Title: ICUTogether a web based recovery program for intensive care survivors: a randomized controlled trial protocol

Abstract

Background: Those who experience a critical illness/event requiring admission to an intensive care unit frequently experience physical and psychological complications as a direct result of their critical illness/event and intensive care unit experience. Complications, if left untreated, can affect the quality of life of survivors and impact upon health care resources. Explorations of potential interventions to reduce the negative impact of an intensive care unit experience have failed to establish an evidence based intervention. The aim of this study is to evaluate the impact of a web based intensive care recovery program on the mental well-being of intensive care survivors and to determine if it is a cost effective approach.

Methods: One hundred and sixty-two patients that survived an intensive care unit experience will be recruited and randomized into one of two groups. The intervention group will receive access to the web based intensive care recovery program, ICUTogether, two weeks after discharge (n=81) and the control group will receive usual care (n=81). Mental well-being will be measured using the Hospital Anxiety and Depression Scale, The Impact of Events Scale-Revised and the EQ-5D at three time points (2 weeks, 6 months and 12 months post discharge). Analysis will be conducted on an intention to treat basis using regression modelling. Covariates will include baseline outcome measures, study allocation (intervention or control), age, gender, length of intensive care unit stay, Apache III score, level of family support and hospital readmissions. Participants’ evaluation of the mobile website will be sought at 12 months post discharge.

A cost utility analysis conducted at 12 months from a societal perspective will consider costs incurred by individuals as well as health care providers.

Discussion: This study will evaluate a novel intervention in a group of intensive care unit survivors. The findings from this study will inform a larger study and the wider debate about an appropriate intervention in this population.

Trial Registration:

Australian New Zealand Clinical Trial Registry: ACTRN12618000252213

Key words:

Intensive care, survivorship, survivor, recovery program
Background

An intensive care unit (ICU) admission is a stressful, potentially traumatic event for survivors and their families. Admission to an ICU usually means that the individual has suffered a critical illness/event which is a threat to their lives, and they are among the most critically ill and vulnerable patients in the hospital. It is thought that the complications of a critical illness/event are not only related to the severity of the illness but also to the ICU experience [1, 2]. Intensive care survivors often struggle to return to their previous role in the family and to their pre-illness state of health due to prolonged physical and neuropsychological disability [3-5].

Over 172,000 people were admitted to ICUs across Australia during 2014 -2015. As survival rates from ICU have increased over the last 30 years there has been a concomitant rise in the number of survivors, increasing the number of people who may develop chronic illness as a direct result of their ICU experience [6, 7]. It has become increasingly apparent that those who survive ICU and are discharged home suffer myriad physical, cognitive, and mental health impairments as a direct result of their ICU experience and critical event [8-10]. These impairments can persist over a long period of time [4, 11]. Psychological complications have been estimated to be as high as 44% of survivors at hospital discharge [1] and in some populations have been noted to increase during the year following hospital discharge [12].

Despite awareness of the high risk of complications post ICU discharge, support to anticipate and address physical and psychological complications is not routinely offered through existing health care services. Many survivors report being unaware of what to expect during recovery and lack knowledge of what is normal and when they need to seek help [13]. The onus to seek help post discharge sits in the hands of the survivor, and it is unknown how many “suffer in silence”, unaware if what they are experiencing is a usual part of recovery.

The purpose of this study is to determine if a web based intensive care recovery program improves the mental health and well-being of ICU survivors. As a mobile website, availability of the program will be unrestricted, enabling participants to access it at anytime and anywhere via a smart device. The program will enable participants to access support, advice and guidance during their recovery post discharge from ICU.

Methods

A parallel, prospective randomized controlled study will determine if a web based intensive care recovery program improves the mental health and well-being of ICU survivors. The study design for the protocol is outlined in a flow diagram in Figure 1.

Ethical approval was obtained from the participating study site and the University where the researchers are employed.
Study duration

Recruitment will begin in January 2018 and data collection completed within 2 years.

Participants

Participants will be screened and recruited from a general 10 bed ICU within a 750 bed hospital in Metropolitan Western Australia (WA) following discharge from ICU and admission to a general ward. Eligibility for inclusion are (1) aged 18 years and over at time of randomization, (2) ventilation in ICU for a minimum period of 24 hours, (3) speak and understand English and (4) able to give informed consent. Participants will be informed which group they have been randomized to immediately after providing written informed consent.

Randomization

Permuted block randomization will be conducted in blocks of 20 using a computer random numbers generator. Allocation concealment will be conducted by an independent researcher using sequentially numbered, opaque, sealed envelopes. The independent researcher will provide the researcher conducting the consent process with the sequentially numbered, sealed, opaque envelopes. Envelopes containing the treatment allocation will only be opened by the recruiting researcher on participant enrolment.

