# The effect of a therapeutic early mobility position on the haemodynamic stability in a critically ill patient population

by

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## Declaration

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# Abstract

## Introduction

Bed rest is routinely prescribed during critical illness which leads to significant inactivity in an adult critically ill population. Survivors will possibly encounter difficulties in their health related quality of life (HRQoL) and physical functioning. The therapeutic use of positioning in the management of an adult critically ill population could minimise the negative effects of bed rest.

## Method

A scoping review was conducted to describe the therapeutic use of positioning in the management adult of critically ill patients. Six electronic data bases were searched by two researchers using specific search strategies. Papers were identified and included using predefined inclusion criteria. Data was extracted into an Excel spreadsheet. Data describing the therapeutic use of positioning was reported in a scoping review and the focussed review explored the effect of the semi-recumbent position on a critically ill patient population. This information was used in planning of the primary study. A non-randomised experimental design was used to evaluate the feasibility of using an *adapted early mobility readiness protocol* (protocol) to identify patients who could tolerate the therapeutic early mobility position (testing position). We reported on the effect of the testing position on two haemodynamic parameters including the mean arterial pressure (MAP) and the percentage central venous oxygen saturation ($ScvO_2$%). The secondary aim was to describe the current nursing positions used in the surgical and respiratory units (the units) and to describe any adverse events. Twice weekly, all patients nursed in the units were screened with the inclusion/exclusion criteria and the protocol. The patients included were tested in the baseline nursing position followed by the testing position. The MAP and $ScvO_2$% were measured at 0 minutes, 3 minutes and 10 minutes. Data were described using repeated measures of ANOVA. A 5% significant level ($p < 0.05$) was used. If data were skewed, medians ranges 95% confidence intervals (CI), mean differences and 95% CI of mean differences were used.

## Results

Nine hundred and thirty-six full text papers were assessed for inclusion into the review. One hundred and thirty-four papers described the therapeutic use of positions. Twelve papers, of which six papers described the effect of the semi-recumbent position and six

papers described the clinical outcome of the semi-recumbent position, were included in the focussed review. Uncertainties still surround the haemodynamic stability and the ability of a patient to maintain the 45° semi-recumbent position. A longer period in the 45° semi-recumbent position is needed to evaluate the dynamic interaction of variables like the MAP and $ScvO_2$%. We screened 138 patients using the inclusion/exclusion criteria which 82 patients failed. Eleven (7.9%) patients passed the protocol: male/female (9/2) with a median (range) age of 47 (20-67) years. The placement from the baseline nursing position to the testing position resulted in a mean difference (95% CI) of 2.03 (-1.12 - 5.18) in the MAP and a mean difference (95% CI) of 0.79 (-3.15 - 4.74) in the $ScvO_2$%. Both did not reach statistical significance.

## Conclusion

Guidelines for the use of the 45° semi-recumbent position as a preventative intervention for ventilator associated pneumonia and aspiration do exist but therapeutic use of a position as an early mobility position still needs investigation. The protocol was not able to adequately identify patients who would be able to tolerate the testing position. Further work is needed to refine the criteria of protocol. Our data can inform the process. The outcome of patients nursed in this position needs further investigation.

# Opsomming


## Inleiding

Bed rus word gewoonlik voorgeskryf tydens die mediese versorging van kritieke siek pasient. Dit lei tot onaktiwiteit van kritieke siek pasiënt. Pasiënte sal moontlik probleme teëkom in hul gesondheidsverwante lewenskwaliteit en fisiese funksionering na hul herstel. Die negatiewe gevolge van bed rus kan moontlik verminder word en daarom word n beter begrip van die terapeutiese gebruik van posisionering in die hantering van volwasse pasiente in n kritieke siektetoestand benodig.

## Metode

'n Literatuur oorsig is gedoen om die terapeutiese gebruik van posisies te beskryf in volwasse kritieke siek pasiente. Ses data basisse is ondersoek deur twee navorsers met behulp van spesifieke soekstrategieë. Relevante artikels is geïdentifiseer en ingesluit aan die hand van vooraf gedefinieerde kriteria. Data is onttrek en opgesom in 'n self-ontwikkelde datablad. Data wat die terapeutiese gebruik van posisionering beskryf is in die oorsig studie beskryf en die gefokusde studie rapporteer die effek van die semi-geligte posisie op kritieke siek pasiente. Hierdie inligting is gebruik om te help in die beplanning van die primêre studie. 'n Nie-ewekansige eksperimentele studie is gebruik om die toepaslike gebruik van 'n aangepaste vroeë mobiliteits-gereedheidsprotokol te evalueer en om moontlike pasiënte te identifiseer wat die terapeutiese vroeë-mobiliteitsposisie kan verdra. Die primere doel was om die uitwerking van die toetsposisie op twee hemodinamiese parameters, die gemiddelde arteriele druk (MAP) en die sentrale veneuse suurstof persentasie ($ScvO_2$%), te beskryf. Die beskrywing van die huidige verpleegsposisies in die eenhede en die newe-effekte wat daarmee gepaard gaan was die sekondere doel. Alle pasiënte wat in die chirurgiese en respiratoriese eenhede verpleeg word, is twee maal per week gëevalueer met die insluiting- en uitsluiting kriteria. Indien hul ingesluit is, is hul verder gëevalueer met die protokol. Pasiënte, wat dan slaag, is getoets in die basislyn-verplegingsposisie, gevolg deur die toetsposisie. Die MAP en die $ScvO_2$% is gemeet by 0, 3 en 10 minute. Data is beskryf deur middel van herhalende metings van ANOVA en n p-waarde van 5% is gebruik ($p < 0.05$) Data is beskryf met mediane (rykwydtes) en 95% vertrouensintervalle, gemiddelde verskille sowel as 95% vertrouensintervalle van gemiddelde verskille tydens skewe distribusie.

## Resultate

936 volledige teks dokumente is uitgelig vir insluiting. 134 dokumente is gevind wat die terapeutiese gebruik van posisies beskryf. Twaalf dokumente is in die gefokusde literatuur oorsig ingesluit waarvan ses die effek van die semi-geligte posisie beskryf en ses die kliniese uitkoms van die semi-geligte posisie beskryf. Die hemodinamiese stabiliteit en die vermoë van 'n pasiënt om die $45^0$ semi-geligte posisie te verdra word bevraagteken. 'n Langer tydperk in die $45^0$ semi-geligte posisie is nodig om die dinamiese interaksie van veranderlikes, die MAP en die $ScvO_2$%, te evalueer. 138 pasiënte is gëevalueer met die insluitings en uitsluitings kriteria waarvan 82 pasiente nie geslaag het nie. Daarna is die oorblywende 46 pasiente gëevalueer met die protocol. Elf (7.9%), manlike / vroulike (9/2) pasiente met 'n mediaan (rykwydte) ouderdom van 47 (20-67) jaar, slaag die protokol. Die gemiddelde verskil van die MAP (95%CI) was 2.03 (-1.12 – 5.18) tydens posisionering vanaf die basislynverplegingsposisie na die toetsposisie en dit was nie statisties beduidend nie. Die gemene verskil van die $ScvO_2$% (95%CI) was 0.79 (-3.15 - 4.74) tydens posisionering vanaf die basislynverplegingsposisie na die toetsposisie was ook nie statisties beduidend nie.

## Gevolgtrekking

Riglyne bestaan wel vir die gebruik van die $45^0$ semi-geligte posisie vir die voorkoming van ventilator geassosieerde pneumonie en aspirasie van maag inhoud. Die gebruik van hemodinamiese parameters om die veiligheid en toepaslikheid van 'n vroeë mobiliteitsposisie te bepaal is nie ten volle beskryf nie. Die aangepaste vroeë mobiliteits-gereedheidsprotokol kon nie daarin slaag om toepaslike pasiente te identifiseer wat in die toets posisie geplaas kon word nie. Ons stel voor dat kriteria van die protokol verfyn word voor verdere gebruik. Ons data kan hierdie proses inlig. Die uitkoms van pasiënte wat vir n langer periode verpleeg word in hierdie posisie, benodig verdere ondersoek.

## Dedication

Thank you to my husband, family and friends for all the support, help and understanding.

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## Glossary of Terms

**ARDS** is previously known as acute respiratory distress syndrome (ARDS), acute lung injury, adult respiratory distress syndrome, or shock lung, is a severe, life-threatening medical condition characterised by widespread inflammation in the lungs. While ARDS may be triggered by a trauma or lung infection, it is usually the result of sepsis[1].

**Arterial pressure** is described as an average blood pressure in an individual. It is defined as the average arterial pressure during a single cardiac cycle[2].

**Aspiration** is described as the movement of gastric content to the lower airways in patients receiving mechanical ventilation with a nasogastric tube in place[3].

**Atelectasis** is described as a partial or complete decrease closure of lung units and loss of elastic recoil of lungs[4].

**Beach chair** is defined where the head of bed is elevated to $75^0$ and the knees bent at -$75^{0}$[5].

**Bed rest** is defined as confinement of a patient to bed as part of treatment[6].

**Bundle care** is a structured way of improving the processes of care and patient outcomes: a small, straightforward set of evidence-based practices generally three to five that, when performed collectively and reliably, have been proven to improve patient outcomes[7].

**Cardiac index** is a haemodynamic parameter that relates the cardiac output (CO) from the left ventricle in one minute to the body surface area (BSA), thus relating heart performance to the size of the individual. The unit of measurement is litres per minute per square metre ($L/min/m^2$)[8].

**Cardiac output** expressed in litres/minute, is the amount of blood the heart pumps in one minute. Cardiac output is logically equal to the product of the stroke volume and the number of beats per minute (heart rate)[8].

**Central venous oxygen saturation** assesses the changes in the global oxygen supply to demand ratio[9]. Normal value of above 70%[34].

**Cerebral blood flow (CBF)** is the blood supply to the brain in a given period of time. In an adult, CBF is typically 750 millilitres per minute or 15% of the cardiac output. This

equates to an average perfusion of 50 to 54 millilitres of blood per 100 grams of brain tissue per minute [10].

**Cerebral perfusion pressure (CPP)** is defined as the difference between the Mean Arterial Pressure (MAP) and the Intracranial Pressure (ICP). CPP = MAP - ICP. This represents the pressure gradient driving cerebral blood flow (CBF) and hence oxygen and metabolite delivery[10].

**Cerebral vasospasm** is a sustained arterial constriction reducing its diameter and flow rate which results in cerebral ischemia and infarction[10].

**Central venous pressure (CVP)**, also known as mean venous pressure (MVP), is the pressure of blood in the thoracic vena cava, near the right atrium of the heart. CVP reflects the amount of blood returning to the heart and the ability of the heart to pump the blood into the arterial system[11].

**Gravitational equilibrium** is described as a prolonged period in a stationary position[12].

**Haemodynamic instability** is most commonly associated with an abnormal or unstable blood pressure, especially hypotension[11].

**Haemodynamic monitoring** includes measurement of heart rate, arterial pressure, cardiac filling pressures or volumes, cardiac output, and mixed venous oxygen saturation ($SvO_2$)[13].

**Haemodynamic parameters** are parameters that determine blood flow[13].

**Health related quality of life (HRQoL)** is described by the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36), which measures the health-related quality of life and consist of eight multiple-item scales that assess physical functioning, social functioning, physical role, emotional role, mental health, pain, vitality, and general health[14].

**Hypoxemia** is described as oxygen desaturation due to arterial oxygen desaturation occurs which results in a decrease in arterial carbon dioxide and an increase in arterial pH[4].

**ICU acquired weakness** is described as clinically apparent weakness caused by being critically ill[15].

**Intra-cranial pressure** is the pressure of the cerebrospinal fluid in the subarachnoid space, the space between the skull and the brain; the normal range is between 50 and 180 mm$H_2O$ (approximately 4 to 13 mmHg)[10].

**Kinetic bed** is a therapy also known as continuous lateral rotational therapy, oscillation therapy, and continuous postural oscillation, involves nursing the patient on a bed that continuously rotates in an attempt to prevent the respiratory complications of immobility[16].

**Mean arterial pressure (MAP)** is defined as the average pressure in a patient's arteries during one cardiac cycle[11]. Normal value of above 65 mmHg[34].

**Mean systemic filling pressure** is defined as the mean pressure that exists in the circulatory system when the blood has had a chance to redistribute evenly to all vessels and organs. Mean systemic filling pressure is approximately 7 mmHg. Maas et al[17] defined it as the extrapolation of the linear line regression to zero flow[17].

**Neuromuscular impairments** include critical illness polyneuropathy, myopathy and disuse atrophy[18].

**Orthostatic intolerance** is a disorder of the autonomic nervous system occurring when an individual upper body is raised. Requires rapid and effective circulatory and neurologic compensations to maintain blood pressure, cerebral blood flow, and consciousness[6].

**Physical functioning impairments** are described as impairments of activities and instrumental activities of daily living and the six minute walk distance[18].

**Pulmonary artery pressure** is a measurement of the blood pressure found in the pulmonary artery. This is measured by inserting a catheter into the pulmonary artery. The mean pressure is typically 9-18 mmHg, and the wedge pressure measured in the left atrium may be 6-12 mmHg[2].

**Pulmonary impairment** is described as an impairment of the diffusion capacity of the lung and is inversely associated with the duration of mechanical ventilation[18].

**Pulmonary wedge pressure** is the pressure produced by an inflated latex balloon against the inner wall of a pulmonary artery. A pulmonary artery catheter or similar balloon-tipped catheter is inserted through a subclavian, jugular, or femoral vein to the vena cava and on through the right atrium and ventricle to the pulmonary artery. The balloon is

inflated briefly, during which time it measures left ventricular diastolic pressure. The procedure is used in the diagnosis of congestive heart failure, myocardial infarction, and other conditions[2].

**Recumbancy** is described as lying supine in bed[4].

**Reverse (anti-) Trendelenburg** is where the body of a person is tilt with head higher than the feet by $15^0$ to $30^{017}$.

**Semi-recumbent position** is defined as a degree of elevation of the head of the bed. During this position the upper body is elevated[19].

**Stroke volume** (SV) is the amount of blood pumped out of the heart (left ventricle - to the body) during each contraction measured in millilitres per beat (ml/b)[8].

**Stroke volume variation** is defined as the percentage change between the maximal and minimal stroke volumes (SV) divided by the average of the minimum and maximum over a floating period of 30 s, continuously displayed by the continuous cardiac output monitor[8].

**Therapeutic early mobility intervention** is described as the 45° semi-recumbent position that has been adapted to a position called the therapeutic early mobility position which is defined as a 45° semi-recumbent position with the knees bent appropriately to prevent the patient from sliding out of the position.

**Tilt** is described as standing with the use of a tilt table and allows a patient to be passively tilted to varying angles to the horizontal[20].

**Trendelenburg** is when the body is laid flat on the back (supine position) with the feet higher than the head by 15-30 degrees[17].

**VAP** is ventilator-associated pneumonia and is defined as nosocomial infection occurring more than 48 hours after patients have been intubated and received mechanical ventilation[1]

**Units** refer to a specialised section of a hospital that provides comprehensive and continuous care for persons who are critically ill and who can benefit from treatment. The surgical critically ill unit refers to the unit where critically ill patients are nursed after surgery and the respiratory unit refers to the critically ill unit where patients are nursed with respiratory conditions.

# List of Abbreviations and Symbols

| | |
|---|---|
| ABCDE | Awakening and breathing coordination, delirium monitoring and management, and early mobility |
| ADL | Activities of daily living |
| ALI | Acute lung injury |
| APACHE | Acute Physiology and Chronic Evaluation |
| ARDS | Acute respiratory distress syndrome |
| BC | Beach chair |
| BiPAP | Bi-level positive airway pressure |
| BP | Blood pressure |
| bpm | Beats per minute |
| BRE | Back rest elevation |
| CA | Cancer |
| CAP | Community acquired pneumonia |
| CBF | Cerebral blood flow |
| CCI | Continuous cardiac index |
| CCO | Continuous cardiac output |
| CDCP | Centre of Disease Control and Prevention |
| CI | Cardiac index |
| CI | Confidence interval |
| CO | Cardiac output |
| CPAP | Constant positive airway pressure |
| cpm | Counts per minute |
| CPP | Cerebral perfusion pressure |
| CVP | Central venous pressure |
| DBP | Diastolic blood pressure |
| $DO_2$ | Oxygen delivery |
| ECG | Electro cardiogram |
| ET | Endotracheal tube |
| GER | Gastroesophageal reflux |
| GSW | Gunshot wound |
| HOB | Head of bed |
| HR | Heart rate |
| HRQoL | Health related quality of life |

| | |
|---|---|
| Hrs | Hours |
| $I^2$ | Heterogeneity |
| ICP | Intra-cranial pressure |
| ICU | Intensive care unit |
| Lab | Laboratory |
| LOS | Length of stay |
| MAP | Mean arterial pressure |
| mcg/kg/min | Microgram per kilogram per minute |
| MFV | Mean flow velocity |
| Mg | Milligram |
| Min | Minutes |
| Ml | Milliliter |
| mmHg | millimeter mercury |
| MVA | Motor vehicle accident |
| N | No |
| n | Number |
| NG | Nasogastric |
| Pa | Arterial pressure |
| $PaO_2/FiO_2$ | Ratio of arterial oxygen partial pressure to fractional inspired oxygen |
| PAP | Pulmonary artery pressure |
| PCWP | Pulmonary wedge pressure |
| PEEP | Positive end expiry pressure |
| pH | Acidity |
| PI | Principal investigator |
| PICOS | Population Intervention Comparison Outcome Studies |
| PLR | Passive leg rise |
| Pmsf | Mean systemic filling pressure |
| RAc | Radio-isotopic count |
| RASS | Richard Agitation Sedation Scale |
| RCT | Randomised control trials |
| RR | Respiratory rate |
| $SpO_2$ | Peripheral capillary oxygen saturation |
| SBP | Systolic blood pressure |

| | |
|---|---|
| $ScvO_2$% | Percentage central venous oxygenation saturation |
| SD | Standard deviation |
| SIMV | Synchronised intermittent mandatory ventilation |
| SV | Stroke volume |
| Temp | Temperature |
| Type I | Type one |
| VAE | Vascular air emboli |
| VAP | Ventilator associated pneumonia |
| VO2 | Oxygen consumption |
| WBC | White blood cell count |
| X | Parameter not used |
| Y | Yes |
| Yrs | Number of years |
| % | Percentage |
| ✓ | Parameter used |
| $^0$ | Degrees |

# Chapter 1: Introduction

## 1.1 Background

Bed rest is associated with poor health related quality of life (HRQoL) and physical functioning of survivors after recovering from critical illness[18]. Physical-, pulmonary- and neuromuscular impairments have been reported as possible causes for the poor HRQoL[18]. The physical impairments include poor daily activities like gripping and a decrease in the six minute walk distance[18]. Poor diffusion capacity and lung volumes have been reported as pulmonary impairments[18]. Intensive care unit (ICU) acquired weakness including disuse atrophy of muscles, polyneuropathy and myopathy have been reported as neuro-muscular impairments[18]. These impairments can be seen as detrimental effects of bed rest and can possibly be prevented through early mobilisation during the acute phase of critical illness[21].

Early mobilisation has been described as an interdisciplinary, goal-directed therapeutic intervention with the aim of preventing the detrimental effects of bed rest and improving patient outcome through various activities[21]. Early mobilisation refers to a facilitation of movement intervention and includes positioning, continuous lateral rotating therapy, active and passive range of movement exercises, dangling of feet, moving out of bed to a chair, moving into an upright position in bed, walking, tilting on table, use of resistance exercises and the use of electrical muscle stimulation[21].

Early mobilisation of critically ill patients is considered to be safe[22-23] and well tolerated[23]. The physical functioning of patients seems to improve when early exercise therapy is started after cardiorespiratory stability is gained[24]. The ICU associated delirium[25-26] seems to be minimised to a mean of two days[23] when early mobilisation starts before 72 hours of ventilation. The unit[23] and hospital length of stay is shorter[27]. The ICU acquired weakness[27-30] shows a possible improvement. Schweikert et al[23.]reported that the independent functional status of patients improved with early mobilisation. There is a possibility of improving pulmonary drainage, oxygenation and ventilation with the change in position and of possibly decreasing the risk of developing ventilator associated pneumonia (VAP) as well as decreasing the time of ventilation[21]. Early mobilisation into the upright position helps with weaning from the ventilator as stated in a concept analysis by Amidei[21]. All the above positive effects of early mobility urge

a physical therapist to start facilitating early mobility as soon as possible to help prevent the detrimental effects of bed rest[21]. However, it has been reported by Amidei[21] that the readiness of patients is still being questioned by the interdisciplinary team. The implementation is also delayed until physiological stability is gained[31-32]. Therefore early mobility often begins after the acute phase of critical illness[21].

Haemodynamic instability[33-34] which forms part of the cardiovascular reserve of physiological stability[35-36] has been proposed as a possible reason for delaying early mobility during the acute phase of critical illness[21,35]. Addressing the haemodynamic instability[33-34], Stiller et al[35] suggested that before the start of mobilisation a patient's clinical status and ability need to be screened with a comprehensive protocol to evaluate if mobilisation will be safe. Protocols have been developed over the years to help ICU teams with early mobility of critically ill patients[12, 23, 36-38]. The screening of patients with a protocol could address the major concern of haemodynamic instability[33-34] which may occur during early mobility. A protocol could also facilitate early mobilisation, like a therapeutic early mobility position. By using a protocol, early mobility can be initiated as early as possible to prevent the detrimental effects of bed rest and improve a patient's HRQoL and physical functioning after recovering from critical illness, as discussed earlier.

Addressing the inability to reach the specific goal-directed position[19, 34, 39], the poor HRQoL and physical functioning and the detrimental effects of bed rest[18], the need was identified for an appropriate therapeutic intervention. Therefore, the researchers decided to investigate ways to facilitate optimal positioning, as early as possible from time of admission to the unit, as a therapeutic early mobility intervention in an adult critically ill population. The aim of this thesis was to investigate the therapeutic use of positions in an adult critically ill population.

## 1.2 Thesis outline

The thesis is presented in "Masters by publication" format.

**Chapter 2** makes use of a scoping review to describe therapeutic use of positioning in the management of an adult critically ill population with the aim of answering the following research question: Which nursing positions are currently used as therapeutic positioning in the management of an adult critically ill population? The objectives were to identify all primary papers, systematic reviews and meta-analyses describing the use of a therapeutic position;

describe the therapeutic positions used; identify the countries where therapeutic positioning is used; identify the year of publication of therapeutic positioning; describe the critically ill population where therapeutic positioning is used and to identify any gaps in the evidence of therapeutic positioning. This chapter will be prepared as a manuscript for submission to the Worldviews on Evidence-based Nursing journal under the title "A Scoping Review: The therapeutic use of positioning in the management of an adult critically ill population". Instructions for author for the specific journal are presented in Addendum A.

**Chapter 3** makes use of a focussed review to explore the effect of the semi-recumbent position (semi-fowler or head-up position) on an adult, critically ill, mechanically ventilated or intubated population with the aim of answering the following research question: What is the effect of the semi-recumbent position on an adult, critically ill, mechanically ventilated or intubated population? The objectives of this review were to describe the semi-recumbent positions used; describe the methodology used in papers on the semi-recumbent position; describe the critically ill population where the semi-recumbent positioning is used; describe the effect of the semi-recumbent position on haemodynamic and pulmonary parameters; describe the cerebrovascular dynamics during the semi-recumbent position; describe the adverse effects of the semi-recumbent position; describe the effect of the semi-recumbent position on the clinical outcome (VAP and aspiration) of a critically ill population. This chapter will be prepared as a manuscript for submission to the Worldviews on Evidence-based Nursing journal under the title "A Focussed Review: The effects of the semi-recumbent position on an adult critically ill population". Instructions for author for the specific journal are presented in Addendum A.

**Chapter 4** describes the primary research study. A non-randomised experimental study was used with a primary aim of identifying patients who could tolerate the therapeutic early mobility position by using an adapted early mobility readiness protocol. The effect of a therapeutic early mobility position on two haemodynamic parameters was investigated including: 1) the mean arterial pressure (MAP) and; 2) the oxygen consumption via the percentage central venous oxygen saturation ($ScvO_2$%). The secondary aim is to describe the current nursing positions used in the units and to describe any adverse events. This chapter will be prepared as a manuscript for submission to Critical Care, a journal of BMC, under the title: "A pilot study: The effect of a therapeutic early mobility position on an adult critically ill population". Instructions for author for the specific journal are presented in Addendum B. The abstract of this manuscript was

presented at the Critical care Society of Southern Africa (CCSSA) congress, Adventures in Critical Care 2015 and published in the Southern African Journal of Critical Care 2015;31(1)nr5:24-28 (Addendum C).

**Chapter 5** discusses the current understanding of literature, the aims of the primary study, achievements of aims, limitations and suggestions of future research with a take home message and a final conclusion.

**References** are presented in a chapter together and all manuscripts which will be prepared from Chapter 2, Chapter 3 and Chapter 4 will adhere to the guidelines provided by each of the specific journals chosen for submission.

**Addenda** include: All data related to the methodology; the description of the pilot study with the result; the description of the results of the pulmonary compliance (Addendum D) not described in Chapter 4 and the results not described or presented in Chapter 4.

# Chapter 2: Scoping Review

**This chapter will be prepared as a manuscript for submission to the Worldviews on Evidence-based Nursing journal (Addendum A) under the title "A Scoping Review: The therapeutic use of positioning in the management of an adult critically ill population".**

## 2.1 Introduction

Bed rest is routinely used to nurse critically ill patients. Winkelman[6] defined bed rest as prescribed immobilisation in the recumbent position. Immobilisation prohibits weight bearing activities which contribute to significant inactivity in a patient[6]. Due to patient inactivity, multiple changes in organ systems occur[6]. The affected organs include the circulatory, pulmonary, muscular, skeletal, nervous, and digestive systems[6] which in turn could affect patient outcome.

The effects of inactivity on the circulatory system include a decrease in blood volume, orthostatic intolerance and a decrease in blood flow in the lower extremities[4, 6, 12]. Therefore inactivity leads to a decrease in the stroke volume (SV) which leads to a decrease in the cardiac output (CO) and increases the resting heart rate (HR)[4, 6, 12].

Lung volumes and the mechanism of breathing change with the persistence of inactivity[4]. These changes lead to hypoxemia through atelectasis, aspiration and pneumonia[4, 6]. During the supine position a patient's diaphragm moves cephalic and decreases the size of the thorax. As a result, the pulmonary blood flow decreases below the amount of blood flow in the lungs which leads to poor lung volumes, poor clearance of secretions, a loss of cough and desaturation of arterial blood[4].

Inactivity during bed rest also leads to muscle atrophy[40]. Muscle atrophy is noted in the antigravity muscle groups at a faster rate than the muscles used for gripping[40]. The type I fibres of the antigravity muscles lose myofilaments[40]. This deconditioning of the antigravity muscles at a faster rate is a problem for ICU teams as it makes turning, sitting on the edge of the bed and ambulation of a critically ill patient difficult[40].

Other detrimental effects of inactivity include changes in the autonomic and cognitive nervous system which occur during a period of inactivity[6]. Peripheral nervous system injuries[6] have also

been reported. Pressure ulcers and skin breakdown caused by the shearing forces on the sheet are also noted during inactivity[6].

The physiological adverse effects lead to a poor HRQoL including pulmonary, neuromuscular and physical functioning impairments[18]. Physical functioning impairments are slow to improve and can last for up to five years post ICU admission and include difficulty in walking and weak grip strength[18]. Poor activity of daily living (ADL) has also been reported in most of the ICU survivors during the first week at home[18]. This poor ADL has been reported to be more prevalent in ICU survivors who have been ventilated for more than 48 hours[18].

It has been reported that the detrimental effects of inactivity can be minimised by early rehabilitation in the critically ill environment[18]. Therefore, designing effective interventions as well as the timing of interventions are essential to address the detrimental effects of bed rest[18]. Early mobilisation is defined as an inter-disciplinary, goal-directed therapy aimed at facilitating movement and improving outcomes in critically ill patients[21]. Early mobility has also been described as mobilisation which consists of active limb exercises, actively moving or turning in bed, sitting on the edge of the bed, sitting out of bed in a chair while using special equipment and manoeuvres, standing and walking activities[41]. The effects of early mobility have been summarised in a number of systematic reviews[41-42]. The studies reviewed showed that early activities are feasible and safe[41-42]. Most of the studies included critically ill patients who received mechanical ventilation for four or more days and only one study reported safety of physical therapy performed within two days of intubation[23].

It has been hypothesised that mobilisation can be started within eight hours of intubation if the patient meets the specific criteria[12, 38]. Mobilisation starts with elevation of the head of the bed to an angle greater than $30^0$ and progresses to out of bed movements if a patient can tolerate it[12]. However the feasibility of head of bed elevation to an angle greater than $30^o$ has been questioned by a number of studies [19, 34, 43]. A wide variation in the standard nursing care position has been documented, varying between $22.9^0$ and $28^0$[19, 43]. Elevating a patient up to a $45^o$ semi-recumbent position was found to be a risk which is associated with a significant drop in the MAP and $ScvO_2$%[34].

Early mobility away from the bedside is time and resource intensive and the effects on therapist related injuries have not been described well[44]. The inclusion of weight bearing positions during

the routine nursing of critically ill patients could be a novel approach to decreasing the effects of immobility in this population. These positions are not dependent on the patient's participation and could be implemented within eight hours of intubation[12]. However, positioning during the early stages of critical illness, and which therapeutic positions have the possibility of forming part of an early mobility intervention and routine nursing care, have been poorly investigated[21]. Therefore two researchers conducted a scoping review to investigate the use of therapeutic positioning in the management of an adult, critically ill patient.

## 2.2 Research Question

Which nursing positions are currently used as therapeutic positioning in the management of an adult critically ill population?

## 2.3 Aim

The aim of this scoping review was to describe the therapeutic use of positions in the management an adult critically ill population.

## 2.4 Objectives

The objectives of this review were to:

1. Identify all primary papers, systematic reviews and meta-analyses describing the use of a therapeutic position;
2. Describe the therapeutic positions used;
3. Identify the countries where therapeutic positioning is used;
4. Identify the year of publication of therapeutic positioning;
5. Describe the critically ill population where therapeutic positioning is used;
6. Identify any gaps in the evidence of therapeutic positioning.

## 2.5 Methodology

Two researchers (EC & SS) used the methodology described by Arksey and O'Malley[45] who published the first methodological framework for conducting scoping reviews in 2005. This process incorporates five steps which include identifying the research question, identifying relevant papers, study selection, charting the data and collating, summarising and reporting the results. No critical appraisal is performed on relevant papers.

### 2.5.1 Search strategies

Two researchers (EC & SS) independently searched six electronic databases including *CINAHL*, *Science Direct*, *Scopus*, *Pubmed*, *Google Scholar* and *Web of Science* from inception to June 2013 through the Stellenbosch University E-Library. A specific search strategy was developed for each of the databases. Key words included the relevant terms for therapeutic positions like "backrest elevation", head-up position", "beach chair position", "prone position", "lateral position", "semi-recumbent position", "supine position", "head down tilt" AND "adult" and "mechanically ventilated" OR "critically ill" were used. The terms were searched as MeSH terms, subject headings and also as "free text" keywords. Retrieval was limited to English publications. Addendum E contains the full search strategies with the keywords used in all the databases and the number of hits.

### 2.5.2 Trail eligibility

#### *2.5.2.1 Inclusion criteria*

All papers were included which reported on:

a) The use of a therapeutic position;

b) A description of standard nursing position;

c) The effect of a therapeutic position.

#### *2.5.2.2 Exclusion criteria*

All papers reporting on children, animals, books, surgical procedures, foreign language papers, healthy participants, reviews, commentary on papers and editorials were excluded.

### 2.5.3 Study design

All primary papers with descriptive and analytical observational designs, and all analytical experimental designs were included. Secondary papers which gave a systematic review or a meta-analysis were also included.

### 2.5.4 Study selection

All books and duplicates found in each of the three databases were excluded by each fellow researcher. The remaining titles were combined and all duplicates found were excluded again.

The titles were divided between the two researchers (EC & SS). Abstracts of titles were reviewed by each of the two researchers (EC & SS) and full-text publications of potentially relevant papers were obtained. The second-level screening of all titles, abstracts and full-text papers was reviewed by both researchers independently to identify relevant potential full-text papers for inclusion. A third researcher (SH), a Professor in Physiotherapy, was consulted to resolve discrepancies between the two researchers (EC & SS) and reach consensus on the inclusion or exclusion of unclear potentially relevant papers at each level (Addendum F: Complete flow chart of paper selection).

### 2.5.5 Data extraction

Data were extracted and moved into a Microsoft Excel spreadsheet from relevant included papers. Data extracted included the study design, the therapeutic positions and the standard nursing positions found; the country of origin, the year of publication and the characteristics of the populations. Random checks of the extracted date were completed by an independent reviewer to ensure the quality of data.

