Development of a structured nurse-led follow-up for patients after discharge from the intensive care unit and testing of its effectiveness

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Thesis for the degree of Philosophiae Doctor

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HJÚKRUNARFRÆÐIDEILD OG LÆKNADEILD

Þróun skipulagðrar, hjúkrunarstýrðrar eftirgæslu til sjúklinga eftir útskrift af gjörgæsludeild og prófun á áhrifum hennar

Rannveig J. Jónasdóttir

Ritgerð til doktorsgráðu

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Ágrip

Bakgrunnur: Bráð og alvarleg veikindi og lega á gjörgæsludeild geta haft áhrif á líkamlegt og sálrænt heilsufar sjúklinga eftir útskrift af gjörgæsludeild. Vísbendingar eru um mögulegan ávinning sjúklinga af hjúkrunarstýrðri eftirgæslu eftir útskrift af gjörgæsludeild en áhrif hennar eru lítt þekkt og samanburðarrannsóknir fáar.

Markmið: Markmið rannsóknarinnar var að þróa íhlutunina: skipulögð, hjúkrunarstýrð eftirgæsla eftir útskrift af gjörgæsludeild – og mæla áhrif hennar á langtíma líkamlegt og sálrænt heilsufar sjúklinga eftir útskrift af gjörgæsludeild og bera saman við hefðbundna þjónustu.

Aðferðir: Ritgerðin samanstendur af þremur rannsóknargreinum. Rannsókn I var samþætt kerfisbundið yfirlit á innihaldi, skipulagi og mælingum á árangri hjúkrunarstýrðrar eftirgæslu sjúklinga eftir útskrift af gjörgæsludeild. Jafnframt var unnið að þróun íhlutnunarinnar: skipulögð hjúkrunarstýrð eftirgæsla sjúklinga eftir útskrift af gjörgæsludeild. Rannsóknir II og III voru framsýnar samanburðarrannsóknir þar sem íhlutunin var veitt sjúklingum eftir útskrift af gjörgæsludeild. Íhlutunin samanstóð af: (i) bæklingi, afhentur við útskrift af gjörgæsludeild, (ii) staðlað, klínískt eftirlit og stuðningur gjörgæsluhjúkrunarfræðinga á legudeild, (iii) símtal í fyrstu viku heima eftir útskrift af legudeild og, (iv) endurkoma þremur mánuðum eftir útskrift af gjörgæsludeildinni sem innihélt hálf-staðlað viðtal og heimsókn á gjörgæsludeildina. Samanburðarhópurinn fékk hefðbundna þjónustu. Þátttakendur voru sjúklingar ≥18 ára sem höfðu dvalið ≥72 klukkustundir á gjörgæsludeild. Í rannsókn II voru áhrif íhlutunarinnar á heilsufar (spurningalistinn Short-Form 36v2) borin saman milli tilraunahóps (N=73) og samanburðarhóps (N=75) með slembiþáttalíkani (mixed effects model). Mælingar voru gerðar fimm sinnum: Fyrir innlögn á gjörgæsludeild (mælt á legudeild), við útskrift af legudeild og þremur, sex og 12 mánuðum eftir útskrift af gjörgæsludeild. Í rannsókn III voru einkenni áfallastreituröskunar (spurningalistinn Impact of Event Scale-Revised), kvíða og þunglyndis (spurningalistinn Hospital Anxiety and Depression Scale) borin saman með slembiþáttalíkani milli tilraunahóps (N=68) og samanburðarhóps (N=75) yfir þrjú og fjögur skipti á 12 mánaða tímabili eftir útskrift af gjörgæsludeild. Truflandi minningar frá legu á gjörgæsludeild og sálræn viðbrögð (sjúklingur taldi líf sitt vera í hættu, taldi að líkami hans væri vanvirtur eða honum

misboðið, upplifði að vera hjálparvana, upplifði hrylling, var skelfingu lostinn) voru mæld þremur mánuðum eftir útskrift af gjörgæsludeild. Spáð var fyrir um einkenni áfallastreitu þremur mánuðum eftir útskrift af gjörgæsludeild með aðhvarfsgreiningarlíkani (regression model).

Niðurstöður: Rannsókn I: Þrenns konar fyrirkomulag hjúkrunarstýrðrar eftirgæslu sjúklinga eftir útskrift af gjörgæsludeild kom fram: i) komur gjörgæsluhjúkrunarfræðinga á legudeild; ii) komur gjörgæsluhjúkrunarfræðinga á legudeild og endurkoma sjúklinga tveimur mánuðum eftir gjörgæsluútskrift; iii) heimsókn á gjörgæsludeild og símtal tveimur mánuðum eftir útskrift af gjörgæsludeild. Niðurstöður sýndu óljósan árangur hjúkrunarstýrðrar eftirgæslu sjúklinga eftir útskrift af gjörgæsludeild. **Rannsókn II:** Íhlutunin: skipulögð hjúkrunarstýrð eftirgæsla sjúklinga eftir útskrift af gjörgæsludeild – bætti ekki heilsufar sjúklinga borið saman við hefðbundna þjónustu. Heilsufar beggja, tilraunahóps og samanburðarhóps, versnaði frá því fyrir innlögn á gjörgæsludeild að 12 mánuðum eftir útskrift þaðan. Meiri verkir mældust á rannsóknartímanum hjá konum í tilraunahópi en konum í samanburðarhópi og karlmönnum úr báðum hópunum. Jafnframt var heilsufar kvenna í tilraunahópi almennt verra en karla í sama hópi. Algengast var að starfsemi öndunarfæra væri metin hjá sjúklingum í tilraunahópi á legudeild og inntu 30 gjörgæsluhjúkrunarfræðingar matið af hendi (spönn 1 – 6 gjörgæsluhjúkrunarfræðingar) en þeir komu að meðaltali þrisvar sinnum til hvers sjúklings (spönn 2 – 10 komur á hvern sjúkling). Sjúklingarnir vildu heldur tala um hversu veikburða og úthaldslitlir þeir voru en fá upplýsingar um endurhæfingu og virkni þegar hringt var í þá í fyrstu viku eftir útskrift af legudeild og heim. Af þeim 68 sjúklingum sem þáðu endurkomu voru 56% (n=38) sem heimsóttu gjörgæsludeildina. Tilraunahópur lá marktækt skemur á legudeild en samanburðarhópur. **Rannsókn III:** Tilraunahópurinn hafði fremur einkenni áfallastreituröskunar en samanburðarhópur yfir 12 mánuði eftir útskrift af gjörgæsludeild. Hlutfallslega fleiri sjúklingar úr báðum hópum sem höfðu einkenni áfallastreituröskunar við þrjá mánuði (n=34) áttu truflandi minningar úr gjörgæslulegunni og höfðu sálræn viðbrögð samanborið við sjúklinga án einkenna áfallastreituröskunar (n=96). Lægri aldur, að vera á örorkubótum, hafa upplifað hjálparleysi, eiga truflandi minningar og hafa orðið skelfingu lostinn í gjörgæslulegu spáði fyrir um einkenni áfallastreituröskunar sjúklings þremur mánuðum eftir útskrift af gjörgæsludeild.

Ályktun: Íhlutunin: skipulögð, hjúkrunarstýrð eftirgæsla sjúklinga eftir útskrift af gjörgæsludeild – bætti ekki heilsufar sjúklinga samanborið við hefðbundna þjónustu sem sjúklingar í samanburðarhópi fengu. Hinir ólíku hópar sjúklinga

og fjöldi gjörgæsluhjúkrunarfræðinga sem veittu íhlutnina gætu skýrt ómarktækar niðurstöður. Frekari rannsóknir þarf til að þróa og mæla útkomu hjúkrunarstýrðrar eftirgæslu gjörgæslusjúklinga. Niðurstöðurnar sýna að heilsufar ófárra sjúklinga sem lifa af gjörgæsludvölina er slæmt fyrsta árið eftir útskrift. Þær gefa til kynna að bæta þarf líðan þeirra með markvissum aðgerðum.

Lykilorð: bráð og alvarleg veikindi, eftirbati, gjörgæsludeild, heilsufar, klínísk hjúkrunarrannsókn

Abstract

Background: The physical and psychological health status of patients after intensive care is frequently compromised due to the consequences of critical illnesses and the intensive care stay. There are indications that patients may benefit from receiving nurse-led follow-up after intensive care but the nature of the intervention and its effects have not been sufficiently investigated.

Aims: The aim of this thesis was to develop an intervention of structured nurse-led follow-up for patients after intensive care and test its effectiveness on patients' long-term physical and psychological health status after intensive care discharge compared with standard care.

Methods: The thesis consists of three studies. In Study I, an integrative review of a nurse-led follow-up of patients after discharge from intensive care was performed and an intervention of structured nurse-led follow-up for patients after intensive care was constructed. Studies II and III were prospective, quasi-experimental studies of patients who received a structured nurse-led follow-up after intensive care discharge. The intervention consisted of: (i) a booklet delivered at intensive care discharge, (ii) protocolised clinical surveillance and support with general ward visits from intensive care nurses, (iii) contact during the first week after discharge from the general ward to home and, (iv) an appointment comprising a semi-structured interview and an intensive care visit three months after discharge from intensive care. The control group received standard care. Participants were patients ≥ 18 years of age with ≥72 hour's intensive care stay. In Study II, the effectiveness of the intervention on health status (Short-Form 36v2 questionnaire) was compared between the experimental (N=73) and control groups (N=75) over five time points, from before admission to intensive care (collected during the ward stay), at ward discharge, three, six and 12 months after intensive care discharge using a mixed effects model. In Study III, symptoms of post-traumatic stress disorder (Impact of Event Scale-Revised), anxiety and depression (Hospital Anxiety and Depression Scale) were compared between the experimental (N=68) and control groups (N=75) three and four times over 12 months after intensive care discharge. Patients' disturbing memories of the intensive care stay and their psychological reactions (feeling that their life was in danger, sensing a threat to physical integrity, intense fear, helplessness, horror) were collected three months after discharge from

intensive care. A mixed effect model tested differences between the groups over time and a regression model predicted post-traumatic stress at three months.

Results: Study I: Three patterns of intensive care nurse-led follow-up were detected: i) ward visits, ii) ward visits and appointment(s) to an intensive care follow-up clinic, and iii) a follow-up visit to an intensive care and a phone call two months after intensive care discharge. The results indicated uncertain, primarily descriptive, outcomes of intensive care nurse-led follow-up. There was a lack of continuity between intervention structures. **Study II:** The structured nurse-led follow-up did not improve patients' health status compared to standard care. Health status within both groups decreased from before the intensive care admission and over one year after the intensive care discharge. Females in the experimental group reported more bodily pain over the time points than females in the control group and men in both groups. Another trend was an overall worse health status of women in the experimental group compared to men in that group. Patients' respiratory status was most commonly assessed during an average of three ward visits (range 2 – 10 visits per patient) with a total of 30 intensive care nurses (range 1 – 6 nurses) providing the visits to the experimental group. Rather than focusing on rehabilitation information and activities the patients were most concerned about how weak they were and their lack of endurance when contacted in the first week after discharge from the general ward to home. Of the 68 patients attending the three-month appointment, 56% (n=38) accepted the invitation to re-visit the intensive care. The length of the general ward stay was shorter in the experimental group compared to the control group. **Study III:** The experimental group had significantly more post-traumatic stress symptoms and anxiety than the control group over the 12 months after intensive care discharge. Proportionally more patients in both groups with post-traumatic stress symptoms at three months (n=34) had disturbing memories of the intensive care stay and psychological reactions compared to patients without post-traumatic symptoms (n=96). Younger age, receiving disability benefits, experiencing helplessness, disturbing memories and intense fear during the intensive care predicted symptoms of post-traumatic stress three months after the intensive care discharge.

Conclusion: The intervention of structured nurse-led follow-up for patients after intensive care did not improve patients' health status compared to the standard care that the control group received. The heterogeneity of the patient groups and the number of nurses providing the intervention might explain the insignificance of the findings. Further effort is needed to develop

and measure outcomes of intensive care nurse-led follow-up. The findings indicate that the health status of a large number of patients who survive the intensive care stay is severely compromised over the first year after the ICU discharge, which necessitates a concerted effort to improve that situation.

Keywords: Aftercare, Clinical Practice Nursing Research, Critical Illness, Health Status, Intensive Care Units.

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Contents

List of abbreviations

ANOVA: Analysis of Variance

APACHE II: Acute Physiology and Chronic Health Evaluation II

CCO: Critical Care Outreach

CReDECI 2: Criteria for Reporting the Development and Evaluation of Complex Interventions 2

HADS: Hospital Anxiety and Depression Scale

ICU: Intensive Care Unit

IES-R: Impact of Event Scale-Revised

LOS: Length of stay

NHS: National Health Service

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PTSD: Post-traumatic stress disorder

RCT: Randomised controlled trial

SF-36v2: Short-Form-36 version 2® Health Survey

TISS-28: Therapeutic Intervention Scoring System-28

UK: United Kingdom

List of figures

List of tables

List of original papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I-III):

I. Jónasdóttir, R. J., Klinke, M. E., & Jónsdóttir, H. (2016). Integrative review of nurse-led follow-up after discharge from the ICU. *Journal of Clinical Nursing, 25*(1-2), 20-37. doi: 10.1111/jocn.12939. *

II. Jónasdóttir, R. J., Jones, C., Sigurdsson, G. H., & Jónsdóttir, H. Structured nurse led follow-up for patients after discharge from the intensive care unit: prospective quasi-experimental study. *Journal of Advanced Nursing*, accepted for publication 10th of October, 2017. doi: 10.1111/jan.13485 *

III. Jónasdóttir, R. J., Jónsdóttir, H., Gudmundsdottir, B., & Sigurdsson, G. H. (2017). Psychological recovery after intensive care: outcomes of a long-term quasi-experimental study of structured nurse-led follow-up. *Intensive and Critical Care Nursing*, [Article in press]. doi.org/10.1016/j.iccn.2017.06.001. **

Declaration of contribution

Study I: Rannveig J. Jónasdóttir (RJJ), Marianne E. Klinke (MEK) and Helga Jónsdóttir (HJ) were responsible for the study conception and design. RJJ performed the initial literature searches. RJJ and HJ performed the data analysis. RJJ was responsible for drafting the manuscript and HJ and MK made critical revisions to the article for important intellectual content.

Study II: RJJ, HJ, Christina Jones (CJ) and Gísli H. Sigurðsson (GHS) were responsible for the design of the study and interpretation of the results. RJJ conducted the study and performed the statistical analysis. Statistical assistance was received from the Statistical counselling center, School of Health Science, University of Iceland (www.trhvs.hi.is - trhvs@hi.is). RJJ was responsible for drafting the manuscript with supervision from HJ and GHS. RJJ, CJ, GHS and HJ made critical revisions to the article for important scientific and intellectual content.

Study III: RJJ, HJ, GHS and Berglind Guðmundsdóttir (BG) were responsible for the design of the study and interpretation of the results. RJJ conducted the study and performed the statistical analysis. Statistical assistance was received from the Statistical counselling center, School of Health Science, University of Iceland (www.trhvs.hi.is - trhvs@hi.is). RJJ, HJ and GHS were responsible for drafting the manuscript and RJJ, HJ, BG, and GHS, made critical revisions to the article for important scientific and intellectual content.

