Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

Site procedures

ICU inclusion criteria

Intensive care units (ICUs) (clusters) were defined as either ICUs or combined ICU/high-dependency units (HDUs). Stand-alone HDUs and specialist critical care units (e.g. cardiothoracic) were excluded.

ICUs were eligible to take part in the trial if they were active participants in the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme (CMP) and able to commit to the following further criteria:

- show that recruitment to target, timely data collection, and delivery of the preventive, complex psychological intervention were feasible - via completion of a site feasibility questionnaire;
- commit to dedicate adequate resources to carry out the preventive, complex psychological intervention;
- agree to adhere to randomization into either the control group or the intervention group;
- have two joint Principal Investigators (PIs) identified to lead the trial at the ICU (a lead nurse and a lead doctor);
- agree, where possible, to recruit all eligible patients to the trial and to maintain a screening and enrolment log to include reasons why eligible patients were not recruited;
- agree to use the Confusion Assessment Method for the ICU (CAM-ICU)[1] for assessing delirium and Richmond Agitation Sedation Scale (RASS)[2] for assessing sedation status for the duration of the trial; and
- continue active participation in the CMP.

The CMP, coordinated by ICNARC, is the national clinical audit for critical care and has 100% coverage for adult, general ICUs in England, Wales and Northern Ireland.

ICUs that took part in the POPPI intervention feasibility study (ISRCTN61088114) were not eligible for selection for the cluster-randomized clinical trial (cluster-RCT).

ICU set-up/training

Site initiation visits were held at each participating ICU prior to the commencement of patient screening. The purpose of these visits was to present the background/rationale to the trial and to train local teams in the trial procedures (e.g. screening, recruitment and data collection). An investigator site file was provided to all participating ICUs during the visits.

Randomization procedures

Restricted randomization approach: Simulations of alternative ways to balance on size of unit were performed and compared:

i. balancing on teaching status and number of beds;
ii. balancing on teaching status and number of Level 3 admissions; and
iii. balancing on teaching status, number of beds and number of Level 3 admissions.

The best combination on the above three factors (balance on teaching status and number of Level 3 admissions) was used to perform the final random allocation.

ICU-selected nurses

ICUs randomized to the intervention group were then required to identify three ICU nurses who would lead local delivery of the preventive, complex psychological intervention based on the following criteria:

- registered nurse with at least three years critical care clinical experience;
- effective communicator, with patients, families, colleagues and collaborators;
- able to work flexibly;
- interested in improving psychological care of patients; and
- organised and able to manage a busy schedule.

The PIs were provided with the person specification, and decisions on nurse selection were made locally, as would be the case in usual practice.

Patient procedures

Eligibility

Inclusion criteria

- ≥18 years of age
- At least 48 hours in ICU
- Receipt of Level 3 (intensive) care during first 48 hours in ICU
- Between +1 and -1 on the Richmond Agitation Sedation Scale[2]
- Glasgow Coma Scale[3] score of 15
- English-speaking
- Ability to communicate orally

Exclusion criteria

- Pre-existing chronic cognitive impairment, such as dementia
- Pre-existing psychotic illness, such as schizophrenia
- Pre-existing chronic PTSD
- Receiving end-of-life care
- Previously recruited to POPPI

Screening procedure

On admission to ICU, all patients were added to a screening and enrolment log. Once the patient had stayed 48 hours in the ICU, they were screened by the local ICU research team for the following 'stable' criteria (i.e. those unlikely to change after this time-point):

- ≥18 years of age;
- receipt of Level 3 (intensive) care during first 48 hours in ICU;
- English-speaking;
- no pre-existing:
    - chronic cognitive impairment (e.g. dementia);
    - psychotic illnesses (e.g. schizophrenia); or
    - chronic PTSD; and
- not previously recruited into POPPI.

If the patient met all the above criteria, daily screening of the following 'transient' criteria (i.e. those which could fluctuate) commenced:

- current RASS score between +1 and −1;[2]
- current Glasgow Coma Scale score of 15;[3]
- not receiving end-of-life care;
- currently able to communicate orally; and
- able to give informed consent (e.g. not deemed delirious by the CAM-ICU).[4]

If any of the daily screening criteria were not met, the patient would be re-screened each day until either fully meeting the criteria or discharge from ICU. Once the patient met all eligibility criteria simultaneously, they were approached for informed consent in the ICU.

Informed consent

Patients who met the eligibility criteria were approached in the ICU. Patients were provided with written and verbal information about the trial by a member of the local ICU research team. Potential participants were given the opportunity to ask questions and time to discuss the trial with family or friends before making their decision. After the person seeking consent was satisfied that the information had been understood and questions had been answered, they invited potential participants to sign the consent form.

In providing informed consent, participants were agreeing for the trial team to access their medical records for data collection and to receive a follow-up questionnaire at six months. In addition, participants recruited at intervention ICUs during the transition period (month 6) and intervention period (month 7 onwards) were offered the option to provide consent to receive an assessment with the Intensive care Psychological Assessment Tool (IPAT),[5] and subsequent stress support sessions and relaxation and recovery programme (where applicable).

To minimize selection bias between the intervention and control ICUs, it was possible for a patient at an intervention ICU, during the transition and intervention periods, to provide consent to receive the follow-up questionnaire but decline participation in the intervention (i.e. assessment with the IPAT, stress support sessions and relaxation and recovery programme).

Follow-up procedure

The follow-up process started at 157 days post-recruitment for the six-month follow-up to allow for the administrative processes. Patients who had died since leaving hospital were logged and the follow-up process ended. For survivors, questionnaire packs were sent to participants either by post or email (as requested by the participant) and included a self-addressed stamped envelope and pen (if sent by post). Participants could indicate if they no longer wished to complete the questionnaire.

Non-responders were telephoned three weeks later to check whether they had received the questionnaire and were given the option to complete the questionnaire over the telephone with a trained member of the ICNARC Clinical Trials Unit (CTU) trial team.

For patients identified as either being a hospital in-patient, or resident in a care home or rehabilitation centre, the relevant institution was contacted to establish the most appropriate way to proceed with follow-up. If a patient was identified as having no fixed abode but was registered with a General Practitioner (GP) or known at a homeless shelter, then the questionnaire was sent to be passed to them at their next visit.

If a completed questionnaire received at the ICNARC CTU indicated the presence of signs of serious post-traumatic stress (score of ≥18 on the PTSD Symptom Scale – self report questionnaire (PSS-SR)), anxiety or depression (scores of >7 on the relevant Hospital Anxiety and Depression Scale (HADS) subscale), then a referral letter from the lead clinical investigator (DW) was sent to the patient's GP or the local Principal Investigators at the recruiting ICU.

Intervention

Overview of the preventive, complex psychological intervention
An overview of the three elements of the preventive, complex psychological intervention is provided below. The intervention, and its development, is described in detail elsewhere.[6]

Element 1: Promotion of a therapeutic environment in ICU
Key components of this element were:

- increasing awareness and understanding by staff of acute stress and poor psychological outcomes suffered by ICU patients;
- identifying and reducing stressors in the ICU such as loud noise, unnatural light, pain, sleep deprivation and psychoactive drug effects;
- improving communication between staff, families and distressed patients, particularly those who are delirious or experiencing hallucinations and/or delusions; and
- promoting a sense of hope and optimism during the psychological and physical recovery period.

Element 2: Three stress support sessions for patients screened as acutely stressed
Sessions started when the patient was awake and alert, either in the ICU or following discharge to the hospital ward. The aim of the stress support sessions was for nurses to develop a trusting relationship with patients, so patients could discuss concerns which they might feel embarrassed or worried about communicating, and to reduce emotional distress. The components included establishing a collaborative relationship focused on reducing distress; managing patient concerns, including hallucinations and delusions; psychological education to reduce distressing interpretations of unusual experiences; reducing stigma and encouraging open communication; and provision of active coping strategies.

There are three common components to each stress support session: Starting the session; Building Rapport; and Finishing the session. In addition, each session is structured as follows:

- Stress support session one – “helping patients understand and cope with stress”
    - Normalise reactions (discuss common psychological reactions and their causes in critical care)
    - Encourage communication (encourage patient to start opening up about worries and concerns)
    - Teach coping strategies (encourage patients to get information from staff and to use the relaxation and recovery programme)

- Stress support session two – “managing frightening thoughts from critical care”
    - Stress reactions (encourage further talk about worries and fears, normalise concerns and take note of stressful thoughts)
    - Explain stressful thinking (explain how unrealistic fears can create extra stress. Identify one stressful thought the patient agrees to work on)
    - Teach “check out my fear” technique (“check out my fear” is a combination of two common CBT approaches: challenging automatic thoughts, and behavioural experiments to find out if fears are accurate – in this case, by asking staff for information, talking to family, writing down a brief description of a fear to pass on; thinking about evidence for and against fears)

- Stress support session three – “creating confidence and hope for a good recovery”
    - Summarise and review (reinforce key messages from sessions one and two; identify persisting problems to pass on)

- Action plan (nurse and patient co-design a personal action plan to cope with challenges ahead and build on the stress support sessions)
- Future expectations (encourage realistic optimism and hope about progress made and recovery)

Element 3: Relaxation and recovery programme for patients screened as acutely stressed
The programme was split into two parts. The first, delivered using an app on a tablet computer during the patient's hospital stay, was designed to:

- provide meaningful activity and distraction;
- help people practise new coping strategies to reduce stress and improve sleep; and
- learn from other patients' experiences, between and following the stress support sessions.

The app was loaded onto a tablet to use in-hospital between stress support sessions. It had a green nature-scene background and large coloured buttons for easy navigation between sections. App contents included a "safe-place" visualization and relaxation exercise, muscle and breathing relaxation exercises; a body scan and other mindfulness meditations; relaxing classical music (from Bach to Vivaldi), calming modern ambient music; and restful nature sounds and videos. The app also included a section of former ICU patients' recovery stories, to help to normalise emotional reactions and unusual psychological experiences in ICU, and to encourage hope and optimism for recovery. There were five stories from patients of differing age, gender and ethnicity, illustrating a range of ICU experiences.

The second part of the relaxation and recovery programme, consisting of a digital video disc (DVD) and patient self-help booklet, was designed to give information on making a good psychological recovery after an ICU stay. The DVD included a shorter selection of relaxation exercises and music from the app, and longer versions of the patient recovery stories, assuming longer concentration spans as patients got closer to hospital discharge or go home.

The "*Getting well, staying well*" patient self-help booklet built on the support patients had already received during the stress support sessions. It was a 'readable' guide focusing on psychological well-being and positive coping strategies to help patients deal better with the challenges of recovery. It included:

- a personal action plan;
- information about what to expect after ICU in the early days;
- seven tips for psychological wellbeing;
- advice on coping with difficulties (worries, panic, low mood, memories);
- further information on sources of psychological support;
- information about the relaxation and recovery programme DVD; and
- information for family and friends.

The personal action plan is used to address the potential challenges ahead and create an individual psychological recovery plan based on advice and information in the rest of the booklet, as relevant to the patient's current needs.

Description of training, transition and support
The education package included training courses tailored for each element of the preventive, complex psychological intervention with materials to support training and delivery of the intervention.

Promotion of a therapeutic environment in ICU
The POPPI online training course (entitled *'Key skills in psychological care'*) was designed to give a balance of concise, readable text with graphics and other visual or audio aids. The online training course was divided into four sections:
1. Understanding the stresses of intensive care patients
2. Reducing stress and fear in patients
3. Communicating with distressed patients
4. Inspiring patients with confidence and hope

Test-yourself questions were included at the end of each section (with informative feedback), and the training ended with a summary and assessment. Videos included former patients talking about their experiences of ICU, and nurses and psychologists modelling good communication strategies with patients. Staff members who passed the assessment (a score of 80% or more) received a certificate.

Materials to aid and encourage completion of the online training course included flyers, cards and posters advertising the course. Posters and cards of key messages from the online training were distributed and displayed around the ICUs.

Three stress support sessions and the relaxation and recovery programme for patients screened as acutely stressed
The three-day, face-to-face course for ICU-selected nurses had a main focus on practical delivery of the stress support sessions and relaxation and recovery programme. Psychological principles were also taught. A significant amount of time was devoted to skills practice (role play) in delivering the sessions, with simulated patients (actors), and the training team (a psychologist, senior nurses, patient representatives and a research assistant) observing and offering feedback. In addition, two patient representatives talked about their ICU experiences each day; games and exercises were used to enhance learning, and a video of a sample stress support session delivered by a clinical psychologist specialist in psychosis was shown and analysed. Education for element three covered how to use the relaxation and recovery programme; theories of relaxation and mindfulness; and co-designing the personal action plan with the patient.

Associated training materials for the ICU nurses included a stress support session training manual, a set of slides for the three-day training course, and a training folder. All were designed for readability and clarity, with short sections, clear signposting, photographs, graphics and colourful diagrams. The writing of the stress support session manual was led by the lead adult ICU health psychologist with input from the wider trial team, including clinical psychologists, experts in cognitive behavioural therapy for psychosis and trauma, and senior nurses – under the supervision of the Expert Psychology Advisory Group. The manual begins with an introduction covering acute and post-traumatic stress, overview of the stress support sessions and relaxation and recovery programme, and how to use the manual. There is a section on each stress support session, including a two-page summary of the session in words and diagrams, and example scripts. At the end there is a glossary of patient-friendly terms and phrases, and a reading list. Other materials included course hand-outs for the three days, games and exercises to practice stress support skills such as 'guided discovery' and 'psychological education', example patient scenarios for the skills practice sessions, laminated stress thermometers, summaries of each stress support session and structured reflective note sheets for the ICU-selected nurses.

Ahead of the three-day training course, ICU-selected nurses were given a short pre-course theory booklet to read before attending the course. This booklet contained an overview of their new role and the psychological theory behind the stress support sessions – including details of key techniques used (e.g. normalization and psychological education). The stress support session manual and early access to the online training course were also given to the ICU-selected nurses ahead of the three-day training course.

Transition period timeline

Following an intervention site initiation visit and the three-day, training course for ICU-selected nurses, the intervention ICUs commenced delivery of the preventive, complex psychological intervention.

During the transition period, each ICU-selected nurse aimed to deliver stress support sessions to ≥1 recruited patient screened as acutely stressed. In parallel, the trained ICU-selected nurses and local education/research teams encouraged staff in their ICU to create a therapeutic environment by ensuring all clinical ICU staff completed the POPPI online training and through other educational activities (e.g. seminars and short presentations, bedside teaching, and display of the provided materials reinforcing key messages from the POPPI online training). At the end of the transition period, the ICU nurses underwent a skills development (competency) assessment. Following the transition period, the preventive, complex psychological intervention was delivered until the end of the recruitment period.

Debriefing and support for ICU-selected nurses

A clinical supervision structure, with one of the trainers acting as a supervisor (psychologist or senior nurse), was set up to allow regular “debriefing and support” phone calls and an ICU visit. The first debriefing and support call was made during or soon after the ICU-selected nurse delivered stress support sessions to their first patient. Subsequent calls would be scheduled every two months, or on nurses’ request. The focus of these calls was on enhancing nurses’ skills and discussing patient cases. A debriefing and support visit was held to support the ICU-selected nurses once each nurse at the ICU had delivered sessions to at least one patient. The visit included group and individual discussions and the skills development (competency) assessment with the trainer. Anyone who lacked confidence in the assessment would receive further training to repeat the assessment. Emails could be exchanged between nurses and trainers about issues arising from stress support sessions at any time. Peer support teleconferences were also held monthly.

Process evaluation

The process evaluation involved field observation and discussion of the cluster-RCT and preventive, complex psychological intervention with ICU staff, so it was important that the researcher was sufficiently independent to minimize the introduction of bias into the evaluation and for it to remain credible.[7] This independence helped ensure the external researcher would neither view the intervention too positively, nor be unduly critical. The relationship between the process evaluation team and the wider trial team was defined at the planning stage.

At the end of the cluster-RCT patient recruitment, interviews were conducted at intervention ICUs visits with both Principal Investigators and the trained ICU-selected nurses with the aim of giving ICUs an overall implementation grade and categorising them into lowest, moderate, or highest adherers. In addition, routinely-collected cluster-RCT data were summarized by the trial team in the form of individual ICU profiles and sent to the researcher to help understand how ICUs were engaging with the cluster-RCT and preventive, complex psychological intervention. The ICU profiles provided information to evaluate the dose and reach of the intervention, and comprised the following:

1. Uptake of the online training over time
2. Number of patients assessed with the IPAT
3. Number of stress support sessions received by patients screened as acutely stressed

Interview data were combined with the routine cluster-RCT data so that all four components of the preventive, complex psychological intervention had a score. The components were (1) POPPI online training, (2) creation and promotion of a therapeutic environment, (3) IPAT assessments and stress support sessions and (4) relaxation and recovery programme. The scores addressed the fidelity, dose and reach of the intervention. Scores on each of the components were combined to give an overall implementation grade for each intervention ICU.