### 2.5.6 Analysis

Results were descriptively reported in histograms and tables to identify the gap in the body of evidence reported in the full-text papers that were included.

## 2.6 Results

Of the 936 titles found, 134 (100%) full text papers[2, 5, 8, 10, 17, 19, 20, 34, 43, 46-170], which were included for analysis. Figure 2.1 displays a consort flow diagram of the summarised literature search.

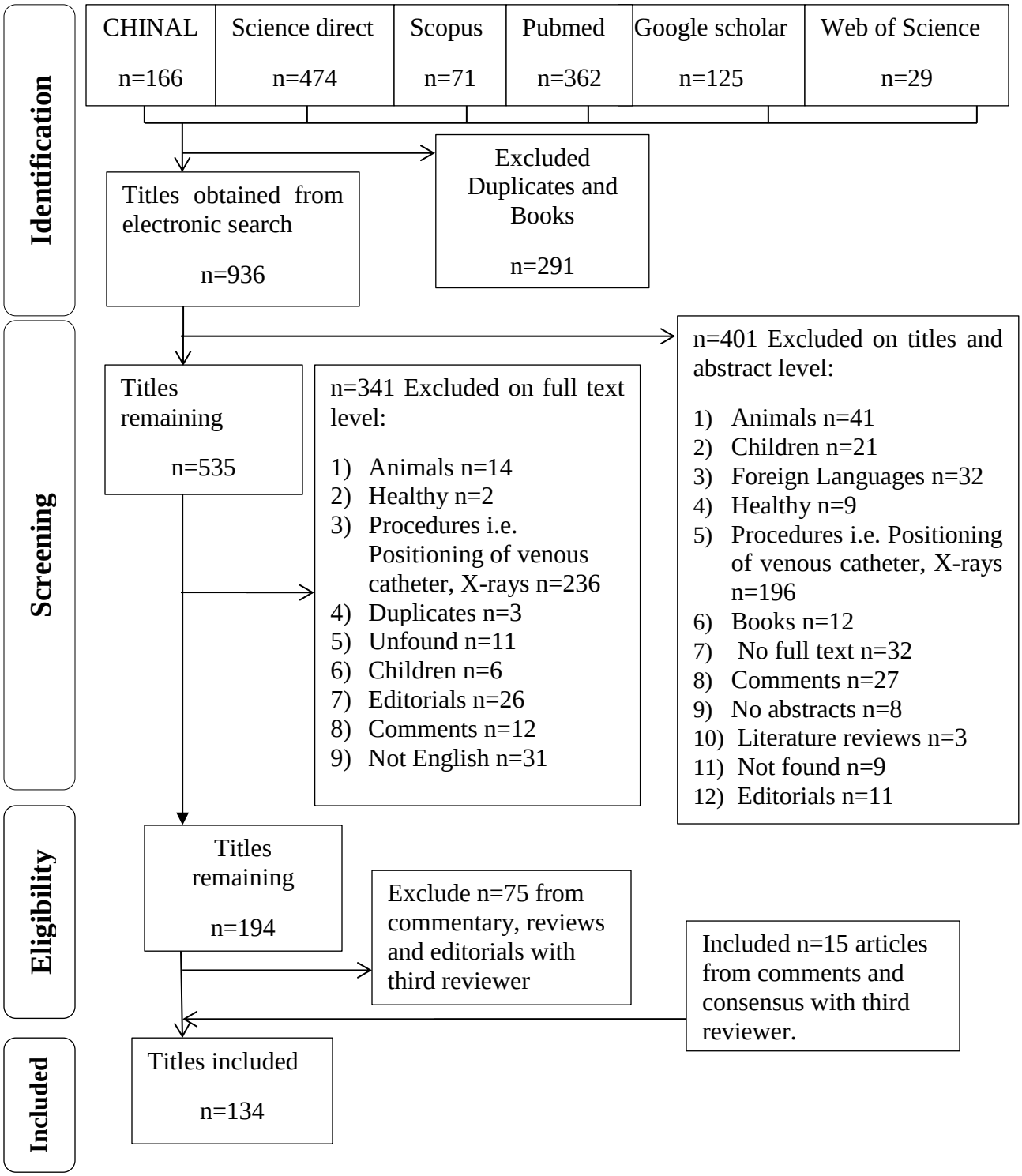



**Figure 2.1: Consort flow diagram summary of paper search**

The majority of papers were 122 (91%) primary studies[2, 5, 8, 10, 17, 19-20, 34, 43, 46-66, 68-130, 133-134, 139-141, 143-146, 149-156, 158-163, 165-170] and 12 (8.9%) papers[67, 131-132, 135-138, 142, 147-148, 157, 164] were secondary studies (Table 2.1).

The secondary papers included six (50%) meta-analyses[132, 135-136, 147-148, 164], four (33%) systematic reviews[67, 131, 137-138] and two (16.6%) papers[142, 157] were a combination of a systematic review and a meta-analysis. The secondary papers mostly reported on the use of positioning in the management of acute respiratory distress syndrome and acute lung injury (ARDS/ALI); incidences of VAP; mortality; prevention of VAP and the management of the critically ill population. Two different combinations of positioning were investigated, including five (41.6%) prone versus supine papers[132, 135-136, 157, 164] and one (8.3%) prone and $45^0$ semi-recumbent position paper[147] as an intervention. Mostly the effects of prone positioning on ARDS/ALI were investigated in five (41.6%) meta-analyses[132, 135-136, 148, 164]. Table 2.1 gives a summary of PICOS investigated in the systematic reviews and the meta-analyses in this review.

## Table 2.1: Summary of systematic reviews and meta-analysis PICOS up to June 2013

| Study | Country | M/S | Population | Intervention | Comparison | Outcome | Studies included |
|---|---|---|---|---|---|---|---|
| Tiruvoipati et al[132] | UK | M | Adults with ALI / ARDS | Prone & Supine | Prone ventilation vs supine ventilation | Mortality; Oxygenation; VAP; Pressure ulcers. | 5 RCT's |
| Abroug et al[136] | Tunisia | M | Adults with ALI / ARDS | | Prone ventilation vs supine position; Disease severity; Clinical outcomes; Adverse events. | Effects of prone ventilation on mortality of patients with ALI / ARDS. | 7 RCT's |
| Alsaghir et al[135] | Canada | M | Adults with ARDS | | Comparing >6 hrs of prone position with supine position. | Mortality; Improvement in oxygenation; Days of MV; VAP. | 5 RCT's |
| Sud et al[157] | Canada | S/M | Adults, AHRF and severe hypoxemia | | Prone vs Supine ventilation | Mortality | 10 RCT's |
| Abroug et al[164] | Tunisia | M | Adults, intubated, ALI / ARDS with Hypoxemia | | Prone vs Supine relationship between studies' effect size and daily prone duration. | Mortality; Effects of prone positioning on major adverse airway complications. | 7 RCT's |
| Curley et al[67] | USA | S | Adults with ARDS | Prone | Techniques, patients responses and complications. | Recommendations to prevent complication. | 20 RCT's |
| Sud et al[142] | USA | S/M | Aduts with AHRF | | Effects of prone ventilation. | Mortality, oxygenation, duration of ventilation and adverse events. | 13 Randomised & Quasi-randomised trials |
| Nortje et al[138] | UK | S | Adults, intubated | | Effects of complications, oxygenation and haemodynamic outcomes compared with the different prone positioning protocols. | Development of evidence-based nursing guidelines. | 45 RCT's |
| Kopterides et al[148] | Greece | M | AHRF patients | | Assess the effect of prone positioning. | Mortality; Days of MV; LOS; Incidence of VAP and pneumothorax; Associated complications. | 4 RCT's |
| Thomas et al[131] | Australia | S | Adults, intubated | Lateral position | Benefit vs Detrimental; Incidence of VAP; LOS; Mortality. | Efficacy and safety | 11 RCT's, quasi-randomized, cross-over control trials. |
| Alexiou et al[147] | Greece | M | Adults, intubated | Prone & 45° Semi-recumbent | Prone vs 45° semi-recumbent positional strategies | Incidence of VAP | 7 RCT's |
| Arabi et al[137] | USA & Saudi-Arabia | S | Adults, intubated | Different treatments methods | Compared different countries incidence rate, microbiology, and outcome of VAP. | LOS, mortality, and the impact of interventions used to reduce VAP rates | 22 Observational and interventional studies |

**Legend:**

**UK =** United Kingdom of Britain; **ARDS =** Acute lung injury / Acute Respiratory Distress Syndrome; **VAP =** Ventilator Associated Pneumonia; **Vs =** Versus**; AHRF =** Acute hypoxemia and respiratory; failure; **> =** Greater; **USA =** United States of America; **PLR** = Passive leg raise; **CO** = Cardiac output; **S** = Systematic reviews; **M** = Meta-analysis; **RCT's** = Randomised control trials; **LOS** = Length of stay; **Rx** = Treatment; **PEEP** = Positive end expiratory pressure; **ICU** = Intensive Care Unit; **MV** = Mechanical ventilation.

### 2.6.1 Positions

A total of 15 different positions were investigated (Figure 2.2). Some papers investigated more than one position. The trendelenburg[105], 30° lateral recumbent[59], continuous rotation[77], sitting in a chair and walking[155] were all investigated in one (0.8%) primary paper. Some papers[7, 130] investigated bundle care which is described as best care practice and includes the elevation of bed to 30° or 45°, continuous removal of secretion, the change of the ventilator circuit every 48 hours as well as washing of hands before and after patient contact. The prone position was investigated in 78 (63.9%) papers[47, 50-55, 57-58, 60-64, 68, 70, 73, 75-78, 80-83, 85-92, 95-104, 106-112, 115-119, 122-123, 126-127, 129, 139-141, 144-146, 149-150, 153-154, 159-163, 166-167, 170]. The semi-recumbent position with 24 (20.4%) papers[2, 8, 10, 17, 19, 34, 43, 65-66, 69, 71-72, 93-94, 112, 120-121, 124, 128, 134, 152, 156, 158, 168] and the beach chair position with one paper[5] were the only positions investigating the up-right position in the bed.

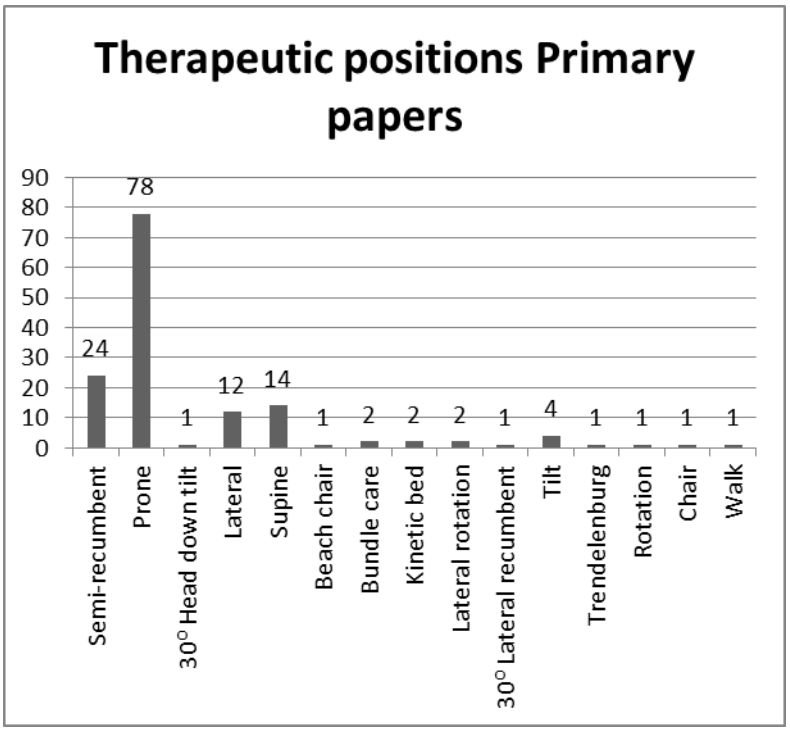
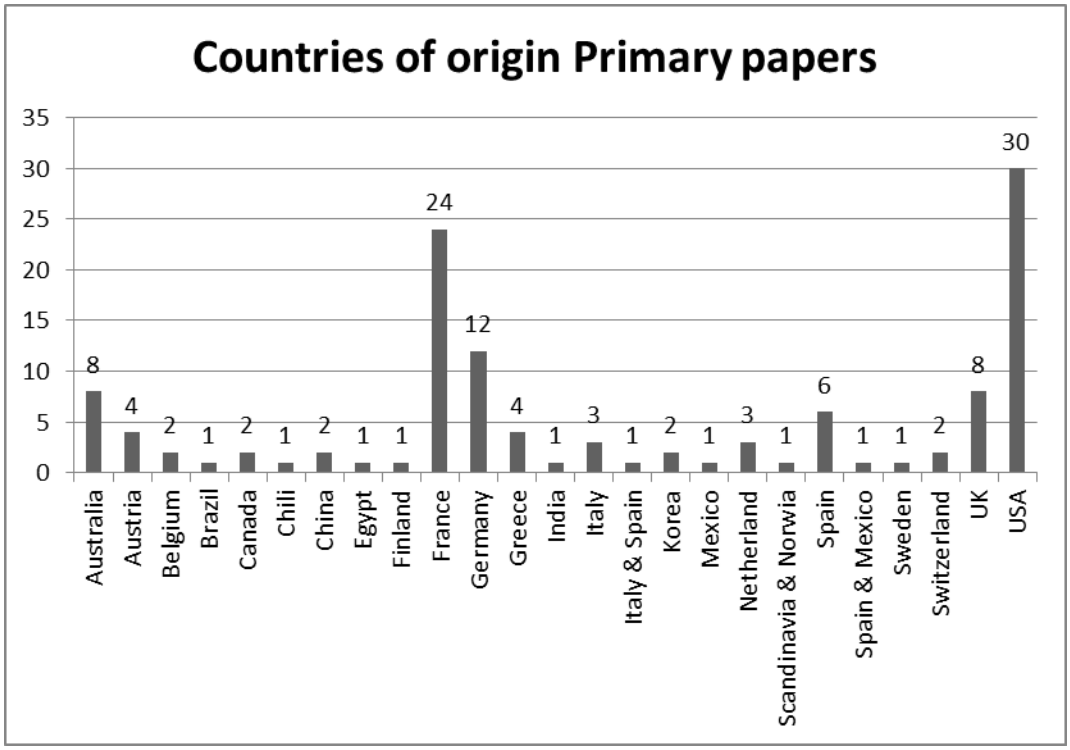



**Figure 2.2: Summary of all the therapeutic positions in the primary papers up to June 2013**

### 2.6.2 Countries

Primary papers were published in 25 countries (Figure 2.3). Three (2.4%) papers[58, 115, 145] reported on a combination of two (1.6%) countries. The majority of papers were published in the United State of America (USA), 30 (24.5%) papers[5, 8, 10, 17, 43, 46, 49, 52, 56, 59, 66, 68-69, 73, 79, 82, 84, 87, 93-94, 120, 124, 127, 130, 141, 146, 149, 152, 158, 166], France 24 (19.6%) papers[53, 61, 64, 75, 81, 86, 95, 96, 101-102, 106-107, 111, 113, 123, 126, 129, 150, 154-155, 160-162, 170] and Germany 12 (9.8%) papers[34, 47-48, 63, 80, 85, 104-105, 109, 116, 140, 159]. Australia conducted eight (6.5%) papers[2, 20, 50, 74, 114, 125, 151, 156], Britain eight (6.5%) papers[90-91, 97, 99, 103, 122, 128, 133], Spain six (4.9%) papers[55, 62, 65, 71, 117, 121] and four (3.2%) papers were published in Greece[70, 108, 112, 119] and Austria[51, 60, 77, 110]. Most of the studies were conducted in the northern hemisphere.




**Legend**:
**UK =** United Kingdom of Britain; **USA =** United States of America.

**Figure 2.3: Countries that primary papers originated from up to June 2013**

### 2.6.3 Year of publication

The investigation of therapeutic positioning in a critically ill population grew from two (1.6%) papers[46-47] in 1993 to 11 (9%) papers[76-86] in 2001 (Figure 2.4). The majority of primary papers reporting on the therapeutic use of positioning were published between 1999 and 2010 in 94 (77%) papers[5, 8, 10, 17, 19-20, 43, 60-66, 68-130, 133-134, 139-141, 143-146, 149-156].

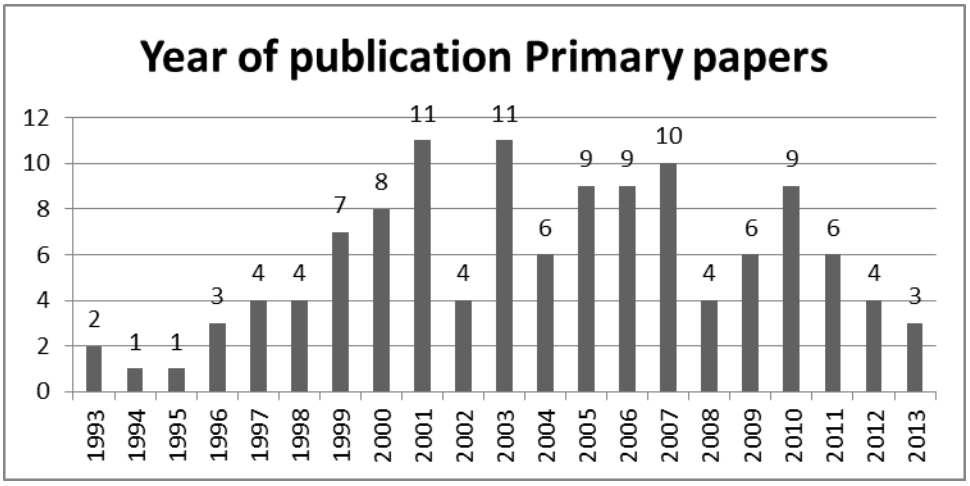
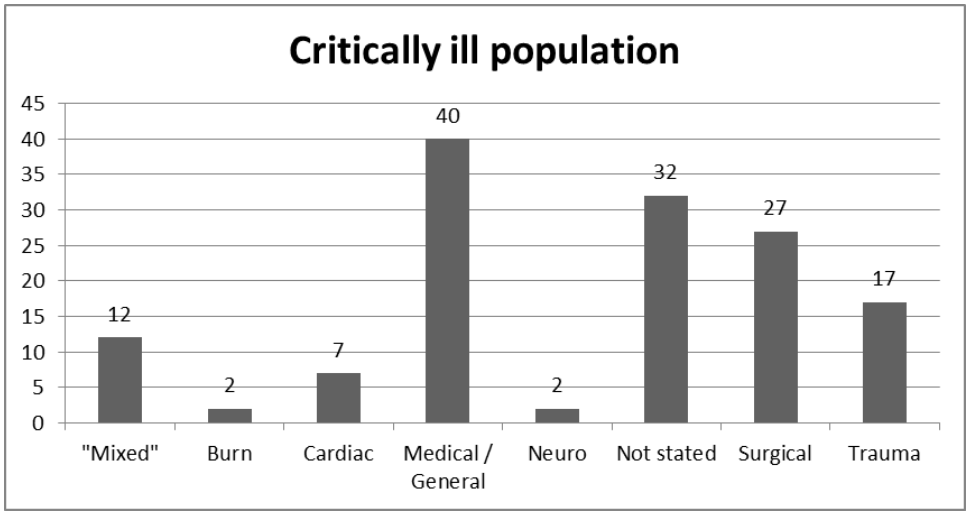



**Figure 2.4: Summary of the number of primary study papers published each year up to June 2013**

### 2.6.4 Population

Five different types of critical ill populations were identified in the studies reported in the primary papers (Figure 2.5). The medical/general populations were reported in 40 (32.7%) papers[5, 8, 43, 53, 55, 57-58, 60-62, 65-66, 71, 74-75, 78, 79, 81, 88, 92-94, 96, 101-102, 106, 111, 113, 121, 123, 128, 134, 139, 143, 149-151, 155, 160, 169]. The surgical populations were reported in 27 (22.1%) papers[5, 8, 10, 17, 34, 47, 58-59, 73, 75, 81-82, 87, 92-94, 105, 117, 127, 134, 139, 141, 143-144, 150, 158, 169].




**Legend:**
**"Mixed"** = No indication of population only reported as "mixed".

**Figure 2.5: Totals of therapeutic positioning studies in different types of critical care units up to June 2013**

It is evident that therapeutic positioning was investigated primarily in a variety of populations as indicated by the included papers. The total number of participants reported on in the primary papers were 11041 participants. The ages of the participants ranged between 23 and 76 years. Two (1.6%) papers[5, 19] did not report the mean age of the participants.

## 2.7 Discussion

Therapeutic positioning is widely used in the management of critically ill patients as indicated by the number of papers published. The USA seems to be investigating the therapeutic positions the most. Currently the investigation of therapeutic positioning has sloped downwards during the last years from 2010 till 2013. This identifies a gap in current evidence of therapeutic positioning with a lesser amount of new data to inform clinicians. The therapeutic use of the prone position has drawn most attention while other therapeutic positions have been poorly reported.

Therapeutic positioning has been used in the management of critically ill patients to optimise the clinical outcome of critically ill patients. The optimisation of the clinical outcome included the prevention of VAP and the optimisation of the outcome of ARDS/ALI.

It is also noted that positioning has been used in a wide variety of populations. In all the populations investigated, however, positioning during the early stages of critical illness, and

which therapeutic positions could possibly form part of an early mobility intervention and routine nursing care, were poorly investigated.

Two therapeutic positions were found which elevated the head of the bed, the semi-recumbent position and the beach chair position. The beach chair position can possibly help prevent a patient from sliding out of the position[19] which has been reported as a reason for not reaching the optimal position for treatment in the semi-recumbent position. It is noted that the use of the beach chair position[5], is not yet well described and needs further investigation regarding the safety of this position. The beach chair position is described as a 70º semi-recumbent position with -75º knee bend. The beach chair position could possibly be a good position to form part of an early mobility intervention as it is not labour intensive and has the potential to be used during the early stage of intubation as the position does not need the patient to be fully awake. The beach chair position is also an anti-gravity position as the patient is sitting upright in the bed which possibly may help prevent the detrimental effects[18] of bed rest. However, an electrical bed is needed to place a patient in the beach chair position and that is not always available.

The semi-recumbent position has been poorly investigated compared to the prone position, although it is recommended by the CDCP as good practice for the prevention of VAP and aspiration[1]. Haemodynamic instability[34] and inability to maintain the position[19, 34, 43] have been possible reasons for not reaching this optimal position for treatment.

This scoping review has some limitations. We excluded trials that were conducted in resource-limited areas as all papers conducted in settings, where mechanical ventilation was not available, were excluded. Therefore the relevance of this review to clinicians in resource-limited areas may be limited. Strengths of this review are that all papers with relevant therapeutic positions used in the critical care environment were included.

Strengths of this literature review were the comprehensive search strategy as it included all the papers published from inception till June 2013. No search strategies were performed after this date. The researcher acknowledged that the review will need to be updated and the search strategies will be performed again and any new evidence will be included in the manuscript.

This review was limited to English papers conducted in adult critically ill units and we acknowledge that incorporating papers published in all languages as well as papers conducted in

other populations such as paediatrics or neonates, emergency departments or the operating room may also inform the use of therapeutic positioning in the management of an adult critically ill patient population.

## 2.8 Conclusion

It is evident that therapeutic positioning was investigated through the years in a variety of populations and countries. The number of different positions also indicates that a wide range of positions have been investigated already, but it is still unclear what therapeutic positions can be used effectively as an early mobility intervention. It is not clear which therapeutic positions may possibly form part of standard nursing care to improve the HRQoL of critically ill survivors, while the semi-recumbent position was identified as a potential early mobility position and in this regard further work is needed.

## 2.9 Take Home Message

1. Therapeutic positioning is widely used in the management of critically ill patients.
2. It is still unclear which therapeutic positions may form part of standard nursing care.
3. The semi-recumbent position as a potential early mobility position needs further investigation.

# Chapter 3: Focussed Review

**This chapter will be prepared as a manuscript for submission to the Worldviews on Evidence-based Nursing journal (Addendum A) under the title "A Focussed Review: The effects of the semi-recumbent position on an adult critically ill population".**

## 3.1 Introduction

Mobilisation starts with elevation of the head of the bed to an angle greater than $30^0$. If a patient can tolerate it[12], mobilisation will progress to out of bed movements like sitting on the edge, standing, sitting in chair and walking activities[41]. However the feasibility of head of bed elevation to an angle greater than $30^o$ has been questioned by a number of studies [19, 34, 43]. Reasons for not reaching the optimal position for treatment recommended by the CDCP[1] were haemodynamic instability and inability to maintain the position[19, 34, 43].

A wide variation in the standard nursing care position has also been documented, varying between $22.9^0$ and $28^0$[19, 43]. Elevating a patient up to a $45^o$ semi-recumbent position was found to be a risk which is associated with a significant drop in the MAP and $ScvO_2$%[34], although the values of the MAP and the $ScvO_2$% were still within normal ranges (MAP > 65mmHg, $ScvO_2$% > 70%).

Therefore a scoping review (Chapter 2) was conducted to investigate which nursing positions are currently used as therapeutic positioning in the management of an adult critically ill population. Investigating the evidence found, only 25 (20.4%) primary papers[2, 5, 8, 10, 17, 19, 34, 43, 65-66, 69, 71-72, 93-94, 112, 120-121, 124, 128, 134, 152, 156, 158, 168] investigated the semi-recumbent position while 78 (63.9%) papers[47, 50-55, 57-58, 60-64, 68, 70, 73, 75-78, 80-83, 85-92, 95-104, 106-112, 115-119, 122-123, 126-127, 129, 139-141, 144-146, 149-150, 153-154, 159-163, 166-167, 170] investigated the prone position. The semi-recumbent position still needs further investigation. Uncertainties still exist regarding the haemodynamic stability[34] and tolerance[19] of the semi-recumbent position. This leads the researcher to probe deeper into the body of evidence pertaining to the semi-recumbent position.

## 3.2 Research question

What is the effect of the semi-recumbent position on an adult, critically ill, mechanically ventilated or intubated population?

## 3.3 Aim

The aim of this focussed review was to explore the effect of the semi-recumbent position (semi-fowler or head-up position) on an adult, critically ill, mechanically ventilated or intubated population.

## 3.4 Objectives

The objectives of this review were to:

1. Describe the semi-recumbent positions used.
2. Describe the methodology used in papers on the semi-recumbent position.
3. Describe the critically ill population where the semi-recumbent positioning is used.
4. Describe the effect of the semi-recumbent position on haemodynamic and pulmonary parameters.
5. Describe the cerebrovascular dynamics during the semi-recumbent position.
6. Describe the adverse effects of the semi-recumbent position.
7. Describe the effect of the semi-recumbent position on the clinical outcome (VAP and aspiration) of a critically ill population.

## 3.5 Methodology

The researcher team (E & SS) developed a systematic approach to further explore the papers identified in the scoping review. All the semi-recumbent positions, described in degrees as well as the supine position described as the $0^{o}$ semi-recumbent position (supine position) were included.

***Trial eligibility***

All 25 (20.4%) papers[2, 5, 8, 10, 17, 19, 34, 43, 65-66, 69, 71-72, 93-94, 112, 120-121, 124, 128, 134, 152, 156, 158, 168] reporting on the semi-recumbent position, identified through the scoping review were eligible for inclusion. In addition, the reference lists of the 25 (20.4%) papers[2, 5, 8, 10, 17, 19, 34, 43, 65-66, 69, 71-72, 93,

[94, 112, 120-121, 124, 128, 134, 152, 156, 158, 168] were searched independently by one researcher (EC) for possible papers not found by the scoping review.

***Inclusion criteria***

Papers were included when reporting on:

a) The effect of semi-recumbent positioning on the haemodynamic, pulmonary and cerebrovascular parameters was described in a critically ill population.
b) The therapeutic application of the semi-recumbent position on the clinical outcome (VAP and aspiration) of a critically ill population.

***Methodological quality of papers***

The quality of papers was evaluated for internal validity, independently by the researcher (EC), with a quantitative critical review form since this review included experimental trials and observational trials. This critical review form for quantitative studies was developed by the McMaster University Occupational Therapy Evidence-Based Practice Research Group[171] (Addendum G). Four points were added to evaluate the process of participants' randomisation into groups, blinding was used as well if any adverse events were reported. It consisted of a set of twenty questions to which the researcher can answer 'yes' or 'no' which were seen as a positive or a negative point. If a point was not reported it was also seen as a negative point against the paper's score. Papers were scored according to this process and received a point out of twenty which in turn was converted to a percentage (Addendum H).

***Hierarchy of papers***

Each paper was given a level of evidence in accordance with the National Health Research Council of Australia Evidence Hierarchy (Addendum I).

***Data extraction***

Collectively the research team determined which variables to extract into a data chart to analyse and report the description of papers, patients' characteristics, the process of sampling, inclusion and exclusion criteria, the time before measurements, the intervention, time spent in the position, results, outcome measures and safety measures. The inclusion and exclusion criteria were subdivided into ventilator, pulmonary, cardiac, vascular, orthopaedic and other inclusion or other exclusion criteria. The outcome measures were also subdivided into pulmonary, cardiac, vascular

and other outcome measures. Safety measures were also subdivided into observational, safety measurements from the monitor, adverse events and other safety measurements. This process was done independently by each of the two researchers (EC & SS). To eliminate discrepancies a data extraction sheet was checked and compared in consultation with the supervisor (SH).

***Data analysis***

Data were evaluated and reported in tables and odds ratios were calculated. All data of results which were comparable were reported in forest plots using the mean difference, pooled effect size, heterogeneity, $I^2$ and the p-values. The mean difference is the expected value of the difference of two random variables in a normal distribution. The pooled effect size describes the weighted effect size of all the papers included in the analysis so that papers with big sample sizes can be identified and have more weight. Heterogeneity refers to the variation in study outcomes between papers and is calculated as the weighted sum of squared differences between individual papers effects and the pooled effect across the studies included. The heterogeneity test results were considered alongside the outcome of the quantitative critical review form assessment of all the papers combined. $I^2$ statistic describes the percentage of variation across the papers that are due to heterogeneity rather than chance and is a simple expression of the inconsistency of papers' results. The p-value is the probability of obtaining the observed effect under a null hypothesis.

## 3.6 Results

Twelve (44.4%) papers[2-3, 5, 8, 10, 17, 19, 34, 65, 72, 128, 172] were identified as relevant papers for data analysis (Figure 3.1). Fifteen (55.5%) papers were excluded of which eight (29.6%) papers[43, 66, 93-94, 121, 134, 156, 158] investigated standard nursing care, five (18.5%) papers[69, 112, 124, 152, 168] compared the semi-recumbent position to an alternative position (prone, lateral or tilt position) and two (7.4%) papers[71, 120] did not report the degrees of the semi-recumbent position. Another two (7.4%) papers[3, 172] were included by pearling.

Six (50%) papers[2, 8, 10, 17, 34, 72] used haemodynamic, pulmonary and cerebrovascular parameters to determine the effect of the semi-recumbent position and six (50%) papers[3, 5, 19, 65, 128, 172] used the clinical outcome of participants to evaluate the therapeutic application of the semi-recumbent position.

