

A nurse-led, preventive, psychological intervention to reduce PTSD symptom severity in critically ill patients: the POPPI feasibility study and cluster RCT

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Scientific summary

The POPPI feasibility study and cluster RCT

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Scientific summary

Background

Over 170,000 patients are admitted to adult, general critical care units in the NHS each year. Meta-analyses of outcome data for survivors have identified high rates of clinically important post-traumatic stress disorder (PTSD) (25%), depression (34%) and anxiety (40%) in the 6 months after unit discharge. Experiencing acute stress and early memories of frightening critical care experiences (e.g. hallucinations, delusions and nightmares) in the unit are known risk factors for longer-term psychological morbidity.

Research estimates that $\approx 50\%$ of patients in the critical care unit experience acute stress, and up to two-thirds experience hallucinations and delusions. Acute stress, including symptoms of anxiety, low mood and panic, may be caused by a range of difficult, cumulative experiences that are common for patients in critical care units: fear of dying, invasive treatments, pain and discomfort, inability to communicate and hallucinatory delusions.

Owing to a lack of strong evidence about what may help, little is currently done to alleviate patients' acute stress in critical care with a view to preventing the development of longer-term psychological morbidity. Rigorous and relevant evidence is therefore urgently needed to reduce the burden of serious psychological morbidity on patients and their carers, and cost-effective strategies are needed to reduce the burden on the NHS.

Very few NHS critical care units have regular access to psychologists. Acknowledging this, and evidence that indicates that non-experts can be trained to deliver effective psychological interventions in other settings, a preventive, complex psychological intervention was developed to be led by existing, but specially trained, critical care nurses, who were selected by their local critical care unit team. The intervention, developed using the Medical Research Council (MRC) framework for developing and evaluating complex interventions, aimed to alleviate acute stress and prevent development of longer-term psychological morbidity. It comprised three elements:

1. creating a therapeutic environment in critical care
2. three stress support sessions for patients identified as acutely stressed
3. a relaxation and recovery programme for patients identified as acutely stressed.

Objectives

The Psychological Outcomes following a nurse-led Preventative Psychological Intervention for critically ill patients (POPPI) study consisted of standardisation of the intervention, followed by feasibility testing, and, if feasible, a cluster randomised clinical trial (RCT). The overall objectives were to:

- standardise the proposed POPPI intervention
- develop an education package and support tools to deliver the POPPI intervention
- test the feasibility and acceptability of the education package, support tools and delivery of the intervention to patients and staff (i.e. an intervention feasibility study)
- test the feasibility of the proposed procedures for the cluster RCT (i.e. a RCT procedures feasibility study)
- refine the education package, support tools, the POPPI intervention and cluster RCT procedures based on results of the feasibility studies
- evaluate, using a parallel-group cluster RCT design, the clinical effectiveness and cost-effectiveness of the POPPI intervention, including an integrated process evaluation (if deemed feasible).

The active patient and public involvement group was involved across all aspects of the study, including development of the research question, development/refinement of the intervention, training of key trial staff and as members of oversight committees.

Standardisation of the intervention

The proposed POPPI intervention was standardised to ensure that it could be delivered consistently by non-experts across a number of different units. To do this, stage one of the MRC framework was completed by updating the evidence base for an intervention to reduce patients' acute stress, developing a theoretical understanding of the probable process of change in reducing acute stress and modelling the process to progressively refine the intervention. To support the delivery of the intervention, an education package and support tools were developed, to be tested for feasibility and acceptability. The education package comprised an online training course (POPPI online training) for completion by all clinical unit staff and a central 3-day training course for POPPI nurses, who were selected by their local critical care unit team to lead the intervention, followed by 1 day for assessment and feedback.

Feasibility, piloting and refinement

Two feasibility studies were carried out: (1) an intervention feasibility study – to test the feasibility and acceptability of the education package and support tools and to test the acceptability of the intervention delivery to patients and staff and (2) a RCT procedures feasibility study – to test the proposed procedures for the cluster RCT. The same patient eligibility and screening procedures were applied in both studies. Both were approved by the South Central – Oxford B Research Ethics Committee and were sponsored by the Intensive Care National Audit & Research Centre (ICNARC) and managed by ICNARC Clinical Trials Unit (CTU).

Intervention feasibility study

Two adult, general critical care units ('sites') were recruited. Both identified POPPI nurses to participate in the education package and to support and deliver the intervention. A total of 127 eligible patients were recruited over a 5.5-month period; all (100%) were screened for acute stress using the Intensive Care Psychological Assessment Tool (IPAT). Of these, 51 patients were identified as acutely stressed and eligible to receive stress support sessions. Of these, 25 (49%) received all three sessions, 14 (28%) received two sessions, five (10%) received one and seven (14%) received none. A total of 84% of unit staff completed the POPPI online training.