1 Introduction

Intensive care unit (ICU) nurse-led follow-up is a service designed for supporting patient's health and recovery after the ICU discharge (Cuthbertson et al., 2009). The recovery is impacted by consequences of the ICU stay and of the critical illness that originally led to the ICU admission (Desai et al., 2011). The consequences can be profound, affecting physical and psychological health status, and recovery, which is frequently slow and incomplete despite the cure of the disease causing the ICU admission (Jones & Griffiths 2002; Oeyen et al., 2010). The consequences of critical illness and the ICU stay can be extensive and numerous, including effects on physical health, impacts on function in activities of daily living, effects on psychological health causing anxiety, depression and post-traumatic stress disorder (PTSD), and effects on cognition and social health status, as shown in Figure 1 (Granja et al., 2005; Griffiths & Jones 2007; Needham et al., 2012;

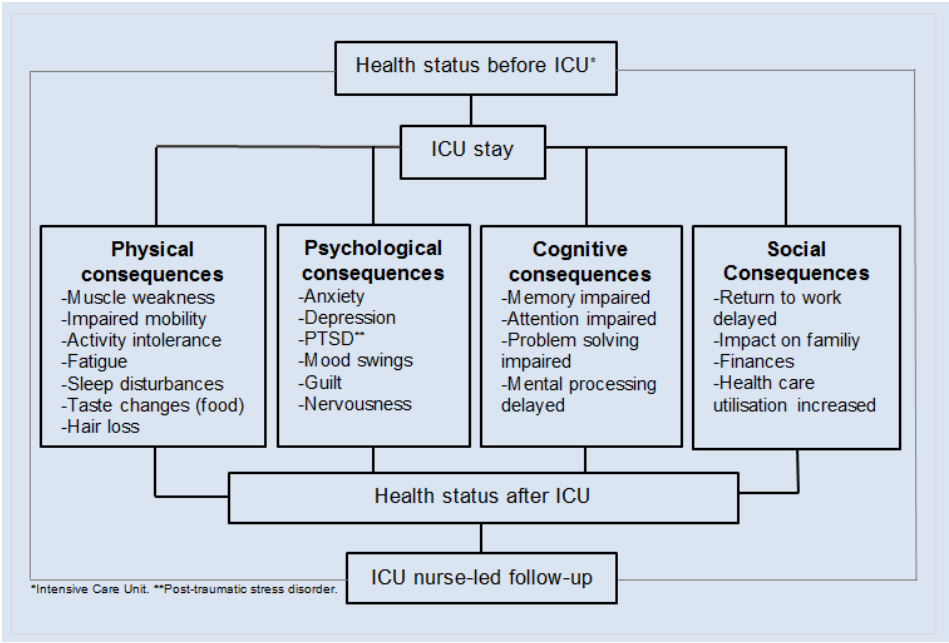

Figure 1. Consequences of the intensive care stay on patients' health status and relation of ICU nurse-led follow-up in supporting patients' recovery after intensive care stay.

Sharland, 2002; van der Schaaf et al., 2009). The patient's health status before the ICU admission has also been shown to be a significant factor affecting the health status post-hospital (Feemster et al., 2015). Impairment in patient's health status can be persistent, compared to their health status before the ICU admission and compared to the health status of the general population, from a few months up to several years after the ICU discharge (Cuthbertson et al., 2010; Herridge et al., 2011).

Because of increased awareness of the effect of the aftermath of critical illness and ICU stay on health status, means to improve patients' outcomes have commenced. These are mainly hospital services, implemented by experienced ICU nurses and physicians, and provided after patients' ICU discharge. The services are, for example, medical emergency teams, rapid response teams and Critical Care Outreach (CCO) teams (Chan et al., 2010; Hillman et al., 2005; McDonnell et al., 2007). Nurse-led follow-up of patients after discharge from the ICU is one of the services and has been reported to be a means to support patients' recovery after discharge from the ICU (Egerod et al., 2013).

In the following sections, a brief description of the ICU environment and patients' experiences and memories of the ICU stay is given. The background of the consequences of critical illness and patients' ICU stay on physical and psychological health status is outlined, which is the primary reason for the development of ICU nurse-led follow-up. The section is completed with a history of ICU nurse-led follow-up. This gives the context and rationale for the study.

1.1 The intensive care: environment, treatment, experience and memories

The fundamental treatment that patients receive during the ICU stay aims at supporting and restoring the function of vital organs and preventing further organ failure and mortality (Lone & Walsh, 2012). The ICU treatment is provided in an environment that is unlike other hospital units. It is characterised by continuous surveillance from nurses and physicians and the use of machines and drugs for supporting and monitoring organ function. This includes invasive vascular lines, tubes and machinery, inserted into or attached to the patient, such as arterial lines, central venous catheters, urinary catheters, mechanical ventilators or dialysis machines. The intravenous drugs commonly used are vasopressors and fluids for supporting

the haemodynamics, and pain killers and sedatives to ensure patients comfort (Christensen & Probst, 2015). When discharged from the ICU to a general ward, the patients may still be critically ill and have not returned to their former state of health; the convalescence after critical illness is starting (Angus & Carlet, 2003). Additionally, the change from the secure and continuous monitoring of the ICU to the more intermittent transaction with health care staff at the general ward is vast (Field et al., 2008).

Being admitted to the ICU can be a stressful experience for patients (Engström et al., 2013; Rotondi et al., 2002; Samuelson, 2011). The stressfulness is caused by several factors. Among those are the ICU environment and the ICU treatment received, as well as emotions and memories during the ICU stay (Karlsson et al., 2012; Meriläinen et al., 2013; Samuelson, 2011). Patients have described the stressfulness of noises, bright lights, staff conversations and hearing other patients in the ICU (Burry et al., 2015; Elliott et al., 2013; Meriläinen et al., 2013) and being connected to lines and tubes (Engström et al., 2013). Intubated patients have difficulties communicating. A substantial proportion of the communication exchange between patients and ICU nurses is unsuccessful for the patients (Happ et al., 2011). Among the worst experiences during the ICU stay are difficulties when patients become voiceless/cannot make a sound when intubated and on a ventilator, combined with breathlessness, helplessness and powerlessness (Karlsson et al., 2012). Patients can remember feelings of security and comfort during their ICU stay (Engström et al., 2013; Samuelson, 2011), but at the same time they may experience cold, thirst, pain, fear, distress (Löf et al., 2008; Meriläinen et al., 2013), being dependent on staff and confrontations with death (Almerud et al., 2007).

Patients frequently have amnesia about the ICU stay, concurrent with positive and disturbing memories (Chahraoui et al., 2015; Löf et al., 2008). The experience of amnesia and disturbing memories can occur despite being considered awake when the depth of sedation is measured with assessment tools such as the *Richmond Agitation-Sedation Scale* (Burry et al., 2015). The memories of the ICU stay can be vivid and strong and can remain unchanged from one to five years after the ICU discharge (Löf et al., 2008; Zetterlund et al., 2012). The memories can be factual, such as remembering the family, emotional, such as fear and pain, or delusional, such as dreams, nightmares, hallucinations and feelings that people were trying to hurt them (Jones et al., 2001; Burry et al., 2015). Putting the ICU experience into perspective can be difficult for patients (Löf et al., 2008). That is, delusional memory can be misinterpreted in the context or circumstances in which it

occurred. Patients who have frightening memories of their ICU stay (delusions, hallucinations, nightmares) can have symptoms of PTSD at two months (Jones et al., 2001; Samuelson et al., 2007), three months (Jones et al., 2010) and up to at least six months (Granja et al., 2008) after the ICU stay.

1.2 Health status after intensive care

The reasons for patients' slow recovery after ICU discharge are manifold (NICE, 2009). Muscle weakness – also referred to as physical weakness – is one of the main reasons. Patients experience muscle weakness because of muscle wasting, produced by complex pathophysiological processes in the body during critical illness in addition to immobility, i.e. bed rest, during the hospital stay (Hashem et al. 2016; Truong et al., 2009). Muscle wasting can be profound during the acute period of critical illness (Koukourikos et al., 2014). The muscle weakness presents itself as loss of muscle strength, apparent in the hand grip, and a deficiency in the distance walked over a timed six minutes (Fan et al., 2014). It also emerges in restrictions in other activities of daily living such as lifting and carrying objects/groceries, shopping, doing housework and transport (van der Schaaf et al., 2009). Due to the restrictions, patients need help at home, after discharge from hospital (Chaboyer and Grace, 2003; Chelluri et al., 2004) and a delay in returning to the previous employment or workplace can be inevitable (Chaboyer & Grace, 2003; van der Schaaf et al., 2009). Multiple other physical consequences have been reported, such as problems with swallowing, joint stiffness and motor and sensory polyneuropathy (Hermans et al., 2009; Jones & Griffiths, 2002) (Figure 2). During the first (van der Schaaf et al., 2009) and the second year (Fan et al., 2014) after the ICU discharge, physical function is heavily impacted by muscle weakness. In the first year after the ICU discharge there is, nevertheless, a significant improvement in patients' physical health (Elliott et al., 2011; Fan et al., 2014).

A combination of time, case-mix, pre-ICU health and age add to the complexity of ICU patients' post-ICU health status. Despite the improvement, the overall health status of former ICU patients is worse than that of the general population from one year (Cuthertson et al., 2005; Herridge et al. 2003) up to five years post-ICU (Deja et al. 2006; Herridge et al. 2011). Although physical functioning is usually worse than that of the general population (Cuthbertson et al., 2005; Feemster et al., 2015) mental health

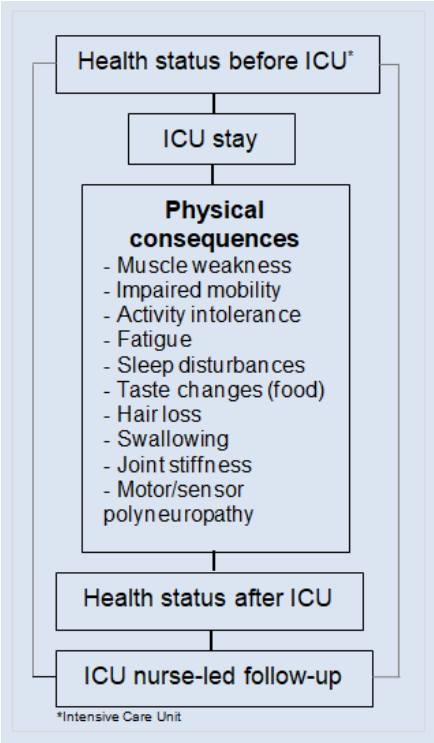

Figure 2. Consequences of intensive care stay on physical health status.

can be equal or even better compared to the general population from three to 12 months after ICU discharge (Cuthbertson et al., 2005). Regardless of this, the health status of elderly patients (Jeitziner et al., 2015), the mixed ICU patient population (Cuthbertson et al., 2005) and patients with certain ICU admission diagnoses, such as respiratory dysfunction (Deja et al., 2006), sepsis (Longo et al., 2007), or trauma (Ringdal et al., 2009), is revealed to be worse compared to the general population from seven months (Longo et al., 2007) up to five years post-ICU (Deja et al., 2006). This is evident although the precipitating factor that caused the critical illness in the first place is long gone. Among the ICU patient groups there are two that have been shown to have a health status comparable to the general population from six months (Cronberg et al., 2015) to five years (Faulhaber-Walter et al., 2016) after ICU discharge. The groups are patients with ICU admission diagnosis of cardiac arrest (Cronberg et al., 2015) and acute kidney injury (Faulhaber-Walter et al., 2016).

ICU patients have more comorbidity and worse health status when admitted to the ICU compared to the general population (Cuthertson et al., 2005; Wehler et al., 2003). Additionally, the pre-ICU health status has been shown to be a significant factor in the health status post-hospital (Feemster et al., 2015; Myhren et al., 2010; Wehler et al., 2003). Orwelius et al. (2010) showed that the pre-existing disease explained the reduction in health status over three years after ICU discharge. Moreover, pre-existing disease was the primary factor causing reduced health status after ICU, and not ICU factors such as length of ICU stay, ICU admission diagnosis and APACHE II score (Orwelius et al., 2010). This underscores the importance of assessing ICU patients' health status before hospital admission in order to realistically

indicate changes in health status post-hospital that may be expected (Feemster et al., 2015; Wehler et al., 2003). Measuring patients' health status before the ICU is, nevertheless, not a routine procedure in research on ICU patients (Feemster et al., 2015; Oeyen et al., 2010) as the patients' serious condition hinders them from answering questionnaires when in the ICU (Hofhuis et al., 2003).

Older age along with high burden of pre-existing diseases is associated with worse physical health post-ICU (Myhren et al, 2010). Despite a decrease in quality of life post-ICU, compared to younger ICU patient controls, the elderly adapt to their health status (Kaarlola et al., 2006; Merlani et al., 2007) and report good quality of life one year after ICU, particularly in mental health (Kaarlola et al., 2006). Acceptance of disability is greater by older patients than younger (Montuclard et al., 2000).

Some gender differences have been reported post-ICU. The lowest scores of health status six months after ICU discharge that have been reported are of single men on sick leave before the ICU admission (Orwelius et al., 2013). In a mixed cohort of ICU patients there was a tendency for women to have worse health status than men 12 months post-ICU in all of the eight items of SF-36, although this was significant in only two of the items (role physical, social functioning) (Myhren et al., 2010). Additionally, women had more bodily pain than men before ICU and bodily pain increased significantly more for women than for men from before ICU to 12 months post-ICU (Myhren et al., 2010).

Furthermore, focusing on the psychological health of patients during and after ICU treatment there is emerging evidence that the critical illness and the treatment in the ICU can be difficult and stressful experiences for patients and this may contribute to PTSD, anxiety and depression after ICU discharge (Davydow et al., 2013; Jones et al., 2001; Perrins et al., 1998). The psychological distress post-ICU adds to the slow course of recovery, comparable to the consequences of critical illness on physical health post-ICU (Rattray et al., 2010; Samuelson et al., 2007). This signifies the importance of the presence and provision of follow-up after critical illness (NICE, 2009).

PTSD is defined as a stress-related response after witnessing or experiencing a traumatic event (American Psychiatric Association, 2013). The event can be experiencing extreme stress during the ICU stay (Wade et al., 2013) or the injury that led to the ICU admission (O´Donnell et al., 2010). The response of an individual can be to re-experience the event via flashback,

dreams or memories (intrusion), avoiding thoughts, feelings, places, people or activities related to the event (avoidance) or being hypervigilant, resulting in having sleep disturbances or being irritable (hyperarousal) (American Psychiatric Association, 2005). In 2013 a new category, negative thoughts and feelings, was added to the definition of PTSD. Negative thoughts and feelings are characterised by symptoms of negative beliefs about oneself, fear, guilt, and diminished interest in previously enjoyable activities (American Psychiatric Association, 2013). PTSD has been described in various groups and circumstances such as after avalanches (Thordardottir et al., 2015), burn injuries (Cakir et al., 2015), mothers of infants with extremely low birth weight (Zerach et al., 2015) and patients after an ICU stay (Asimakopoulou & Madianos, 2015). If symptoms of PTSD are present one month after the traumatic event, the PTSD is considered acute, but chronic if the symptoms are persistent at three months after the event (American Psychiatric Association, 2013).

The majority of people recover from their PTSD-related symptoms without professional help within the first three months of a traumatic event, indicating a natural recovery period (Riggs et al., 1995; Rothbaum et al., 1992). Watchful waiting together with general and concerned support is recommended in the first months after the event (NICE, 2005; NICE update, 2013). Even though some patients recover naturally after the ICU, a substantial proportion of patients report symptoms of PTSD from three months up to two years after ICU discharge (Bienvenu et al., 2015). The point prevalence of PTSD symptoms from one to 12 month post-ICU ranges from 4% to 62% (Parker et al., 2015). The pooled prevalence of severe symptoms of PTSD measured with the Impact of Event Scale (score ≥ 36) one to six months after ICU is 24% and at seven to 12 months it is 22% post-ICU, as reported in a meta-analysis (Parker et al., 2015). The primary risk factors for developing symptoms of PTSD post-ICU are receiving benzo-diazepam medication during ICU treatment (Girard et al., 2007), psychopathology before the ICU admission (Wade et al., 2012), anxiety and depression before the ICU admission (Davydow et al., 2013; Nickel et al., 2004) and disturbing or frightening memories during the ICU stay (Samuelson et al., 2007). Being female (Girard et al., 2007; Samuelson et al., 2007) and of younger age (there is an indication of declining PTSD symptoms after the age of 50 (Girard et al., 2007)) have been shown to be predictors of PTSD (Figure 3). Severity of illness (Girard et al., 2007; Ratzer et al., 2014) and length of ICU stay (Parker et al., 2015; Samuelson et al., 2007) are, however, generally not associated with symptoms of PTSD post-ICU.

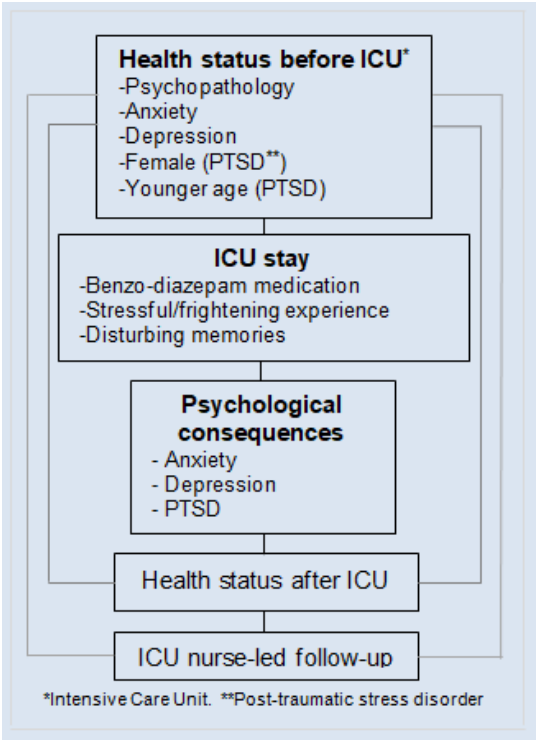

Figure 3. The impact of health status before the ICU stay and the ICU stay on patients' psychological health status after ICU.

