Early Mobilization of the Critically Ill

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ABBREVIATIONS

CIM	Clinical Illness Myopathy
CIP	Critical Illness Polyneuropathy
CIPNM	Critical Illness Polyneuromyopathy
EM	Early Mobilization
ICU	Intensive Care Unit
ICUAW	Intensive Care Unit-Acquired Weakness
KT	Knowledge Translation
LOS	Length of Stay
MDFG	Multidisciplinary Focus Group
MDs	Physicians
MRC	Medical Research Council
NMES	Neuromuscular Electrical Stimulation
OR	Odds Ratio
PFG	Physicians' Focus Group
PT	Physiotherapist
PTs	Physiotherapists
RCT	Randomized Controlled Trial
RR	Risk Ratio
RTs	Respiratory Therapists
TDF	Theoretical Domain Framework

ABSTRACT

Many patients who are admitted to the intensive care unit (ICU) experience a reduction in their level of mobility that can have detrimental physiological effects on several body systems. Early mobilization (EM) is an intervention that reduces the level of immobility during critical illness. There is evidence that EM is associated with more ventilator-free days, shorter ICU and hospital length of stay, improved functional status and increased quality of life after hospital discharge. However, implementation of EM is not without challenges. The overall aim of this thesis, which contains four manuscripts, is to provide insight into the barriers and facilitators to the implementation of EM in local area ICUs and to contribute to the existing body of knowledge in order to ultimately to help improve the practice of EM.

The first study involved a survey of 138 clinicians from three local area ICUs to identify the barriers and practice patterns of EM. The results showed that many clinicians did not perceive EM as a top priority, were not fully aware of the benefits of EM, and did not feel well trained to mobilize mechanically ventilated patients. It also showed that most ICUs required a physician's order for initiation of physiotherapy care and that physiotherapy services were unavailable during evening hours and limited on weekends. Key identified barriers were medical instability, safety concerns of nurses, limited staffing, insufficient equipment, risk of dislodgement of devices or lines, excessive sedation, lack of coordination among providers, slow recognition of when patients should begin EM, inadequate training, conflicting perceptions among physicians about the suitability of EM, and lack of effective communication.

The second study involved follow-up exploratory focus group discussions with physiotherapists, nurses, physicians and respiratory therapists to explore their perspectives regarding the barriers, facilitators, and potential solutions for improving EM practice. The key barriers to EM were a lack of conviction or knowledge regarding the available evidence on EM, lack of attention to the provision of optimal care, poor ICU organization, poor communication and the unpredictable nature of the ICU. Other barriers included limited staffing, equipment, time and clinical knowledge. Identified facilitators included individual-level factors such as intrinsic motivation, positive outcome expectations, conscious effort to mobilize early, good planning and coordination, presence of ICU champions and expert support by a physiotherapist; and organizational level

facilitators: reminder system, pro-EM culture, implementation of an EM protocol, and improved ICU organization. Based on the results of these two initial studies, knowledge translation interventions were determined to be necessary to help reduce the identified barriers and enhance the identified facilitators.

The third study, a systematic review and meta-analysis of randomized controlled studies, evaluated the impact of EM and neuromuscular electrical stimulation on the incidence of intensive care unit-acquired weakness (ICUAW), ventilator dependency, discharge location, ICU and hospital length of stay, and acute mortality. The results indicated that EM and neuromuscular electrical stimulation interventions were associated with a lower likelihood of development of ICUAW and a greater likelihood of being discharged home. The evidence was inconsistent regarding these interventions being associated with reduced ventilator dependency, ICU length of stay, and hospital length of stay. Moreover, these interventions were not associated with an increased odds of acute mortality.

Finally, the last manuscript initiated the process of creating a Physical Therapy Critical Care Learning Needs Assessment Tool. This tool will eventually be used to help guide the creation of educational modules in an effort to bridge the knowledge gaps of physiotherapists working in the ICU. Specifically, a scoping review of the literature was performed, followed by a survey and focus group discussions, as well as consultation with experienced physiotherapists to identify and select the knowledge and skill topics deemed as relevant for inclusion in the future Learning Needs Assessment Tool. The items that were identified and selected covered several domains including foundational knowledge with subdomains of anatomy, physiology, exercise physiology, pathophysiology and presenting features of common ICU conditions, pharmacology, medical therapies and procedures, lines, leads and/or ICU equipment. Other domains included tests and laboratory findings, assessment, clinical reasoning, evaluation skills, physiotherapy interventions, as well as professional and ethical practice.

In summary, these four studies have identified key barriers and facilitators to EM, elucidated practice patterns for EM in several local area ICUs, contributed to the available evidence regarding the positive impact of EM and initiated a process to help to bridge the critical care knowledge/skill gaps of physiotherapists.

ABRÉGÉ

De nombreux patients admis dans l'unité de soins intensifs voient leur niveau de mobilité diminuer, ce qui peut avoir des effets physiologiques préjudiciables sur plusieurs systèmes corporels. La mobilisation précoce est une intervention qui réduit le niveau d'immobilité pendant une maladie grave. Il a été prouvé que la mobilisation précoce est associée à plus de jours sans ventilateur, des soins intensifs de courte durée ainsi que la durée d'hospitalisation, l'amélioration de l'état fonctionnel et une meilleure qualité de vie après la sortie de l'hôpital. Cependant, la mise en œuvre de la mobilisation précoce n'est pas sans défis. L'objectif global de cette thèse, qui contient quatre manuscrits, est de fournir un aperçu des obstacles et des facilitateurs à la mise en œuvre de la mobilisation précoce dans les unités de soins intensifs locaux et de contribuer à l'ensemble des connaissances existantes afin d'améliorer la pratique de la mobilisation précoce.

La première étude a consisté en une enquête auprès de 138 cliniciens de trois unités de soins intensifs de la région afin d'identifier les barrières et les modèles de pratique de la mobilisation précoce. Les résultats ont montré que de nombreux cliniciens ne considéraient pas la mobilisation précoce comme une priorité absolue, ne connaissaient pas pleinement les avantages d'une mobilisation précoce et ne se sentaient pas bien formés pour mobiliser des patients ventilés mécaniquement. On a également démontré que la plupart des unités de soins intensifs nécessitaient l'ordonnance d'un médecin pour l'initiation aux soins de physiothérapie, et que les services de physiothérapie n'étaient pas disponibles pendant les heures du soir et limités les fins de semaines. Les principaux obstacles identifiés étaient l'instabilité médicale, les problèmes de sécurité des infirmières, la pénurie de personnel, l'équipement insuffisant, le risque de délogement des appareils ou des lignes, la sédation excessive, le manque de coordination entre les prestataires, reconnaissance tardive du moment où les patients devraient commencer la mobilisation précoce, une formation inadéquate des conflits de perception de mobilisation précoce, et un manque de communication efficace.

La deuxième étude comportait des discussions exploratoires de groupe de suivi avec des physiothérapeutes, des infirmières, des médecins et des inhalothérapeutes afin d'évaluer leur point de vue sur les obstacles, les facilitateurs et les solutions possibles afin d'améliorer les pratiques de mobilisation précoce. Les principaux obstacles à la mobilisation précoce étaient le manque de conviction ou de connaissances des preuves disponibles sur la mobilisation précoce, le manque

d'attention de prodiguer des soins optimaux, l'organisation médiocre des unités de soins intensifs, la mauvaise communication et la nature imprévisible de l'unité de soins intensifs. Parmi les autres obstacles, mentionnons la ressource en personnel limitée, l'équipement, le temps et les connaissances cliniques limitées. Les facilitateurs identifiés comprenaient des facteurs individuels comme la motivation intrinsèque, les attentes positives en matière de résultats, les efforts conscients pour une mobilisation précoce, une bonne planification et coordination, la présence de champions en soins critiques et le soutien d'un physiothérapeute spécialisé; et des facilitateurs au niveau organisationnel : système de rappel, culture de mobilisation précoce, mise en place d'un protocole de mobilisation précoce et organisation améliorée des unités de soins intensifs. Selon les résultats de ces deux études initiales, les interventions d'application des connaissances ont été jugées nécessaires pour aider à réduire les obstacles identifiés et améliorer les facilitateurs identifiés.

La troisième étude, une revue systématique et une méta-analyse d'études contrôlées randomisées, a évalué l'impact de la mobilisation précoce et de la stimulation électrique neuromusculaire sur l'incidence des poly-neuropathie chez les patients à l'état critique admis aux soins intensifs, la dépendance ventilatoire, l'unité de soins où le congé a été assigner, la durée du séjour hospitalier, et la mortalité aiguë. Les résultats ont indiqué que la mobilisation précoce et les interventions de stimulation électrique neuromusculaire étaient associées à une plus faible probabilité de développer une poly-neuropathie en soins intensifs et une plus grande probabilité d'être renvoyé chez soi. La preuve était incohérente en ce qui concerne ces interventions qui sont associées à une réduction de la dépendance au ventilateur, de la durée du séjour en unité de soins intensifs et de la durée du séjour à l'hôpital. De plus, ces interventions n'étaient pas associées à une probabilité accrue de mortalité aiguë.

Enfin, le dernier manuscrit a initié le processus de création d'un outil d'évaluation des besoins d'apprentissage en soins intensifs de physiothérapie. Cet outil servira éventuellement à guider la création des modules éducatifs dans le but de combler le manque de connaissances des physiothérapeutes travaillant dans une unité de soins intensifs. Plus précisément, un examen exploratoire de la documentation a été effectué, suivi d'un sondage et de discussions de groupe, ainsi que de consultations avec des physiothérapeutes expérimentés pour identifier et sélectionner les connaissances et les compétences jugées pertinentes pour l'inclusion des paramètres et des

données pertinentes dans le futur outil d'évaluation des besoins. Les items identifiés et sélectionnés couvraient plusieurs domaines incluant les connaissances fondamentales avec les sous-domaines de l'anatomie, physiologie, physiologie de l'exercice, physiopathologie et caractéristiques des unités de soins intensifs communs, pharmacologie, thérapies et procédures médicales, lignes, pistes et/ou équipement d'unité de soins intensifs. Les autres domaines comprenaient les tests et les résultats de laboratoire, l'évaluation, le raisonnement clinique, les compétences d'évaluation, les interventions de physiothérapie, ainsi que la pratique professionnelle et éthique.

En résumé, ces quatre études ont identifié des barrières et des facilitateurs à la mobilisation précoce, des schémas de pratique élucidés pour une mobilisation précoce dans plusieurs unités de soins intensifs locaux, ont contribué aux preuves disponibles concernant l'impact positif de la mobilisation précoce et ont initié un processus pour les lacunes dans les connaissances et les compétences en soins intensifs des physiothérapeutes.

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PREFACE AND CONTRIBUTION OF AUTHORS

PREFACE

Statement of Originality

The research projects included in this thesis are the products of my own original work with guidance from my supervisor, Dr. Jadranka Spahija. The topic for my thesis work is the result of my personal interest in preventing avoidable complications related to reduced mobility and enhancing the quality of care provided for the critically ill. This interest came from my ten years of clinical experience as a physiotherapist and from my discussions with my supervisor as a Master's student.

This thesis has made novel and unique contributions to the practice and science of early mobilization in the ICU. First, this was the first study to identify perceived gaps, barriers and facilitators to early mobilization using a survey methodology and followed up by an exploratory focus group methodology to further elucidate the involved barriers and facilitators. This thesis thus provides unique and new insight into the barriers and facilitators that are related to clinician behavior, not identified in earlier studies. These unique findings also provide a framework for the design of theory-based knowledge translation interventions that may improve early mobilization practice in the ICU. Second, this thesis is the first to provide evidence that early mobilization reduces the likelihood of developing intensive care unit-acquired weakness. Thirdly, the theoretical and practical knowledge, and skills that physiotherapists may require for practice in the ICU have also been identified and summarized in this thesis. This knowledge was tailored to the patient population within a given hospital in preparation for the development of a Physical Therapy Critical Care Learning Needs Assessment Tool to be used for identifying knowledge gaps in physiotherapists intending to practice in the ICU setting.

Thesis Overview and Organization

This thesis contains four overarching projects which are presented in a manuscript-based format consisting of four manuscripts. As required by McGill Graduate and Postdoctoral Studies, additional chapters have been incorporated to form a coherent thesis. Given the manuscript-based structure, a few repetitions are inevitable.

Chapter 1 presents a brief introduction to the subject of EM and the rationale for this research thesis.

Chapter 2 is a review of the literature that summarizes the negative effects of bed rest and decreased mobility on the human body. It also contains a dedicated section to intensive care unit-acquired weakness because it is an essential component of one of the studies in this thesis. It further discusses the concept of EM, and finally, presents the topic of learning needs assessment, given the last project is the first step in the process the development of a learning needs assessment tool.

Chapter 3 presents the objectives of the studies presented in this thesis.

Chapter 4 provides a preface to manuscript one.

Chapter 5 presents manuscript one which is entitled "Interprofessional Survey of Perceived Barriers and Facilitators to Early Mobilization of Critically Ill Patients in Montreal, Canada".

Chapter 6 is the preface to the second manuscript and it links the first two manuscripts.

Chapter 7 presents the second manuscript which is entitled "ICU Clinicians' Perspectives on Early Mobilization: A Qualitative Study".

Chapter 8 is the preface to the third manuscript, linking the first two manuscripts with the third.

Chapter 9 presents the third manuscript entitled "Early Mobilization and Neuromuscular Electrical Stimulation to reduce intensive care unit-acquired weakness: A Systematic Review and Meta-Analysis."

Chapter 10 is the preface to the fourth manuscript linking the first two manuscripts with the fourth.

Chapter 11 presents the fourth manuscript entitled "The Identification and Selection of Items for a Physical Therapy Critical Care Learning Needs Assessment Tool."

Chapter 12 presents a summary of the findings, conclusions of the four manuscripts, as well as the implications for future research.

Corresponding figures and tables are presented at the end of each manuscript or section. All references are presented at the end of the thesis. The appendices include information that was submitted as appendices in the published manuscripts or that may be submitted as an appendix. Ethics approval was obtained for all relevant studies and was stated in the manuscripts.

Contribution of authors

The candidate was responsible for the conceptualization, designing, protocol writing, obtaining ethics, data collection, analysis, and writing of all the manuscripts, as well as coordinating the overall activities of the studies. J. Spahija provided guidance and feedback in all stages, as well as extensive editing of all the manuscripts. M. de Marchie participated in the design and data collection for manuscript one and two. K. Koo, P. Goldberg, and D. Jayaraman were collaborators for manuscript one. S. Milner was involved as a second independent coder in the analysis of the manuscript two. A. Bussieres was a member of the supervisory committee and provided methodological guidance in the analysis of manuscript two, three and four as well as editing of the manuscripts. S. Biswas acted as the second reviewer for manuscript three. S. Katz, L.Gillespie, and G.Moullec were collaborators for manuscript four. Additionally, S. Katz and L.Gillespie contributed to study conceptualization and facilitated the data collection phases. With the exception of P. Goldberg, D. Jayaraman, S. Katz, L.Gillespie, and G.Moullec, all coauthors participated in the review of their respective manuscripts.

CHAPTER 1: INTRODUCTION

Intensive care unit (ICU) survivors are often faced with medical complications that develop during hospitalization and which may be unrelated to the diagnosis associated with ICU admission.[1-3] Available literature shows a high prevalence of long-lasting restrictions in physical function among survivors of critical illness.[4-7] These complications sometimes culminate in a condition known as ICU acquired weakness (ICUAW) and are known to be associated with decreased mobility.[3] Patients often experience decreased mobility during their ICU stay.[8,9] Mechanically ventilated patients are especially at risk because they often remain relatively motionless for lengthy periods of time.[10-12] Prolonged recumbent positions have been associated with many negative and deleterious effects on the cardiovascular, integumentary, renal, gastrointestinal, nervous and musculoskeletal systems of the body. [13-15] Even in apparently healthy subjects, immobility has been demonstrated to be associated with losses in functional capacity of the musculoskeletal[16-18] and cardiovascular systems.[19,20] It is therefore important that individuals in the ICU (especially those on mechanical ventilation) should be mobilized as early as possible. This intervention is known as early mobilization (EM).

Recent scientific literature has shown that EM is safe and feasible in critically ill patients.[10,21] Survival rates in the ICU are on the rise because of advances in the medical sciences and in patient management.[10] It is therefore important to increase the implementation of EM in order to prevent and reduce the prevalence and incidence of complications among these survivors. This goal underlies the projects included in this PhD thesis.

The overall aim of this thesis, which contains four manuscripts, is to provide insight into the barriers and facilitators to the implementation of EM in local area ICUs and to contribute to the existing body of knowledge in order to ultimately to help improve the practice of EM.

To achieve these goals, four studies are presented in this thesis. The first study identified perceived gaps in clinical practice and assessed the perceived barriers to EM in critically ill patients. The second explored a deeper understanding of these barriers: why they exist, what could be done to lower them, and how facilitators can be enhanced to improve the practice of EM from the perspective of ICU clinicians. The third study contributed evidence to the effect of EM interventions on intensive care unit-acquired weakness (ICUAW), ventilator dependency,

discharge location, ICU length of stay (LOS) and hospital LOS, and the relationship of ICUAW with acute mortality using a systematic review and meta-analysis of randomized controlled studies. The fourth study identified the theoretical and practical knowledge as well as skills required for physiotherapy practice in the ICU, and selected the items that will be used to develop a learning needs assessment tool. This initiates the process for the development of a critical learning needs assessment for physiotherapists aiming to work in the ICU.

