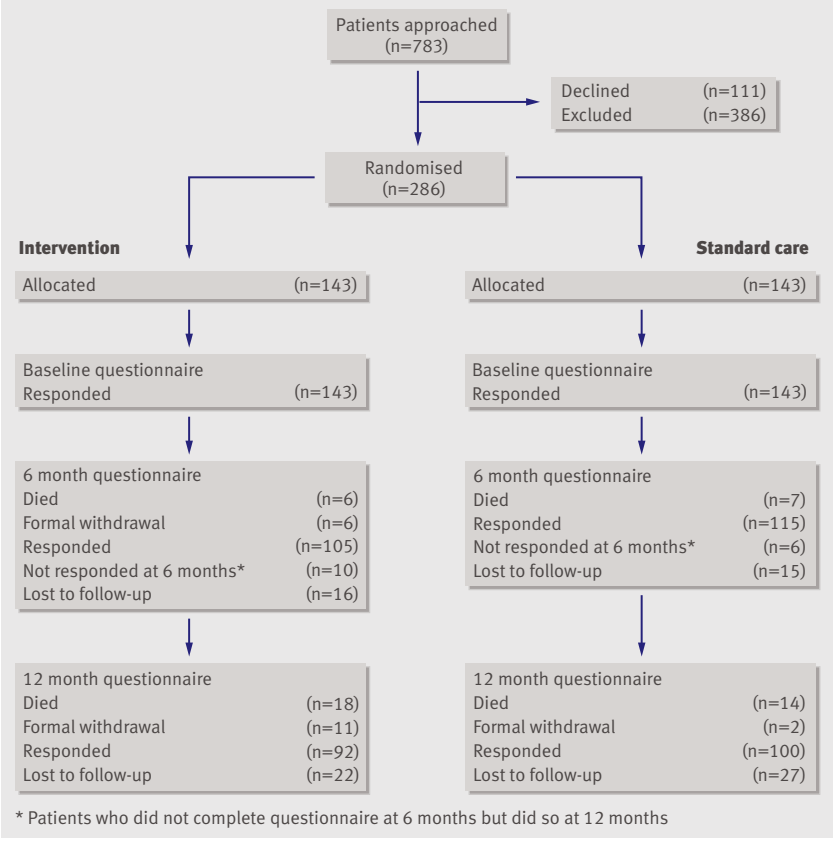



**Fig 1 | Consort flow diagram of patient recruitment and retention for the study. "Not responded" relates to patients who did not complete a questionnaire at six months but did so at 12 months (primary outcome point).**

### Intervention

Patients randomised to the intervention joined a manual based, self directed, physical rehabilitation programme developed by physiotherapists and introduced by a study nurse. This started in hospital and continued for three months after discharge. Patients monitored their own compliance and progress with the manual treatments and were formally reviewed at nurse led clinics at three months and nine months after discharge. The timing and format of this intervention was determined by the results of a survey of clinical practice conducted by our group, a national survey, and a national guideline,[11 23 24] as well as experiences of intensive care follow-up from one of the trial centres. The nurses followed a set format with standardised intervention and assessment requirements. An intensive care consultant was immediately available for support or to assess the patients for onward referral to other medical services and on patient request.

Clinic appointments had the following components: structured case review, discussion of experiences of intensive care, formal assessment of requirement for specialist medical referral, and screening for psychological morbidity relating to admission to the intensive care unit (using the Davidson trauma score and HADS).[27 28] Patients with "caseness" or in whom there was clinical concern were referred for review by a mental health professional, review of current drug treatment, visit to the intensive care unit if appropriate, and physiotherapy if appropriate, and a review letter on the patient's progress was sent to each patient's general practitioner. For more details of the intervention, see protocol paper.[29]

All interventions and referrals used standard NHS pathways. The exception was for psychological services, for which we developed assured referral pathways owing to the lack of identifiable clinical pathways for this patient group. The intervention was rigorously applied in each centre to avoid dependence on the aptitude of individual nurses. Trial nurses were trained together by nurses who carried out intensive care follow-up to ensure standardisation.

The "standard care" group had follow-up in accordance with standard clinical practice with no intensive care follow-up after hospital discharge. They were followed up by their general practitioners and primary hospital specialty as indicated by these teams.

### Outcomes

The primary outcome measures were health related quality of life (HRQoL) scores at 12 months measured with the SF-36 questionnaire by means of a postal survey. Secondary outcomes included HRQoL at six months, quality adjusted life years (QALYs) at 12 months, incidence and severity of post-traumatic stress disorder (Davidson trauma score) and anxiety and depression (using HADS) at six and 12 months, cost effectiveness at 12 months, primary and secondary healthcare costs in the year after hospital discharge, and mortality in the 12 months after discharge. All outcomes were measured by postal questionnaire to

prevent the follow-up becoming a clinical intervention. The researchers handling the outcome surveys were blinded to the intervention group.