To ensure each component of the intervention was weighted to account for its anticipated importance, the POPPI investigators were asked to independently weight the components using a total of 15 points each, representing likely overall importance. These weighted scores would be used in subgroup analyses.

Outcome measures

Patient reported PTSD symptom severity at six months

PTSD symptom severity at six months was measured using the PTSD Symptom Scale – Self Report version (PSS-SR).[8] The PSS-SR conforms to all DSM-IV diagnostic criteria for PTSD and has been validated for use in ICU survivors.[9,10] The scale is made up of 17 items and scores range from 0 to 51 (with higher scores indicated greater symptom severity).

PTSD symptom severity was reported for survivors at six months post-recruitment. The minimum clinically important difference (MCID) was considered to be 4.2 points, based on observing an improvement equal to the reliable change index among patients receiving stress support sessions.

As part of the preparation for the cluster-RCT, we conducted a feasibility study in two ICUs, including follow-up with the PSS-SR, and undertook a psychometric evaluation of the results (see eTable 1 and eTable 2 and eFigure 3 for details).

Costs up to six months

The resource use categories considered were chosen *a priori* and according to those where differences between the treatment groups were judged as being possible and likely to drive incremental costs, these were: resource use associated with the preventive, complex psychological intervention, hospital admissions (index admission and readmissions), and visits to outpatients and community healthcare services. Information on visits to outpatient and community healthcare services were collected via a health service questionnaire sent to patients at six months post-recruitment. Total costs at six months were calculated by combining the resource use with unit costs at 2015/16 prices (£ GBP), and then converted to US dollars using the currency conversion factor $1 equals £0.703.

Intervention

The costs of the preventive, complex psychological intervention were estimated based on experience of delivering the intervention in a typical ICU and considering the rolling-out of the intervention into routine NHS practice. Costing was based on the following guiding principle: key elements of the intervention that were deemed important to outcomes and would be provided in routine practice were considered, and elements that would incur costs in routine practice but were provided free of charge in the POPPI cluster-RCT were costed and included. The cost items associated with the intervention were grouped into three elements (eTable 3). The base case intervention costs were estimated using resource use data recorded on the POPPI cluster-RCT electronic case report form and informed by expert clinical opinion and the process evaluation reflecting the most plausible assumption for routine practice in a majority of ICUs, with alternative levels considered in the sensitivity analyses.

Hospital stay

The duration and location of the index hospital admission (the hospital stay following recruitment) was recorded for each patient up to six months post-recruitment on the electronic case report form. The total duration of the index admission included the time spent in ICU and on general medical wards. The length of stay in ICU was calculated as the total duration in days (including fractions of days), from the date and time of admission for the stay in ICU during which the patient was recruited until the time of discharge from critical care or death. Within the index admission, the total duration of ICU stay included all the time spent in ICU between admission to the ICU unit and discharge from acute hospital, and included any transfers to ICUs in other hospitals, as well as those within the hospital where the patient was recruited. For each day in ICU, data on the number of organs supported was recorded in the CMP database. Each critical care episode was then assigned a Healthcare Resource Group (HRG) applying standard HRG grouper algorithm.[11] For the index

admission, the total length of stay was calculated as the total duration in days from the date of recruitment to the date of ultimate hospital discharge, or death.

A hospital readmission was defined as a further hospital admission following ultimate hospital discharge from the index admission. The information on readmissions was collected from two sources. Firstly, data on readmissions to ICU were accessed from the CMP database.[12] From the CMP database, information was accessed on the duration of stay within ICU, and the total hospital stay including subsequent transfer to other care areas (e.g. general medical wards) within the same hospital and to other hospitals. Secondly, information on readmissions that did not include a further stay in ICU was collated from responses to the health services questionnaire administered to patients surviving to six months post-recruitment.

The resource use items considered included the total number of hospital outpatient visits and community service use following discharge from the index admission but before six months post-recruitment. The resource use included was for reasons both related and unrelated to the initial ICU admission in which the patient was recruited. The items of community service use included visits to the GP, nurses (i.e. from the GP clinic, hospital or a psychiatric nurse), health visitor, occupational therapist, speech and language therapist, counsellor, physiotherapist, psychiatrists, psychologist and critical care follow-up clinics. The levels of resource use were taken from responses to the health services questionnaire administered to patients surviving to six months post-recruitment.

Unit costs

The unit costs required for valuing the resource use data were taken from national unit cost databases and are listed in eTable 4. The unit costs associated with the additional staff time required to deliver the preventive, psychological complex intervention were taken from national sources.[13] The costs per critical care bed day by HRG and general medical bed day were taken from the 'Payment by Results' database.[14] Unit costs for hospital outpatient visits and community service use were obtained from a recommended published source for Health and Social Care costs.[13] All unit costs were reported in 2015-16 prices.

Quality-Adjusted Life Years (QALYs) at six months

POPPI cluster-RCT data were linked with national death registrations using the Medical Research Information Service Database Administrative System held by NHS Digital. Information on the date and time of deaths were used to calculate the survival time up to six months for each recruited patient. QALYs at six months post-recruitment were calculated by valuing each patient's survival time by their HrQoL at baseline (i.e. self-completed by patients at the time of consent) and six months according to the 'area under the curve' approach.[15] For patients surviving to six months, QALYs were calculated using the HrQoL at baseline and six months, applying linear interpolation. For decedents between recruitment and six months, a linear interpolation was applied between the baseline HrQoL, and the date of death when a zero HrQoL was applied.

Incremental net monetary benefit at six months

Incremental net monetary benefit of the preventive, complex psychological intervention at six months was calculated by multiplying the mean gain or loss in QALYs by the UK NICE recommended threshold of willingness to pay for a QALY gain in England (£20,000 [US $28,450]) and subtracting the incremental cost.

Days alive and free from sedation to day 30

For patients surviving to 30 days following recruitment, the number of days alive and free of sedation to day 30 was defined as the number of calendar days (00:00 to 23:59) on which sedatives/anxiolytics/anaesthetics were not received at any time. Patients dying between randomisation and day 30 will be assigned a value of 0. The specific agents included in the definition of sedatives/anxiolytics/anaesthetics were: chlordiazepoxide, clobazam, clonidine,

desflurane, dexmedetomidine, diazepam, etomidate, halothane, isoflurane, ketamine, lorazepam, midazolam, propofol, sevoflurane, thiopentone.

Duration of ICU stay (days)
Duration of ICU stay was be calculated as the sum of the duration (in days) from the date and time of recruitment (for the ICU admission during which the patient was recruited) or the date and time of admission to the ICU (for any subsequent admissions) to the date and time of discharge from the ICU or death in the unit for all admissions to ICU during the acute hospital stay.

PSS-SR greater than 18 points at six months
The proportion of patients scoring greater than 18 on the PSS-SR was reported amongst survivors at six months post-recruitment. A cutoff of 18 has been identified as a threshold for predicting likely current or future PTSD.[16]

HADS anxiety score at six months
Anxiety at six months was measured using the Hospital Anxiety and Depression Scale (HADS).[17] Scores on the anxiety subscale of HADS range from 0 to 21 with higher scores indicating worse severity. A value of 8 points is considered the threshold for likely anxiety. The mean (SD) score on the anxiety subscale of the HADS questionnaire was reported amongst survivors at six months post-recruitment. Among survivors of acute respiratory failure, a MCID of 2.0 to 2.5 ha been suggested for the anxiety subscale.[18]

HADS depression score at six months
Depression at six months was measured using the HADS.[17] Scores on the depression subscale of HADS range from 0 to 21 with higher scores indicating worse severity. A value of 8 points is considered the threshold for likely depression. The mean (SD) score on the depression subscale of the HADS questionnaire was reported amongst survivors at six months post-recruitment. Among survivors of acute respiratory failure, a MCID of 1.9 to 2.3 has been suggested for the depression subscale.[18]

EQ-5D-5L Health-related Quality of Life (HrQoL) utility score at six months
HrQoL at six months was measured using the EQ-5D-5L[19] which requires patients to describe their health on five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The responses to the EQ-5D questionnaire were used to report each patient's described health, which was then valued according to health state preferences from the general population to calculate EQ-5D utility scores, anchored on a scale from 0 (death) to 1 (perfect health).[20] The EQ-5D-5L HrQoL utility scale ranges from −0.285 to 1 with lower scores indicating worse health-related quality of life. The mean (SD) was reported amongst survivors at six months post-recruitment. Among patients with chronic respiratory disease, a MCID of around 0.05 has been suggested;[21] no studies have been conducted to establish a MCID for patients recovering from critical illness.

Analysis of uncertainty and sensitivity in cost-effectiveness at six months
The uncertainty around the differences in average costs and QALYs between the treatment groups was illustrated on the cost-effectiveness plane.[22] We estimated the incremental costs and QALYs with a multilevel regression model. To express the uncertainty in the estimation of the incremental costs and QALYs, we used the estimates of the means, and variances from the multilevel regression model, to generate 500 estimates of incremental costs and QALYs from the joint distribution of these endpoints, assuming asymptotic normality. These incremental costs and QALYs were then plotted on the cost-effectiveness plane. We also reported cost-effectiveness acceptability curves, by calculating the probability that, compared to usual care, the preventive, complex psychological intervention is cost-effective given the data, at alternative levels of willingness to pay for a QALY gain.

The main assumptions made in the base case scenario, and how each was relaxed in sensitivity analyses are detailed below and summarised in eTable 25:

- *Nurse's time for IPAT assessment:* In the base case analysis, we assumed that IPAT assessment involves 10 minutes of nurse's time per patient. The time per IPAT assessment could vary between 5-20 minutes as there may be a learning curve effect, which was varied in the sensitivity analysis.
- *Nurse's time for delivering stress support session:* In the base case analysis, we assumed that delivering the stress support sessions requires 1.5 hours of an ICU-selected nurse's time. However, evidence from the process evaluation suggests that the time required to deliver the stress support sessions varied widely across the cluster-RCT intervention ICUs. It could vary depending on experience with delivering stress support sessions. In the early stage of delivering stress support sessions, it may require up to 2 hours of nurse's time and at later stage it could take up to 1 hour of nurse's time. In the sensitivity analysis, ICU-selected nurse's time for stress support session was varied between 1 to 2 hours.
- *Readmissions from Health Services Questionnaire:* The base case analysis included readmissions recorded on the CMP Database (to critical care) but also those recorded from responses to the Health Services Questionnaire. To consider the possible impact of double-counting the same readmissions across both sources, this sensitivity analysis only included readmissions from the CMP Database.
- *HrQoL at time of consent:* In the base case analysis, QALYs at six months post recruitment were calculated by valuing each patient's survival time by their HrQoL at the time of consent and six months according to the 'area under the curve' approach. HrQoL at the time of consent was measured using a visual analogue scale. In the sensitivity analysis, zero HrQoL at the time of consent instead of the actual self-reported HrQoL measured from the visual analogue scale was considered for both treatment groups.
- *Distributional assumptions for costs and QALYs:* The base case analysis assumed that costs and QALYs were normally distributed when reporting the 95% confidence intervals around incremental costs and QALYs. In sensitivity analyses we assessed the robustness of the cost-effectiveness results to alternative distributional assumptions about both outcomes. Following methodological guidance,[23,24] the sensitivity analysis considered a gamma distribution for costs as they had a right-skewed distribution. For QALYs, the sensitivity analysis also considered a gamma distribution because a large proportion of decedents had zero QALYs, and the remainder of the distribution was again right-skewed.
- *Unit level SMR:* The base case analysis model followed the pre-specified regression model as per the SAP and did not adjust for SMR which may vary across units. These mortality rates at the unit level was adjusted in the sensitivity analysis by including the natural logarithm of the SMR (as it is a ratio measure) as an additional site-level covariate in the multilevel regression models.

The results of the sensitivity analysis are reported as mean INBs with corresponding 95% confidence intervals.

Lifetime costs-effectiveness

Lifetime cost-effectiveness was projected by summarising the relative effects of alternative strategies on long-term survival, and HrQoL as compared with that of age-gender matched general population.[25,26] The survival of POPPI cluster-RCT patients who survived up to six months post-recruitment was extrapolated over the lifetime by comparing survival and HrQoL of POPPI cluster-RCT patients to those of the age and gender matched general population. In the POPPI cluster-RCT, the survival probability of patients at one year was similar to those of the age-gender matched general population. There is evidence in support

of decrement in quality of life for up to five years following discharge from critical care.[27] In the POPPI cluster-RCT, HrQoL of survivors at six months was approximately 87% of that of the age-gender matched general population.[28] We therefore considered a decrement in HrQoL in the first year, but with improvement over five years to match the age-gender matched quality of life. After five years, we applied HrQoL values for the age-gender matched general population. Lifetime QALYs were reported by combining life years and HrQoL.

To project lifetime costs attributable to the initial episode of critical illness we considered the readmission costs (critical care and general wards) recorded up to one-year post-recruitment in the POPPI cluster-RCT. Mean annual readmission costs in critical care and general ward were calculated for patients who survived at least six months and were not censored between six and 12 months. We applied these six-month costs to the subsequent six months for patients who survived at least six months and were not censored between six and 12 months and calculated mean annual outpatient and community costs. These mean costs were applied annually for up to five years over which HrQoL decrement is applied to POPPI cluster-RCT patients as compared to those of the age-gender matched general population. All future costs and life years were discounted at the recommended rate of 3.5%.[23]

Elicitation methods

Just over 20% of patients who survived to six months did not return completed follow-up questionnaires. In the primary analysis, the resulting missing outcomes are assumed to be 'missing at random' (MAR), which assumes that the probability of a patient's outcome being missing does not to depend on the patient's outcome after conditioning on observed variables (e.g. the patient's baseline characteristics). In this section, we describe a sensitivity analysis that allows the probability that a patient returns their questionnaire to be dependent on their predicted state of health, for example, the expectation may be that patients in relatively poor health may be less likely to complete the requisite questionnaires and so these outcome data may be 'missing not at random' (MNAR). This additional analysis required: adapting the statistical models used for the primary analysis; developing an elicitation questionnaire about the PSS-SR and EQ-5D-5L outcomes; identifying experts; conducting the elicitation; and converting the elicited information into a range of priors.

Bayesian pattern-mixture models

Our approach to modelling MNAR data uses fully Bayesian pattern-mixture models,[1] which allow a patient's outcome to be calculated differently depending on whether the outcome is observed (pattern 1) or missing (pattern 2). For pattern 1, the outcome is calculated from the observed data using the statistical model specified for the primary analysis. For pattern 2, this model is adjusted, by specifying an offset from the mean of the observed data. This offset term, also known as a sensitivity parameter, is allowed to vary by treatment group and, as POPPI has a heterogeneous patient population, by patient type. [2]

As, in POPPI, missing outcomes occur because some patients do not return a completed PSS-SR or EQ-5D-5L questionnaire, an offset can be interpreted as the difference in the outcome between patients who did and did not return a completed questionnaire. Because the offset cannot be estimated from the observed data, expert opinion about their likely values is required to inform the prior for these parameters. Minimally informative priors are placed on all other unknown parameters.

Pattern-mixture models for the primary outcome (PTSD symptom severity), health-related quality of life (HRQOL) and the cost-effectiveness analysis (CEA) were fitted using the WinBUGS software.[3] To improve the mixing of the MCMC chains the random effects have not been hierarchically centred. For the CEA, the primary analysis is followed and separate models are used for the QALYs and costs. The personal health services costs which have missing values, are modelled conditionally on the fully observed costs (intervention and hospital costs) and assumed to be MAR.

Elicitation tool

The purpose of the elicitation is to quantify differences in the mean scores relating to two important outcomes (PTSD symptom severity and HRQoL) between patients who did and did not complete questionnaires at 6 months. Accordingly, two versions of the POPPI elicitation tool, which we will refer to as the PSS version and the HrQoL version, were created using Shiny, a web application framework within a widely used statistical software, R.[4,5]

Our starting point was the elicitation tool developed for the IMPROVE trial.[2] This allowed experts to represent their opinion as a normal distribution, using two sliders to control its shape: one to position the value they considered most likely (mode) and the other to indicate their uncertainty about this value (sd). For POPPI, we adopted a similar approach but allowed greater flexibility in the distribution by using an additional slider so that the uncertainty on each side of the mode was controlled separately. The underlying distribution is a (truncated) split normal distribution controlled by 3 sliders: mode, left sd and right sd.

The patient population for the POPPI trial is heterogeneous, with outcomes affected by patient characteristics including age, sex and level of anxiety after regaining capacity in the

ICU. To allow for this, the elicitation tool incorporated questions about 3 types of patients, characterized as A) female, younger and anxious in unit; B) male, older and anxious in unit and C) male, younger and not anxious in unit.