CHAPTER 2: LITERATURE REVIEW

The Great Antiquity of Physical Activity and the Emergence of Bed Rest

History of Physical Activity and Health

Advocacy for the beneficial effects of physical activity on health and longevity started about 2000 years ago with the legendary physicians Hippocrates and Galen.[22] A paper titled 'Diseases of Workers' by Italian physician Berbardino Ramazzini in the late seventeenth to early eighteen century described the occupational hazards of sedentary life associated with certain occupations.[23] However, objective data on the injurious effects of a sedentary lifestyle began to emerge in the mid-19th century with Guy's[24] publication in the *Journal of the Statistical Society of London* showing that workers who used the least amount of muscular effort during work were more prone to poor health outcomes, while exercise had a tendency to counteract the injurious effects of a sedentary life. Other studies in the 19th and 20th centuries supported the reports of Guy which lead to further research on the relationship between physical activity and health. For example, Morris et al.[25] showed that drivers of London's double-decker buses and government clerks were more likely to die from cardiovascular-related deaths compared to active bus conductors and postmen. Similarly, another study which examined mortality secondary to acute coronary occlusion showed that mortality rates were higher among sedentary white-collar-job individuals compared to more active laborers.[26] Siversten[27] showed carcinoma to occur more predominantly among people who used less muscular activity. Paffenbarger et al.[28] demonstrated that the death rate (primarily due to cardiovascular or respiratory cause) was lower among 16,936 Harvard alumni who expended more than 2000kcal energy per week (mainly in walking, stair climbing, and sports) when compared to those who did not, irrespective of smoking status, hypertension, parental death and extreme gains in body weight. Exercise and increased physical activity have therefore been promoted as important health determinants for about 2000 years.[22]

Nonetheless, at that time, the benefits of exercise and physical activity were not extended to patients with acute or critical illness. According to Paffenbarger et al.,[22] a 1926 report from the US Surgeon General's office in *Exercise and Health* (Supplement No. 24 to the Public Health Reports 1926) stated that daily exercise in an amount just short of fatigue was necessary for all, "*except those who are actually and acutely ill"*. Prolonged bed rest, which was assumed to be therapeutic, therefore became a common medical prescription for many ailments.

The Emergence of Bed Rest in Hospital Wards

From the 5th century BC until now, rest has been known as a therapeutic approach for illness and acute injuries. Hippocrates[29] in his work, translated by Chadwick and Mann, stated that rest is restorative in all disturbances of the body, as soon as there is pain, but cautioned that the whole body should not be rested more than is usual, since a long period of inactivity would result in deterioration. However, modern clinical practice, which evolved greatly in the 19th and 20th centuries, did not follow the advice of the legendary physician in limiting rest for people with illness, but rather adopted prolonged periods of bed rest as a medical therapy. According to the literature, prior to the 19th century, sick people rarely took to bed until they were too sick to stand or sit.[30] The prescription of bed rest as a medical therapy is believed to have begun in 1863 with the published lecture 'Therapeutic Influence of Rest in Accidents and Surgical Diseases', given by John Hilton, a professor of Anatomy and Surgeon Extraordinary to Her Majesty the Queen in United Kingdom.[31] Although some believe that physicians grossly misinterpreted Hilton's position,[32,33] the practice of prolonged bed rest thereafter became an unchallenged model of medical treatment until about the middle of the 20th century.[22,30] By this time, prescribed lengths of bed rest were as long as 4 - 6 weeks following surgery or treatment for myocardial infarction.[30]

Objective data on the deleterious physiological consequences of prolonged bed rest began to emerge around the middle of the 20th century.[16,30,34] Nonetheless, there was no change in clinical practice until certain physicians, began to challenge the predominant medical culture of their day, using the limited evidence available at that time.[13,32,35] As early as 1944, Dock[35] in his paper entitled "The evil sequelae of complete bed rest" warned of the deleterious effect of immobility. Similarly, in an article published in British Medical Journal in 1947, Dr. Asher[13] wrote, "Teach us to live that we may dread unnecessary time in bed. Get people up and we may save our patients from an early grave''. In a meta-analysis of 39 randomized trials conducted in 1999, Allen et al.[36] showed that bed rest, was potentially harmful rather than just not beneficial. These initial efforts led to other efforts that gradually diminished the practice of bed rest as a medical practice in many hospital wards across the globe.

The Emergence of Bed Rest in the Intensive Care Unit

The initial efforts to discourage the clinical practice of bed rest in the hospital wards[13,32] incidentally coincided with the birth of the ICU in 1953 to manage poliomyelitis victims with

respiratory failure.[37] Over the years, the concept of the ICU evolved from the treatment of poliomyelitis victims with respiratory failure to the treatment of critically ill patients irrespective of pathology (critical care).[38] History repeated itself, as these critically ill patients were again assumed to be too sick for any form of physical activity. Bed rest, which was being campaigned against in the hospital wards, easily found its way into the ICU resulting in a prolonged stay in the lying position (usually supine) for such patients, especially for those on mechanical ventilation. Reduced mobility in the ICU has since then been a menace that has besieged critically ill patients for over six decades and is associated with many complications that the medical practice has had to deal with for years.

Effects of Prolonged Bed Rest and Inactivity

Bed rest is typically associated with the recumbent position and a decreased level of physical activity. The effects of immobility stem from the loss of the vertical gravitational stress gradient (secondary to the recumbent position) and from the loss of exercise stress on all the body systems (secondary to inactivity). These result in many negative effects on the physiological systems of the body and leads to an overall decrease in physical fitness.

Cardiovascular Effects of Bed Rest and Inactivity

The immediate short-term cardiovascular effects of bed rest and inactivity are due to the alterations in the cardiovascular system homeostasis. These alterations in homeostasis occur secondary to fluid shifts associated with the loss of gravitational stress. The erect position of the body results in a hydrostatic pressure gradient of about 2 mmHg for each 2.5cm of vertical height.[39] This pressure gradient causes an arterial blood pressure differential of about 140 mmHg between the head and the toe (65 mmHg and 205 mmHg in the head and toe, respectively, with a mean blood pressure of 90 mmHg at the level of the heart) in a normal male of about 1.75m height.[39] In the lying position, there is a loss of this cephalo-caudal pressure differential which is accompanied by a loss of the gravitational pull of blood towards the lower limbs, resulting in a fluid shift from the lower limbs to the central circulation in the thorax (increased venous return). This fluid shift gives rise to a higher end-diastolic volume in the reclined position (compared to the upright position), i.e. a higher preload and subsequently a higher stroke volume (based on Frank-Starling law[40]) and cardiac output[41] (Figure 1). These effects are associated with increases in myocardial work.[42,43] Within days, renal compensation occurs resulting in a reduced plasma volume leading to a

decreased preload and a consequent reduction in stroke volume. Reduced stroke volume leads to decreased cardiac output and an attempt at compensation by an increase in heart rate.[44,45] There is also increased venous compliance and venous stasis which contributes to decreased venous return.[45] According to Fick's equation[46] *(maximum oxygen consumption = cardiac output*[the arterial oxygen content- the mixed venous oxygen content])*, the decreased cardiac output will lead to a decrease in maximal oxygen consumption. Bed rest is also associated with a decreased red blood cell volume and decreased capillarization, which in turn contributes to a decreased blood flow at the tissue level.[44,45] These decreases also contribute to a reduction in maximal oxygen consumption (Figure 2). Data from nineteen investigations showed that bed rest reduces aerobic capacity (VO_{2max}) by 0.9% per day over 30 days of bed rest[45] (Figure 3) independent of the disease state. The reduction in VO_{2max} secondary to reduced mobility is of special interest in critically ill patients who are already threatened by impaired oxygen delivery secondary to critical illness itself.

Beyond impaired oxygen delivery, other factors that may comprise the cardiovascular system with a prolonged recumbent position include increased blood viscosity. Increased blood viscosity results from decreased plasma volume[47] which could occur secondary to renal compensation to central fluid overload. Higher blood viscosity is associated with increased venous blood stasis which increases the risk of deep venous thrombosis.[48] Higher blood viscosity will also increase the pressure against which the heart must pump and thereby increase afterload and lead to an increase in myocardial work. [22,23]

The recumbent position is also associated with diminished reflex sympathetic nervous system response[49] which decreases venous tone and diminishes splanchnic vasoconstriction (altered arterial baroreceptor response). This reflex sympathetic system response is required to restore blood to the central circulation and maintain blood pressure in the erect position.[50-53] The diminished reflex sympathetic system response and the associated decrease in venous tone and splanchnic vasoconstriction lead to orthostatic hypotension. Orthostatic hypotension is further worsened by lower limb muscle weakness because these muscles act as a venous pump in the erect position.[50,51]

Similar to the skeletal muscle, the cardiac muscle responds to reduced loading conditions which further compromises the cardiovascular system after bed rest. Prolonged bed rest decreases the oxygen requirement of the body tissues and organs, resulting in decreased activity of the

myocardial fibres which may lead to myocardial muscle fibre atrophy. Perhonen et al[54] showed a 8.0 ± 2.2% (P = 0.005) decrease in left ventricular mass after 6 weeks of bed rest in 5 sedentary men with an additional decrease of 7.6 +/- 2.3% in 3 subjects who remained in bed for 12 weeks with no change in mass for 5 controls. The decrease in ventricular mass was associated with a corresponding decrease in left ventricular thickness. This finding suggests that cardiac atrophy can occur with bedrest secondary to physiological adaptation to reduced myocardial load.

Pulmonary Effects of Bed Rest and Inactivity

The effects of bed rest and inactivity on the pulmonary system also stem primarily from the loss of the vertical gravitational stress gradient related to the recumbency. Movement from the erect to a reclined position is associated with a restriction in chest wall movement and cephalad displacement of the diaphragm by the abdominal viscera, both of which result in decreased thoracic gas volume. An increased thoracic blood volume resulting from central fluid shift to the thoracic region in the reclined position also contributes to the reduced lung volume.[55] Available evidence show a decrease in functional residual capacity with the change from the upright to the recumbent position,[56,57] which mainly reflects the decrease in expiratory reserve volume[57] since the expiratory reserve volume is a component of the functional residual capacity (functional residual capacity = expiratory reserve volume + residual volume). Reduced functional residual capacity moves the lungs to the flatter part of the lung compliance curve thus leading to reduced compliance and increased risk of atelectasis. A 20% decrease in lung compliance from sitting to supine (0.21-0.16 L.cm H2O-1) was reported in healthy young adults.[58] An increase in the lung compliance could further contribute to increased elastic work of breathing.[59]

Both vital capacity and forced vital capacity have also been shown to decrease with the recumbent position. Blair et al.[57] showed a 6.5% decline in vital capacity with a change in position from standing to supine (4.94 L and 4.64 L, respectively). Manning et al.[55] also reported a ~3% lower forced vital capacity in right and left side-lying compared to sitting in older individuals without cardiac or pulmonary disease. This was accompanied by a reduction in the forced expiratory volume in one second (FEV_1 % predicted: 6.2% and 4% for the right and left side-lying, respectively) which further suggests that the recumbent positions also limit expiratory flow rate.[55] Behrakis et al.[58] showed that, independent of disease, flow-resistance increased by 40% with a change in position from sitting to supine (1.78 to 2.5 cm H_2O/L-1.s, respectively). Tidal volume

and minute ventilation are also decreased in the recumbent position. Gisolf et al.[60] reported a 50% increase in tidal volume, when healthy subjects changed from a supine to a standing position (490 ml and 734 ml, respectively). This was accompanied by a corresponding 24% increase in minute ventilation despite a 19% decrease in the respiratory rate. Thus lung ventilation is also decreased in the recline position.

Decreased ventilation-perfusion ratio has been reported to be lower in healthy individuals in the reclined compared to the erect position,[56,61] which shows lower gas exchange across the lungs in the reclined position. In individuals with lung disease, the decrease in functional residual capacity with the recumbent position[57] brings tidal breaths closer to the closing capacity, thereby subjecting dependent areas of the lungs to closure during normal tidal breaths.[56,61] The later reduces the surface area available for gas exchanges and leads to a decrease in the ventilation-perfusion ratio and results in hypoxia.[62]

Muscular Effects of Bed Rest and Inactivity

Unlike the cardiovascular and the pulmonary systems, the effects of bed rest and inactivity on the skeletal muscles stem primarily from a loss of exercise stress, related to inactivity. Consequently, these effects take longer to occur after the onset of bed rest and inactivity, unlike the effects on the cardiovascular and the pulmonary systems which begin immediately after the onset of recumbency.

Initial interest and inquiry into the effect of reduced mobility on the body was spurred by findings of its effect on the muscles, particularly the discovery of increased urinary nitrogen excretion in individuals with reduced activity, on bed rest or immobilized.[16,63] The increased nitrogen excretion occurs from a net catabolic protein metabolism (muscle protein breakdown),[16,64] which is an indication of muscle atrophy. Muscle atrophy has been noted as the predominant response of skeletal muscles to decreased activity and bed rest.[44] Bed rest induced muscle atrophy is accompanied by a decrease in muscle cross-sectional area[65,66] and fiber cross-sectional area.[67,68] While these studies indicate the effect of disuse atrophy independent of any disease condition, muscle atrophy associated with a disease condition is known to be more profound and rapid.[63] The loss of muscle mass is often accompanied by a reduction in muscle strength. Suetta et. al [68] reported a 13% - 20% decline in maximal quadriceps muscle contractile strength after 14 days of limb unloading using a knee brace and a cast in both younger and older individuals. Another study

showed that after 7 days of bed rest in healthy subjects,[65] maximum leg press and leg extension strength declines by 7% and 8% decline, respectively. There is also a decrease in peak torque and angle-specific torque with inactivity.[66]

Structural changes that disorganise the muscle contractile machinery and lead to altered oxygen delivery and impaired metabolism have also been reported to occur with reduced activity and bed rest.[69] Such changes also contribute to the observed muscle atrophy, decreased muscle strength, and reduced muscle endurance. Total immobility of the muscles further results in a shortening of muscle length (both fibre and total muscle lengths).[70]

Effects of Bed Rest and Inactivity on Other Body Organs and Systems

Almost all body organs and systems are affected directly or indirectly by prolonged bed rest and inactivity, including the bones, joints, and ligaments. The loss of bone mass resulting from resorption of calcium and phosphorous during bed rest has long been established.[16,71,72] Mineral resorption (bone disuse atrophy), which occur due to the loss of gravitational stress loading on the bones, increases the risk of pathologic fractures. With reduced joint mobility, there is loss of the buffering volume of water and increased synovial fluid viscosity.[73] These lead to the development of fibrogenous crosslinks, which harden with time and lead to stiffness.[70,73] The collagenous fibres of the capsules, tendons, and ligaments also adapt to the shortened position, and give rise to reduced flexibility and limited joint range of motion.[74]

At the skin, shearing forces, friction, and moisture, as well as pressure which occurs in prolonged bed rest may lead to the development of pressure sore.[75] When the pressure between the bony prominences and the bed is higher than capillary refill pressure, capillary circulation is impaired and ischemia occurs leading to the skin breakdown referred to as pressure sores.[75]

In the digestive systems, propulsion of the contents of the colon correlates with physical activity level.[76] Immobility therefore contribute, among other causes, to the development of constipation and faecal impaction due to incomplete emptying of the bowels.[77]

Bed rest and immobility leads to loss of gravitational pull of fluid to the ureters which results in incomplete voiding and stagnation of fluid. These provide a conducive environment for the development of infection. The stagnation of fluid also contributes to the development of calculosis from urinary calcium (which is also increased because of the excretion of calcium from bone).

Bed rest and inactivity also affect the metabolic process of glucose. Physical inactivity reduces the sensitivity of skeletal muscles to the presence of insulin (insulin resistance).[78] Since the skeletal muscles are the largest insulino-sensitive organs in the body, this resistance gives rise to an increased blood sugar (hyperglycaemia) which stimulates beta cell secretion of insulin leading to increased blood insulin levels.[79] The resulting hyperinsulinism is usually not sufficient to address the insulin resistance, thus the persistence of hyperglycaemia. The insulin resistance occurs secondary to a decreased concentration of glucose transporter 4 (GLUT-4) present in the muscle membranes with inactivity.[80] Isometric resistance training during bed rest has been shown to induce a 30% increase above the value of GLUT-4 before bed rest, suggesting that inactivity is the precursor to the reduced insulin sensitivity and not the recumbent position.[80] Hyperglycaemia resulting from increased insulin resistance is a predisposing factor to critical illness myopathy in immobile ICU patients.

There may also be depression, anxiety and other psychological disorders although these seem to be more related to the restricted and unfamiliar environment and isolation from friends rather than direct effect of bed rest.[81-83]

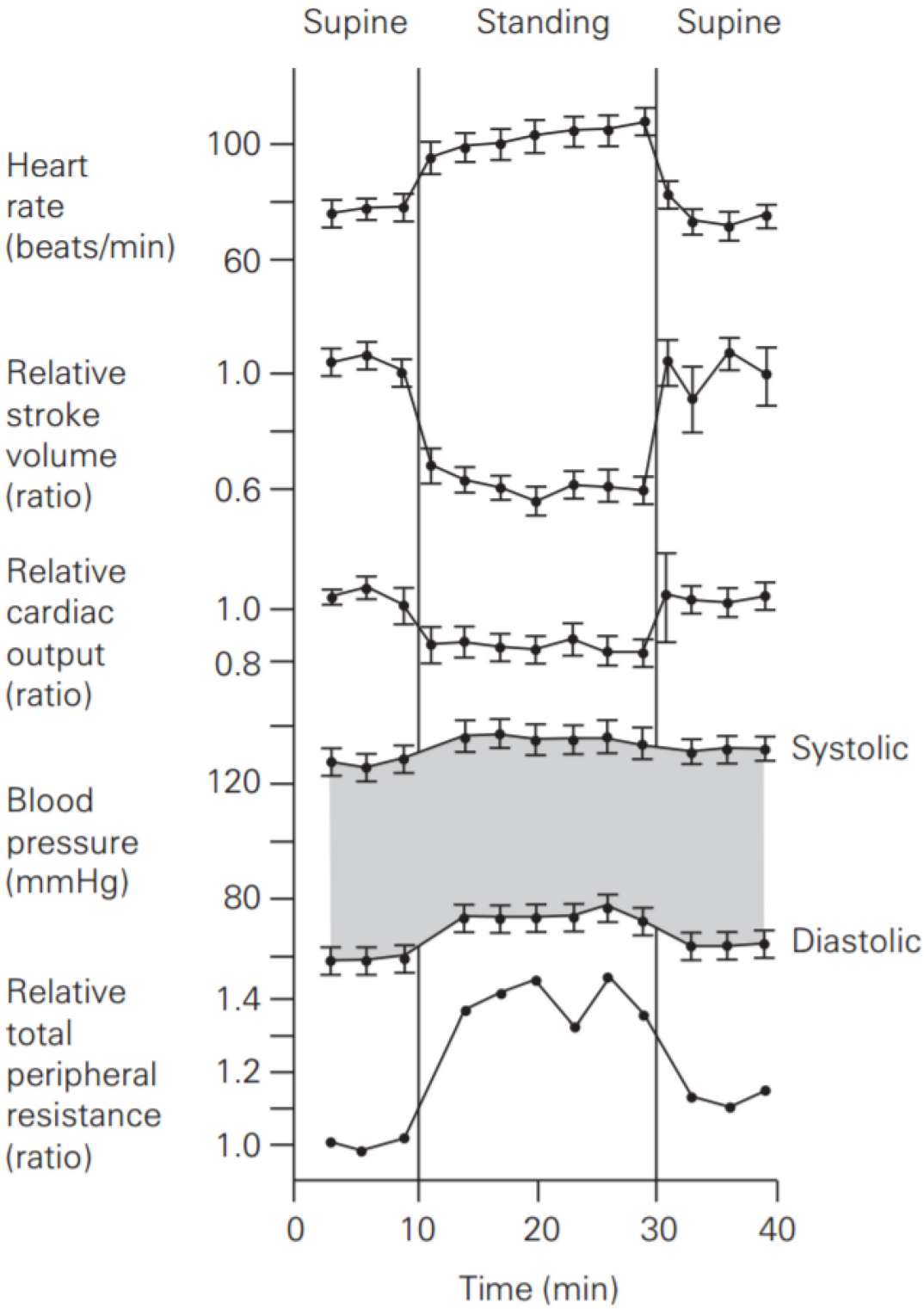

Figure 1. Mean Cardiovascular Responses (± SD) in Supine and Standing positions in normal subjects. *From Smith et al., 1970*[41]