### Sample size

Previous studies have shown the intensive care patients had a mean physical component score of the SF-36 of 35 (SD 14) at one year after discharge from intensive care.[2] We powered the study to detect a effect size of a 5 point increase on the SF-36 physical component score (about a 0.36 effect size) in the intervention group at one year. This suggested that 123 patients per group were required to complete the one year outcome measure to detect this difference with 80% power and an α of 0.05. However, the analysis was planned to adjust for baseline measurement and that the correlation between baseline, three month, and 12 month SF-36 scores was 0.6 (as had been seen in other studies of health related quality of life[2]), implying a sample size reduction of 36% was feasible. A conservative reduction of 30% in the estimated sample size could be achieved without a concomitant loss of power. Therefore, we required only 86 patients per group to complete the one year outcome measure. Assuming a 20% loss to follow-up[2 7 9] and a further 20% mortality in the first year, the total number of patients needed to be recruited into the study was estimated as 135 per group.

The primary analyses were based on the principle of intention to treat. The outcomes were compared between the groups using analysis of covariance, adjusting for minimisation factors and the baseline measurement of the outcome variable (with the exception of the Davidson trauma score, which was not measured at baseline), with two tailed $P<0.05$. Dichotomous outcomes were analysed using logistic regression. A priori subgroup analyses of the primary outcome were undertaken for APACHE II severity of illness, APACHE II comorbidity, intensive care experience (ICE score), and length of stay in intensive care, using tests for treatment by subgroup interaction (two tailed $P<0.01$). Data were analysed using SAS version 9.1 software. Sensitivity analyses were also undertaken around the primary outcome measures using the treatment received and per protocol methods. Patients were considered to have received the treatment if they attended at least one of the two clinics. Sensitivity analysis for loss to follow-up was performed using multiple imputation methods. Results are presented as effect sizes and odds ratios where relevant with confidence intervals.

**Table 1 | Baseline characteristics of patients recruited after discharge from intensive care to a nurse led follow-up programme (intervention) or standard care. Values are numbers (percentages) of patients unless stated otherwise**

| | Intervention (n=143) | Standard care (n=143) |
|---|---|---|
| Male | 86 (60) | 86 (60) |
| Median (IQR) age (years) | 59 (46–49) | 60 (46–71) |
| Median (IQR) APACHE II score | 19 (15–24) | 19 (15–24) |
| Median (IQR) APACHE II predictive mortality | 28.1 (12.3–45.2) | 28.5 (12.8–44.9) |
| APACHE II system failure: | | |
| Respiratory | 48 (33.6) | 42 (29.4) |
| Cardiovascular | 43 (30.1) | 42 (29.4) |
| Neurological | 5 (3.5) | 11 (7.7) |
| Gastrointestinal | 27 (18.9) | 27 (18.9) |
| Renal | 5 (3.5) | 3 (2.1) |
| Metabolic or endocrine | 2 (1.4) | 2 (1.4) |
| Haematological | 0 | 1 (0.7) |
| Trauma | 13 (9.1) | 15 (10.5) |
| APACHE II chronic health evaluation | 19 (13) | 12 (8) |
| Ventilated during intensive care | 139/141 (99)* | 139 (97) |
| Renal replacement therapy during intensive care | 19 (13) | 13 (9) |
| Inotropes during intensive care | 85 (59) | 77 (54) |
| Median (IQR) length of stay in intensive care (days) | 2.9 (1.7–9.5) | 3.1 (1.2–7.5) |
| Median (IQR) time from discharge to randomisation (days) | 9.5 (6.7–16.1) | 8.6 (4.8–13.3) |
| Mean (SD) SF-36 score: physical component | 33.4 (10.0) | 32.6 (9.9) |
| Mean (SD) SF-36 score: mental component | 40.9 (15.2) | 41.4 (14.2) |
| Median (IQR) EQ-5D score | 0.52 (0.26–0.73) | 0.49 (0.19–0.69) |
| Median (IQR) HADS: anxiety component | 7 (3–10) | 7 (4–10) |
| Median (IQR) HADS: depression component | 6 (3–9) | 5 (3–9) |
| Median (IQR) ICE score: awareness | 34 (27–38) | 34 (28–40) |
| Median (IQR) ICE score: frightening | 17 (12–20) | 16 (12–21) |
| Median (IQR) ICE score: recall | 14 (12–17) | 15 (12–18) |
| Median (IQR) ICE score: satisfaction | 16 (14–17) | 15 (14–17) |
| Sedative use during intensive care: | | |
| Propofol | 115 (80) | 112 (78) |
| Morphine | 8 (6) | 21 (15) |
| Short acting opiate (fentanyl or remifentanil) | 114 (80) | 108 (76) |
| Benzodiazepines | 17 (12) | 21 (15) |

IQR=interquartile range. APACHE=acute physiology, age and chronic health evaluation. SF-36=short form 36. EQ-5D= EuroQol quality of life measure. HADS=hospital anxiety and depression scale. ICE=intensive care experience questionnaire.
*Two missing values.