Symptoms of PTSD can have negative effect on the patient's health status, including physical, mental and social health and recovery, after the ICU discharge. A correlation has been reported between symptoms of PTSD and health-related quality of life (health status), six months after hospital discharge, where having symptoms of PTSD impaired health-related quality of life (Girard et al., 2007). Measures of the general population are comparable, which show a negative association between PTSD and general health (Pacella et al., 2013). A long-term, negative association has also been reported between symptoms of PTSD and physical functioning, 24 months after patients' ICU discharge (Bienvenu et al., 2015). ICU patients, who have a high symptom score of PTSD, have worse mental health one year after ICU, compared to patients that score lower on symptoms of PTSD and compared to a general population (Deja et al., 2006). The impact of symptoms of PTSD on social health, measured three months post-ICU, is substantiated with an increased likelihood of patients' emergency department admission the following nine months (Davydow et al., 2014). On the other hand, social support during post-ICU recovery could benefit patients, sustained by decreased measures of PTSD symptoms one year after ICU (Deja et al., 2006).

Measures of anxiety and depression have repeatedly shown a negative impact on psychological health and recovery of patients after their ICU discharge (Kowalczyk et al., 2013; Ringdal et al., 2009). Depression and anxiety can reduce patients' quality of life for a period ranging from three up

to 24 months after the ICU discharge (Paparrigopoulos et al., 2014; Stevenson et al., 2013). Additionally, anxiety and depression post-ICU can have an impact on the effectiveness of physical recovery (delayed) (Sukantarat et al., 2007). The pooled prevalence of clinically significant anxiety and depression is around 17% (Hospital Anxiety and Depression Scale (HADS) cut-off score of ≥11) from two to 14 months post-ICU (Nikayin et al., 2016; Rabiee et al., 2016).

The trajectory of measured anxiety and depression has shown a significant decrease from ICU patients' hospital discharge to three months (Castillo et al., 2016) and again during the first two to 12 months post-ICU (Rattray et al., 2005; Samuelson et al., 2007). At the same time, the severity of depression and anxiety scores remains relatively stable from two to six and 12 months after ICU discharge (Castillo et al., 2016; Rattray et al., 2005; Rattray et al., 2010). To add to the complexity, ICU patients' anxiety and depression scores have been shown to fluctuate in severity or between being clinically significant and non-significant from hospital discharge to six months after ICU (Castillo et al., 2016).

Patients who have a history of anxiety, depression or other psychiatric disorders before the ICU admission are at risk of experiencing anxiety and/or depression from two up to 24 months after ICU (Paparrigopoulos et al., 2014; Samuelson et al., 2007; Stevenson et al., 2013) (Figure 3). Patients' experience of the ICU stay also plays a significant role in relation to anxiety and depression post-ICU. Those who have a stressful or frightening ICU stay have significantly more anxiety and depression compared to patients who do not have such experiences during their ICU stay when measured at two months post-ICU (Samuelson et al., 2007). Furthermore, having delusional memories during the ICU stay significantly increases anxiety, as measured at six months post-ICU, compared to those who do not have such ICU memories (Jones et al., 2003). Stress or frightening experiences during the ICU or ward stay also predicts the risk of anxiety and depression over the 12 months post-ICU (Davydow et al., 2013; Rattray et al., 2005; Wade et al. 2012). An association between age, severity of illness and ICU or hospital length of stay and anxiety and depression post-ICU has not been established (Nikayin et al., 2016; Rabiee et al., 2016). Moreover, gender and ICU diagnosis have not been shown to be associated with anxiety post-ICU (Nikayin et al., 2016).

1.3 Nurse-led follow-up of patients after discharge from intensive care

In the late eighties and beginning of the nineties, studies of the quality of life of ICU patients started to appear (Jacobs et al., 1988; Ridley & Wallace, 1990). Those studies investigated ICU patients' survival, mortality and severity of illness (Chassin, 1982; Knaus et al., 1982) and supported emerging awareness of ICU patients' outcomes compared to merely measuring short-term mortality after the ICU (Ledingham et al., 1989; Shiell et al., 1990). A decade later, the National Health Service (NHS) in the United Kingdom (UK), published the Comprehensive Critical Care recommendations of critical care services (Department of Health, 2000). The recommendation arose from disorganised ICU services, a need for more ICU beds, increasing costs and an ongoing need for outcome measures (Audit Commission, 1999). The recommendations were a milestone in intensive care services in the UK. There, the "Intensive Care without walls" was introduced, with recommendations for Critical Care Outreach (CCO) services with the aim of preventing readmissions to the ICU, supporting earlier discharges from the ICU, and sharing critical care skills with staff in the general wards (Department of Health, 2000). Long-term support and follow-up of ICU patients after discharge from hospital was also included in the recommendations (Department of Health, 2000). The limitation of this pivotal work was the lack of recommendations for a structure of follow-up services, resulting in various health care professionals' teams attending patients at any time after ICU discharge, such as consultant nurses and nurse-led teams with or without medical participation (Ball, 2002). Nevertheless, the recommendations remained as the foundation for formal post-ICU services, albeit implemented with numerous structures and contents throughout the UK (NHS Modernisation Agency, 2003).

While hospitals in the UK were fulfilling obligations outlined in the policy of the NHS, in Australia, ICU nurse-led follow-up had already started as a "bottom-up" initiative (Chaboyer et al., 2004). In the mid-nineties, the Australians began a service for patients after discharge from the ICU to general wards, later called the ICU liaison nursing (Russell, 1999b). The initiative was inspired by the research of Russell (1996, 1999a) and presented to the Royal Melbourne Hospital in 1994 to 1995 (Russell, 1999b). The cornerstone of this work was the high rate of readmission of patients to ICUs from general wards, the lack of support for ward nurses in caring for the critically ill, and the lack of support for patients and their families after critical illness. Subsequently, from 1995, ICU follow-up nurses at the Royal

Melbourne Hospital started working systematically on reducing ICU readmissions, emphasising continuity of patients' and family care when discharged from the ICU to the ward, and increasing the clinical expertise of ward staff (Russell, 1999a, 1999b). The benefits of this service were a lower readmission rate and indications of a timely readmission to the ICU (Russell, 1999a). Chaboyer et al. (2004) published a description of the role of five ICU liaison nurse services in Australia. In total, six ICUs in Australia were identified as having such services in 2004, with one ICU liaison nurse at each ICU. The role encompassed support and education for ward staff, and care of patients on general wards that included ICU therapies and support for them and their families (Chaboyer et al., 2004).

Looking more closely into the history of the nurse-led follow-up services in the UK before the NHS recommendations were published in 2000, it is clear that post-ICU services were already in place there, as summarised in Table 1. One of the first ICU follow-up clinics in the UK was established in 1990 at Whiston Hospital, Merseyside, Liverpool, where patients received ward visits and were invited to attend with their family at two and six months post-ICU. From the beginning, the clinic was led by an experienced ICU nurse and the patients also met an experienced ICU physician. The aim was to support the recovery of patients after discharge from the ICU (Griffiths & Jones, 2002). There were more hospital ICU-follow-up-clinics to follow. In 1994 a clinic was established at the Homerton Hospital in London (Hall-Smith et al., 1997) where a clinical nurse-specialist provided ward visits and interviewed patients about their psychological and physical recovery three months after ICU discharge. At the Royal Berkshire Hospital in Reading in 1995, an ICU follow-up clinic was established with ICU nurses and ICU physicians (Waldmann, 2002; Waldmann & Gaine, 1996). There, the patients were referred to other professionals as needed (e.g. a pain clinic and an ophthalmology service). The time during the ICU stay was discussed as well, and support of physical and psychological health and recovery was provided. Also in 1995, an ICU nurse-led follow-up clinic at Southampton University Hospitals NHS Trust was established, providing ward visits and appointments for patients after ICU discharge (Sharland, 2002). Furthermore, around 1995, Manchester Royal Infirmary established an ICU clinic and engaged in data collection for the ICU rehabilitation study of Jones et al. (2003).

Table 1. The location, year of establishment and content of the first ICU nurse-led follow-up services in the United Kingdom.

Location and year	Content
Whiston Hospital, Merseyside, Liverpool, 1990.	Ward visits to patients discharged from ICU and appointment two and six months post-ICU, for supporting psychological and physical recovery, where the patient and the family met an experienced ICU nurse and ICU physician who provided the service (Griffiths & Jones, 2002).
Homerton Hospital, London, 1994.	Ward visits from a clinical -nurse specialist to patients staying > 5 days in ICU for supporting the transition from the ICU to the ward, and an interview at three months post-ICU, aiming at psychological and physical recovery (Hall-Smith et al., 1997).
Royal Berkshire Hospital, Reading, 1995.	Patients and family staying > 4 days in ICU met an ICU nurse and ICU physician at two, six and 12 months post-ICU, providing information and discussing the post-ICU physical and psychological recovery (Waldmann, 2002; Waldmann & Gaine, 1996).
Southampton University Hospitals NHS Trust, 1995.	Patients and family staying > 4 days in ICU received ward visits and appointments from an ICU nurse-led clinic. The ICU experience and the recovery were addressed at two months, and the progress of recovery was monitored at six- and 12-month sessions (Sharland, 2002).

In the NHS policy of the year 2000, two forms of ICU follow-up services were recommended, the long-term follow-up (interpreted here as ICU nurse-led follow-up) and the CCO (Department of Health, 2000). The assignment of patients to the CCO is an early identification of the clinically deteriorating condition of patients during the ward stay. This is done in close collaboration with ward staff. The CCO is led and implemented by experienced ICU nurses and/or nurse consultants with backup from ICU physicians (Dawson & McEwen, 2005; Pittard, 2003; Priestley et al., 2004). From the outset, these two forms of service in the UK, i.e. the CCO and the ICU nurse-led follow-up, have had slightly different emphases. The primary differences are the patient populations and the timing of the services. The CCO was implemented for all patients staying in general wards regardless of ICU admissions or discharges and without further follow-up after the ward discharge (Dawson & McEwen, 2005; Pittard, 2003; Priestley et al. 2004). However, the ICU nurse-led follow-up was provided two to 12 months post-ICU (Griffiths et al., 2006) and included ward visits in some hospitals (Griffiths & Jones, 2002; Hall-Smith et

al., 1997) (Table 1). The ward visits of the ICU nurse-led follow-up were possibly separated from the ICU nurse-led follow-up in some hospitals because of the CCO ward based service. Likewise, the CCO seems not to have been regarded as a part of an ICU nurse-led follow-up. The probability remains that from the beginning these services were considered separate, which might have added to a discontinuous follow-up, set to occur directly after the patient's ICU discharge.

1.4 Context and rationale for the study

The necessity of a comprehensive follow-up for patients after discharge from an ICU with the purpose of supporting their recovery has been recognised (NICE, 2009). A structured nurse-led follow-up for patients, from ICU discharge to three months after the ICU discharge, was not in place at Landspítali – The National University Hospital of Iceland – where the study was performed. That prompted the development of this study. Additionally, there is a need internationally to substantiate the empirical evidence of ICU nurse-led follow-ups, by exploring and developing structure and content for the care of patients discharged from the ICU.

This thesis describes the development of a structured, nurse-led follow-up of patients after discharge from the ICU and the testing of its effectiveness on physical and psychological health status. The thesis is intended to increase knowledge of the content and structure of ICU nurse-led follow-up and its long-term effectiveness on patients' physical and psychological health status after ICU discharge.

2 Aims

There are three original studies that comprise the thesis. The overall aim of the thesis was to develop an intervention of structured nurse-led follow-up for patients after ICU and test its effectiveness on patients' long-term physical and psychological health status after ICU discharge versus standard care.

The aims of the three papers described in this thesis were:

I. To analyse and synthesise the structure, content and types of outcome variables of nurse-led follow-up of patients after discharge from ICU.

II. To describe the intervention of structured nurse-led follow-up for patients after ICU — at ICU discharge, during the ward stay after ICU discharge, from ward discharge to home, and three months after discharge from the ICU — and to measure the effect of the follow-up on health status versus standard care, from ward discharge to 12 months after ICU discharge, of patients staying ≥72 hours in mixed ICUs.

III. The aim was threefold. First, to measure the difference between patients receiving the structured nurse-led follow-up after ICU discharge versus standard care over time on symptoms of PTSD at three, six and 12 months after discharge from the ICU, and anxiety and depression at ward discharge and three, six and 12 months after discharge from ICU. Second, to compare background, memories of ICU stay and psychological reactions related to the memories of patients with and without symptoms of PTSD three months after ICU and third, to identify predictors of symptoms of PTSD three months after the ICU.

The research questions in each study and study hypothesis are presented in Table 2.

Table 2. Research questions and hypotheses.

Study	Research question	Study hypothesis
I	What is the structure, content and types of outcome variables of nurse-led follow-up of adult patients in any time after discharge from ICU as described in quantitative and qualitative studies?	There is evidence of effective structure, content and types of outcome variables of nurse-led follow-up of adult patients in any time after discharge from ICU.
II	What is the effectiveness of a structured nurse-led follow-up on patient's health status over 12 months after ICU discharge compared to standard care?	Structured ICU nurse-led follow-up significantly improves the health status of patients over 12 months after ICU discharge, compared to standard care.
III	What is the effectiveness of a structured ICU nurse-led follow-up on patient's psychological health over 12 months after ICU discharge compared to standard care?	Structured ICU nurse-led follow-up significantly improves psychological health of patients over 12 months after ICU discharge compared to standard care.

3 Materials and methods

This study was performed at Landspitali – The National University Hospital of Iceland which is a tertiary care hospital, located in Reykjavik, the main capital of Iceland. The hospital has two intensive care units, each with 10 beds, located in two separate buildings (buildings I and II) with around 1400 admissions a year. Patients admitted to the ICUs are level II and III patients (Intensive Care Society Standards, 2009). Approximately two thirds of the admitted patients are discharged from the ICUs within 72 hours. Both units have a 1:1-2 patient nurse ratio and 24 hours/day availability of intensive care physicians.

In 2012 the doctoral student prepared a research protocol for a Randomised Controlled Trial (RCT) for a PhD thesis which included a structured nurse-led follow-up to be tested at Landspitali. Ethical approvals for the trial were completed and accepted, along with approvals of the hospital and the ICUs. The trial was launched in May 2012 but after randomising the first patients the trial was stopped at the request of the ICU located in building II, i.e. the building where the general wards of the control site are located in the current thesis. The reason for the rejection was that some form of ward visits – described as the standard care in the current thesis – to patients discharged from the ICU in building II to general wards in building II was already ongoing, and had begun in 2007. Consequently, the research protocol had to be changed to a quasi-experimental study. A decision was made to carry out the study by having patients discharged from the ICUs in buildings I and II to general wards in building I as the experimental group and patients discharged from the ICUs in buildings I and II to general wards in building II as the control group.

Study I was an integrative review of the nurse-led follow-up after discharge from the ICU. The integrative review in study I guided the structure and content of the structured nurse-led follow-up intervention tested in Studies II and III and the outcome variables that were measured.

Study II was a prospective, longitudinal, quasi-experimental study of the structured nurse-led follow-up intervention and tested its effectiveness by measuring patient's health status from before the patient's ICU admission, at ward discharge and three, six and 12 months after the ICU discharge.

Study III was also a longitudinal, quasi-experimental study of symptoms of PTSD, anxiety and depression from ward discharge (only anxiety and depression) and at three, six and 12 month post-ICU. Additionally, patients' memories of the ICU stay and psychological reactions related to their

memories at three months were analysed and used in a prediction model. A description of each study is given in Table 3.

Table 3. The aims, designs, variables, data sources and analysis of Studies I, II, and III.