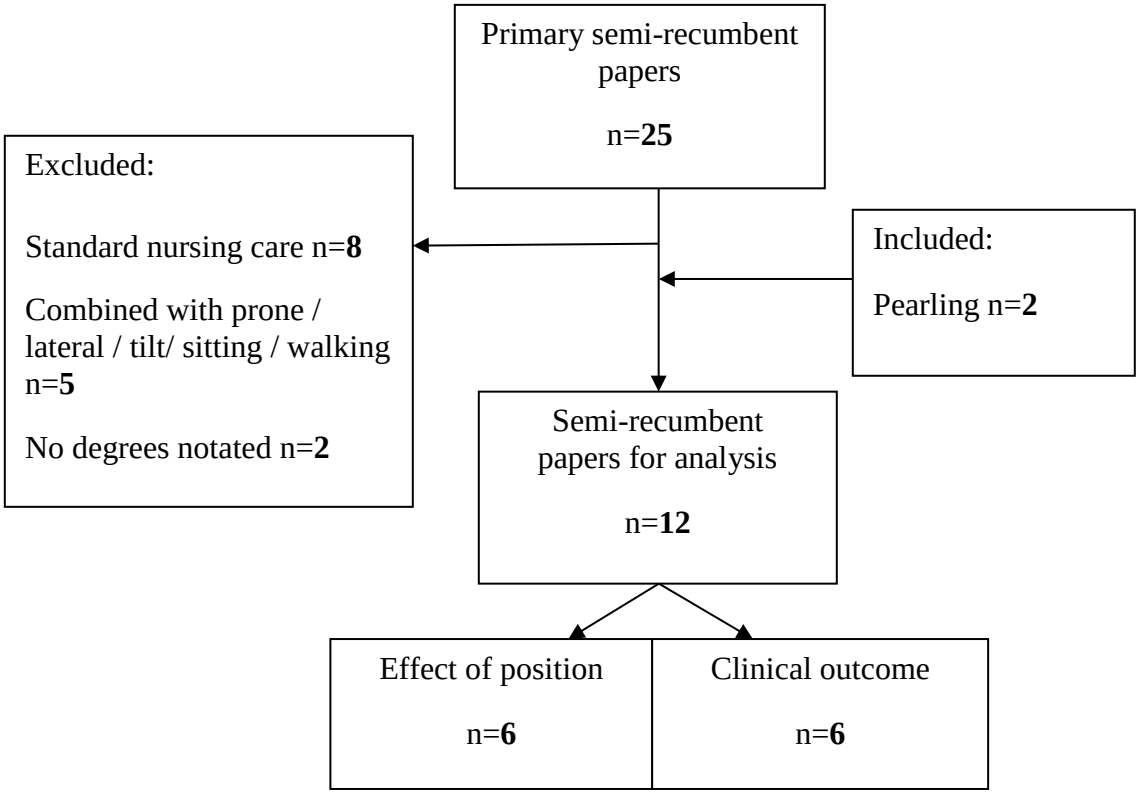



**Figure 3.1: Consort diagram of relevant semi-recumbent papers**

### 3.6.1 The semi-recumbent positions used

During a period of 21 years, only 12 (9.8%) primary papers[2-3, 5, 8, 10, 17, 19, 34, 65, 72, 128, 172] investigated the effect of the semi-recumbent position (Table 3.1). Ten (83.3%) papers[2-3, 8, 10, 19, 34, 65, 72, 128, 172] compared the $45^0$ semi-recumbent position with a range of other degrees of semi-recumbent positions ($0^0$, $15^0$, $20^0$, $25^0$ and $30^0$ semi-recumbent position) and one (8.3%) paper[5] tested the beach chair position.

**Table 3.1: Summary of the semi-recumbent positions used in critically ill papers up to June 2013**

| Study | Year | Semi-recumbent position | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 0° | 15° | 20° | 25° | 30° | 45° | BC |
| Torres, A et al[3] | 1992 | ✓ | | | | | ✓ | |
| Driscoll, A et al[2] | 1995 | ✓ | | | | | ✓ | |
| Orozco-Levi, M et al[172] | 1995 | ✓ | | | | | ✓ | |
| Drakulovic, MB et al[65] | 1999 | ✓ | | | | | ✓ | |
| Moraine, JJ et al[72] | 2000 | ✓ | ✓ | | | ✓ | ✓ | |
| Giuliano, KK et al[8] | 2003 | ✓ | | | | ✓ | ✓ | |
| Blissitt, P et al[10] | 2006 | ✓ | | ✓ | | | ✓ | |
| Van Niewenhoven, CA et al[19] | 2006 | ✓ | | | | | ✓ | |
| Libby Keeley[128] | 2007 | | | | ✓ | | ✓ | |
| Maas, JJ et al[17] | 2009 | ✓ | | | | ✓ | | |
| Caraviello, KAP et al[5] | 2010 | | | | | | | ✓ |
| Gocze, I et al[34] | 2013 | ✓ | | | | ✓ | ✓ | |

**Legend:**
**(°) =** Degrees; **BC** = Beach Chair → Hip Flexion 70° with knee bend 75°

### 3.6.2 The methodology of papers

The level of evidence of papers investigating the effect of the semi-recumbent position varied from level II[34, 72] to III-2[8, 10, 17] while the papers investigating the clinical outcome varied from a level II[3, 19, 65, 128, 172] to a level III-3[5] (Table 3.2).

***Study design***

An experimental design was used in ten (83.3%) papers[2-3, 5, 10, 19, 34, 65, 72, 128, 172] (Table 3.2). Five (41.6%) papers[3, 19, 65, 128, 172] reporting on the clinical outcome of the semi-recumbent position used randomisation of participants into the treatment group and the control group while three (25%) papers[2, 34, 72] reporting on the safety of the semi-recumbent position used randomisation of participants.

**Table 3.2: Summary of study structures of semi-recumbent papers**

| Study | | Study design | Type of study | Level of Evidence |
|---|---|---|---|---|
| **Effect of position** | Driscoll et al[2] | Two-group quasi-experimental design, randomised in groups. | Experimental | III -1 |
| | Moraine et al[72] | Prospectively randomised experimental clinical design | Experimental | II |
| | Giuliano et al[8] | Cohort design | Observational | III-2 |
| | Blissitt et al[10] | With-in pt repeated measure design | Experimental | III-2 |
| | Maas et al[17] | Cohort design | Observational | III-2 |
| | Gocze et al[34] | Randomised experimental design | Experimental | II |
| **Clinical outcome** | Torres et al[3] | Randomised, crossover design | Experimental | II |
| | Orozco-Levi et al[172] | Randomised, crossover design | Experimental | II |
| | Drakulovic et al[65] | Randomised two group design | Experimental | II |
| | Van Niewenhoven et al[19] | Randomised prospective multi-centre trial | Experimental | II |
| | Keeley, L[128] | RCT | Experimental | II |
| | Caraviello et al[5] | Nonrandomised cohort study compared with retrospective cohort | Experimental/ Observational | III-3 |

**Legend:**
**RCT =** Randomised controlled trail; **Level of Evidence =** National Health and Medical Research Council of Australia, Evidence Hierarchy.

***Quality of papers***

The internal validity of papers reporting on the effect of the semi-recumbent positioning scores ranged from 65%[8] to 85%[10, 72] (Addendum H). The scores of papers reporting on the clinical outcome of a critically ill population in the semi-recumbent position ranged from 55%[172] to 95%[65]. Randomisation of participants to a specific position was used in eight (66.6%) papers[2-3, 19, 34, 65, 72, 128, 172]. The avoidance of contamination, three (25%) papers[2, 8, 172]; co-intervention, four (33.3%) papers[2-3, 8, 172]; and drop out, two (16.6%) papers[3, 172] were not reported. Blinding of investigators was found in two (16.6%) papers[19, 65].

***Study procedures***

Great variation was noted in the time periods used for adjustment before measurements were obtained as well as the time spent in the therapeutic position (Table 3.3). The time for adjustment before outcomes were measured varied between 0 minutes[8] and 12 hours[3, 172]. The time of therapeutic positioning varied between 1 minute[2] and up to 160 hours[128].

**Table 3.3: Time for adjustment and time of intervention up to June 2013**

| Study | | Position | Time before measurement | Time in position |
|---|---|---|---|---|
| **Effect of position** | Driscoll et al[2] | 0°; 45° | 5 min | 1 min |
| | Moraine et al[72] | 0°; 15°; 30°; 45° | 10 min | not stated |
| | Giuliano et al[8] | 0°; 30°; 45° | 0 min | 10 min |
| | Blissitt et al[10] | 0°; 20°; 45° | 2 min | 2-5 min |
| | Maas et al[17] | 30° | 2 min | not stated |
| | Gocze et al[34] | 0°; 30°; 45° | 3 min | 3 min |
| **Clinical outcome** | Torres et al[3] | 0°; 45° | 12 hrs | 12 hrs |
| | Orozco-Levi et al[172] | 0°; 45° | 12 hrs | 5 hrs |
| | Drakulovic et al[65] | 0°; 45° | not stated | 145 hrs |
| | Van Nieuwenhoven et al[19] | 0°; 45° | not stated | not stated |
| | Libby Keeley[128] | 25°; 45° | not stated | 160 hrs |
| | Caraviello et al[5] | Beach chair | not stated | 1 hr 4x daily |

**Legend:**
**Hrs/hr** = hours/hour; **(°) =** Degrees; **min** = minutes.

## 3.6.3 Description of the population

All papers reported on studies conducted in well developed countries with all resources available (Table 3.4). The majority of papers were conducted in Europe, eight (66.6%) papers[3, 17, 19, 34, 65, 72, 128, 172]. The sample sizes of the populations ranged from 12 participants[17] to 221 participants[19].

**Table 3.4: Characteristics of the population of semi-recumbent critically ill trials up to June 2013**

| Study | | Year | Location | n | Mean Age | M/F | Unit |
|---|---|---|---|---|---|---|---|
| Effect of position | Driscoll et al[2] | 1995 | Australia | 30 | 66.4 | 20/10 | not stated |
| | Moraine et al[72] | 2000 | Belgium | 37 | 52 | 22/15 | N |
| | Giuliano et al[8] | 2003 | USA | 26 | 58.2 | 15/11 | M T S |
| | Blissitt et al[10] | 2006 | USA | 20 | 50.25 | 5/15 | S |
| | Maas et al[17] | 2009 | Netherland | 12 | 64 | 10/2 | S |
| | Gocze et al[34] | 2013 | Germany | 200 | 60 | 131/69 | S |
| Clinical outcome | Torres et al[3] | 1992 | Spain | 19 | 66 | 13/6 | M |
| | Orozco-Levi et al[172] | 1995 | Spain | 15 | 56 | 11/4 | not stated |
| | Drakulovic et al[65] | 1999 | Spain | 86 | 65 | 65/21 | M |
| | Van Nieuwenhoven et al[19] | 2006 | Netherland | 221 | not stated | 140/81 | M |
| | Libby Keeley[128] | 2007 | UK | 132 | 66 | 115/17 | M |
| | Caraviello et al[5] | 2010 | USA | 152 | not stated | not stated | M S N |

**Legend:**
**M** = Medical unit; **N** = Neurology unit; **S** = Surgical unit; **T** = Trauma unit; **n =** number; **M/F** = Male/Female.

Data reported the effect of the semi-recumbent position on a total population of 950 participants. The mean age ranged between 50.25[10] and 66.4[2] years. Male participants were investigated more than female participants in 11 (91.6%) papers[2-3, 5, 8, 17, 19, 34, 65, 72, 128, 172]. One (8.3%) paper[10] investigated more female than male participants. Participants were ventilated in the medical critically ill unit in six (50%) papers[3, 5, 8, 19, 65, 128].

### 3.6.4 The effect of the semi-recumbent position

The effect of the semi-recumbent position was investigated including haemodynamic- and pulmonary parameters, cerebrovascular dynamics as well as the adverse effects during study procedures.

***Haemodynamic and pulmonary parameters***

Haemodynamic and pulmonary parameters have been reported to describe the effect of the specific position on the cardiac and pulmonary systems (Table 3.5). The haemodynamic parameters indicate if the haemodynamic status of the participant is not compromised. The effects of 0°, 30° and 45° semi-recumbent position on the haemodynamic parameters were investigated in four (33.3%) papers[2, 8, 17, 34].

**Table 3.5: Papers reporting haemodynamic parameters up to June 2013**

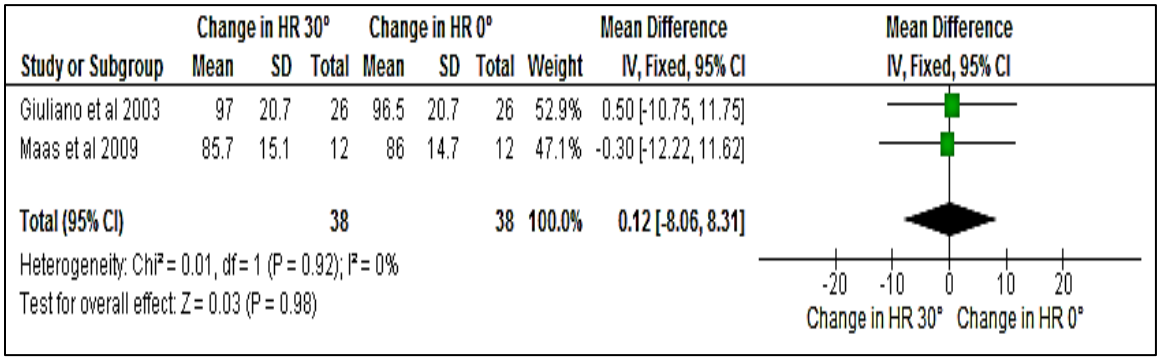
| Study | Type of Units | Position tested | Hemodynamic Parameters | | | | | | | | | | Pulmonary Parameters | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | CI | SV | CO | Pa | MAP | CVP | $ScvO_2$% | HR | CCI | Pmsf | PAP | PCWP |
| Driscoll et al[2] | not stated | 0°; 45° | | | ✓ | ✓ | | ✓ | | ✓ | | | ✓ | ✓ |
| Giuliano et al[8] | Medical, Surgical, Trauma | 0°;30°; 45° | ✓ | ✓ | ✓ | ✓ | ✓ | | | ✓ | ✓ | | | |
| Maas et al[17] | Surgical | 0°; 30° | | | ✓ | ✓ | ✓ | ✓ | | ✓ | | ✓ | | |
| Gocze et al[34] | Surgical | 0°; 30°; 45° | | | | ✓ | ✓ | | ✓ | | | | | |

**Legend**:
**CI** = Cardiac Index; **SV =** Stroke Volume; **CO** = Cardiac Output; **Pa** = Arterial pressure; **MAP** = Mean arterial pressure; **CVP** = Central Venous Pressure; **$ScvO_2$%** = Percentage Central Venous Oxygen saturation; **HR** = Heart Rate; **CCI** = Continuous cardiac index ; **Pmsf** = Mean systemic filling pressure**; PAP** = Pulmonary artery pressure**; PCWP = P**ulmonary wedge pressure; ✓ = parameter used**; (°) =** Degrees; **Blank** = not reported.

A total of nine different measures were used to report the haemodynamic parameters of participants. Arterial pressures were reported in four (33.3%) papers[2, 8, 17, 34]. The HR[2, 8, 17], MAP[8, 17, 34], central venous pressure (CVP)[2, 17] and CO[2, 8, 17] were measured in three (25%) papers each. The MAP and HR were reported together in one (8.3%) paper[8]. The $ScvO_2$%[34], SV[8], continuous cardiac index (CCI)[8] and cardiac index (CI)[8] were each reported in one (8.3%) paper. Two pulmonary parameters, the pulmonary wedge pressure (PCWP) and the pulmonary artery pressure (PAP), were investigated in one (8.3%) paper[2]. The surgical units were used in three (25%) papers[8, 17, 34].

***Heart rate***

Data from two (16.6%) papers[8, 17] were comparable and could be pooled into a forest plot (Figure 3.2). When comparing the effect of the 30° semi-recumbent position and the 0° semi-recumbent position on the HR of 38 participants, the pooled effect showed no significant difference in the HR between the two groups [Weighted mean difference (WMD) 0.12, 95% CI -8.06, 8.31].



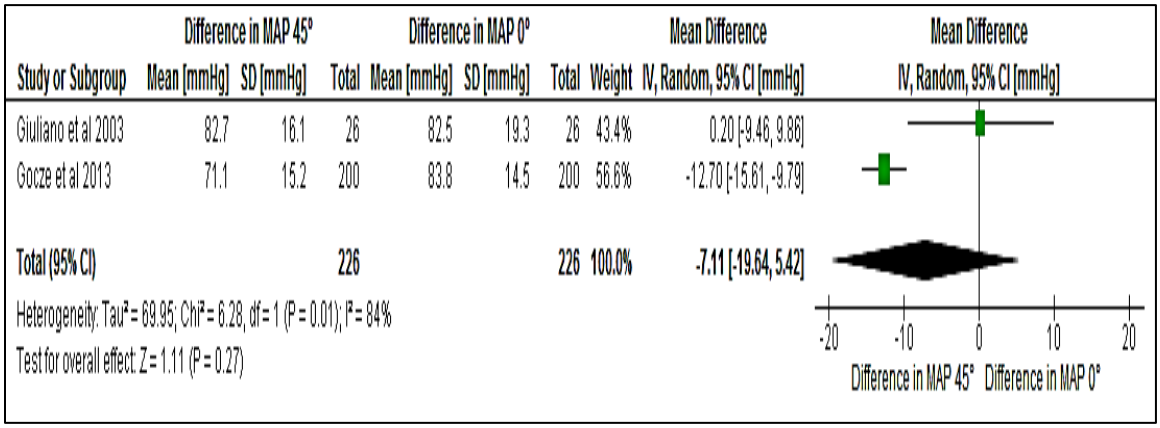

**Legend:**
**HR** = Heart rate; **SD =** Standard deviation; **CI** = Confidence interval; **30° =** 30° semi-recumbent position; **0° =** 0° semi-recumbent position.

**Figure 3.2: Forest plot reporting the effect of 30° position on the HR**

This indicates that the change in position had no effect on the HR which remained stable within the normal range of 60 to 120 beats per minute (bpm). The heterogeneity was $I^2$=0% with a p-value of p=0.92 which indicated that the papers were similar. However, the internal validity differed between the two papers scoring 13 (65%)[8] and 15 (75%)[17] respectively (Addendum H). The characteristics of the populations differed including the amount of male versus female participants and the type of population (Table 3.4). The inclusion and exclusion criteria of the papers also differed (Addendum J & Addendum K). Maas et al[17] included coronary heart disease participants while Giuliano et al[8] included participants with a continuous cardiac output (CCO) catheter in place. The sample sizes were not justified and dropouts were not reported in one (8.3%) papers[17].

***MAP***

Two (16.6%) papers[8, 34] reported on the MAP and the 45° semi-recumbent position and data were compared (Figure 3.3). A decrease in the MAP (WMD -7.11; 95%CI -19.64, 5.42)) could be expected if placing a participant into the 45° semi-recumbent position from the 0° semi-recumbent position which stayed within the normal range of above 65mmHg[34]. But the pooled effect indicates that placing a participant in the 45° semi-recumbent position has no significant effect on the MAP. The heterogeneity was $I^2$=84% with a p-value of p=0.01 which indicated that the papers were different. The internal validity differed, scoring 16 (80%)[34] and 13 (65%)[8] respectively (Addendum H).

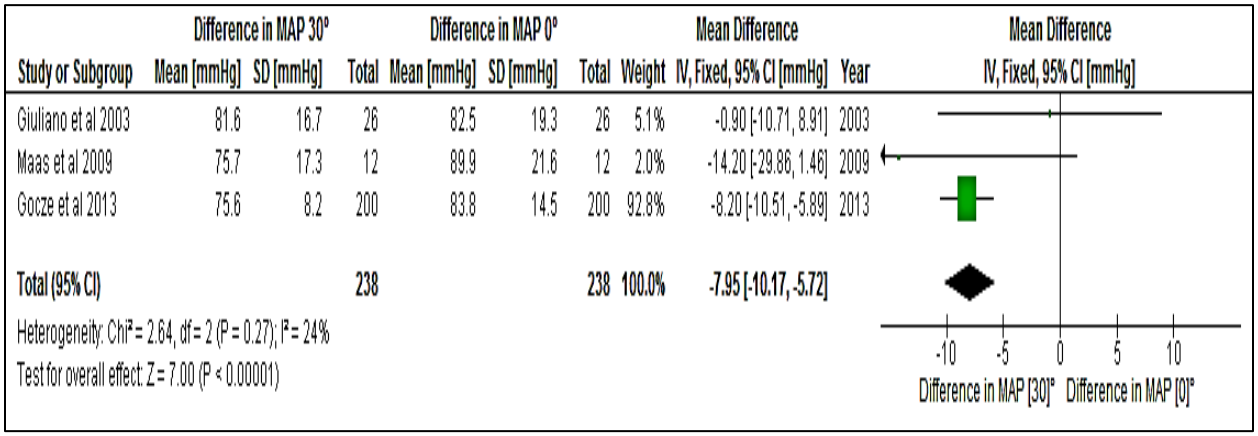



**Legend:**
**MAP** = Mean arterial pressure; **SD =** Standard deviation; **CI** = Confidence interval; **45° =** 45° semi-recumbent position; **0° =** 0° semi-recumbent position.

**Figure 3.3: Forest plot reporting the effect of 45° position on the MAP**

The population differed regarding the type and the amount of male versus female participants (Table 3.4). Participants were recruited from the medical, trauma and surgical units in Guiliano et al[8] paper while Gocze et al[34] recruited participants from the surgical unit. Gocze et al[34] reported on 131 (65.5%) male participants and 69 (34.5%) female participants while Giuliano et al[8] reported on 15 (57.7%) male participants and 11 (42.3%) female participants. A sample of convenience was used in both papers[8, 34] but one (8.3%) paper[34] used randomisation of participants to a position. The inclusion and exclusion criteria also differed between the papers (Addendum J & Addendum K).

Data of three (25%) papers[8, 17, 34] were comparable reporting on the MAP and the 30° semi-recumbent position (Figure 3.4). The pooled effect showed a significant effect on the MAP in the 30° semi-recumbent group (WMD -7.95mmHg, 95%CI -10.17mmHg, -5.72mmHg) with a heterogeneity of $I^2$=24% and p-value of p=0.27. This indicates that a decrease in MAP can be expected when placing a participant into the 30° semi-recumbent from the 0° semi-recumbent position. The internal validity differed, scoring 13 (65%)[8], 15 (75%)[17] and 16 (80%)[34] respectively (Addendum H).




**Legend:**
**MAP** = Mean arterial pressure; **SD =** Standard deviation; **CI** = Confidence interval; **30° =** 30° semi-recumbent position; **0° =** 0° semi-recumbent position.

**Figure 3.4: Forest lot reporting the effect of 30° semi-recumbent position on the MAP**

The type of population and the number of males versus females differed (Table 3.4). Variations were also found between the three (25%) papers[8, 17, 34] inclusion criteria (Addendum J) as well as the exclusion criteria (Addendum K). Maas et al[17] investigated participants after elective bypass surgery or valve replacement while Giuliano et al[8] and Gocze et al[34] investigated participants with a specific haemodynamic stability status.

***Cerebrovascular dynamics***

Our search terms revealed two (16.6%) papers[10, 72] exploring the cerebrovascular dynamics of different semi-recumbent positions (Table 3.6). Both papers investigated the effect of the 0° semi-recumbent position as well as the 45° semi-recumbent position combined with one or two other positions on a critically ill population with head injuries.

The mean flow velocity in the middle cerebral artery and the internal carotid artery were measured to investigate if a mild to moderate vasospasm occurred after an aneurysmal subarachnoid haemorrhage occurred in the brain. The participants were placed in the $0^0$, $15^0$, 30° and $45^0$ semi-recumbent positions.

**Table 3.6: Papers reporting cerebrovascular dynamics up to June 2013**

| Paper | Year | Position | MFV (bilateral) | CPP | CBF | ICP | Blood gas |
|---|---|---|---|---|---|---|---|
| Moraine et al[72] | 2000 | 0°; 15°; 30°; 45° | ✓ | ✓ | ✓ | ✓ | ✓ |
| Blissitt et al[10] | 2006 | 0°;20°;45° | | | ✓ | ✓ | ✓ |

**Legend:**
**CPP** = Cerebral perfusion pressure; **CBF** = Cerebral blood flow; **ICP** = intra-cranial pressure;
**MFV** = Mean flow velocity in the middle cerebral artery and internal carotid artery; ✓= Parameter used;
**Blank** = parameter not reported.

Cerebral perfusion pressure (CPP)[10, 72], cerebral blood flow (CBF)[10, 72], intra-cranial pressure (ICP)[10, 72] and blood gases were reported. Only one (8.3%) paper[10] was found in this review reporting the mean flow velocity in the middle cerebral artery and the internal carotid artery.

***Adverse effects***

Adverse events were reported in six (50%) papers[5, 8, 10, 17, 34, 65] (Table 3.7). Four (33.3%) papers[8, 10, 17, 65] reported no changes in the haemodynamic status or no adverse events. This was seen as a positive event.

Two (16.6%) papers[5, 34] reported negative adverse events including two severe events of hypotension which required volume and inotropic support[34] and indicated intolerance to the beach chair position[5]. These were seen as negative events. However, most of the papers have small sample sizes and were not powered to detect adverse events.

**Table 3.7: Adverse events reported Yes/No (✓/X) and type of event up to June 2013**

| Study | | Reported Yes=✓/No = X | (+/-) event | Description ofAdverse event |
|---|---|---|---|---|
| Effect of position | Driscoll et al[2] | X | | |
| | Moraine et al[72] | X | | |
| | Giuliano et al[8] | ✓ | (+) | No changes in MAP or CCO. |
| | Blissitt et al[10] | ✓ | (+) | Stop of study never evoked; no neurological changes. |
| | Maas et al[17] | ✓ | (+) | Haemodynamic stable with no change in vasoative drug. |
| | Gocze et al[34] | ✓ | (-) | 2 severe hypotention required volume & inotropic support. |
| Clinical outcome | Torres et al[3] | X | | |
| | Orozco-Levi et al[172] | X | | |
| | Drakulovic et al[65] | ✓ | (+) | No adverse events. |
| | Van Nieuwenhoven et al[19] | X | | |
| | Libby Keeley[128] | X | | |
| | Caraviello et al[5] | ✓ | (-) | 4.8% did not tolerate position: 36%cardiovascular events(tachycardia, hypertension and hypotension), 21% neurological events and 8% respiratory events. |

**Legend**:
**MAP** = Mean arterial pressure; **CCO** = Continuous Cardiac Output; **(+)** = Positive event;
**(-)** = Negative event; **Blank =** not reported.

### 3.6.5 Clinical outcome of the semi-recumbent position

Over the years the clinical outcome of participants has been investigated including the influence of the semi-recumbent position on the development of VAP and the possibility of aspiration during semi-recumbent positioning.

***VAP***

Four (33.3%) papers[5, 19, 65, 128] reported on the frequency of nosocomial pneumonia of ventilated critically ill adult participants including the odds ratios (Table 3.8). Microbiological confirmation and clinical suspicion of VAP were reported in three (25%) papers[19, 65, 128]. One (8.3%) paper[5] reported only the odds ratio as a result. A variety of other tests were performed during the procedures of papers including gastric retention, the development of pressure sores, the average back rest elevation, tolerance for the position, the type of nasogastric feed and the MAP (Table 3.9).

**Table 3.8: Summary of the effect of the semi-recumbent position on VAP up to June 2013**

| Study | Position | Suspected VAP (%) | Odds ratio (95%CI) | Microbiologically confirmed VAP(%) | Odds ratio (95% CI) | Incidence of VAP |
|---|---|---|---|---|---|---|
| Drakulovic et al[65] | 0° | n=16 (34%) | 0.1615(0.043-0.6064) | n=11 (23%) | 0.1762 (0.0366-0.8546) | 41·2 / 1000 ventilator days |
| | 45° | n=3 (18%) | | n=2 (5%) | | 10·9 / 1000 ventilator days |
| Van Nieuwenhoven et al[19] | 0° | n= 20 (14.3%) | 0.74(0.36-1.52) | n= 8 (7.3%) | 1.6578 (0.6585-4.1739) | 7.8/1000 days |
| | 45° | n=16 (18.3%) | | n=13 (11.6%) | | 10.2/1000 ventilator days |
| Libby Keeley[128] | 25° | n= 2 (15%) | 0.41(0.035-4.82) | n=7 (54%) | 0.64 (0.1516-2.7) | |
| | 45° | n=1 (6%) | | n=5 (29%) | | |
| Caraviello et al[5] | 70° HOB & -75°Knee flexion | | | | 0.321(not reported) | |

**Legend**:
**cpm** = count per minute; **HOB** = Head of bed; **CI** = Confidence Interval; **n** = number; **Blank =** not reported.

Two (16.6%) papers[65, 128] reported a lesser amount of microbiologically confirmed VAP in the 45° semi-recumbent position (Table 3.8). Van Niewenhoven et al[19] found a lower incidence of VAP in the 0° semi-recumbent position than in the 45° semi-recumbent position which contradicted the findings of two (16.6%) papers[65, 128].

An odds ratio value smaller than one, for the microbiologically confirmed VAP, favoured the 45° semi-recumbent position in two papers[65,128] and indicates that the risk of developing VAP is smaller in the 45° semi-recumbent position (Table 3.8). However, Keeley[128] compared the 45° semi-recumbent position with the 25° semi-recumbent position and found four (29%) participants diagnosed with microbiologically confirmed VAP in the 45° semi-recumbent position and seven (54%) participants diagnosed with VAP in the 25° semi-recumbent position. Van Nieuwenhoven et al[19] found a lower risk of developing VAP in the 0° semi-recumbent position. One paper's[5] odds ratio of smaller than one, favoured the beach chair position and

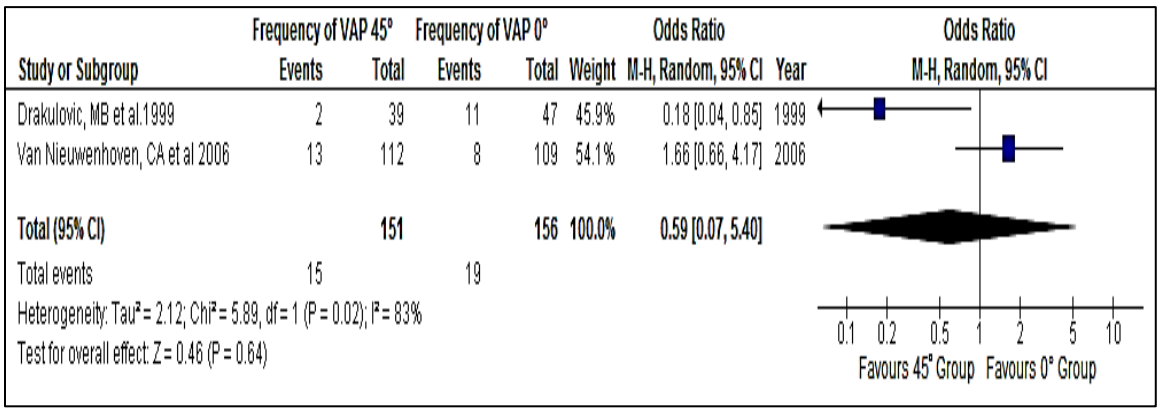
indicates that the risk is lower to develop VAP. The criteria used for clinical suspicion and microbiological confirmation of VAP are summarised in Table 3.9.

**Table 3.9: Summary of the parameters used to investigate the effect of the semi-recumbent position on VAP up to June 2013**

| Study | Position | Criteria for clinically suspicion | Criteria for microbiologically confirmation | Other tests |
|---|---|---|---|---|
| Drakulovic et al[65] | 0°,45° | • Y,<br>• WBC;<br>• Temp.;<br>• X-rays;<br>• Purulent tracheal secretions. | • Y, one pathogenic micro-organism isolation<br>• Tracheobronchial aspirate,<br>• Broncho alveolar lavage,<br>• (+) blood cultures or pleural fluids. | • Gastric retention;<br>• Development of pressure sores. |
| Van Nieuwenhoven et al[19] | 0°, 45° | • Y,<br>• WBC;<br>• Temp.<br>• X-rays<br>• (+) cultures tracheal aspirate | • Y,<br>• (+) blood cultures; or<br>• (+) Cultures of bronchial lavage≥$10^4$. | • Average BRE day 1;<br>• Average BRE day7. |
| Libby Keeley[128] | 25°,45° | • Y,<br>• WBC;<br>• Temp.;<br>• X-rays;<br>• Lab confirmed; | • Y, one pathogenic micro-organism isolation:<br>• Tracheobronchial aspirate,<br>• Broncho alveolar lavage, or<br>• (+) blood cultures or pleural fluids. | • Endotracheal tube;<br>• (+) NG feed;<br>• MAP;<br>• Pressure areas |
| Caraviello et al[5] | 70° BRE & -75° knee bend | •N | •Rate of VAP reported | • Tolerance of position. |

**Legend:**
**VAP =** Ventilator associated pneumonia; **WBC =** White blood cell count; **MAP =** Mean Arterial Pressure; **BRE**= Back rest elevation; **(+)** = positive; **Temp.** = Temperature; **Lab** = Laboratory; **NG** = Nasogastric; **(°) =** Degrees; **Blank** = not reported.

Data of two (16.6%) papers[19, 65] were comparable and could be pooled in a forest plot (Figure 3.5). When comparing the frequency of VAP in the 45° semi-recumbent position with 152 participants with the frequency of VAP in the 0° semi-recumbent with a total of 156 participants, the pooled effect indicated that none of the two positions are favoured (Odds ratio = 0.59; 95% CI of 0.07 to 5.40).




**Legend:**
**SD =** Standard deviation; **CI** = Confidence interval; **45°** = 45° semi-recumbent position; **0°** = 0° semi-recumbent position.