### Economic analysis

Cost per participant for each arm of the trial was calculated. We estimated use of healthcare resources per patient by means of patient questionnaires and hospital note review over the first year. Unit costs or prices were obtained using published estimates[30-32] and study-specific estimates. QALYs were calculated using the area under the curve method with responses to the EQ-5D questionnaire valued using UK population tariffs.[25] Patients who died were assigned a zero utility weight from their death to the end of the follow-up. QALYs before death were calculated using linear extrapolation. Point estimates for mean costs and mean QALYs were derived for treatment and standard groups to obtain incremental cost per QALY gained. Deterministic and stochastic sensitivity analyses (based on bootstrapped estimates) addressed different types of uncertainties within the economic evaluation, such as the exploration of the effect of those participants with the greatest costs on the estimates of mean cost effectiveness.

## RESULTS

Baseline characteristics showed that groups were well balanced in respect of key prognostic variables (table 1). Fig 1 shows details of patient recruitment

and retention for the study. In the year after randomisation 18 (13%) of patients in the intervention group died compared with 14 (10%) of control patients (odds ratio 1.32 (95% confidence interval 0.59 to 3.01)). Thirteen (4.5%) patients formally withdrew from the study, and 49 (17.1%) were lost to follow-up. Table 2 shows the delivery of the intervention in the treatment group.

No difference between groups was observed in any of the primary or secondary outcome measures at six or 12 months (tables 3 and 4). For the SF-36 physical component, the intervention group had a mean score of 42 (SD 10.6) compared with 40.8 (11.9) for the standard group (effect size 1.1 (95% confidence interval −1.9 to4.2), P=0.46). For SF-36 mental component, the intervention group had a mean score of 47.1 (SD 12.7) versus 46.8 (12.4) for the standard group (effect size 0.4 (−3.0 to 3.7), P=0.83). Table 3 presents the results of the sensitivity analyses for the primary outcome measure (10 patients in the intervention group did not attend either of the nurse led clinics and so were deemed to have not had the intervention): these showed a slight increase in the observed effect sizes for the primary outcomes, but they remained non-significant. Fig 2 shows the a priori subgroup analyses.

At six and 12 months after discharge from intensive care, similar percentages of patients in each group had returned to work (at six months, 40% (16/40) of intervention group *v* 37% (15/41) of controls, odds ratio 1.16 (95% confidence interval 0.43 to 3.12); at 12 months, 56% (18/32) *v* 55% (17/31); odds ratio 1.06 (0.35 to 3.21)). Likewise, similar percentages of patients in each group had seen their general practitioner (at 6 months, 90% (92/102) *v* 89% (98/110), odds ratio 1.13 (0.42 to 3.06); at 12 months, 82% (75/92) *v*88% (85/97), odds ratio 0.62 (0.25 to 1.49)). There were also no significant differences in satisfaction rates between groups (data not shown). There were no serious adverse events in either group.

The mean cost of care was £7126 for the intervention compared with £4810 for standard care (difference £2316 (95% credible interval −£269 to £4363)). The mean total QALY was 0.423 in the intervention group versus 0.426 in the control group (difference −0.003 (−0.065 to 0.060)). The difference in cost was significant at the 5% level, but the difference in QALYs was not. Based on the bootstrapped estimates of cost effectiveness, it is unlikely that follow-up programmes after intensive care are cost effective at typical threshold values for society's willingness to pay for a QALY. The sensitivity analysis revealed that the results of the study were not affected by loss to follow-up.

**Table 2 | Delivery of a nurse led follow-up programme* to 143 patients after discharge from intensive care. Values are numbers (percentages) of patients unless stated otherwise**