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Blinding of the participant to allocation status will not be possible due to the nature of the intervention. The researchers conducting the data analysis will be blinded.

**Intervention**

Patients in the intervention group will receive access to a web based recovery program, called ICUTogether, accessible via smart devices and personal computers. The mobile website will provide information about health and wellbeing during recovery including advice about exercise, sleep and nutrition. Information will be provided on the recovery process, the signs and symptoms of potential complications during recovery, and when and how participants should seek professional help. Participants will be encouraged to keep a journal to promote reflection on progress over time and to explore their thoughts and feelings during their recovery. A chat room will also be available and participants will be able to post items to share with other participants in the study.

Participants will be given access to the mobile web site two weeks following discharge from hospital. A hard copy self-help guide and telephone call will guide participants in the use of the site. If the participant is still unable to use the website a researcher will visit their home and provide direct support with it. A demonstration of the functionality of the mobile website by a researcher will also be given at that time. The frequency of use of the website is at the discretion of the participants who will be encouraged to use the site as frequently as they wish. Each time a participants log in they will be prompted to complete a symptoms checker that will identify material most useful to the participant at that point in time. The score from the symptom checker will be monitored and an alert notification will be sent to the researchers when the scores reaches a certain level and therefore gives cause for concern. Participants will receive a weekly email summarising their participation over the previous seven days and indicating any days they have not participated along with a prompt to continue participating.

The mobile website was developed by an external provider in collaboration with the researchers. The mobile website is being tested for ease of use and navigation properties by the researchers, clinicians and a group of ICU survivors prior to commencement of the study.

**Control Group**

The comparator, the control group, will receive usual care. Usual care defined as ongoing management by the participants’ general practitioner (GP). There is no specific after care provision for ICU survivors offered at the study site. At the time of discharge from hospital, survivors are discharged back to the care of their GP with additional services provided as necessary. These services do not include any specific ICU aftercare provision, for instance follow-up by the ICU team. There will be no contact with the control group beyond consent and postal surveys.

**Data Collection and Measures**

Following the consent process, demographic data will be collected from the participants’ health records, this will include age, gender, admission diagnosis, severity of illness (APACHE III), existing co-morbidities and ICU length of stay. Data will be collected from participants at three time points: (1) two weeks post discharge, (2) six months post discharge and (3) 12 months post discharge (primary timepoint). Three outcome measures will be used in the study: the Hospital Anxiety and Depression Scale (HADS), the Impact of Events Scale Revised (IES-R) and the five-level five-dimension EuroQoL (EQ-5D-5L). All three measures will be completed at each of the time points. Table 1 provides a brief description of each of the outcome measures. Participants in the intervention group will receive the Intervention study protocol V2
three surveys by post two weeks post discharge from hospital to complete the first data collection time point. The first data collection point for the control group and the following two data collection time points for both groups will be sent by post with a stamp-addressed envelope. Participants will also be contacted by telephone to provide a prompt to complete the surveys.

Table 1 Summary of outcome measures and description

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of items</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
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<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>14 on a 4 point scale</td>
<td>Used to identify the incidence of anxiety and depression in patients with a range of diseases and medical conditions [14]</td>
</tr>
</tbody>
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| **Secondary Outcomes** | | |
| Impact of Events Scale Revised (IES-R) | 24 on a 5 point scale | Measure of subjective distress in response to a traumatic event [15]. It comprises three subscales which represent the major symptom clusters of post-traumatic stress disorder (PTSD): intrusion, avoidance and hyperarousal [16]. |

| 5-level 5-dimension EuroQoL (EQ-5D-5L) | 5 on a 5point scale And a visual analogue scale | Measure changes to health-related quality of life over time or between/ following interventions [17]. The five dimensions within the survey are: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. |

For participants in the intervention group at time point three, 12 months after discharge, an evaluation will be conducted via the website on the acceptability and usability of the website. The evaluation will be conducted through the web portal and completed online. The evaluation was developed by the research team and consists of questions on the acceptability and content of the web based recovery program. In addition, web based analytics will be collected. This includes the frequency and duration of access to the site, frequency and duration of interaction with content areas and frequency of journaling.

**Sample size**

Sample size and statistical power were calculated for the primary outcome measure using G*Power 3.1.9.2 (Faul et al. 2007). In order to detect a 2-point difference (effect size 0.44) between the two groups on the HADS with an alpha of 0.05 and 80% power requires 81 participants in each group for a total sample size of 162 participants. Given the discharge rate of 80 patients per month and a recruitment rate of 30% it is estimated that it will take seven months to recruit the required sample size.