For each patient type, the expert was asked to think about a group of 100 patients, all with the same specified characteristics, who were included in the POPPI trial, received usual care in the unit and returned a completed questionnaire. The expert was shown the outcome scale with our best estimate of the average score based on early data for this group of patients from the cluster-RCT baseline period, marked by a line and our uncertainty about this estimate shown by a shaded area. They were then asked for their views about the average score for two more groups of 100 patients: I) similar to the original group, except they did not return their questionnaire and II) similar to the original group, except they received the preventive, complex psychological intervention and did not return their questionnaire. At this stage they were provided with graphical feedback showing the difference/overlap in their views about the two groups (I and II) and asked to revise their answers if this seemed unreasonable. To allow for the possibility that the elicited values for the non-responding usual care and intervention patients are related, we also asked the expert to reconsider their views about the average score for the intervention patients (I) in the light of new information about the usual care patients (II). Eliciting this third distribution provided sufficient information to formulate a joint distribution for the sensitivity parameters for each group allowing correlation between them.

The elicitation tool also included free text questions asking the expert about the basis of their views, in terms of what they have observed about patients and any other factors. These were to provide useful context and to facilitate an assessment of the expert's responses to the main questions.

PSS-SR (PTSD system severity) scores can take values from 0 to 51, with 0 indicating no symptoms. For interpretability, in the PSS version the expert is presented with a continuous scale of symptom severity starting with none and ranges marked as 'mild', 'moderate', 'moderate to severe' and 'severe' rather than numerical values. These ranges and their link to the numerical scale are based on published literature.

The EQ-5D-5L (HrQoL) used a numeric scale from -28 to 100 (the original scale for the EQ-5D-5L utility score multiplied by 100 for ease of completion), anchored at 0 (death) and 100 (perfect health). An arrow was marked on the scale, linked to the quality of life score calculated from specific answers to the 5 contributing questions: mobility, self-care, usual activities, pain or discomfort and anxiety or depression. All the answers are originally set to 'moderate', but the expert is invited to select other combinations of answers from the 5 available levels of severity using drop-down menus, to see how the quality of life score changes.

Internal and external piloting was carried out prior to use in the POPPI cluster-RCT.

Selection of experts and conduct of the elicitation

To identify participants to take part in the study, the chief investigator (KR) sent a call for expressions of interest via email to the medical directors of all adult, general ICUs participating in the CMP. This call was also sent to Principal Investigators of recent/ongoing ICU trials. All contacts were identified from a database maintained by ICNARC. The recipients were asked to identify the person most involved/interested in long-term follow-up of patients at their unit and to provide their contact details to ICNARC.

Those identified as having an interest in this area were then contacted via email, by the chief investigator (KR), to confirm whether they would be interested in participating in the study. Potential participants were told that they would be offered a £20 Amazon gift voucher as a thank you for their participation. This approach resulted in a final sample of 113 individuals, of which 57 were randomly allocated to receive the PSS version of the elicitation questionnaire, and the other 56, the QoL version.

Participants were sent a link to the relevant questionnaire, along with the participant information sheet, in early December 2017, with reminder emails sent at one week and four weeks. Consent was taken electronically using the on-line tool.

Conversion of expert information into informative priors

The elicited information was independently examined by two statisticians (AM and DHa) to identify experts who had provided 'usable' responses (usable experts) and of those, the subgroup in whom we have 'high confidence' (high confidence experts). The criteria for the usable group were designed to identify any experts who had clearly misunderstood the task. Inclusion in the high confidence group required consistency and a high level of engagement with the elicitation exercise. The criteria were based on a combination of the quantitative and qualitative responses and were predefined but operationalized retrospectively. The categorizations of AM and DHa were compared, and discrepancies resolved through discussion.

To fully explore the sensitivity of the trial results to a range of expert opinion, we formulated two pooled priors (usable experts and high confidence experts) and also used two individual priors (the 'most sceptical' expert and the 'most enthusiastic' expert from the high confidence group). The pooled priors are an average of the individual distributions of all the experts in the group, based on linear pooling with equal weights,[6] and specified as a mixture of bivariate split normal distributions.

Elicited information was collected from three subgroups of patients (A, B and C), based on three stratifying variables: age, sex and anxiety in the unit. Eliciting from the full eight subgroups defined by these variables was considered impractical and would have overburdened the experts. Individuals in the five non-elicited sub-groups were assigned a prior or mixture of priors from the elicited sub-groups, assuming a priori that the observed differences in the distributions of the sub-groups would carry through to differences in the priors. The same allocation was reasonable for both outcomes.

Analysis

All the models were run with two chains initialized using diffuse starting values to produce a sample of 100,000 after convergence for posterior inference. Convergence is assumed if the Gelman-Rubin convergence statistic[7] for individual parameters is less than 1.05 and a visual inspection of the trace plot for each parameter is satisfactory. The results from the Bayesian MNAR sensitivity analyses are compared with Bayesian MAR and complete case analysis.

eResults

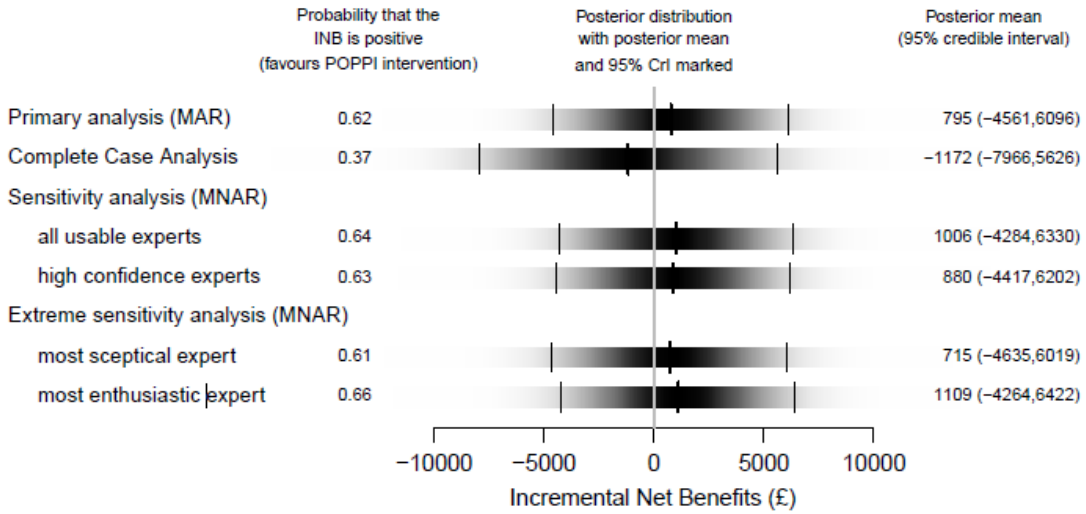
Cost-effectiveness analysis

The cost-effectiveness outcomes at six-months are presented in eTable 20. The mean (SD) cost of delivering the preventive, complex psychological intervention was £140 (£128) [US $199 ($182)] per patient out of a total six-month cost of £30,100 (£25,403) [US $42,817 ($36,135)] (eTable 21 to 23). The incremental cost at six months was −£755 (95% CI −£5,883 to £4,374) [US −$1,074 (95% CI −$8,368 to $6,222)]. Mean EQ-5D utility scores were similar between treatment groups.

On average, the intervention decreased costs and slightly improved QALYs, leading to positive INB at six months (£835 [US $1188]), but the statistical uncertainty surrounding this result was substantial (95% CI −£4,322 to £5,992) [US −$6,148 to $8,523] (eFigure 8). A higher mortality was observed at intervention ICUs during the baseline period (eFigure 9 and eTable 24). The net effect was a small favourable effect on QALYs (mean 0.004; 95% CI −0.023 to 0.031).

The probability that the preventive, complex psychological intervention is more cost-effective than usual care at six months is about 60% when willingness to pay for a QALY gain is zero, and this probability is never greater than 65%, irrespective of how much society is willing to pay for a QALY gain (

eFigure 10. Sensitivity Analysis That Reports the Incremental Net Benefit (at £20,000 per QALY) Within Six Months Post-recruitment According to Alternative Missing Not at Random Assumptions Compared to the Primary and Complete Case Analyses



MAR denotes missing at random; and MNAR missing not at random.

Each shaded rectangular strip shows the full posterior distribution. The darkness at a point is proportional to the probability density, such that the strip is darkest at the maximum density and fades into the background at the minimum density. The posterior mean and 95% credible interval are marked.

The INB is calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 and subtracting from this value the incremental cost.

eFigure 11). These results were similar across all subgroups, and when alternative assumptions, including using expert opinion, were made in sensitivity analyses (eFigure 12 and eFigure 13 and eTable 25).

When extrapolated to lifetime, the INB was £4,158 ($5,915) with wide 95% CI that again included zero (eTable 26) and the probability of the preventive, complex psychological intervention being cost-effective is around 70% at the NICE recommended threshold (eFigure 14).

Expert elicitation exercise

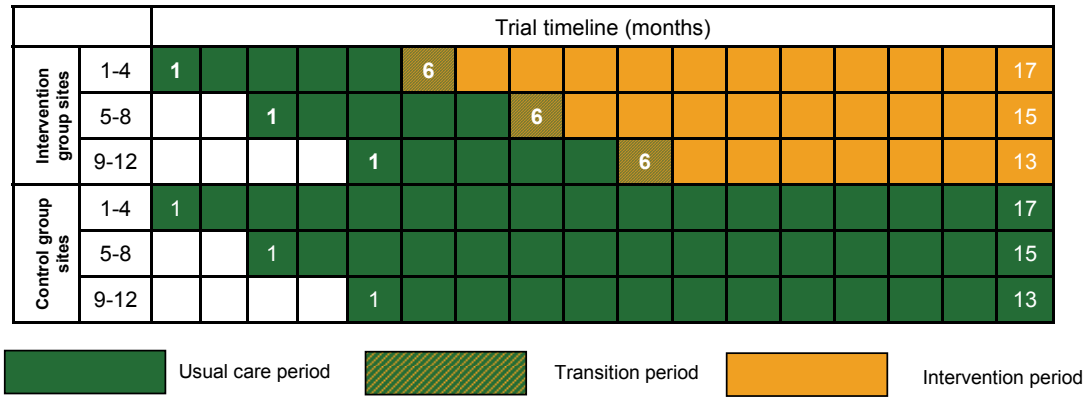
Thirty-one experts completed the PSS-SR version of the elicitation tool, of which 29 were classified as usable and 15 high confidence. For the HrQoL version, 37 responses were received (30 usable and eight high confidence). Across both questionnaires, of the usable experts, 58% were medical doctors and 22% clinical nurses, 73% have been in their current role for over 10 years and 88% have work that involves following-up patients in person after intensive care.

eTable 18 and eTable 19 summarize the elicitation responses across all usable experts for the PSS-SR and HrQoL scores respectively. Overall, for patients receiving usual care, the elicited average PSS-SR scores were higher for patients who did not return their questionnaire compared with the corresponding average from the observed data for all three patient sub-groups. For patients with missing PSS-SR scores, the elicited values were higher for those receiving usual care versus the intervention for all subgroups. The HrQoL scores show the same direction of change (higher scores are a better outcome for HrQoL, whereas a lower score is a better outcome for PSS-SR), but there is more variation in the magnitude between the patient types. For both PSS-SR and HrQoL there is a wide diversity in the elicited scores across experts, as indicated by the standard deviations.

The results of the sensitivity analysis compared to the primary analysis and complete case analysis are summarized in eFigure 6, 7 and 10 for the primary treatment effect (PSS-SR), HrQoL and the INB, valuing QALY at £20,000 per QALY. These show (1) the posterior probability that the outcome favors the preventive, complex psychological intervention, and (2) the posterior distribution of the treatment effect (interaction between treatment group and time period)/INB. The full posterior distribution is shown as a density strip,[1] where the darkness at a point is proportional to the probability density. The results from the sensitivity analysis are broadly similar to the primary analysis in terms of point estimates and uncertainty about these, with little difference between those based on all usable experts versus the smaller high confidence group. The extreme individual priors provide greater differences, in particular for the primary outcome, where the probability that the mean PSS-SR score is lower for the preventive, complex psychological intervention is 94% and 43% for the ‘most enthusiastic’ expert and the ‘most sceptical’ expert respectively.

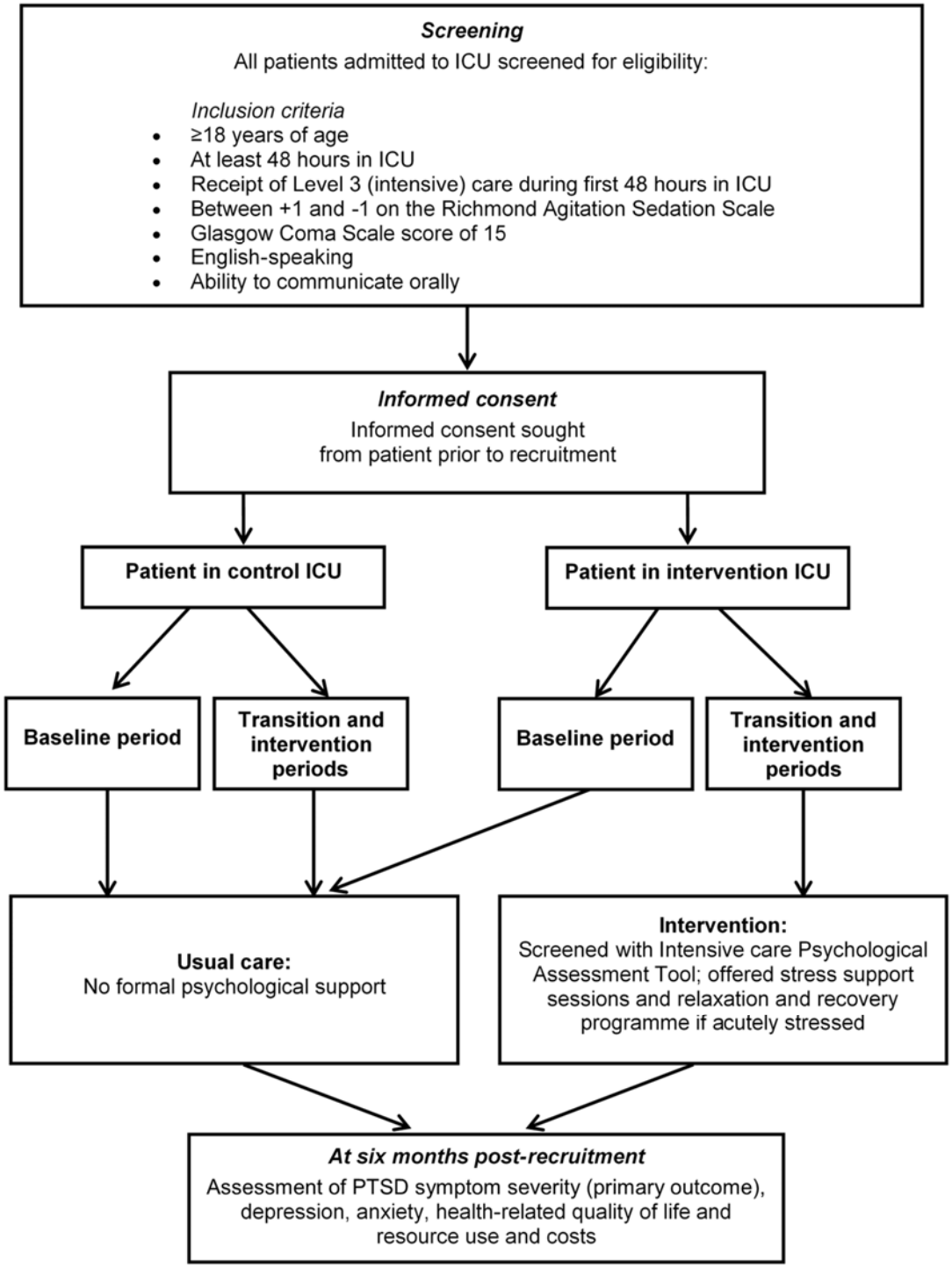
Supplementary Figures

eFigure 1. POPPI Cluster-RCT Schedule



The POPPI cluster-RCT recruited patients over a 17-month period. All ICUs commenced delivering usual care, during a baseline period of data collection. ICUs randomized to the intervention group then received training and began roll-out of the intervention during a transition period in month 6 and then continued to deliver the preventive, complex psychological intervention until the end of the recruitment period. Control group ICUs delivered usual care throughout.