	Study I	**Study II**	**Study III**
Aim	Analyse and synthesize the structure, content and types of outcome variables of nurse-led follow-up of patients after discharge from intensive care units.	Describe the intervention of structured ICU* nurse- led follow-up — at ICU discharge, during ward stay, first week after ward discharge to home, and three months after the ICU discharge — and to measure the effectiveness of the follow-up on health status versus standard care, from ward discharge up to 12 months after ICU discharge.	Measure the difference between patients receiving structured nurse-led follow-up after ICU discharge versus standard care over time on: 1) symptoms of PTSD** at three, six and 12 months after discharge from ICU, and anxiety and depression at ward discharge and three, six and 12 months after discharge from ICU, 2) compare background, memories of ICU stay and psychological reactions related to the memories of patients with and without symptoms of PTSD three months after ICU, and 3) identify predictors of symptoms of PTSD three months after ICU.
Design	Integrative review	Prospective, longitudinal, quasi-experimental	Prospective, longitudinal, quasi-experimental
Variables	Structure, content and types of outcome variables of ICU nurse-led follow-up.	Intervention and standard care (independent variables). Health status (dependent variable).	Intervention, standard care, memories of ICU stay and psychological reactions (independent variables). PTSD, anxiety, depression, (dependent variables).
Data	Online databases from January 2003 to June 2014: PubMed, CINAHL, ScienceDirect, Scopus	Questionnaire answers of patients in the experimental group (N=83) and the control group (N=85) from before the ICU admission (collected during ward stay), at ward discharge, three, six and 12 months after ICU discharge.	Questionnaire answers of patients in the experimental group (N=68) and control group (N=75) at ward discharge, three, six and 12 months after ICU discharge.
Analysis	Extraction and synthesis of data.	Independent sample t-test, Mann-Whitney U test, Friedman Test, Mixed effect model.	Independent sample t-test, Mann-Whitney U test, Chi-square test, Mixed effect model, Multiple linear regression.

3.1 Design, search methods and quality appraisal of Study I

A systematic approach of integrative review was applied to investigate the structure, content and types of outcome variables of nurse-led follow-up of adult patients (≥18 years) after discharge from the ICU. Studies with quantitative and qualitative designs published from the first of January 2003 to the first of June 2014 were analysed, targeting literature of full-text articles and their reference lists for eligible studies. The review was built on the approach of Whittemore and Knafl (2005), where analysis and synthesis of studies with different methodologies is described, as well as using the PRISMA guidelines (Liberati et al., 2009) to structure the report. The inclusion criteria of the studies were follow-up service or intervention provided by nurses or a multidisciplinary team that included a nurse, within a hospital or a hospital clinic for patients after discharge from the ICU. A comprehensive search in PubMed, CINAHL, ScienceDirect and Scopus was applied. The search terms and search criteria of the online databases are presented in Figure 4.

Quality appraisal of selected articles was applied with four instruments from the Joanna Briggs Institute (2011); i) The Meta-Analysis of Statistics Assessment and Review Instrument for randomised and pseudorandomised studies, ii) The Meta-Analysis of Statistics Assessment and Review Instrument for cohort/case-control studies iii) The Qualitative Assessment and Review Instrument for qualitative studies, and iv) The Narrative, Opinion and Text Assessment and Review Instrument for Text/Opinion. The appraisal was graded by answering questions with yes (1), no (2), unclear (3) and not applicable (0) with a higher total score of the answer 'yes' indicating more quality. Two reviewers independently assessed the methodological quality of the articles and ambiguity was resolved by dialogue with the third reviewer. The authors of two original studies were contacted and gave information needed from their studies.

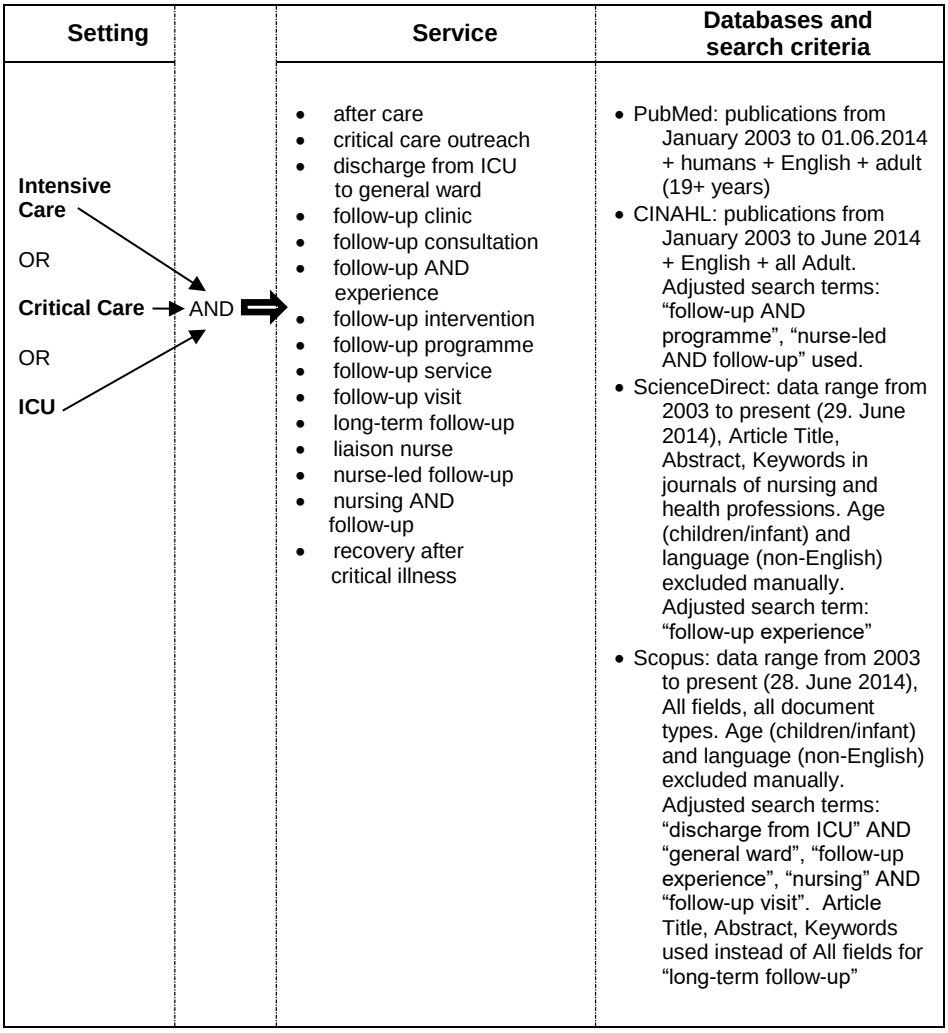

Figure 4. Search terms and search criteria used in the online databases.

3.2 Outcomes of Study I: Designing the ICU structured nurse-led follow-up intervention

The analysis and synthesis of the integrative review in Study I elicited the decision to design the structure and content of an ICU structured nurse-led follow-up, connecting the components from the ICU discharge to three months post-ICU. The synthesis of the findings is presented in Figure 5.

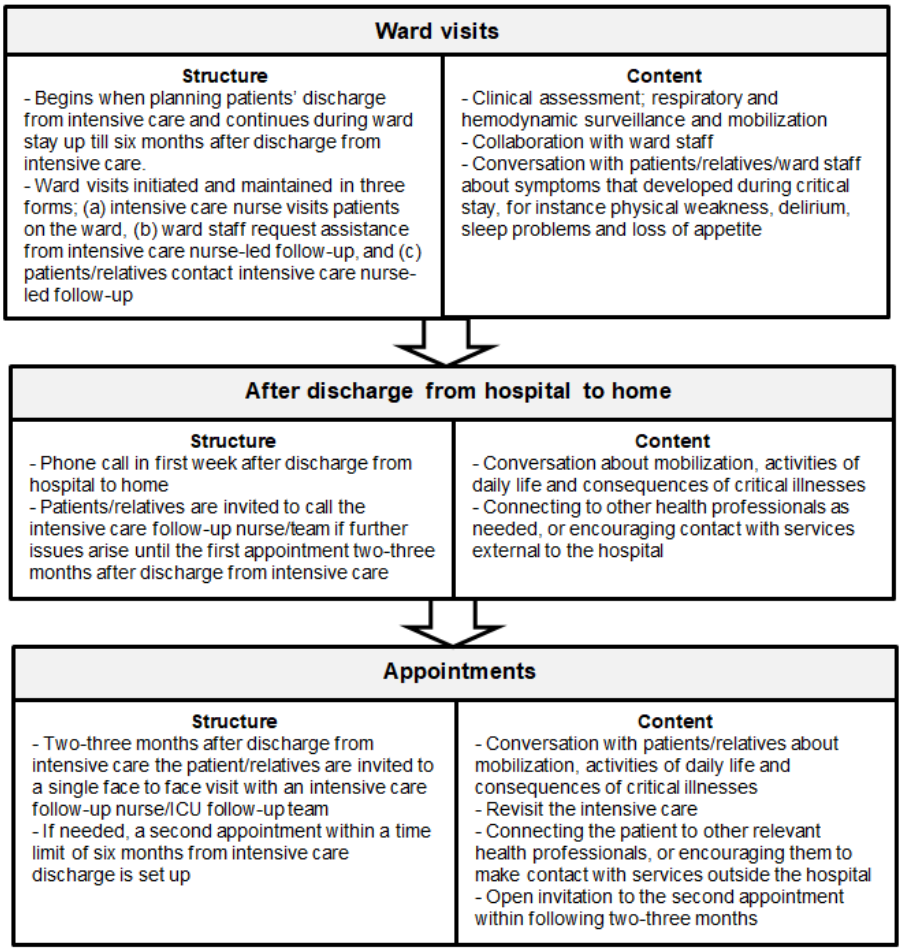

Figure 5. Synthesis of the findings of the content and structure of the ICU nurse-led follow-up after discharge from intensive care.

3.2.1 The intervention of structured nurse-led follow-up for patients after intensive care

The content and structure of the structured ICU nurse-led follow-up intervention is comprised of four components of care for patients from ICU discharge to three months thereafter. It is based on the findings of the integrative review (Study I), see Figure 5, and pilot testing (Study II). The components of the structured ICU nurse-led follow-up intervention are as follows; i) booklet delivered at ICU discharge, ii) ward visits, iii) contact during the first week after discharge from the ward to home and, iv) and an appointment three months after discharge from the ICU:

I. *Booklet*. The booklet was delivered at ICU discharge with the purpose of facilitating transition from the ICU to the ward for the patient/closest relative, and provided a sense of continuing ICU surveillance. The booklet was partially built on the work of Bench et al. (2011) and Odell et al. (2010). Designed and delivered by the researcher (doctoral student), the booklet contained handwritten information about each individual patients' ICU stay and printed, standardised material about ICU discharge, ward visits, stay in the ward, and the appointment at three months. Additionally, phone-numbers of the ICU ward visit service and the researcher were included, with an invitation to make contact when needed during and after the ward stay (Appendix 1).

II. *Ward visits*. The purpose of ward visits was to promote recovery and prevent ICU readmission. ICU nurses, working at the ICU in building I, with a minimum of two years of ICU work experience, visited patients staying ≥72 hours in the ICU after discharge to the wards in building I, using an observation scheme at each ward visit (see Appendix 2) (Ball et al., 2003; Garcea et al., 2004; Samuelson & Corrigan 2009). All of the nurses had a BSc degree in nursing, in addition to two years of ICU experience. The visits began on the ICU discharge day or the day after, with a minimum of two visits per patient on two consecutive days and availability 24/hrs. Ward nurses could call the ICU for advice and talk directly to ICU nurses if needed. The number of patients' visits each time was determined by the assessment of the ICU nurse and ward nurses and the requests of the patient or the patient's closest relative.

The surveillance provided in the ward visits consisted of clinical and proactive assessment of the patients' physical and psychological condition.

This assessment was conducted in collaboration with ward staff. The surveillance also included support to the ward staff, which consisted of formal and informal conversations, guidance and recommendations. General, compassionate support to patients' relatives was provided if the relatives were present. Consultations with other health professionals regarding the patients' condition were arranged as needed. At ward discharge the researcher gave information to each patient about what to expect regarding recovery after critical illness and she also introduced the three-month appointment. The researcher informed the patients that they would be contacted two weeks before the appointment invitation and were told that their closest relative was welcome to attend the appointment also.

III. *Contact during the first week after discharge from the ward to home*. The purpose of the contact was to facilitate patients' recovery. The researcher phoned the patients the first week after discharge from the general ward to home and conducted a semi-structured interview focusing on patients' concerns regarding their health, especially in relation to mobilisation, nutrition and sleep. In addition, relevant information regarding each patient's recovery was provided.

IV. *Appointment three months after discharge from the ICU*. The appointment had the purpose of supporting recovery and assessing the current physical and psychological health status of the patient. The appointment was semi-structured, lasting a maximum of one hour, and was conducted by the researcher. Before the appointment the patient answered a questionnaire on current health status (SF-36v2), anxiety and depression (HADS) and PTSD (IES-R). The patient also wrote about disturbing memories and answered questions about psychological reactions related to that memory. It was not obligatory for the patient to answer these questions. The questions guiding the appointment are shown in sequential order as follows:

- What is on your mind now regarding your health?
- How is your current physical recovery?
    - Mobilisation, appetite/nutrition, sleep?
- How is your current psychological recovery?
    - What was your experience of the ICU stay?
    - What are your memories of the ICU stay?
    - Are the memories disturbing in your daily life?

Discussion and information on recovery after critical illness were offered during the appointment, for example, the information that recovery can take a long time. Typical symptoms after critical illness such as tiredness, lack of

endurance and muscle strength, and the normality of not being prepared to work full time were explained as well. If the patients had problems with tiredness or endurance they were encouraged to contact their physician and get a prescription for physical therapy. If they had symptoms of PTSD they were encouraged to contact a psychologist of their own choice which was only possible at their own expense. The patients were also encouraged to seek health professionals for other health problems that were brought up in the appointment as well.

The appointment was recorded. At the end of the appointment the patient and the closest relative were invited to visit the ICU, see the ICU room and talk to the staff. The ICU staff were informed before each visit. An open invitation was given to further contact the researcher after the appointment.

3.2.2 The implementation of the intervention

The implementation of the intervention included two interconnected factors. The first was to provide information on the research to the ward head nurses and chief ward physicians in the hospital and the ICU at the intervention site. Second, there was the implementation itself, with an introduction, instructions and discussion with ICU nurses about the structure, content and delivery of the ward visits and the consequences of critical illness on patients' recovery, as shown in Table 4.

Table 4. Implementation of the structured nurse-led follow-up intervention.

Components and description of the implementation of the intervention
Information of the structured ICU nurse-led follow-up intervention at general wards (building I and II) and the ICU at the intervention site (building I) **Strategy:** (Grol & Grimshaw 2003; Ivers et al., 2012) 1) Information was provided from the researcher of the structured ICU nurse-led follow-up to all head nurses and chief physicians at the 14 general wards of the hospital, verbally and via email. 2) An email, containing information about the intervention from the researcher, forwarded by head nurses and chief physicians of the seven general wards at the intervention site to their staff, and additionally announcing the intervention at staffs' ward-meetings 3) All ICU staff at the intervention site received information about the intervention through ICU ward-meetings and emails from the researcher. 4) All ICU nurses, regardless of length of ICU work experience, received information on documenting in an observation scheme, at ICU discharge, the clinical condition of patients ≥72 hours stay in the ICU. **Material**: Poster with information and availability of the structured ICU nurse-led follow-up hung up in the seven wards at the intervention site (building I).
Interactive meeting for the ICU nurses providing delivery of the ward visits **Strategy:** (Forsetlund et al., 2009; O´Brien et al., 2007) A 60-minute interactive meeting conducted by the researcher with the ICU nurses with a minimum of two years of ICU work experience. The subject was the structure and content of the ward visits and the consequences of critical illness on patients' recovery at and after ICU discharge. The ICU nurses could choose when to attend but a total of five meetings were held for 40 ICU nurses. During the research period the meeting was repeated once and the ICU nurses received feedback twice with a summary of the number and content of the ward visits at an ICU nurses' meetings and via email. **Material**: Observation scheme for the ICU nurses' documentation of the assessment of patients' clinical condition during each ward visit.

3.2.3 Standard care

The standard care included ward visits. Patients who were considered in need of continuing surveillance might get ward visits from ICU clinical nurse specialists working in the ICU in building II during morning shifts on weekdays, and from other ICU nurses working in the ICU in building II during evenings and weekends. This applied, in particular, to patients with high oxygen demands, who had tracheostomy, critical illness polyneuropathy, and those who were in need of intermittent non-invasive ventilation. Some patients discharged from the ICU in building II and/or relatives received a booklet with printed, standardised information about the discharge from the ICU and the ward stay. Patients discharged from the ICU in building I to wards in building II did not receive such a booklet. The ICU in building II was

notified when patients were discharged from the ICU in building I to wards in building II. After discharge from the general ward the patients received no further ICU follow-up.

The description of the standard care was read by an ICU clinical nurse-specialist, the ICU head nurse and ICU head physician in building II and two experienced nurses working in the ICU of building II. One clinical nurse-specialist and one head nurse of the general wards in building II confirmed this description as well after commenting on the procedure of the ward visits, that is the times of visits, those who visited, and the recordings of the visits.