**Figure 3.5: Forest plot reporting the frequency of VAP**

This indicates that a participant's risk of developing VAP in the 45° semi-recumbent position is the same than in the 0° semi-recumbent position. The heterogeneity of $I^2$=83% with a p-value of p=0.02 indicates that the two papers[19,65] were different. The internal validity differed scoring 18 (90%)[19] and 19 (95%) [65] (Addendum H). Differences were the number of male versus female participants (Table 3.4) and the criteria for diagnosis of clinically suspected or microbiological confirmation of VAP (Table 2.10). The inclusion criteria only differed regarding the time of intubation[19, 65] (Addendum J) and the exclusion criteria differed regarding the pulmonary[65] and neurological[65] exclusion criteria as well as any change in the position[65] (Addendum K). Only the diagnosis of VAP and non-randomisation were used in one (8.3%)[19] paper. Both papers used blinded randomisation of participants to the testing position but Van Niewenhoven et al[19] did not report the adverse events of the position tested.

***Aspiration***

Two (16.6%) papers[3, 172] investigating the 0° and 45° semi-recumbent position, measured the radio-isotopic count (RAc) after an amount of isotopes were instilled via the nasogastric tube (Table 3.10). Investigating the amount of gastro-oesophageal reflux (GER) in participants with a nasogastric tube during mechanical ventilation was the main purpose of these two (16.6%) papers[3, 172]. Orozco-Levi et al[172] obtained samples of the RAc and the microbiological cultures at baseline as well as during the study procedures from the gastric, pharyngeal, bronchial and blood samples, while Torres et al[3] obtained the samples of RAc from the endo-bronchial aspirate and the microbiological cultures isolation from the stomach, trachea and pharynx. A summary of the

parameters used to investigate the effect of a semi-recumbent position on aspiration is given in Table 3.10.

**Table 3.10: Summary of parameters used to investigate the effect of the semi-recumbent position on aspiration up to June 2013**

| Study | Position | Mean RAc of endotracheal secretions | Mean RaC in blood | Mean RAc in gastric content | Microorganism isolated | Other tests |
|---|---|---|---|---|---|---|
| Torres et al[3] | 0°, 45° | Y | | | Y | Cuff pressure of ET tube and pH. |
| Orozco-Levi et al[172] | 0°, 45° | Y | Y | Y | Y | Cuff pressure of ET tube. |

**Legend**:
RAc = Radio-activity count; **(°) =** Degrees; **ET** = Endotracheal tube; **pH** = Acidity; **Y** = Yes; **Blank** = Not reported.

Torres et al[3] and Orozco-Levi et al[172] found a lower radioactivity count and a lower count of micro-organism isolation in the 45° semi-recumbent position. A summary of the results found is given in Table 3.11.

**Table 3.11: Summary of the results of papers reporting the effect of position on aspiration up to June 2013**

| Study | Micro-organisms isolated | | Radioactivity count | |
|---|---|---|---|---|
| | 0° | 45° | 0° | 45° |
| Torres et al[3] | Isolated in n=13 (68%) pts in all 3 sites (gastric juice, endobronchial secretions, pharyngeal specimens) | Isolated in n=6 (32%) pts in all 3 sites (gastric juice, endobronchial secretions, pharyngeal specimens) | 4154 ± 1959 cpm | 954 ± 217 cpm |
| Orozco-Levi et al[172] | | Colonization from stomach to pharynx in n=6 pts (n=4, first studied in 0° then 45°) | In bronchial secretions significantly higher; 2.54 ± 0.49cpm | Values from pharynx significantly lower; 1.66 ± 0.45 cpm (from 3 hrs to 5 hrs) |

**Legend**:
**(°) =** Degrees; **pts =** patients; **cpm** = count per minute; **n** = number of participants; **GER** = Gastroesophageal reflux; **Blank =** not reported; **hrs** = Hours.

## 3.7 Discussion

A range of different semi-recumbent positions testing a variety of different outcomes was found. Therefore, the following aspects of the body of evidence are discussed.

### 3.7.1 The semi-recumbent position

This review describes the existing body of evidence of the therapeutic, semi-recumbent position which investigated a wide variety of different semi-recumbent positions with some similarity in the testing procedures as well as the evaluation of the therapeutic application of the semi-recumbent position.

The majority of papers investigating the semi-recumbent position described mainly the effect of the position on major organ systems and the prevention of VAP and aspiration. None of the literature reviewed investigated the possibility of using the semi-recumbent position as an early mobility intervention during the early stages of critical illness. Therefore, the effect of mobilisation on a critically ill patient during the early stages of critical illness is questionable. Is it the semi-recumbent position itself or the physical activity of sitting in the position on the awakened patient that has an effect on the organ systems? No specific guidelines could be compiled for the use of the semi-recumbent positioning in the management of a critically ill patient as a therapeutic early mobility position. This indicates that unanswered questions still exist regarding the therapeutic use of the semi-recumbent position and that researchers are not yet satisfied with the positive or negative effect of the semi-recumbent position.

The quality of papers and internal validity were inconsistent and future papers should ensure that all relevant outcomes are reported, like the adverse events during positioning as this is a good indicator if the position is tolerated. However, most of the papers were not powered to detect adverse events for safety. Blinding of measurers was also a shortcoming in papers reviewed and future papers need to blind measurers to prevent performance and detection bias.

Inconsistencies were found in the time before measurements were obtained in the semi-recumbent position, thus the time needed for adjustment was unclear. The time spent in a specific testing position was also not reported. Is the outcome a true result of the intervention or are there other factors that may have caused that specific outcome? We found it difficult to compare the results of these papers and this also created uncertainty on how to interpret the

results. Therefore no analysis could be made for future use in clinical practice. This review recommends that future studies need to report the exact duration of adjustment before measurements of parameters are obtained as well as the time spent in the specific position.

The population of critically ill patients in this review were predominately elderly, male participants, mostly admitted to the medical critically ill units. Therefore, studies need to include younger participants as well as more female participants to investigate possible age and gender specific differences in the testing population. The neurological units have been poorly investigated and need further investigation for more population specific guidelines for the use of the semi-recumbent position. Recommendation for future studies investigating therapeutic positioning is to report the type of unit as this describes the characteristics of a specific population of critically ill patients and their co-morbidities. The literature reviewed was located in countries in the northern hemisphere with only one paper published in a country located in the southern hemisphere. This indicates that a need exists for more research in southern hemisphere countries.

### 3.7.2 The effect of the semi-recumbent position

The papers in this review can be categorised into two major areas of investigation namely the effect of the semi-recumbent position and the influence of the semi-recumbent position on the clinical outcome of participants. Haemodynamic and pulmonary parameters, cerebrovascular dynamics and adverse events described the effect of the semi-recumbent position while the development of VAP and the possibility of aspiration during semi-recumbent positioning described the clinical outcome of participants.

***Haemodynamic stability***

Haemodynamic stability forms part of physiological stability which includes an adequate cardiovascular and respiratory reserve as described by Stiller et al[35] and Hanekom et al[36]. Haemodynamic stability refers to adequate blood flow to the organ systems[35-36]. The cardiovascular reserve is measured by the MAP which is a good approximation for adequate organ perfusion according to Pinsky and Payen[11]. The monitoring of haemodynamic stability currently includes the measurement of HR, arterial pressures, cardiac filling pressures or volumes and the percentage of mixed venous oxygen saturation ($SvO_2$%) according to Pinsky and Payen[11] and Vincent et al[13]. The measurement of haemodynamic stability is complex and

future research should use the principles of Vincent et al[13] as guidelines for the measurement of haemodynamic stability when investigating the effect of a semi-recumbent position on the haemodynamic stability. The measurement of multiple variables and their interaction also quantify if the position is effective or not[13].

This review concluded that the change in position from the 0° semi-recumbent to the 30° semi-recumbent position did not have an effect on the HR, but only two papers[8, 17] published the results of the heart rate with differences in internal validity and the characteristics of the population. Thus, the HR alone is not a good indicator of haemodynamic stability and other haemodynamic parameters should be considered together to form a good understanding of the haemodynamic stability.

The results of the papers investigated indicated that the effect of the semi-recumbent position on the MAP is questionable. The measurement of the MAP is considered to be the gold standard as recommended at the International Consensus Conference, Paris, France, April 2006[13]. The tests performed by Lehman et al[173] confirmed that the MAP is a consistent metric measure for monitoring blood pressure in the intensive care units and is independent of the measurement modality by comparing the invasive arterial blood pressure measurements with non-invasive blood pressure measurements. The results of the tests which Lehman et al[173] performed showed agreement between these two methods of blood pressure measurement in the ICU. Therefore the MAP as an outcome measure can be regarded as valid and is easily accessible in a clinical setting.

However, the 20$^0$ to 30$^0$ semi-recumbent position was recommended by Gocze et al[34] as a haemodynamic stable position but the 45° semi-recumbent position was found by Gocze et al[34] to be an unstable position during the early onset of critical illness in sedated patients but the findings of MAP in the study of Gocze et al[34] were still within normal ranges (MAP > 65mmHg). This finding was based on results of the MAP obtained after a period of three minutes in the specific position and opposes the recommendation of 30° to 45° semi-recumbent position of the CDCP[1]. However, a study conducted by Giuliano et al[8] reported no decrease in the MAP after 10 minutes in each position (0°, 30° and 45° semi-recumbent positions)[8]. Both Gocze et al[34] and Giuliano et al[8] evaluated the correctness of the arterial catheter measurements. This indicates

that additional work is needed to clarify the effect of the 45° semi-recumbent position on the MAP for a period longer than three minutes.

Only one paper[34] was found which investigated the $ScvO_2$%. The measurement of the $ScvO_2$% is seen as a good reflection of the interaction between the oxygen delivery ($DO_2$) and the oxygen consumption ($VO_2$) of the body[13]. The following equation explains the interaction: $DO_2 = CO \times CaO_2$ [(Hb x Sat/100 x 1.34) + ($PaO_2$ x 0.0031)][181]. Active mobilisation into the semi-recumbent position maybe increases the activity of a patient and thus maybe increases the oxygen consumption of the body. Oxygen delivery ($DO_2$), maybe compromised by any haemodynamic changes[34]. Therefore, the preload is likely to decrease in the semi-recumbent position[181]. The contractility of the heart should be unchanged unless myocardial ischemia or arrhythmia is introduced. The afterload can decrease or increase. The HR is likely to increase during initial activity but may return towards the baseline afterwards, unless orthostatic hypotension is associated with a sustained tachycardia. The $ScvO_2$% thus reflects the complex cardiorespiratory interaction. There is a good correlation between the mixed venous oxygen saturation ($SvO_2$) and the central venous oxygen saturation ($ScvO_2$)[13]. It has been proposed as a good surrogate for the $SvO_2$ although $ScvO_2$ represents only an approximation of the $SvO_2$[13].

This review recommends that future papers investigate the MAP and the $ScvO_2$%, together with their dynamic interaction in response to time, in order to quantify whether a therapeutic position is effective or not as Vincent et al[13] stated. The need exists to investigate the oxygen consumption during mobilisation into the semi-recumbent position which is likely to increase the activity of a patient. Therefore, to use the 45° semi-recumbent position as a therapeutic early mobility position needs further investigation.

***Cerebrovascular dynamics***

Cerebrovascular dynamics are determined by complex factors including the auto regulation system of the body, ICP, CPP and vasospasm[10]. The paired middle cerebral artery arises from the internal carotid artery and it supplies the cerebrum with blood[10]. Vasospasm in these arteries is monitored by the mean velocity blood flow measured with a transcranial Doppler to detect elevated blood velocity which indicates cerebral vasospasm[174].

The literature reviewed indicated that the influence of a 45° semi-recumbent position on the cerebrovascular dynamics was similar regarding the ICP in different populations[10,72]. Morraine et al[72] investigated comatose participants while Blissitt et al[10] investigated surgical participants with mild to moderate vasospasm after aneurysmal subarachnoid haemorrhage and with coils placed in the aneurysmal sac. However, Morraine et al[72] found a decrease in the cerebral blood flow and CPP when placing a participant from the 30° semi-recumbent position to the 45° semi-recumbent position which could be a possible danger to comatose patients. Therefore, future research is needed to clarify the influence of position on the CPP and cerebral blood flow in different population groups.

***Adverse events***

Adverse events were not reported well in the literature reviewed. The small sample sizes of the papers included indicate that the studies were not powered to detect adverse events. Therefore the safety of the semi-recumbent position cannot be evaluated by the presence or absence of an adverse event and can only be an indication if a position is tolerated. Out of the six papers[5,8,10,17,34,65] reporting the adverse events, four papers[8,10,17,65] reported adverse events as positive events which encourage the use of the semi-recumbent position in clinical practice. However, two severe events of hypotension were reported by Gocze et al[34] which required volume and inotropic support during their study as well as intolerance to the position. Reporting of adverse events needs a bigger priority during the positioning of participants. The time of an adverse event, duration, action taken, the time of recovery and abortion of study procedures needs to be reported and will give better guidelines for clinical practice.

***VAP***

The routine use of the 45° semi-recumbent position is recommend for the beneficial effects it has on the prevention of VAP as recommended by the CDCP[1]. This recommendation is not supported by the pooled effect of two papers[19,65]. The heterogeneity test was significant (p=0.02) and indicates that these two papers were different. Therefore, uncertainties existed regarding the feasibility and the routine use of the 45° semi-recumbent position. The influence of this position on pressure areas is still unclear and further investigation is needed regarding the placement in this position to prevent the possible development of pressure ulcers[19].

Another position, the beach chair position, has been investigated by Caraviello et al[5]. This position was safely used and required fewer personnel to be present during the positioning, although special beds were needed to place patients in this position. Caraviello et al[5] found a lower rate of VAP when comparing the beach chair group to a historical comparison group. The beach chair position may be a possible intervention to prepare a patient for sitting on the edge of the bed, but the influence of this position on a critically ill patient is still unknown and needs to be further investigated.

The mean degree of elevation is found to be lower than the recommended degree of the semi-recumbent position[19,34]. Possible reasons for not reaching the 45° semi-recumbent position were the severity of illness[19] and the discomfort of the position[19, 128]. Literature reviewed indicated that uncertainties still surround the use of the 45° semi-recumbent position, its effect on the frequency of VAP and the feasibility and the effect of the position.

***Aspiration***

Metheney et al[175] found that a lower back rest elevation (back rest elevation of ≥ 30° semi-recumbent position) was a risk for aspiration of gastric content. This finding is supported by the results of Torres et al[3] and Orozco-Levi et al[175] which found a lower radio-activity count in the 45° semi-recumbent position. However, a systematic review of Metheney et al[175] reported that the optimal position for elevation to prevent the critically ill from aspiration is still unknown. This indicates that a need exists for future research to investigate aspiration and pressure ulcers as an outcome in different semi-recumbent positions, as recommended by Metheney et al[175].

## 3.8 Limitations

Limitations of this review were the variable methodological quality of papers included as well as the difference in study design and internal validity. The diverse range of study sample sizes as well as the diverse range of interventions used made the pooling of results difficult for statistical analysis. Strengths of this literature review were that it included all the papers published from inception till June 2013. No search strategies were performed after this date. The researcher (EC) acknowledged that the review will need to be updated and the search strategies will be performed again and any new evidence will be included in the manuscript. Additional strengths are that all papers with relevant semi-recumbent positions used in the critical care environment were

included as well as two researchers independently searched three data bases each. Moreover, this review investigated a wide and diverse body of research evidence.

## 3.9 Conclusion

The methodology of this review was aimed at answering the questions about the therapeutic use of positions in an adult critically ill population. Uncertainty still surrounds the haemodynamic stability of the 45° semi-recumbent position[34] and a patient's inability to maintain this position[19, 39, 176-177]. These are all factors which could affect the feasibility of this nursing position as a therapeutic early mobility position. A longer period in the 45° semi-recumbent position is needed to evaluate the dynamic interaction of variables, like the MAP and $ScvO_2$%, to quantify the effectiveness of the position as a therapeutic intervention.

## 3.10 Take Home Message

- Although the 45° semi-recumbent position is recommended by the CDCP[1] for the prevention of VAP, the pooled results of two papers[19,65] indicate that the patient position might not affect the development of VAP in all patient populations. Further work is needed to identify the patients who would most benefit from upright positioning.
- Neurological units were the least investigated.
- The haemodynamic stability is complex and nine different measures were used to report haemodynamic stability of participants including the CI[8], SV[8], CO[2, 8, 17], Pa[2, 8, 17, 34], MAP[8, 17, 34], CVP[2, 17], $ScvO_2$%[34], HR[2, 8, 17], CCI[8], and the Pmsf[17]. The $ScvO_2$% was used only once, in a study conducted by Gocze et al[34]. The measurement of $ScvO_2$% determines adequate tissue oxygenation and is a good reflection of the interaction between the oxygen delivery ($DO_2$) and the oxygen consumption ($VO_2$).
- The HR remained stable during the placement of participants from the 0° semi-recumbent position to 30° semi-recumbent position.
- The MAP decreased during the placement of participants from the 0° semi-recumbent position to the 30° semi-recumbent position and the 45° semi-recumbent position but did not drop below 65 mmHg[34] which indicated that a good perfusion of organ systems was sustained. However, the time spent in the 45° semi-recumbent position was short and the effect of the position on the MAP after three minutes needs further investigation. The

dynamic interaction of this variable, the MAP, in response to time is important to quantify whether or not a therapeutic position is effective.

- Reporting of adverse events needs to be prioritised during the positioning of participants. Only two severe incidents of hypotension and intolerance of position were reported. The time of the adverse events, duration, action taken, the time of recovery and abortion of study procedures needs to be reported. Future studies need bigger sample sizes with enough power to detect adverse events.

# Chapter 4: Primary Research Study

**This chapter will be prepared as a manuscript for submission to Critical Care, a journal of BMC (Addendum B) under the title "A Pilot study: The effect of a therapeutic early mobility position on haemodynamic parameters, the MAP and the $ScvO_2$% ."**

## 4.1 Introduction

Early mobility has been described as a goal-directed therapeutic intervention[21] with the aim of preventing the detrimental effects of bed rest through various activities. Activities consist of active limb exercises, the patient actively moving or turning in bed, sitting in bed, on the edge of the bed, out of bed in a chair, standing and walking[23, 27, 41]. These activities are included in the awakening and breathing coordination, delirium monitoring and management, and early mobility (ABCDE) protocol[25] as early mobility and exercises. Protocols[12, 23, 36-38] have been developed to initiate early mobility and ensure the feasible and safe intervention of early mobility.

The following advantages of early mobility have been proposed: the possibility of improving ICU acquired weakness[27-30]; decreased unit and hospital length of stay[27]; and improvement in ICU associated delirium[25-26]. However, utilising early mobility as a therapeutic intervention has known barriers. These barriers can be seen as patient or staff specific barriers. Patient specific barriers include haemodynamic instability[33-34], falls[22] and inability to reach the specific goal-directed position[19, 34, 39]. Physiotherapy staff specific barriers have not been investigated but could include the possibility of being labour intensive and an increased burden of injury[44].

The therapeutic use of positioning in the critically ill population has been investigated. Positions include proning for the management of ARDS[178], while a 30° to 45° semi-recumbent position is recommended to prevent aspiration[1]. While protocols[12, 23, 35-38] have been developed to facilitate early mobility of awakened patients, work still needs to be done on ensuring that unconscious patients are being positioned optimally. The 45° semi-recumbent position has been described as a positional intervention in various papers[12, 23, 27, 36]. The position can prevent aspiration[3, 172] and can be utilised to prevent the detrimental effects of bed rest. However, various papers[19, 34, 39] have reported that the 30° to 45° semi-recumbent position is not reached in clinical practice, although it is being recommended by the CDCP as an intervention for patients at high risk of aspiration

pneumonia[1]. Uncertainties still surround the haemodynamic stability[33-34] of the 45° semi-recumbent position and the patient's inability to maintain the position[19, 34, 39, 179].

The primary aim of this study was to identify patients, with an adapted early mobility readiness protocol, who could tolerate the therapeutic early mobility position[a]. We measured the effect of a therapeutic early mobility position on two haemodynamic parameters including: 1) The MAP and; 2) The oxygen consumption via the $ScvO_2$%. The secondary aim was to describe the current nursing positions used in the units and to describe any adverse events in the therapeutic early mobility position. The preliminary results will inform the planning of a larger study.

## 4.2 Materials and Methods

### 4.2.1 Study design

A non-randomised experimental design (Addendum L).

### 4.2.2 Ethical consideration

Ethical permission was granted by the Institutional Health Research Ethics Committee (Ethics no: S13/10/194) and the chief executive officer of the tertiary teaching hospital in accordance with the Provincial Research Policy and tertiary teaching hospital notice No 40/2009 (Addendum M).

Informed consent was obtained from the participants themselves retrospectively, next of kin or an appropriate surrogate if the participant's next of kin was unreachable (Addendum N).

### 4.2.3 Research setting

A tertiary teaching hospital in the Cape Metropole, Western Cape, South Africa.

[a] The 45° semi-recumbent position has been adapted to a position called the therapeutic early mobility position which is defined as a 45° semi-recumbent position with the knees bent appropriately to prevent the patient from sliding out of the position.

***Research team***

**Principal Investigator (PI)**

All demographic data and clinical parameters of participants as well as all the measurements from the monitor and the ventilator were recorded by the PI (Addendum O). The measurements of the baseline nursing position and the placement of the participant in the therapeutic early mobility position were performed by the PI (Addendum O; Addendum P).

A pilot study was conducted to determine the reliability of repeated measurements from the monitor and ventilator as well assessing the ability of the PI to place the participant in the therapeutic early mobility position during the study's procedures. The results of the pilot study indicated that it was possible and enough time was available to record measurements and observations and to perform the intervention (Addendum Q). The monitors and ventilators were calibrated for accuracy on a daily basis in accordance with standard practice.

Results of blood gas samples were received via email from the laboratory and recorded by the PI. Adverse events were recorded by the PI during study procedures as well as post hoc analysis of $ScvO_2$% (Addendum O). The results of the blood samples were reliable as they were analysed at a national laboratory which adheres to standard practice.

**Nursing specialist**

All blood samples from the CVP-catheter and the arterial catheter were drawn by the nursing specialist who adhered to the standard practice of drawing blood samples and placing them into a container with ice blocks.

**Research assistant**

A container with blood samples was taken every five minutes during the study procedures of each participant to the laboratory of the tertiary teaching hospital by the research assistant to eliminate any chance of the blood samples expiring.

### 4.2.4 Sample

***Population***

All patients nursed in a seven bed respiratory unit with a nursing ratio of 2:1 and a 12 bed surgical unit with a nursing ratio of 2:1 of a tertiary teaching hospital from July 2014 to September 2014 were eligible for inclusion in the study. A sample of convenience was used. The respiratory unit admits critically ill respiratory patients while the surgical unit admits critically ill surgical and trauma patients after surgery to the unit.

***Sample size***

The sample size was calculated in consultation with a statistician. The MAP was used as the primary outcome of the study and the calculation were based on the results of Gocze et al[34], who found a statistical significant difference in the MAP of 4 mmHg ($p < 0.05$). Including 73 participants in the study would provide us with 80% power to detect a difference in the MAP ($p < 0.05$).

***Sample***

Twice weekly all patients nursed in the respiratory and surgical units were screened by the PI for inclusion in the study. Patients were eligible for inclusion if they were 18 years and older, eight hours after admission or intubation to the units, optimal CVP-values were reached, nursed with a CVP and arterial line in situ; and the level of adrenaline infusion was smaller than 0.06 microgram per kilogram per minute (mcg/kg/min).

All patients were excluded if deemed moribund by the attending intensivist. Patients with acute brain or spinal injuries as well as patients who presented with an increased intracranial pressure were also excluded. Unstable lumbar, pelvic or other fractures, which are contra-indicated for testing position also excluded patients from the study, and combative patients were also excluded. After inclusion patients were screened eight hours after admission to the units or intubation using the adapted early mobility readiness protocol (Table 4.1). This protocol was first published by Vollman[12] and Bassett et al[38] under a 'Mobility Assessment for Readiness' tool[12] and a 'Progressive Mobility Continuum' tool[38]. The amount of PEEP was adapted from PEEP < 10mmHg to PEEP ≤ 10mmHg as well as the lower limit of the MAP from 55mmHg to 65mmHg in consultation with an intensivist.

**Table 4.1: Adapted early mobility readiness protocol**

| Adapted Early mobility Readiness Protocol | | | | |
|---|---|---|---|---|
| Start with early mobility protocol if all YES | Yes | $PaO_2/FiO_2 \geq 250$ | NO | Postpone early mobility positioning if one is NO |
| | | PEEP≤10mmHg | | |
| | | $SpO_2 \geq 90\%$ | | |
| | | RR 10-30/min | | |
| | | No new cardiac arrhythmic or ischemia events | | |
| | | HR>60<120 | | |
| | | MAP>65<140mmHg | | |
| | | SBP>90<180mmHg | | |
| | | N0 New or ↑vasopressor | | |
| | | RASS > -3 | | |

**Legend:**
**$PaO_2/FiO_2$ =** Ratio of arterial oxygen partial pressure to fractional inspired oxygen; **PEEP** = Positive end -expiratory pressure; **mmHg** = millimetre mercury; **$SpO_2$** = peripheral capillary oxygen saturation; **RR** = Respiratory rate; **HR** = Heart rate; **MAP** = Mean arterial pressure; **SBP** = Systolic blood pressure; **RASS** = Richmond Agitation Sedation Scale.

### 4.2.5 Positioning

Two positions were utilised: 1) the baseline nursing position; and 2) the therapeutic early mobility position. Measurements were taken in both positions after the correct placement of the participant's position had been observed as well as the safety of the testing area (Addendum R). A Bosch digital angle and level measurer (Addendum P) were used to measure the position. The participant was placed in the therapeutic early mobility position through an incremental process (Addendum L). From the baseline nursing position using a 90 second pause with each 15° increase till the 45° semi-recumbent position was reached. Thereafter, the legs of the participant were bent until a maximum of 150° knee bend was reached.

### 4.2.6 Measurements

***Demographic data and clinical parameters***

Demographic data of participants were extracted from the two unit's documentation systems (Addendum O). This included the age (years), gender (male/female), Acute Physiology And Chronic Evaluation II score (APACHE II), admission diagnosis, time on the ventilator (unit

admission time / time of intubation – intervention) (hours), positive end expiratory pressure (PEEP) ($cmH_2O$), the ventilation mode, the fraction of inspired oxygen ($FiO_2$) (%), the sedation of participant, type and dose (mg/hour) and the Richardson Agitation Sedation Score (RASS) score. The ICU length of stay (hours) on testing day, level of inotropic support, fluid balance (ml/24hours) and latest haemoglobin (g/dL), platelets (cells/$mm^3$), and white blood cell count (cells/$mm^3$), were measured before study procedures commenced.

***Haemodynamic parameters***

The MAP, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP) and peripheral capillary oxygen saturation ($SpO_2$%) were measured thrice at 0 minutes, 3 minutes and 10 minutes in each position from the bedside monitor using the electrocardiogram electrodes connected to patient via the monitor, the arterial line catheter in situ and the peripheral capillary oxygen meter.

***$ScvO_2$% and arterial blood gasses***

One millilitre of blood was obtained from the CVP-catheter at the 0 minute, 3 minute and 10 minute time intervals as well as from the arterial catheter at the 10 minute time interval in each of the two positions. A one millilitre heparinized blood gas syringe (BD A-line 1ml syringes, product code 364356) was used to obtain the blood sample after a 5ml to 10ml volume of fluid and blood was taken from the line to eliminate all saline and heparin infused.

***Adverse events***

Adverse events were records at three time levels: 1) Placement of participant in position; 2) During the position and 3) Post hoc analysis of $ScvO_2$% values.

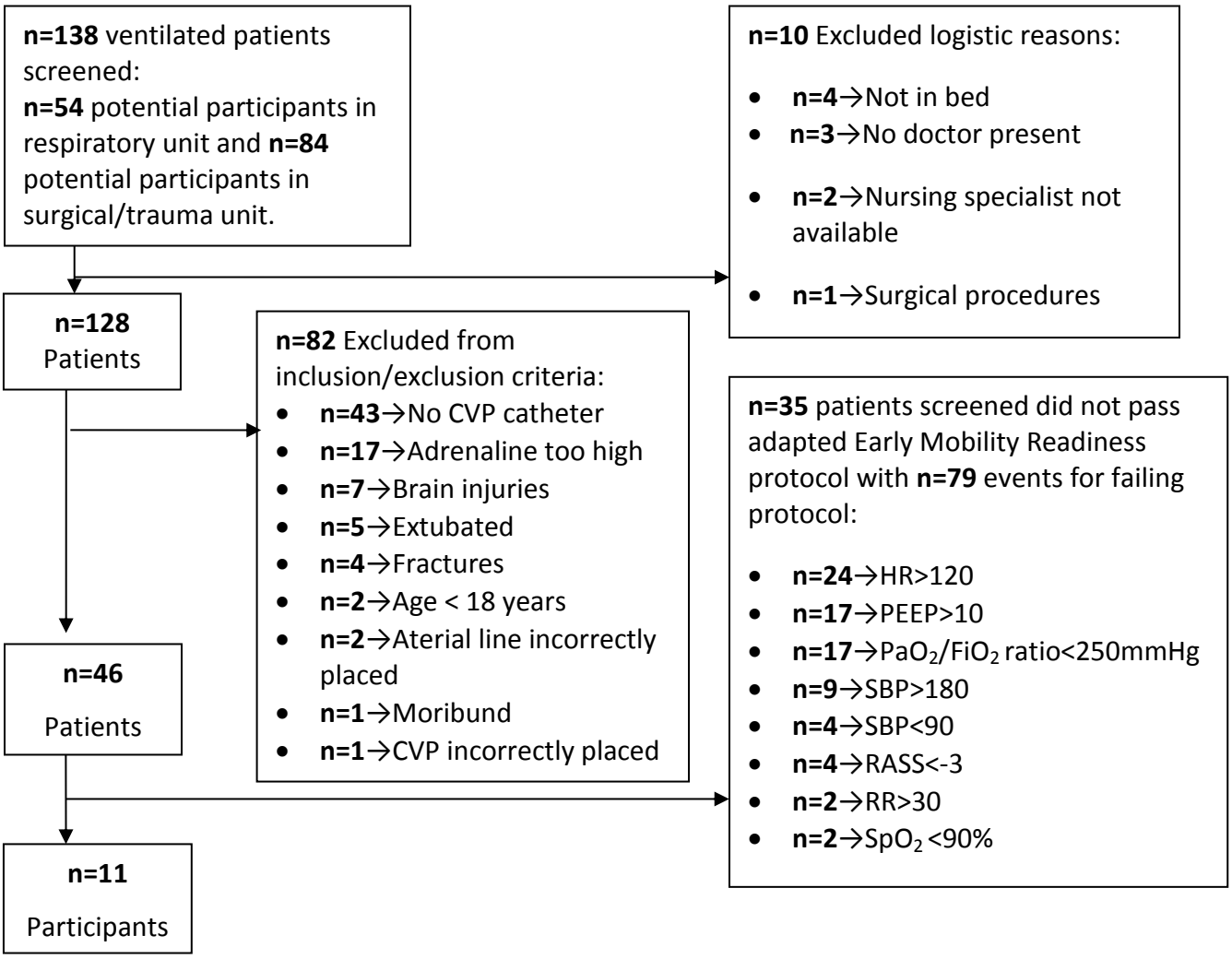
Predefined adverse events were recorded while placing the participant in the position and during the position, which included a possible increase or decrease in HR, arrhythmia of ECG on monitor, a drop or increase of MAP below normal values (MAP < 65mmHg[34]), increase in respiratory rate and any change in tidal volumes (ml). Any signs of discomfort, pain or suppression of consciousness or fainting were recorded as an adverse event. Any signs and symptoms of vascular air emboli (VAE) were recorded as an adverse event. A drop in the $ScvO_2$% below 70% was recorded on post analysis of values, as an adverse event.

### 4.2.7 Data processing and statistical analysis

Data were captured and analysed in an Excel datasheet by the PI after each study day and checked for accuracy at the end of each week. Descriptive statistics were used to describe the clinical parameters of the study population using medians (ranges) and means (standard deviations). Data were analysed in Statistica version 9 (Statsoft, Tulsa, Oklahoma, USA) by a statistician. The baseline nursing position and the therapeutic early mobility position were compared using repeated measures ANOVA. A 5% significant level ($p < 0.05$) was used. Evenly distributed data were descriptively described by using means (standard deviations). If data were skewed, medians (ranges) were used as well as 95% confidence intervals (CI), mean differences and 95% CI of mean differences.

## 4.3 Results

One hundred and thirty eight patients were screened (Figure 4.1). Ten patients were excluded due to logistical issues and a further 82 patients were excluded based on the exclusion criteria. Only 11 of 46 patients (7.9%) passed the adapted early mobility readiness protocol. Seventy nine events were recorded in 35 patients that failed the protocol. The most prevalent events included HR above 120 bpm (n=24), PEEP above 10 $cmH_2O$ (n=17) and $PaO_2/FiO_2$ ratio smaller than 250 mmHg (n=17).