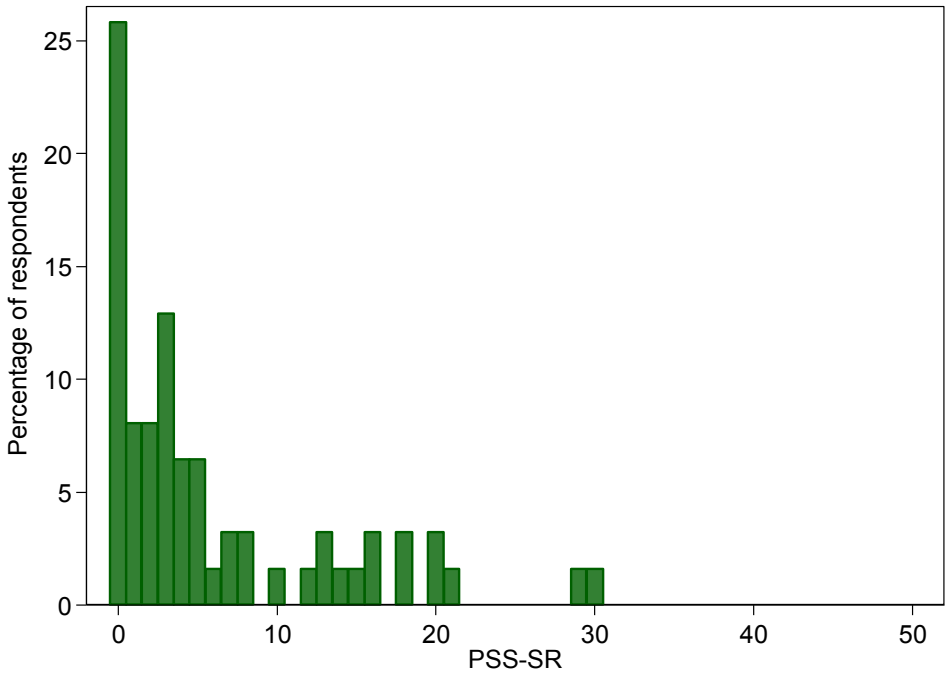
eFigure 2. POPPI Cluster-RCT Patient Flow



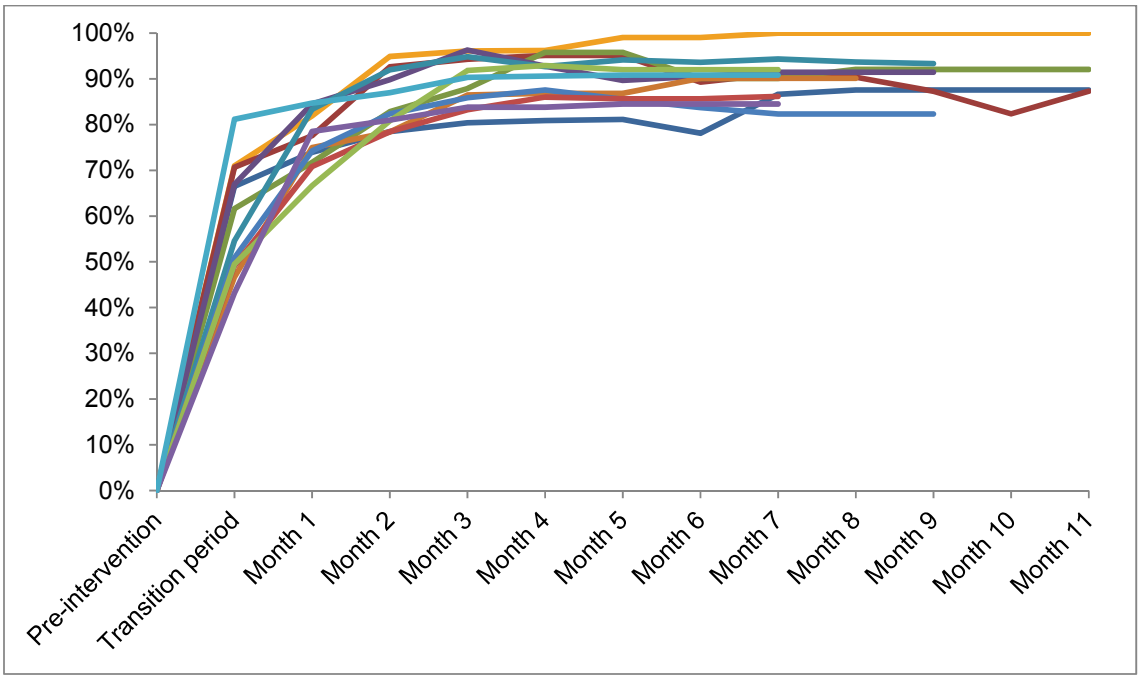
PTSD denotes Post-Traumatic Stress Disorder.

Presents the flow of patients through the POPPI cluster-RCT; from screening, informed consent, treatment allocation through to follow-up for outcomes at six-months post-recruitment.

eFigure 3. Histogram of PSS-SR Scores (n=62) From the POPPI RCT Processes and Procedures Study

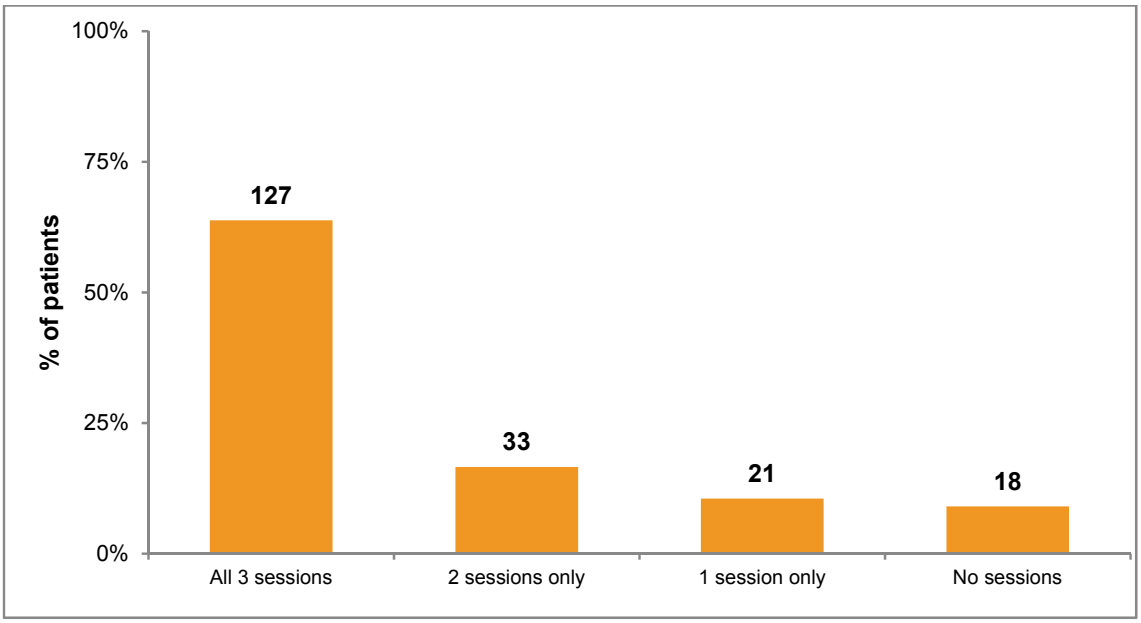


eFigure 4. Monthly POPPI Online Training Uptake at Each Intervention ICU



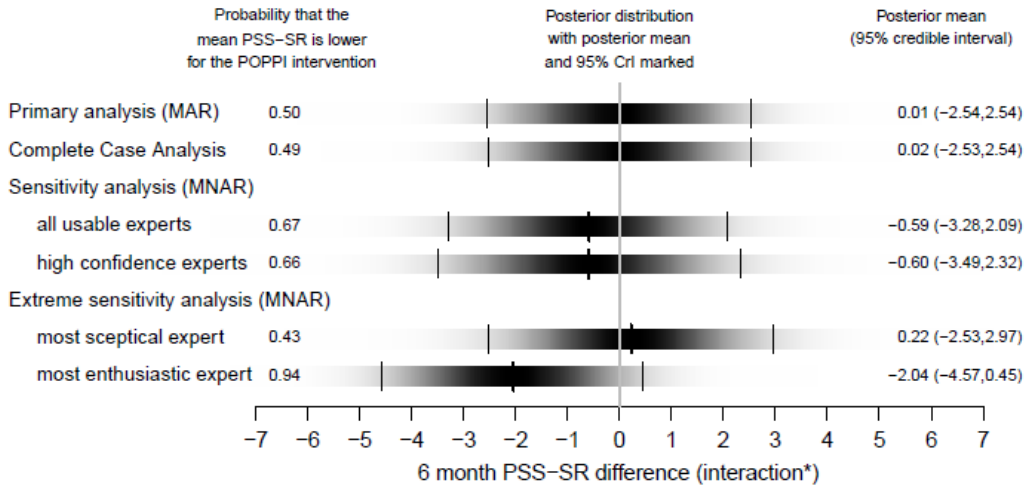
The Monthly POPPI online training uptake at each intervention ICU (N=12) from transition month until end of intervention period. Each line represents the percentage of staff having completed the POPPI online training out of all ICU staff at each intervention ICU.

eFigure 5. Number of Stress Support Sessions Received by Patients



The number of stress support sessions received by patients screened as high-risk (acutely stressed) (IPAT score ≥7 points) (n=199).

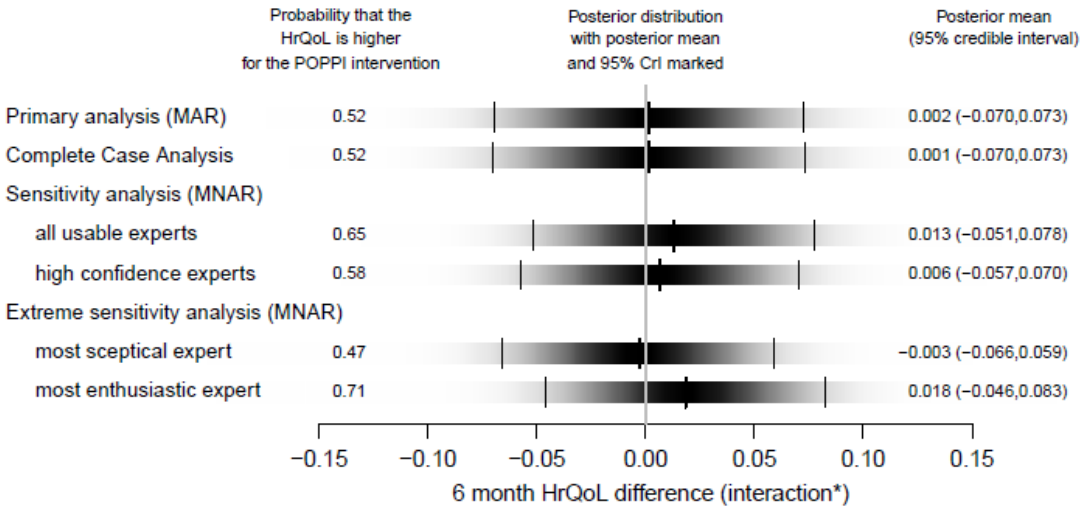
eFigure 6. Sensitivity Analysis That Reports the Primary Treatment Effect Estimate at Six-Months According to Alternative Missing Not at Random Assumptions Compared to the Primary and Complete Case Analyses



* interaction between treatment group and time period.

Each shaded rectangular strip shows the full posterior distribution. The darkness at a point is proportional to the probability density, such that the strip is darkest at the maximum density and fades into the background at the minimum density. The posterior mean and 95% credible interval are marked. For PSS-SR, negative differences favor preventive, complex psychological intervention.

eFigure 7. Sensitivity Analysis That Reports the Treatment Effect on Health-Related Quality of Life Score at Six Months According to Alternative Missing Not at Random Assumptions Compared to the Primary and Complete Case Analyses

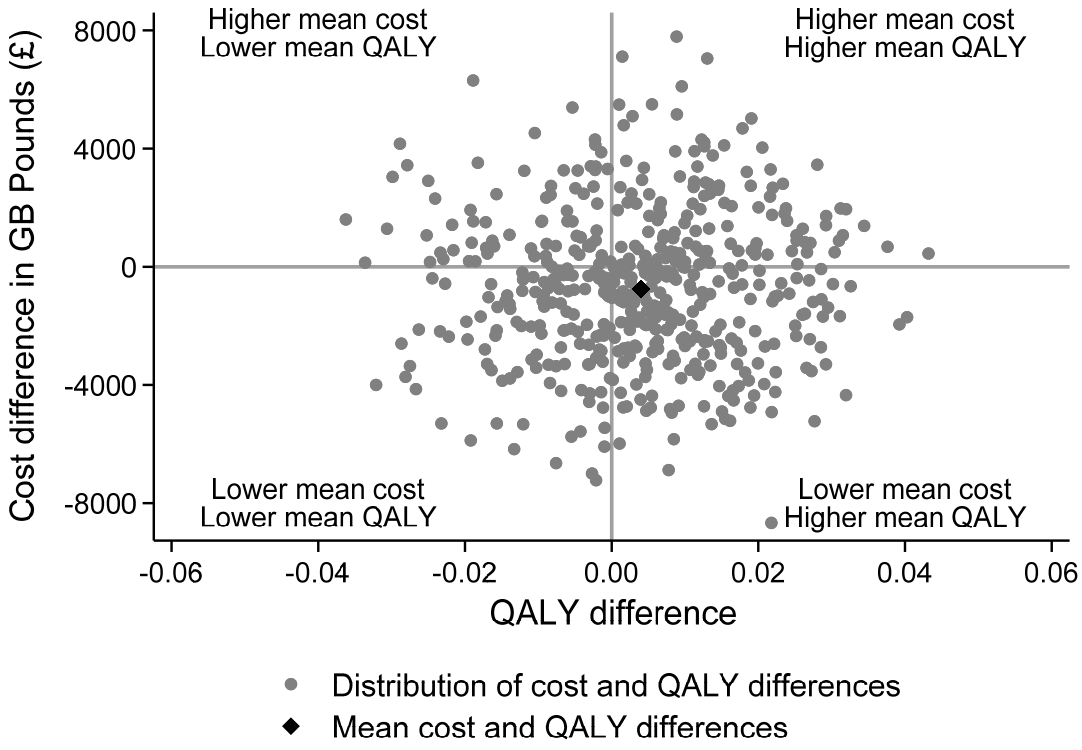


* interaction between treatment group and time period.

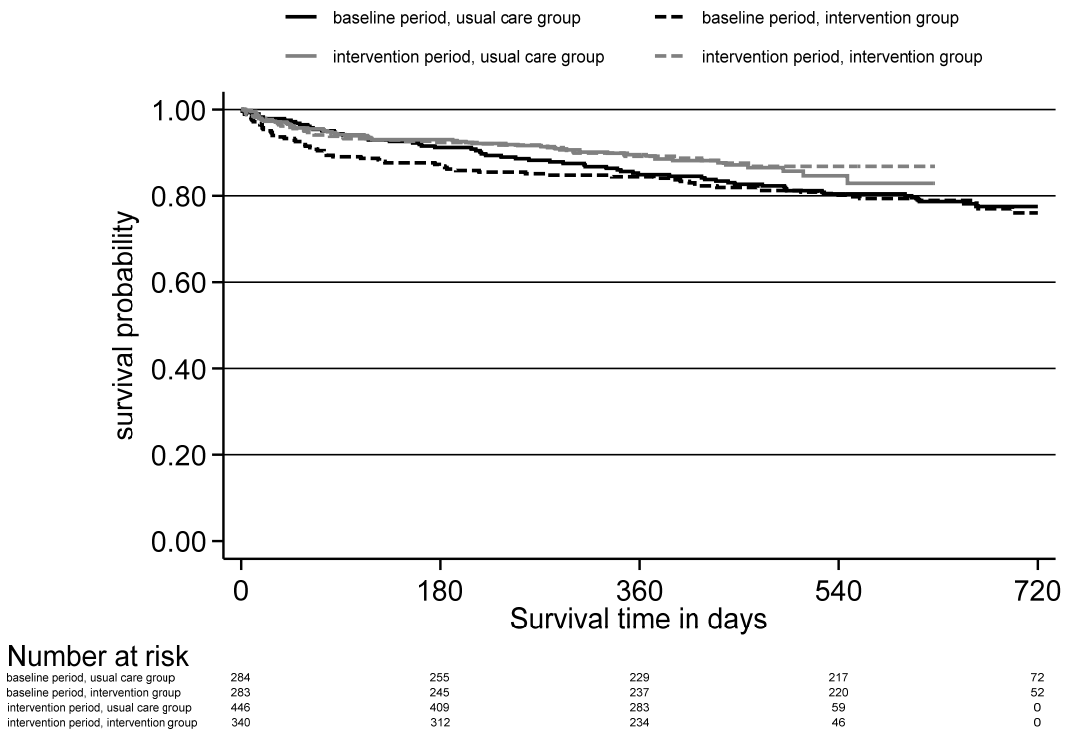
MAR denotes missing at random; and MNAR missing not at random.