Randomised clinical trial procedures feasibility study

Two different sites were recruited to test the proposed procedures (including recruitment and retention). A total of 86 eligible patients were recruited over a 2-month period, and 80.5% of survivors completed the follow-up questionnaire at 5 months. Overall, completeness of the primary outcome measure [PTSD Symptom Scale – Self Report (PSS-SR) questionnaire] was very good. Of 1054 fields, only 24 (2.3%) had missing data.

Refinements

Based on data from both feasibility studies, the education package, support tools and intervention were refined for evaluation in the cluster RCT and were used to inform a review of the power calculation for the cluster RCT.

Cluster randomised clinical trial methods

Trial design and governance

The trial was a multicentre, parallel-group, cluster RCT, with a baseline (pre-intervention) period and a staggered roll-out of the POPPI intervention. Integrated process and economic evaluations were embedded. It was nested in the Case Mix Programme (CMP) (the national clinical audit for adult critical care). The South Central – Oxford B Research Ethics Committee approved the cluster RCT. The National Institute for Health Research (NIHR) convened a Trial Steering Committee and an independent Data Monitoring and Ethics Committee. The cluster RCT was sponsored by ICNARC and coordinated by ICNARC CTU.

Participants: sites and patients

The cluster RCT aimed to recruit a representative sample of 24 adult, general critical care units ('sites') and at least 1378 patients. A total of 24 sites opened to recruitment in three groups of eight sites at 2-month intervals and recruited participants over a 17-month period. Control group sites delivered usual care for the duration of the recruitment period. Intervention group sites delivered usual care from months 1 to 5. Participating sites did not offer formal psychological support to patients. Sites were randomised (12 to the intervention group and 12 to the control group), using a restricted randomisation algorithm to minimise imbalance, in their second month of recruitment. After month 5, intervention group sites underwent a 1-month transition period, during which the education package was rolled out and they transitioned from delivering usual care to delivering the POPPI intervention. The intervention was then delivered until the end of the recruitment period. Patients meeting the following inclusion criteria were approached for consent:

- aged ≥ 18 years
- spent > 48 hours in the critical care unit
- received level 3 critical care during first 48 hours in the critical care unit
- scored between 1 and -1 on the Richmond Agitation–Sedation Scale
- had a Glasgow Coma Scale score of 15
- spoke English
- able to communicate orally.

Outcome measures

The primary clinical effectiveness outcome was mean patient-reported PTSD symptom severity measured using the PSS-SR at 6 months. The primary cost-effectiveness outcomes were incremental costs, quality-adjusted life-years (QALYs) and net monetary benefit at 6 months. Secondary outcomes were:

- days alive and free from sedation to day 30
- duration of critical care unit stay
- PSS-SR score of > 18 points at 6 months
- depression and anxiety at 6 months, measured using the Hospital Anxiety and Depression Scale
- health-related quality of life (HRQoL) at 6 months, measured by the EuroQoL-5 Dimensions, five-level version questionnaire
- estimated life-time cost-effectiveness.

Data sources

A secure, electronic case report form enabled cluster RCT data to be entered by site staff. Participants completed follow-up questionnaires at 6 months post recruitment. Data were linked to the CMP and NHS Digital to provide additional information on sites and patient characteristics and outcomes.

Analysis principles

All analyses were by intention-to-treat, following a prespecified statistical analysis plan. A p -value of < 0.05 was considered statistically significant. All tests were two-sided with no adjustment for multiple comparisons. Missing data were handled by multiple imputation. The primary analysis for the clinical evaluation determined if there was a significant difference in the mean PSS-SR score at 6 months between participants recruited

during the intervention period at intervention group sites compared with participants recruited at control group sites using a generalised linear mixed model at the individual-patient level (patients nested within sites and time periods), including a random effect of site and a fixed effect of period (baseline or intervention) and adjusted for site-level factors included within the restricted randomisation algorithm.

A full cost-effectiveness analysis (CEA) was undertaken to assess the relative cost-effectiveness of the POPPI intervention versus usual care. The CEA was reported for two time periods: 6 months and lifetime. For each time period, the analysis took NHS and Personal Social Services perspectives, using information on HRQoL at 6 months combined with information on survival status to report QALYs, valued using the National Institute for Health and Care Excellence recommended threshold of willingness to pay for a QALY gain (i.e. £20,000). The main assumptions were subjected to extensive sensitivity analyses.

Results

Sites and patients

A total of 1458 participants were recruited between 1 September 2015 and 3 February 2017. Five withdrew consent. Treatment groups across time periods were well matched at baseline, and 79.3% of participants surviving to 6 months completed the follow-up questionnaire.

Process evaluation

By the end of the transition period, 971 out of 1669 critical care staff had completed the online training, equating to a median percentage of staff completing the POPPI online training of 58% (interquartile range 49% to 69%), with all sites achieving 80% (i.e. the prespecified target) by intervention period month 3. Local initiatives to translate the online training into practice included: optimisation of sleep (e.g. through sleep packs, night-time lighting and clustering of care), reduction of noise (e.g. through soft-close bins, minimisation of alarm and telephone noise), improved patient orientation (e.g. through clocks, staff-patient interaction and white boards) and increased family involvement. Some intervention sites found it challenging to change long-standing practices and some were restricted by the physical environmental limitations of the unit.