| | Nurse led clinic | |
|---|---|---|
| | 3 months | 9 months |
| No of patients who attended clinic | 104 | 94 |
| Mean (SD) time after randomisation to clinic appointment (days) | 91.3 (19.5) | 270 (20.2) |
| Relative accompanied patient to clinic | 46 (44) | 31 (33) |
| Case review | 99 (95) | 92 (98) |
| Discussion of intensive care experiences | 104 (100) | 92 (98) |
| Assessment of medical referral | 94 (90) | 83 (88) |
| Patients referred for specialist review | 25 (25) | 16 (17) |
| Total number of specialist referrals: | 34 | 29 |
| Ear, nose, and throat | 4 | 5 |
| Medical or surgical | 8 | 6 |
| Neurology or neurosurgery | 0 | 1 |
| Sexual medicine or urology | 1 | 2 |
| Physiotherapy or occupational therapy | 7 | 6 |
| Dietician | 6 | 1 |
| Speech therapy | 2 | 1 |
| Other | 6 | 7 |
| Psychological screen | 103 (99) | 93 (99) |
| Referral for psychological review | 25 (24) | 6 (6) |
| Review of current drug therapy | 101 (97) | 91 (97) |
| Changes to current medications | 3 (3) | 2 (2) |
| Visit to intensive care unit: | | |
| Offered | 87 (84) | 48 (51) |
| Performed | 22 (21) | 13 (14) |
| Physiotherapy or occupational therapy assessment requested | 7 (7) | 5 (5) |
| Intensive care doctor consulted | 15 (14) | 15 (16) |
| Intensive care doctor reviewed case | 17 (16) | 14 (15) |
| Review letter to patient's general practitioner | 104 (100) | 93 (99) |

*Patients received a physical rehabilitation handbook from baseline until 3 months, and were reviewed at nurse led clinics at 3 months and 9 months. Individual patients could have referrals for more than one treatment.

## DISCUSSION

This study is the first randomised controlled trial of a nurse led follow-up programme over the year after discharge from intensive care. It achieved its target sample size, and the intervention was reliably delivered. The outcome measures included both general and specific measures of health related quality of life and mental health and were appropriate to the research questions asked. The intervention was not effective in improving health related quality of life in the year after discharge from intensive care with regard to the outcome measures. The intervention also did not show effectiveness in any of the a priori subgroups, which included severity of illness, chronic comorbidity, intensive care experience, and length of stay in intensive care.

We believe that this study has high internal validity. The study recruited from three centres, one of which had an existing follow-up service and two that did not. The expert centre taught the other centres in the delivery of the intervention. The patients recruited to the trial are broadly representative of UK intensive care admissions.[1] However, those included in our study were likely to have been more severely ill than patients admitted to intensive care in other countries as our patients represented level 3 dependency care or the requirement for support of multiorgan failure.[24] This may affect the external validity and generalisability of the result. Study baseline quality of life scores were

**Table 3 | Primary outcome of trial of a nurse led rehabilitation programme for patients discharged from intensive care. Results were analysed on the basis of intention to treat (adjusted for minimisation covariates*), per protocol, and the treatment received**

| SF-36 score at 12 months | Intervention | | Standard care | | Effect size (95% CI) | P value |
|---|---|---|---|---|---|---|
| | No of patients | Mean (SD) score | No of patients | Mean (SD) score | | |
| **Intention to treat analysis** | | | | | | |
| Physical component score | 90 | 42.0 (10.6) | 97 | 40.8 (11.9) | 1.1 (−1.9 to 4.2) | 0.46 |
| Mental component score | 90 | 47.1 (12.7) | 97 | 46.8 (12.4) | 0.4 (−3.0 to 3.7) | 0.83 |
| **Per protocol analysis** | | | | | | |
| Physical component score | 80 | 42.3 (10.8) | 97 | 40.8 (11.9) | 1.6 (−1.6 to 4.8) | 0.33 |
| Mental component score | 80 | 48.5 (11.8) | 97 | 46.8 (12.4) | 1.7 (−1.7 to 5.1) | 0.33 |
| **Treatment received analysis** | | | | | | |
| Physical component score | 80 | 42.3 (10.8) | 107 | 40.7 (11.7) | 1.7 (−1.4 to 4.8) | 0.27 |
| Mental component score | 80 | 48.5 (11.8) | 107 | 45.8 (13.0) | 2.6 (−0.8 to 6.0) | 0.14 |

*Minimisation covariates were age, sex, HADS score, APACHE II score, ICE score, and trial centre (see table 1 for definitions of abbreviations).

measured in hospital after discharge from the intensive care unit and mean scores for the mental and physical components of the SF-36 questionnaire were consistent with previous literature.[2 33 34] Baseline HADS scores showed a moderately high overall level of anxiety and depression, as found in previous studies in this population.

The intervention was delivered with high reliability in all centres and mirrored UK practice at the time of development. Markers of this include that more than 90% of patients had the main elements of the intervention delivered. Despite encouragement to do so, only a minority of patients brought a relative with them to the clinic. With the key role of relatives in delivering care, we were surprised this number was not higher. Also, about a third of the patients required specialist medical referrals and a further third psychological referral. These data reflect the high, and presumably often unmet, need for specialist care in this patient group. Intensive care doctors were involved in the care of up to half of the patients at the clinics, mainly at the request of the nurses rather than of the patients, and were involved in all specialist referrals. The vast majority of patients were offered a visit to the intensive care unit, and three quarters took up this offer independently of the clinic appointment. From these data it is clear that the intervention was coordinated at the clinics but was delivered across the entire first year after discharge from the intensive care unit. Losses to the study over the first year were due to deaths (11.2%), withdrawal, and loss to follow-up (21.7%). Such mortality figures are in keeping with previous reports from similar patient cohorts.[2 34] A 20% withdrawal or loss to follow-up is also broadly in keeping with other studies in this patient cohort.[2 34] However, we performed sensitivity analysis to analyse the effects of such losses to follow-up, which showed that the results were not affected by such losses.