Each shaded rectangular strip shows the full posterior distribution. The darkness at a point is proportional to the probability density, such that the strip is darkest at the maximum density and fades into the background at the minimum density. The posterior mean and 95% credible interval are marked. For health-related quality of life positive differences favour the preventive, complex psychological intervention.

eFigure 8. Mean Cost and QALY Differences at Six Months; Distribution for the Preventive, Complex Psychological Intervention Versus Usual Care

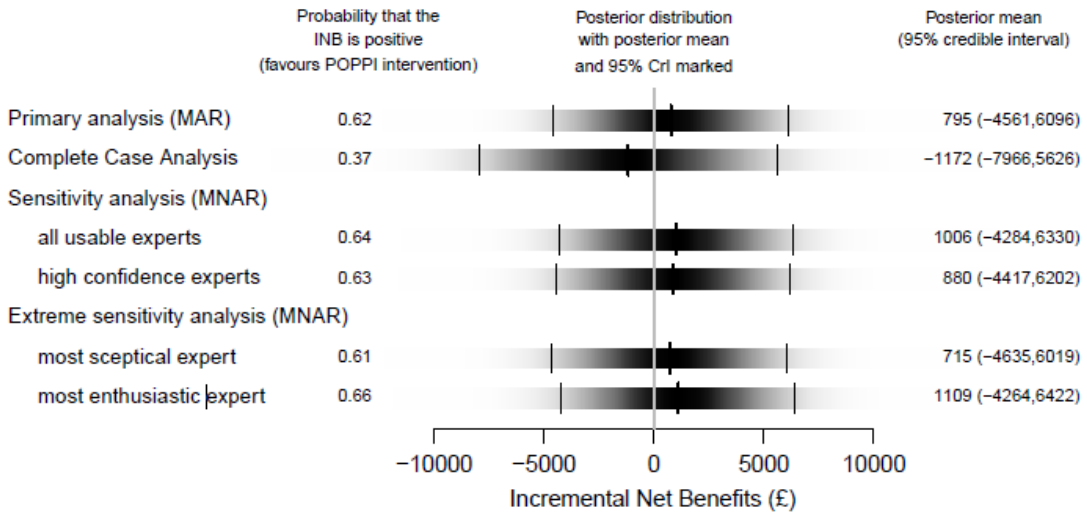


eFigure 9. Kaplan-Meier Survival Curves



Reports the Kaplan-Meier survival curves for each treatment group and time period.

eFigure 10. Sensitivity Analysis That Reports the Incremental Net Benefit (at £20,000 per QALY) Within Six Months Post-recruitment According to Alternative Missing Not at Random Assumptions Compared to the Primary and Complete Case Analyses

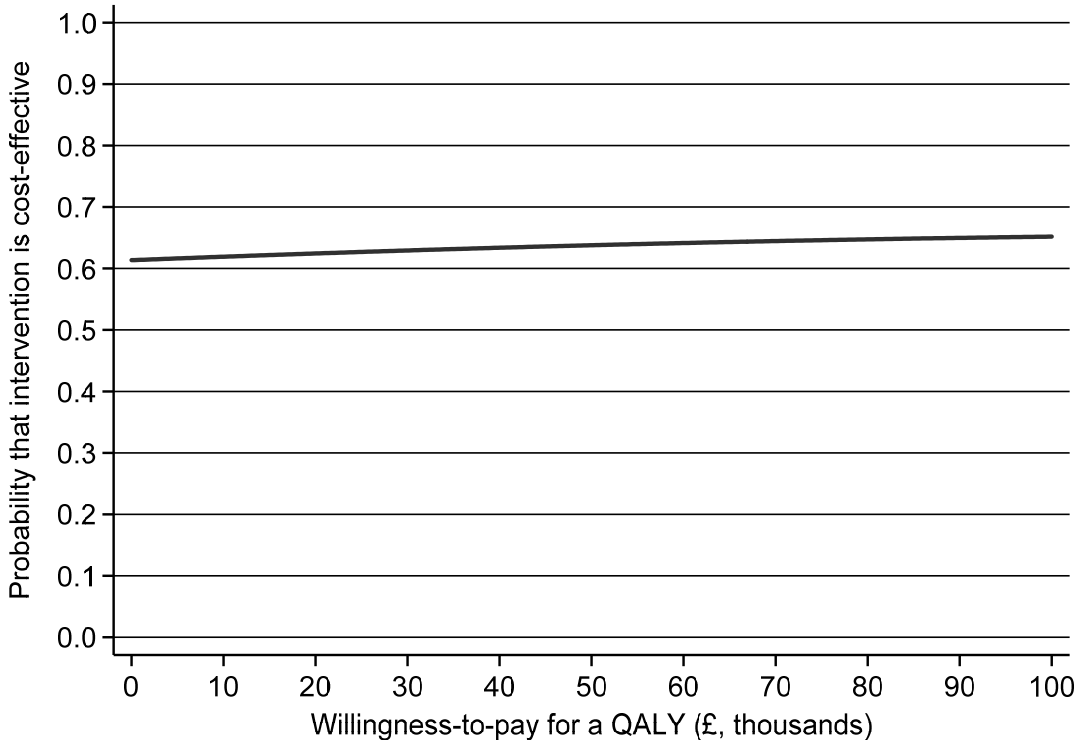


MAR denotes missing at random; and MNAR missing not at random.

Each shaded rectangular strip shows the full posterior distribution. The darkness at a point is proportional to the probability density, such that the strip is darkest at the maximum density and fades into the background at the minimum density. The posterior mean and 95% credible interval are marked.

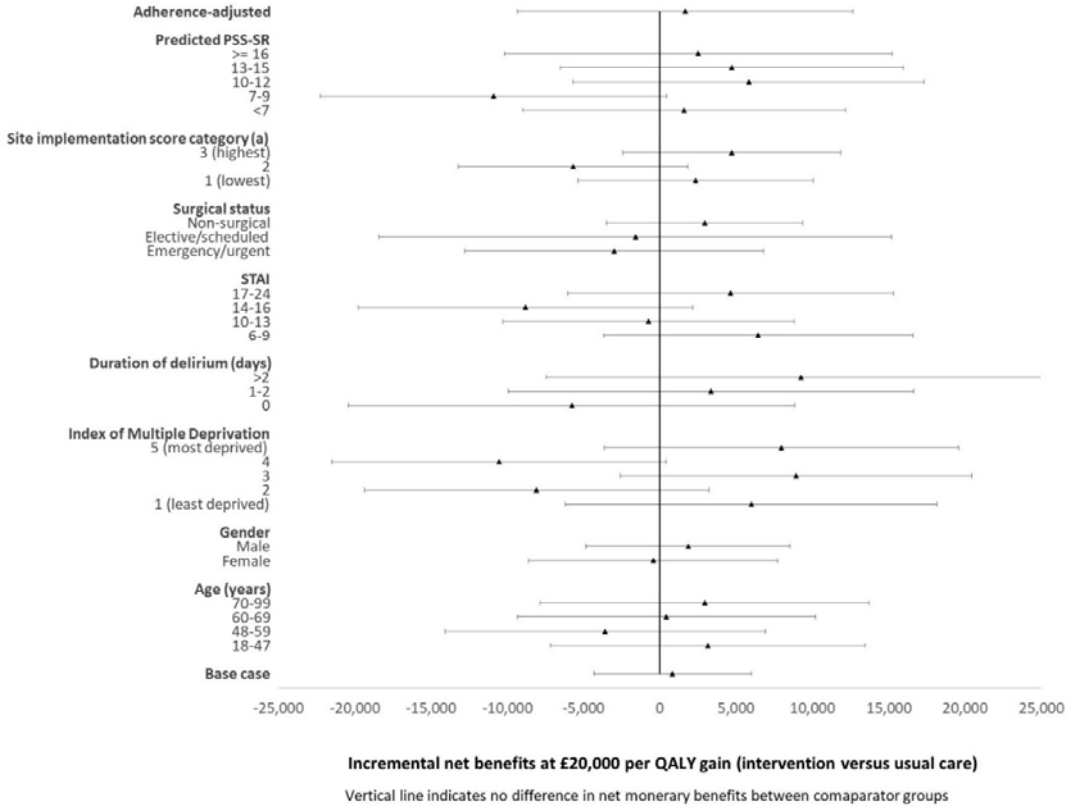
The INB is calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 and subtracting from this value the incremental cost.

eFigure 11. Cost-effectiveness Acceptability Curve – At Six-Months



Reports the probability that the preventive, complex psychological intervention is cost-effective at six months post-recruitment, at alternative levels of willingness to pay for a QALY gain.

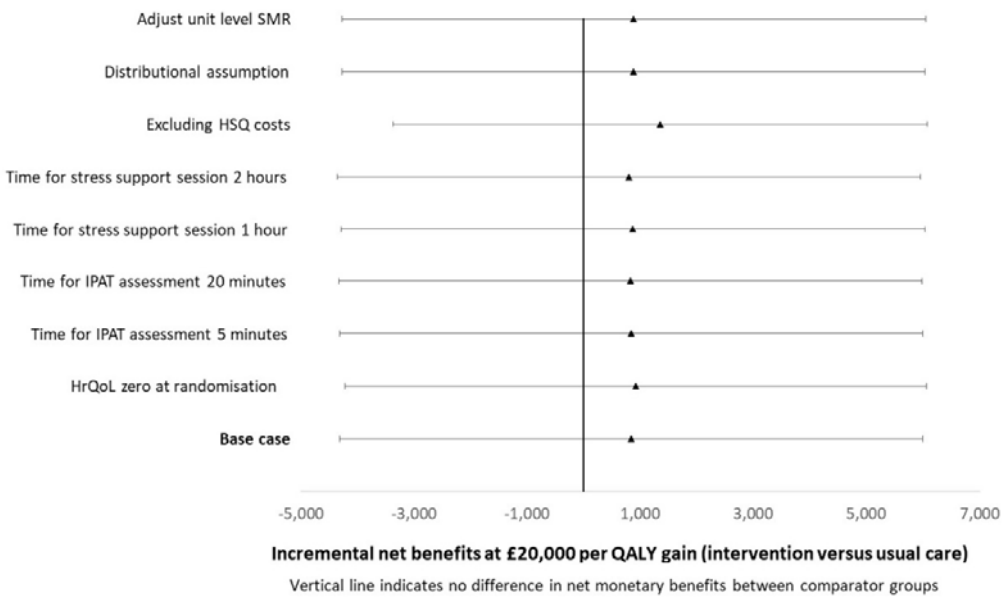
eFigure 12. Subgroup Analyses for Incremental Net Benefit at Six Months at £20,000 per QALY



Reports the mean with 95% confidence interval of the incremental net benefit (at £20,000 per QALY) for the sub-groups, compared with the base case. The INB is calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 and subtracting from this value the incremental cost. The solid vertical line indicates no difference in net monetary benefits between the treatment groups.

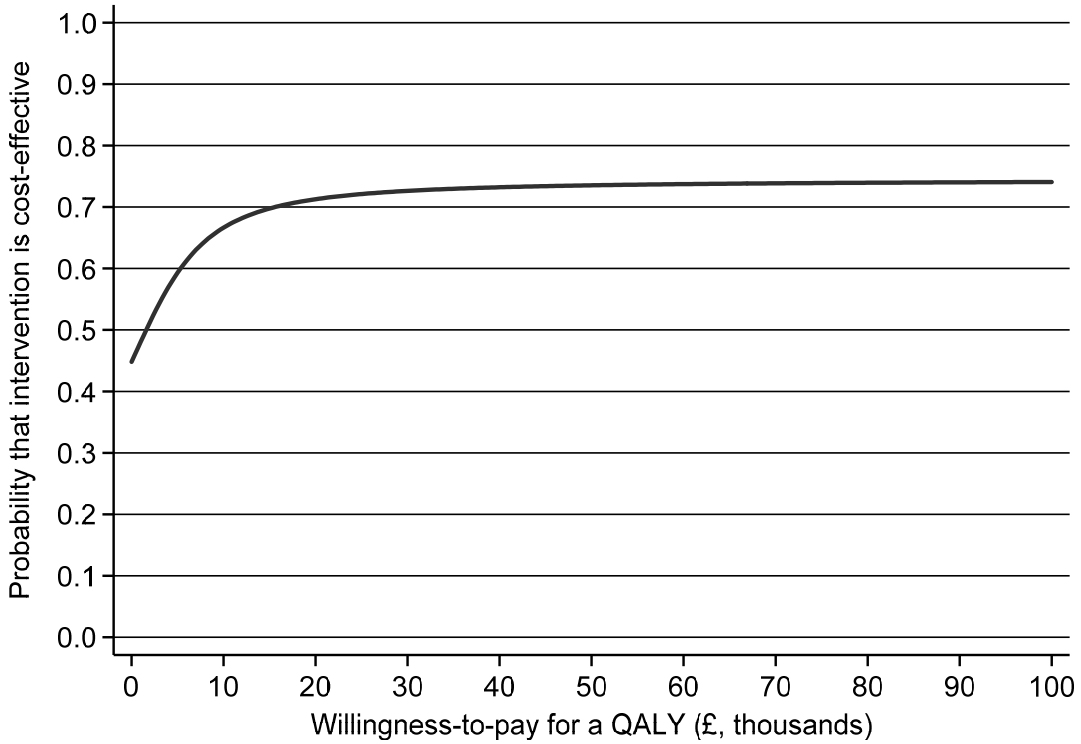
As a post-hoc sub-group analysis, the model was refitted according to the natural logarithm of the standardised mortality ratio (ratio of observed deaths to predicted deaths from the $ICNARC_{H\text{-}2015}$ risk prediction model[29]) from the period April 2014 to March 2015. All other sub-groups were pre-specified in the statistical and health economic analysis plan.

eFigure 13. Sensitivity Analyses for the Cost-effectiveness Analysis at Six Months



Reports the mean with 95% confidence interval of the incremental net benefit (at £20,000 per QALY) according to alternative assumptions, compared with the base case. The INB is calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 ($28,450) and subtracting from this value the incremental cost. The solid vertical line indicates no difference in net monetary benefits between the treatment groups.

eFigure 14. Cost-effectiveness Acceptability Curve – Lifetime Extrapolation



Reports the probability that the preventive, complex psychological intervention is cost-effective when extrapolated to the lifetime at alternative levels of willingness to pay for a QALY gain.

Supplementary Tables

eTable 1. PSS-SR Item Responses (n=62) From the POPPI RCT Processes and Procedures Study

	How often has each problem bothered you in the past month?	No response	Not at all	Once per week or less	2–4 times per week	5 or more times per week	Mean (SD)	Item to scale correlation	Cronbach's alpha if removed	Factor loading in confirmatory PCA
1	Have you had upsetting thoughts or images about your time in intensive care that came into your head when you didn't want them to?	1 (1.6)	52 (85.2)	7 (11.5)	2 (3.3)	0 (0)	0.18 (0.47)	0.64	0.89	0.71
2	Have you had bad dreams or nightmares about your time in intensive care?	0 (0)	52 (83.9)	7 (11.3)	3 (4.8)	0 (0)	0.21 (0.52)	0.59	0.89	0.65
3	Have you relived your time in intensive care, acting or feeling as if it were happening again?	0 (0)	48 (77.4)	12 (19.4)	2 (3.2)	0 (0)	0.26 (0.51)	0.75	0.89	0.77
4	Have you felt emotionally upset when you were reminded of your time in intensive care (e.g. feeling scared, angry, sad, guilty)?	0 (0)	45 (72.6)	15 (24.2)	2 (3.2)	0 (0)	0.31 (0.53)	0.56	0.89	0.63
5	Have you had physical reactions when you remember your time in intensive care (e.g. breaking into a sweat, heart beating fast)?	1 (1.6)	54 (88.5)	5 (8.2)	2 (3.3)	0 (0)	0.15 (0.44)	0.55	0.89	0.56
6	Have you tried not to think, talk or have feelings about your time in intensive care?	0 (0)	52 (83.9)	9 (14.5)	1 (1.6)	0 (0)	0.18 (0.43)	0.47	0.90	0.52
7	Have you tried to avoid activities, people or places that remind you of your time in intensive care?	0 (0)	59 (95.2)	2 (3.2)	1 (1.6)	0 (0)	0.06 (0.31)	0.40	0.90	0.46
8	Have you found that you were not able to remember an important part of your time in intensive care?	3 (4.8)	44 (74.6)	11 (18.6)	2 (3.4)	2 (3.4)	0.36 (0.71)	0.63	0.89	0.62
9	Have you had much less interest in important activities?	0 (0)	48 (77.4)	5 (8.1)	7 (11.3)	2 (3.2)	0.40 (0.82)	0.80	0.88	0.78
10	Have you felt distant or cut off from people around you?	0 (0)	47 (75.8)	6 (9.7)	5 (8.1)	4 (6.5)	0.45 (0.90)	0.83	0.88	0.79