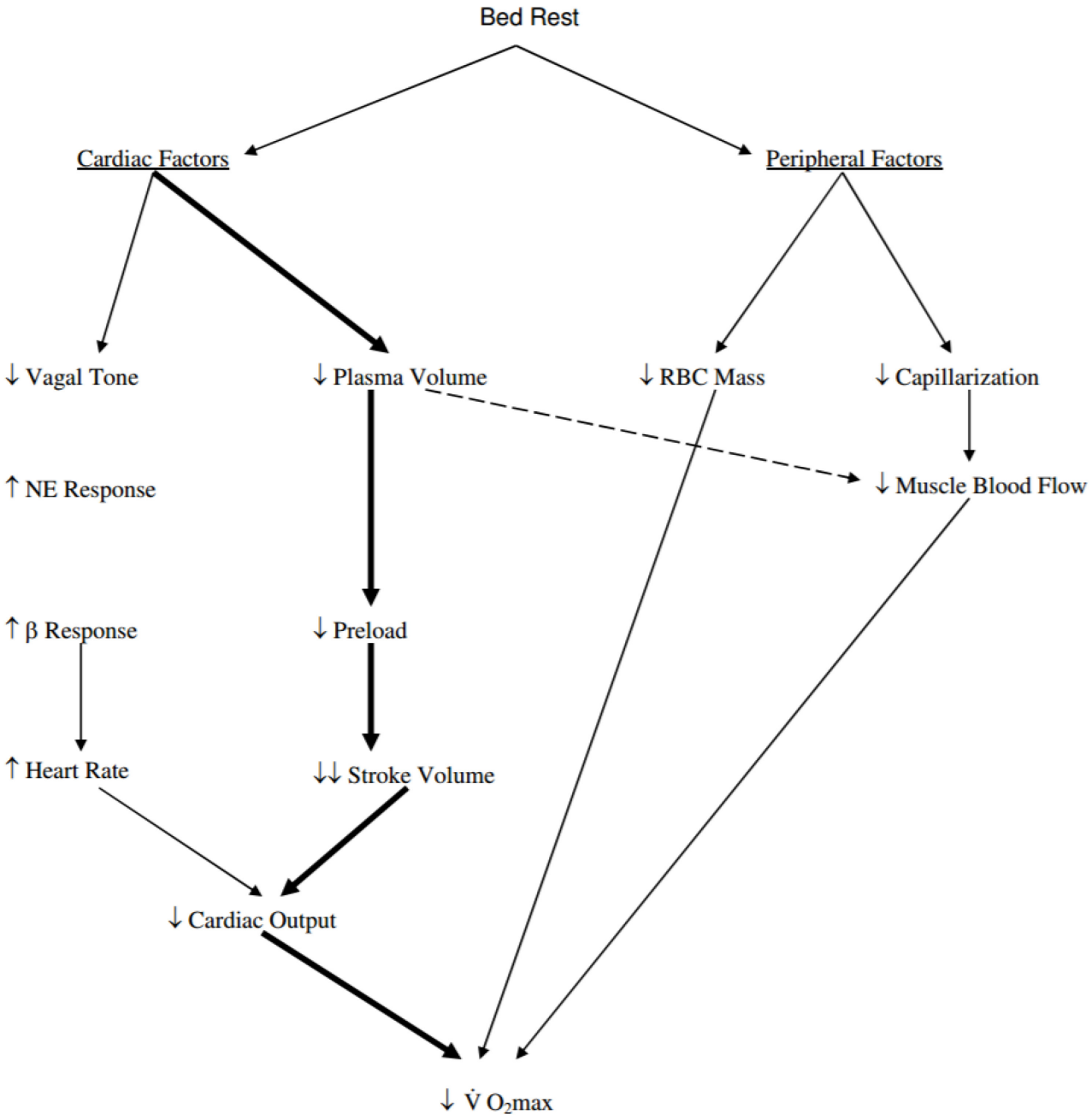

Figure 2. Cardiovascular mechanisms affecting VO2 max following best rest. *NE; norepinephrine, RBC: red blood cells. Adapted from Convertino*[45]

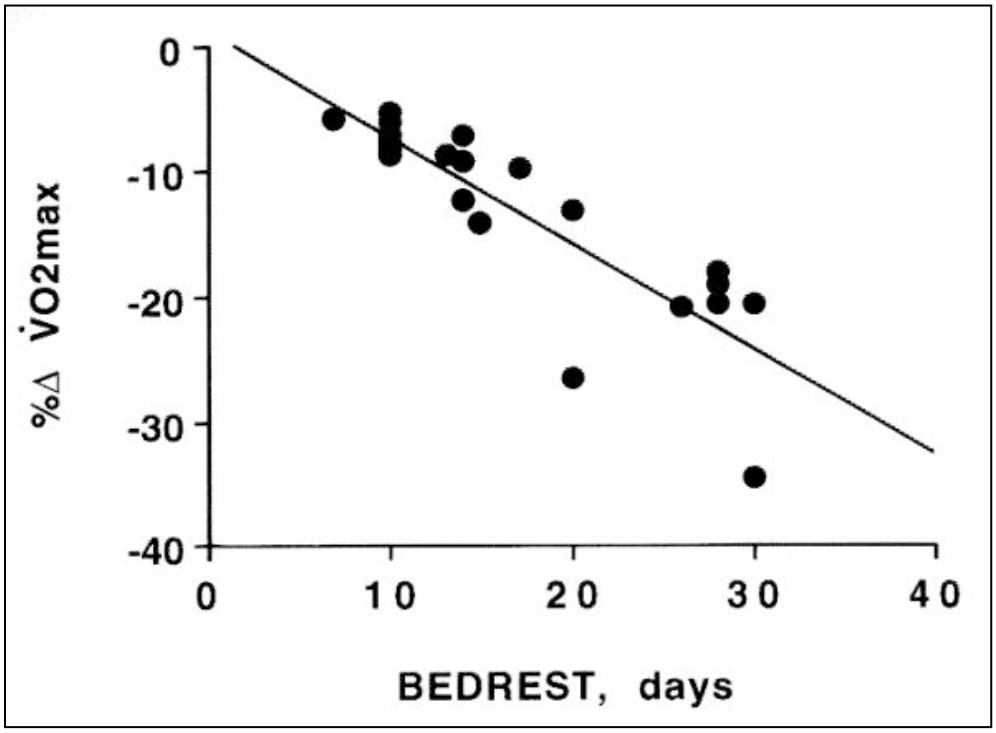

Figure 3: Regression of percent change in VO2max on duration of bed rest. The linear regression equation of best fit is %ΔVO2max =+1.4 -0.85 (days)]; r = -0.73. *Figure from Convertino 1997*[45]

Critical Illness and Reduced Activity

Impact of Reduced Activity in Critically Ill Individuals

Reduced activity has profound consequences in critically ill patients because it can accentuate the pathophysiology of underlying illnesses such as cardiac dysfunction, respiratory dysfunction, anemia, muscle wasting, muscle weakness, neuropathy, glucose intolerance, and reduced bone density. Moreover, critical illness itself can also accentuate the effects of immobility on several body organs and systems. Using a rat model of sepsis and immobility, Fink et al[84] showed that both inflammation (present in critical illness) and immobility independently induce atrophy, and the combination of these two factors further accentuates atrophy beyond that which may be caused by inflammation or inactivity in isolation.[84]

Consequently, ICU survivors are faced with impairments in body function,[85-87] which occur as a result of reduced physical activity[9,88,89] and that is further compounded by the presence of inflammation that manifests itself during critical illness. These impairments include, but are not limited to, neuromuscular dysfunction, heterotopic ossification, frozen joints, compression neuropathies, and pulmonary dysfunction, along with abnormalities in memory, attention, concentration and executive function, anxiety and depression, post-traumatic stress disorder / post-traumatic stress-related symptoms.[90] These complications are usually non-existent before ICU admission and unrelated to the pathology underlying the ICU admission.[1-5] Sometimes, they culminate in a condition known as ICU acquired weakness (ICUAW) which is an important consequence of critical illness that is associated with reduced activity and prolonged bed rest in critically ill patients. In a study by Zanni et al,[7] 55% of surviving patients, who were living at home before hospital admission, required inpatient rehabilitation after discharge from the medical facility due to their physical impairments. These complications may persist long after discharge. A study by van der Schaaf et al[6], in a cohort of 255 consecutive patients admitted to the ICU for more than 48 hours, showed that 54% of the patients had restrictions in their daily functioning, one year after discharge from the ICU. The net consequence is a decreased physical and health-related quality of life, increased costs and increased use of health care services among survivors of acute critical illness.[91-94]

Intensive Care Unit-Acquired Weakness

Intensive care unit-acquired weakness is a syndrome that can be defined as 'bilateral, global, diffuse and symmetrical muscle weakness acquired in the ICU, and for which there is no plausible cause other than critical illness'. The syndrome consists of three pathological categories: clinical illness myopathy (CIM), critical illness polyneuropathy (CIP) and critical illness polyneuromyopathy (CIPNM). Clinical illness myopathy was first described in a twenty-four-year-old woman who was admitted to the ICU on account of status asthmaticus.[95] The woman, with no previous history of muscle weakness, developed severe respiratory and limb muscle weakness after eight days of ICU admission, and subsequent electrophysiological testing confirmed CIM.[95] In a case report, Bolton et al.[96] reported 5 patients admitted to the ICU between 1977 and 1981, without previous history of muscle weakness, who all developed motor and sensory polyneuropathy during ICU admission.

Incidence of Intensive Care Unit-Acquired Weakness

The incidence of ICUAW varies with the patient population studied, the clinical syndromes evaluated (CIM, CIP or CIPNM), the timing of evaluation (ICU awakening, 7-days post-awakening, ICU discharge etc.), and the method of assessment (clinical, electrophysiological, etc.). There is a lower incidence with clinical diagnosis (32%, 95% CI:30-35) when compared to electrophysiological diagnosis (47%, 95% CI:45-50%) or histological diagnosis (52%, 95% CI:33-71%).[97] The latest systematic review involving 2686 adult ICU patients shows a combined incidence of 40% (95% CI:38-42%)[97] in the general medical and surgical ICU.

Clinical illness myopathy

Clinical illness myopathy refers to acute primary myopathy, characterized by reduced muscle membrane excitability, and a preferential loss of the heavy chain molecular motor protein myosin.[98-100] The protein loss results in rapid severe atrophy beyond that which may be expected from disuse alone,[101,102] which is an indication that critical illness potentiates the effect of immobility.

The major feature of CIM is acute generalized flaccid paralysis affecting the limbs, neck, respiratory, and often the facial muscles[103,104] (usually spared in CIP[105]). Patients with CIM are usually difficult to wean from mechanical ventilators secondary to the involvement of the diaphragm.[103] As is common in other myopathies, muscle weakness is usually more pronounced in the proximal compared to the distal muscles.[106] Although Apte-Kakade[107] reported more severe weakness distally in her case reports, the electrophysiological tests she reported did not rule out the co-existence of CIP, which presents with predominantly distal weakness. Tendon reflexes may be reduced or normal.[103,104] Sensation is usually spared in CIM, but that does not distinguish it from CIP, because of the difficulty in assessing sensation in the critically ill secondary to edema, impaired cognition, and other technical factors.[108] Therefore, sensory impairment does not rule out CIM.

Clinical illness polyneuropathy

Clinical illness polyneuropathy refers to symmetrical distal axonal sensorimotor polyneuropathy of the limbs and respiratory muscles that is characterised by a reduction in amplitude of the compound action potentials of both the sensory and motor nerves, with preserved or mildly reduced nerve conduction velocities, and acute primary denervation of sensory and motor nerves

supplying the limbs and respiratory muscles.[105,109] Previous terminologies for CIP include polyneuropathy in critically ill patients,[96] critically ill polyneuropathy,[105] critical illness polyneuropathy[110] and critical illness neuropathy.[111]

Clinical features in CIP are characterised by limb and respiratory muscle weakness, difficulty to wean from a mechanical ventilator, reduced deep tendon reflexes (often), and mild sensory loss usually in a stocking and glove pattern,[104,105] as is common in other peripheral neuropathies.[112] The presence of intact sensation may not rule out CIP, as intact sensation has been documented in cases of CIP.[113] Head and facial muscles are usually preserved in CIP,[105] and muscle weakness and other signs and symptoms seem more pronounced distally compared to proximally,[105,109] as is common in most peripheral neuropathy with axonal degeneration.[112] Although a study by Hund et al.[114] did not confirm the predominance of muscle weakness distally, the presence of co-existing primary myopathy was ruled out in only three of the seven patients, and a number of patients may have presented with co-existing CIM (CIPNM).

Clinical illness polyneuromyopathy

Clinical illness polyneuromyopathy is a more common presentation of ICUAW and represents a combination of CIM and CIP.[104,115] In a study by De Jonghe et al.,[106] all patients with clinically detected ICUAW showed sensorimotor axonopathy (CIP) on electrophysiological study, and those who underwent a muscle biopsy also had specific muscle involvement unrelated to the nerve involvement (CIM).

Clinical illness polyneuromyopathy presents with features of both CIM and CIP and the major clinical feature may depend on whether CIM or CIP is more predominant or whether both syndromes are predominantly present.

Pathological Mechanisms of ICUAW

The pathogenesis of ICUAW involves a complex mechanism of several related factors which are yet to be fully understood. It is believed to be driven by inflammatory related mechanisms and their interaction with immobility.[2,109,116,117] The complex interactions between these mechanisms and other risk factors of ICUAW ultimately result in the complications of bioenergetic failure, mitochondrial dysfunction, proteolysis within the muscles, glucose toxicity, Na^+ channel dysfunction, membrane excitability abnormalities, microvascular injury, membrane

depolarization, neuromuscular disconnection and axonal injury, which give rise to the clinical features ultimately seen with ICUAW.[109,117-120] While the interactions between the involved processes and mechanisms are complex and interwoven, several pathways may be more prominent in the development of either CIM or CIP.

Consequences of Intensive Care Unit-Acquired Weakness

The burden of ICUAW has far-reaching consequences that go beyond ICU survival and hospital discharge. ICUAW has been associated with prolonged weaning from mechanical ventilation,[106,121-124] increased ICU and hospital LOS,[87,121,123,124] and increased costs.[124,125] Available evidence suggests that ICUAW is associated with increased short- and long-term mortality,[121,125,126] though this is not consistent across all studies at all time points.[106,127] Notably, the only propensity score matching analysis (the best option to answer the question related to mortality in the absence of an RCT) supports an association between ICUAW and mortality at one year.[125] Reduced quality of life has also been generally reported after critical illness.[94,128] Although quality of life may not have been compared directly between survivors with and without ICUAW, studies from the general population[129] and some patient populations[130,131] have shown that muscle weakness impacts negatively on physical functioning and quality of life, although none of these studies was in the ICU.

Intensive care unit-acquired weakness is particularly pronounced in patients undergoing invasive mechanical ventilation because these patients commonly encounter reduced mobility for lengthy periods of their ICU stay [10-12] and because other factors which are closely associated with mechanical ventilation (such as sedation and neuromuscular blockers) are also risk factors for ICUAW. There is currently no treatment for ICUAW, efforts are therefore focused on reducing the risk factors, with reduced mobility being one of the factors of interest.

Association between Reduced Mobility and Intensive Care Unit-Acquired Weakness

Decreased mobility is one possible pathogenesis of CIM.[101,102,132-134] Furthermore, muscle inactivity predisposes to insulin resistance,[135] which causes hyperglycemia and possibly leading to CIP. Indirect reflectors of the duration of immobility, such as duration of mechanical ventilation and ICU LOS, have also been shown to be positively associated with ICUAW.[136-142] Such relationships, however, do not imply causality as ICUAW could precede such outcomes. Nonetheless, minimizing immobility during ICU stay is anticipated to reduce the risk of ICUAW.

Further evidence, however, is needed to confirm this assertion. As the prevalence of ICU survivors is increasing secondary to advancements in medical technology[10] attention should be given to identifying interventions that may prevent and/or reduce the prevalence and incidence of ICUAW among ICU survivors.

Causes of Reduced Activity in the ICU

The Impact of Illness

Critical illness itself has been associated with impairment of one or more body organs and systems which may result in multiple organ dysfunction syndrome that directly impacts activity level. Many pathological conditions managed in the ICU (neuromuscular disease, head injury, burns, morbid obesity, spinal cord injury, musculoskeletal trauma, sepsis and others) can lead to an impaired functioning of the cardiovascular system. The resulting impact on the oxygen transport system limits the energy available for normal activity which gives rise to general fatigue and reduced level of physical activity.

The Prescription of Bed Rest

Patients admitted to the ICU may have some conditions that necessitate limitation of movement or they may be assumed by ICU clinicians to be too sick to move.[22,30] They are, therefore, restricted to passive turning in bed for the prevention of pressure sores with or without contemplation on the detrimental implications of bed rest for already compromised body systems. Such contemplation may necessitate an assessment of their underlying cardiopulmonary reserve and tailoring of activities that can safely challenge their cardiopulmonary system.