**Table 4 | Secondary outcome measures of trial of a nurse led rehabilitation programme for patients discharged from intensive care. Results were analysed on the basis of intention to treat (adjusted for minimisation covariates*)**

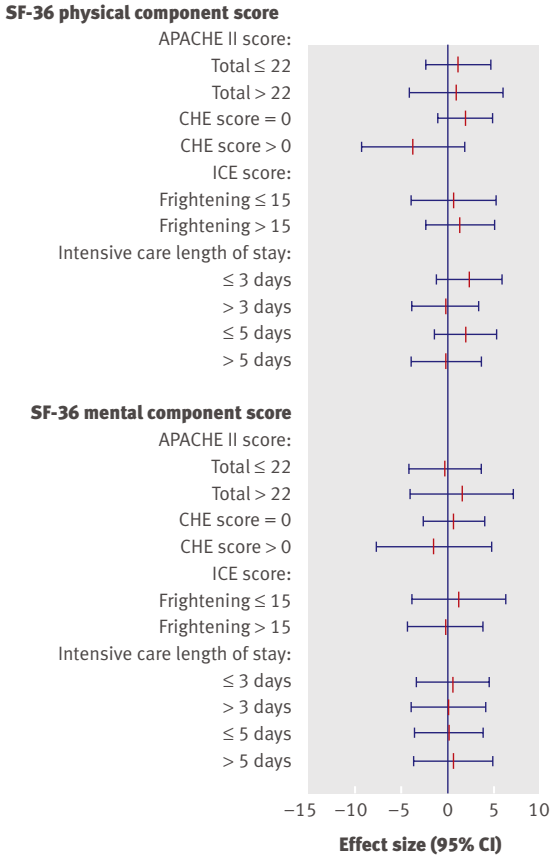
| | Intervention | | Standard | | Effect size (95% CI) | P value |
|---|---|---|---|---|---|---|
| | No of patients | Mean (SD) score | No of patients | Mean (SD) score | | |
| SF-36 score at 6 months: | | | | | | |
| Physical component score | 102 | 39.8 (9.5 | 110 | 40.1 (11.7 | −0.8 (−3.6 to 2.0) | 0.59 |
| Mental component score | 102 | 44.7 (14.2 | 110 | 45.2 (12.0 | −0.6 (−3.9 to 2.8) | 0.74 |
| EQ-5D quality of life score: | | | | | | |
| At 6 months | 110 | 0.63 (0.31 | 121 | 0.62 (0.3 | 0.0 (−0.1 to 0.1) | 0.83 |
| At 12 months | 108 | 0.58 (0.37 | 113 | 0.60 (0.3 | −0.0 (−0.1 to 0.1) | 0.57 |
| Davidson trauma score: | | | | | | |
| Incidence at 6 months | 102 | 16.1 (15.7 | 111 | 19.5 (16.7 | −3.6 (−7.6 to 0.4) | 0.07 |
| Incidence at 12 months | 90 | 13.7 (14.5 | 99 | 17.1 (14.7 | −3.7 (−7.4 to 0.0) | 0.05 |
| Severity at 6 months | 101 | 12.3 (14.1 | 111 | 15.1 (15.8 | −3.1 (−6.7 to 0.6) | 0.10 |
| Severity at 12 months | 89 | 10.3 (13.9 | 98 | 11.9 (13.3 | −1.6 (−5.0 to 1.9) | 0.37 |
| HADS score: | | | | | | |
| Anxiety at 6 months | 105 | 6.0 (4.5 | 115 | 7.0 (4.6 | −0.9 (−2.0 to 0.1) | 0.09 |
| Anxiety at 12 months | 92 | 5.5 (4.6 | 100 | 6.4 (4.4 | −0.8 (−1.9 to 0.4) | 0.18 |
| Depression at 6 months | 105 | 5.3 (4.3 | 115 | 5.3 (4.0 | −0.0 (−1.0 to 1.0) | 0.99 |
| Depression at 12 months | 92 | | 100 | | −0.1 (−1.2 to 1.0) | 0.86 |

*Minimisation covariates were age, sex, HADS score, APACHE II score, ICE score, and trial centre (see table 1 for definitions of abbreviations).