3.3 Design of Studies II and III and reporting

The design of Studies II and III was prospective, longitudinal and quasi-experimental. The aim, research questions and hypotheses are described in chapter two. Studies II and III were reported according to the TREND (Transparent Reporting of Evaluations with Nonrandomised Designs guideline) (Des Jarlais et al., 2004). The structured nurse-led follow-up intervention was reported in Study II according to CReDECI 2 (Criteria for Reporting the Development and Evaluation of Complex Interventions 2) (development, feasibility/piloting, evaluation) (Möhler et al., 2015).

3.3.1 Setting of Studies II and III

This was a single centre quasi-experimental study, which was conducted in a tertiary, national university hospital, Landspítali – The National University Hospital of Iceland, Reykjavik. There were two ICUs with mixed patient populations, located in two separate buildings (buildings I and II) each having ten ICU beds.

3.3.2 Participants in Studies II and III

Eligible patients were ≥18 years of age with ICU stay of ≥72 hours in either of the two ICUs at Landspítali. Patients were excluded who were non-native speakers, unlikely to survive the general ward stay, unlikely to be alert or mentally able to communicate after the ICU discharge, had dementia, or were active drug or alcohol users. The reason for excluding active drug or alcohol users was the risk of attrition.

Patients in the experimental group were those that were discharged from the ICUs in buildings I and II to general wards in building I (Figure 6). The patients in the experimental group received the structured nurse-led follow-up intervention described in chapter 3.2.1.

Patients in the control group were those that were discharged from the ICUs in buildings I (ICU I) and II (ICU II) to general wards in building II (Figure 6). Patients in the control group received standard care.

Power analysis was assessed for the measures of health status using the SF-36v2 measurement tool, and presented in Study II. The sample size needed to achieve 80% power to detect an effect size of 0.5 difference between groups was estimated prior to the data collection, using the G*Power 3 software, calculated by a two-tailed t-test for means of independent groups (Faul et al., 2007). The suggested sample size of 64 was needed in each group when assuming a significance level of 0.05 and accounting for 20% loss to follow-up of 80 patients in each group.

All 3142 ICU patient admissions to the two ICUs at Landspítali from 25th of November 2012 to 10th of May 2015 were screened for participation. There were 2939 patients discharged alive from the ICUs (203 died), 574 patients stayed ≥72 hours in the ICUs (only the patients' first eligible ICU admission counted). This gave a total of 168 recruited patients; 83 in the experimental group and 85 in the control group. All patients in the experimental group were discharged from the ICU in building I to the wards in building I (N=83) (Figure 6). Overall, a majority of patients in the control group were discharged from the ICU in building II to the wards in building II (N=80) except for five patients discharged from the ICU in building I to wards in building II (Figure 6).

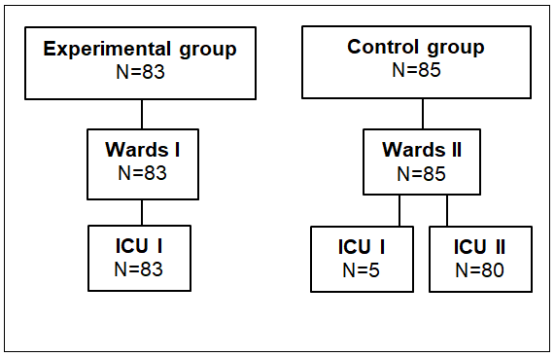

Figure 6. Patients recruited from ICUs I and II, and discharged to wards I or II.

In total of 20 recruited patients were lost to follow-up during the ward stay, ten from the experimental group and ten from the control group, and these were excluded from further analysis (Figure 7 and Figure 8). Therefore, 73 patients in the experimental group and 75 patients in the control group were included from the analysis in Study II (Figure 7). In Study III, 68 patients in the experimental group received the three-month intervention and 75 patients in the control group were included in the analysis (Figure 8).

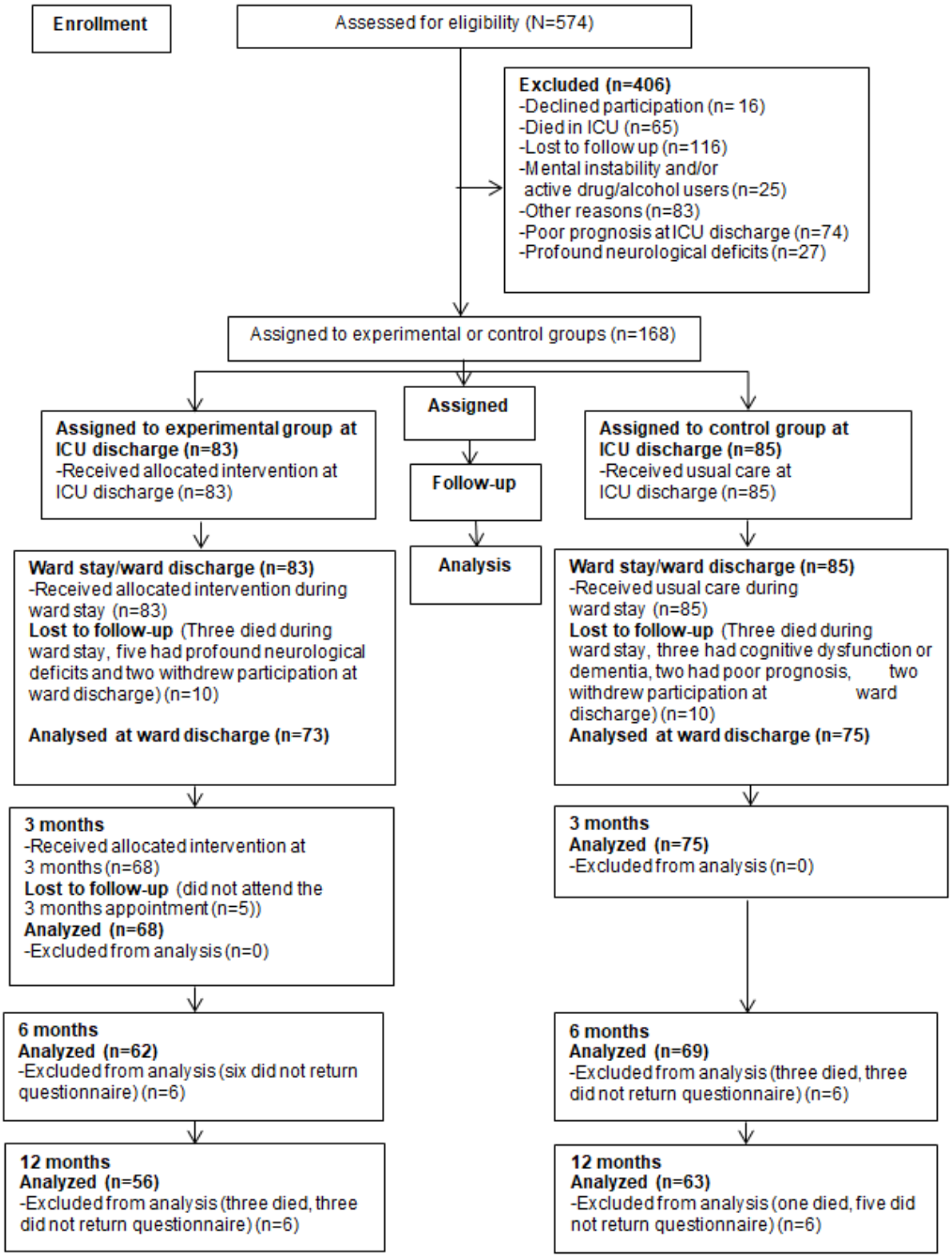

Figure 7. Flow chart of participants in Study II.

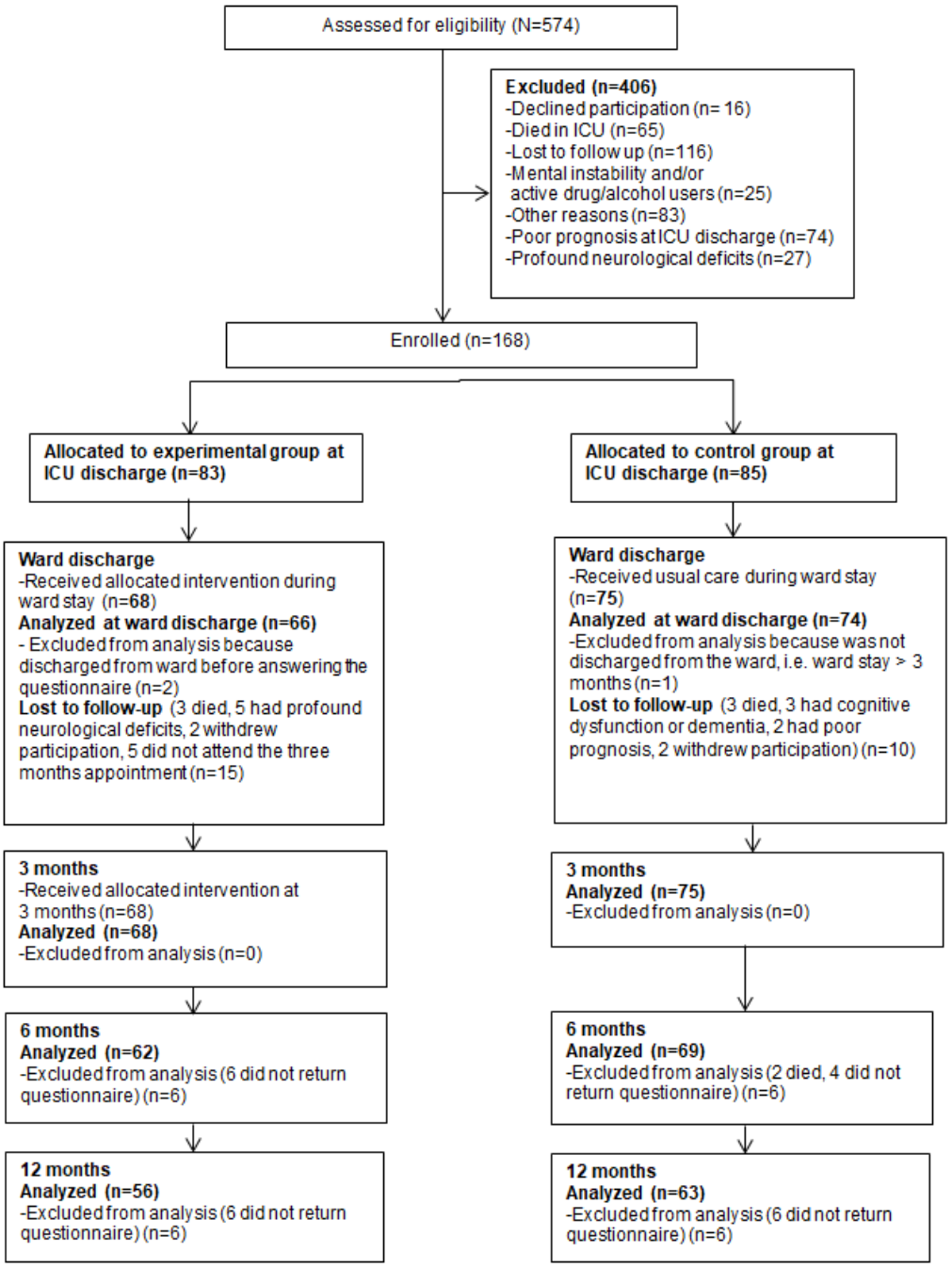

Figure 8. Flow chart of participants in Study III.

3.4 Outcome measures in Studies II and III

3.4.1 Outcomes in Study II

The outcomes were as follows. The primary outcome was health status over time, i.e. the difference between and within the experimental group and the control group after discharge from the general ward to 12 months after the ICU discharge. Secondary outcomes were health status within and between gender, length of ward stay, and ICU readmission rate within 48 and 120 hours after the first eligible ICU discharge.

3.4.2 Outcomes in Study III

The outcomes were: 1) difference between the experimental group and the control group over time in symptoms of PTSD at three, six and 12 months after the ICU discharge, and anxiety and depression after discharge from the general ward, three, six and 12 months after ICU discharge, 2) comparison of background, memories of the ICU stay and psychological reactions related to the memories of patients with and without symptoms of PTSD three months after the ICU stay and, 3) predictors of symptoms of PTSD three months after the ICU.

3.5 Instruments

3.5.1 Health status

The Short-Form-36 version 2® Health Survey (SF-36v2) was used for measuring health status. The SF-36 was developed in the United States in the eighties as a generic scale to measure health outcomes in the Medical Outcome Study (Ware & Sherbourne, 1992). The SF-36v2 questionnaire is the second version of the SF-36 measurement scale (Ware et al., 2007). The instrument has 36 questions answered on an ordinal scale of eight domains of health status: 1) physical functioning, 2) role physical, 3) bodily pain, 4) general health, 5) vitality, 6) social functioning, 7) role emotional, and, 8) mental health. The first four domains are included in the physical summary measure and the latter four domains in the mental summary measure (Maruish, 2011).

Both SF-36 and SF-36v2 are widely used in research on intensive care patients (Denehy et al., 2013; Orwelius et al. 2013) and have been translated

and back-translated, according to standards of *International Quality of Life Assessment*, in over 100 non-English translations, including Icelandic (Optum, n.d.; Ware et al, 2007). Their reliability and validity have been tested in various patient groups and general populations (Maruish, 2011; Sullivan et al., 1995). A psychometric testing of the scale on Icelandic university students (Cronbach's *α* 0.95) and in patients with chronic pain (Chronbach's *α* 0.92) revealed good internal consistency (Eiríksdóttir, 2011). The internal consistency of the SF-36v2 in a nationwide Icelandic sample was .78 to .94 Cronbach's *α* (Jonsdottir et al. 2014). The internal consistency (Cronbach's *α*) of the scales in the sample in Study II ranged from 0.70 to 0.93 in all domains except social functioning where it was 0.62 Cronbach's *α*.

3.5.2 Symptoms of PTSD

The Impact of Event Scale-Revised (IES-R) was used to measure symptoms of post-traumatic stress disorder (PTSD). The scale includes 22 questions on distress (intrusion, avoidance, hyperarousal) in the past seven days, scoring from 0 (never) to 4 (very often), with a total score range from 0 to 88 and a higher score indicating more symptoms of PTSD (Weiss & Marmar, 1997). The original scale is the IES, measuring only intrusion and avoidance (Horowitz et al., 1979). The IES and the IES-R are the most frequently used scales measuring patients' PTSD post-ICU (Parker et al., 2015). The IES-R is built on the PTSD criteria presented in the 4th edition of *Diagnostic and statistical manual of mental disorders* (American Psychiatric Association, 2005). A diagnosis of PTSD cannot be made using the IES-R, but it is possible to differentiate between having or not having PTSD (Beck et al., 2008). The IES-R has been psychometrically tested on patients after critical illness by comparing it with the Clinician-Administered PTSD Scale. The results showed that a score of ≤22 on the IES-R signifies no symptoms of PTSD, score of ≥ 23 represents partial PTSD and a score of ≥ 36 signifies full PTSD (Bienvenu et al., 2013). IES has been translated from English into Icelandic and back-translated and psychometrically tested with internal reliability 0.99 (Cronbach's alpha) for the whole scale as well as for questions of intrusion and avoidance (Árnadóttir, 1995). The revised part of the scale was translated into Icelandic by Unnur Jakobsdóttir Smára, psychologist and translated back into English by Sjöfn Ágústsdóttir psychologist (personal information).

3.5.3 Anxiety and depression

Anxiety and depression was measured with the HADS. The HADS contains 14 questions on anxiety (HADS-Anxiety (HADS-A) (seven questions) and depression (HADS-Depression (HADS-D) (seven questions) with answers rated from 0 to 3 and a total score of 0 to 21 for anxiety and 0 to 21 for depression (Zigmond & Snaith, 1983). A score of seven and less is within the normal range, a score of 8 to 10 suggests anxiety and/or depression, and a score of 11 or higher indicates caseness of anxiety and/or depression (Snaith, 2003). The HADS has been translated into Icelandic and has been psychometrically tested (Schaaber et al., 1990).

3.5.4 Disturbing memories of the ICU stay

Disturbing memories of the ICU stay and psychological reactions related to that memory three months after the ICU discharge were measured by asking the patients to write down their disturbing memories of the ICU stay in the three-month questionnaire. They were also asked to answer questions (yes/no) in the three-month questionnaire on psychological reactions experienced and related to that memory: Did you experience: a) that your life was in danger? b) threat to your physical integrity? c) intense fear? d) helplessness? and e) horror? The psychological reactions were the two items of criteria A for PTSD, 4th edition (American Psychiatric Association, 2005): 1) witnessing death or experiencing threatened death or serious injury or threat to the physical integrity of self or others, and 2) the person's response to that event was intense fear, helplessness or horror.