The Sedative Practices and the Use of Neuromuscular Blocking Agents

Bjorn Ibsen, an anesthesiologist, was the first ICU physician to use sedative drugs in his practice.[37] This early use of sedatives in the ICU resulted in the practice of sedation becoming common in the ICU. Sedatives were originally designed for short-term usage as in surgery. No guideline was available to guide its prolonged use in critically ill patients until 1995.[143] The administration of sedatives was thus largely over-used without an understanding of the potential hazards of prolonged deep sedation and paralysis (especially for patients on mechanical ventilation was common practice[144,145]). A survey conducted in 1982 revealed that most patients were over-sedated and completely detached from the environment,[145] which is associated with immobility. Similarly, the use of neuromuscular blocking agents, which results in therapeutic paralysis, was also common

in most ICUs.[144,145] Therefore, deep sedation and paralysis have contributed to reducing physical activity levels during critical illness.

The ICU Lines, Leads, and the Physical Environment

Patients in the ICU are usually connected to life-sustaining and monitoring equipment via leads and they also have lines that are used for the delivery of medication and drainage of fluids. These lines and leads constitute a physical barrier to the movement of critically ill patients. The fear of dislodging such lines and leads often results in limiting patient movement in the ICU environment.

Other Factors

Other factors that may contribute to prolonged bed rest and decreased physical activity in the ICU include the side effects of some medications (such as fatigue, drowsiness, hypotension etc.), nutritional status of the patients, and certain e conditions such as post-fracture movement restrictions.

It is therefore necessary to consciously improve mobility in ICU patients even during the early stages of critical illness. This realization has given birth to the concept of EM.

Early Mobilization

The Concept of Early Mobilization

According to the European Respiratory Society and the European Society of Intensive Care Medicine, mobilization refers to physical activity sufficient to elicit acute physiological effects that enhance ventilation, central and peripheral perfusion, circulation, muscle metabolism, and alertness.[146] These acute physiological effects are also countermeasures for venous stasis and deep vein thrombosis.[146] Evidence suggests that mobilization can be started as early as about 24-48 hours after ICU admission,[21,138,142,147] in which case it is termed EM.[148]

Evidence of Effectiveness of Early Mobilization

Evidence from systematic reviews,[149-151] randomised controlled trials,[142,152,153] and other study types[88,89] have shown that EM is a countermeasure to immobility and is associated with more ventilator-free days in the ICU, shorter ICU and hospital LOS, improvement in peripheral and respiratory muscle strength, improved functional status at hospital discharge, and increased quality of life after hospital discharge. All these positive outcomes were not confirmed in some studies.[154-156] The cardinal difference between studies with and without positive results is the timing of the

mobilization intervention. Most studies showing a positive outcome started the mobilization at approximately 24-48 hours after admission to the ICU or the initiation of mechanical ventilation[21,138,142,147] when compared to studies that do not confirm these results which started mobilization at approximately 5 days or more after admission to the ICU.[154-156] All Clinical trials[21,138,142,153,156-158] and systematic reviews[150,159-161] have also shown that EM is safe and feasible for most patients even in the acute stages of critical illness. But it is still unknown if EM reduces the likelihood of developing ICUAW. Till date, no RCT has shown a significant positive effect of EM on the likelihood of developing ICUAW. Three RCTs have reported no difference in the incidence of ICUAW in ICU patients randomized to EM compared to usual care.[142,147,156] None of these studies were powered to detect a difference in ICUAW. Two previous systematic reviews[159,162] attempted to synthesize this evidence by pooling a number of studies together; however, the results were limited by the limited studies available at the time of the reviews, and by the methodological and statistical approaches of the meta-analysis. A more current systematic review would therefore still be required to answer this clinical question.

Realities of Practice

Early mobilization is not without its challenges, despite the evidence favouring its adoption into clinical practice.[163,164] Despite the availability of some protocols/guidelines to direct the implementation of EM,[138,141,146,165,166] as in all areas of clinical practice, evidence-based practice of EM seems difficult to implement clinically. Available research evidence does not guarantee transference to clinical practice.[167] A Canadian national survey reported that about two-thirds of ICU clinicians claimed to be familiar with the current literature on EM in the ICU;[168] however, evidence from observational studies showed that most ICU patients were not routinely mobilized.[88,89,140] A point-prevalence study across 38 Australian and New Zealand ICUs, no patient on mechanical ventilation was mobilized out of bed or walked on the day of the study.[88] A similar study across 116 ICUs in Germany showed that only 13% of the 783 mechanically ventilated patients were mobilized to a chair or standing/walking level on the day of the study.[89] In the same study, only 2% of the 401 patients with an endotracheal tube achieved the same level of mobility.[89] These results show the existence of a knowledge-to-practice gap in the clinical practice of EM.

Barriers that Hinder Knowledge Implementation

Several studies that have examined obstacles to the implementation of evidence-based practice of EM reported barriers existing at the patient-level (clinical factors), institutional-level (organizational factors), or provider-level (behavioural and non-behavioural factors).[168-173] A recent review involving about 40 studies, reported 28 unique barriers and over 70 strategies to address such barriers.[172] Studies have examined barriers at both the national,[89,174-178] and local hospital levels.[170,179] Whereas the studies conducted nationally provide a general snapshot of the existing barriers, they do not specifically identify barriers at a particular local facility, information that would be necessary for the development of knowledge translation interventions to overcome practice gaps at such a local level. A systematic review by Dubb et. al[172] revealed that barriers vary across ICUs depending on the patient population, setting, and ICU culture. However, there are no studies to date that have examined the practice of EM in any Montreal area hospitals (Quebec, Canada); we therefore do not know the current state of EM practice in these hospitals, the barriers being experienced, and facilitators that might improve this practice. Such information would be necessary to be able to design effective KT interventions at such facilities.

Physiotherapists in the Intensive Care Unit

The increased demand for the provision of EM in the ICU has necessitated greater involvement of physiotherapists in critical care. Nonetheless, limited knowledge and training, and limited availability of physiotherapists are barriers to meeting this demand. [168,172,177,180] Practice in the ICU requires familiarity with ICU environment viz-a-viz equipment, common ICU conditions, medications, therapies and procedures, tests and laboratory investigations and how these may impact on physiotherapy interventions. It also requires an understanding of the safety parameters that should be assessed before and during mobilization in critically ill patients. Traditionally across the globe and currently in some jurisdictions, physiotherapy entry-level training does not provide adequate competency in critical care.[181-183] There is therefore the need to bridge the critical care knowledge and skill gaps of practicing physiotherapists and the necessary first step in this process is to identify these gaps, which leads to the concept of a learning needs assessment.

Learning Needs Assessment

What is a learning needs assessment

A needs assessment is a systematic exploration of the way things are and the way they should be.[184] It is a process to determine the size and nature of the gap between current and more desirable knowledge, skills, attitudes, behaviours, and outcome.[185] A learning needs assessment is a systematic process to collect and analyze information on what a target group needs to learn.[186] Determination of a person's knowledge, skills, attitudes, and behaviours could be in the form of examination of the person's current practices and then measuring them against a template of what practice should be,[187] which may be more properly referred to as 'Gap or discrepancy analysis'.[188,189]

Types of learning needs in professional education

Learning needs among clinicians can be classified on the basis of who is determining the needs (i.e. the learner, educator, etc.) as well as what personal or professional standards are used as the metric for identifying such needs.[186] A review by Ratnapalan and Hilliard[186] described six types of learning needs, which were not mutually exclusive, and may be better viewed when categorized as: i) standard (normative and prescribed learning needs), ii) self-recognized needs (perceived and expressed learning needs) and iii) unknown needs (comparative and unperceived learning needs).

Standard needs

Normative needs refers to a gap in knowledge (learning needs) that is defined by an individual's or group's current level of knowledge, skills, attitudes, and behaviour in comparison to some level based on established standards.[186] The standards are usually determined by the certifying bodies and are based on value judgements, expert opinions, or information that emerges from research. In contrast, prescribed needs are learning needs that are judged by educators or program planners as being inadequate yet essential for the individual or group of clinicians.[186] Usually, the prescribers' (judges') decisions are established in reference to standards set by a certifying body or program requirement.[186]

Self-recognized needs

Felt or perceived needs are those identified by individuals or a group as being what they want and need to learn.[186] These are usually a result of an interaction between their knowledge, experience, and current or intended work environment, and are characterised by the sentence "I know what I

don't know." An expressed need is a sub-type of felt and perceived needs. It is simply what an individual or group express as their needs, by translating felt or perceived needs into the action of seeking help.[186] Usually, not all felt/perceived needs are expressed because of the presence of barriers to expressing needs.

Unknown needs

Comparative learning needs are identified by comparing two similar groups or individuals to determine discrepancies in knowledge, skills, attitudes, and behaviours; whereas, unperceived learning needs are unknown to the learner and are characterized by the sentence, "I do not know what I don't know."[186] These two types of learning needs are usually discerned by external entities such as clinical supervisors, teachers, professional bodies, clients or patients, allied health professionals, and national and international organizations or by research studies such as epidemiological reviews of health care problems within an institution or community.[186]

Other uncategorized types of needs assessment that have also been reported in the literature include miscalculated or misperceived needs, which refer to learning that the learner thinks that he/she has but does not have (I think I know something I don't), and emergent needs which are discovered when additional information is gained.[190,191]

Methods of learning needs assessment

The literature lists up to 46 formal and informal methods of learning needs assessment.[188] These methods include but may not be limited to the use of questionnaires, focus groups, interviews, chart audits, standardized patients, environmental scans, clinical recall interviews, objective structured clinical examinations, nominal groups, and the Delphi technique. Among these, questionnaires and structured interviews seem to be the most commonly employed methods.[192]

While each of these methods has several pros and cons, some of which have been discussed in previous literature,[186] the choice of method to be used is largely influenced by the type of learning needs to be assessed. Previous publications have mapped learning needs according to the different types of methods used for assessment of such needs.[186,190,191]

Nonetheless, when the targets users of a learning needs assessment tool development are licensed clinicians for whom there is no obligation to use the tool other than for self-directed learning, it

will be more pragmatic to find out from the target audience what method of learning needs assessment will be most suitable for them.

Summary of Evidence Gaps Addressed in this Thesis

In summary, bed rest and decreased activity in the critically ill is associated with the development of ICUAW and other poor health outcomes. Early mobilization has been suggested as a possible preventive therapy for ICUAW but no RCTs have been powered to detect a difference in the likelihood of developing ICUAW. There is, therefore, the need to pool studies together in a meta-analysis to provide evidence on this proposition.

Furthermore, while the implementation of EM practice in the ICU has been advocated in the literature, the wide-scale adoption is challenged by many barriers which vary depending on the clinical setting. No study has evaluated the current practice of EM in Montreal area ICUs. To improve practice in this local context, it is important to first identify and characterize the existing barriers.

Finally, while it is important to identify barriers, efforts should be made to develop interventions to address them. Some important barriers to EM that has been consistent across many studies is the limited availability of physiotherapists and limited training/knowledge.[168,172,177,180,193]

The conceptual framework to improving patient outcomes in clinical practice described by Cabana et al.[194] in "Why don't physicians follow clinical practice guidelines? A framework for improvement." asserts that before a knowledge translation intervention can affect patient outcomes, it first affects the clinician's knowledge, then attitudes, and finally behavior. It further asserts that indirect manipulation of behaviour alone is more difficult to sustain if knowledge and attitudes have not been affected. Currently, no tool exists to identify the gaps in critical care knowledge and skills of physiotherapists aiming to work in the ICU. Such gaps need to be addressed in order to improve knowledge, attitudes and ultimately patient outcomes.

The aim of the projects included in this doctoral thesis is, therefore, to bridge the evidence gaps identified in this literature review by providing insight into the barriers and facilitators to the implementation of EM in local area ICUs and contributing to the existing body of knowledge in order to ultimately to help improve the practice of EM. These projects are situated in the knowledge creation funnel and action cycle of the Knowledge to Action Framework developed by

Graham et al.[195] The first and second projects assessed barriers and identified problems to be addressed and therefore encompass two steps, “assess barriers to knowledge use” and “identify a problem” in the action cycle. The third project falls under the “knowledge synthesis” step of the knowledge creation component. Finally, the fourth project involves the development of a learning needs assessment tool and falls under the “knowledge tools/products” step of the knowledge creation component.

CHAPTER 3: OBJECTIVES OF THE RESEARCH THESIS'S PROJECTS

OVERALL OBJECTIVE

The overall aim of this thesis, which contains four manuscripts, is to provide insight into the barriers and facilitators to the implementation of EM in local area ICUs and to contribute to the existing body of knowledge in order to ultimately to help improve the practice of EM.

OBJECTIVE ONE

The objective of the first project was to identify perceived gaps in clinical practice and to assess the perceived barriers to EM in critically ill patients in three McGill University affiliated teaching hospitals (Montreal, Canada).

OBJECTIVE TWO

The objective of the second project was to obtain a deeper understanding of the barriers to the practice of EM in the ICU from the perspective of ICU clinicians: why these barriers exist, what could be done to reduce them, and the facilitators that might enhance this practice.

OBJECTIVE THREE

The objective of the third project was to estimate the extent to which EM and neuromuscular electrical stimulation interventions compared to usual care, reduce the incidence of ICUAW among patients in the ICU.

The secondary objective was to assess the extent to which EM and NMES interventions impact other outcomes (ventilator dependency, discharge location, ICU and hospital LOS, and acute mortality) that may be associated with ICUAW.

OBJECTIVE FOUR

The objective of the fourth project was to identify and select the theoretical and practical knowledge and skill areas that will inform the development of a critical care learning needs assessment tool for physiotherapists aiming to work in the ICU.

CHAPTER 4: PREFACE TO MANUSCRIPT ONE

Chapter two presents the evidence to support that EM is a safe and feasible intervention that is associated with positive health outcomes in patients with critical illness. Nonetheless, there are barriers that exist to the implementation of EM in clinical practice. This chapter reveals that these barriers vary from one local context to another. This difference may be attributed to differences in ICU culture, patient population, staffing level, availability of expertise to implement the intervention and other resource issues. Consequently, there are also differences in the practice patterns of EM from one hospital to another. As stated earlier, no study has looked at EM practice in the Montreal area. Therefore, before this study was conducted, there was no knowledge as to the current state of EM practice, as well as the existing barriers and facilitators. Acquiring knowledge regarding the current state of practice and the existing barriers in the region is be an important first step towards being able to develop knowledge translation interventions that may close any existing knowledge-to-practice gaps.

In this manuscript, we present the results of a study that used surveys to explore the practice pattern, identify perceived barriers, and assess perceived gaps in the clinical practice of EM among critically ill patients in three Montreal-area ICUs.

CHAPTER 5: MANUSCRIPT ONE

INTERPROFESSIONAL SURVEY OF PERCEIVED BARRIERS AND FACILITATORS TO EARLY MOBILIZATION OF CRITICALLY ILL PATIENTS IN MONTREAL, CANADA

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LIST OF ABBREVIATIONS IN MANUSCRIPT 1

Abbreviation	Meaning
EM	Early mobilization
ICU	Intensive care unit
KT	Knowledge translation
MDs	Physicians
PTs	Physiotherapists
RTs	Respiratory therapists

Keywords: Early Ambulation, Clinical Practice Patterns, Intensive Care Units, Critical Illness, Physical Therapy Specialty, Barriers.

ABSTRACT

Objective: Early mobilization is safe, feasible and associated with better outcomes in patients with critical illness. However, barriers to mobilization in clinical practice still exist. The objective of this study was to assess the knowledge and practice patterns of intensive care unit (ICU) clinicians, as well as the barriers to early mobilization.

Design: Cross-sectional survey.

Setting: Intensive care units of three university-affiliated hospitals in Montreal, Canada.

Subjects: One hundred and thirty-eight ICU clinicians, including nurses, physicians (MDs), respiratory therapists (RTs), and physiotherapists (PTs).

Interventions: None

Measurements: Perceived barriers, knowledge and practice pattern of early mobilization were assessed using a previously validated mobility survey tool.

Main Results: The overall response rate was 50.0% (138/274). Early mobilization was not perceived as a top priority in 49% of respondents. Results showed that clinicians were not fully aware of the benefits of early mobilization as per current literature. About 58% of clinicians did not feel well trained and informed to mobilize mechanically ventilated patients. Perceptions on patient-level barriers varied with clinicians' professional training, but there was a high degree of inter- and intra- professional disagreement on the permissible maximal level activity in different scenarios of critically ill patients.

Conclusions: Our survey shows limited awareness, among our respondents, of the clinical benefits of early mobilization, and high level of disagreement on the permissible maximal level of activity in the critically ill. Future studies should evaluate the role of knowledge translation in modifying these barriers and improving early mobilization.

BACKGROUND

Intensive care unit (ICU) survivors are at risk of deconditioning, weakness and functional disability.[94,117] These complications are known to be associated with reduced mobility[117] which is common in many ICUs.[8,9,88,89] Emerging evidence suggests that early mobilization (EM) in the ICU is associated with better outcomes in survivors of critical illness.[142,147,151,153,162,196] There is also strong evidence on the safety and feasibility of initiating EM for mechanically ventilated patients in the ICU.[21,89,142,147,149] Despite increasing concern and advocacy for changing the current ICU culture to promote EM in the critically ill,[9,10,197] translating the available knowledge into clinical practice remains a serious problem because of numerous patient-level, institutional-level, and clinician-level barriers. Studies in several countries have focused on identifying these barriers nationally[89,168,174,198] and locally.[170,179] While the national studies have succeeded in providing an overview of the existing barriers and their magnitude, only regional studies highlighted problems within a local context.

The aim of this present study was to identify possible perceived gaps in clinical practice and to assess the perceived barriers to EM in critically ill patients in three McGill University affiliated teaching hospitals (Montreal, Canada). This survey examined the perspectives of clinical professionals involved in the mobilization of the critically ill patients.

METHODS

The survey respondents

We simultaneously surveyed all physicians (MDs), physiotherapists (PTs), nurses, respiratory therapists (RTs) and occupational therapists who work in the ICU in three McGill University affiliated teaching hospitals, namely the Royal Victoria Hospital, the Montreal General Hospital, and the Jewish General Hospital. The surveys were self-administered through a central pick-up box within each ICU, and were conducted between September 2014 and February 2015. Potential clinician respondents were contacted through mini-presentations at the clinical meetings of the participating departments of each hospital, through email communications with the clinicians and through direct contact. Clinicians were eligible if they had worked in an ICU within Canada for at least six months in the preceding eight years. Ethics approval was obtained from the Research Ethics Board of McGill University (Montreal, Quebec), and from participating hospitals.