**Statistical Analysis**

Data will be reported in accordance with the Consolidated Standards of reporting Trial (CONSORT). Data analysis will be conducted using IBM SPSS and Stata. Characteristics of participants in each arm of the study will be summarised using descriptive statistics. The three outcome measures (HADS, IES, QoL) at follow-up will be analysed as dependent variables using regression modelling. Covariates will include baseline outcome measures, study allocation (intervention or control), age, gender, length of ICU stay, Apache II score, and level of family support. Analysis will be conducted on an intention to treat basis. A sub-analysis of the intervention group based on those who engaged with the mobile website compared to those who did not will also be conducted. Characteristics of people who
withdraw from the study will be compared to those who remain in the study. Missing data will be addressed using multiple imputation assuming variables are missing at random. The person who completes the data analysis will be blind to participant allocation status.

Summary statistics of frequency of use, time spent using the site, most frequently used elements and time spent on each screen will be reported.

**Economic outcomes**

A cost utility analysis will be conducted at 12 months to determine whether the web based recovery program is a cost effective approach for improving the quality of life of ICU survivors when compared to usual care. The perspective taken for the economic analysis will be a societal perspective and will include costs incurred by individuals as well as health care providers.

*Identification of costs and benefits*

The primary outcome measure for assessing benefits will be quality of life. The identification of costs will be across four main areas: i) *intervention costs* includes ongoing mobile website maintenance such as hosting costs as well as the cost of promoting the mobile website to future ICU survivors. The cost for developing the mobile website and implementing the intervention for the study will not be included as these costs will not be incurred in future implementation of the mobile website; ii) *health care costs* includes general practitioner (GP) visits, other health practitioner consultations such as counselling services, dieticians, and physiotherapists, emergency department (ED) visits, hospital inpatient stays in acute or mental health settings, mental health outpatient visits, and medication use; iii) *personal and family costs* includes the use of alternative therapies such as massage and reflexology, use of health promotion resources such as sporting facilities and support groups. Travel costs to attend health services and health promotion activities will also be included. The time cost for using the mobile website will not be included as this will occur during leisure time and is expected to be minimal; and iv) *productivity costs* includes time spent absent from work due to illness.

*Measurement of costs and benefits*

Benefits will be measured using the EQ-5D. Intervention costs will be measured through discussion with the mobile website developers about the requirements to maintain the website for a one-year period. A plan for promoting the mobile website to future ICU survivors will be prepared detailing the elements that will be included. Health care costs will be measured by a patient diary for GP visits, health practitioner visits and medication use. Linked data will be used to measure ED visits, outpatient visits, and hospital usage. Personal and productivity costs will be measured by a patient diary which will record the number of times health related services and health promotion resources are accessed, travel details to access these resources, as well as time spent absent from paid work.

*Valuation of costs and benefits*

Benefits will be valued by calculating quality adjusted life years (QALYs) from the EQ-5D data using Australian derived utility weights [18]. Intervention costs will be valued by obtaining three quotes from service providers. The average of the three quotes will be used in the calculations. Health care costs will be valued using the Australian Medicare Benefits Schedule [19], Pharmaceutical Benefits Scheme data [20] and the National Hospital Cost Data Collection [21]. Personal and family costs will be valued by cost prices recorded in the patient diaries. Travel costs will be valued by the number of visits to providers or facilities, the average distance travelled, and the Australian Taxation Office (ATO).

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guidelines for car expenses (cents per kilometre method)[22] or the cost of public transport. Productivity costs for time spent absent from paid work will be valued using the human capital approach[23].

Data and Sensitivity Analysis

The incremental cost effectiveness ratio will be calculated by dividing the difference in costs between the intervention and control arms by the difference in QALYs.

Probabilistic sensitivity analysis using Monte Carlo simulations will be performed. Uncertainty exists around the estimate of the intervention effect on quality of life, and around costs, including health provider, individual and productivity costs and these will be included in the sensitivity analysis with the distributions to be determined from the data. Results will be presented as scatterplots and cost effectiveness acceptability curves for a range of willingness to pay thresholds.

No discounting is required as all costs and benefits will be measured within a one-year time period. All costs will be valued using 2018 AUD. No modelling of costs and benefits into the future will be undertaken.

Discussion

ICU survivors face many challenges during their recovery and many may never achieve a level of recovery which is acceptable to them. Despite the evidence which confirms that this group have an increased uptake of health care resources and poor outcomes, they are not routinely offered dedicated programs to support them post discharge from ICU.

This research study is an innovative approach to provide an evidence based recovery program for ICU survivors; a group who experience significant levels of physical and psychological morbidity. The findings from this study will inform a larger study and the wider debate on approaches to engage and support survivors post ICU.

Authors’ contributions

BE, HM, LW, DS & JH were involved in the conception and organisation of the research and the review and critique of the manuscript. KS & BE wrote the first draft of the manuscript.

Competing interests

The authors declare that they have no competing interests.

References

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