3.6 Data collection of Studies II and Study III

The data collection was performed by the doctoral student. Demographic data on age, sex, marital status, residency, educational level and employment status was collected from patients after recruitment during the ward stay. Moreover, the questionnaire on health status four weeks before the ICU admission, or before admission to a general ward if the patient was first admitted to a general ward, was also answered during the ward stay. Data on comorbidities and on use of depression and/or anxiety drugs before the ICU admission was collected from the patient's electronical hospital journal. The APACHE II (*Acute Physiology and Chronic Health Evaluation II*) was measured during the patient's ICU stay and the TISS-28 (*Therapeutic*

Intervention Scoring System-28) score was measured at the patient's ICU discharge. Clinical data on length of ICU-, ward-, and hospital stay, and length of mechanical ventilation was retrieved from the hospital data warehouse. The measurement scales and time of measurements of questionnaires submitted are shown in Table 5.

Table 5. Measurement scales and time of measurement for Studies II and III.

Instruments*	Variables measured	Before ICU admission**	Ward discharge	3, 6, and 12 months after ICU discharge
SF-36v2	Health status	X	X	X
IES-R	PTSD***			X
HADS	Anxiety and Depression		X	X

*SF-36v2 (*Short-Form 36v2 Health Survey*), IES-R (*Impact of Event Scale-Revised*), HADS (*Hospital Anxiety and Depression Scale*). **Health status around four weeks before the ICU admission; data collected during patients' ward stay. ***Post-traumatic stress disorder.

Additionally, in the questionnaire at three months, patients were asked to write down any memories from the ICU stay that were disturbing to them now, and were asked questions on psychological reactions felt while they experienced such memories (Figure 9).

Question 1: Please, describe a memory from your intensive care stay that is disturbing to you now (free text, hand written).

Question 2: Please, answer the next questions in relation to the memory or the experience that you described (yes or no). During the memory or the experience, did you experience: a) that your life was in danger? b) threat to your physical integrity? c) intense fear? d) helplessness? e) horror?

Figure 9. Measuring patient's disturbing memories of the intensive care stay and psychological reactions related to that memory at three months after the intensive care discharge.

Data on the ward visits to the experimental group were collected from the observation scheme (Appendix 2) and entered in a computer spreadsheet.

Data on ward visits to patients in the control group were collected from the hospital electronic database and from ICU handwritten reports of visit(s).

For the experimental group only, the researcher phoned the patients during the first week after their ward discharge home. Patients discharged from the ward to other places than home (rehabilitation centre, another hospital) did not receive a phone call.

The three-month appointment of participants in the experimental group took place at the hospital or places chosen by the patients (home, rehabilitation centre). If the patient was still hospitalised, the appointment took place there, in a quiet room.

The questionnaires at three, six and 12 months were sent home to patients with a pre-paid envelope. If a questionnaire had not been returned two weeks later, a reminder letter was sent, and then there was a phone call from the researcher two weeks thereafter. Patients in the experimental group answered the three-month questionnaire before attending the appointment with the researcher, and handed the questionnaire to her. If patients were hospitalised they were approached there. Participants reporting difficulties in answering the questionnaire were offered a meeting with the researcher at a location of the patients' choice (home, hospital buildings). At that meeting, the researcher read the questions aloud.

3.6.1 Data analysis in Study II

Data analysis was performed using the IBM® SPSS® Statistics 22 and 24. Frequency, means, standard deviation and range of demographic and clinical characteristics were measured. The independent t-test measured differences between the experimental group and the control group in demographic and clinical characteristics and SF-36v2 at the five time points: before the ICU admission (T1), at ward discharge (T2), at three (T3), six (T4) and 12 (T5) months after ICU discharge. The Friedman Test (one-way repeated measures analysis of variance) measured change in health status within group over the five time points (T1-T5). The independent t-test and the Mann-Whitney-U test measured the differences between and within gender within and between the groups.

A mixed effects model tested differences in the SF-36v2 between the experimental group and the standard care group over time. The model assessed the effectiveness of the intervention over time and accounted for

dependence in repeated measures within individuals (Beumont, 2011). Dependence in repeated measures refers to including in the analysis individuals that did not answer the questionnaire at all time points (T1 – T5) — e.g. some patients may not have answered at three months but did answer at all other time points — and was preferred over repeated measures ANOVA where dependence is not assumed. The measure of SF-36v2 before the ICU admission was a covariate in the model, adjusting for baseline differences between the groups, making the mixed effect model more robust regarding possible any imbalance between the groups that might influence the outcome, i.e. the difference between the groups in health status (SF-36v2) over time.

The model tested for differences in health status between the experimental group and the control group over time, with the following formula: Y_ij = u + g_i + b_i + S_i + E_ij, where Y_ij was the health status of individual i at time j (ward discharge, three, six, 12 months), g_i was the fixed effect for group, b_i was the fixed effect of health status before the ICU stay, S_i was the random effect of individual i, and E_ij was the random error for time j and individual i. An exchangeable correlation structure was assumed such that S_i was N(0, sigma^2_s) and E_ij was N(0, sigma^2_e). Multiple testing was accounted for using the Bonferroni method where the Bonferroni threshold of $p \leq .006$ indicated the statistical significance of the model. Significance in Study II was otherwise set at $p \leq .05$.

3.6.2 Data analysis in Study III

Patients' sociodemographic and clinical variables, disturbing memories and psychological reaction variables were measured as median, interquartile range, frequency, mean and standard deviation. Differences between the experimental group and the control group in baseline characteristics, IES-R scores, HADS-A and HADS-D scores were measured with the independent t-test, a Mann-Whitney U test and a Chi-square test. Data analysis was performed using the IBM® SPSS® Statistics 24. Significance in Study III was set at $p \leq .05$ unless otherwise indicated.

A mixed effects model tested difference in the IES-R, the HADS-A and HADS-D between the experimental group and the standard care group over time. The measure of IES-R at three months and the measure of HADS-A and HADS-D at ward discharge were covariates in the model. The use of covariates is further explained in the formula of the model, which also shows

how the model was fitted (Table 6). A Bonferroni threshold of p ≤ .017 indicated the statistical significance of PTSD measures (IES-R) and a Bonferroni threshold of p ≤ .012 indicated the statistical significance of anxiety (HADS-A) and depression (HADS-D) measures of the mixed effects model.

Table 6. Formula of the mixed methods model in Study III.

The formula of the mixed methods model testing differences in symptoms of PTSD*, anxiety and depression between groups over time: Y_ij = u + g_i + b_i + S_i + E_ij	
Y_ij	PTSD, anxiety, depression of individual i at time j ((three) **, six, 12 months)
g_i	Fixed effect for group
b_i	Fixed effect of baseline PTSD (three months post-ICU), anxiety and depression (ward discharge)
S_i	Random effect of individual i
E_ij	Random error for time j and individual i
Exchangeable correlation structure was assumed such that S_i was N(0, sigma^2_s) and E_ij was N(0, sigma^2_e)	

*PTSD: Post-traumatic stress disorder
**Measures of PTSD over six and 12 months and measures of anxiety and depression over three, six and 12 months

Multiple linear regression with forward selection was used for assessing variables predictive of IES-R scores (predictive of symptoms of PTSD) of patients from the experimental group and the control group at three months post-ICU. Sociodemographic and clinical variables (continuous and binary), memories of the ICU stay, and psychological reaction variables (binary) at three months post-ICU that significantly correlated (Pearson) with the IES-R total score at three months, were added to the model, one at a time, until further addition did not improve the model. Then the observed IES-R scores (true IES-R scores) were compared with the predicted IES-R scores on a continuous scale. In addition to reporting the adjusted R^2 of the final linear model, the results were put in a potentially clinical perspective by comparing the dichotomised IES-R scores (IES-R ≤22=no symptoms of PTSD and IES-R ≥23=symptoms of PTSD) and the predicted IES-R scores (measuring accuracy) and the sensitivity (true predictive rate) and specificity (true negative rate) were calculated using predictive IES-R ≥23 as a cut-off to classify patients as having symptoms of PTSD. Binary logistic regression,

predicting symptoms of PTSD (IES-R scores ≤22 and IES-R scores ≥23), was an option but was not chosen because of the limited number of patients (n=34) who had IES-R scores ≥23, restricting the number of variables to be used when building a logistic regression model. The sensitivity of the prediction model is the proportion of PTSD cases with pIES-R≥23 and is estimated to be #(pIES-R≥23 and IES-R≥23)/#(IES-R≥23), the specificity is estimated to be #(pIES-R≤22 and IES-R≤22)/#(IES-R≤22) and the accuracy as (#(pIES-R≥23 and IES-R≥23) + #(pIES-R≤22 and IES-R≤22)) / #individuals.

3.7 Ethics

Approval for the study was obtained from the Chief Medical Officer of Landspítali – The National University Hospital of Iceland (Reference: 2012/16 ÞH/ei), the Landspítali Bioethics Committee (#5/2012 JSn/js) and the Data Protection Authority (Raudararstig 10, 105 Reykjavik, Iceland; Protocol no. 2012010068HGK/-). Additionally, information on the study and on the structured nurse-led follow-up intervention was given verbally and via email to head nurses and chief physicians at the 14 general wards of the hospital. The head nurses and the chief physicians at the ICU in building I and the ICU in building II were informed of the study and gave their approval. The patients, or their closest relative, signed an informed consent during the ICU stay, later to be confirmed by each patient during the ward stay.

4 Results

A summary of the main results from individual studies (Studies I, II and III) are presented as follows:

4.1 Study I

Seventeen papers met the inclusion criteria. They were based on different methodologies, i.e.; nine descriptive and evaluative studies, four before-and after studies, two RCTs, a case-control study, and a qualitative study. Three patterns of structure, content and type of outcome variables of intensive care nurse-led follow-up were detected: i) ward visits (in the immediate time after discharge from the ICU), ii) ward visits and appointment(s) to an ICU follow-up clinic, and iii) follow-up visit to an ICU and a phone call two months after discharge from the ICU. Collectively, the results indicated uncertain, primarily descriptive, outcomes of ICU nurse-led follow-up, but confirmed the consequences of critical illness on physical and psychological and social health. Ward visits, with the main focus of clinical surveillance, were beneficial regarding earlier ICU readmission and hospital survival. There was an indication of less anxiety due to having the appointments. Physical functioning improved in patients who received a self-directed rehabilitation manual and phone calls after discharge from hospital to home. Importantly, patients were satisfied with the ICU nurse-led follow-up. The ICU nurse-led follow-up was not a continuous service from ICU discharge until the appointment(s). The ICU nurse-led follow-up was presented as merely ward visits or appointment(s) and disconnected from each other if both were presented in a study.

4.2 Study II

There was a difference between the groups in clinical background variables and demographics. The patients in the experimental group (n=73) were younger, had less severity of illness as indicated by a lower APACHE II score, were more frequently employed, and fewer were retired compared with the control group (n=75). The reasons for the ICU admission were medical for two thirds of the experimental group and surgical for one third and vice versa for the control group. The experimental group had a shorter general

ward stay, better physical function and more bodily pain before the ICU admission than the control group.

All patients in the experimental group (n=73) received ward visits with the mean of three visits per patient and an average two ICU nurses visiting each patient. There were 224 ward visits in total and the mean time of each visit was 17 minutes. In total, there were 30 nurses who provided the experimental ward visits. The component that was most frequently assessed was the respiratory status. There were 32/73 patients that received a phone call during the first week after discharge from the ward to home, 68/73 patients came to the appointment at three months post-ICU, and 27/73 were accompanied by their closest relative. In the control group documented ward visits existed for 16/75 patients.

The experimental group had significantly more bodily pain compared with the control group over the 12 months but there was no difference between the groups over time in other items of health status (Table 7).

Table 7. Mixed effects model for the eight scales of health status (SF-36v2) of patients in the experimental group (n=73) and the control group (n=75)[a].

Parameter	Estimate	Std.Error	Sign.	95% CI	
				Lower Bound	Upper Bound
Physical Function Treatment[b]	0.984	2.02	0.627	-3.00	4.96
Role Physical Treatment	0.203	2.55	0.937	-4.81	5.22
Bodily Pain Treatment	-7.30	2.26	0.001*	-11.74	-2.86
General Health Treatment	-1.42	1.58	0.368	-4.54	1.68
Vitality Treatment	-2.95	1.67	0.078	-6.23	0.330
Social Function Treatment	0.206	2.32	0.929	-4.36	4.77
Role Emotional Treatment	1.01	2.45	0.678	-3.80	5.84
Mental Health Treatment	-3.16	1.40	0.025	-5.92	-0.402

[a]Adjusted for health status before the ICU admission (i.e., the eight scales of the SF-36v2 before the ICU admission). [b]Treatment: 0 = usual care, 1 = intervention.
Statistical significance indicated with Bonferroni correction, $p \leq .006$.

There was a significant difference in health status (SF-36v2) within the experimental group and within the control group over the five time points, i.e from before the ICU admission, at ward discharge and three, six and 12 months after the ICU discharge. In the experimental group the difference was in all SF-36v2 scales except mental health and bodily pain and in the control group in all SF-36v2 scales except mental health. The mean values of the SF-36v2 items over the five time points indicated decreased health status over time in both groups (Table 8).

Table 8. Health status (SF-36v2 scores) of the experimental group and the control group from before the ICU (T1), at ward discharge (T2) and three (T3) and six (T4) and (T5) 12 months after discharge from the ICU.

SF -36v2	Groups	Before the ICU T1	Ward discharge T2	3 months T3	6 months T4	12 months T5	*p**
Physical Function	Experimental	72,6 (30,6)[a] (N=73)	27,2 (26,2) (N=71)	54,5 (31,5)[a] (N=68)	55,7 (30,9) (N=62)	58.5 (28.6) (N=56)	<0.001
	Control	61,3 (30,3)[a] (N=75)	26,2 (20,0) (N=74)	44,5 (26,0)[a] (N=75)	56,3 (25,0) (N=68)	56.1 (27.5) (N=63)	<0.001
Role Physical	Experimental	65.7 (31.3) (N=73)	40.1 (30.7) (N=71)	38.9 (31.1) (N=68)	41.3 (33.0) (N=61)	44.8 (34.8) (N=56)	<0.001
	Control	57.7 (33.4) (N=75)	43.9 (28.5) (N=73)	31.6 (24.9) (N=73)	41.7 (26.0) (N=66)	47.0 (29.4) (N=60)	<0.001
Bodily Pain	Experimental	63.6 (32.4)[a] (N=73)	61.0 (31.5)[a] (N=70)	57.7 (31.1) (N=68)	49.8 (28.0)[a] (N=60)	49.3 (29.7) (N=56)	0.204
	Control	74.1 (29.7)[a] (N=75)	77.1 (23.0)[a] (N=73)	66.2 (27.6) (N=75)	62.1 (28.7)[a] (N=69)	63.8 (29.2) (N=63)	0.001
General Health	Experimental	66.6 (23.4) (N=73)	65.8 (20.9) (N=70)	60.5 (21.4) (N=68)	55.7 (21.7) (N=62)	54.8 (25.5) (N=56)	0.001
	Control	63.0 (21.9) (N=75)	67.5 (18.1) (N=74)	58.9 (19.8) (N=75)	56.5 (19.2) (N=69)	55.3 (22.5) (N=63)	0.001
Vitality	Experimental	54.1 (21.8) (N=73)	53.9 (21.7) (N=70)	50.5 (22.5) (N=68)	49.1 (25.0) (N=60)	43.5 (23.2) (N=56)	0.002
	Control	56.0 (23.9) (N=75)	58.4 (18.2) (N=73)	51.1 (22.2) (N=75)	52.0 (19.4) (N=69)	52.6 (24.6) (N=62)	0.026
Social Function	Experimental	76.3 (26.3) (N=73)	70.8 (26.6) (N=69)	65.2 (28.6) (N=68)	67.5 (29.6) (N=60)	64.5 (30.0) (N=56)	0.045
	Control	80.5 (27.0) (N=75)	76.9 (23.9) (N=73)	60.3 (30.0) (N=75)	68.4 (28.1) (N=69)	71.4 (30.0) (N=63)	<0.001
Role Emotional	Experimental	83.0 (25.2) (N=72)	90.6 (19.6) (N=68)	73.4 (29.5) (N=66)	64.7 (33.3) (N=59)	64.5 (30.0) (N=56)	<0.001
	Control	83.9 (26.6) (N=75)	92.0 (19.3) (N=71)	72.0 (28.7) (N=71)	63.5 (31.2) (N=65)	65.6 (31.9) (N=59)	<0.001
Mental Health	Experimental	73.3 (19.0) (N=73)	76.3 (19.8)[a] (N=70)	72.5 (21.7) (N=68)	72.5 (20.6) (N=60)	71.3 (20.9) (N=56)	0.409
	Control	79.0 (20.2) (N=75)	84.0 (16.0)[a] (N=73)	77.8 (19.7) (N=75)	79.0 (17.2) (N=69)	76.5 (22.2) (N=62)	0.110

SF-36v2 scores (from 0-100) with higher scores indicating better health status. Values presented as mean (standard deviation)**.** Significance set at $p \leq 0.05$.