The survey instrument

The survey was conducted using a modified version of a previously validated Mobility Survey Questionnaire (see survey instrument, Appendix I) that was developed using rigorous methodology in collaboration with the Canadian Critical Care Trials Group.[168] The survey tool has good reliability and validity.[168] It has three major domains to evaluate clinicians' perceptions of barriers, knowledge and clinical practice of EM in the ICU.[168] The survey instrument defined EM on its front page as 'physical therapy and acute rehabilitation measures initiated as soon as possible following admission to the ICU'. It also made a distinction between non-mobility physiotherapy such as passive range of motion and mobility physiotherapy (Appendix I).

Modification of the survey tool was done by our research team to adapt the tool to the practice in the Montreal area ICUs. The modifications primarily consisted of the addition of a question (*Who performs passive range of motion exercises for the patients in your ICU? – current Q17)* Also, the previous Q17 was split into two parts (current Q18a and Q18b). In 18a, a new question (*On average, what is the daily duration of passive range of motion performed by physiotherapists in YOUR ICU on the following types of critically ill patients?)* was added with the response items 'a' and 'b' of the original Q17 retained, while Q18 retained the original question (Q17) and its remaining response items 'c' and 'd'. A similar procedure was performed for previous Q18 (currently Q19a and 19b). This was necessary to reflect the practice in our local ICUs since unconscious, inattentive and uncooperative patients (described in response items a & b) are not usually mobilized in our ICUs (by the definition of mobilization in the tool). Finally, 'respiratory therapist and occupational therapist' were added to the question on clinician demographics, and 'PCCU' (paediatric critical care unit) was removed from all items since we were surveying only ICUs in which patients were all adults.

Data Analysis

Descriptive statistics were carried out for all variables. Frequency distributions and proportions were computed for discrete variables, and means and standard deviations for continuous variables. The number of respondents was used as the denominator for each survey item. Response items were collapsed where necessary to summarize the responses in a presentable manner. Association between the professional groups and right or wrong response on the knowledge domain question

items was assessed using the chi-square statistics. The SPSS 22 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) was used for all analysis.

RESULTS

Response Rate and Respondents

Overall, 274 surveys were administered and 138 completed and returned (response rate of 50.4%). **Table 1** shows the survey response rates by hospital and profession. Most respondents 127 (92.0%) reported working in a medical-surgical ICU while also covering cardiovascular 72 (52.2%), neurological 38 (27.5%), and trauma 39 (28.3%) ICUs. One respondent did not provide this information

Perceptions

Perceived Importance of Early Mobilization

Overall, 16 clinicians (11.6%) perceived EM as crucial, 54 (39.1%) as very important, 50 (36.2%) as important and 9 (6.5%) as somewhat important. Figure 1 suggests that PTs and MDs value EM more than RTs and nurses.

Perceived Barriers to Early Mobilization

Figure 2 and Appendix II shows the perceived patient-level, institutional-level and provider-level barriers. Medical instability (123 [89.1%] respondents), nurse safety concerns (87 [63.0%]), limited number of physiotherapists (85 [61.6%]) and insufficient equipment (85 [61.6%]) were perceived to be the greatest barriers to EM. While nurses and RTs were most frequently concerned about the risk of dislodgement of devices and lines, PTs were more frequently concerned about excessive sedation, and MDs were equally concerned about both barriers. Insufficient equipment was the greatest institutional barrier reported by MDs, nurses, and RTs, whereas PTs perceived the requirement of a physician order as the greatest institutional barrier.

A further probe into the medical instability of ICU patients in several scenarios with changing diagnosis/condition, device/drug, and physiologic status (section 1.3, questions 5 and 6 of Appendix I) showed a great variability in the maximum level of physical activity that clinicians reported that they would permit in intubated and mechanically ventilated patients. **Figure 3** and

Appendix III shows the maximal activity level identified by clinicians which we dichotomized into bed bound activities (bed rest, passive and active range of motion) and gravitational challenging activities (standing, transfers to chairs and ambulation) for the purposes of analysis. Physiologic status was perceived to pose the greatest limitation to activity progression.

Perceptions on when to initiate EM

Most respondents (122 [88.4%]) felt that EM should be started as soon as a patient's cardiorespiratory status has been stabilized. About 75 (54.3%) were also of the opinion that EM should be started as soon as the patient is conscious and cooperating, whereas 62 (44.9%) responded that EM should be started as soon as possible following ICU admission. Some felt that being off all vasoactive infusions (46 [33.3%]), sedative infusions (46 [33.3%]) or extubated (30 [21.7%]) was necessary to begin EM. Table 2 shows the relative perceptions among the professions on when to initiate EM.

Knowledge and Skills

Many of our respondents 90 (65.2%) reported to be sufficiently familiar with the literature and clinical studies on EM in the ICU, but only 56 (40.6%) respondents had a correct response to the incidence of intensive care unit-acquired weakness (ICUAW) in the general medical and surgical ICU (62 [44.9%] clinicians underrated it and 12 [8.7%] reported to be unaware).[97,199] The Chi-square statistic did not show any association between professional group and right or wrong response on incidence of ICUAW (p=0.050).

A series of five true or false questions regarding the benefits of EM as has been shown in clinical trials[21,138,142,153,196,200] and systematic reviews[149,151,160,162] showed disparity between the clinicians' perceived knowledge and actual knowledge of the benefits of EM. The number of clinicians who gave correct responses to 0, 1, 2, 3, 4 and 5 questions were 1 (0.7%), 5 (1 3.6%), 44 (31.9%), 64 (46.4%), 15 (10.9%) and 5 (3.6%), respectively (4 [2.9%] invalid responses). There was a significant association between the professional group and a right or wrong response to the question items that pertained to the effect of EM on functional independence, delirium and time requiring ventilation. Figure 4a shows the perceived and actual knowledge of our respondents by professional group.

Only 58 (42%) clinicians perceived that they were well trained and informed to mobilize mechanically ventilated patients. Perceived knowledge and skill in EM varied with clinical profession with more PTs and nurses feeling well trained and informed compared to MDs and RTs (Figure 4b).

Practice

Only 22 (15.9%) respondents believed that critically ill patients are screened automatically for appropriateness to begin mobilization by the PTs (34 [24.6%] clinicians were unsure). About 101 (73.2%) reported that the initial PT assessment on each patient in their ICU requires a physician medical order. Most clinicians (88 [63.8%]) responded that the registered nurse is the first to identify when a patient is ready for mobilization, although a greater percentage of PTs believed that the Physician (4 [44.4%]) or PT (3 [33.3%]) is the first. About one third (45 [32.6%]) of clinicians were not aware if a written protocol to guide EM exists in their ICU.

About half of the respondents, 23 (46.0%) and 29 (67.4%) in hospitals A and C, respectively, reported that their ICU had an EM champion compared to 8 (17.8%) in hospital B. More respondents believed the champion was a critical care physician in hospital A (13 [26.0%]) and a registered nurse in hospital C (28 [65.1%]). Each profession group, with the exception of the RTs (most RTs were unsure), believed that the clinician champion was in their profession (it should be noted that overall, 26 [18.8%] of respondents did not respond to this question).

Our respondents reported that nurses (135 [97.8%] of respondents), PTs (131 [94.9%]), health aids (112 [81.2%]), RTs (98 [71.0%]), family member/home care givers (38 [27.5%]), OTs (17 [12.3%]) and physicians (13 [9.4%]) participate in EM in their ICU.

Reported Physiotherapy Availability, Workload and ICU Treatments

A subgroup analysis of PT responses shows that PTs are not available during the evening hours (9 [100% of PT respondents]) while two hospitals provide limited services on the weekends. These PTs see an average of 9 (SD 3.1, IQR 8.5-10.5) hospital patients daily out of which an average of 6 (SD 3.6, IQR 3-9) are ICU patients. The average work duration reported was 7.1 hours (SD 0.33, IQR 7-7) and only one-third work full-time in the ICU.

The subgroup analysis further shows that chest physiotherapy, ROM exercises, in and out of bed activities, as well as transfers, are frequently used, whereas neuromuscular electrical stimulation, tilt table, gait training, treadmill walking, and cycle ergometry are never or infrequently used (Table 3). In summary, technology-driven PT interventions and gravitationally-challenging interventions beyond transfers to the chair are not used frequently.

ICU culture

Only 9 [6.5%] respondents reported that patients with suspected ICUAW are routinely referred to an outpatient clinic after ICU discharge for long-term rehabilitation, whereas 77.5% reported that they are only sometimes referred.

About 3 (21.4%), 5 (35.7%) and 4 (28.6%) of physicians stated that daily interruption of sedation or sedation protocols were routinely, frequently, and sometimes used in their ICU, respectively. Also, 11 physicians (78.6% of physician respondents) reported to routinely use standardized sedation scales or a protocol to adjust sedation to waken patients so as to promote activity, whereas 7.1% reported to frequently do so (2 physicians [14.3%] had no response to these two questions). A substantial number of other professionals gave 'no response' or were not sure of the answer to this question (PTs 3[33%], Nurses 31[35.6%], and RTs 18[64.3%]).

DISCUSSION

The findings of this study show that perceived barriers to EM are largely influenced by the trainings and expertise of professionals, and that there is high variability between clinicians in the maximum level of activity that they deem appropriate for a given critically ill patient. The study further highlights the need for knowledge translation (KT) interventions that will augment the clinicians' knowledge of the potential benefits of EM while enhancing their skills to safely and effectively mobilize mechanically ventilated critically ill patients.

It is expected that EM practice will be largely influenced by the knowledge and skills of ICU clinicians on EM, the priority they place on EM, the barriers they encounter, and by the health care provider's profession as also shown by Garzon-Serrano et al.[179] We found a disparity between clinicians' perceived knowledge and actual knowledge on the benefits of EM as also shown by Koo et. al.[168] While knowledge in itself may not be sufficient to generate a change in practice,[201]

it is a necessary foundation for evidence-based clinical practice. Further knowledge translation of available evidence is needed to guide practicing clinicians.

Half of the respondents in our study did not identify EM as a top priority in patients' care. An earlier study also showed that EM was not perceived as a top priority in about a third (31.2%) of the respondents.[168] While the value placed on EM was higher in that study, it did not include nurses and RTs who also play a role in the day-to-day management of ICU patients. Nurses were about 63% of the respondents in our study and their opinion added value to our results. The priority placed on EM may be a reflection of the ICU clinicians' knowledge of the importance of EM or the interpretation of the existing evidence on the benefits of EM. Despite the overwhelming expert advocacy for EM[9,10,117,197,202] and the benefits shown from many clinical trials,[21,138,142,153,196] some studies have not confirmed the benefits.[154-156] Most studies which did not show benefits with EM often began EM later (about 5-7 days from ICU admission)[154-156] whereas those which showed benefits started earlier (about 1.5 days)[21,138,142,147] suggesting that the timing of mobilization plays an important role.[162,203] In our study, many clinicians were of the opinion that EM should start as soon as possible following ICU admission and as soon as the patient's cardio-respiratory status has stabilized, which is in line with current recommendations.[163,203,204] A previous systematic review, which attempted to tease out the effect of timing differences on study outcomes, were unable to do so due to an inability to obtain the required information.[162] This underscores the need for another systematic review that can obtain the needed information to tease out this difference. Limited skills in the mobilization of mechanically ventilated patients can be a potential barrier to EM. Our study found that over half of the clinicians did not feel well-trained to mobilize patients on mechanical ventilation and this finding was similar to that of a previous study on EM.[168] A point prevalence study showed that no patient requiring mechanical ventilation sat out of bed or walked in 38 Australian and New Zealand ICUs on the day of the study.[88] Improving the skills and knowledge of ICU health professionals in the mobilization of mechanically ventilated patients may promote the EM of this patient population.

The barriers identified by clinicians in this study were similar to the barriers identified in other studies.[167,168,171,179,198,205] Overall, the barriers most highly rated by all clinicians were medical instability, nurse safety concerns, limited physiotherapists, and insufficient equipment. Interestingly, the priority placed on most barriers varied with the clinician's profession as also

previously shown.[168,179] This supports the notion that multidisciplinary teams which complement each other are needed to surmount the multiple barriers of EM in the ICU environment.[21,198,206,207]

Further examination of medical instability using clinical vignettes showed a high variability with regards to the highest level of activity that clinicians perceived to be safe in the critically ill. Fewer than half of the clinicians agreed on the maximum level of activity in ten of the thirteen clinical condition/diagnosis scenarios, eight of the fifteen devices/drug scenarios and ten of the twelve physiologic status scenarios. This high non-agreement ratio among clinicians in a given institution and/or profession cannot be explained by patients' clinical condition, diagnosis, physiologic status, devices or drugs being administered but likely reflects the actual degree of variability in clinical practice. This may be an indication that evidence is lacking on the specifics of mobilization safety in many patient populations, although it may also imply that clinicians are not fully aware of the evidence that does exist.[208] Clinical practice variability, defined by Kennedy et al.[209] as a situation in which 'patients with similar diagnoses, prognoses and demographic status receive different levels of care depending on when, where and by whom they are treated, despite agreed and documented evidence of "best practice"', represents a lack of patient-focused care, and compromised quality and safety of care.[209] Therefore, there is a need for further KT studies to explore the source of the heterogeneity of opinion on the maximum level of permissible activity, in order to close the knowledge to practice gap and lead to greater standardization of care. Heterogeneity of practice may also be linked to lack of protocol to guide practice.[210] About 52%, 42% and 5% of the clinicians in the three ICUs believed that they had a protocol to guide EM. This suggests that either the ICUs did not have a protocol or they had a protocol that was not really used. Earlier studies have identified the absence of written guidelines as a barrier to EM,[168] whereas the existence of a written protocol can act as a facilitator.[138,142,171]

Safety concerns by nurses was rated as a big barrier to EM in this study despite consistent evidence that EM is safe and feasible in critically ill patients.[21,142,204,211] This perception could lead to late initiation of mobilization since most nurses, MDs and RTs believe that the registered nurse is the first to identify when a patient is ready for mobilization; this underscores the need for KT-interventions to address this knowledge barrier among nurses.

The limited number of PTs and nurses was perceived as the greatest provider-level barrier. A third of PTs in this study work full-time in the ICU while 2/3 also covered other hospital units. Dedicated ICU PTs can promote EM. Furthermore, nurses have an enormous burden of responsibility in the

critical care environment, and our survey results additionally showed that EM was not a top priority in their schedule. This supports the findings of Morris et al.[138] that better staffing and use of an interprofessional mobility team can enhance EM in the ICU.[141]

Study Limitations

The major limitation of the current study relates to the common limitations of studies using a survey design methodology. Barriers and practice patterns in this study were as stated by clinicians who responded to the survey and were not observed. Cross-sectional and prospective observational study designs might provide a deeper understanding of practice patterns and barriers to EM. The current study was also limited to clinicians who worked in McGill-affiliated hospitals which were all Montreal English hospitals. These findings may not apply to community hospitals or other regions. It should also be noted that a higher number of nurses and RTs completed the current survey compared to MD and PTs, although this represents the reality of the distribution of professionals in our ICUs. Early mobilization was defined in this study as 'physical therapy and acute rehabilitation measures initiated as soon as possible following admission to the ICU' without any time frames. This could have led to different interpretations on what was considered as EM. The requisite of 6 months' experience in the last eight years might also reflect limited ICU experience or experience that was not up-to-date in some of our respondents. Because the survey was self-administered, we were unable to determine if participants completed it more than once. However, this is unlikely given the time burden involved in completing the survey. Finally, our survey tool did not capture data on the years of experience of the respondents.

CONCLUSION

Our survey shows that there are many clinician-perceived barriers to EM in the ICU and that these barriers vary with clinical profession. This suggests that the involvement of an interprofessional team may enhance EM. It also shows limited awareness of the clinical benefits of EM, and that most clinicians do not feel well trained or well informed to mobilize mechanically ventilated patients. Future knowledge translation research may be helpful in modifying these barriers and improving EM. Furthermore, the findings of this study may guide and/or provide initiatives to the design of EM quality improvement projects in other institutions. Real-time audit of daily activity levels, barriers and facilitators may also be helpful to promote mobility.

Take-home message:

Our results show lack of standardization of care in the clinical practice of EM which suggests the existence of knowledge-to-practice gap. There is a need for knowledge translation interventions to close the knowledge-to-practice gap and translate the research evidence on EM into clinical practice.