	How often has each problem bothered you in the past month?	No response	Not at all	Once per week or less	2–4 times per week	5 or more times per week	Mean (SD)	Item to scale correlation	Cronbach's alpha if removed	Factor loading in confirmatory PCA
11	Have you felt emotionally numb (e.g. unable to cry, have loving feelings)?	0 (0)	50 (80.6)	6 (9.7)	5 (8.1)	1 (1.6)	0.31 (0.69)	0.71	0.89	0.70
12	Have you felt as if your future plans or hopes would not come true?	0 (0)	41 (66.1)	9 (14.5)	7 (11.3)	5 (8.1)	0.61 (0.98)	0.84	0.88	0.84
13	Have you had trouble falling or staying asleep?	0 (0)	38 (61.3)	7 (11.3)	8 (12.9)	9 (14.5)	0.81 (1.14)	0.63	0.90	0.56
14	Have you felt irritable or had fits of anger?	0 (0)	38 (61.3)	15 (24.2)	8 (12.9)	1 (1.6)	0.55 (0.78)	0.59	0.89	0.53
15	Have you had trouble concentrating (e.g. forgetting what you read, losing track of a story on television)?	1 (1.6)	38 (62.3)	6 (9.8)	13 (21.3)	4 (6.6)	0.72 (1.02)	0.56	0.90	0.47
16	Have you been too alert (e.g. checking to see who is around you, not being comfortable with your back to a door)?	1 (16)	54 (88.5)	5 (8.2)	1 (1.6)	1 (1.6)	0.16 (0.52)	0.42	0.90	0.44
17	Have you been jumpy or easily startled (e.g. when someone walks up behind you)?	1 (16)	45 (73.8)	10 (16.4)	4 (6.6)	2 (3.3)	0.39 (0.76)	0.65	0.89	0.66

PCA, principal components analysis; SD, standard deviation. No items had non-response > 10%; Red = possible floor effect (>70% of responses at lowest value), no items had possible ceiling effects; Amber = borderline for lack of internal consistency (item to scale correlation 0.4-0.5), no items had item to scale correlation < 0.4; Green = possible redundancy (item to scale correlation > 0.8); There were no items for which removal resulted in an increase in Cronbach's alpha; Blue = borderline for construct validity (factor loading 0.4-0.5), no items had factor loading <0.4.

eTable 2. PSS-SR Total Score (n=62) From the POPPI RCT Processes and Procedures Study

Measure	Floor, n (%)	Ceiling, n (%)	Mean (SD)	Median (IQR)	Range	Cronbach's alpha (95% CI)
PSS-SR total score	16 (25.8)	0 (0)	6.1 (7.5)	3 (0, 8)	(0, 30)	0.90 (0.84, 0.95)

CI, confidence interval; IQR, interquartile range; SD, standard deviation.

eTable 3. Resource Use Associated With the Preventive, Complex Psychological Intervention

Elements of intervention	Content /delivery of element	Action	Level of resource use
Element one: Promoting a therapeutic environment in the ICU	Delivery of online training	Take course (including test), coordinate delivery in unit	Absorbed in the NHS mandatory training cost
	Creating a therapeutic environment	Seminars/teaching, core groups meetings/activities, individual activities/actions	
Element two: Three stress support sessions for patients screened as acutely stressed	IPAT assessment	Screening patient with questionnaire	10 minutes of bed side nurse's (band 5) time
	Delivery of stress support sessions	Prepare for stress support sessions Carry out stress support sessions Write up stress support sessions	1.5 hours of ICU nurse's (band 7) time
	Three-day training course	Attending the training course Delivering the training course Other costs	Per patient costs calculated from the actual training costs incurred
	Debriefing and support	Trainee/clinical supervisor's meeting time	0.5 hours per month of 3 ICU nurses & a trainer (band 8) per ICU
Element three: Relaxation and recovery programme for patients screened as acutely stressed	Relaxation and recovery programme	Delivering the programme via tablet computer app, DVD and booklet	Absorbed in the NHS routine cost

NHS denotes National Health Service, IPAT Intensive care Psychological Assessment Tool; and DVD digital video disc.

eTable 4. Unit Costs in GB Pounds (£)

Items	Unit costs	Source
Staff time for delivering the preventive, complex psychological intervention		
Hospital nurse – band 5 (per hour)	35	PSSRU
Hospital nurse (ICU nurse to lead intervention) – band 7 (per hour)	53	PSSRU
Health psychologist – band 8 (per hour)	60	PSSRU
Hospital costs (bed day)		
Critical care bed day – 0 organ supported	759	NHS Reference Costs
Critical care bed day – 1 organ supported	1,031	NHS Reference Costs
Critical care bed day – 2 organs supported	1,399	NHS Reference Costs
Critical care bed day – 3 organs supported	1,619	NHS Reference Costs
Critical care bed day – 4 organs supported	1,794	NHS Reference Costs
Critical care bed day – 5 organs supported	1,977	NHS Reference Costs
Critical care bed day – 6+ organs supported	2,274	NHS Reference Costs
General Medical bed day	298	NHS Reference Costs
Outpatient & community health services		
Hospital outpatient	135	PSSRU
GP practice visit (per visit)	36	PSSRU
GP home visit (per visit)	118	PSSRU
GP nurse visit†	11	PSSRU
GP nurse home visit†	18	PSSRU
Hospital nurse†	9	PSSRU
Health visitor†	8	PSSRU
Health visitor home visit†	18	PSSRU
Occupational therapist†	8	PSSRU
Physiotherapist†	8	PSSRU
Psychiatrist†	16	PSSRU
Psychologist†	13	PSSRU
Counsellor†	8	PSSRU
Speech and language therapist†	8	PSSRU

PSSRU denotes Personal Social Services Research Unit; and NHS National Health Service.

† 15 minutes of consultation time.

eTable 5. Variables Considered for Multiple Imputation and Form of Imputation Model

Variable	Missing values, n (%)	Imputation model
ICU level covariates		
Teaching status of hospital	0 (0)	None required
Number of beds in the ICU	0 (0)	None required
Number of ICU admissions receiving Level 3 care staying at least 48 hours	0 (0)	None required
Allocated treatment group	0 (0)	None required
Patient level covariates		
Time period	0 (0)	None required
Age	0 (0)	None required
Gender	0 (0)	None required
Ethnicity	0 (0)	None required (not stated retained as separate category)
IMD 2015	3 (<0.1)	Singly imputed to category 3 (middle quintile)
Pre-existing anxiety/depression	0 (0)	None required
Elective surgical admission	0 (0)	None required
ICNARC Physiology Score	0 (0)	None required
NEWS	0 (0)	None required
HrQoL health thermometer score	1 (<0.1)	Singly imputed to mean
STAI-6	2 (<0.1)	Missing items singly imputed to mode
Duration of stay in the ICU	0 (0)	None required
Number of days of delirium	0 (0)	None required (not assessed retained as separate category)
Number of days receiving sedatives/anxiolytics/anaesthetics	0 (0)	None required
Number of days receiving sleep medications	0 (0)	None required
Receipt of benzodiazepines	0 (0)	None required

Variable	Missing values, n (%)	Imputation model
Patient level covariates		
Number of days receiving antipsychotics	0 (0)	None required
Number of days receiving vasoactive agents	0 (0)	None required
Number of days receiving analgesics	0 (0)	None required
Number of days receiving antidepressants	0 (0)	None required
Number of days receiving mechanical ventilation	0 (0)	None required
Duration of stay in hospital following discharge from the ICU	0 (0)	None required
Adherence to intervention	0 (0)	None required
Length of stay in general medical wards	0 (0)	None required
Outcomes and resource use at six months		
Costs of ICU stay	0 (0)	None required
Mortality	0 (0)	None required
PSS-SR	283 (21.4)	Predictive mean matching
HADS anxiety score	303 (22.9)	Predictive mean matching
HADS depression score	302 (22.8)	Predictive mean matching
EQ-5D-5L health utility	302 (22.8)	Predictive mean matching
Health services questionnaire costs	631 (47.7)	Predictive mean matching

IMD denotes Index of Multiple Deprivation; ICNARC Intensive Care National Audit & Research Centre; NEWS National Early Warning Score; HrQoL Health-related Quality of Life; STAI State-Trait Anxiety Inventory; PSS-SR PTSD Symptom Scale – Self Report version; HADS Hospital Anxiety and Depression Scale and EQ-5D-5L European Quality of Life-5 Dimensions five-level questionnaire.

eTable 6. Criteria for Component Adherence Scoring From Process Evaluation

<table>
<tr><td></td><td colspan="4">Component adherence scoring</td></tr>
<tr><td rowspan="2">1. POPPI online training</td><td colspan="2">Dose</td><td colspan="2">Reach</td></tr>
<tr><td colspan="2">Time to achieving 80% uptake:
3 = By end month 1
2 = By end month 2
1 = By end month 3
0 = > 3 months</td><td colspan="2">% Staff completing POPPI online training:
3 = > 90%
2 = 85-89%
1 = 80-84%
0 = < 80%</td></tr>
<tr><td rowspan="2">2. Creation of a therapeutic environment</td><td colspan="4">Fidelity</td></tr>
<tr><td colspan="4">Qualitative interview:
3 = Full adherence
2 = Mostly adhering
1 = Some adherence
0 = Low adherence</td></tr>
<tr><td rowspan="2">3. IPAT assessments and stress support sessions</td><td>Fidelity</td><td>Dose</td><td colspan="2">Reach</td></tr>
<tr><td>Qualitative interview:
3 = Full adherence
2 = Mostly adhering
1 = Some adherence
0 = Low adherence</td><td>% patients receiving ≥ 2 SSS
3 = ≥ 90%
2 = 80-89%
1 = 70-79%
0 = < 70%</td><td>% acutely stressed patients receiving 0 SSS
3 = 0%
2 = 1-10%
1 = 11-20%
0 = > 20%</td><td>% used tablet computer
3 = > 80%
2 = 70-79%
1 = 60-69%
0 = < 60%</td></tr>
<tr><td rowspan="2">4. Relaxation and recovery programme</td><td colspan="4">Reach</td></tr>
<tr><td colspan="4">% patients receiving relaxation and recovery programme to take home (either DVD or booklet given)
3 = 100%
2 = 90-99%
1 = 80-89%
0 = < 80%</td></tr>
<tr><td rowspan="4">Implementation grade (composite score)</td><td>Component 1
(0-6)</td><td>Component 2
(0-3)</td><td>Component 3
(0-12)</td><td>Component 4
(0-3)</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="3">TOTAL SCORE
(0-24)</td><td></td></tr>
<tr><td colspan="3">ICU RANKING (1-12)</td><td></td></tr>
</table>

IPAT denotes Intensive care Psychological Assessment Tool; SSS stress support sessions and; DVD digital video disc.

eTable 7. Representativeness of Participating ICUs, n/N (%)

ICU characteristic	ICUs in POPPI cluster-RCT	ICUs in CMP[a]
	N = 24	N = 191
Type of hospital		
Teaching	8/24 (33.3)	56/191 (29.3)
Non-teaching	16/24 (66.7)	135/191 (70.7)
Region		
North	8/24 (33.3)	55/191 (28.8)
Midlands/East	3/24 (12.5)	35/191 (18.3)
London/South East	2/24 (8.3)	50/191 (26.2)
South West/South Central	9/24 (37.5)	29/191 (15.2)
Wales	1/24 (4.2)	14/191 (7.3)
Northern Ireland	1/24 (4.2)	8/191 (4.2)
Size of unit		
Fewer than 8 beds	2/24 (8.3)	33/191 (17.3)
8 to 11 beds	5/24 (20.8)	68/191 (35.6)
12 to 15 beds	7/24 (29.2)	36/191 (18.8)
16 or more beds	10/24 (41.7)	54/191 (28.3)
Annual admissions		
Fewer than 500 admissions	2/24 (8.3)	47/191 (24.6)
500 to 749 admissions	5/24 (20.8)	62/191 (32.5)
750 to 999 admissions	8/24 (33.3)	41/191 (21.5)
1000 or more admissions	9/24 (37.5)	41/191 (21.5)

[a] Adult, general, ICUs that did not participate in the POPPI cluster-RCT and whom participated in the Case Mix Programme (CMP) between April 2014 and March 2015.

eTable 8. Screening and Recruitment by Treatment Group and Period

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
Screened, N	4257	7290	5051	8106
Not eligible, n/N (% of screened)	3724/4257 (87.5)	6432/7290 (88.2)	4543/5051 (89.9)	7240/8106 (89.3)
Did not meet stable criteria, n [a]	n = 3131	n = 5393	n = 3644	n = 5828
Age <18 years, *n (%)*	19 (0.6)	30 (0.6)	26 (0.7)	59 (1.0)
<48 hours in ICU, *n (%)*	1898 (60.6)	3461 (64.2)	2129 (58.4)	3351 (57.5)
No Level 3 care in first 48 hours in unit, *n (%)*	1089 (34.8)	1652 (30.6)	1407 (38.6)	2253 (38.7)
Not English-speaking, *n (%)*	27 (0.9)	27 (0.5)	45 (1.2)	80 (1.4)
Previously recruited to POPPI, *n (%)*	16 (0.5)	24 (0.4)	16 (0.4)	33 (0.6)
Chronic cognitive impairment*, *n (%)*	49 (1.6)	97 (1.8)	92 (2.5)	113 (1.9)
Psychotic illness*, *n (%)*	76 (2.4)	134 (2.5)	77 (2.1)	134 (2.3)
Chronic PTSD*, *n (%)*	2 (0.1)	23 (0.4)	9 (0.2)	23 (0.4)
Did not meet transient criteria, n [a]	n = 593	n = 1039	n = 899	n = 1412
Not able to communicate orally, *n (%)*	118 (19.9)	214 (20.6)	384 (42.7)	426 (30.2)
RASS not between +1 and −1, *n (%)*	76 (12.8)	158 (15.2)	172 (19.1)	239 (16.9)
GCS score <15, *n (%)*	304 (51.3)	563 (54.2)	543 (60.4)	814 (57.6)
Receiving end of life care, *n (%)*	248 (41.8)	394 (37.9)	289 (32.1)	404 (28.6)
Not able to consent, *n (%)*	81 (13.7)	191 (18.4)	199 (22.1)	323 (22.9)
Potentially eligible, n	n = 533	n = 858	n = 508	n = 866
Missed (e.g. out-of-hours, no staff), *n (%)*	144 (27.0)	247 (28.8)	96 (18.9)	194 (22.4)
Other reasons not recruited, *n (%)*	28 (5.3)	75 (8.7)	32 (6.3)	46 (5.3)
Approached for informed consent, *n (%)*	361 (67.7)	536 (62.5)	380 (74.8)	626 (72.3)
Eligible and approached for consent, n	n = 361	n = 536	n = 380	n = 626
Declined consent, *n (%)*	76 (21.1)	194 (36.2)	95 (25.0)	180 (28.8)
Provided informed consent, *n (%)*	285 (78.9)	342 (63.8)	285 (75.0)	446 (71.2)
Withdrew consent, n (%)	2 (0.7)	2 (0.6)	1 (0.4)	0 (0)
Analysed, n	283	340	284	446

PTSD denotes Post-Traumatic Stress Disorder; RASS Richmond Agitation Sedation Scale; and GCS Glasgow Coma Scale.

[a] The individual numbers and percentages do not add up to the total as patients are included in multiple categories if they met >1 criteria.

eTable 9. Patient Characteristics – Demographics

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Age (years)				
Mean (SD)	59.5 (16.0)	60.4 (15.0)	57.2 (16.2)	57.2 (15.6)
Median (IQR)	62 (48, 72)	62 (51, 70)	60 (46, 69)	58 (47, 68)
Gender, n/N (%)				
Female	115/283 (40.6)	153/340 (45.0)	105/284 (37.0)	178/446 (39.9)
Male	168/283 (59.4)	187/340 (55.0)	179/284 (63.0)	268/446 (60.1)
Ethnicity,[a] n/N (%)				
White	254/283 (89.8)	320/340 (94.1)	264/284 (93.0)	406/446 (91.0)
Mixed	0/283 (0.0)	1/340 (0.3)	1/284 (0.4)	2/446 (0.4)
Asian	4/283 (1.4)	1/340 (0.3)	3/284 (1.1)	6/446 (1.3)
Black	7/283 (2.5)	3/340 (0.9)	1/284 (0.4)	2/446 (0.4)
Other	8/283 (2.8)	2/340 (0.6)	0/284 (0.0)	4/446 (0.9)
Not stated	10/283 (3.5)	13/340 (3.8)	15/284 (5.3)	26/446 (5.8)
Quintile of IMD 2015,[b] n/N (%)				
1 - Least deprived	41/283 (14.5)	57/338 (16.9)	57/284 (20.1)	95/445 (21.3)
2	46/283 (16.3)	74/338 (21.9)	65/284 (22.9)	107/445 (24.0)
3	56/283 (19.8)	76/338 (22.5)	52/284 (18.3)	73/445 (16.4)
4	71/283 (25.1)	73/338 (21.6)	57/284 (20.1)	88/445 (19.8)
5 - Most deprived	69/283 (24.4)	58/338 (17.2)	53/284 (18.7)	82/445 (18.4)
Documented pre-existing anxiety/depression,[c] n/N (%)				
Anxiety	3/283 (1.1)	12/340 (3.5)	4/284 (1.4)	9/446 (2.0)
Depression	19/283 (6.7)	32/340 (9.4)	19/284 (6.7)	33/446 (7.4)
Both	17/283 (6.0)	21/340 (6.2)	8/284 (2.8)	13/446 (2.9)
None	244/283 (86.2)	275/340 (80.9)	253/284 (89.1)	391/446 (87.7)

IQR, interquartile range; SD, standard deviation.