***p** value of Friedman Test (one-way repeated measures analysis of variance) representing change in health status within group over the five time points with significance set at $p \leq 0.05$.

[a]Significant difference detected between the experimental group and the control group and measured with independent t-test at, T1: physical function ($t(146)= 2.26$, $p = .025$), bodily pain ($t(146)= -2.06$, $p = 0.041$); T2: bodily pain ($t(126.1)= -3.47$, $p = 0.001$), mental health ($t(132.7)= -2.55$, $p = 0.012$); T3: physical function ($t(130.5)= 2.06$, $p = 0.041$); T4: bodily pain ($t(127)= -2.44$, $p = 0.016$); T5 bodily pain ($t(114.9)= 2.68$, $p = 0.009$), vitality ($t(115.7)= 2.06$, $p = 0.041$).

There was a gender difference in the experimental group, where females had significantly worse health status than males in all of the SF-36v2 domains at several time points from before the ICU until 12 months post-ICU. The difference of gender in the control group was on physical function, where females had worse health status compared with males at all time points, and in role physical and general health at 12 months (see Appendix 3).

4.3 Study III

As in Study II, there were baseline differences in Study III between the groups. The patients in the experimental group (n=68) were younger, had lower APACHE II scores, were more frequently employed, and fewer were retired than in the control group (n=75).

Symptoms of PTSD increased from three months to six and 12 months in both groups. The average IES-R score was 16 (three months) 18 (six months) and 20 (12 months) in the experimental group and 12 (three months) 13 (six months) and 14 (12 months) in the control group.

The experimental group had significantly more symptoms of post-traumatic stress and anxiety compared with the control group over the 12 months, but there was no difference between the groups over time in depression (Table 9).

Table 9. Mixed effects model for (A) symptoms of Post-traumatic stress disorder measured with Impact of Event Scale-Revised 6 and 12 months after ICU discharge[a] and for (B) Anxiety and Depression of the Hospital Anxiety and Depression Scale three, six and 12 months after intensive care[a].

Parameter	Estimate	Std.Error	Sign.	95% CI	
				Lower Bound	Upper Bound
A					
PTSD					
Treatment[b]	4.06	1.62	.013	.870	7.25
B					
Anxiety					
Treatment[b]	1.07	.320	.001	.442	1.70
Depression					
Treatment[b]	.362	.327	.268	-.280	1.00

[a]Adjusted for total score of IES-R at 3 months post-ICU. Adjusted for HADS-A score and HADS-D score at ward discharge.
[b]Treatment: 0 = standard care, 1 = intervention. *Bonferroni correction of PTSD measures .017 (.05/3 = .017). **Bonferroni correction of anxiety and depression measures .012 (.05/4 = .012).

Between 9% (n=12) and 15% (n=15) of patients in the experimental group and the control group respectively at three, six and 12 months had severe symptoms of PTSD. Five patients, three from the experimental group and two from the control group, had severe PTSD symptoms at all three time points.

Patients with symptoms of PTSD at three months in both groups had disturbing memories and psychological reactions (that their life was in danger, a threat to physical integrity, helplessness, horror, intense fear) related to the experience of the memories during their ICU stay compared to patients without symptoms of PTSD at three months (Table 10).

Table 10. Background, memories of the ICU stay and psychological reactions related to the memories of patients with IES-R[≠] score ≤22 (no symptoms of PTSD) and IES-R score ≥23 (symptoms of PTSD) three months after ICU discharge.

Variables	IES-R score ≤22 n=96	IES-R score ≥23 n=34	*p*
Sociodemographic variables			
Age, years	65 (13)	55 (15)	.001**
Male/Female, n (%)	62 (65)/34 (35)	19 (56)/15 (44)	.368
Employed, n (%)	36 (38)	18 (53)	.116
Retired, n (%)	47 (49)	6 (18)	.001**
Disability benefits, n (%)	7 (7)	9 (26)	.003**
Clinical variables			
APACHE II	18 (8)	17 (6)	.310
Surgical/medical reason of ICU admission, n (%)	51 (53)/45(47)	14 (41)/20 (59)	.231
Mechanical ventilation, days	7 (8)	9 (9)	.213
ICU LOS, days	11 (11)	12 (9)	.775
Ward LOS, days	24 (24)	14 (8)	.001**
Disturbing memories			
Disturbing memories, n (%)	24 (25)	17 (50)	.007**
Psychological reactions			
That your life was in danger, n (%)	27 (28)	16 (47)	.044*
Threat to physical integrity, n (%)	4 (4)	7 (20)	.003**
Helplessness, n (%)	37 (39)	27 (79)	.000**
Horror, n (%)	10 (10)	14 (41)	.000**
Intense fear, n (%)	10 (10)	15 (44)	.000**

Measure presented as mean (SD) unless indicated otherwise. * ≤ .05 ** ≤ .01
[≠]Impact of Event Scale-Revised.

The regression model predicted that patients who were younger, were on disability benefits, experienced helplessness, or had disturbing memories and intense fear during the intensive care stay would have symptoms of post-

traumatic stress three months after ICU discharge. Age and intense fear contributed the most to the model (Figure 10).

Parameters	Unstandardised coefficients		Standardised coefficients	Sig.	95% CI	
	B	Std.error	Beta		Low	High
(Constant)	22.35	5.38		.000	11.70	33.00
Age	-.231	.078	-.226	.004	-.386	-.076
Disability benefits	7.30	3.48	.162	.038	.412	14.18
Helplessness	4.22	2.49	.143	.092	-.704	9.15
Disturbing memories	4.41	2.61	.138	.094	-.757	9.58
Intense fear	8.62	3.40	.229	.012	1.90	15.33

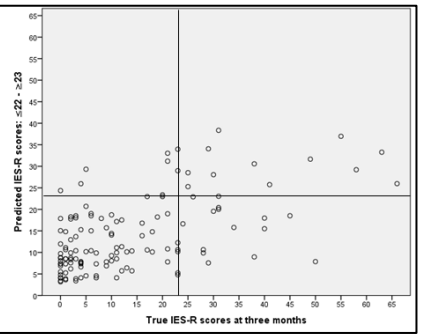

Figure 10. Multiple linear regression model between total IES-R scores three months after intensive care discharge and independent variables and a scatterplot of true (observed) and predicted IES-R scores at three months of the multiple linear regression model. The true predictive rate of patients with IES-R score ≥23 is shown in the upper right quadrant of the scatterplot.

5 Discussion

The present thesis constitutes a pivotal work for ICU patients and ICU nursing practice. The integrative review of nurse-led follow-up of patients after discharge from the ICU (Study I) is the first synthesis of findings from studies on nurse-led follow-up which reports on structure, content and outcomes. The use of rigorous guidelines (PRISMA) for such a review is also innovative. This synthesis was the foundation for the development and testing of the effectiveness of a structured nurse-led follow-up intervention (Studies II and III). The long duration of the nurse-led follow-up, i.e. from ICU discharge until three months post-ICU, as well as the statistical approach that was used, i.e. a mixed effect model and reporting the intervention according to the CReDECI 2 guidelines (Study II) is also a novelty in this thesis. Furthermore, a comparative design is uncommon in research on the present subject, and only three other published studies have presented the topic by using a comparison group (Cuthbertson et al., 2009; Jensen et al., 2016; Jones et al, 2003). This work also illustrates the severity and the heterogeneity of the illnesses that ICU patients deal with, especially those who stay longer than three days in a mixed patient population ICU. Measuring the health status of the patients before the ICU admission is seldom reported in ICU research and provides extra volume to the present work (Studies II and III). In summary, the integrative review (Study I) revealed limited evidence of effective structure and content of nurse-led follow-up of adult patients after discharge from the ICU. From the synthesis of the results, a four-component intervention of structured nurse-led follow-up was developed and their effectiveness tested. The intervention did not significantly improve the health status of patients over time, compared with standard care, from the ICU discharge until 12 months thereafter. Furthermore, the intervention did not significantly improve the psychological health of patients, over 12 months after ICU discharge, compared to standard care.

In the following pages there is a is discussion of the effectiveness of the intervention on patients' physical and psychological health status, reflections on the structured nurse-led follow-up intervention, suggestions for refinement of the intervention for future research and practice, as well as a consideration

of the strengths and limitations of the studies. This is an addition to the discussions that are reported in the published papers of Studies I, II and III.

5.1 Outcomes of the structured nurse-led follow-up intervention on physical and psychological health status

The patients allocated to the experimental and control groups had baseline differences, as was reported in Studies II and III. The experimental group was younger and had lower APACHE II scores at ICU admission, indicating a reduced severity of illness compared with the control group. Furthermore, before the ICU admission the experimental group had significantly better physical functioning and more bodily pain than the control group. The difference between the groups was also substantiated by the different reasons for the ICU admission. About two thirds of the ICU admissions in the experimental group were medical and one third surgical and vice versa in the control group (Studies II and III). Therefore, the two groups varied on some important parameters at the outset of the study.

The difference in bodily pain between the groups over all the time points or, from before ICU admission to 12 months after ICU, originated in the characteristics of the females in the experimental group and was detected through sub-group analysis (Study II). The females in the experimental group had also other components that further exaggerated the difference between the groups. Their health status was worse, in general, compared to males in the experimental group before the ICU, at three and six months. Meanwhile, the difference between genders in the control group was in physical functioning at all of the five time points and in role physical and general health at 12 months, to the benefit of the males. Compared to females in the control group and males in either group, the females in the experimental group had on average the highest anxiety symptoms at ward discharge and at three and six months and they had the highest depression symptoms at three and six months. There were also more females in the experimental group (12/15) than the control group (3/15) with symptoms of PTSD (IES-R score ≥23-88) at three months post-ICU. Females in the experimental group were considerably younger than females in the control group (mean age difference 13 years). The majority of the females in the experimental group were admitted to the ICU because of respiratory failure (14/29) but in the control group females were admitted for cardio-thoracic surgery (8/27), cardiovascular reasons (7/27) and respiratory failure (7/27).

There were significant negative changes in health status within the groups over the five time points, i.e. from better health before the ICU admission to worse health at 12 months. The changes were in all SF-36v2 items of both groups except bodily pain and mental health in the experimental group and mental health in the control group. Descriptively, the health status of both groups was similar to a cohort of ICU patients reported by Cuthbertson et al. (2005) indicating the profound and long-term impact of critical illness and ICU stay on patients' health status in the first year after discharge from the ICU. Further analysis (not reported in Study II) revealed that the physical functioning of the experimental group was significantly worse at 12 months compared to before the ICU stay (paired t-test: t(55)=4.18, $p < .001$). The same was not found in the control group (paired t-test: t(62)=1.55, p .127). Seeking explanations for this, it is possible that the severity of the critical illness and the consequences of a shorter ward stay had such profound influences on the experimental group that despite receiving the structured nurse-led follow-up it was not possible for them to reach the pre-ICU status. Also, the patients in the experimental group were younger and had fewer comorbidities than patients in the control group. This is supported by earlier studies showing that elderly patients accept limited recovery while younger ones expect full recovery after the critical illness that led to the ICU admission (Kaarlola et al., 2006; Montuclard et al., 2000; Orwelius et al., 2005).

The mental health of patients in both groups was stable over time. The mental health scale of the SF-36v2 measures anxiety, depression, emotional and psychological well-being. High scores reflect being calm and at peace (Marush, 2016). The mental health scale of the SF-36v2 was in concordance with results of anxiety and depression as measured by the HADS instrument. In both groups at ward discharge, and three, six and 12 months thereafter, anxiety and depression were both within normal limits, i.e. scores between 0 and 7 on the HADS (Zigmond & Snaith, 1983). Conversely, there were 34 patients – 19/66 in the experimental group and 15/64 in the control group – who had indications of partial or full PTSD (IES-R score ≥23-88) at three months post-ICU (Bienvenu et al., 2013). PTSD increased from three months to six and 12 months. Similar results have been shown in some cohort studies (Bienvenu 2013; Myhren et al., 2010). Furthermore, there are indications that the presentation of the PTSD symptoms can be complex over the first year after ICU, reflected in persistent symptoms, delayed onset, recovering, or even no symptoms of PTSD (Myhren et al., 2010; Rattray et al., 2010). This complexity should emphasise the importance of prevention measures and support for symptoms of PTSD in patients after ICU discharge.

5.2 Reflections on the structured nurse-led follow-up intervention

The intervention tested in this thesis was built on analysis and synthesis of research of nurse-led follow-up of patients after discharge from the ICU. The intervention was further substantiated in a model presented for utilisation in this thesis (Study I). An important outcome of the integrative review (Study I) was the reporting of a single component of an ICU nurse-led follow-up, such as a three-month appointment, but separated from ward visits. Additionally, there was a complete lack of studies of ICU nurse-led follow-up measuring patients' health status before the ICU admission, and therefore no reference point for the post-ICU measures. There was also a limited number of studies comparing the effectiveness of ICU nurse-led follow-up within and between groups over time.

Reflecting on what this thesis adds to the structure, content and measured outcomes of an ICU nurse-led follow-up intervention reveals its novelty. Furthermore, the rationale for the structure and content of each component of the structured nurse-led follow-up intervention that was tested is reiterated.

I. *Booklet.* The provision of a booklet with written and verbal information to patients and/or their closest relatives at ICU discharge was the first component of the structured nurse-led follow-up intervention, although not included in the model presented in Study I. The work of Bench et al. (2011) suggested that providing verbal and written information to patients/closest relative at ICU discharge was valuable in supporting recovery. A booklet, handed over at ICU discharge had not been integrated in an ICU nurse-led follow-up intervention that included ward visits and appointment(s) post-ICU, which was confirmed when reading the articles of the integrative review of Study I. Furthermore, providing information at ICU discharge had not been tested by measuring physical or psychological health status over time in studies of ICU nurse-led follow-up.

II. *Ward visits.* The novelty of the ward visits intervention in this thesis was in the protocolised structure and content of ward visits applied for patients staying ≥ 72 hours in ICU that was added to the daily work of experienced ICU nurses. Clinical surveillance and support was determined to be pivotal content of the ward visits because of patients' risk of clinical deterioration due to consequences of critical illness at that time point. A prospective study comparing a ward visit intervention and standard care had not been presented at the launch of this study. Additionally, outcomes of ward visits had primarily concerned readmission rate, length of stay and survival (Ball et

al., 2003; Eliott et al., 2008) but not patients' health status. As reported in Study I, an ICU nurse-led follow-up, which included ward visits with clinical surveillance, similar to ICU liaison nursing intervention or CCO, and appointment(s) three months post-ICU, had been tested in the study of Jones et al. (2003) (affirmed by the first author of that study). However, this structure was not mentioned in the study of Jones et al. (2003) or in any other studies.

III. *Contact during the first week after discharge from the ward to home.* A telephone call asking patients how they were doing and providing a consultation regarding the recovery is a relatively new addition in the development of ICU nurse-led follow-up. Contact (telephone call), with patients during the first week after discharge from a general ward to home, was included in one study of an ICU nurse-led follow-up intervention (Jones et al., 2003). The aims of the three weekly telephone calls were to encourage patients and remind them of a self-help rehabilitation manual. The telephone calls and the self-help rehabilitation manual proved beneficial with improved physical function compared to standard care (Jones et al., 2003).

IV. *Appointment three months after discharge from the ICU.* As previously mentioned, the novelty of this thesis is the interconnected components of the intervention concluded with an appointment at three months. Study I showed that in 2012, the first year of working on this thesis, there were two RCTs that included ICU follow-up appointments, which suggested that such an appointment might be important. As it turned out, there was only one RCT that tested the effectiveness of an ICU nurse-led follow-up appointment intervention (Cuthbertson et al., 2009). In the other RCT the effectiveness was tested of a rehabilitation self-help manual that was an add-on intervention in a routine ICU follow-up that included ward visits, telephone calls to home and appointments (Jones et al., 2003). Later, or in the year 2016, the RCT of Jensen et al., reported no difference between a post-ICU recovery program and standard care. Other studies that included appointments in their ICU follow-up were descriptive and evaluative (Glimelius Petersson et al., 2011; Schandl et al., 2011) and underscored the need for empirical research of ICU nurse-led follow-up.