TABLES

Table 1: Survey Response Rate

Hospital	MDs	PTs	Nurses	RTs	*Total by Hospital*
Hospital 1	4/6	3/4	35/69	8/35	50/114
	(66.7%)	(75.0%)	(50.7%)	(22.9%)	(43.9%)
Hospital 2	5/10	3/5	23/47	14/22	45/84
	(50.0%)	(60.0%)	(48.9%)	(63.6%)	(52.4%)
Hospital 3	5/9	3/3	29/31	6/21	43/76
	(55.6%)	(100%)	(93.5%)	(28.6%)	(56.6%)
Total by Clinician	14/25	9/12	87/147	28/78	**138/274**
	(56.0%)	(75.0%)	(59.2%)	(35.9%)	**(50.4%)**

Ratio of 'returned' to 'distributed surveys' (percentage)

Table 2: Perceptions on when to Initiate Mobilization in the ICU

Response Option	PTs n(%)	MDs n(%)	Nurses n(%)	RTs n(%)	All n(%)
As soon as possible following ICU admission	4 (44)	6 (42.9)	43 (49.4)	9 (32.1)	62 (44.9)
As soon as the patient's cardio-respiratory status has stabilized	8 (88.9)	11 (78.6)	79 (90.8)	24 (85.7)	122 (88.4)
As soon as the patient is extubated	3 (33.3)	0 (0.0)	19 (21.8)	8 (28.6)	30 (21.7)
As soon as the patient is off all vasoactive infusions	3 (33.3)	3 (21.4)	29 (33.3)	11 (39.3)	46 (33.3)
As soon as the patient is conscious and can cooperate	4 (44.4)	7 (50.0)	46 (52.9)	18 (64.3)	75 (54.3)
As soon as all sedative infusions are discontinued	4 (44.4)	1 (7.1)	31 (35.6)	10 (35.7)	46 (33.3)
As soon as the patient is ready to be transferred out of the ICU	0 (0.0)	0 (0.0)	13 (14.9)	2 (7.1)	15 (10.9)
Others	1 (11.1)	0 (0.0)	4 (4.6)	0 (0.0)	5 (3.6)

Number of 'no response' = 0. Respondents were asked to select all that applies

Table 3: Physiotherapy ICU Treatments

Type of physiotherapy	Never n (%)	Infrequently n (%)	Sometimes n (%)	Frequently n (%)	Routinely n (%)	Unsure n (%)
Chest physiotherapy	0 (0)	0 (0)	0 (0)	4 (44.4)	5 (55.6)	0 (0)
Passive range of motion	0 (0)	2 (22.2)	3 (33.3)	3 (33.3)	1 (11.1)	0 (0)
Active range of motion	0 (0)	0 (0)	0 (0)	6 (66.7)	3 (33.3)	0 (0)
Strengthening exercises	0 (0)	0 (0)	1 (11.1)	6 (66.7)	2 (22.2)	0 (0)
Bed mobility	0 (0)	0 (0)	0 (0)	2 (22.2)	7 (77.8)	0 (0)
Transfers	0 (0)	0 (0)		4 (44.4)	5 (55.6)	0 (0)
Pre-gait activities	0 (0)	0 (0)	1 (11.1)	4 (44.4)	4 (44.4)	0 (0)
Gait training /ambulation	0 (0)	0 (0)	5 (55.6)	1 (11.1)	3 (33.3)	0 (0)
Treadmill	9 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Neuromuscular electrical stimulation	9 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cycle ergometer	4 (44.4)		3 (33.3)	2 (22.2)	0 (0)	0 (0)
Dynamic tilt table	5 (55.6)	3 (33.3)	1 (11.1)	0 (0)	0 (0)	0 (0)
Other, please specify	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

FIGURES

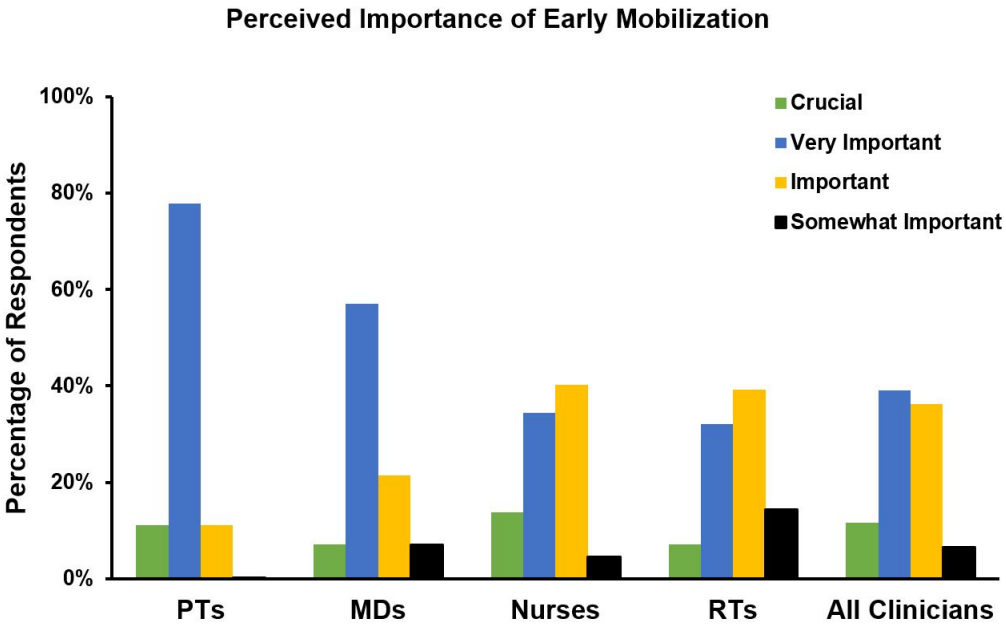

Figure 1: Clinicians perceptions on the importance of early mobilization. Only 11.6% of clinicians felt that early mobilization was crucial. *PTs = Physiotherapists, MDs = Medical Doctors, RTs = Respiratory Therapists.*

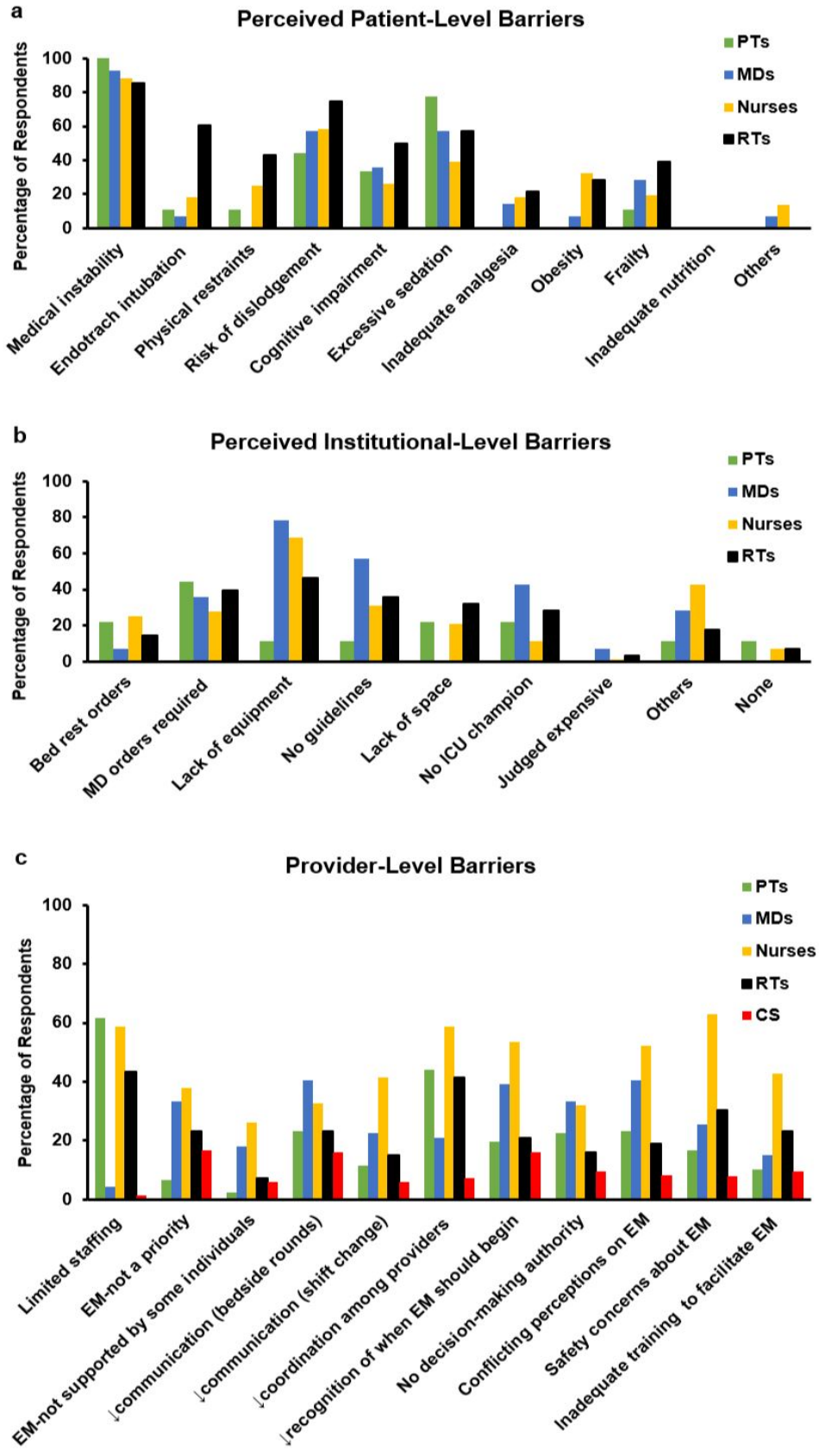

Figure 2: Percentage of clinicians who rated each identified barrier as a challenge to clinical practice in their ICU. PTs = Physiotherapists, MDs = Medical Doctors, RTs = Respiratory Therapists, CS = referring Consultants/primary Surgeon.

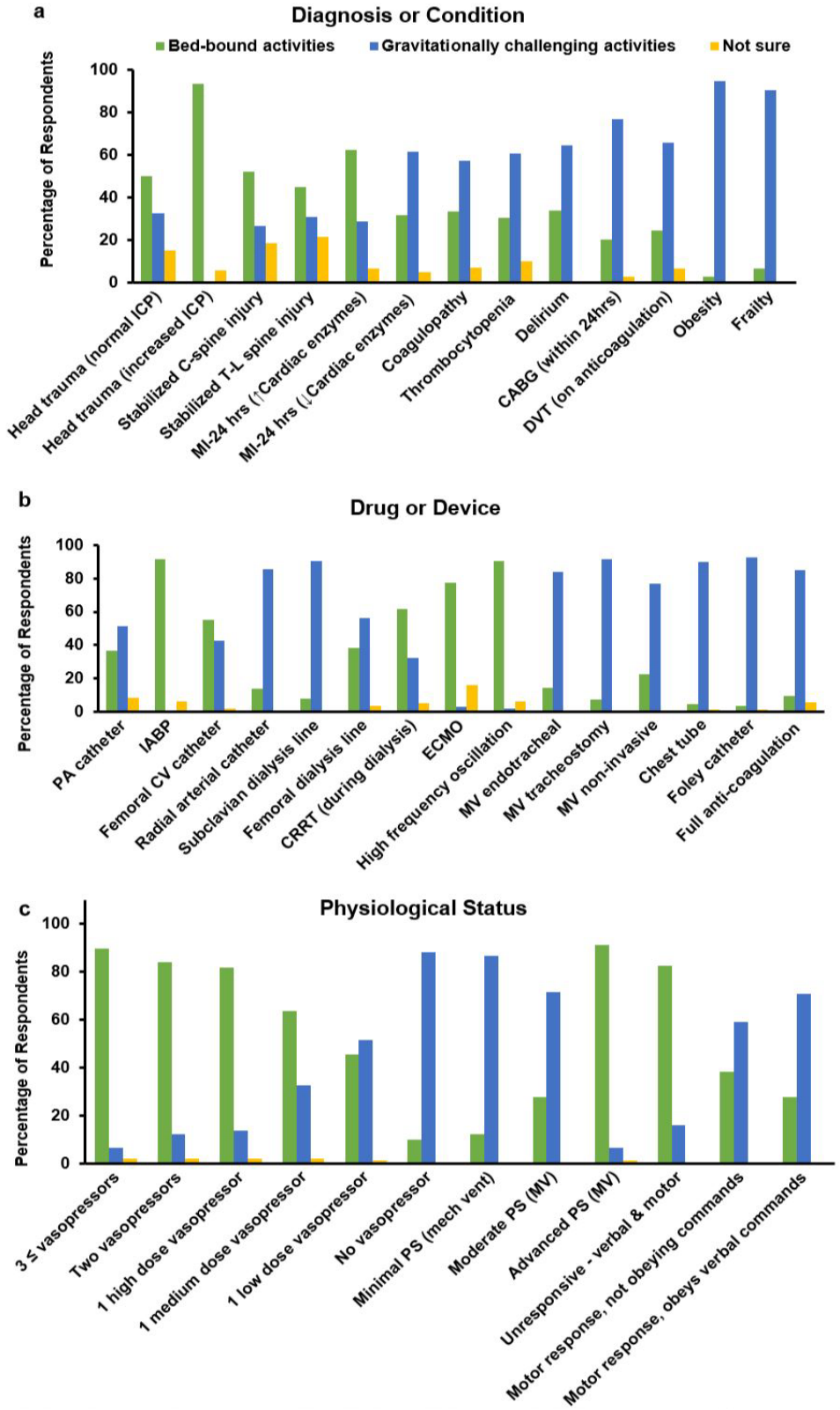

Figure 3: Clinicians' perceived level of maximum activity in different scenarios in a given mechanically ventilated patient. Physiologic status was perceived to pose the greatest limitation to activity progression (58% of scenarios in this category were limited to bedbound activities). ICP: intracranial pressure, C-spine: cervical spine, T-L spine: thoraco-lumbar spine, MI: myocardial infarction, CABG: coronary artery bypass grafting, DVT: deep venous thrombosis, PA: pulmonary artery, IABP: intra-aortic balloon pump, CV: central venous, CRRT: continuous renal replacement therapy, ECMO: extracorporeal membrane oxygenation, MV: mechanical ventilation, PS: pressure support.

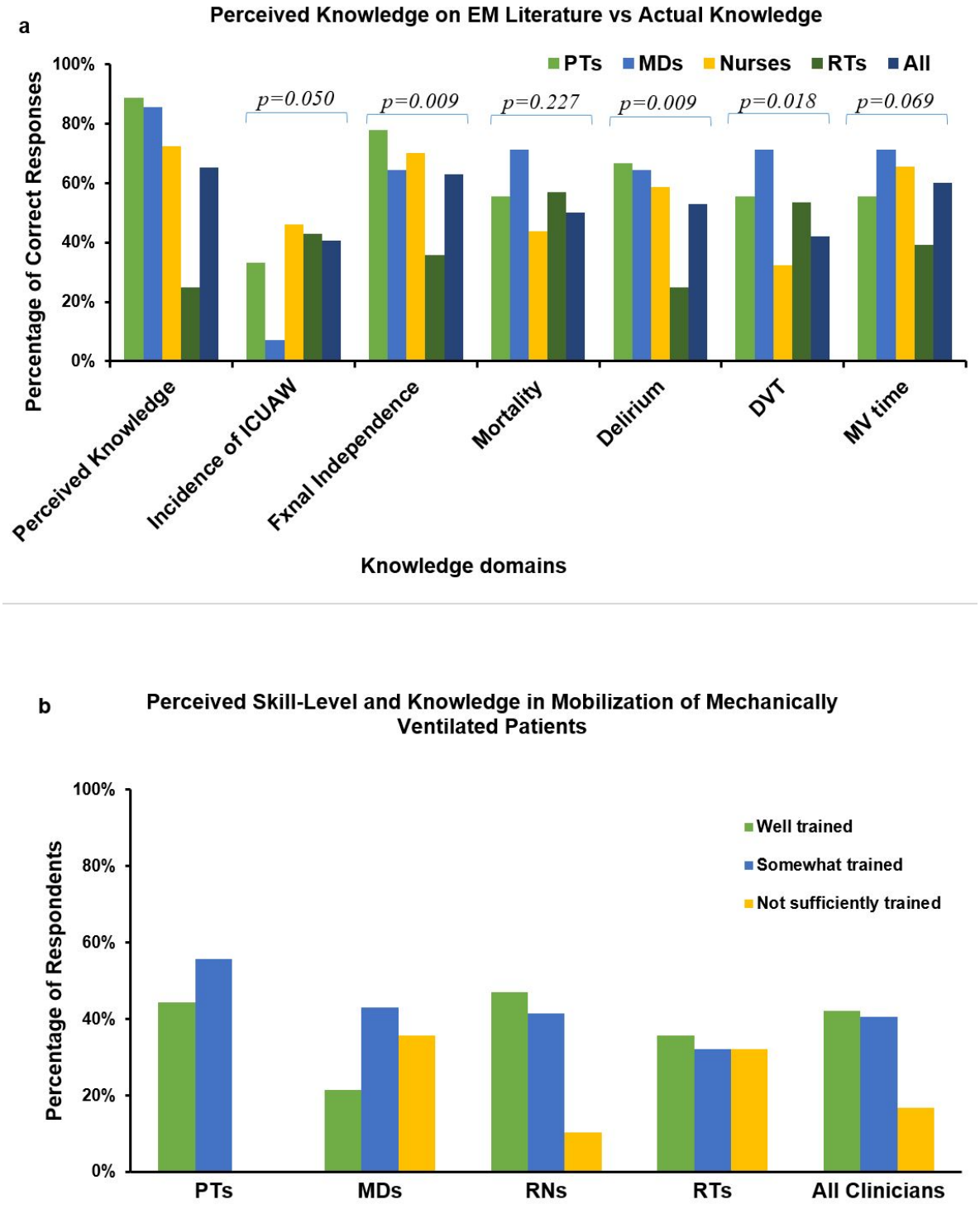

Figure 4: Knowledge and skill-level in mobilization of mechanically ventilated patients. About 58% of clinicians did not feel well trained and informed to mobilize mechanically ventilated patients. Percentage of clinicians with no response PTs: 0.00 %, MDs 0.00 %, RNs: 1.10 %, RTs: 0.00 %, All clinicians: 0.70 %. PTs = Physiotherapists, MDs = Medical Doctors, RNs = Registered Nurses, RTs = Respiratory Therapists.

APPENDICES

Appendix I: Survey Instrument

Survey of early Mobilization if ICU Patients: Current Knowledge, Perspectives and Practices

Please complete the following questions. All responses will be held in confidence.

Glossary of Terms

ICU: Intensive Care Unit

ICU-acquired weakness: polyneuropathy, polyneuromyopathy or neuropathy acquired during critical illness.

Mobilization: physical therapy that involves active or assisted patient mobility. This may include bed mobility, sitting, standing, ambulation or active exercise training. This does not include passive range of motion.

Early Mobilization (EM): physical therapy and acute rehabilitation measures initiated as soon as possible following admission to the ICU. Patients who receive EM will be progressively rehabilitated through a series of exercises that may begin while they are still receiving life support (i.e., mechanical ventilation).

Non-Mobility Physiotherapy
• **Cardio-respiratory/Chest physiotherapy:** physical therapies to improve ventilation-perfusion matching and respiratory mechanics including deep breathing exercises, airway secretion clearance, and percussion techniques • **Passive Range of Motion:** passive movement facilitated by providers
Mobility Physiotherapy
• **Active Assisted Motion:** Patient movement that is assisted by the therapist • **Active Range of Motion:** unassisted patient movement • **Strengthening exercises:** muscle strengthening (can include bedside cycle ergometer), neuro-developmental play (i.e., play activities to facilitate fine and gross motor development) for infants and developmentally delayed children. • **Bed mobility:** activities done while recumbent (e.g., active or partially assisted repositioning in bed or rolling from side to side) • **Transfers:** trunk control, unsupported sitting, sitting on edge of bed, sit to stand, from bed to chair or commode • **Pre-Gait:** weight shifting, stepping in place and sideways • **Ambulation:** walking/gait training with or without walking aid or assistance

PERCEPTIONS

1.0 Personal view of Early Mobilization in the ICU

1. Please select ONE option below that best describes your view of early mobilization:

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
crucial, should be top priority in the care of ICU patients	very important, should be a priority in the care of ICU patients	important, should be a priority in the care of ICU patients	somewhat important, should be considered in the care of ICU patients	not of great importance, but clinicians should bear it in mind	of minimal importance to the care of ICU patients	of no importance to the care of ICU patients

1.1 Barriers to Early Mobilization in the ICU

2. a) What is (are) the <u>most</u> important institutional barrier(s) to early mobilization in YOUR ICU? By institutional barriers we mean customs and behavior patterns in your work environment. Please check ALL that apply or "no institutional barriers"· if there are none.