The scores for the physical and mental components of the SF-36 rose from baseline values at six and 12 months' follow-up in both groups but remained below population norms at all times, in line with previous findings.[2 18 33 34] Psychological distress scores tended to improve over the year but still represented a significant degree of psychological morbidity in both groups. As above, nearly a third of these patients required psychological referral, and ready access to such care is simply not available currently in the UK. Clearly, despite the results of this study, more needs to be done to identify patients with significant morbidity and suitable assessment and treatment options put in place.

As part of a sensitivity analysis, we analysed the primary outcomes according to treatment received and per protocol. These analyses show a slight increase in the intervention effect, but it remained non-significant. This may suggest that greater penetration of the intervention contributes to an improved outcome but will not on its own bring about important improvements. Subgroup analyses also did not yield any notable differences between intervention and control groups.

A key part of the economic evaluation was to explore under what circumstances the conclusions would alter.




CHE = chronic health evaluation
ICE = Intensive care evaluation

**Fig 2 | A priori subgroup analyses of SF-36 scores (physical and mental components) adjusted for minimisation covariates.**

This was undertaken using sensitivity analysis but the results remained robust to different underlying assumptions. Furthermore, given that there was no evidence of differences in QALYs, follow-up programmes could only be cost effective if they had the same or lower cost than standard care. This seems implausible over a 12 month follow-up period given the data we have. However, for the average difference in cost of £2316, follow-up programmes would need to provide 0.12 QALYs above standard care over a 12 month period to have an incremental cost per QALY of £20 000. This value is well above the upper limit of the 95% credible interval obtained in the base case or any of the sensitivity analyses.

There may be a variety of reasons why an improvement in health related quality of life was not observed in this study. Firstly, our complex intervention package may truly be ineffective. The intervention was developed from the experiences of an existing intensive care follow-up programme with many years experience, with additional regard to current UK practice in this field and with detailed knowledge of the morbidity that occurs in the year after discharge from intensive care.[2 7 9] However, although well informed, these follow-up programmes are not strongly evidence based. A further reason may be that our intervention did not account for important aspects of a patient's illness such as delirium and cognitive dysfunction and the complexity of the role of patients' relatives in their recovery (these aspects have emerged in the literature as important factors in patient recovery since our trial intervention was designed).[35-37] It may be that medical review is always appropriate for such complex patients and that a multiprofessional approach is required for this group at all times.

Our intervention differed from standard UK practice in that we included all intensive care patients with level 3 dependency irrespective of their length of stay in intensive care. Many centres invite only those patients with longer lengths of stay to their programmes, believing that these patients may gain greater benefit. However, our subgroup analysis did not show a significant treatment effect in patients with longer lengths of stay. Further, patients with short stays are known to have significant physical and psychological morbidity after admission to intensive care.

The timing of the intervention may have contributed to the non-significant findings (the first follow-up clinic was held at three months after discharge), and different results might have been seen if there had been more emphasis on early interventions occurring in hospital or in the immediate period after hospital. Our physical rehabilitation package did, however, start in hospital but may have been inadequate for the needs of these patients. A previous study has suggested that a physical rehabilitation programme does improve physical outcome when delivered in hospital after discharge from intensive care through to three months after discharge.[38] The knowledge of physical rehabilitation requirements after critical illness has advanced since we designed the intervention, with more attention

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Critically ill patients who require intensive care have severe and prolonged physical and psychological morbidity, and excess mortality, in the years after discharge from intensive care

Intensive care follow-up programmes have been developed in an attempt to improve the quality of life of these patients, but evidence for the effectiveness of such programmes is lacking

## WHAT THIS STUDY ADDS

This pragmatic study showed that nurse led follow-up clinics were neither effective nor cost effective in improving patients' quality of life in the year after their discharge from intensive care

Use of such follow-up programmes should be reviewed in light of these results

being paid to starting rehabilitation while the patient is still in the intensive care unit.[39]

Elements of our intervention might also have strayed inadvertently into the practice for our control patients (that is, contamination across groups might have occurred). However, the data indicate that there were higher referral rates to specialist services in the intervention group than the control group (data not shown), suggesting that the management of patients in the intervention group was indeed different from that in the control group. This gives some reassurance that contamination was minimal. The intervention effect was also consistent across the centres, suggesting there was not differential drift of the components of the intervention group into the control group across centres, which might have been expected if contamination had occurred in individual sites.

Finally, the conduct of the study may have inadvertently impaired the delivery of the intervention. Although it is often stated that the conduct of a research project can improve the studied outcome through the Hawthorne effect, it may be that this was not the case in this study. After the study, the nurses who delivered the intervention indicated that the completion of detailed questionnaires at the clinic appointments (most of which were part of the clinical assessment at that time as well as of the outcomes assessment at the main outcome points) did sometimes feel intrusive, potentially making the clinic reviews feel more like a research follow-up session rather than a review and treatment session. This may have reduced the effectiveness of the intervention.