**Legend:**
**HR** = Heart rate; **PEEP** = Positive end expiratory pressure; **$PaO_2/FiO_2$ ratio** = Arterial oxygen partial pressure to fractional inspired oxygen ratio; **SBP** = Systolic blood pressure; **RASS** = Richardson Agitation Sedation Score; **RR** = Respiratory rate; **$SpO_2$** = Peripheral capillary oxygen saturation; **CVP =** Central venous pressure.

**Figure 4.1: Consort flow diagram of screening process and participant inclusion/exclusion**

Mostly male participants with a median (range) age of 47 (20-67) years and with a median (range) APACHE II score of 8 (2-27) were tested. Baseline characteristics of all participants are listed in Table 4.2 and individual clinical parameters are listed in Table 4.3.

**Table 4.2: Characteristics of participants**

| Demographics | | | n(%) |
|---|---|---|---|
| **Gender:** Male | | | 9 (81.1) |
| Female | | | 2 (18.9) |
| **Unit admitted:** | Respiratory | | 2 (18.1) |
| | Trauma/Surgical | | 9 (81.8) |
| **Admission diagnosis:** | CAP | | 1 (9) |
| | Pneumonia | | 1 (9) |
| | MVA | | 1 (9) |
| | GSW | | 3 (27) |
| | Emergency surgery | Acute abdomen | 1 (9) |
| | Elective surgery | Ca Pancreas head | 1 (9) |
| | | Ca Oesophagus | 1 (9) |
| | | Ca Colon | 1 (9) |
| | | Oesophageal perforation | 1 (9) |
| **RASS sore of 0:** | | | 11 (100) |
| **Sedation & Dose:** | Morphine 50mg & Dormicum 60mg | | 1 (9) |
| | Morphine on request 10mg 6hourly | | 2 (18) |
| | Epidural | | 1 (9) |
| | None | | 7 (63) |
| **Ventilation mode:** | Bipap | | 9 (81) |
| | SIMV | | 2 (18) |

**Legend:**

**CAP** = Community Aquired Pneumonia; **MVA** = Motor Vehicle Accident; **GSW** = Gun Shot Wounds; **Ca** = Cancer; **RASS =** Richmond agitation sedation scale; **BiPAP** = Bilevel positive airway pressure; **SIMV** = Synchronized Intermittent Mandatory Ventilation; **(mg)** = microgram.

Nine participants were nursed in the surgical unit and two in the respiratory unit. All participants were awake and calm. The participants who were included were four participants with cancer having elective surgery, three participants with gunshot wounds, two participants with pneumonia and one participant having had emergency surgery for an acute abdomen. The time participants spent on the ventilator ranged between 14 hours and 298 hours. The median (range) arterial oxygen partial pressure to fractional inspired oxygen ratio (P/F ratio) (mmHg) was 414.3 mmHg (292.5 mmHg-577.5 mmHg).

**Table 4.3: Individual clinical parameters of participants**

| Participant | Age (yrs) | BP (°) | Vent. Time(hours) | PEEP ($cmH_2O$) | LOS (hours) | Fluid balance (ml) | Platelets ($cells/mm^3$) | Hb(g/dL) | WBC ($cells/mm^3$) | P/F ratio ($mmHg/O_2\%$) | APACHE |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A002 | 33 | 22,4 | 84 | 10 | 84 | 495 | 109 | 10,1 | 11,1 | 427,5 | 7 |
| A003 | 67 | 34,2 | 298 | 5 | 298 | -493 | 293 | 8 | 13 | 577,5 | 27 |
| A004 | 20 | 34 | 66 | 10 | 66 | 1055 | 112 | 10 | 2,5 | 478,1 | 7 |
| A005 | 39 | 25,4 | 18 | 5 | 18 | 414 | 67 | 7 | 16 | 414,3 | 24 |
| A006 | 54 | 36,6 | 16 | 8 | 16 | 345 | 114 | 9,9 | 10 | 356,35 | 16 |
| A007 | 21 | 50,9 | 14 | 10 | 14 | 247 | 138 | 17 | 12,85 | 427,5 | none |
| A008 | 64 | 37,5 | 88 | 10 | 345 | 3000 | 221 | 9,8 | 7,2 | 350 | 16 |
| A009 | 47 | 26,5 | 138 | 10 | 138 | 6500 | 174 | 11,2 | 10,13 | 369,3 | none |
| A010 | 33 | 33 | 53 | 10 | 53 | 90 | 177 | 9 | 7,07 | 313,1 | 2 |
| A011 | 64 | 40 | 113 | 10 | 113 | 1949 | 174 | 9,5 | 18,9 | 448,12 | 5 |
| A012 | 62 | 40,1 | 27 | 10 | 27 | 2497 | 288 | 7,8 | 19,1 | 292,5 | 8 |
| **Median** | 47 | 34,2 | 66 | 10 | 66 | 775 | 174 | 9,8 | 11,1 | 414,3 | 8 |
| **Range** | 20-67 | 22.4-50.9 | 14-298 | 5-10 | 14-345 | 90-6500 | 67-293 | 7-17 | 2.5-19.1 | 292.5-577.5 | 2-27 |
| **Mean** | 45,82 | 34,60 | 83,18 | 8,91 | 106,55 | 1659,2 | 169,73 | 9,94 | 11,62 | 404,93 | 12,3 |
| **SD** | 17,6 | 8,00 | 82,45 | 2,02 | 114,24 | 1985,27 | 73,20 | 2,64 | 5,10 | 81,13 | 8,76 |

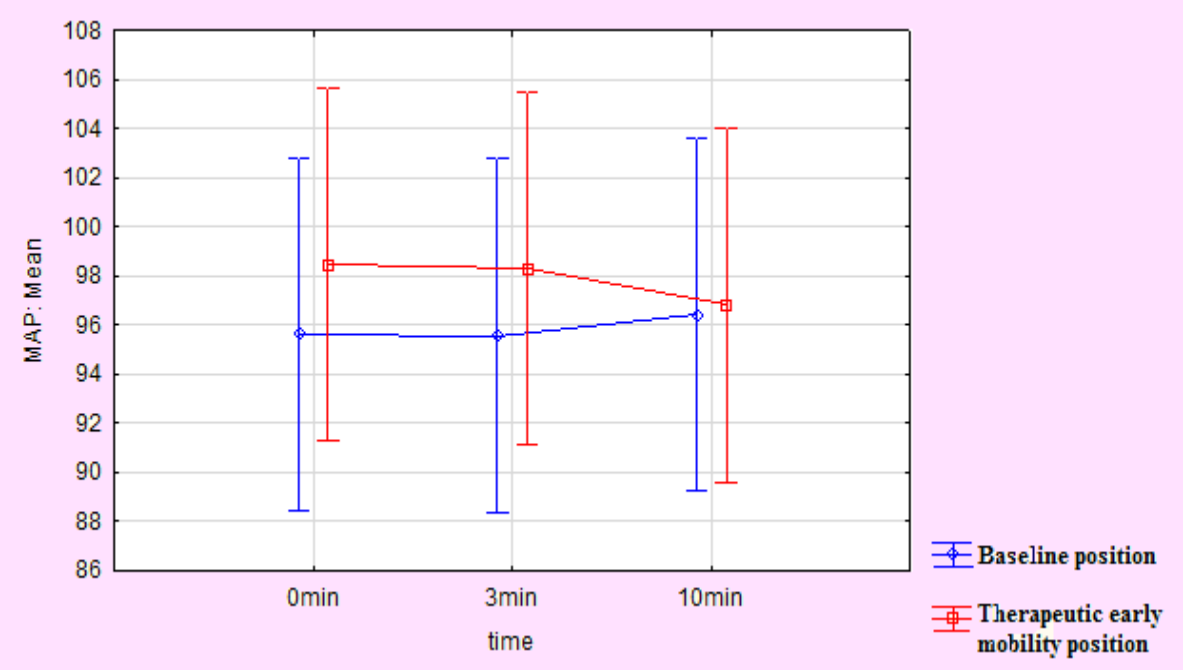
**Legend:**

**Yrs** = Years; **BP (°) =** Baseline position (degrees); **Vent. time =** Ventilation time in unit; **PEEP($cmH_2O$) =** Positive end expiratory pressure (centimetre water); **LOS (hours)** = Length of stay in hours; **Fluid balance(ml) =** Fluid balance (millilitre); **Hb (g/dL) =** Hemoglobin count (gram per decilitre); **WBC ($cells/mm^3$)** = White blood cell count (cells per cubic millimetre); **P/F ratio ($mmHg/O_2\%$)** = Arterial oxygen partial pressure to fractional inspired oxygen (millimetre mercury per percentage oxygen); **APACHE =** Acute physiology chronic evaluation score; **SD** = Standard Deviation.

The positions that participants were nursed in were used as the baseline nursing position for this study. It is noteworthy that there were no standard nursing positions. Positions varied from 22.4° to 50.9° in the units (Table 4.3). Ten of 11 participants were not nursed in the 45° semi-recumbent position and did not adhere to the CDCP's guideline for optimal positioning for intention to treat[1].

**MAP**

There was an increase noted in MAP when participants were moved from the baseline nursing position to the therapeutic early mobility position with a mean difference (95% CI) of 2.03 (-1.12 - 5.18) mmHg. This difference did not reach statistical significance in this sample ($p < 0.05$). The difference in MAP was negligible. All values of the MAP were still within normal ranges of above 65mmHg (MAP > 65mmHg)[34] (Figure 4.2).



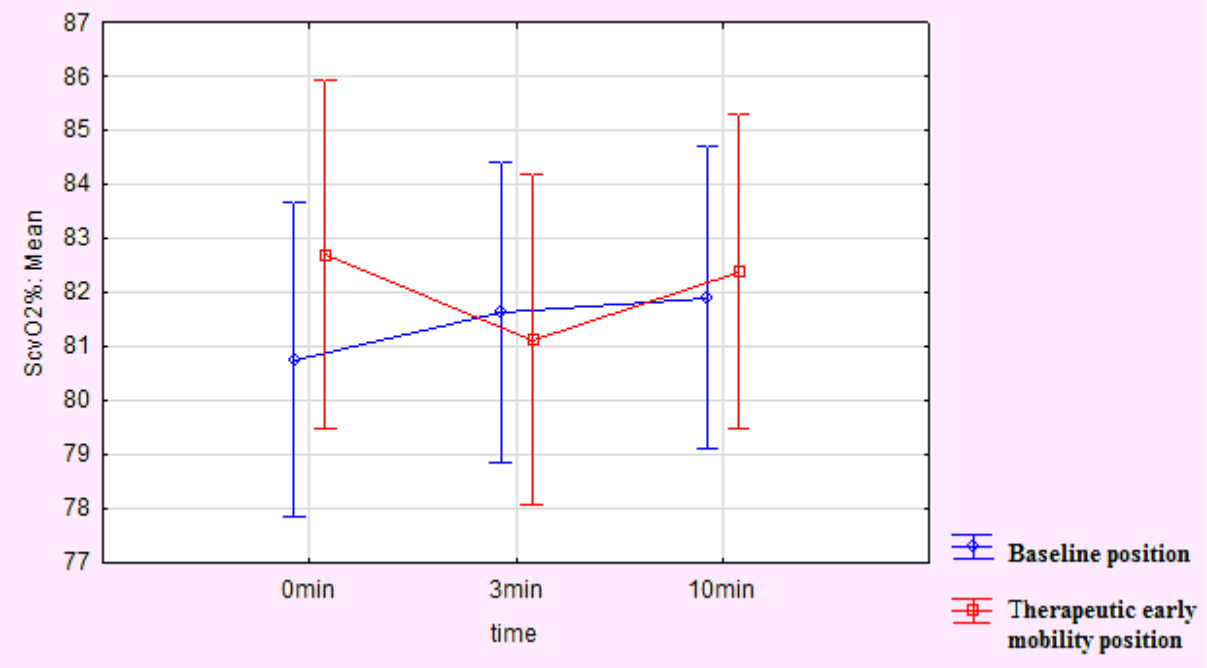

**Legend:**
**MAP =** Mean arterial pressure in millimetre mercury; **min** = minute.

**Figure 4.2: Mean arterial pressure values of the baseline nursing position and the therapeutic early mobility position at 0 minutes, 3 minutes and 10 minutes**

**$ScvO_2$%**

After the initial increase noted in the $ScvO_2$% at 0 minutes when participants were placed in the therapeutic early mobility position from the baseline nursing position [mean difference (95% CI) of 0.79 (-3.15 - 4.74)], no difference was found at 3 or 10 minutes. The mean $ScvO_2$% of the therapeutic early mobility position dropped below the mean $ScvO_2$% in the baseline nursing position after 3 minutes and increased to a mean $ScvO_2$% higher than the baseline nursing position

after 10 minutes as illustrated in a line graph (Figure 4.3). The $ScvO_2$% stayed within normal range of the greater than 70% ($ScvO_2 > 70\%$)[34] through the study procedures as indicated by the 95%CI.




**Legend:**
**$ScvO_2$%**= Central venous oxygen saturation percentage; **min** = minute.

**Figure 4.3: Mean $ScvO_2$% values in the baseline nursing position and the therapeutic early mobility position at 0 minutes, 3 minutes and 10 minutes**

### Adverse events

Four incidences of adverse events were noted in four participants during the 220 (11 participants x 20 minutes) minutes of the study and none needed abortion of study procedures. Two adverse events occurred in the baseline nursing position. A SBP of 182mmHg which lasted for 30 seconds and recovered to 177mmHg and one drop in the $SpO_2$% to 89% which returned to 90% after finger oximetry meter was adjusted. One adverse event occurred during the therapeutic early mobility position, blocking of the Clave port with clotted blood, which was replaced and no data were collected at that point and study procedures continued. One post hoc incidence occurred at the baseline nursing position 3 minute time period where the $ScvO_2$% dropped below 70%.

## 4.4 Discussion

This study's results indicate that only 7.9% of patients screened with the adapted early mobility readiness protocol could be placed in the therapeutic early mobility position. The adapted early mobility readiness protocol consists of ten criteria and all need to be passed before a patient could be placed in a position higher than the 30° semi-recumbent position (Table 4.1). Patients were

screened eight hours after intubation. Although the individual criteria do provide an indication of the physiological stability of the patient, we argue that using single criteria as suggested by Vollman[12] and Bassett et al[38] to exclude patients from early mobility, is not clinically viable. Using the protocol, which gives equal weighting to all criteria, may lead to the exclusion of patients who would be routinely mobilised safely. This observation is confirmed by literature[23,35,38]. In developing criteria for the early mobilisation of awake patients Stiller et al[35] and Hanekom et al[38] have advocated a less stringent approach of looking at the sufficient cardiovascular reserve and the respiratory reserve of a patient. Although criteria are recommended to guide the decision making process the clinical interpretation of all values are also advocated. Based on our results a similar approach is advocated for the refinement of the adapted early readiness protocol. The data presented in this paper can be used to inform the process.

Although only 11 participants could be placed in the therapeutic early mobility position, our findings supports the results already reported[34]. A study performed by Gocze et al[34] found a statistical significant difference in the value of the MAP (decrease of 4 mmHg) in the 45° semi-recumbent position after a sequence of six combinations of the 0°, 30° and 45° semi-recumbent positions[34]. However, the MAP remained within the normal ranges of above 65 mmHg. Although statistical significance could be attained due to the large sample the clinical significance of a 4mmHg decrease in MAP is questionable. Guiliano et al[8] found similar results in the MAP during their study. This supports our finding that the therapeutic early mobility position had no negative effect on the MAP. These preliminary findings must be confirmed in an adequately powered study.

Our study showed an initial increase in the $ScvO_2$% from the 10 minute baseline nursing position ($ScvO_2$ = 81.9%) to the placement in the 0 minute therapeutic early mobility position ($ScvO_2$ = 82.7%) which indicated that the oxygen delivered ($DO_2$) to the lungs was adequate for the oxygen demand of the body created by the initial placement of the participants in the therapeutic early mobility position. The drop in the $ScvO_2$% at 3 minutes possibly indicates that the body consumes more oxygen from the 0 minutes to the 3 minutes time interval when a patient is placed in the therapeutic early mobility position. Our results have clinical relevance and indicate that a therapist using the therapeutic early mobility position can expect an initial drop in the $ScvO_2$% after the 0 minutes which stabilized again between three and ten minutes. The results of our study indicated that the 11 patients who passed the screening with the adapted early mobility readiness protocol, could tolerate the therapeutic early mobility position. No adverse events were documented. More participants need to be recruited to confirm these preliminary findings.

Ten of the 11 participants were not nursed in the optimal position of 45° semi-recumbent position to prevent aspiration as recommended by the CDCP[1] (Table 4.3). Studies[19, 34, 39] investigating the mean average degrees of semi-recumbent positioning during usual care in the critically ill units found that they varied between 22.9° and 28°[19, 34, 39]. Reasons for not reaching the 45° semi-recumbent position were discomfort[177], sliding out of bed[179] possible severity of illness[39] and heamodynamic instability[34], none of which were found during our study.

Placing a patient in the therapeutic early mobility position is an easy task which is not labour-intensive and does not need any special equipment to perform. The therapeutic early mobility position can be used as a stepping stone towards getting a patient ready for mobilisation out of bed as it does not challenge the haemodynamic parameters of a patient. The patient can be positioned optimally while still having a minus three on the RASS score. The therapeutic early mobility position can form part of a patient's daily routine in the unit to start early mobility and can be continued as long as a patient tolerates the position and no adverse events occur.

## 4.5 Limitations

The screening of the participants on specific days led to the late inclusion of participants or loss of potential candidates resulting in a small sample size. However, the characteristics of participants indicated that a wide variety of participants were included. The great variation noted in our sample indicated that the protocol was sensitive enough to identify suitable candidates who can tolerate the therapeutic early mobility position. Although, 138 patients were screened, only 11 participants passed the adapted early mobility readiness protocol. This indicates that the protocol is not a clinical viable tool. It would be valuable in future studies to refine the criteria which can be used for the early identification of suitable patients in order to deter the detrimental effects of bed rest.

We positioned the participants with the knees bent in a bid to prevent the participants from sliding down in bed. However, this has the potential to increase pressure on specific areas. While patients could tolerate the position, it would be valuable to also assess the effect of the position on pressure areas.

While larger numbers could confirm that placing a participant in the therapeutic early mobility position can increase the MAP, the 95% CI of our study indicated that the effect does not cause instability as the values remained within acceptable ranges of above 65mmHg[34]. The recruitment of 73 participants would have given enough power to detect a significant difference in the MAP. Even though 138 patients were screened, only 11 participants were included. On evaluation of results and after consultation with the intensivist it became clear that the criteria included in the protocol could

be too strict. Many patients, who would be excluded from the therapeutic early mobility position when applying the protocol, were routinely mobilised safely in the unit. This highlights the difficulty with the clinical viability of the protocol.

The PI performed most of the procedures and measurements of the study which could lead to potential performance and detection bias as no blinding of participants or the PI were performed. The instruments used in the units were calibrated on a daily basis and adhered to standard practice which ensured accurate measurements as well as observing that the position of the arterial line transducer was still in the mid-axillary line. The pilot study confirmed that enough time was available to perform the intervention, measurements and observations. However, blinding of participants and the PI in future studies would help prevent performance and detection bias and would have given an objective consideration to the research question but would possibly have increased the costs of the study as more personnel would be needed.

## 4.6 Conclusion

The adapted early mobility readiness protocol was not able to adequately identify suitable patients who could tolerate the therapeutic early mobility position. More work is needed to refine and clarify the criteria of clinical importance. Data reported can be used to inform this process. While participants were not physiologically challenged during the study procedures, these preliminary results must be confirmed in an adequately powered study. The effect of the therapeutic early mobility position on patient outcome needs further investigation.

## 4.7 Key Message

- The use of an early mobility readiness protocol succeeded in identifying only 7.9% patients suitable for positioning. More work is needed to refine the protocol criteria. Our data will inform this process.
- Measurement of $ScvO_2$% over time (multiple points) is recommended for future studies as it provides an indication of the changing demands of therapeutic positioning on oxygen delivery and oxygen consumption.
- The MAP values remained within normal range of above 65mmHg[34] in our 11 participants.
- The therapeutic early mobility position did not physiologically challenge our 11 participants.
- Preliminary findings need to be confirmed in an adequate powered sample.
- There is no standardized routine position used for nursing of critical ill patients in our units.

# Chapter 5: General Discussion

The aim of this thesis was to investigate the therapeutic use of positions for a critically ill population. A scoping review was conducted to describe the therapeutic use of positioning in the management of an adult critically ill population (Chapter 2). The scoping review led to a focussed review (Chapter 3) with the aim of exploring the effect of the semi-recumbent position (semi-fowler or head-up position) in the management of an adult, critically ill, mechanically ventilated or intubated population. The literature was not clear on the effect or feasibility of the 45° semi-recumbent position. Following the focussed review the PI decided to conduct a primary study (Chapter 4) with the aim of identifying patients who could tolerate a therapeutic early mobility position by using an adapted early mobility readiness protocol. The effect of a therapeutic early mobility position on two haemodynamic parameters including the MAP and the oxygen consumption via the $ScvO_2$% were investigated. The secondary aim was to describe the current nursing positions used in the units and to describe any adverse events and the preliminary results would inform future research.

## 5.1 Current Understanding of Literature

The therapeutic use of positioning in the management of critical ill patients has been investigated since 1992. A wide variety of positions have been investigated with the main focus on the prone position. The majority of papers were conducted in the northern hemisphere in the medical and general critical ill populations. Therapeutic positioning has mostly been used to optimise the clinical outcome of patients including the prevention of VAP and aspiration as well as the improvement of the outcome of ARDS.

### 5.1.1 The therapeutic use of the semi-recumbent position

The therapeutic use of the semi-recumbent position has been investigated, but discrepancies still exist. Clear guidelines[12], standardised protocols[38] and clinical management algorithms[36, 41] do exist for early mobility but were not used in any of the papers discussed in the scoping review (Chapter 2). Papers investigating the semi-recumbent position mainly explored the effect of the semi-recumbent position and the effect of the position on the clinical outcome (VAP and aspiration) of participants. However, the focussed review (Chapter 3) concluded that no clear description exists of the therapeutic use of the 45° semi-recumbent position as an optimal position for treatment during the acute phase of critical illness in sedated patients. One paper[34] in the review reported haemodynamic instability during positioning of sedated patients in the 45° semi-recumbent position which was not of clinical relevance as the MAP stayed within normal range of above 65 mmHg[34].

The authors in this paper[34] considered that a difference of 4mmHg was clinically meaningful. However our study confirmed the findings of Gocze et al[34] that the MAP remained stable. We found that using the protocol, described in Chapter 4, we could identify less than 10% of participants who could tolerate the therapeutic early mobility position. We argue that the adapted early mobility readiness protocol is not a clinical viable tool and that more work is needed to refine the criteria.

### 5.1.2 Quality of papers

The quality of papers varied from level II to level III-3 of the hierarchy which indicates that shortcomings of level I evidence exist. A shortcoming of randomised control trials was identified and evidence is not robust enough to be used in clinical practice. Bias can be prevented by blinding of participants and the research team. The internal validity of papers also varied and future research needs to plan concisely the methodology of experimental trials which will rule out contamination and bias.

### 5.1.3 Therapeutic positioning and haemodynamic parameters

A wide variety of haemodynamic parameters were described, including the CI[8], SV[8], CO[2, 8, 17], Pa[2, 8, 17, 34], MAP[8, 17, 34], CVP[2, 17], $ScvO_2$%[34], HR[2, 8, 17], CCI[8], and the Pmsf[17]. Out of nine parameters, four can be directly monitored from the bedside monitor during positioning of a patient. However, uncertainties still exist regarding the effect of therapeutic positioning on the haemodynamic parameters.

One paper[34] investigating the effect of the semi-recumbent position indicated that the MAP decreases when a patient was placed in the 45° semi-recumbent position while another paper's[8] results indicated that the MAP remained stable. However, our study indicated that the MAP remained stable within its normal ranges of above 65mmHg[34] when 11 participants were placed in the 45° semi-recumbent position with the knees bent. By using the protocol, only 11 patients were identified and could tolerate the therapeutic early mobility position.

Papers[8, 17, 34] investigating the effect of the 30° semi-recumbent position, reported a decrease in the MAP which was stable and within normal ranges of above 65 mmHg. It also seemed that the HR remained stable within its normal ranges during the 30° semi-recumbent positioning.

The results of the $ScvO_2$% in one paper[34] indicated that the $ScvO_2$% decreases when a patient is placed in the 30° and 45° semi-recumbent position from the 0° semi-recumbent position. The placement of a participant in a higher head of bed elevation possibly leads to a participant consuming more oxygen during the positioning. However, our study's results indicated that the

$ScvO_2$% increased initially, decreased from 0 minutes to three minutes but stayed within normal ranges of above 70%[34]. The $ScvO_2$% returned to the same value again at 10 minutes as at the 0 minute time interval of therapeutic early mobility position. The body consumed more oxygen initially but returned to normal values ($ScvO_2$% > 70%) again after three minutes. Our findings indicate that the participants could tolerate the position, however only 11 participants were recruited and data can now be used to inform future studies. The effect of the therapeutic early mobility position on this haemodynamic variable after 10 minutes needs further investigation.

### 5.1.4 Therapeutic positioning and cerebrovascular dynamics

Cerebrovascular dynamics were described in two papers[10, 72]. The ICP, CPP, CBF and the cerebral metabolic rate of oxygen ($CMRO_2$) seem to decrease as well as the CI of comatose patients during the placement of a patient in the 45° semi-recumbent position[72], while surgical patients, showed no indication of a possible increase in vasospasm, during the 45° semi-recumbent positioning in another paper[10]. Future research is needed in comatose patients to investigate the effect of the 45° semi-recumbent position on the ICP and the CPP. The presence of adverse events was not reported consistently as well as the studies included in the focussed review did not have enough power to detect adverse events. Therefore, future studies with enough power need to be investigating adverse events.

### 5.1.5 VAP

As described in the Chapter 3, four papers[5, 19, 65, 128] investigated the influence of the semi-recumbent position on VAP. Only two papers[65, 128] odds ratios favours the 45° semi-recumbent position and one paper's[5] odds ratio favours the beach chair position. Pooling of results in a forest plot indicates that the risk to develop VAP in the 45° semi-recumbent position was equal to the risk to develop VAP in the 0° semi-recumbent position. The heterogeneity ($I^2$ = 83%) was significant and the two papers[65,128] differed regarding the population included, the inclusion and exclusion criteria as well as the time of intubation. However, this variable was not investigated in our study and future research is needed to clarify the influence of the therapeutic early mobility position on VAP.

### 5.1.6 The population

In the papers described in Chapter 3, samples were of more elderly, male participants. The sample sizes also varied as well as the type of population. The medical units were mostly described. In the primary study (Chapter 4) the adapted early mobility readiness protocol was able to identify younger participants, mostly male surgical patients but was not a clinical viable tool to identify

enough patients suitable for the therapeutic early mobility position that would give enough power to detect a significant difference.

## 5.2 Achievement of Aims for Primary Study

Within the context of the literature reviewed, a primary study was planned as a first step to include an optimal position for patients unable to actively engage with mobilisation. Our first aim was to identify patients who could be positioned in a therapeutic early mobility position by using an adapted early mobility readiness protocol (Chapter 4). Secondly we used two (Chapter 4 haemodynamic parameters, the MAP and the oxygen consumption via the $ScvO_2$% to describe the effect of the therapeutic early mobility position on an adult critically ill patient population. Our first aim was achieved but less than 10% participants passed the screening with the adapted early mobility readiness protocol and could be placed in the therapeutic early mobility position. We argue that the adapted early mobility readiness protocol is too strict and therefore not clinically viable in the current format. We concluded that more work is needed to refine the criteria and to clarify which criteria of the protocol were of clinical importance. Our data will inform this process. The 11 participants who passed the protocol screening could tolerate the therapeutic early mobility position as indicated by the MAP and $ScvO_2$% which stayed within normal ranges.

Measurements of the $ScvO_2$% were done to determine adequate tissue oxygenation. A decrease in the $ScvO_2$% measurement was seen as a reflection of the balance between oxygen delivery ($DO_2$) and consumption ($VO_2$) of the body. A low $ScvO_2$% either indicated an increase in oxygen consumption ($VO_2$) or a decrease in $DO_2$[180]. The placement of the tip of central venous catheter was evaluated by the attending doctor for correctness before testing commenced, the standardised method of drawing blood from the CVP-line by the attending nursing specialist, the standardised equipment used by the laboratory as well as the five minute time of transportation, ensured accurate measurement of the $ScvO_2$%. Therefore the $ScvO_2$% measurements can be trusted.

We tested the $ScvO_2$% and measured the MAP at 0 minutes, 3 minutes and 10 minutes before placing the participants in the therapeutic early mobility position for the same time interval. Testing was performed in the baseline nursing position which is the current nursing position at 0, 3 and 10 minutes and in the therapeutic early mobility position thereafter, at the same time intervals. This was done to investigate the results found by the Gocze et al[34] which only tested participants for three minutes. We discovered that even though we only had data of 11 participants, the narrow 95% CI indicated precise measurements of both the $ScvO_2$% and the MAP. The values of mean MAP remained within normal ranges above 65mmHg. The $ScvO_2$% stayed within normal range ($ScvO_2$ > 70%)[34] throughout the study procedures as indicated by the 95% CI. A drop in the $ScvO_2$% from 0

minute to 3 minutes which will correct again by 10 minutes could possibly be expected but these preliminary findings need to be confirmed in an adequately powered study. These preliminary findings can be used to inform future research.

Another aim was to describe the current nursing positions in the units. This aim was achieved and 10/11 participants did not reach the 45° semi-recumbent position. The results of the primary study indicated that optimal positioning was not yet reached and the 45° semi-recumbent position is not currently used during usual care. This was only preliminary results and future studies with bigger sample sizes need to investigate this further.

## 5.3 Limitations

- All the literature investigating therapeutic positioning was included from inception till June 2013, but the evidence found was not robust enough for clinical practice because of the variability of the methodological quality of papers.
- The diverse range of study sample sizes and the diverse range of interventions used made the pooling of results difficult for statistical analysis. However, the focussed review described applicable results which could be pooled, including the heterogeneity and $I^2$.
- Only six electronic data bases were included in the search and the fact that only English publications were investigated can be seen as a limitation. Grey literature was not included and can be seen as a limitation. However, this scoping review included all the papers published from inception till June 2013 with the relevant therapeutic positions used in the adult critical care environment, and two researchers (EC & SS) independently searched the six electronic data bases. Additionally, this review investigated a wide and diverse body of research evidence which indicated that unanswered questions still exist regarding the therapeutic positioning.
- No search strategies were performed after June 2013 of the literature investigating therapeutic positioning. The researcher (EC) acknowledges that the scoping review and the focussed review will need to be updated and the search strategies will be performed again and any new evidence will be included in the manuscripts before submission for review.
- The screening of patients using the adapted early mobility readiness protocol led to the exclusion of potential candidates from the therapeutic early mobility position who would be routinely mobilised safely during usual care.
- The screening of participants twice weekly led to the late inclusion of participants, or to loss of potential candidates, and resulted in a small sample size. This was identified as a limitation

of the primary study. It will be valuable in the future to screen patients bi-daily to initiate optimal positioning early after admission to the unit.

- The small sample size indicates that the adapted early mobility readiness protocol is not a clinical viable tool to use and is possibly too strict. It would be valuable in the future to refine the criteria and clarify which of the criteria are of clinical importance.
- The positioning of participants with the knees bent in a bid to prevent the patient from sliding out of the position could possibly increase pressure on certain areas. While participants could tolerate the position it would be valuable to assess the effect of the position on pressure areas.
- The short time period spent in the therapeutic early mobility position can be a possible limitation. It will be valuable in the future to assess the effect of this position on muscle activity during the placement of a participant in this position, and a longer time period spent in the position will also be valuable.
- The participants and the PI were not blinded and could lead to potential performance and detection bias but would lead to employment of more personnel to conduct the study and would have increased the costs of the study.

## 5.4 Future Research

The adapted early mobility readiness protocol needs more work before it is utilised in units. Future research needs to investigate which criteria of the adapted early mobility readiness protocol are too strict and needs refinement. Future research needs to confirm the preliminary findings of the MAP and $ScvO_2$%. Our data can inform the size of the sample needed.

The therapeutic early mobility position needs further investigation. A longer period of time spent in the position is needed to investigate the effect of the position on the same haemodynamic parameters and to evaluate if any risk factors are associated with this position. Future research is needed to evaluate the effect of this position on pressure areas as this position might cause an increase in pressure on specific areas. The effect of the therapeutic early mobility position on the muscle activity and blood flow in the lower extremities is needed to investigate the influence of the increased gravitational force on the body as the drop in the $ScvO_2$% at three minutes needs further investigation. The effect of the therapeutic early mobility position on the HRQoL of survivors needs investigation.