- ☐ routine bed rest orders on ICU admissions
- ☐ physician orders required prior to mobilization
- ☐ insufficient equipment for early mobilization (e.g. ceiling lifts, chairs, walkers etc)
- ☐ no written guidelines or protocols for early mobilization
- ☐ not enough physical space
- ☐ no clinician champion/advocate to promote early mobilization in the ICU
- ☐ perceived to be an expensive intervention by administrators or unit leader
- ☐ no institutional barriers
- ☐ other institutional barrier(s), please specify _____

_____

2. b) What is (are) the most important patient level barrier(s) to early mobilization in YOUR ICU? Please check ALL that apply or "no patient barriers• if there are none.

- ☐ medical instability
- ☐ endotracheal intubation
- ☐ physical restraints
- ☐ risk of dislodgement of devices or lines
- ☐ cognitive impairment/cognitive age
- ☐ excessive sedation
- ☐ inadequate analgesia
- ☐ obesity
- ☐ frailty

- ☐ inadequate nutritional status
- ☐ no patient barriers
- ☐ other patient barrier(s), please specify _____

_____

3. Providers are critical care physicians (MD), physiotherapists (PT), registered nurses (RN), respiratory therapists (RT), referring consultants/primary surgeons (CS). What is (are) the most important provider level barrier(s) to early mobilization (EM) in YOUR ICU? If you believe that the listed barrier is important, please select ALL provider(s) who contribute to the existence of that barrier. Alternatively, if you believe the listed barrier is NOT an important barrier, select "None".

Potential Provider Barrier	MD	PT	RN	RT	CS	None
a) limited staffing to routinely mobilize patients						
b) EM in the ICU is generally supported but it is not perceived as a priority in the care plan of a critically ill patient						
c) EM in the ICU is generally not supported by some specific individuals						
d) lack of communication among clinician groups during bedside rounds to facilitate EM						
e) lack of communication about rehabilitation during hand- over at shift change						
f) lack of coordination among providers to facilitate EM						
g) slow to recognize when patients should begin EM						
h) lack of specific decision-making authority to initiate EM						
i) conflicting perceptions about suitability of EM in some patients						
j) safety concerns about EM						
k) inadequate training to facilitate EM						
I) other provider level barrier(s), please specify: _____ _____						

1.2 When to Initiate Mobilization in the ICU

4. Generally speaking, when do YOU think mobilization should be initiated in the ICU? Please select ALL that apply.

- ☐ as soon as possible following ICU admission
- ☐ as soon as the patient's cardio-respiratory status has stabilized (i.e. no escalation in hemodynamic or ventilatory support)
- ☐ as soon as the patient is extubated
- ☐ as soon as the patient is off all vasoactive infusions

- ☐ as soon as the patient is conscious and can cooperate
- ☐ as soon as all sedative infusions are discontinued
- ☐ as soon as the patient is ready to be transferred out of the ICU
- ☐ other, please specify

1.3 Level of Activity

5. For each of the following scenarios, assume that the patients are previously ambulatory and are currently physiologically stable on mechanical ventilation, no inotropes and on minimal sedation infusion. These patients have purposeful motor response and can obey verbal commands (unless otherwise stated). In YOUR opinion, what would you consider as the greatest permissible level of activity for a patient with the following diagnosis, condition, device or drug? Please select **ONE** response for each diagnostic group.

Diagnosis, Condition, Device or Drug	**Bed rest**	**Passive range of motion**	**Active range of motion**	**Stand-ing**	**Transfers to chair**	**Ambulat-ion**	**Not sure**
Diagnosis/Condition a) head trauma without increased intracranial pressure							
b) head trauma with increased intracranial pressure							
c) stabilized cervical spinal injury							
d) stabilized thoraco-lumbar spinal injury							
e) within 24 hrs of treated myocardial infarction (cardiac enzymes persistently elevated)							
f) within 24 hrs of treated myocardial infarction (cardiac enzymes decreasing)							
g) coagulopathy (INR > 3)							
h) thrombocytopenia (platelet count < 20 x10g/L)							
i) delirium (fluctuating level of consciousness, at							

times inattentive or agitated)							
j) within 24 hrs of uncomplicated coronary bypass surgery							
Diagnosis, Condition, Device or Drug	**Bed rest**	**Passive range of motion**	**Active range of motion**	**Stand-ing**	**Transfers to chair**	**Ambulat-ion**	**Not sure**
k) deep vein thrombosis (receiving therapeutic anti-coagulation)							
I) obesity							
m) frailty							
<u>Devices</u> n)pulmonary artery catheter							
o) intra-aortic balloon pump							
p) femoral central venous catheter							
q) radial arterial catheter							
r) dialysis line inserted at the subclavian site (during non-dialysis periods)							
s) dialysis line inserted at the femoral site (during non-dialysis periods)							
t) continuous renal replacement therapy (during dialysis such as PRISMA)							
u) extra corporeal membrane oxygenation							
v) high frequency oscillation							

w) conventional mechanical ventilation with an endotracheal tube							
x) conventional mechanical ventilation with a tracheostomy							
Diagnosis, Condition, Device or Drug	**Bed rest**	**Passive range of motion**	**Active range of motion**	**Stand-ing**	**Transfers to chair**	**Ambulat-ion**	**Not sure**
y) non-invasive positive pressure ventilation (e.g. BiPAP)							
z) chest tube							
aa) foley catheter							
Drugs (bb) full anti-coagulation (i.e. heparin infusion, warfarin)							

6. Consider a patient admitted to the ICU who is intubated and mechanically ventilated (unless otherwise stated). What maximum level of activity would you prescribe for this patient under each of the following independent circumstances?

Please select **ONE** response for each condition.

Physiological Status	**Bed rest**	**Passive range of motion**	**Active range of motion**	**Standing**	**Transfers to chair**	**Ambulation**	**Not sure**
Cardiovascular a) three or more vasopressors or inotropic infusions							
b) two vasopressors or inotropic infusions							
c) one high dose							

vasopressor or inotropic infusion							
d) one medium dose vasopressor or inotropic infusion							
e) one low dose vasopressor or inotropic infusion							
f) no vasopressors or inotropes							

Diagnosis, Condition, Device or Drug	Bed rest	Passive range of motion	Active range of motion	Standing	Transfers to chair	Ambulation	Not sure
Respiratory g) minimal pressure support on conventional mode of mechanical ventilation							
h) moderate pressure support on conventional mode of mechanical ventilation (e.g., FiO_2 0.5,PEEP 10)							
i) advanced mode of mechanical ventilation (e.g., high frequency oscillation)							
Neurologic j) unresponsive to verbal and motor							
k) purposeful motor response, not obeying verbal commands							
i) purposeful motor response, obeys verbal commands							

KNOWLEDGE

2.0 Intensive Care Unit-Acquired Weakness (ICU-AW)

7. What do YOU think is the approximate incidence of ICU-AW in the population of general medical-surgical ICU patients?

- ☐ < 5%
- ☐ 5-10%
- ☐ 11-20%
- ☐ 21-40%
- ☐ > 40%
- ☐ Don't know

2.1 Current Literature

8. Are YOU familiar with any clinical trials or literature evaluating early mobilization of critically ill patients?

- ☐ yes
- ☐ no

9. What do the clinical studies about early mobilization of critically ill patients (i.e., general medical surgical ICU population) show? Select ALL TRUE responses only.

- ☐ I am not sufficiently familiar with the current literature/clinical studies on early mobilization in the ICU.
- ☐ early mobilization of critically ill patients can improve their functional independence (i.e. activities of daily living) at hospital discharge
- ☐ early mobilization of critically ill patients is associated with reduced mortality at hospital discharge
- ☐ early mobilization of critically ill patients is associated with a reduced incidence of delirium
- ☐ early mobilization of critically ill patients reduces the incidence of deep vein thrombosis
- ☐ early mobilization of critically ill patients reduces their time requiring mechanical ventilation

2.2 Practical and Technical Skills

10. How well trained and informed do you feel to mobilize mechanically ventilated patients? Please select ONE response only.

- ☐ I feel well trained and informed to mobilize mechanically ventilated patients.

- ☐ I feel somewhat trained and informed to mobilize mechanically ventilated patients.
- ☐ I do not feel sufficiently trained or informed to mobilize mechanically ventilated patients

PRACTICE

3.0 Assessment for Need of Rehabilitation

11. Are all patients automatically assessed for appropriateness to begin mobilization by the physiotherapist in YOUR ICU without prompting or requests by other clinician groups?

- ☐ yes
- ☐ no
- ☐ unsure

12. Who is generally the first health care provider to identify if a patient is ready for mobilization? Please select **ONE** response only.

- ☐ registered nurse
- ☐ physician
- ☐ physiotherapist
- ☐ occupational therapist
- ☐ respiratory therapist
- ☐ other, please specify _____

13. Does the initial physiotherapist assessment on each patient require a written medical order by a physician?

- ☐ technically, yes
- ☐ no
- ☐ unsure

14. Does YOUR ICU have written protocols or policies that provide guidelines on when a patient should begin mobilization?

- ☐ yes
- ☐ no
- ☐ unsure

15. Does YOUR ICU have at least one clinician who serves as a champion for early mobilization?

- ☐ yes
- ☐ no
- ☐ unsure

16. If the ICU you work in has at least one champion who promotes early mobilization, what discipline is the main champion from?

- ☐ Physiotherapist
- ☐ Critical care physician
- ☐ Registered nurse
- ☐ Respiratory therapist
- ☐ unsure

17. Who performs passive range of motion exercises for the patients in your ICU?

- ☐ Physiotherapists
- ☐ Nurses
- ☐ Family members
- ☐ Others. Specify_____

3.1 Intensity & Frequency of Mobilization

18 a) On average, what is the daily duration of passive range of motion performed by physiotherapists in **YOUR ICU** on the following types of critically ill patients?

Condition	None	<15 min	16-30 min	31-45 min	46-60 min	>60 min	Unsure
i) a patient who is intubated, mechanically ventilated, deeply sedated and unconscious							
ii) a patient who is intubated, mechanically ventilated, inattentive and uncooperative							

18. b) On average, what is the daily duration of mobilization performed by physiotherapists in YOUR ICU on the following types of critically ill patients?

Condition	None	<15 min	16-30 min	31-45 min	46-60 min	>60 min	Unsure
i) a patient who is intubated, mechanically ventilated, alert, interactive and co-operative **but cannot ambulate yet**							
ii) a patient who is intubated, mechanically ventilated, alert, interactive/cooperative **and can ambulate**							

19. a) On average, how frequently is passive range of motion performed by physiotherapists in YOUR ICU on the following types of critically ill patients?

Condition	None	<1 /wk	1-2 /wk	3-4 /wk	5-6 /wk	once daily	twice daily	> twice daily	unsure
i) a patient who is intubated, mechanically ventilated, deeply sedated and unconscious sedated and unconscious									
Condition	**None**	**<1 /wk**	**1-2 /wk**	**3-4 /wk**	**5-6 /wk**	**once daily**	**twice daily**	**> twice daily**	**unsure**
ii) a patient who is intubated, mechanically ventilated, inattentive and uncooperative									

20. b) On average, how frequently is mobilization performed by physiotherapists in YOUR ICU on the following types of critically ill patients?

Condition	**None**	**<1 /wk**	**1-2 /wk**	**3-4 /wk**	**5-6 /wk**	**once daily**	**twice daily**	**> twice daily**	**unsure**
i) a patient who is intubated, mechanically ventilated, alert, interactive and co-operative **but cannot ambulate yet**									
Condition	**None**	**<1 /wk**	**1-2 /wk**	**3-4 /wk**	**5-6 /wk**	**once daily**	**twice daily**	**> twice daily**	**unsure**
ii) a patient who is intubated, mechanically ventilated, alert, interactive/cooperative **and can ambulate**									

3.2 Staffing in the ICU

21. Who participates in the mobilization of patients in YOUR ICU? Please select ALL that apply.

- ☐ registered nurse
- ☐ physician
- ☐ physiotherapist
- ☐ occupational therapist
- ☐ health care aide (i.e. physical therapy assistant, nurse aide, orderlies etc)
- ☐ respiratory therapist
- ☐ family member or home caregiver
- ☐ others, please specify_____

22. Is there a designated physiotherapist working in YOUR ICU during the following times?

Time	Available for full assessments & mobilization	Available for limited assessments & mobilization	Available only for cardiorespiratory /chest physiotherapy	Not available	Unsure
Regular weekday hours (Mon-Fri)					
Weekend evenings (after 17:00, Mon-Fri)					
Weekends (Sat, Sun) & holidays					

3.3 Types of Physiotherapy Techniques Performed

23. In general, how often are these physiotherapy techniques used in ICU patients who are eligible/suitable for rehabilitation? Please select only ONE answer for each type of treatment.

Type of physiotherapy	Never	Infrequently	Sometimes	Frequently	Routinely	Unsure
a) chest physiotherapy						
b) passive range of motion						
c) active range of motion						
d) strengthening exercises						
e) bed mobility						
f) transfers						
g) pre-gait activities						
h) gait training/ambulation						
i) treadmill						
j) neuromuscular electrical stimulation						
k) cycle ergometer						
I) dynamic tilt table						
m) other, please specify						

3.4 Workload of the Physiotherapist *(If you are not a PT, got to section 3.6)*

24. Please answer the following questions about YOUR workload in the ICU:

a) On average, how many ICU patients do you see each day? _____

b) On average, how many hospital patients (including ICU) do you see per day? _____

c) Do you work full time or part time in the ICU?

- ☐ full time
- ☐ part time

d) What is the duration of your shift? ___ hours

3.5 Sedation Practices

25. Are daily interruption of sedation or sedation protocols used in YOUR ICU?

- ☐ routinely
- ☐ frequently
- ☐ sometimes
- ☐ infrequently
- ☐ never
- ☐ unsure

26. Do YOU use standardized sedation scales to titrate sedation, according to patient activity level?

- ☐ Routinely
- ☐ Frequently
- ☐ Sometimes
- ☐ Infrequently
- ☐ Never
- ☐ Unsure

3.6 Rehabilitation following ICU Discharge

27. Are patients with suspected ICU acquired weakness routinely referred to an outpatient clinic after ICU discharge for long term rehabilitation?

- ☐ yes
- ☐ no
- ☐ unsure

28. To whom are the patients with suspected ICU acquired weakness referred?

- ☐ family physician
- ☐ general internist/pediatrician
- ☐ neurologist
- ☐ physiotherapist
- ☐ occupational therapist
- ☐ rehabilitation specialist
- ☐ intensivist
- ☐ other, please specify _____
- ☐ patients with ICU acquired weakness are not routinely referred to outpatient clinics
- ☐ unsure

4.0 Clinician Demographics

29. What type of clinician are you?

- ☐ physiotherapist
- ☐ physician
- ☐ registered nurse
- ☐ respiratory therapist
- ☐ occupational therapist

30. What type(s) of ICU(s) do you work in? Please select ALL that apply.

- ☐ medical-surgical ICU
- ☐ cardiovascular ICU
- ☐ neurological ICU
- ☐ trauma ICU

Thank you very much for completing this survey!

Once the survey is completed, please seal it in the envelope provided and deposit the envelope in the designated reception box in your ICU.