### Strengths and limitations of study

Strengths of this study include it being the first multicentre randomised controlled trial of nurse led follow-up of patients over the year after their discharge from intensive care. We achieved the target sample size, and the intervention was delivered with high validity. The outcomes used were robust and well validated in a variety of clinical areas. We believe the study was delivered with high internal reliability. The external validity and generalisability may be reduced by the high severity of illness of patients treated in UK intensive care practice. Limitations include a comparatively small sample size to detect important changes in less common outcomes, including some physical and psychological outcomes. Patient selection may also have been too inclusive for this study. We selected all patients who had required intensive care, but the intervention may have been of greater benefit to more severely ill patients or those who required longer stay in intensive care.

### Future research

Further studies should attempt to identify effective ways to select patients most likely to benefit from follow-up after intensive care. They also need to elucidate more clearly the role of delirium and cognitive dysfunction on recovery and indeed on patients' ability to complete clinical and outcome questionnaires. A greater understanding of the complexity of the role of patients' relatives in their recovery and rehabilitation after critical illness is also required. Finally, the role of early physical rehabilitation based in the intensive care unit itself needs to be further explored.[36]

### Conclusions

Our study showed no evidence that a nurse led follow-up programme was effective or cost effective in improving patients' health related quality of life in the first year after their discharge from intensive care. Hospitals using intensive care follow-up programmes with a similar model of care should review their practice in light of our results.

Members of the PRaCTICaL study group were A McDonald, G McPherson, CR Ramsay, L Vale, C Pflanz-Sinclair, University of Aberdeen; JAW Wildsmith, Ninewells Hospital and Medical School, Dundee; S Rose, Berkshire Healthcare Foundation NHS Trust, Bracknell; and B Williams, Intensive Care Society, London. Chairman of the trial steering committee was Timothy Walsh, Royal Infirmary of Edinburgh, Edinburgh.

**Contributors:** BHC, JR, MKC, MG, SR, AH, JN, RH, MJ, EW, and CW participated in the study design, data collection, data analysis, and in writing the final paper; had access to all data; and approved the final version of the paper. AS, SB, and DJ participated in the data collection, data analysis and in writing the final paper; had access to all data; and approved the final version of the paper. BHC is guarantor for the study.
**Funding:** The study is supported by a research grant from the Chief Scientist Office of the Scottish Government Health Directorates. The Health Services Research Unit is also funded by the Chief Scientist Office of the Scottish Government Health Directorates. The researchers are completely independent of the funders, and the views expressed are those of the authors alone. The study sponsor was the University of Aberdeen, which had no role in the study design; collection, analysis, and interpretation of data; writing of the article; or the decision to submit it for publication. The researchers are completely independent of the sponsors in their research activities.
**Competing interests:** None declared.
**Ethical approval:** The project gained full ethical approval.
**Data sharing:** No additional data available.

1 Scottish Intensive Care Society. Annual audit. 2007. http://www.sicsag.scot.nhs.uk/.
2 Cuthbertson B, Scott J, Strachan M, Kilonzo M, Vale L. Quality of life before and after intensive care. *Anaesthesia* 2005;60:332-9.
3 Williams T, Dobb G, Finn JC, Knuiman MW, Geelhoed E, Lee KY, et al. Determinants of long-term survival after intensive care. *Crit Care Med* 2008;36:1523-30.
4 Wright JC, Plenderleith L, Ridley SA. Long-term survival following intensive care: subgroup analysis and comparison with the general population. *Anaesthesia* 2003;58:637-42.
5 Broomhead RL, Brett SJ. Intensive care follow-up—what has it told us? *Crit Care* 2002;6:411-7.
6 Crocker C. A multidisciplinary follow-up clinic after patients' discharge from ITU. *Br J Nurs* 2003;12:910-4.