[a] Ethnicity was collected as part of the Case Mix Programme dataset and was ascertained by review of medical records. This field was collected to help describe the demographics of the patient population and assess the representativeness of the sample

[b] The Index of Multiple Deprivation (IMD) 2015 is reported by quintiles, with higher values indicating greater deprivation.

[c] Documented pre-existing anxiety/depression was ascertained by review of medical records.

eTable 10. Patient Characteristics – at ICU Admission

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Elective surgical admission, n/N (%)				
Yes	17/283 (6.0)	20/340 (5.9)	24/284 (8.5)	37/446 (8.3)
No	266/283 (94.0)	320/340 (94.1)	260/284 (91.5)	409/446 (91.7)
ICNARC Physiology Score[a]				
Mean (SD)	21.1 (7.0)	21.0 (7.6)	21.2 (7.1)	21.4 (7.2)
Median (IQR)	21 (16, 26)	20 (16, 25)	21 (16, 25)	21 (17, 26)
APACHE II score[b]				
Mean (SD)	16.9 (6.5)	17.7 (6.4)	16.7 (5.8)	16.9 (6.2)[c]
Median (IQR)	16 (12, 21)	17 (13, 22)	16 (13, 20)	16 (13, 21)[c]

IQR denotes interquartile range; and SD standard deviation.

[a] Scores on the Intensive Care National Audit & Research Centre (ICNARC) Physiology Score range from 0 to 100, with higher scores indicating greater severity of illness. The ICNARC Physiology Score was calculated using physiology readings from the first 24 hours following ICU admission.

[b] Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating greater severity of illness. APACHE II score was calculated using physiology readings from the first 24 hours following ICU admission.

[c] n=444 as data were missing for two patients.

eTable 11. Patient Characteristics – at Time of Consent

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Duration of ICU stay prior to consent (days)	n = 283	n = 340	n = 284	n = 446
Mean (SD)	9.8 (8.8)	12.1 (13.2)	9.1 (7.4)	11.0 (11.6)
Median (IQR)	7 (4, 12)	7 (4, 14)	6 (4, 11)	7 (4, 13)
CAM-ICU positive (delirium) days in ICU prior to consent	n = 162	n = 147	n = 113	n = 180
Mean (SD)	1.4 (2.2)	1.7 (3.0)	2.3 (3.2)	2.8 (3.5)
Median (IQR)	1 (0, 2)	1 (0, 2)	1 (0, 3)	2 (1, 3)
Days from ICU admission to consent	n = 283	n = 340	n = 284	n = 446
Mean (SD)	10.5 (9.1)	13.2 (13.4)	9.6 (7.5)	11.9 (11.7)
Median (IQR)	7 (4, 13)	9 (5, 15)	7 (4, 12)	8 (5, 14)
Proportion of patients consented in ICU, n/N (%)	225/283 (79.5)	224/340 (65.9)	236/284 (83.1)	337/446 (75.6)
Last NEWS prior to consent[a]	n = 283	n = 340	n = 284	n = 446
Mean (SD)	3.2 (2.2)	2.8 (2.1)	3.1 (2.4)	2.8 (2.4)
Median (IQR)	3 (2, 5)	3 (1, 4)	3 (1, 5)	2 (1, 4)
STAI-6 score at time of consent[b]	n = 282	n = 340	n = 284	n = 445
Mean (SD)	45.0 (16.0)	43.8 (17.1)	43.6 (15.5)	42.1 (14.2)
Median (IQR)	43 (33, 57)	43 (30, 55)	43 (30, 53)	43 (33, 50)
HrQoL (health thermometer score) at time of consent[c]	n = 283	n = 340	n = 284	n = 445
Mean (SD)	52.4 (25.7)	51.0 (25.6)	52.9 (23.3)	54.9 (23.3)
Median (IQR)	50 (35, 70)	50 (30, 70)	50 (40, 70)	50 (40, 70)

IQR denotes interquartile range; SD standard deviation; CAM-ICU Confusion Assessment Method for the Intensive Care Unit; NEWS National Early Warning Score; STAI State-Trait Anxiety Inventory; and HrQoL Health-related Quality of Life.

[a] Scores on the National Early Warning Score (NEWS) range from 0 to 20, with higher scores indicating greater severity of illness. NEWS was calculated from the last physiology readings prior to consent.

[b] Score on the six-item State Trait Anxiety Inventory (STAI-6) range from 20 to 80, with higher scores indicating greater anxiety. STAI-6 was self-completed by patients at the time of consent.

[c] HrQoL health thermometer scores range from 0 (“the worst health you can imagine”) to 100 (“the best health you can imagine”). The HrQoL health thermometer was self-completed by patients at the time of consent.

eTable 12. Nesting of POPPI Patients in Case Mix Programme Data

	POPPI cluster-RCT patients	POPPI eligibility applied to CMP Database[a]	
		POPPI ICUs	Non-POPPI ICUs
	N = 1,453	N = 8,189	N = 50,208
Age (years)			
Mean (SD)	58.0 (15.8)	58.7 (17.1)	59.3 (17.0)
Median (IQR)	60 (48, 70)	61 (47, 72)	62 (48, 73)
Gender, %			
Female	41.2	39.6	41.0
Male	58.8	60.4	59.0
Ethnicity, %			
White	96.4	93.0	89.4
Mixed	0.3	0.3	0.7
Asian	1.2	3.0	4.8
Black	1.1	1.9	3.3
Other	1.0	1.8	1.9
Quintile of IMD 2015, %			
1 - Least deprived	18.0	16.2	14.6
2	21.0	17.8	17.4
3	19.2	19.9	19.4
4	21.8	21.5	22.6
5 - Most deprived	20.0	24.6	26.0
Elective surgical admission, %			
Yes	7.1	7.8	6.7
No	92.9	92.2	93.3
ICNARC Physiology Score[c]			
Mean (SD)	21.2 (7.3)	20.8 (7.3)	20.4 (7.2)
Median (IQR)	21 (16, 26)	20 (16, 25)	20 (15, 25)
APACHE II score[d]			
Mean (SD)	17.1 (6.3)	17.4 (6.6)	16.7 (6.4)
Median (IQR)	17 (13, 21)	17 (13, 22)	16 (12, 21)
ICU length of stay			
Mean (SD)	11.3 (13.5)	9.3 (12.5)	9.9 (12.0)
Median (IQR)	6 (3, 13)	5 (3, 10)	5 (3, 11)

CMP denotes Case Mix Programme; IQR interquartile range; SD standard deviation; IMD Index of Multiple Deprivation, ICNARC Intensive Care National Audit & Research Centre; and APACHE Acute Physiology And Chronic Health Evaluation.

[a] Best approximation of the POPPI eligibility criteria applied to the Case Mix Programme (CMP) database (aged ≥18 years, received Level 3 care during the first 24 hours of admission, not a readmission to the unit, length of stay ≥48 hours, survived to unit discharge, not discharged whilst receiving Level 3 care, not discharged to die or for palliative care) for admissions between June 2015 and March 2017.

[b] The Index of Multiple Deprivation (IMD) 2015 is reported by quintiles, with higher values indicating greater deprivation.

[c] Scores on the Intensive Care National Audit & Research Centre (ICNARC) Physiology Score range from 0 to 100, with higher scores indicating greater severity of illness. The ICNARC Physiology Score was calculated using physiology readings from the first 24 hours following ICU admission.

[d] Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating greater severity of illness. APACHE II score was calculated using physiology readings from the first 24 hours following ICU admission.

eTable 13. Reasons for Not Receiving Stress Support Sessions*

	n/N (%)
Patients who received no stress support sessions (N=18)	
Patient declined sessions	6/18 (33.3)
Patient was discharged	7/18 (38.9)
Trained ICU nurse was unavailable	2/18 (11.1)
Other reasons	3/18 (16.7)
Patients who received one stress support session only (N=21)	
Patient declined further sessions	5/21 (23.8)
Patient was discharged	13/21 (61.9)
Patient died	1/21 (4.8)
Trained ICU nurse was unavailable	1/21 (4.8)
Other reasons	1/21 (4.8)
Patients who received two stress support sessions (N=33)	
Patient declined further session	3/33 (9.1)
Patient was discharged	29/33 (87.9)
Trained ICU nurse was unavailable	1/33 (3.0)

* For patients scoring ≥7 points on the Intensive care Psychological Assessment Tool (IPAT).

eTable 14. Stress Support Session Delivery Locations

Delivery location	n/N (%)
Stress support session one (N=181)	
ICU	72/181 (39.8)
Outside ICU	109/181 (60.2)
Stress support session two (N=160)	
ICU	27/160 (16.9)
Outside ICU	133/160 (83.1)
Stress support session three (N=127)	
ICU	14/127 (11.0)
Outside ICU	113/127 (89.0)

eTable 15. Medical Interventions Received in the ICU by Treatment Group and Time Period

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Sedatives/anxiolytics/anaesthetics				
n/N (%) receiving intervention	264/283 (93.3)	311/340 (91.5)	263/284 (92.6)	413/446 (92.6)
Median (IQR) days among those receiving intervention	4 (2, 8)	4 (2, 9)	3 (2, 7)	4 (2, 7)
Mean (SD) days among all patients	5.5 (6.4)	6.2 (7.9)	5.2 (5.2)	5.6 (7.0)
Sleep medication				
n/N (%) receiving intervention	73/283 (25.8)	99/340 (29.1)	78/284 (27.5)	143/446 (32.1)
Median (IQR) days among those receiving intervention	3 (1, 7)	5 (2, 9)	3 (2, 6)	3 (1, 9)
Mean (SD) days among all patients	1.6 (4.9)	2.7 (10.0)	1.2 (3.1)	2.1 (5.4)
Benzodiazepines[a]				
n/N (%) receiving intervention	64/283 (22.6)	92/340 (27.1)	75/284 (26.4)	129/446 (28.9)
Median (IQR) days among those receiving intervention	2 (1, 5)	2 (1, 4)	2 (1, 5)	2 (1, 5)
Mean (SD) days among all patients	1.0 (4.1)	1.2 (4.5)	1.0 (2.4)	1.3 (4.0)
Antipsychotics				
n/N (%) receiving intervention	77/283 (27.2)	89/340 (26.2)	68/284 (23.9)	123/446 (27.6)
Median (IQR) days among those receiving intervention	3 (1, 7)	2 (1, 5)	3 (1, 7)	4 (2, 11)
Mean (SD) days among all patients	1.3 (3.5)	1.4 (4.8)	1.2 (3.2)	2.0 (5.4)
Analgesics				
n/N (%) receiving intervention	277/283 (97.9)	335/340 (98.5)	280/284 (98.6)	443/446 (99.3)
Median (IQR) days among those receiving intervention	7 (4, 12)	7 (4, 13)	7 (4, 11)	7 (4, 13)
Mean (SD) days among all patients	9.8 (9.9)	10.9 (13.3)	8.7 (7.1)	10.7 (10.6)
Antidepressants				
n/N (%) receiving intervention	63/283 (22.3)	66/340 (19.4)	57/284 (20.1)	101/446 (22.6)
Median (IQR) days among those receiving intervention	7 (3, 11)	7 (3, 17)	5 (3, 11)	7 (4, 14)
Mean (SD) days among all patients	2.3 (7.1)	2.6 (9.0)	1.7 (5.3)	2.6 (8.1)

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Vasoactive agents				
n/N (%) receiving intervention	227/283 (80.2)	287/340 (84.4)	237/284 (83.5)	383/446 (85.9)
Median (IQR) days among those receiving intervention	3 (2, 5)	3 (2, 6)	3 (2, 5)	3 (2, 5)
Mean (SD) days among all patients	3.7 (4.2)	4.2 (6.3)	3.3 (3.7)	4.1 (6.4)
Mechanical ventilation				
n/N (%) receiving intervention	267/283 (94.3)	306/340 (90.0)	269/284 (94.7)	415/446 (93.0)
Median (IQR) days among those receiving intervention	4 (2, 8)	3 (2, 9)	3 (2, 7)	3 (2, 8)
Mean (SD) days among all patients	6.8 (9.5)	7.6 (11.8)	5.9 (6.6)	6.8 (10.2)

IQR denotes Interquartile Range; and SD Standard Deviation.

[a] Benzodiazepines also included as either sedatives/anxiolytics/anaesthetics or sleep medications as appropriate.

eTable 16. Patient Follow-up by Treatment Group and Time Period

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Outcome at six months, n/N (%)				
Alive	245/283 (86.6)	314/340 (92.4)	259/284 (91.2)	415/446 (93.0)
Dead	38/283 (13.4)	26/340 (7.6)	25/284 (8.8)	31/446 (7.0)
Lost to follow-up	0/283 (0.0)	0/340 (0.0)	0/284 (0.0)	0/446 (0.0)
Returned questionnaire, n/N (% of alive at six months)				
Completed	193/245 (78.8)	251/314 (79.9)	203/259 (78.4)	331/415 (79.8)
Refused	25/245 (10.2)	19/314 (6.1)	22/259 (8.5)	31/415 (7.5)
Lost to follow-up	27/245 (11.0)	44/314 (14.0)	34/259 (13.1)	53/415 (12.8)
Method of completion, n/N (% of completed questionnaires)				
Paper	173/193 (89.6)	240/251 (95.6)	178/203 (87.7)	315/331 (95.2)
Telephone	20/193 (10.4)	11/251 (4.4)	25/203 (12.3)	16/331 (4.8)
Method of refusal, n/N (% of refused)				
Paper	8/25 (32.0)	10/19 (52.6)	13/22 (59.1)	15/31 (48.4)
Telephone	17/25 (68.0)	9/19 (47.4)	10/22 (45.5)	16/31 (51.6)
Complete responses by instrument, n/N (% of completed questionnaires)				
PSS-SR	191/193 (99.0)	250/251 (99.6)	201/203 (99.0)	330/331 (99.7)
HADS anxiety	186/193 (96.4)	246/251 (98.0)	196/203 (96.6)	327/331 (98.8)
HADS depression	186/193 (96.4)	247/251 (98.4)	196/203 (96.6)	327/331 (98.8)
EQ-5D-5L	188/193 (97.4)	248/251 (98.8)	197/203 (97.0)	320/331 (96.7)
Health services questionnaire	122/193 (63.2)	161/251 (64.1)	135/203 (66.5)	226/331 (68.3)

PSS-SR denotes PTSD Symptom Scale – Self-Report questionnaire; HADS Hospital Anxiety and Depression Scale; and EQ-5D-5L European Quality of Life-5 Dimensions five-level questionnaire.

eTable 17. Response Rate by Patient Characteristics

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 245	N = 314	N = 259	N = 415
Age (years)				
18-49	50/68 (73.5)	47/68 (69.1)	53/81 (65.4)	89/123 (72.4)
50-59	41/50 (82.0)	61/73 (83.6)	42/51 (82.4)	84/103 (81.6)
60-69	57/67 (85.1)	77/91 (84.6)	63/69 (91.3)	83/102 (81.4)
70+	45/60 (75.0)	66/82 (80.5)	45/58 (77.6)	75/87 (86.2)
Gender				
Female	77/104 (74.0)	113/145 (77.9)	67/94 (71.3)	129/164 (78.7)
Male	116/141 (82.3)	138/169 (81.7)	136/165 (82.4)	202/251 (80.5)
Ethnicity[a]				
White	177/223 (79.4)	239/294 (81.3)	190/240 (79.2)	298/377 (79.0)
Non-white	9/14 (64.3)	2/7 (28.6)	3/5 (60.0)	9/13 (69.2)
Not stated	7/8 (87.5)	10/13 (76.9)	10/14 (71.4)	24/25 (96.0)
Quintile of IMD 2015[b]				
1 (least deprived)	27/31 (87.1)	46/55 (83.6)	50/54 (92.6)	79/89 (88.8)
2	28/40 (70.0)	55/67 (82.1)	45/55 (81.8)	84/97 (86.6)
3	43/51 (84.3)	56/66 (84.8)	32/48 (66.7)	52/70 (74.3)
4	47/64 (73.4)	56/71 (78.9)	40/51 (78.4)	63/83 (75.9)
5 (most deprived)	48/59 (81.4)	36/53 (67.9)	36/51 (70.6)	52/75 (69.3)
Pre-existing anxiety/depression[c]				
Anxiety	0/1 (0.0)	9/11 (81.8)	3/4 (75.0)	6/9 (66.7)
Depression	13/18 (72.2)	24/31 (77.4)	13/19 (68.4)	25/32 (78.1)
Both	13/17 (76.5)	13/21 (61.9)	4/8 (50.0)	9/11 (81.8)
None	167/209 (79.9)	205/251 (81.7)	183/228 (80.3)	291/363 (80.2)
Elective surgical admission				
Yes	9/11 (81.8)	18/19 (94.7)	16/19 (84.2)	29/36 (80.6)
No	184/234 (78.6)	233/295 (79.0)	187/240 (77.9)	302/379 (79.7)
ICNARC Physiology Score[d]				
<17	55/75 (73.3)	73/95 (76.8)	59/73 (80.8)	83/105 (79.0)
17-21	48/64 (75.0)	82/91 (90.1)	56/75 (74.7)	89/118 (75.4)
22-26	50/61 (82.0)	48/64 (75.0)	44/55 (80.0)	82/103 (79.6)
≥27	40/45 (88.9)	48/64 (75.0)	44/56 (78.6)	77/89 (86.5)