## 5.5 Take Home Message

- Therapeutic positioning has been investigated in ARDS and VAP.
- The semi-recumbent position needs further investigation.

- More randomised control trials are needed for robust evidence.
- The adapted early mobility readiness protocol in its current format cannot be used in units to initiate the early mobility of patients. More work is needed to refine and clarify which of the criteria can guide clinicians in their decision making regarding early mobility (within eight hours of admission) of a critically ill patients.
- The 11 participants who passed the protocol screening could tolerate the therapeutic early mobility position as indicated by the MAP and $ScvO_2$% which stayed within normal ranges. These preliminary findings need to be confirmed in an adequately powered study.
- Placing a patient in the therapeutic early mobility position does not need any special equipment to perform.
- The results of the primary study indicate that the optimal semi-recumbent position is not currently used during usual nursing care of critically ill patients.

## 5.6 Final Conclusion

Therapeutic positioning of critically ill patients has been well reported. However, the semi-recumbent position needs further investigation. The adapted protocol described in this thesis is cannot recommended to be used by clinicians in its current format. More work is needed to identify criteria for the early identification of suitable patients for early mobilisation.

The preliminary findings describing the minimal effect of the early mobility position on hemodynamic stability need to be confirmed in an adequately powered study. Whether the therapeutic early mobility position has the potential to be used as a stepping stone for mobilisation out of bed needs to be confirmed in an adequately powered study. The preliminary hemodynamic results of the 11 patients included in this preliminary study can inform future studies. The effect of a therapeutic early mobility position on the HRQoL of survivors must now be investigated.

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**Note to NIH Grantees**

Pursuant to NIH mandate, Wiley-Blackwell will post the accepted version of contributions authored by NIH grant-holders to PubMedCentral upon acceptance. This accepted version will be made publicly available 12 months after publication. For further information, seewww.wiley.com/go/nihmandate. Frequently asked questions are answered here.

# Addendum B: Instructions for authors to Critical Care a journal of BMC

## Critical Care a journal of BMC

- **Instructions for authors**

- **Research Articles**

See 'About this journal' for descriptions of different article types and information about policies and the refereeing process.

- **Submission process**

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Manuscripts must be submitted by one of the authors of the manuscript, and should not be submitted by anyone on their behalf. The submitting author takes responsibility for the article during submission and peer review.

Please note that all content published in *Critical Care* is entirely open access. *Critical Care* levies an article-processing charge on all accepted Research Articles that have not been directly invited by the journal; if the submitting author's institution is a BioMed Central member the cost of the article-processing charge may be covered by the membership (see About page for detail). Please note that the membership is only automatically recognised on submission if the submitting author is based at the member institution. Authors of invited Research Articles are entitled to a full waiver on the journal article processing charge and should complete a waiver request during the submission process.

To facilitate rapid publication and to minimise administrative costs, *Critical Care* prefers online submission.

Files can be submitted as a batch, or one by one. The submission process can be interrupted at any time; when users return to the site, they can carry on where they left off.

See below for examples of word processor and graphics file formats that can be accepted for the main manuscript document by the online submission system. Additional files of any type, such as movies, animations, or original data files, can also be submitted as part of the manuscript.

During submission you will be asked to provide a cover letter. Use this to explain why your manuscript should be published in the journal, to elaborate on any issues relating to our editorial policies in the 'About *Critical Care*' page, and to declare any potential competing interests.

Assistance with the process of manuscript preparation and submission is available from BioMed Central customer support team.

We also provide a collection of links to useful tools and resources for scientific authors on our Useful Tools page.

- **File formats**

The following word processor file formats are acceptable for the main manuscript document:

- Microsoft word (DOC, DOCX)
- WordPerfect (version 5 and above)
- Rich text format (RTF)
- Portable document format (PDF)

- TeX/LaTeX (use BioMed Central's TeX template)

TeX/LaTeX users: Please use BioMed Central's TeX template and BibTeX stylefile if you use TeX format. During the TeX submission process, please submit your TeX file as the main manuscript file and your bib/bbl file as a dependent file. Please also convert your TeX file into a PDF and submit this PDF as an additional file with the name 'Reference PDF'. This PDF will be used by internal staff as a reference point to check the layout of the article as the author intended. Please also note that all figures must be coded at the end of the TeX file and not inline.

If you have used another template for your manuscript, or if you do not wish to use BibTeX, then please submit your manuscript as a DVI file. We do not recommend converting to RTF.

For all TeX submissions, all relevant editable source must be submitted during the submission process. Failing to submit these source files will cause unnecessary delays in the publication procedures.

## • Preparing main manuscript text

General guidelines of the journal's style and language are given below.

### • Overview of manuscript sections for Research Articles

Manuscripts for Research Articles submitted to *Critical Care* should be divided into the following sections (in this order):

- Title page
- Abstract
- Keywords
- Article headings
- Introduction
- Methods
- Results and discussion
- Conclusions
- Key messages
- List of abbreviations used (if any)
- Competing interests
- Authors' contributions
- Authors' information
- Acknowledgements
- Endnotes
- References
- Illustrations and figures (if any)
- Tables and captions
- Preparing additional files

The **Accession Numbers** of any nucleic acid sequences, protein sequences or atomic coordinates cited in the manuscript should be provided, in square brackets and include the corresponding database name; for example, [EMBL:AB026295, EMBL:AC137000, DDBJ:AE000812, GenBank:U49845, PDB:1BFM, Swiss-Prot:Q96KQ7, PIR:S66116].

The databases for which we can provide direct links are: EMBL Nucleotide Sequence Database (EMBL), DNA Data Bank of Japan (DDBJ), GenBank at the NCBI (GenBank), Protein Data Bank (PDB), Protein Information Resource (PIR) and the Swiss-Prot Protein Database (Swiss-Prot).

For reporting standards please see the information in the About section.

- ## Title page

The title page should list

- the title of the article
- the full names
- institutional addresses
- email addresses for all authors

The corresponding author should also be indicated.

Please note that the title should include the study design, for example "A versus B in the treatment of C: a randomised controlled trial" or "X is a risk factor for Y: a case control study". Please see the policy section in 'About *Critical Care*' for further details.
Please note that if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "acknowledgements" section in accordance with the instructions below. Please note that the individual names may not be included in the PubMed record at the time a published article is initially included in PubMed as it takes PubMed additional time to code this information.

- ## Abstract

The Abstract of the manuscript should not exceed 350 words and must be structured into separate sections: **Introduction**, the context and purpose of the study; **Methods**, how the study was performed and statistical tests used; **Results**, the main findings; **Conclusions**, brief summary and potential implications; **Trial registration**, if your research reports the results of a controlled health care intervention, please list your trial registry, along with the unique identifying number (e.g. **Trial registration**: Current Controlled Trials ISRCTN73824458). Please note that there should be no space between the letters and numbers of your trial registration number. We recommend manuscripts that report randomised controlled trials follow the CONSORT extension for abstracts.
Please minimise the use of abbreviations and do not cite references in the abstract. Please see also our guide for writing an easily accessible abstract.

- ## Keywords

Three to ten keywords representing the main content of the article.

- ## Introduction

The Introduction section should be written in a way that is accessible to researchers without specialist knowledge in that area and must clearly state - and, if helpful, illustrate - the background to the research and its aims. Reports of clinical research should, where appropriate, include a summary of a search of the literature to indicate why this study was necessary and what it aimed to contribute to the field. The section should end with a brief statement of what is being reported in the article.

- ## Methods

The methods section should include the design of the study, the setting, the type of participants or materials involved, a clear description of all interventions and comparisons, and the type of analysis used, including a power calculation if appropriate. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses in the methods section.

For further details of the journal's data-release policy, see the policy section in 'About this journal'.

- ## Results and discussion

The Results and discussion may be combined into a single section or presented separately. Results of statistical analysis should include, where appropriate, relative and absolute risks or risk reductions, and confidence intervals. The Results and discussion sections may also be broken into subsections with short, informative headings.

- ## Conclusions

This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.

- ## Key messages

These should be up to five bullet points summarising the main findings of your study.

- ## List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations can be provided, which should precede the competing interests and authors' contributions.

- ## Competing interests

A competing interest exists when your interpretation of data or presentation of information may be influenced by your personal or financial relationship with other people or organizations. Authors must disclose any financial competing interests; they should also reveal any non-financial competing interests that may cause them embarrassment were they to become public after the publication of the manuscript.

Authors are required to complete a declaration of competing interests. All competing interests that are declared will be listed at the end of published articles. Where an author gives no competing interests, the listing will read 'The author(s) declare that they have no competing interests'.

When completing your declaration, please consider the following questions:

*Financial competing interests*

- In the past three years have you received reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? Is such an organization financing this manuscript (including the article-processing charge)? If so, please specify.
- Do you hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? If so, please specify.
- Do you hold or are you currently applying for any patents relating to the content of the manuscript? Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript? If so, please specify.
- Do you have any other financial competing interests? If so, please specify.

*Non-financial competing interests*

Are there any non-financial competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify.

If you are unsure as to whether you, or one your co-authors, has a competing interest please discuss it with the editorial office.

- ## Authors' contributions

In order to give appropriate credit to each author of a paper, the individual contributions of authors to the manuscript should be specified in this section.

According to ICMJE guidelines, An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. To qualify as an author one should 1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; 3) have given final approval of the version to be published; and 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.
We suggest the following kind of format (please use initials to refer to each author's contribution): AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, a department chair who provided only general support, or those who contributed as part of a large collaboration group.

- ## Authors' information

You may choose to use this section to include any relevant information about the author(s) that may aid the reader's interpretation of the article, and understand the standpoint of the author(s). This may include details about the authors' qualifications, current positions they hold at institutions or societies, or any other relevant background information. Please refer to authors using their initials. Note this section should not be used to describe any competing interests.

- ## Acknowledgements

Please acknowledge anyone who contributed towards the article by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for each author, and for the manuscript preparation. Authors must describe the role of the funding body, if any, in design, in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. Please also acknowledge anyone who contributed materials essential for the study. If a language editor has made significant revision of the manuscript, we recommend that you acknowledge the editor by name, where possible.

The role of a scientific (medical) writer must be included in the acknowledgements section, including their source(s) of funding. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.'

If you would like the names of the individual members of a collaboration Group to be searchable through their individual PubMed records, please ensure that the title of the collaboration Group is included on the title page and in the submission system and also include

collaborating author names as the last paragraph of the "acknowledgements" section. Please add authors in the format First Name, Middle initial(s) (optional), Last Name. You can add institution or country information for each author if you wish, but this should be consistent across all authors.

Please note that individual names may not be present in the PubMed record at the time a published article is initially included in PubMed as it takes PubMed additional time to code this information.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

- ## Endnotes

Endnotes should be designated within the text using a superscript lowercase letter and all notes (along with their corresponding letter) should be included in the Endnotes section. Please format this section in a paragraph rather than a list.

- ## References

All references, including URLs, must be numbered consecutively, in square brackets, in the order in which they are cited in the text, followed by any in tables or legends. Each reference must have an individual reference number. Please avoid excessive referencing. If automatic numbering systems are used, the reference numbers must be finalized and the bibliography must be fully formatted before submission.

Only articles, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited; unpublished abstracts, unpublished data and personal communications should not be included in the reference list, but may be included in the text and referred to as "unpublished observations" or "personal communications" giving the names of the involved researchers. Obtaining permission to quote personal communications and unpublished data from the cited colleagues is the responsibility of the author. Footnotes are not allowed, but endnotes are permitted. Journal abbreviations follow Index Medicus/MEDLINE. Citations in the reference list should include all named authors, up to the first six before adding 'et al.'

Any *in press* articles cited within the references and necessary for the reviewers' assessment of the manuscript should be made available if requested by the editorial office.
An Endnote style file is available.
Examples of the *Critical Care* reference style are shown below. Please ensure that the reference style is followed precisely; if the references are not in the correct style they may have to be retyped and carefully proofread.
All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Authors may wish to make use of reference management software to ensure that reference lists are correctly formatted. An example of such software is Papers, which is part of Springer Science+Business Media.

- **Examples of the *Critical Care* reference style**

*Article within a journal*

Smith JJ. The world of science. Am J Sci. 1999;36:234-5.

*Article within a journal (no page numbers)*

Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Medicine. 2013;11:63.

*Article within a journal by DOI*

Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

*Article within a journal supplement*

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.

*Book chapter, or an article within a book*

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

*OnlineFirst chapter in a series (without a volume designation but with a DOI)*

Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. Top Curr Chem. 2007. doi:10.1007/128_2006_108.

*Complete book, authored*

Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

*Online document*

Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. http://www.rsc.org/dose/title of subordinate document. Accessed 15 Jan 1999.

*Online database*

Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998. http://www.healthwise.org. Accessed 21 Sept 1998.

*Supplementary material/private homepage*

Doe J. Title of supplementary material. 2000. http://www.privatehomepage.com. Accessed 22 Feb 2000.

*University site*

Doe, J: Title of preprint. http://www.uni-heidelberg.de/mydata.html (1999). Accessed 25 Dec 1999.

*FTP site*

Doe, J: Trivial HTTP, RFC2169. ftp://ftp.isi.edu/in-notes/rfc2169.txt (1999). Accessed 12 Nov 1999.

*Organization site*

ISSN International Centre: The ISSN register. http://www.issn.org (2006). Accessed 20 Feb 2007.

*Dataset with persistent identifier*

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (Sorghum bicolor). GigaScience Database. 2011. http://dx.doi.org/10.5524/100012.

## • Preparing illustrations and figures

Illustrations should be provided as separate files, not embedded in the text file. Each figure should include a single illustration and should fit on a single page in portrait format. If a figure consists of separate parts, it is important that a single composite illustration file be submitted which contains all parts of the figure. There is no charge for the use of color figures.

Please read our figure preparation guidelines for detailed instructions on maximising the quality of your figures.

- **Formats**

The following file formats can be accepted:

- PDF (preferred format for diagrams)
- DOCX/DOC (single page only)
- PPTX/PPT (single slide only)
- EPS
- PNG (preferred format for photos or images)
- TIFF
- JPEG
- BMP

*Critical Care* will edit all figures supplied by the author. For this reason it is especially important that authors should supply figures in vector form, to facilitate such editing.

- **Figure legends**

The legends should be included in the main manuscript text file at the end of the document, rather than being a part of the figure file. For each figure, the following information should be provided: Figure number (in sequence, using Arabic numerals - i.e. Figure 1, 2, 3 etc.); short title of figure (maximum 15 words); detailed legend, up to 300 words.

**Please note that it is the responsibility of the author(s) to obtain permission from the copyright holder to reproduce figures or tables that have previously been published elsewhere.**

## • Preparing tables

Each table should be numbered and cited in sequence using Arabic numerals (i.e. Table 1, 2, 3 etc.). Tables should also have a title (above the table) that summarises the whole table; it should be no longer than 15 words. Detailed legends may then follow, but they should be concise. Tables should always be cited in text in consecutive numerical order.

Smaller tables considered to be integral to the manuscript can be pasted into the end of the document text file, in A4 portrait or landscape format. These will be typeset and displayed in the final published form of the article. Such tables should be formatted using the 'Table object' in a word processing program to ensure that columns of data are kept aligned when the file is sent electronically for review; this will not always be the case if columns are generated by simply using tabs to separate text. Columns and rows of data should be made visibly distinct by ensuring that the borders of each cell display as black lines. Commas should not be used to indicate numerical values. Color and shading may not be used; parts of the table can be highlighted using symbols or bold text, the meaning of which should be explained in a table legend. Tables should not be embedded as figures or spreadsheet files.

Larger datasets or tables too wide for a landscape page can be uploaded separately as additional files. Additional files will not be displayed in the final, laid-out PDF of the article, but a link will be provided to the files as supplied by the author.

Tabular data provided as additional files can be uploaded as an Excel spreadsheet (.xls ) or comma separated values (.csv). As with all files, please use the standard file extensions.

## Preparing additional files

Although *Critical Care* does not restrict the length and quantity of data included in an article, we encourage authors to provide datasets, tables, movies, or other information as additional files.

Please note: All Additional files **will be published** along with the article. Do not include files such as patient consent forms, certificates of language editing, or revised versions of the main manuscript document with tracked changes. Such files should be sent by email to editorial@ccforum.com, quoting the Manuscript ID number.

Results that would otherwise be indicated as "data not shown" can and should be included as additional files. Since many weblinks and URLs rapidly become broken, *Critical Care* requires that supporting data are included as additional files, or deposited in a recognized repository. Please do not link to data on a personal/departmental website. The maximum file size for additional files is 20 MB each, and files will be virus-scanned on submission.

Additional files can be in any format, and will be downloadable from the final published article as supplied by the author.

Certain supported files formats are recognized and can be displayed to the user in the browser. These include most movie formats (for users with the Quicktime plugin), mini-websites prepared according to our guidelines, chemical structure files (MOL, PDB), geographic data files (KML).

If additional material is provided, please list the following information in a separate section of the manuscript text:

- File name (e.g. Additional file 1)
- File format including the correct file extension for example .pdf, .xls, .txt, .pptx (including name and a URL of an appropriate viewer if format is unusual)
- Title of data
- Description of data

Additional files should be named "Additional file 1" and so on and should be referenced explicitly by file name within the body of the article, e.g. 'An additional movie file shows this in more detail [see Additional file 1]'.

### Additional file formats

Ideally, file formats for additional files should not be platform-specific, and should be viewable using free or widely available tools. The following are examples of suitable formats.

- Additional documentation
  - PDF (Adode Acrobat)
- Animations
  - SWF (Shockwave Flash)
- Movies
  - MP4 (MPEG 4)
  - MOV (Quicktime)
- Tabular data
  - XLS, XLSX (Excel Spreadsheet)
  - CSV (Comma separated values)

As with figure files, files should be given the standard file extensions.

### Mini-websites

Small self-contained websites can be submitted as additional files, in such a way that they will be browsable from within the full text HTML version of the article. In order to do this, please follow these instructions:

1. Create a folder containing a starting file called index.html (or index.htm) in the root.
2. Put all files necessary for viewing the mini-website within the folder, or sub-folders.
3. Ensure that all links are relative (ie "images/picture.jpg" rather than "/images/picture.jpg" or "http://yourdomain.net/images/picture.jpg" or "C:\Documents and Settings\username\My Documents\mini-website\images\picture.jpg") and no link is longer than 255 characters.
4. Access the index.html file and browse around the mini-website, to ensure that the most commonly used browsers (Internet Explorer and Firefox) are able to view all parts of the mini-website without problems, it is ideal to check this on a different machine.
5. Compress the folder into a ZIP, check the file size is under 20 MB, ensure that index.html is in the root of the ZIP, and that the file has .zip extension, then submit as an additional file with your article.

## Style and language

### General

Currently, *Critical Care* can only accept manuscripts written in English. Spelling should be US English or British English, but not a mixture. There is no explicit limit on the length of articles submitted, but authors are encouraged to be concise.

### Language editing

For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz. BioMed Central has arranged a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. Please contact Edanz directly to make arrangements for editing, and for pricing and payment details.

### Help and advice on scientific writing

The abstract is one of the most important parts of a manuscript. For guidance, please visit our page on Writing titles and abstracts for scientific articles.

Tim Albert has produced for BioMed Central a list of tips for writing a scientific manuscript. American Scientist also provides a list of resources for science writing. For more detailed guidance on preparing a manuscript and writing in English, please visit the BioMed Central author academy.

### Abbreviations

Abbreviations should be used as sparingly as possible. They should be defined when first used and a list of abbreviations can be provided following the main manuscript text.

### Typography

- Please use double line spacing.
- Type the text unjustified, without hyphenating words at line breaks.
- Use hard returns only to end headings and paragraphs, not to rearrange lines.
- Capitalize only the first word, and proper nouns, in the title.

- All pages should be numbered.
- Use the *Critical Care* reference format.
- Footnotes are not allowed, but endnotes are permitted.
- Please do not format the text in multiple columns.
- Greek and other special characters may be included. If you are unable to reproduce a particular special character, please type out the name of the symbol in full. **Please ensure that all special characters used are embedded in the text, otherwise they will be lost during conversion to PDF.**

## Units

SI units should be used throughout (liter and molar are permitted, however).

# Addendum C: Abstract of presentation

**Paper was presented at the Critical Care Society of Southern Africa congress July 2015**

## Abstract of presentation

### Screening critical ill patients with an adapted early mobility readiness protocol ensures safety of a therapeutic early mobility position

Conradie, Elmarie*; Dr Fourie, Cate; Prof. Hanekom, Susan.

*University of Stellenbosch, Department of Physiotherapy.*
vanheerden.elmarie@gmail.com

**Background:** The effect of the 45° semi-recumbent position on the haemodynamic stability of critically ill patients are questioned. This routine nursing position, could minimise the negative effects bed rest has on the cardiac and pulmonary systems.

**Aim:** The aim was to evaluate the feasibility of an *adapted early mobility readiness protocol* (protocol) and the effect of a *therapeutic early mobility position* (testing position) on two haemodynamic parameters, the mean arterial pressure (MAP) and central venous oxygen saturation ($ScvO_2$%).

**Methods:** Twice weekly, all patients nursed in the surgical and respiratory units were screened with the protocol. Patients, who passed the protocol and inclusion criteria, were tested in the baseline nursing position followed by the testing position. Haemodynamic parameters were measured at 0, 3 and 10 minutes.

**Results:** We screened 138 patients. Eleven patients passed, male/female (9/2) with a median (range) age of 47 (20-67) years. The mean MAP (95%CI) increased from 95.87 mmHg (91.72 mmHg-100.03 mmHg) to 97.86 mmHg (94.16 mmHg-101.57mmHg) and the mean $ScvO_2$% (95%CI) increased from 81.43 (79.43%-83.42%) to 82.06 (79.43%-84.2%) when the baseline nursing position was followed by the testing position.

**Conclusion:** Patients who passed the protocol were not physiologically challenged when placed in the testing position. The protocol can be used by clinicians to identify patients suitable for the testing position. Additional work is needed to investigate the outcome of patients nursed in this position.

**Southern African Journal of Critical Care 2015;31(1)nr5:24-28.**

# Addendum D: Pulmonary compliance

## Dynamic pulmonary compliance

The results of the dynamic pulmonary compliance were not reported on in Chapter 3 due to the insufficient size of the sample as well as not being a primary outcome.

## Measurement of dynamic pulmonary compliance

The Tidal volume ($V_T$), Peak inspiratory pressure (PIP) and PEEP were recorded from ventilator using three ventilator breaths at the 8 minute time interval in the baseline nursing position and the therapeutic early mobility position. The dynamic pulmonary compliance ($C_{dyn}$) was calculated using the following equation:

$$C_{dyn} = \frac{V_T}{PIP - PEEP}$$

### *Results*

There was a decrease noted in the mean $C_{dyn}$ when placing a participant in the therapeutic early mobility position. This difference did not reach statistical significance.

**Table 4.6: Results of dynamic pulmonary compliance**

| Variable | Valid N | Mean | Confidence Interval | | Std. Dev. |
|---|---|---|---|---|---|
| | | | -95% | 95% | |
| $C_{dyn}$ BP | 11 | 56.35 | 39.54 | 73.16 | 25.02 |
| $C_{dyn}$ TP | 11 | 55.38 | 38.42 | 72.33 | 25.23 |
| $C_{dyn}$ Mean Difference | 11 | -0.97 | -4.39 | 2.44 | 5.09 |

**Legend:**
**$C_{dyn}$ =** Dynamic pulmonary compliance; **BP** = Baseline nursing position; **TP** = Therapeutic early mobility position; **n** = number; **Std. Dev.** = Standard deviation.

### *Conclusion*

Placing a participant in the therapeutic early mobility position decreased the pulmonary compliance of participants. A possible reason could be the short time spent in the position and the small sample size.

# Addendum E: Summary of search strategies

**Search strategy: Data bases searched**

**CINALH**

Limit applied to data base:

Species: Human

Age: ALL adults

Language: English

| Search terms | HITS |
|---|---|
| 1. (backrest elevation*) AND (mechanical* ventilated OR critical* ill*) | 20 |
| 2. (head-up position*) AND (mechanical* ventilated OR critical* ill*) | 2 |
| 3. (beach chair position*) AND (mechanical* ventilated OR critical* ill*) | 1 |
| 4. (prone position*) AND (mechanical* ventilated OR critical* ill*) | 17 |
| 5. (lateral position*) AND (critical* ill* OR mechanical* ventilated) | 35 |
| 6.(semirecumbent position*) AND (critical* ill* OR mechanical* ventilated) | 23 |
| 7. (supine position*) AND (critical* ill* OR mechanical* ventilated) | 40 |
| 8. (head down tilt) AND (critical* ill* OR mechanical* ventilated) | 28 |
| Total | 166 |

**Scopus**

| Search terms | HITS |
|---|---|
| 1.(prone position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT(animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT (infant) | 16 |
| 2. (lateral position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT (animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) | 10 |
| 3.(semirecumbent position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT (animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT (infant) | 11 |
| 4. (supine position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*) | 28 |
| 5.(head down position*) AND (critical* ill* OR mechanical* ventilated) AN (adult*)) AN D NOT (animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT (infant) | 1 |

| | |
|---|---|
| 6. (beach chair position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT (animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT (infant) | 0 |
| 7. (head up position*) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT (animals) AND NOT (baby) AND NOT(children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT (infant) | 5 |
| 8. (back rest elevation) AND (critical* ill* OR mechanical* ventilated) AND (adult*)) AND NOT (animals) AND NOT (baby) AND NOT (children) AND NOT (pediatric) AND NOT (neonatal) AND NOT (newborn) AND NOT(infant) | 0 |
| Total | 71 |

**Science Direct**

| Search terms | HITS |
|---|---|
| 1. prone position AND "critical illness" OR "mechanically ventilated" AND adults AND NOT animals AND NOT babies AND NOT children AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 67 |
| 2. "lateral position" AND "mechanically ventilated" AND "critical illness"AND (adult) and NOT (animals) and NOT (baby) and NOT (infant) and NOT (children) and NOT (neonatal) | 3 |
| 3. (semi-recumbent) AND (critical* ill* OR mechanical* ventilated) AND (adult) AND NOT animals AND NOT baby AND NOT child AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 45 |
| 4. (supine position*) AND (critical* ill* OR mechanical* ventilated) AND (adults) AND NOT animal AND NOT baby AND NOT children AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 317 |

| | |
|---|---|
| 5. (head down tilt) AND (critical* ill* OR mechanical* ventilated) AND (adults) AND NOT animal AND NOT baby AND NOT children AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 19 |
| 6. (beach-chair-position) AND (critical* ill* OR mechanical* ventilated) AND (adults) AND NOT animal AND NOT baby AND NOT children AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 1 |
| 7. (back rest elevation) AND (critical illness OR mechanically ventilated) AND (adults) AND NOT animals AND NOT babies AND NOT children AND NOT infant AND NOT neonatal AND NOT pediatric AND NOT newborn AND NOT premature | 22 |
| Total | 474 |

**Google scholar**

| Search terms | HITS |
|---|---|
| 1. (icu OR (critically ill)) AND (mechanical ventilation) AND (therapeutic positioning OR (body positioning)) AND (supine OR prone OR lateral OR (head-down tilt) position) -infants -babies -neonatal -newborn -children -animals –books) | 95 |
| 2. (icu OR (critically ill)) AND (mechanical ventilation) AND (therapeutic positioning OR (body positioning)) AND (semi-recumbent OR head-up OR beach chair position) -infants -babies -neonatal -newborn -children -animals –books) | 30 |
| Total | 125 |

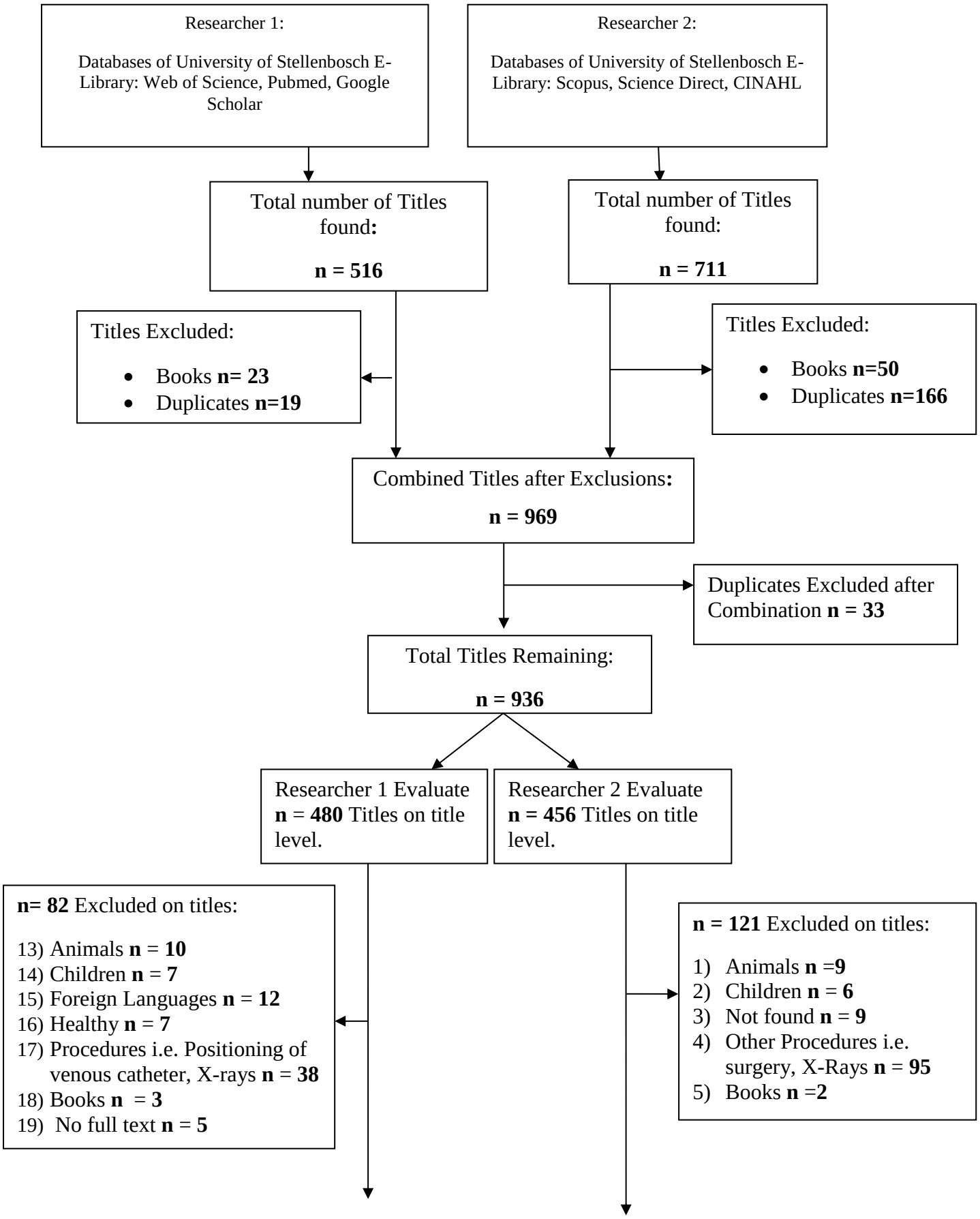
**Pubmed**

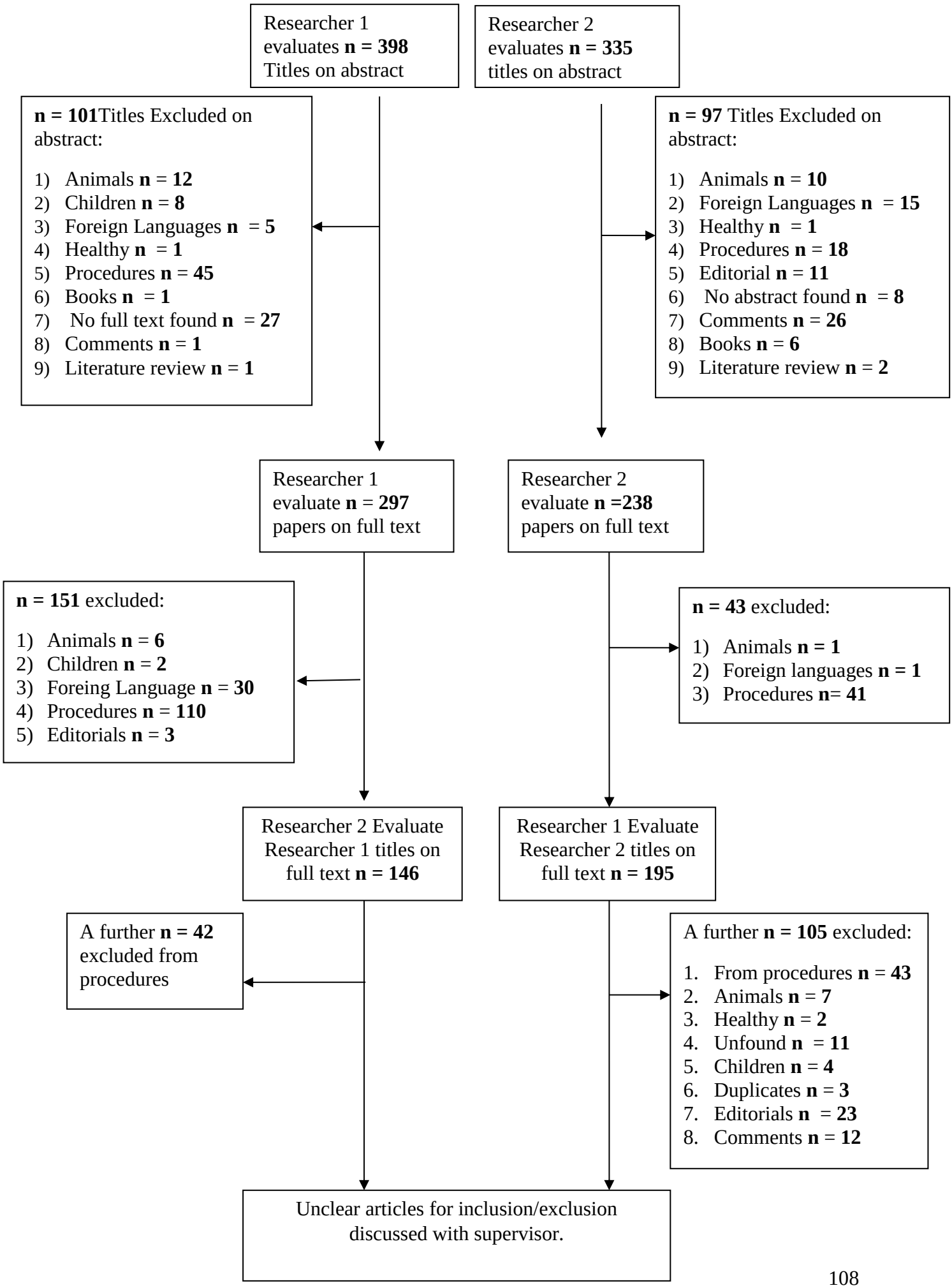
| Search terms | HITS |
|---|---|
| 1.("Critical Illness" AND "Adult" AND "Patient Positioning" AND "Supine Position" OR "Prone Position" OR "Head-Down Tilt") AND "Respiration, Artificial" NOT "Infant" NOT "Infant, Newborn" NOT "Pediatrics" | 362 |
| Total | 362 |