5.3 The effectiveness of the structured nurse-led follow-up intervention

The results of the thesis call for reviewing the structure and content of the structured nurse-led follow-up intervention. A mean of three ward visits per patient were provided by 30 ICU nurses and the visits were an addition to the nurses' daily workload. A selected team of ICU nurses and/or ICU clinical nurse specialists, with expert knowledge of ICU patients' recovery, and having time dedicated to the ICU nurse-led follow-up, might be more likely to lead to greater effectiveness of the ward visits. This was though not implied by the results of the standard care showing the same number of visits per patient (a mean of three per patient), although only a few patients' records were retrieved that documented the ward visits of patients (n=16). The ward visits in standard care were delivered by one or two clinical nurse specialists, as well as an unknown number of ICU nurses. Another consideration is the duration of the intervention. The results of Studies II and III show that patients' recovery is in its early stages three months after ICU discharge, as already verified by other research (Cuthbertson et al., 2005; Herridge et al., 2011). That can signify the necessity of follow-up beyond the two to three months post-ICU, although the patients in the experimental group did not use the open invitation to contact the structured nurse-led follow-up service after the three months appointment. The structure of the intervention might need to be more affirmative for the patients, including an invitation to a second or even a third appointment during the first year post-ICU.

An important finding during recovery post-ICU concerned the first week after discharge from the ward to home which was shown to be a particularly vulnerable and difficult period for the patients (Study II). This indicates that the nurse-led follow-up needs to be expanded to support patients' recovery at this particular time point. An expansion of the nurse-led follow-up was also implied by the results regarding disturbing memories of the ICU stay (Study III). Disturbing memories of the ICU stay and emotional reactions were associated with patients' PTSD symptoms at three months (Study III). These effects of the ICU stay on patients' psychological recovery suggest the ICU nurse-led follow-up intervention should commence during patients' ICU stay. The negative experience and disturbing memories of the ICU treatment and environment could possibly be dealt with during patients' ICU stay (Long et al., 2014; Papathanassoglou, 2010). ICU nurses could systematically work on ameliorating the challenges of the negative experience of the ICU stay that impact patients' psychological recovery as a part of their comprehensive ICU nursing care. Some of the challenges are pain (Myhren et al., 2010), sleep

problems, noise (Elliott et al., 2013) and communication between the patient and the ICU nurses (Elliott et al., 2013; Khalaila et al., 2011; Meriläinen et al., 2013).

There is a growing body of research on the importance, for patients and their closest relatives, of receiving information at ICU discharge (Bench et al., 2011; Bench et al., 2015). The studies show the complexity of such an intervention regarding the content, timing and method of information delivery and patients' capacity to comprehend information early in the recovery (Bench et al., 2011; Bench et al., 2013; Ramsay et al., 2016). The patients and/or their relatives in Studies II and III received an information booklet on ward discharge. The effectiveness of this single component remains unknown but as one of four components of the structured nurse-led follow-up intervention it was not effective in measures of health status over time. However, the importance of receiving information on recovery after the ICU, for the patient and family, should not be underestimated. Awareness of the consequences of critical illness and the ICU stay is vital for the patients and their closest relatives (Jones, 2002). Of particular importance is to understand why the recovery process is difficult and can take a long time (Jones, 2002). The complexity of informing patients is reflected in approaching patients during the ward stay with the aim of discussing the ICU experience (Glimelius Peterson et al., 2011; Ramsay et al., 2016; Schandl et al., 2011). This practice could demand careful evaluation of its timing and content in relation to PTSD recovery after ICU discharge where a brief, single session, focusing on the traumatic event, is not recommended as an immediate intervention of PTSD recovery (NICE, 2005).

The awareness of the empathetic care that supports patients' first months of natural recovery after a traumatic event is a vital component of ICU nurse-led follow-up (NICE, 2005) and was particularly addressed in Study III. Additionally, screening patients for symptoms of PTSD at the end of the natural recovery period, i.e. preferably one month after the ICU discharge and definitely within three months, is of importance and should be offered to patients, at least if they are still hospitalised (NICE, 2013; NICE 2005). To prevent PTSD symptoms becoming a chronic problem it is of particular importance to treat them within three months from their onset, highlighting the significance of the first appointment, held within three months post-ICU.

The three-month appointment (Studies II and III) had a global content and was without additional professional resources such as physiotherapists or psychologists. The physical and psychological consequences of critical

illness and an ICU stay are multifaceted (Studies I, II and III) and may call for an interdisciplinary approach that includes an ICU nurse. However, there are few studies presenting content and measuring outcomes of interdisciplinary ICU nurse-led follow-up (Crocker 2003; Schandl et al., 2011). It is uncertain whether patients who are referred to other professionals actually received or used the referred service (Cuthbertson et al, 2009; Glimelius Petersson et al., 2011). Early mobilisation of critically ill patients while in the ICU appears to enhance recovery, for example resulting in shortened length of ICU and hospital stay, and increases functional ability measured at hospital discharge (Stiller, 2013; Schweickert et al., 2009). However, the benefits of physical exercises initiated post-ICU remains unknown (Connolly et al., 2015). Mobilisation may also have a positive impact on long-term psychological recovery (Jackson et al., 2014) and remains an essential and pivotal aspect of appointments post-ICU.

Although the structure and content of the ward visits as practiced in this study did not apparently benefit the patients in Studies II and III, it is not only patients that may benefit from ICU nurses' ward visits. The ward visits could be important for the ward nurses and may indirectly increase the quality of care for patients and their families transferring from the ICU to the ward (Cullinane & Plowright, 2013; Häggström & Bäckström, 2014). Chaboyer et al, (2005) showed that the support that ICU liaison nurses provided to ward nurses increased their clinical competence and it helped with patients' and their families' transition from the ICU to the ward. Furthermore, the reduction in ICU readmission rate (Ball et al., 2003), reduced mortality (Garcea et al., 2004) and transfer to an appropriate level of care (Endacott et al., 2010) when providing ICU nurse-led follow-up, cannot be overlooked, as illustrated in the literature. The proactive, clinical focus of the ward visits is therefore important to explore further.

5.3.1 Summary of suggestions for refinement of the intervention and for future practice and research

The suggestions in this thesis for possible refinement of an ICU nurse-led follow-up and future research are plentiful, covering the long-term recovery of patients after ICU. Below are the suggestions summarised for: **I** refinement of future practice and research and, **II** several research questions for an ICU nurse-led follow-up that remain to be addressed and tested.

I. *Summary of suggestions for refinement of the intervention and for future*

practice and research.

- The ICU nurse-led follow-up intervention should begin during patients' ICU stay, because patients' disturbing memories of the ICU stay and emotional reactions associated with symptoms of PTSD hinder psychological recovery after intensive care.
- Patients and their closest relatives should receive information explaining the milestones of the recovery and reasons for the difficult and long recovery process in any time after intensive care.
- The ICU nurse-led follow-up should involve a small and dedicated team of ICU nurses providing the ward visits with proactive, clinical focus on support and surveillance for patients after ICU discharge.
- The ICU nurse-led follow-up team and the ward staff should emphasise empathetic care that supports patients' psychological recovery after ICU discharge and during the ward stay.
- Patients' recovery needs during the first week at home after discharge from the hospital ward should be considered.
- Patients should be screened for symptoms of PTSD within three months from the ICU discharge, which highlights the significance of the first appointment, held within three months post-ICU.
- The ICU nurse-led follow-up should consider the inclusion of an interdisciplinary approach (physiotherapist, psychologist) in addition to comprehensive appointment(s) with an ICU nurse from two to three months up to 12 months after ICU discharge.

II. *Suggestions for future studies in the field of ICU nurse-led follow-up.*

- What is the effect of ICU nurse-led follow-up psychological support during the ICU stay on patient's long-term recovery from symptoms of post-traumatic stress disorder after the ICU compared to standard care?
- What is the effect of location of discharge from the general ward (home) on the recovery of patients discharged from the ICU compared to other locations (rehabilitation centre, other hospital, other)?
- What is the effect of an ICU nurse-led follow-up intervention on patient's recovery experience in the first week after discharge from hospital to home compared to standard care?

- What is the effect of ICU nurse-led follow-up interventions - during the patient's ward stay, during the first week after discharge home from the general ward, and two to three months after ICU discharge - on patient's health status compared to standard care?
- What is the effect of ICU nurse-led follow-up that includes interdisciplinary collaboration on patient's recovery after intensive care compared with ICU nurse-led follow-up without interdisciplinary collaboration?
- What is the effect of ICU nurse-led follow-up on patients' and families' physical and psychological health over 12 months after the ICU discharge compared to standard care?
- Is more emphasis on prolonged physical and psychological support the best way to improve patient's health status after intensive care compared to providing support over a shorter period of time?

5.4 Epilogue

There are abundant challenges for ICU nursing in promoting the recovery of ICU patients. Patients report on a wide variety of individual factors that are helpful for their recovery after critical illness (Aitken et al., 2016). Such individuality is further acknowledged in the definition of Post-intensive care syndrome (PICS) articulating numerous consequences after critical illness on physical and psychological health (Needham et al., 2012) and underscoring the importance of approaching each patient with the realisation of this complexity. When preparing the aims of patients' recovery, an appealing approach is to ask each patient what is important to him or her in the recovery. Simultaneously, ensuring a reference point of health status before the ICU admission is vital for a logical and individual outcome after critical illness and ICU discharge (Feemster et al., 2015).

A favourable outcome of an ICU nurse-led follow-up intervention for patients is possibly challenging to reach. The ICU nurse-led follow-up intervention could nevertheless be beneficial for patients. The heterogeneity of the patients is one of the factors supporting such a hypothesis along with the numerous cofounding variables during a patient's hospitalisation and after discharge to home. A parallel situation has been reported with Rapid Response Teams, such as Critical Care Outreach and the Medical Emergency Teams, which are acute medical ward services for patients

designed to prevent clinical deterioration such as cardiac arrest (Jones et al., 2011). The effectiveness of Rapid Response Teams is not fully substantiated but the team is considered important for patients' safety, survival and treatment while hospitalised at acute general wards (Hillmann et al., 2005; Tee et al., 2008; Winters et al., 2013). Reasons for non-effective results of ICU nurse-led follow-up are certainly plentiful. ICU nurse-led follow-up is, presumably, a relatively well known post-ICU service among ICU professionals, including ICU nurses. When implementing such an intervention and comparing it with standard care at one central hospital, there could be a risk of ICU professionals, at the standard care site, changing their clinical practice accordingly (Hawthorne effect). Furthermore, despite more than a decade of strong focus of ICU researchers on prolonged and insufficient recovery of ICU patients (Desai et al., 2011; Needham et al., 2012), few controlled studies testing interventions for patients' recovery have been published (Melhorn et al., 2014). The possibility also remains that ICU nurse-led follow-up does not improve patient's outcomes. The approach of the ICU nurse-led follow-up could also be too broad with extensive and unspecific measures resulting in non-effectiveness, especially if an individual approach is what the patients need and want.

The physical, psychological, cognitive and social consequences after the ICU stay are plentiful and miscellaneous (Figure 1). In this thesis, only a fraction of the possible consequences post-ICU were chosen to measure the effectiveness of the structured nurse-led follow-up intervention, e.g. general physical and psychological consequences and specific psychological consequences of anxiety, depression, PTSD and disturbing memories of the ICU stay. The ICU nurse-led follow-up faces complexity regarding patients' health status; equally the consequences of ICU stay and the pre-ICU health status on health after the ICU discharge. The complexity is augmented by the constituents of the ICU stay, e.g., the reason of the ICU admission, the severity of the ICU illness, the ICU treatment received and the ICU length of stay. The complexity of developing an ICU nurse-led follow-up is further highlighted in the process of the post-ICU recovery, which is marked by several factors. The first factor being the patient's health status before the ICU admission followed by the patient's ICU stay and discharge. The other factors are the ward stay and the ward discharge, the first week at home after hospital discharge and for months thereafter.

5.5 Strengths and limitations

Several methodological novelties were considered as strengths of the present work. The first was that the content, structure and measured outcomes of the intervention were based on outcomes of previous research that were included and presented in the integrative review (Study I). The second was translating the synthesis of the integrative review into a clinical practice model of nurse-led follow-up, creating continuity of the intervention from the patients' ICU discharge until three months post-ICU. The third was measuring patients' health status before the ICU (Studies II and III).

A systematic review would have been preferred for reviewing the structure, content and outcomes of nurse-led follow-up but it was impossible because of the lack of empirical and RCTs on the subject, hence an integrative review was chosen (Study I). The inability to randomise the patients to the experimental and control groups was a major limitation (Studies II and III). The opposition from the ICU staff at the standard care site where unstructured ward visits had been provided for few years was the main reason but simultaneously a fact of standard care and could therefore not be ignored. To randomise patients only at the experimental site was unrealistic because of the low number of patients with an ICU stay ≥ 72 hours, which extended the time of the recruitment. The consequences of this for the study were substantial as there were baseline differences between the groups. This makes comparison between the groups contradictory, with the conclusions being more about two cohorts rather than two comparable groups. There was also general knowledge among staff in both ICUs of the planned research, which might have influenced the practice for the control group (Hawthorn effect). The staff that provided the ward visits to the control group (building II) might have changed their practice accordingly.

There were fidelity issues in implementing the intervention. To secure the integrity of the ward visit delivery, training of the ICU nurses attending the ward visits needed more sophistication than was provided. The training of the nurses providing the follow-up compromised interactive meetings but not direct training on the scene, implying variability in the implementation. The variability is also underscored by the large number of ICU nurses (30 ICU nurses) providing the visits when implementing the intervention. However, this could also be looked upon as a strength because this shows the clinical reality. The ward visits were an addition to their ICU workload and could have limited the implementation even further.

Thirty-two patients were discharged home from the general ward and received a phone call during the first week at home. Answering a questionnaire was planned, but proved difficult because the patients were more interested in discussing their disbelief at how weak they were and their lack of endurance. This component of the intervention was not piloted and therefore has fidelity limitations.

The data on the number and the actual content of the ward visits at the control site were incomplete due to the deficiency in documentation of the visits. Subsequent is the fidelity of missing and unknown data with the unidentified effects on the comparison between the groups.

6 Conclusions

The results from the three studies that comprise this thesis contribute to the development of nurse-led follow-up of patients after discharge from the ICU. The contribution covers a substantial and important time period in patients' recovery or from the ICU discharge to 12 months thereafter.

The integrative review revealed limited evidence of an effective structure and content of nurse-led follow-up of adult patients after discharge from the ICU. The tentative results of the small number of heterogeneous studies with diverse methodology were primarily measured with descriptive outcomes. From the synthesis of the results, a four-component intervention of structured nurse-led follow-up was developed and its effectiveness tested. The intervention did not significantly improve the health status of patients over time, compared with standard care, from the ICU discharge until 12 months thereafter. Health status within both groups decreased compared to before the ICU admission and over the one year after the ICU discharge. Females in the experimental group reported more bodily pain over the time points than females in the control group and men in both groups. The length of the general ward stay was shorter in the experimental group compared to the control group. Furthermore, the intervention did not significantly improve the psychological health of patients, i.e. symptoms of post-traumatic stress disorder, anxiety and depression, over 12 months after ICU discharge, compared to standard care.

The heterogeneity of the ICU patient population calls for a more individual approach to the structured nurse-led follow-up. Having data on patients' health status before the ICU admission is a prerequisite for supporting patients' recovery after the ICU and setting reasonable aims in the recovery post-ICU. Patients' disturbing memories of the ICU stay and its effect on psychological health suggest the need to initiate patients' first contact with the structured nurse-led follow-up during the ICU stay. Methods to improve patients' experience and memories in the ICU should be integrated in the ICU treatment. The aim is to avert the potential development of symptoms of PTSD and consequently promote long-term psychological recovery. An allocated team of ICU nurses providing ward visits to patients after discharge from the ICU could encourage more consistent surveillance and support. It is imperative for nursing to respond to the implications of the patients' need for

support in their recovery during the first week at home after the discharge from the general ward. An interdisciplinary team approach for supporting patients' recovery at the two-three month appointment could possibly further enhance patients' health status outcomes.

The critical illness and the ICU stay have a tremendous impact on patients' health and recovery. Patients that survive the intensive care stay need support to regain their physical and psychological health. Although the benefits of the intervention applied in this study were below expectations, there is potential to improve the ICU nurse-led follow-up and thus support the recovery of ICU patients, but that requires further research.

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