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 245	N = 314	N = 259	N = 415
APACHE II score[e]				
<14	58/79 (73.4)	65/89 (73.0)	65/80 (81.3)	90/124 (72.6)
14-17	58/71 (81.7)	72/89 (80.9)	58/79 (73.4)	100/117 (85.5)
18-21	37/45 (82.2)	52/61 (85.2)	42/50 (84.0)	74/90 (82.2)
≥22	40/50 (80.0)	62/75 (82.7)	38/50 (76.0)	65/82 (79.3)
Number of days CAM-ICU positive (delirious) in unit prior to consent				
0	50/67 (74.6)	46/61 (75.4)	19/33 (57.6)	20/29 (69.0)
1-2	43/55 (78.2)	35/42 (83.3)	33/41 (80.5)	65/84 (77.4)
>2	17/22 (77.3)	30/35 (85.7)	21/30 (70.0)	42/55 (76.4)
Last NEWS prior to consent[f]				
0-1	48/56 (85.7)	76/92 (82.6)	56/77 (72.7)	124/157 (79.0)
2-3	70/97 (72.2)	88/116 (75.9)	67/81 (82.7)	109/130 (83.8)
4	19/28 (67.9)	35/41 (85.4)	26/35 (74.3)	25/37 (67.6)
≥5	56/64 (87.5)	52/65 (80.0)	54/66 (81.8)	73/91 (80.2)
STAI-6 at time of consent[g]				
20-30	44/53 (83.0)	74/98 (75.5)	54/71 (76.1)	81/103 (78.6)
31-43	59/78 (75.6)	67/73 (91.8)	58/70 (82.9)	111/145 (76.6)
44-53	43/52 (82.7)	50/64 (78.1)	44/58 (75.9)	78/96 (81.3)
54-80	47/61 (77.0)	60/79 (75.9)	47/60 (78.3)	60/70 (85.7)
HrQoL health thermometer score at time of consent[h]				
0-38	48/63 (76.2)	77/92 (83.7)	49/62 (79.0)	71/86 (82.6)
39-50	54/66 (81.8)	61/82 (74.4)	66/82 (80.5)	97/125 (77.6)
51-70	46/58 (79.3)	58/72 (80.6)	41/53 (77.4)	80/102 (78.4)
71-100	45/58 (77.6)	55/68 (80.9)	47/62 (75.8)	83/101 (82.2)
IPAT score < 7	-	103/128 (80.5)	-	-
IPAT score ≥ 7 by number of stress support sessions received				
None	-	9/16 (56.3)	-	-
1	-	13/19 (68.4)	-	-
2	-	24/31 (77.4)	-	-
3	-	102/120 (85.0)	-	-

APACHE denotes Acute Physiology And Chronic Health Evaluation; CAM-ICU Confusion Assessment Method for the Intensive Care Unit; NEWS National Early Warning Score; ICNARC Intensive Care National Audit & Research Centre; IMD Index of Multiple Deprivation; HrQoL Health-related Quality of Life; STAI-6 State-Trait Anxiety Inventory score; and IPAT Intensive care Psychological Assessment Tool.

[a] Ethnicity was collected as part of the Case Mix Programme dataset and was ascertained by review of medical records. This field was collected to help describe the demographics of the patient population and assess the representativeness of the sample.

[b] The Index of Multiple Deprivation (IMD) 2015 is reported by quintiles, with higher values indicating greater deprivation.

[c] Scores on the Intensive Care National Audit & Research Centre (ICNARC) Physiology Score range from 0 to 100, with higher scores indicating greater severity of illness. The ICNARC Physiology Score was calculated using physiology readings from the first 24 hours following ICU admission.

[d] Documented pre-existing anxiety/depression was ascertained by review of medical records.

[e] Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating greater severity of illness. APACHE II score was calculated using physiology readings from the first 24 hours following ICU admission.

[f] Scores on the National Early Warning Score (NEWS) range from 0 to 20, with higher scores indicating greater severity of illness. NEWS was calculated from the last physiology readings prior to consent.

[g] Score on the six-item State Trait Anxiety Inventory (STAI-6) range from 20 to 80, with higher scores indicating greater anxiety.

[h] HrQoL health thermometer scores range from 0 (“the worst health you can imagine”) to 100 (“the best health you can imagine”); and was self-completed by patients at the of consent.

eTable 18. Summary of Elicited PSS-SR Scores Across All Usable Experts (n=29)

	A[a]	**B**[b]	**C**[c]
Most likely patient PSS-SR[d] average scores (i.e. mode), mean (SD)			
Receiving usual care who did not return a PSS-SR	22 (8)	9 (8)	10 (3)
Receiving preventive, complex psychological intervention who did not return a PSS-SR	17 (7)	7 (7)	8 (3)
Differences in most likely patient PSS-SR[d] average scores, mean (SD)			
Receiving usual care: Did not return a PSS-SR minus did return a PSS-SR	3 (8)	5 (8)	2 (3)
Did not return a PSS-SR: Receiving usual care minus receiving the preventive, complex psychological intervention	5 (5)	2 (3)	2 (3)

[a] Female, younger and anxious after regaining capacity in the ICU
[b] Male, older and anxious after regaining capacity in the ICU
[c] Male, younger and not anxious after regaining capacity in the ICU
[d] PSS-SR (PTSD Symptom Scale – Self Report Version) scale is from 0 to 51 with higher scores indicating greater post-traumatic stress symptoms.

eTable 19. Summary of Elicited EQ-5D-5L Scores Across All Usable Experts (n=30)

	A[a]	B[b]	C[c]
Most likely patient EQ-5D-5L[d] average scores (i.e. mode), mean (SD)			
Receiving usual care who did not return an EQ-5D-5L	61 (13)	66 (10)	79 (5)
Receiving preventive, complex psychological intervention who did not return an EQ-5D-5L	69 (10)	70 (9)	83 (4)
Differences in most likely patient EQ-5D-5L[d] average scores, mean (SD)			
Receiving usual care: Did not return an EQ-5D-5L minus did return a EQ-5D-5L	-1 (13)	-14 (8)	2 (3)
Did not return an EQ-5D-5L: Receiving usual care minus receiving the preventive, complex psychological intervention	-8 (10)	2 (3)	2 (3)

[a] Female, younger and anxious after regaining capacity in the ICU
[b] Male, older and anxious after regaining capacity in the ICU
[c] Male, younger and not anxious after regaining capacity in the ICU
[d] EQ-5D-5L (European Quality of Life-5 Dimensions five-level questionnaire) scale is from -28 to 100 with lower scores indicating worse health-related quality of life.

eTable 20. Cost-effectiveness Outcomes – at Six Months.*

Sites	**Intervention ICUs**			**Control ICUs**			**Difference in difference**[c]	**P value**	**ICC (95% CI)**
Time period	**Baseline**[a]	**Intervention**[a]	**Difference**[b]	**Baseline**[a]	**Intervention**[a]	**Difference**[b]			
Number of patients	283	340		284	446				
Costs (US dollars)[d]	$39,579 ($33,845)	$42,817 ($36,135)	$3,240 ($2,841)	$37,235 ($29,811)	$42,131 ($38,815)	$4,893 ($2,731)	-$1,074 (−$8,368, $6,222)	0.77	0.01 (0.00, 0.07)
Quality-adjusted life years[e]	0.26 (0.12)	0.27 (0.12)	0.01 (0.01)	0.29 (0.12)	0.29 (0.11)	0.01 (0.01)	0.00 (−0.02, 0.03)	0.77	0.00 (0.00, 0.28)
Incremental net monetary benefit (US dollars)[f]							$1,187 (−$6,148, $8,523)	0.76	0.01 (0.00, 0.05)

* Reported for all patients after applying multiple imputation to handle missing data.

[a] Mean (standard deviation).

[b] Difference in means (standard error).

[c] Adjusted difference in means (95% confidence interval). Adjusted for age, sex, ethnicity, deprivation, pre-existing anxiety/depression, planned admission following elective surgery and ICNARC Physiology Score.

[d] Costs were collected in UK pounds and converted to US dollars using the currency conversion factor $1 equals £0.703

[e] QALYs for survivors calculated by multiplying the EQ-5D-5L utility score by 0.5 life years (6 month time period), decedents assumed to have zero QALYs.

[f] Calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 ($28,450)[37] and subtracting from this value the incremental cost.

eTable 21. Costs (£) up to Six Months

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Intervention costs	-	140 (128)	-	-
Hospital costs				
Index admission				
ICU	19,221 (19,183)	19,573 (18,083)	17,424 (15,195)	20,495 (21,627)
General medical ward	5,095 (7,435)	5,814 (8,471)	4,149 (5,608)	5,055 (7,618)
Readmission[a]				
ICU	910 (3,897)	873 (6,877)	1,679 (7,486)	782 (4,378)
General medical	279 (1,995)	337 (1,979)	277 (1,401)	170 (1,364)
Outpatient & community costs[*b]	2,319 (4,356)	3,363 (7,026)	2,646 (4,551)	3,118 (5,609)
Total costs up to 6 months[*a,b]	**27,824 (23,793)**	**30,100 (25,403)**	**26,176 (20,957)**	**29,618 (27,287)**

All numbers are mean (SD) unless stated otherwise

* Following multiple imputation to handle missing resource use data:

[a] POPPI cluster-trial and Case Mix Programme (CMP) Database;

[b] Health services questionnaire

eTable 22. Mean (SD) Resource Use up to Six Months

	Intervention ICUs		**Control ICUs**	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
Index admission				
Days in ICU	12.55 (12.13)	12.74 (10.86)	11.46 (9.63)	13.05 (12.98)
General medical bed days	17.10 (24.95)	19.51 (28.42)	13.92 (18.82)	16.96 (25.56)
Readmissions				
N (%) readmissions	32 (11.31)	26 (7.65)	36 (12.68)	32 (7.17)
Days in ICU	0.67 (2.75)	0.58 (3.80)	1.21 (5.28)	0.67 (2.75)
General medical bed days	0.94 (6.70)	1.13 (6.64)	0.93 (4.70)	0.94 (6.70)
Total length of stay up to 6 months (days)	**31.27 (31.04)**	**33.95 (33.66)**	**27.52 (25.06)**	**31.16 (31.96)**

eTable 23. Mean (SD) Resource Use From Health Services Questionnaire Between Hospital Discharge and Six Months*

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 160	N = 187	N = 160	N = 257
Inpatient days (general medical)	5.38 (14.35)	9.53 (28.39)	4.60 (11.83)	6.82 (19.39)
Outpatient visits	4.33 (5.4)	4.69 (6.18)	5.49 (6.7)	5.09 (6.13)
GP contacts	4.69 (5.52)	4.05 (4.77)	4.08 (5.36)	3.59 (5.06)
Nurse contacts	3.97 (5.85)	4.39 (7.83)	3.75 (6.51)	3.31 (5.36)
Health visitor contacts	1.41 (4.76)	1.49 (6.57)	0.59 (1.76)	2.5 (16.64)
Occupational therapist contacts	0.70 (1.54)	1.35 (6.08)	1.37 (6.28)	1.49 (7.71)
Speech therapist contacts	0.27 (1.13)	0.06 (0.31)	0.08 (0.48)	0.19 (0.92)
Physiotherapist contacts	1.30 (2.25)	1.22 (2.49)	0.75 (1.89)	1.87 (6.63)
Psychiatrist contacts	0.11 (0.43)	0.15 (0.72)	0.07 (0.36)	0.22 (1.04)
Psychiatric nurse contacts	0.19 (1.45)	0.17 (1.00)	0.05 (0.31)	0.02 (0.19)
Psychologist contacts	0.06 (0.34)	0.04 (0.28)	0.10 (0.75)	0.21 (1.04)
Counsellor contacts	0.36 (1.59)	0.22 (0.92)	0.05 (0.31)	0.41 (1.51)

GP denotes General Practitioner.

*reported for patients who were alive and completed the health services questionnaire at six months post-recruitment

eTable 24. EuroQol 5-Dimensions, Mortality, and Quality-Adjusted Life Years up to Six Months

	Intervention ICUs		Control ICUs	
	Baseline	**Intervention**	**Baseline**	**Intervention**
	N = 283	N = 340	N = 284	N = 446
EQ-5D (survivors)*	0.661 (0.303)	0.668 (0.302)	0.698 (0.268)	0.690 (0.279)
All-cause mortality, n (%)	38 (13.43)	26 (7.65)	25 (8.80)	31 (6.95)
QALY*	0.263 (0.132)	0.274 (0.120)	0.285 (0.115)	0.291 (0.112)

All numbers are mean (SD), unless stated otherwise.

* The EQ-5D (European Quality of Life-5 Dimensions five-level questionnaire) and QALY (Quality-Adjusted Life Years) results are all reported after applying multiple imputation to handle missing data.

eTable 25. Alternative Assumptions for Cost-effectiveness Sensitivity Analysis

	Base case	**Sensitivity analysis**
Nurse's time for IPAT assessment	10 minutes per patient	5 minutes per patient
Nurse's time for IPAT assessment	10 minutes per patient	20 minutes per patient
Nurse's time for delivering stress support session	Each stress support session requires 1.5 hours	Each stress support session requires 1 hour
Nurse's time for delivering stress support session	Each stress support session requires 1.5 hours	Each stress support session requires 2 hours
Readmissions from Health Services Questionnaires	Included in the analysis	Excluded from the analysis
HrQoL at time of consent	HrQoL measured at time of consent was applied	Zero HrQoL at time of consent was applied
Distributional assumptions	Costs and QALYs normally distributed	Costs and QALYs gamma distributed
Unit level standardised mortality ratios	Not included in the analysis	Adjusted for in the analysis

IPAT denotes Intensive care Psychological Assessment Tool, HrQoL Health-related Quality of Life; and QALY Quality-Adjusted Life Years.

eTable 26. Lifetime Total Costs (£), Lifetime Quality-Adjusted Life Years, and Lifetime Incremental Net Benefit

	Intervention ICUs		Control ICUs		
	Baseline	**Intervention**	**Baseline**	**Intervention**	
	N = 283	N = 340	N = 284	N = 446	**Incremental effect Mean (95% CI)**
Costs (£)	56,319 (25,020)	64,406 (26,482)	56,193 (22,115)	64,254 (28,823)	362 (-5,077 to 5,801)
QALYs	10.58 (6.01)	10.89 (5.29)	11.52 (5.82)	11.81 (5.51)	0.226 (-0.447 to 0.899)
INB (£)[±]					4,158 (-10,354 to 18,670)

CI denotes confidence intervals, QALY Quality-Adjusted Life Years, and INB Incremental Net Benefit.

All numbers are mean (SD), unless stated otherwise. The EQ-5D, QALY, cost and INB results are all reported after applying multiple imputation to handle missing data. The incremental effects are reported after applying case-mix adjustment.

[±] The INB is calculated according to methods of the National Institute for Health and care Excellence (NICE) by multiplying the mean gain or loss in quality-adjusted life-years by £20,000 and subtracting from this value the incremental cost.

eTable 27. Comparison of Baseline and Post-Stress Support Session Three STAI-6a Scores for Patients Completing Both Assessments

Summary	Baseline	Post-stress support session three
No of patients	n = 115	n = 115
Mean (SD)	49.3 (16.9)	40.3 (13.5)
Median (IQR)	47 (37, 60)	40 (30, 50)

IQR denotes Interquartile Range; and SD Standard Deviation.

[a] Score on the six-item State Trait Anxiety Inventory (STAI-6) range from 20 to 80, with higher scores indicating greater anxiety.

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