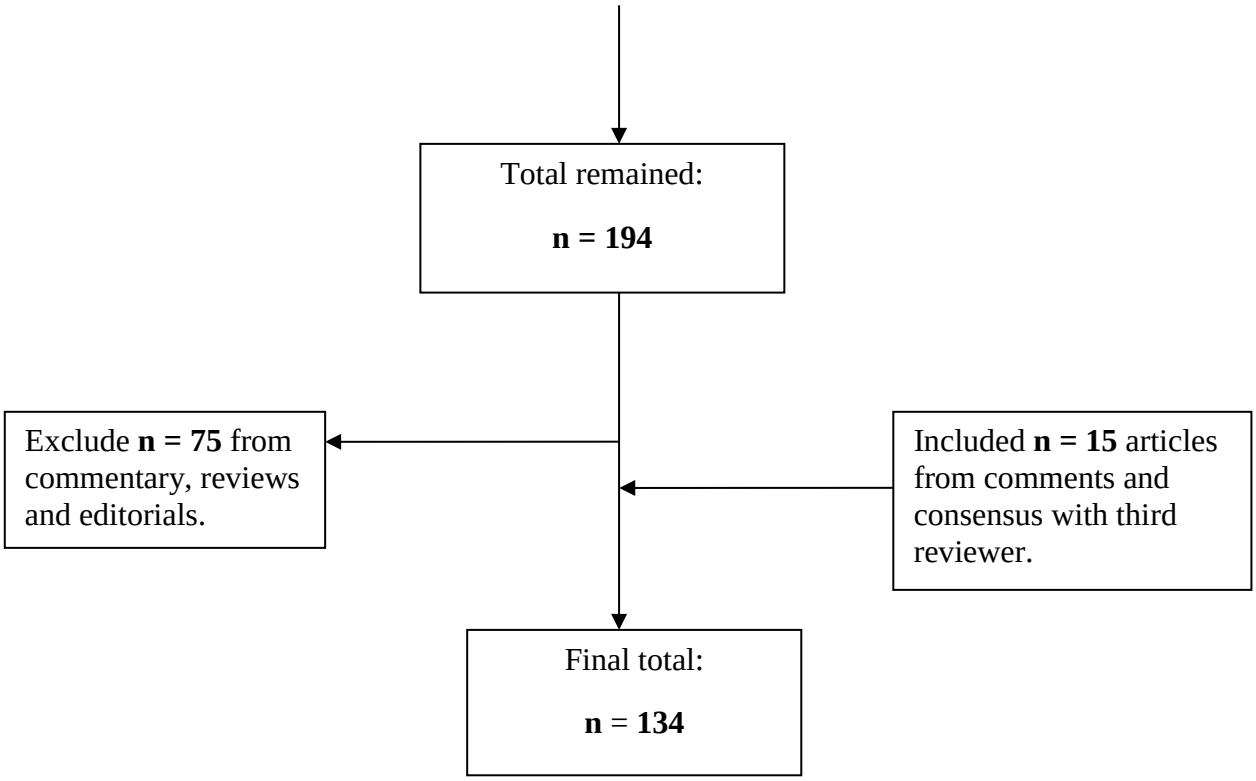
**Web of Science**

| Search terms | HITS |
|---|---|
| (intensive care unit) AND (critical* ill*) AND (mechanical* ventilat*) AND (body position*) NOT (babies) NOT (infants) NOT (newborns) NOT (children) NOT (preterm babies) | 29 |
| Total | 29 |

## Addendum F: Complete flowchart of paper selection







# Addendum G: Quantitative Critical Review Form

## Critical Review Form – Quantitative Studies

**Law, M., Stewart, D., Pollock, N., Letts, L. Bosch, J., & Westmorland, M.**

**McMaster University**

- Adapted Word Version Used with Permission –Instructions: Use tab or arrow keys to move between fields, mouse or spacebar to check/uncheck boxes.

| | |
|---|---|
| **STUDY PURPOSE**<br><br>1. Was the purpose stated clearly?<br>Yes<br>No<br>**LITERATURE**<br>2. Was relevant background literature reviewed?<br>Yes<br>No | Outline the purpose of the study. How does the study apply to your research question?<br><br>Describe the justification of the need for this study: |
| **3. DESIGN appropriate?**<br><br>Randomized (RCT)<br>cohort<br>single case design<br>before and after<br>case-control<br>cross-sectional<br>case study | Describe the study design. Was the design appropriate for the study question? (e.g., for knowledge level about this issue, outcomes, ethical issues, etc.):<br><br>Specify any biases that may have been operating and the direction of their influence on the results: |

<table>
<tr><td>4. SAMPLE stated?<br><br>5. Was the sample described in detail?<br>Yes<br>No<br>6. Was sample size justified?<br>Yes<br>No<br>N/A<br>7. Was sample randomly allocated?<br>Yes<br>No<br>8. Was sample randomised to position?<br>Yes<br>No<br>9. Was blinding used?<br>Yes<br>No</td><td colspan="2">Sampling (who; characteristics; how many; how was sampling done?) If more than one group, was there similarity between the groups?:</td></tr>
<tr><td rowspan="2">OUTCOMES<br><br>10. Were the outcome measures reliable?<br>Yes<br>No<br>Not addressed<br>11. Were the outcome measures valid?<br>Yes<br>No<br>Not addressed</td><td colspan="2">Specify the frequency of outcome measurement (i.e., pre, post, follow-up):</td></tr>
<tr><td>Outcome areas:</td><td>List measures used.:</td></tr>
</table>

| | |
|---|---|
| **INTERVENTION**<br><br>12. Intervention was described in detail?<br>Yes<br>No<br>Not addressed<br>13. Contamination was avoided?<br>Yes<br>No<br>Not addressed<br>N/A<br>14. Cointervention was avoided?<br>Yes<br>No<br>Not addressed<br>N/A | Provide a short description of the intervention (focus, who delivered it, how often, setting). Could the intervention be replicated in practice? |
| **RESULTS**<br><br>15. Results were reported in terms of statistical significance?<br>Yes<br>No<br>N/A<br>Not addressed<br>16.Were the analysis method(s) appropriate?<br>Yes<br>No<br>Not addressed | What were the results? Were they statistically significant (i.e., $p < 0.05$)? If not statistically significant, was study big enough to show an important difference if it should occur? If there were multiple outcomes, was that taken into account for the statistical analysis? |
| 17. Clinical importance was reported?<br><br>Yes<br>No<br>Not addressed | What was the clinical importance of the results? Were differences between groups clinically meaningful? (if applicable) |
| 18. Drop-outs were reported?<br>Yes<br>No | Did any participants drop out from the study? Why? (Were reasons given and were drop-outs handled appropriately?) |
| **CONCLUSIONS AND IMPLICATIONS**<br>19. Conclusions were appropriate given study methods and results<br>Yes<br>No | What did the study conclude? What are the implications of these results for practice? What were the main limitations or biases in the study? |
| 20. Adverse events reported<br>Yes<br>No | |

# Addendum H: Table 3.12: Evaluation of papers using the Quantitative Critical review form

| Study | Safety of position | | | | | | Clinical outcome | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Driscoll et al [2] | Moraine et al [72] | Giuliano et al [8] | Blissit et al [10] | Maas et al [17] | Gocze et al [34] | Torres et al [3] | Orozco-Levi et al [172] | Drakulovic et al [65] | Van Nieuwenhoven et al [19] | Libby Keeley [128] | Caraviello et al [5] |
| ***1. Purpose of study was clearly stated?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***2. Literature review were appropriately?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (-) | (+) | (+) | (+) | (+) |
| ***3. Design was appropriate?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***4. Sample size was stated?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***5. Sample were describe appropriately?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***6. Size of sample was justified?*** | (+) | (+) | (+) | (+) | (-) | (-) | (-) | (-) | (+) | (+) | (+) | (+) |
| ***7. Randomly allocated?*** | (+) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |
| ***8. Randomised to position?*** | (+) | (+) | (-) | (-) | (-) | (+) | (+) | (+) | (+) | (+) | (+) | (-) |
| ***9. Blinded?*** | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (+) | (+) | (-) | (-) |
| ***10. Outcome measures used was reliable?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***11. Outcome measures used was valid?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***12. Intervention descriped?*** | (+) | (+) | (-) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***13. Contamination avoided?*** | NR(-) | (+) | NR(-) | (+) | (+) | (+) | (+) | NR(-) | (+) | (+) | (+) | (+) |
| ***14. Co-intervention avoided?*** | NR(-) | (+) | NR(-) | (+) | (+) | (+) | NR(-) | NR(-) | (+) | (+) | (+) | (+) |
| ***15. Results were reported in terms of significance?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***16. Analysis method appropriate?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***17. Clinical importance reported were appropropriate?*** | (+) | (+) | (+) | (+) | (+) | (+) | (+) | (-) | (+) | (+) | (+) | (+) |
| ***18. Drop outs were reported?*** | (-) | (+) | (-) | (+) | (-) | (+) | NR(-) | NR (-) | (+) | (+) | (+) | (+) |
| ***19. Conclusions were relevent and appropriate?*** | (+) | (+) | (+) | (+) | (+) | (-) | (+) | (+) | (+) | (+) | (+) | (+) |
| ***20. Adverse events reported?*** | (-) | (-) | (+) | (+) | (+) | (+) | (-) | (-) | (+) | (-) | (-) | (-) |
| **Total CAT score /20** | **15** | **17** | **13** | **17** | **15** | **16** | **14** | **11** | **19** | **18** | **17** | **17** |
| ***Total CAT score %*** | **75%** | **85%** | **65%** | **85%** | **75%** | **80%** | **70%** | **55%** | **95%** | **90%** | **85%** | **85%** |

**Legend:**

**(+)** = YES; **(-)** = NO; **NR** = Not Reported also seen as (-).

# Addendum I: Table 3.13: NHMRC Evidence Hierarchy: designations of 'levels of evidence' according to type of research question (including explanatory notes)

| Level | Intervention [1] | Diagnostic accuracy [2] | Prognosis | Aetiology [3] | Screening /Intervention |
|---|---|---|---|---|---|
| I [4] | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies | A systematic review of level II studies |
| II | A randomised controlled trial | A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among consecutive persons with a defined clinical presentation[6] | A prospective cohort study[7] | A prospective cohort study | A randomised controlled trial |
| III-1 | A pseudorandomised controlled trial (i.e. alternate allocation or some other method) | A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among non-consecutive persons with a defined clinical presentation[6] | All or none[8] | All or none[8] | A pseudorandomised controlled trial (i.e. alternate allocation or some other method) |
| III-2 | A comparative study with concurrent controls:<br>▪ Non-randomised, experimental trial[9]<br>▪ Cohort study<br>▪ Case-control study<br>▪ Interrupted time series with a control group | A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence | Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial | A retrospective cohort study | A comparative study with concurrent controls:<br>▪ Non-randomised, experimental trial<br>▪ Cohort study<br>▪ Case-control study |
| III-3 | A comparative study without concurrent controls:<br>▪ Historical control study<br>▪ Two or more single arm study[10]<br>▪ Interrupted time series without a parallel control group | Diagnostic case-control study[6] | A retrospective cohort study | A case-control study | A comparative study without concurrent controls:<br>▪ Historical control study<br>▪ Two or more single arm study |
| IV | Case series with either post-test or pre-test/post-test outcomes | Study of diagnostic yield (no reference standard)[11] | Case series, or cohort study of persons at different stages of disease | A cross-sectional study or case series | Case series |

## Explanatory notes

[1] Definitions of these study designs are provided on pages 7-8 *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000b) and in the accompanying Glossary.

**[2]** These levels of evidence apply only to studies of assessing the accuracy of diagnostic or screening tests. To assess the overall effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes (Medical Services Advisory Committee 2005, Sackett and Haynes 2002). The evidence hierarchy given in the 'Intervention' column should be used when assessing the impact of a diagnostic test on health outcomes relative to an existing method of diagnosis/comparator test(s). The evidence hierarchy given in the 'Screening' column should be used when assessing the impact of a screening test on health outcomes relative to no screening or opportunistic screening.

[3] If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (eg. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

[4] A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review *quality* should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

[5] The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study (Whiting et al 2003).

[6] Well-designed population based case-control studies (eg. population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias or spectrum effect because the spectrum of study participants will not be representative of patients seen in practice (Mulherin and Miller 2002).

[7] At study inception the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in *both* arms of the trial would also meet the criterion for this level of evidence.

[8] All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

[9] This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C with statistical adjustment for B).

[10] Comparing single arm studies ie. case series from two studies. This would also include unadjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C but where there is no statistical adjustment for B).

11 Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. These may be the only alternative when there is no reliable reference standard.

**Note A:** Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms (and other outcomes) are rare and cannot feasibly be captured within randomised controlled trials, in which case lower levels of evidence may be the only type of evidence that is practically achievable; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

**Note B:** When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

**Note c:** Each individual study that is attributed a "level of evidence" should be rigorously appraised using validated or commonly used checklists or appraisal tools to ensure that factors other than study design have not affected the validity of the results.

**Source:** Hierarchies adapted and modified from: NHMRC 1999; Bandolier 1999; Lijmer et al. 1999; Phillips et al. 2001.

**Website:** https://www.health.qld.gov.au/healthpact/docs/gen-docs/lvl-of-evidence.pdf

# Addendum J: Table 3.14: Summary of inclusion criteria of papers included

| Study | Inclusion criteria | | | | |
|---|---|---|---|---|---|
| | **Ventilatory support** | **Pulmonary** | **Cardiac** | **Vascular** | **Other** |
| Drakulovic et al[65] | • Intubated | | | | • Admitted to the ICU. |
| Giuliano et al[8] | | | • CCO catheter in place. | | |
| Van Nieuwenhoven et al[19] | • Intubated within 24 hrs with expected duration of ventilation of at least 48 hrs. | | | | • Undergoing selective decontamination of the digestive tract. |
| Maas et al[17] | | • SIMV;<br>• $PaCO_2$ = 40 -45mmHg;<br>• TV = 6–8 mLkg;<br>• RR = 12–14/min;<br>• $FiO_2$ = 0.4;<br>• PEEP = 5cm $H_2O$. | • Symptomatic coronary artery disease without previous myocardial infarction;<br>• On β- adrenergic block after elective coronary artery bypass surgery or aortic valve replacement. | | |
| Gocze et al[34] | • Over the age of 18 yrs. | | • Haemodynamic stability,stable MAP by constant inotropic support without additional fluid administration. | • CVP in situ in Superior vena cava. | |

**Legend:**

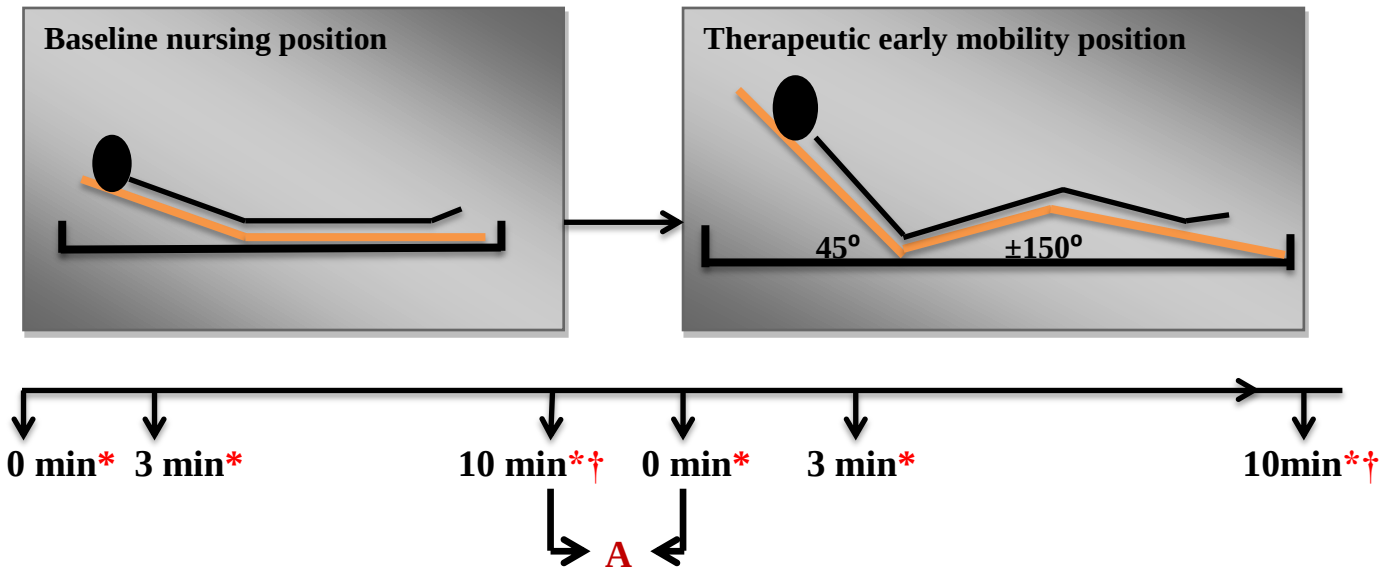
**CCO =** Continuous cardiac output; **ICU** = Intensive care unit; **hrs** = hours; **SIMV =** Synchronised intermittent mandatory ventilation mode; **$PaCO_2$ =** Partial Arterial Carbon dioxide; **TV** = Tidal volume; **RR** = Respiratory rate; **$FiO_2$** = Fractional inspired oxygen content; **PEEP** = Positive end expiratory pressure; **β** = Beta; **yrs =** years; **MAP** = Mean arterial pressure; **CVP** = Central venous pressure.

# Addendum K: Table 3.15: Summary of exclusion criteria of papers included

| Study | Exclusion criteria | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Ventilatory support** | **Pulmonary** | **Cardiac** | **Vascular** | **Orthopedic** | **Neurological** | **Other** |
| Drakulovic et al[65] | Previous intubation (<30 days) | Change in position for > 45min, death during protocol, and weaning trial. | | | | Neurosurgical interventon (<7 days). | Abdominal surgery (<7 days). |
| | Termination of the protocol | | | | | | Shock refractory to vasoactive drugs or volume therapy |
| Giuliano et al[8] | | Within 1 hr of measurement titration of medication which affects on HR or BP. | HR >120 or < 60 bpm, MAP<60 mmHg, CO <2 or >15 lpm, PCWP <10 mmHg. | Hematocrit: <28 or >55 mg/dl. | | | Temp. <35°C or >39°C, CVP < 4 or >20 mmHg. |
| | | | Within 1 hr of measurement titration of medication which affects on HR or BP. | | | | |
| | | | Recent start/completion (within 4 hrs of measurement) of medication affecting HR or BP. | | | | |
| | | | PCWP tracing obtained using <1.25 or >1.5 mls air, Premature ventricular complexes > 3/min. | | | | |
| Van Nieuwenhoven et al[19] | | Diagnosis of VAP | | | | | Could not be randomized. |
| Maas et al[17] | | | CHF, aortic aneurysm, extensive, peripheral arterial occlusive disease, or postop valvular insufficiency. | | | | |
| | | | Post -op arrhythmia, with necessity for artificial pacing, or the use of a cardiac assist device | | | | |
| Gocze et al[34] | | Respiratory support | Acute cardiovascular instability. | Hose with pump-driven circulatory system | Immobilized: spinal injuries or unstable pelvic fractures. | Traumatic brain injury. | |

**Legend:**
**> =** greater than**; Hrs =** Hours; **min =** minute; **HR =** Heart rate; **MAP =** Mean arterial pressure; **CO =** Cardiac Output; **PCWP =** Pulmonary wedge pressure; **bpm** = beats per minute; **mmHg** = millimetre mercury; **mg/dl** = microgram per decilitre; **lpm =** litre per minute; **°c** = Degree of temperature; **mls =** Millilitres; **VAP =** Ventilator associated pneumonia; **CHF =** Congestive heart failure; **Postop** = Post operative.

# Addendum L: Intervention Flow Diagram




**Legend:**
**(A) =** 90s pause with 15° Increase / decrease until 45° semi-recumbent, then knees bend until maximum 150°; (*) = Measurements at 0, 3 and 10 min: Central venous oxygen saturation; Mean arterial pressure; Heart rate; Systolic blood pressure; Diastolic blood pressure; Peripheral capillary oxygen saturation and $SpO_2$ and adverse events; (†) = Measurement at 10 min: Partial oxygen content in arterial blood.

# Addendum M: Ethical Permission:

# 1) Health Research Ethics Committee 2

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jou kennisvennoot • your knowledge partner

## Approval Notice
### Response to Deferral

05-Mar-2014
van Heerden, Elmarie

**Ethics Reference #: S13/10/194**

**Title:** **The effect of a therapeutic early mobility position on the hemodynamic stability and pulmonary compliance in a critically ill patient population**

Dear Ms Elmarie van Heerden,

The **Response to Deferral** - ***(New Application)*** received on , was reviewed by members of **Health Research Ethics Committee 2** via Expedited review procedures on **05-Mar-2014** and was approved.
Please note the following information about your approved research protocol:

Protocol Approval Period: **05-Mar-2014 -05-Mar-2015**

Please remember to use your **protocol number** (**S13/10/194**) on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

**After Ethical Review:**
Please note a template of the progress report is obtainable on www.sun.ac.za/rds and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.
Translation of the consent document to the language applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

**Provincial and City of Cape Town Approval**

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 483 9907) and Dr Helene Visser at City Health (Helene.Visser@capetown.gov.za Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.
For standard HREC forms and documents please visit: www.sun.ac.za/rds
If you have any questions or need further assistance, please contact the HREC office at 0219389207.

**Included Documents:**

CV - van Heerden

CV - Fourie

Declaration - Fourie

Protocol

Declaration - Hanekom

Application form CV - Hanekom

Protocol Synopsis

Declaration - van Heerden

Health General Checklist

Sincerely, Mertrude Davids
HREC Coordinator

Health Research

Ethics Committee

**Ethical Permission:**

## 2) Health & Research Council Provincial Administration Tygerberg Hospital

Western Cape Government
Health

Tygerberg Hospital

REFERENCE: RESEARCH PROJECTS
ENQUIRIES: DR K MAART
TELEPHONE: 021 938 4141

**ETHICS NO: S13/10/194**

**The effect of a therapeutic early mobility position on the hemodynamic stability and pulmonary compliance in a critically ill patient population.**

Dear Ms E Van Heerden

**PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL**

In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital

**DR D ERASMUS**
**CHIEF EXECUTIVE OFFICER**
Date: 22 May 2014

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# Addendum N: Participant Information Leaflet and Consent Form

**TITLE OF THE RESEARCH PROJECT:**

**The effect of a therapeutic early mobility position on the hemodynamic stability (normal blood pressure and oxygen content of blood) and on the pulmonary compliance (lung function) in a critically ill patient population.**

**REFERENCE NUMBER: S13/10/194**

**PRINCIPAL INVESTIGATOR: Elmarie van Heerden**

**ADDRESS: Department of Physiotherapy, University of Stellenbosch**

**CONTACT NUMBER: 021-938 9302**

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research is about and how you could be involved. Also, your taking part is **entirely your own choice** and you are free to say no to take part. If you say no, this will not affect you in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part. A surrogate / proxy who are an experience doctor on the ward, with the necessary expertise, not involved in this study will provide consent for you, till you as a patient can give consent at an appropriate time. If you say no retrospectively, all your data will be destroyed.
This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be carried out according to the ethical (moral) guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research as well as the Bill of Rights and the National Health Act of South Africa.

**What is this research study all about?**

This study will be carried out in the surgical or medical units of Tygerberg Hospital and 73 patients will be recruited for the study.

The aim of this study is to find out if the therapeutic early mobility position has an effect on the hemodynamic stability (normal pressure and oxygen content) of a critically ill adult patient.

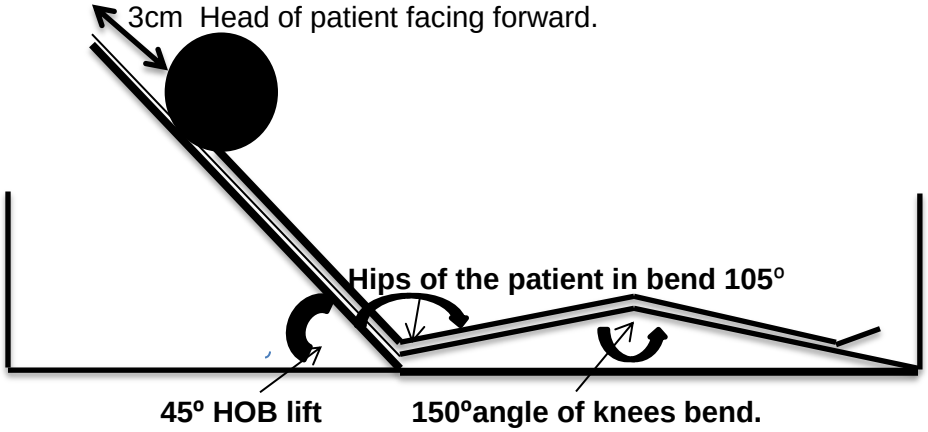



**Fig 1:** *A therapeutic early mobility position* is defined as having the patient's head of the bed elevated to 45º and the knees at 150º angle and the hips at $105^0$ angle.

**Hemodynamic stability** refers to a stable blood pressure and vital signs of a patient.

The **therapeutic early mobility position** refers to 45 degrees lift of the upper body and knees bend at a 150 degrees angle and hips bend at a 105 degrees angle.

The principal investigator will visit the units every morning to screen potential study patients based on early mobility protocol 8 hours after admission to the unit and will continue twice daily till 36 hours. If you pass this process you will be screened for the inclusion and exclusion criteria. This process will be completed in agreement and advice of the unit's doctor to ensures your safety and that no risks are taken. Baseline data, including age, height, date and time of study, gender, Acute Physiology And Chronic Evaluation II(critically functioning and chronic evaluation) (APACHE II score) admission diagnosis, time on ventilator, ventilation mode, level of positive end expiratory pressure, type and dose of sedation, RASS and length of stay and volume status will be collected by principal investigator.

The research assistant will measure and write down the degrees of height of the baseline position before the start of the study. In addition she will position you in the position being tested. MAP (blood pressures), $ScvO_2\%$ (blood oxygen content) and ABG will be recorded in the baseline (current nursing) position and in the position being tested at 0 min, 3 and 10 minutes. The principal investigator will write down the MAP(blood pressures), heart rate and measure the oxygen at fingertip three times at0 minutes, three and ten minutes from the monitor as well as the dynamic lung function at 8minutes from the ventilator. One millilitres of blood will be drawn by the pathology technician of the ward from the tip of distal part of your CVP line to measure the ScvO2 at 0 minutes, three and ten minutes and from the arterial line at ten minutes. The principal investigator will monitor you, the participant and write down the adverse events, the time it took place, duration of the adverse event and the action taken to improve it.

The wards medical and nursing team will be available to respond immediately if any adverse events happen. Adverse events refers to any negative effects that may occurs during the study, like pain, discomfort, increase in breath rate or heart rate, fall or increase in blood pressure, air bubbles in the blood, difficulty breathing, blood clots in lung and change in heart rhythm.

**Why have you been invited to participate?**

You have been invited to take part in this study to clear up the question of the effect of a therapeutic early mobility position will have on the **hemodynamic stability (blood pressure and vital signs)** of an adult, critically ill patient. This position is used frequently in the critically ill environment to prevent pneumonia and swallowing of stomach content. A few studies have been done and the changes during this position need to be documented to determine if this standard care needs adjustments.

**What will your responsibilities be?**

You as a participant will be responsible to relax and stay calm during the study procedure and indicate if you experience any discomfort. If you do not want to take part anymore you may say no and discontinue at any given time. If any signs of discomfort are present the study will stop immediate and you will be made comfortable.

**Will you benefit from taking part in this research?**

You will not benefit at the moment but future patients will benefit from the results. This study will indicate if the therapeutic early mobility position can be used as a treatment tool for the same kind of patients or need adjustment or change.

**Are there any risks involved in your taking part in this research?**

The following were identified as potential risks in this study:

- Discomfort,
- Difficulty to breathing,
- Increase in breath rate,
- Fall or increase in blood pressure,
- Fall in oxygen content in blood,
- Fall or increase in heart rate,
- Air bubbles in your blood,
- Sudden change in heart rhythm,
- Heart attack may occur,
- Blood clots in the lung may occur.
- Dizziness, suppression of consciousness or fainting

**If you do not agree to take part, what alternatives do you have?**

You will be nursed in the original nursing (baseline) position chosen that is best for you by the unit's team.

**Who will have access to your medical records?**

All data collected will be kept confidential using a secure, password files on the principal investigator computer. This data will be stored on an external hard drive in a secured password protected file.

Your identity will stay anonymous in the publication or thesis that will be produced from the results of this study. The principal investigator will have access to this information.

**What will happen in the unlikely event of some form of injury occurring as a direct result of your taking part in this research study?**

If any injury occurs during the procedure of this study, the team of the unit will act immediately to ensure your safety and if any adverse event caused permanent harm, you as a participant are covered by the University of Stellenbosch insurance. (Insurance document attached)

**Will you be paid to take part in this study and are there any costs involved?**

No, you will not be paid to take part and there will be no costs involved.

**Is there anything else that you should know or do?**

- You can contact Elmarie van Heerden…... Attel nr 0823761033…… if you have any further queries or encounters any problems.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

## Declaration by participant

By signing below, I ……..……. agree to take part in a research study entitled: The effect of a therapeutic early mobility position on the hemodynamic stability and pulmonary compliance in a critically ill patient population.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2014.

..... .....

**Signature of participant** **Signature of witness**

…… ……

**Signature of surrogate** **Signature of witness**

### Declaration by investigator

I *(name)* Elmarie van Heerden…..…… declares that:

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2014.

..... .....

**Signature of investigator** **Signature of witness**

Declaration by interpreter

I *(name)* ……..…… declare that:

- I assisted the investigator (*name*) …… to explain the information in this document to (*name of participant*) ……..…….. using the language medium of Afrikaans/Xhosa.
- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) .....….....…….. on (*date*) ……...……..

..... .....