During the intervention period at intervention sites, 340 participants were recruited, of which 313 consented to be assessed by IPAT. All 313 participants were assessed; 199 were identified as acutely stressed and were eligible to receive stress support sessions. A total of 127 (63.8%) participants received all three stress support sessions, 33 (16.6%) received two, 21 (10.6%) received one and 18 (9.0%) received none. A total of 171 participants who received session one were given a tablet containing the relax and recover application to use between sessions and 131 (76.6%) reported use of it to their POPPI nurse. Most were given both the digital versatile disc (DVD) and the booklet to take home. There was variation in delivery of stress support sessions across intervention sites. Facilitators of session delivery included the ability to work flexibly and pre-session preparation by POPPI nurses; barriers to delivery included unanticipated discharge of patients and conflicting clinical workload of POPPI nurses.

Clinical effectiveness

Primary outcome

At 6 months, the mean PSS-SR score for surviving participants in the intervention group had decreased from 11.8 [standard deviation (SD) 11.2] for participants recruited in the baseline period to 11.5 (SD 11.5) for participants recruited in the intervention period. In the control group, the mean PSS-SR score had increased slightly from 10.1 (SD 10.6) in the baseline period to 10.2 (SD 10.0) in the intervention period. This corresponded to a primary treatment effect estimate (i.e. interaction between treatment group and time period) of -0.03 [95% confidence interval (CI) -2.58 to 2.52 ; $p = 0.98$]. This difference remained non-significant after adjustment for intervention adherence and in the prespecified sensitivity analyses.

Secondary outcomes

There were no significant differences between the groups in any secondary outcomes.

Subgroup analyses

There was no statistically significant interaction between the effect of treatment allocation and time period on PSS-SR scores at 6 months in any of the prespecified subgroups.

Cost-effectiveness analysis

Although, on average, the POPPI intervention decreased costs and slightly improved QALYs, leading to a positive incremental net benefit at 6 months (£835, 95% CI –£4322 to £5992), there was considerable statistical uncertainty surrounding the cost-effectiveness results. The probability that the POPPI intervention is cost-effective (at a willingness-to-pay threshold of £20,000 per QALY) is approximately 60%. When extrapolated to the lifetime, the incremental net benefit was larger, although with even greater uncertainty.

Conclusions

This was the first, large, randomised evaluation of a preventive, complex psychological intervention conducted in the challenging setting of NHS critical care. POPPI, a parallel-group, cluster RCT conducted in 24 adult, general critical care units, indicated that among adults who stayed in the critical care unit for ≥ 48 hours and received level 3 intensive care, the delivery of a preventive, complex psychological intervention, led by trained nurses, provided no significant difference in the primary clinical outcome, PTSD symptom severity at 6 months, when compared with usual care. There was considerable statistical uncertainty surrounding the cost-effectiveness results; when extrapolated to the lifetime, the incremental net benefit was larger, although with even greater uncertainty.

The preventive, complex psychological intervention may not have worked for the following reasons:

- The intervention may have been delivered too early: participants may have still been too ill to absorb and remember the therapeutic messages of the stress support sessions
- Although $> 80\%$ of participants received at least two sessions, participants were often discharged from hospital prior to completing all sessions; therefore, an intervention that follows patients into the community may be required.
- Although the trained critical care nurses reported feeling prepared following the 3-day training course, some reported struggling when delivering the session content with more complex patients and situations; therefore, perhaps psychologists should deliver this kind of support.

All intervention group sites reached the minimum target of at least 80% of staff completing the POPPI online training, but this did not seem to consistently convert into higher implementation scores for creating a therapeutic environment.

At 6 months, $> 20\%$ of responders scored > 18 points on the PSS-SR (i.e. the threshold that warrants further investigation for probable PTSD), indicating substantial ongoing psychological morbidity in this patient group.

Implications for health care

The results of the cluster RCT do not support the adoption of this preventive, complex psychological intervention into routine practice. However, the cluster RCT results indicate high levels of acute stress in the critical care unit (64%) and longer-term PTSD symptom severity (20%).

Recommendations for research

Recommendation one

Conducting research in this area is challenging and future research needs to factor in identified challenges such as the short time period for which patients have mental capacity prior to discharge from the critical care unit, and the potential stigma associated with psychological intervention(s).

Recommendation two

Prior to development and evaluation of any subsequent psychological intervention in the critical care unit, there is much to learn from post hoc analyses of the rich quantitative and qualitative data from the cluster RCT to further understand both risk factors for long-term psychological morbidity and why this intervention did not prove beneficial.

Trial registration

This trial is registered as ISRCTN61088114 (feasibility study) and ISRCTN53448131 (cluster RCT).

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