7 Cuthbertson B, Hull A, Strachan A, Scott J. Post-traumatic stress disorder after critical illness requiring general intensive care. *Intensive Care Med* 2004;30:450-5.
8 Kapfhammer HP, Rothenhausler HB, Krauseneck T, Stoll C, Schelling G. Posttraumatic stress disorder and health-related quality of life in long-term survivors of acute respiratory distress syndrome. *Am J Psychiatry* 2004;161:45-52.
9 Rattray J, Johnston M, Wildsmith JAW. The intensive care experience: development of the Intensive Care Experience (ICE) Questionnaire. *J Adv Nurs* 2004;47:64-73.
10 Scragg P, Jones A, Fauvel N. Psychological problems following ICU treatment. *Anaesthesia* 2001;56:9-14.
11 Department of Health. Critical care outreach: progress in developing services. 2003. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4091873.
12 Brooks N. Quality of life after intensive care. *Nurs Crit Care* 1996;1:90-5.
13 Eddlestone J, White P, Guthrie E. Survival, morbidity, and quality of life after discharge from intensive care. *Crit Care Med* 2000;28:2293-9.
14 Lipsett PA, Swoboda SM, Campbell KA, Cornwell E, Dorman T, Pronovost P. Sickness impact profile score versus a modified short-form survey for functional outcome assessment: acceptability, reliability, and validity in critically ill patients with prolonged intensive care unit stays. *J Trauma* 2000;49:737-43.
15 Niskanen M, Ruokenen E, Takala J, Rissanen P, Kari A. Quality of life after prolonged intensive care. *Crit Care Med* 1999;27:1132-9.
16 Schelling G, Stoll C, Haller, M, Briegel J. Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Crit Care Med* 1998;26:651-9.
17 Eddleston J, White P, Guthrie E. Survival, morbidity, and quality of life after discharge from intensive care. *Crit Care Med* 2000;28:2293-9.
18 Ridley SA, Chrispin PS, Scotton H, Rogers J, Lloyd D. Changes in quality of life after intensive care: comparison with normal data. *Anaesthesia* 1997;52:195-202.
19 Granberg A, Engberg I, Lundberg D. Acute confusion and unreal experiences in intensive care patients in relation to the ICU syndrome. Part II. *Intensive Crit Care Nurs* 1999;15:19-33.
20 Jones C, Griffiths R, Humphris G, Skirrow P. Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2001;29:573-80.
21 Rundshagen I, Schabel K, Wegner C, am Esch J. Incidence of recall, nightmares, and hallucinations during analgosedation in intensive care. *Intensive Care Med* 2002;1:38-41.
22 Green A. An exploratory study of patients' memory recall of their stay in an adult intensive therapy unit. *Intensive Crit Care Nurs* 1996;12:131-7.
23 Griffiths JA, Barber VA, Cuthbertson BH, Young JD. A national survey of intensive care follow-up clinics. *Anaesthesia* 2006;61:950-5.
24 Department of Health. Comprehensive critical care: a review of adult critical care services. 2000. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4006585.
25 Dolan P, Gudex C, Kind P, Williams A. A social tariff for EuroQOL of life: results from a general UK General Population Survey. In: *Discussion Paper 138*. Oxford: Centre for Health Economics, 1995.
26 Ware JE, Kosinski M, Dewey JE. *How to score version 2 of the SF-36 health survey.* Lincoln, RI: Quality Metric Incorporated, 2001.
27 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67:361-70.
28 Davidson JR, Book SW, Colket JT. Assessment of a new self-report scale for PTSD. *Psychol Med* 1999;27:153-60.
29 Cuthbertson BH, Rattray J, Johnston M, Wildsmith JA, Wilson E, Hernendez R, et al. A pragmatic randomised, controlled trial of intensive care follow up programmes in improving longer-term outcomes from critical illness. The PRACTICAL study. *BMC Health Serv Res* 2007;23:116.
30 Personal Social Services Research Unit. 2007. http://pssru.ac.uk.
31 Scottish Health Services Costs. 2007. www.isdscotland.org/isd/CCC_FirstPage.jsp.
32 Royal Pharmaceutical Society of Great Britain. *British National Formulary*. London: BMJ Group, 2007. www.bnf.org/bnf/.
33 Dowdy D, Eid M, Dennison C, Mendez-Tellez P, Herridge M. Quality of life after acute respiratory distress syndrome: a meta-analysis. *Intensive Care Med* 2006;32:1115-24.
34 Herridge M, Cheung A, Tansey C, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003;348:683-93.
35 Gordon SM, Jackson JC, Ely EW, Burger C, Hopkins RO. Clinical identification of cognitive impairment in ICU survivors: insights for intensivists. *Intensive Care Med* 2004;30:1997-2008.
36 Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med* 2001;29:1370-9.
37 Cameron JI, Herridge MS, Tansey C, McAndrews MP, Cheung AM. Well-being in informal caregivers of survivors of acute respiratory distress syndrome. *Crit Care Med* 2006;34:81-6.
38 Jones C, Skirrow P, Griffiths R, Humphris GH, Ingleby S, Eddleston J, et al. Rehabilitation after critical illness: a randomized, controlled trial. *Crit Care Med* 2003;31:2456-61.
39 Denehy L, Berney S, Skinner E, Edbrooke L, Warrillow S, Hawthorne G, et al. Evaluation of exercise rehabilitation for survivors of intensive care: protocol for a single blind randomised controlled trial. *Open Crit Care Med J* 2008;1:39-47.


**Accepted:** 26 June 2009