**Signature of interpreter** **Signature of witness**

# Addendum O: Data Sheets 1, 2 and 3

## Data sheet 1

| Patient Data Sheet 1 | | | |
|---|---|---|---|
| Name | | Research number | |
| Age | | Date | |
| Gender | | Time | |
| Weight | | Height | |
| Admission diagnosis | | APACHE II score | |
| Ventilation | Ventilation time | | |
| | PEEP | | |
| | Ventilation mode | | |
| | $FiO_2$ | | |
| Sedation | Type | | |
| | Dose | | |
| | RASS | | |
| Length of stay | | Inotropoc support | |
| Fluid balance | | Hb | |
| Platelets | | WCC | |
| **Richmond Agitation Sedation Scale (RASS)** | | | |
| **Target RASS** | **Description of RASS** | | |
| +4 | Combative, violent, danger to staff | | |
| +3 | Pulls or removes tube(s) or catheters; aggressive | | |
| +2 | Frequent nonpurposeful movement, fights ventilator | | |
| +1 | Anxious, apprehensive , but not aggressive | | |
| 0 | Alert and calm | | |
| -1 | awakens to voice (eye opening/contact) >10 sec | | |
| -2 | light sedation, briefly awakens to voice (eye opening/contact) <10 sec | | |
| -3 | moderate sedation, movement or eye opening. No eye contact | | |
| -4 | deep sedation, no response to voice, but movement or eye opening to physical stimulation | | |
| -5 | Unarousable, no response to voice or physical stimulation | | |

**Legend:**

**APACHE II score =** Acute Physiology And Chronic Evaluation II; **PEEP =** Possitive End Expiratory Pressure; **$FiO_2$ =** Fraction inspired oxygen content; **RASS =** Richards agitation sedation scale: **Hb =** Haemogloblin count; **WCC =** White blood cell count; **sec =** second.

# Data sheet 2

| **Research nr:** | | **Intervention** | | | | | |
|---|---|---|---|---|---|---|---|
| **Max 4.5 minutes allowed for adjustment before start of measurements next position.** | | | | | | | |
| **Position A →Position B** | | | | | | | |
| **Position A** | **0 minutes** | **3 minutes** | **10 minutes** | **Position B** | **0 minutes** | **3 minutes** | **10 minutes** |
| HR (bpm)1 | | | | HR(bpm)1 | | | |
| Systolic BP (mmHg)1 | | | | Systolic BP(mmHg)1 | | | |
| Diastolic BP (mmHg)1 | | | | Diastolic BP(mmHg)1 | | | |
| MAP (mmHg)1 | | | | MAP(mmHg)1 | | | |
| $SpO_2$(%)1 | | | | $SpO_2$(%)1 | | | |
| HR(bpm)2 | | | | HR(bpm)2 | | | |
| Systolic BP(mmHg)2 | | | | Systolic BP(mmHg)2 | | | |
| Diastolic BP(mmHg)2 | | | | Diastolic BP(mmHg)2 | | | |
| MAP(mmHg)2 | | | | MAP(mmHg)2 | | | |
| $SpO_2$(%)2 | | | | $SpO_2$(%)2 | | | |
| HR (bpm)3 | | | | HR(bpm)3 | | | |
| Systolic BP(mmHg)3 | | | | Systolic BP(mmHg)3 | | | |
| Diastolic B(mmHg)3 | | | | Diastolic BP(mmHg)3 | | | |
| MAP(mmHg) 3 | | | | MAP(mmHg)3 | | | |
| $SpO_2$( %)3 | | | | $SpO_2$(%)3 | | | |
| **Adverse events** | **Time** | **Action** | **Duration** | **Adverse events** | **Time** | **Action** | **Duration** |
| | | | | | | | |
| | | | | | | | |
| **Pulmonary Compliance** | | | | | | | |
| **Breath 1** | **8 minutes** | | | **Breath 1** | **8 minutes** | | |
| Tidal volume | | | | Tidal volume | | | |
| Peak pressure | | | | Peak pressure | | | |
| **Breath 2** | | | | **Breath 2** | | | |
| Tidal volume | | | | Tidal volume | | | |
| Peak pressure | | | | Peak pressure | | | |
| **Breath 3** | | | | **Breath 3** | | | |
| Tidal volume | | | | Tidal volume | | | |
| Peak pressure | | | | Peak pressure | | | |

**Legend:**

**HR =** Heart rate; **bpm =** beats per minute; **mmHg =** millimetre mercury; **% =** percentage; **BP =**Blood pressure; **MAP =** Mean arterial pressure; **$SpO_2$ =** Peripheral capillary oxygen saturation.

# Data sheet 3

| Research nr: | | Intervention | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Position A → Position B | | | | | | | | | | |
| Position A | 0 minutes | 3 minutes | 10 minutes | 90s pause for 15° lift (4.5 min max) | | | Position B | 0 minutes | 3 minutes | 10 minutes |
| BRE (°) / knee bend (°) 1 | | | | | | | BRE (°) / knee bend (°)1 | | | |
| BRE (°) / knee bend (°) 2 | | | | | | | BRE (°) / knee bend (°)2 | | | |
| BRE (°) / knee bend (°) 3 | | | | | | | BRE (°) / knee bend (°)3 | | | |
| Adverse events: | | | | | | | Adverse events: | | | |
| Dizziness / Fainting | | | | | | | Dizziness / Fainting | | | |
| ↓ Consciousness | | | | | | | ↓ Consciousness | | | |
| Respiratory | | | | | | | Respiratory | | | |
| Haemodynamic | | | | | | | Haemodynamic | | | |
| Back to position A | YES | NO | | | | | | | | |

**Legend:**

**s** = seconds; **4.5 min max** = 4.5 minute maximum; **BRE =** Back rest elevation; **(°)** = Degrees.

# Addendum P: Bosch digital inclinometer

# Addendum Q: Pilot Study

## Pilot study

The pilot study was performed prior to commencement of the main study.

## Objectives

- To determine if it is possible to record three times the measurements from the monitor at 0 minute, 3 minutes and 10 minutes and from the ventilator at 8 minutes by the PI
- To determine if any adverse events can be observed and recorded by PI.
- To determine if is possible to place the participant in the therapeutic early mobility position during the study procedures.

## Methods

### *Study setting*

The pilot study was conducted in the surgical unit of a tertiary teaching hospital in June 2014.

### *Ethical consideration*

Informed consent was obtained from the participant retrospectively; next of kin or an appropriate surrogate if the participant's next of kin was unreachable.

### *Sample*

One participant was included.

## Measurements

The principal investigator (PI) schedule a pilot study of the measurements from the monitor and ventilator as well as the placement of participant in the therapeutic early mobility position on 25 June 2014. The PI recorded the demographic data and clinical parameters from the records of the participant in the unit. The digital clock was started. Three consecutive measurements were taken from monitor at 0 minute, 3 minutes and 10 minutes of the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and the peripheral capillary oxygen saturation ($SpO_2$%). During the same time period three measurements were taken at each time period of the tidal volume (ml) and peak pressure ($P_{max}$) of three ventilator breaths. Occurrence of any of the predefined adverse events during the study procedures were observed by PI.

**Results**

PI was able to record three repeated measurements of the HR, SBP, DBP, MAP and $SpO_2$ from the monitor at 0 minute, 3 minutes and 10 minutes as well as recording three repeated measurements of the tidal volume and peak pressure of three ventilator breaths from the ventilator at 8 minutes. During the same time period the PI was able to perform the task of placing the participant from the baseline nursing position (current nursing position) into the therapeutic early mobility position. This was measured by the nursing specialist present at the time to evaluate the accuracy of measurement of participant in the testing position. Discomfort was observed by PI at 6 minutes which lasted for 1 minute.

## Table 4.4: Measurements from monitor and ventilator by PI

| Research nr: | A001 | | Intervention | | | | |
|---|---|---|---|---|---|---|---|
| Max 4.5 minutes allowed for adjustment before start of measurements next position. | | | | | | | |
| Position A →Position B | | | | | | | |
| **Position A** | **0 minutes** | **3minutes** | **10 minutes** | **Position B** | **0 minutes** | **3minutes** | **10 minutes** |
| HR (bpm)1 | 93 | 92 | 93 | HR(bpm)1 | 94 | 92 | 92 |
| Systolic BP (mmHg)1 | 150 | 150 | 150 | Systolic BP(mmHg)1 | 150 | 150 | 150 |
| Diastolic BP (mmHg)1 | 89 | 89 | 89 | Diastolic BP(mmHg)1 | 89 | 89 | 89 |
| MAP (mmHg)1 | 128 | 128 | 128 | MAP(mmHg)1 | 128 | 128 | 128 |
| $SpO_2$(%)1 | 98 | 98 | 97 | $SpO_2$(%) 1 | 98 | 98 | 97 |
| HR(bpm)2 | 92 | 92 | 92 | HR(bpm)2 | 93 | 92 | 89 |
| Systolic BP(mmHg)2 | 150 | 150 | 150 | Systolic BP(mmHg)2 | 150 | 150 | 150 |
| Diastolic BP(mmHg)2 | 89 | 89 | 89 | Diastolic BP(mmHg)2 | 89 | 89 | 89 |
| MAP(mmHg)2 | 128 | 128 | 128 | MAP(mmHg)2 | 128 | 128 | 128 |
| $SpO_2$(%)2 | 98 | 98 | 98 | $SpO_2$(%) 2 | 98 | 97 | 97 |
| HR (bpm)3 | 92 | 92 | 91 | HR(bpm)3 | 94 | 92 | 93 |
| Systolic BP(mmHg)3 | 150 | 150 | 150 | Systolic BP(mmHg)3 | 150 | 150 | 150 |
| Diastolic B(mmHg)P3 | 89 | 89 | 89 | Diastolic BP(mmHg)3 | 89 | 89 | 89 |
| MAP(mmHG) 3 | 128 | 128 | 128 | MAP(mmHg) 3 | 128 | 128 | 128 |
| $SpO_2$( %)3 | 97 | 98 | 98 | $SpO_2$(%) 3 | 98 | 98 | 98 |
| **Adverse events** | **Time** | **Action** | **Duration** | **Adverse events** | **Time** | **Action** | **Duration** |
| (-) | (-) | (-) | (-) | discomfort | 6 min | calm | 1 min |
| Lung compliance | | | | | | | |
| **Breath 1** | **8 minutes** | | | **Breath 1** | **8 minutes** | | |
| Tidal volume (ml) | 355 | | | Tidal volume (ml) | 342 | | |
| Peak pressure | 18 | | | Peak pressure | 18 | | |
| **Breath 2** | | | | **Breath 2** | | | |
| Tidal volume (ml) | 250 | | | Tidal volume (ml) | 334 | | |
| Peak pressure | 20 | | | Peak pressure | 18 | | |
| **Breath 3** | | | | **Breath 3** | | | |
| Tidal volume (ml) | 367 | | | Tidal volume (ml) | 324 | | |
| Peak pressure | 19 | | | Peak pressure | 19 | | |

**Legend:**

**HR =** Heart rate; **bpm =** beats per minute; **mmHg =** millimetre mercury; **% =** percentage; **BP =**Blood pressure; **MAP =** Mean arterial pressure; **$SpO_2$% =** Peripheral capillary oxygen saturation; **(-) =** none;

**min** = minute.

**Table 4.5: Measurements taken with Bosch Digital level and angle measurer**

| **Research nr:** | **A001** | **Intervention** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Position A → Position B** | | | | | | | | | | | |
| **Position A** | **0 minutes** | **3 minutes** | **10 minutes** | **90s pause for 15° lift (4.5 min max)** | | | **Position B** | **0 minutes** | **3 minutes** | **10 minutes** |
| BRE (°) /Knees (°) PI 1 | 33° | 33° | 33° | 90s | (-) | (-) | BRE(°)/Knees(°) PI 1 | 45°/150° | 45°/150° | 45°/150° |
| BRE (°)/Knees(°) PI 2 | 33° | 33° | 33° | 90s | (-) | (-) | BRE(°)/Knees (°)PI 2 | 45°/150° | 45°/150° | 45°/150° |
| BRE(°)/Knees(°) PI 3 | 33° | 33° | 33° | 90s | (-) | (-) | BRE(°)/Knees (°)PI 3 | 45°/150° | 45°/150° | 45°/150° |
| BRE(°)/Knees(°) Nurse | Checked ✓ | | | | | | BRE(°)/Knees (°)Nurse | checked ✓ | | |
| **Adverse events:** | | | | | | | **Adverse events:** | | | |
| Dizziness / Fainting | none | none | none | | | | Dizziness / Fainting | none | none | none |
| ↓ Consiousness | none | none | none | | | | ↓ Consiousness | none | none | none |
| Respiratory | none | none | none | | | | Respiratory | none | none | none |
| Haemodynamic | none | none | none | | | | Haemodynamic | none | none | none |
| **Back to position A** | **YES✓** | **NO** | | | | | | | | |

**Legend:**

**s** = seconds; **4.5 min max** = 4.5 minute maximum; **BRE =** Back rest elevation; **(°)** = Degrees; **PI =** Principal investigator.

## Conclusion

It was concluded that three repeated measurements from the monitor and ventilator could be performed accurately by the PI. The PI could place the participant in the correct therapeutic early mobility position. Enough time was available to perform each task and adverse events could be observed and recorded by PI.

# Addendum R: Participant position check sheets

## Participant position checks sheet 1

| Position of tools/patient | Check points | | ✓ | X | Ammend |
|---|---|---|---|---|---|
| Positioning of patient | Comfortable | | | | |
| | 3cm from headboard | | | | |
| | Head is facing forward | | | | |
| | Limbs neutral | | | | |
| | Arterial line arm supported with towel | | | | |
| | Hips positioned in bend of bed | | | | |
| | Position of transducer | | | | |
| | Signs and symtoms of VAE | | | | |
| | Signs of dizziness, fainting or suppression of consiousness | | | | |
| | Patient will be asked to keep calm/ relaxed. | | | | |
| Position of arterial line | Zero/callibration of catheter | | | | |
| | Signs of potential complications | Haemorrhage | | | |
| | | Occlusion of catheter by a blood clot/ kinked tube | | | |
| | | Redness around the catheter, sign of infection | | | |
| | | Air embolism | | | |
| | | Displacement of catheter | | | |
| Position of CVP line | Zero/callibration of catheter | | | | |
| | Signs of potential complications | Haemorrhage | | | |
| | | Occlusion of catheter by a blood clot/ kinked tube | | | |
| | | Redness around the catheter, sign of infection | | | |
| | | Signs of VAE | | | |
| | | Displacement of catheter | | | |
| Bedside table | 8 Blood gas syringes marked with pt research nr and measurement time with B0, B3 and B10 minutes and T0, T3 and T10 minutes | | | | |
| | Blood gas analysis forms filled in correctly | | | | |
| | Timer set to 0 | | | | |
| | Disinfectant on bedside table | | | | |
| | Intervention data sheet | | | | |
| Position of electronic protractor | Protractor set to o degrees | Calibrate inclinometer | | | |
| | | Check acuracy | | | |
| Position of ET tube | ET tube is secure and on the same mark | | | | |

**Legend:**

**Cm** = centimetre; ✓ = correct; **X** = incorrect; **VAE =** Vascular air embolism; **CVP =** Central venous pressure; **ET** = Endotracheal.

## Participant safety check sheet 2

| **Research nr** | | | **Time** | | | |
|---|---|---|---|---|---|---|
| Safety checks | | | | **YES** | **NO** | **Amend** |
| Central venous access points secure | | | | **YES** | **NO** | **Amend** |
| All relevent personel present | | | | **YES** | **NO** | **Amend** |
| Protocol for magament of VAE in place | | | | **YES** | **NO** | **Amend** |
| Ventilated with positive pressure (PEEP) | | | | **YES** | **NO** | **Amend** |
| ALL YES: continue to screening protocol | | | | | | YES |

**Legend:**

**VAE =** Vascular air embolism; **PEEP =** Possitive End Expiratory Pressure

# Addenda Related to Results

## Addendum S: Figure A.1: Normal probability plot of MAP

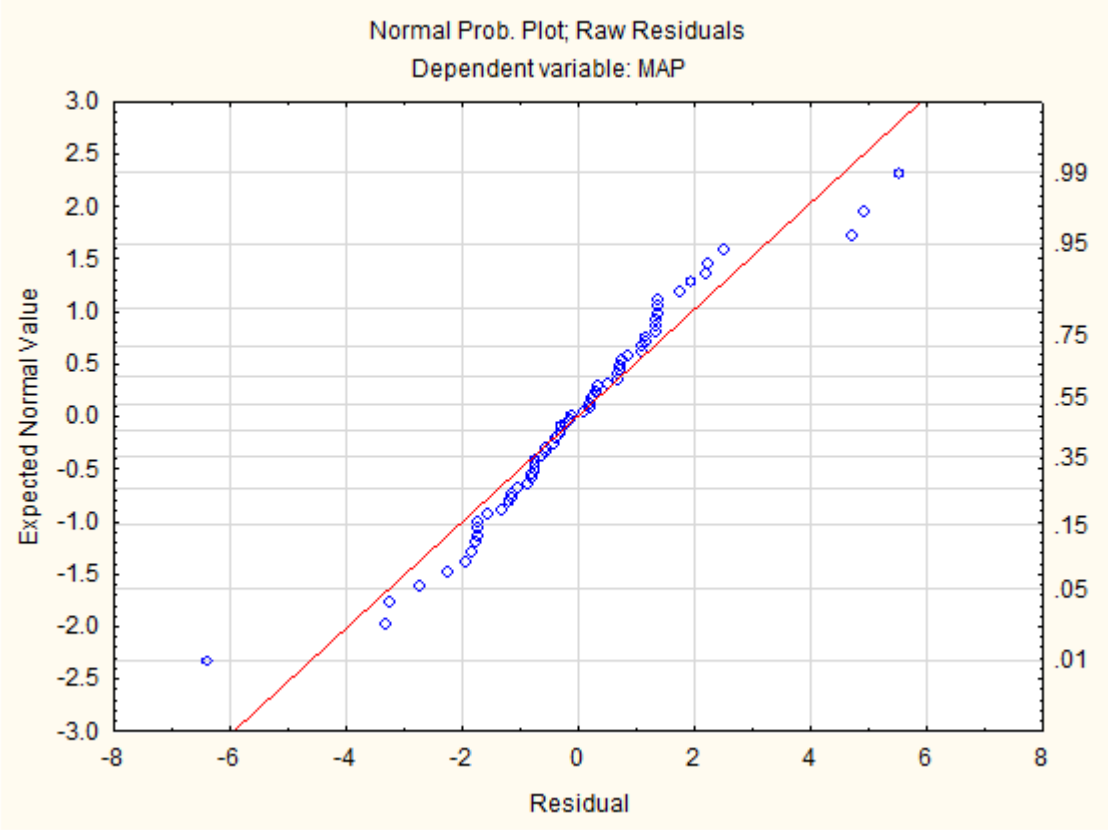



**Figure A.1: Normal probability plot of MAP**

## Addendum T: Figure A.2: Normal probability plot of $ScvO_2$%

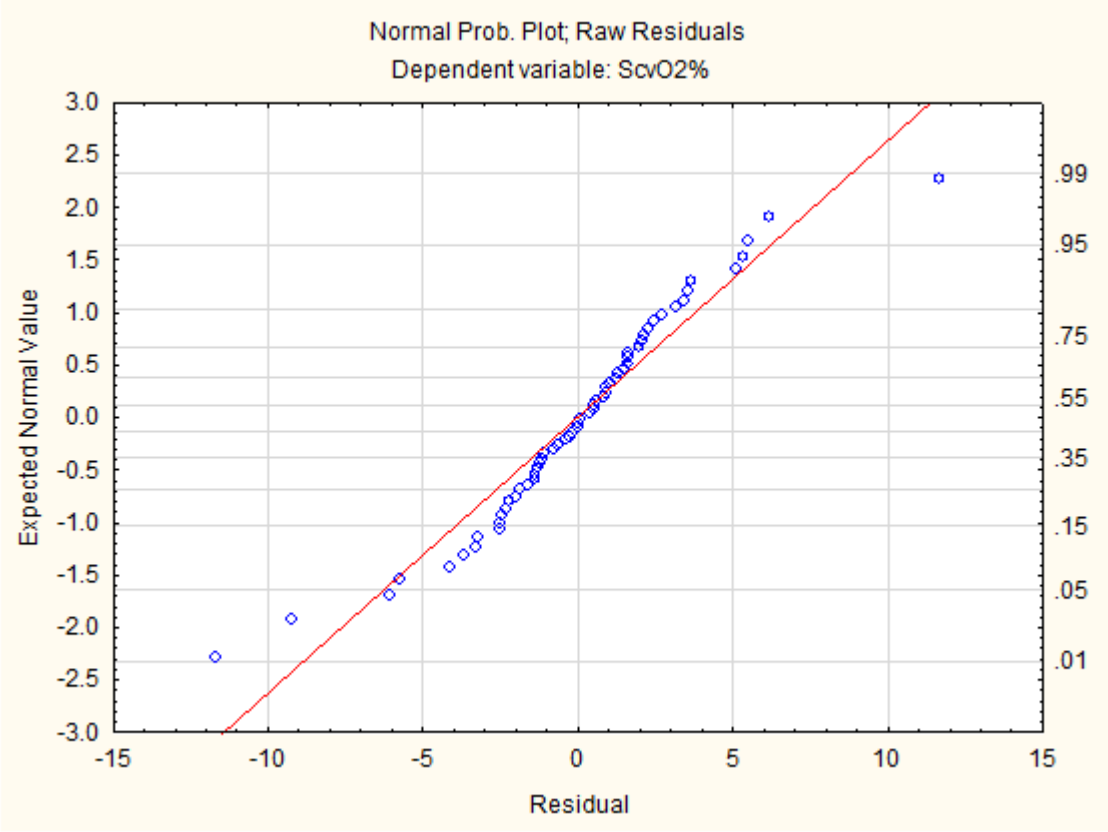
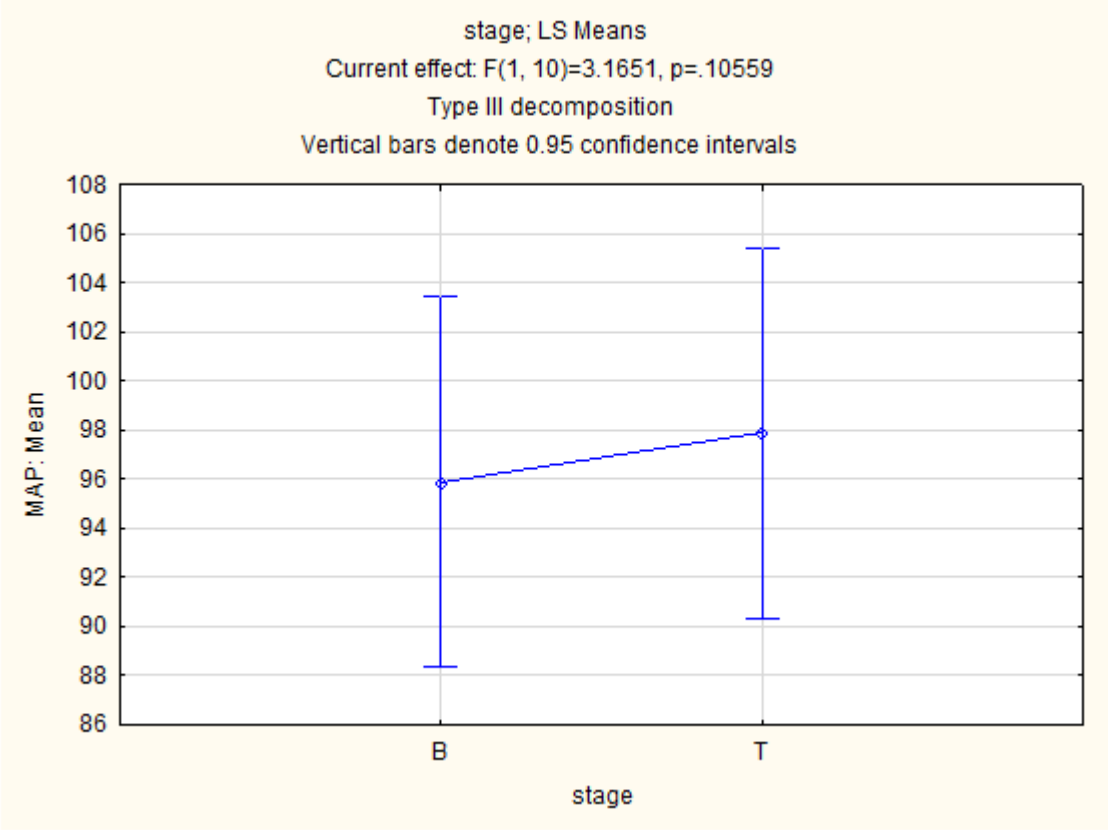



**Figure A.2: Normal probability plot of $ScvO_2$%**

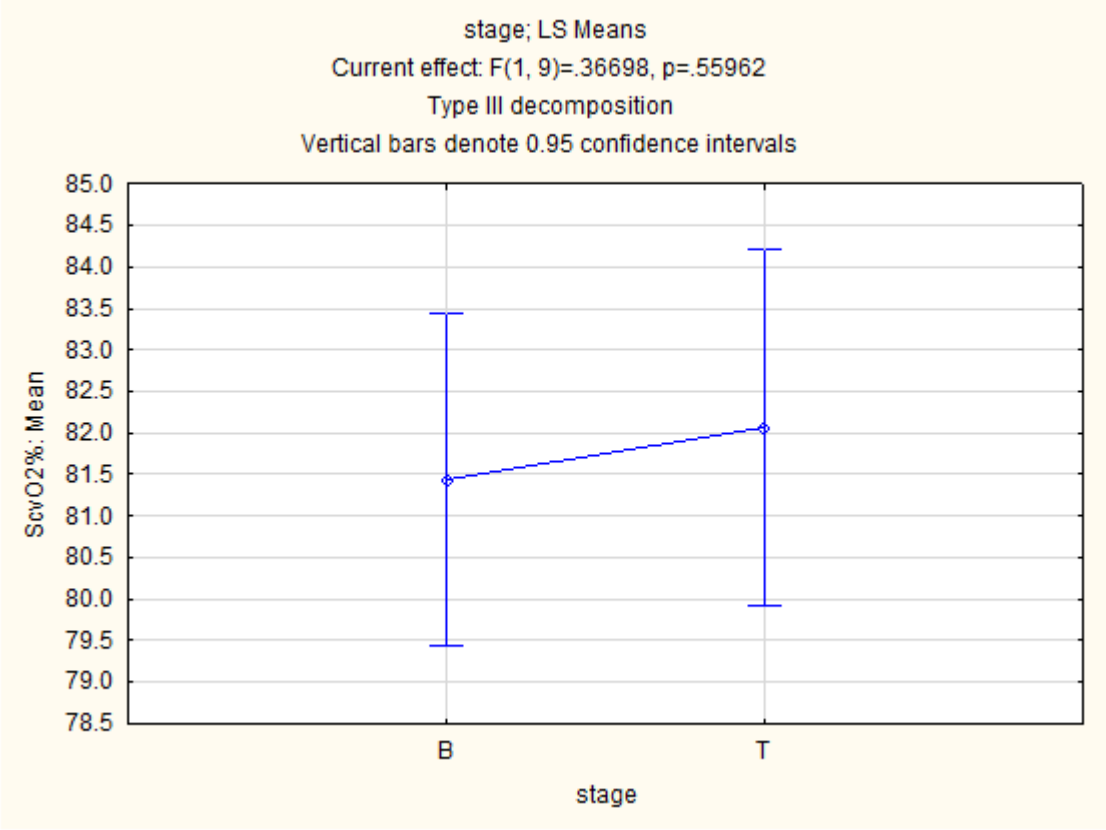
# Addendum U: Figure A.3: Mean difference of the MAP from the baseline position (Stage B) to the therapeutic early mobility position (Stage T)




**Legend:**
**MAP =** Mean arterial pressure; **B =** Baseline nursing position; **T =** Therapeutic early mobility position.

**Figure A.3: Mean difference of the MAP from the baseline position (Stage B) to the therapeutic early mobility position (Stage T)**

# Addendum V: Figure A.4: Mean difference of the $ScvO_2$% from the baseline position to therapeutic early mobility position




**Legend:**
**$ScvO_2$% =** Central venous oxygen saturation; **B** = Baseline position; **T =** Therapeutic early mobility position.

**Figure A.4: Mean difference of the $ScvO_2$% from the baseline position to therapeutic early mobility position**

# Addendum W: Table A1: Mean difference and 95% CI of mean difference the MAP

**Table A1: Mean difference and 95% CI of MAP.**

| 1st Mean | 2nd Mean | Mean Differ. | Standard Error | p | -95.00% | +95.00% |
|---|---|---|---|---|---|---|
| 0min*B | 0min*T | -2.87879 | 1.416722 | 0.055650 | -5.83402 | 0.076442 |
| 0min*B | 3min*B | 0.03030 | 1.190142 | 0.979939 | -2.45229 | 2.512895 |
| 0min*B | 3min*T | -2.69697 | 1.513100 | 0.089870 | -5.85324 | 0.459301 |
| 0min*B | 10min*B | -0.84848 | 1.190142 | 0.484126 | -3.33108 | 1.634107 |
| 0min*B | 10min*T | -1.21212 | 1.513100 | 0.432497 | -4.36839 | 1.944149 |
| 0min*T | 3min*B | 2.90909 | 1.513100 | 0.068889 | -0.24718 | 6.065361 |
| 0min*T | 3min*T | 0.18182 | 1.190142 | 0.880110 | -2.30077 | 2.664410 |
| 0min*T | 10min*B | 2.03030 | 1.513100 | 0.194692 | -1.12597 | 5.186574 |
| 0min*T | 10min*T | 1.66667 | 1.190142 | 0.176719 | -0.81593 | 4.149259 |
| 3min*B | 3min*T | -2.72727 | 1.416722 | 0.068563 | -5.68250 | 0.227958 |
| 3min*B | 10min*B | -0.87879 | 1.190142 | 0.468855 | -3.36138 | 1.603804 |
| 3min*B | 10min*T | -1.24242 | 1.513100 | 0.421263 | -4.39869 | 1.913846 |
| 3min*T | 10min*B | 1.84848 | 1.513100 | 0.236043 | -1.30779 | 5.004755 |
| 3min*T | 10min*T | 1.48485 | 1.190142 | 0.226580 | -0.99774 | 3.967440 |
| 10min*B | 10min*T | -0.36364 | 1.416722 | 0.800052 | -3.31887 | 2.591594 |

**Legend**:
**Mean differ. =** Mean difference; **p =** p value; **min =** minute; **B =** Baseline nursing position; **T =** Therapeutic early mobility position.

# Addendum X: Table A2: Mean difference and 95% CI of mean difference of $ScvO_2$%

**Table A1: Mean difference and 95%CI of the $ScvO_2$%**

| 1st Mean | 2nd Mean | Mean Differ. | Standard Error | p | -95.00% | +95.00% |
|---|---|---|---|---|---|---|
| 0min*B | 0min*T | -1.95018 | 1.888790 | 0.318199 | -5.97604 | 2.075684 |
| 0min*B | 3min*B | -0.88119 | 1.733192 | 0.618556 | -4.57540 | 2.813026 |
| 0min*B | 3min*T | -0.36605 | 1.834603 | 0.844531 | -4.27642 | 3.544313 |
| 0min*B | 10min*B | -1.15391 | 1.733192 | 0.515665 | -4.84812 | 2.540298 |
| 0min*B | 10min*T | -1.62779 | 1.779911 | 0.374903 | -5.42158 | 2.166000 |
| 0min*T | 3min*B | 1.06899 | 1.854675 | 0.572908 | -2.88415 | 5.022139 |
| 0min*T | 3min*T | 1.58413 | 1.928649 | 0.424301 | -2.52669 | 5.694944 |
| 0min*T | 10min*B | 0.79627 | 1.854675 | 0.673787 | -3.15688 | 4.749411 |
| 0min*T | 10min*T | 0.32239 | 1.888032 | 0.866700 | -3.70186 | 4.346631 |
| 3min*B | 3min*T | 0.51513 | 1.788651 | 0.777287 | -3.29729 | 4.327554 |
| 3min*B | 10min*B | -0.27273 | 1.686932 | 0.873723 | -3.86834 | 3.322883 |
| 3min*B | 10min*T | -0.74661 | 1.733753 | 0.672861 | -4.44201 | 2.948801 |
| 3min*T | 10min*B | -0.78786 | 1.788651 | 0.665873 | -4.60028 | 3.024559 |
| 3min*T | 10min*T | -1.26174 | 1.823083 | 0.499454 | -5.14755 | 2.624070 |
| 10min*B | 10min*T | -0.47388 | 1.733753 | 0.788330 | -4.16929 | 3.221528 |

**Legend:**
**Mean differ. =** Mean difference; **p =** p value; **min =** minute; **B =** Baseline nursing position; **T =** Therapeutic early mobility position.