Appendix II

Details on Barriers to Early Mobilization

Perceived Patient-Level Barriers

Patient-Level Barriers	**PTs** **n** **(%)**	**MDs** **n** **(%)**	**Nurses** **n** **(%)**	**RTs** **n** **(%)**	**All** **n** **(%)**
Medical instability	**9** **(100.0)**	**13** **(92.9)**	**77** **(88.5)**	**24** **(85.7)**	**123** **(89.1)**
Endotracheal intubation	1 (11.1)	1 (7.1)	16 (18.4)	17 (60.7)	35 (25.4)
Physical restraints	1 (11.1)	0 (0.0)	22 (25.3)	12 (42.9)	35 (25.4)
Risk of dislodgement of devices or lines	4 (44.4)	8 (57.1)	51 (58.6)	21 (75.0)	84 (60.9)
Cognitive impairment/cognitive age	3 (33.3)	5 (35.7)	23 (26.4)	14 (50.0)	45 (32.6)
Excessive sedation	7 (77.8)	8 (57.1)	34 (39.1)	16 (57.1)	65 (47.1)
Inadequate analgesia	0 (0.0)	2 (14.3)	16 (18.4)	6 (21.4)	24 (17.4)
Obesity	0 (0.0)	1 (7.1)	28 (32.2)	8 (28.6)	37 (26.8)
Frailty	1 (11.1)	4 (28.6)	17 (19.5)	11 (39.3)	33 (23.9)
Inadequate nutritional status	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other patient barriers	0 (0.0)	1 (7.1)	12 (13.8)	0 (0.0)	13 (9.4)

Number (%) of 'no response = 0 (0.0%)

Perceived Institutional-Level Barriers

Institutional-Level Barriers	**PTs** **n** **(%)**	**MDs** **n** **(%)**	**Nurses** **n** **(%)**	**RTs** **n** **(%)**	**All** **n** **(%)**
Routine bed rest orders on ICU	**2** **(22)**	**1** **(7.1)**	**22** **(25.3)**	**4** **(14.3)**	**29** **(21.0)**
Physician orders required prior to mobilization	4 (44.4)	5 (35.7)	24 (27.6)	11 (39.3)	44 (31.9)
Insufficient equipment for EM	1 (11.1)	11 (78.6)	60 (69.0)	13 (46.4)	85 (61.6)
No written guidelines or protocols for EM	1 (11.1)	8 (57.1)	27 (31.0)	10 (35.7)	46 (33.3)
Not enough physical space	2 (22.2)	3 (21.4)	18 (20.7)	9 (32.1)	32 (23.2)
No clinician champion/advocate to promote EM in the ICU	2 (22.2)	6 (42.9)	10 (11.5)	8 (28.6)	26 (18.8)
Perceived to be an expensive intervention by administrators or unit leader	0 (0.0)	1 (7.1)	1 (1.1)	1 (3.6)	3 (2.2)
No institutional barriers	1 (11.1)	0 (0.0)	6 (6.9)	2 (7.1)	9 (6.5)
Other institutional barrier(s)	1 (11.1)	4 (28.6)	37 (42.5)	5 (17.9)	47 (34.1)

Number (%) of 'no response = 1 (0.7%)

Perceived Provider-Level Barriers

Provider-Level Barriers	MD n (%)	PT n (%)	RN n (%)	RT n (%)	CS n (%)	None n (%)	No Response
Limited staffing to routinely mobilize patients	6 (4.3)	85 (61.6)	81 (58.7)	60 (43.5)	2 (1.4)	16 (11.6)	6 (4.3)
EM in the ICU is generally supported but it is not perceived as a priority in the care plan of a critically ill patient	46 (33.3)	9 (6.5)	52 (37.7)	32 (23.2)	23 (16.7)	55 (39.9)	8 (5.8)
EM in the ICU is generally not supported by some specific individuals	25 (18.1)	4 (2.3)	36 (26.1)	10 (7.2)	8 (5.8)	73 (52.9)	12 (8.7)
Lack of communication among clinician groups during bedside rounds to facilitate EM	56 (40.6)	32 (23.2)	45 (32.6)	32 (23.2)	22 (15.9)	56 (40.6)	17 (12.3%)
Lack of communication about rehabilitation during hand- over at shift change	31 (22.5)	16 (11.6)	57 (41.3)	21 (15.2)	8 (5.8)	57 (41.3)	15 (10.9)
Lack of coordination among providers to facilitate EM	29 (21.0)	61 (44.2)	81 (58.7)	57 (41.3)	10 (7.2)	34 (24.6)	15 (10.9)
Slow to recognize when patients should begin EM	54 (39.1)	27 (19.6)	74 (53.6)	29 (21.0)	22 (15.9)	35 (25.4)	14 (10.1)
Lack of specific decision-making authority to initiate EM	46 (33.3)	21 (22.5)	44 (31.9)	22 (15.9)	13 (9.4)	43 (31.2)	19 (13.6)
Conflicting perceptions about suitability of EM in some patients	56 (40.6)	32 (23.2)	72 (52.2)	26 (18.8)	12 (8.2)	35 (25.4)	14 (10.1)
Safety concerns about EM	35 (25.4)	23 (16.7)	87 (63.0)	42 (30.4)	11 (8.0)	33 (23.9)	12 (8.7)
Inadequate training to facilitate EM	21 (15.2)	14 (10.1)	59 (42.8)	32 (23.2)	13 (9.4)	50 (36.2)	18 (13)
Other provider-level barriers	Orderlies had the highest frequency 41(29.7%)						82 (59.3)

Appendix III

Details on Perceived Maximum Level of Activity

Maximum Permissible Level of Activity as influenced by patients' Diagnosis or Condition

Diagnosis or Condition	Bed rest n (%)	Passive range of motion n (%)	Active range of motion n (%)	Standing n (%)	Transfers to chair n (%)	Ambulation n (%)	Not Sure n (%)
a) head trauma without increased intracranial pressure	9 (6.5)	35 (25.4)	25 (18.1)	0 (0)	22 (15.9)	23 (16.7)	21 (15.2)
b) head trauma with increased intracranial pressure	77 (55.8)	31 (22.5)	21 (15.2)	0 (0)	0 (0)	1 (0.7)	8 (5.8)
c) stabilized cervical spinal injury	12 (8.7)	35 (25.4)	25 (18.1)	0 (0)	8 (5.8)	29 (21.0)	26 (18.8)
d) stabilized thoracolumbar spinal injury	11 (8.0)	29 (21.0)	23 (16.2)	2 (1.4)	11 (8.0)	30 (21.7)	30 (21.7)
e) within 24 hrs of treated myocardial infarction (cardiac enzymes persistently elevated)	31 (22.5)	15 (10.9)	40 (29.0)	4 (2.9)	27 (19.6)	9 (6.5)	9 (6.5)
f) within 24 hrs of treated myocardial infarction (cardiac enzymes decreasing)	8 (5.8)	12 (8.7)	24 (17.4)	9 (6.5)	42 (30.4)	34 (24.6)	7 (5.1)
g) coagulopathy (INR > 3)	13 (9.4)	15 (10.9)	18 (13.0)	2 (1.4)	28 (20.3)	49 (35.5)	10 (7.2)
h) thrombocytopenia (platelet count < 20 x10g/L)	14 (10.1)	9 (6.5)	14 (14.1)	10 (7.2)	28 (20.3)	46 (33.3)	14 (10.1)
i) delirium (fluctuating level of consciousness, at times inattentive or agitated)	8 (5.8)	14 (10.1)	25 (18.1)	5 (3.6)	65 (45.7)	21 (15.2)	1 (0.7)
j) within 24 hrs of uncomplicated coronary bypass surgery	3 (2.2)	7 (5.1)	18 (13.0)	5 (3.6)	60 (43.5)	41 (29.7)	4 (2.9)
k) deep vein thrombosis (receiving therapeutic anti-coagulation)	9 (6.5)	10 (7.2)	15 (10.9)	3 (2.2)	24 (17.4)	64 (46.4)	9 (6.5)
I) obesity	0 (0.0)	1 (0.7)	3 (2.2)	5 (3.6)	22 (15.9)	104 (75.4)	1 (0.7)
m) frailty	0 (0.0)	2 (1.4)	7 (5.1)	6 (4.3)	46 (33.3)	73 (52.9)	1 (0.7)

a) head trauma without increased intracranial pressure: Invalid and No response: 1(0.7) and 2(1.4)
b) head trauma with increased intracranial pressure: 0 & 0
c) stabilized cervical spinal injury: Invalid and No response: 1(0.7) and 2(1.4)
d) stabilized thoraco-lumbar spinal injury: Invalid and No response: 1(0.7) and 2(1.4)
e) within 24 hrs of treated myocardial infarction : Invalid and No response: 1(0.7) and 2(1.4)
f) within 24 hrs of treated myocardial infarction : Invalid and No response: 1(0.7) and 1(0.7)
g) coagulopathy: Invalid and No response: 1(0.7) and 1(0.7)
h) thrombocytopenia: Invalid and No response: 1(0.7) and 1(0.7)
i) delirium : Invalid and No response: 1(0.7) and 0(0.0)
j) within 24 hrs of uncomplicated coronary bypass surgery: Invalid and No response: 1(0.7) and 0(0.0)
k) deep vein thrombosis: Invalid and No response: 1(0.7) and 3(2.2)
l) obesity : Invalid and No response: 1(0.7) and 2(1.4)

m) frailty: Invalid and No response: 1(0.7) and 3(2.2)

Maximal Permissible Level of Activity as influenced by patients' drug or device

Device or Drug	Bed rest		Passive range of motion		Active range of motion		Standing		Transfers to chair		Ambulation		Not Sure	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
a) pulmonary artery catheter	12	8.7	12	8.7	27	19.6	4	2.9	54	39.1	13	9.4	12	8.7
b) intra-aortic balloon pump	61	44.2	31	22.5	34	24.6	0	0.0	1	0.7	0	0.0	9	6.5
c) femoral central venous catheter	22	15.9	16	11.6	38	27.5	4	2.9	26	18.8	29	21.0	3	2.2
d) radial arterial catheter	0	0.0	4	2.9	15	10.9	1	0.7	50	36.2	67	48.6	1	0.7
e) dialysis line inserted at the subclavian site (during non-dialysis periods)	0	0.0	3	2.2	8	5.8	1	0.7	16	11.6	108	78.3	1	0.7
f) dialysis line inserted at the femoral site (during non-dialysis periods)	9	6.5	11	8.0	33	23.9	5	3.6	33	23.9	40	29.0	5	3.6
g) continuous renal replacement therapy (during dialysis such as PRISMA)	26	18.8	16	11.6	43	31.2	2	1.4	39	28.3	4	2.9	7	5.1
h) extra corporeal membrane oxygenation	73	52.9	17	12.3	17	12.3	0	0.0	0	0.0	4	2.9	22	15.9
i) high frequency oscillation	76	55.1	33	23.9	16	11.6	1	0.7	1	0.7	1	0.7	9	6.5
j) conventional mechanical ventilation with an endotracheal tube	3	2.2	6	4.3	11	8.0	1	0.7	52	37.7	63	45.7	1	0.7
k) conventional mechanical ventilation with a tracheostomy	1	0.7	4	2.9	5	3.6	1	0.7	43	31.2	82	59.4	1	0.7
l) non-invasive positive pressure ventilation (e.g. BiPAP)	8	5.8	2	1.4	21	15.2	3	2.2	61	44.2	42	30.4	1	0.7
m) chest tube	1	0.7	3	2,2	6	4.3	3	2.2	36	26.1	85	61.6	2	1.4
n) foley catheter	1	0.7	0	0.0	4	2.9	2	1.4	10	7.2	116	84.1	2	1.4
o) full anti-coagulation (i.e. heparin infusion, warfarin)	3	2.2	2	1.4	8	5.8	3	2.2	17	12.3	97	70.3	8	5.8

a) pulmonary artery catheter: Invalid and No response: 0(0.0) and 4(2.9)
b) intra-aortic balloon pump Invalid and No response: 0(0.0) and 2(1.4)
c) femoral central venous catheter: Invalid and No response: 0(0.0) and 0(0.0)
d) radial arterial catheter: Invalid and No response: 0(0.0) and 0(0.0)
e) dialysis line inserted at the subclavian site (during non-dialysis periods) : Invalid and No response: 1(0.7) and 0(0.0)
f) dialysis line inserted at the femoral site (during non-dialysis periods) : Invalid and No response: 1(0.7) and 1(0.7)
g) continuous renal replacement therapy (during dialysis such as PRISMA) : Invalid and No response: 1(0.7) and 0(0.0)
h) extra corporeal membrane oxygenation: Invalid and No response: 0 (0.0) and 4(2.9)
i) high frequency oscillation: Invalid and No response: 0(0.0) and 1(0.7)
j) conventional mechanical ventilation with an endotracheal tube: Invalid and No response: 1(0.7) and 0(0.0)
k) conventional mechanical ventilation with a tracheostomy: Invalid and No response: 1(0.7) and 0(0.0)
l) non-invasive positive pressure ventilation (e.g. BiPAP): Invalid and No response: 0(0.0) and 0(0)
m) chest tube: Invalid and No response: 0(0.0) and 3(2.1)
n) foley catheter: Invalid and No response: 0(0.0) and 2(1.4)

o) full anti-coagulation (i.e. heparin infusion, warfarin): Invalid and No response: 0(0.0) and 0(0.0)

Maximal Permissible Level of Activity as influenced by patients' physiologic status

Physiologic Status of Patient	**Bed rest n (%)**		**Passive range of motion n (%)**		**Active range of motion n (%)**		**Standing n (%)**		**Transfers to chair n (%)**		**Ambulation n (%)**		**Not Sure n (%)**	
Hemodynamic Instability- Cardiovascular	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
a) three or more vasopressors or inotropic infusions	45	32.6	34	24.6	45	32.6	0	0.0	7	5.1	2	1.4	3	2.2
b) two vasopressors or inotropic infusions	29	21.0	39	28.3	48	34.8	2	1.4	13	9.4	2	1.4	3	2.2
c) one high dose vasopressor or inotropic infusion	27	19.6	34	24.6	52	37.7	2	1.4	16	11.6	1	0.7	3	2.2
d) one medium dose vasopressor or inotropic infusion	12	8.7	26	18.8	50	36.2	5	3.6	31	22.5	9	6.5	3	2.2
e) one low dose vasopressor or inotropic infusion	7	5.1	16	11.6	40	29.0	3	2.2	43	31.2	25	18.1	2	1.4
f) no vasopressors or inotropes	2	1.4	1	0.7	11	8.0	1	0.7	31	22.5	90	65.2	1	0.7
Respiratory Instability														
g) minimal pressure support on conventional mode of mechanical ventilation	0	0.0	4	2.9	13	9.4	1	0.7	46	33.3	73	52.9	0	0.0
h) moderate pressure support on conventional mode of mechanical ventilation (e.g., FiO2 0.5, PEEP 10)	3	2.2	11	8.0	24	17.4	5	3.6	59	42.8	35	25.4	0	0.0
i) advanced mode of mechanical ventilation (e.g., high frequency oscillation)	66	47.8	31	22.5	29	21.0	3	2.2	5	3.6	1	0.7	2	1.4
Neurologic														
j) unresponsive to verbal and motor	36	26.1	66	47.8	12	8.7	0	0.0	22	15.9	0	0.0	0	0.0
k) purposeful motor response, not obeying verbal commands	1	0.7	5	3.6	47	34.1	34	24.6	2	1.4	46	33.3	1	0.7
l) purposeful motor response, obeys verbal commands	3	2.2	4	2.9	31	22.5	1	0.7	32	23.2	65	47.1	0	0.0

a) three or more vasopressors or inotropic infusions: Invalid and No response: 0(0.0) and 2(1.4)
b) two vasopressors or inotropic infusions: Invalid and No response: 0(0.0) and 2(1.4)
c) one high dose vasopressor or inotropic infusion: Invalid and No response: 0(0.0) and 2(1.4)
d) one medium dose vasopressor or inotropic infusion: Invalid and No response: 0(0.0) and 2(1.4)
e) one low dose vasopressor or inotropic infusion: Invalid and No response: 0(0.0) and 2(1.4)
f) no vasopressors or inotropes: Invalid and No response: 1(0.7) and 0(0.0)
g) minimal pressure support on conventional mode of mechanical ventilation: Invalid and No response: 1(0.7) and 0(0.0)
h) moderate pressure support on conventional mode of mechanical ventilation: Invalid and No response: 0(0.7) and 1(0.7)
i) advanced mode of mechanical ventilation: Invalid and No response: 0(0.7) and 1(0.7)
j) unresponsive to verbal and motor: Invalid and No response: 0(0.0) and 2(1.4)
k) purposeful motor response, not obeying verbal commands: Invalid and No response: 0(0.0) and 2(1.4)

l) purposeful motor response, obeys verbal commands

CHAPTER 6: PREFACE TO MANUSCRIPT TWO

Manuscript one identified, assessed and reported the practice patterns, perceived barriers, and perceived gaps in clinical practice of EM in three Montreal area ICUs. The study showed that limited awareness of the clinical benefits of EM was an important barrier to EM, as was the fact that most clinicians did not feel well trained or well informed to mobilize mechanically ventilated patients. It also revealed that there was a lack of standardization in the clinical practice of EM, suggesting the presence of a knowledge-to-practice gap. Despite these being significant barriers, little is known about the reasons underlying why they exist. This important information could not be elucidated from the first study due to the inflexibility and inherent inability of surveys to fully explore the reason behind the responses given by the respondents.

The goal of the second manuscript was therefore to explore the cognitive and behavioural factors behind the barriers and facilitators to EM. Use of a qualitative research approach offered the opportunity to deepen our understanding of this complex problem and discover how facilitators can be enhanced to improve the practice of EM. The analysis of the qualitative study was based on a theoretical framework (the TDF) which could also guide the design of an effective KT intervention (by informing the linking of the identified barriers to behavioral change interventions). Additionally, the use of focus group discussions provided us an avenue for developing a partnership with practicing clinicians that was helpful in subsequent stages of the project.

The specific objective of the second manuscript was to gain a deeper understanding of the barriers to EM: why they exist, what could be done to lower them, and how facilitators can be enhanced to improve the practice of EM from the perspective of ICU clinicians.

The combined findings of the first two manuscript provide a thorough understanding of the barriers and facilitators to EM. Such information is essential for the development of future knowledge translation programs that will improve EM practice.

CHAPTER 7: MANUSCRIPT TWO

ICU Clinicians' Perspectives on Early Mobilization: A Qualitative Study

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
EM	Early mobilization
ICU	Intensive care unit
KT	Knowledge translation
TDF	Theoretical domain framework
PT	Physiotherapist
MDFG	Multidisciplinary Focus Group
PFG	Physicians' Focus Group

Keywords: early mobilization, barriers, facilitators, theoretical domain framework, intensive care unit, focus group

ABSTRACT

Objective: Although the deleterious long-term impact of reduced mobility of the critically ill ICU patients is well documented, and early mobilization (EM) offers important health benefits, wide-scale adoption of this practice into standard care remains problematic. The objective of this study was to identify potential barriers and facilitators of EM and solutions to improve such practice among clinicians working in the ICU.

Methods: We conducted four focus group meetings with physicians, nurses, respiratory therapists and physiotherapists from the intensive care units of three university-affiliated hospitals in Montreal, Canada. Two researchers independently performed thematic content analysis on verbatim transcriptions of the audio recordings using the theoretical domains framework (TDF). The analysis was performed in QDA Miner Lite version 2.0.

Main Results: We conducted 4 focus group meetings that included 33 ICU clinicians (data saturation was reached after the third focus group, with recurrent themes occurring in the fourth focus group). Thirty-six barriers were categorized in 13 TDF domains. The key barriers to EM were a lack of conviction or knowledge regarding the available evidence on EM, lack of attention to the provision of optimal care, poor communication, the unpredictable nature of the ICU, limited staffing, equipment, time and clinical knowledge. Four additional barriers not included in the TDF were also identified (obesity, medical instability, sedation, lack of patient comfort or cooperation). Twenty-five facilitators categorized in 10 TDF domains were also identified. These included individual-level facilitators: intrinsic motivation, positive outcome expectations, conscious effort to mobilize early, good planning and coordination, presence of ICU champions and expert support by a physiotherapist; and organizational-level facilitators: reminder system, pro-EM culture, implementation of an EM protocol, and improved ICU organization.

Conclusions: Unique barriers not reported in earlier EM studies were identified in this study. These may inform the design of tailored knowledge translation interventions to promote EM in the ICU.

BACKGROUND

Patients discharged from the intensive care unit (ICU) are prone to impairments in body structure and function,[85-87] limitations in functional activities[85,87,125] and participation restrictions,[85] even after the primary pathology for ICU admission has resolved.[94,117] These impairments, limitations, and restrictions are the result of a number of complex interrelated factors involving reduced mobility, which commonly occurs to patients hospitalized in the ICU.[8,9,88,89,117] Early mobilization — defined as initiating activities within 24-48 hours after ICU admission — has been advocated as a strategy to combat the effects of reduced mobility in the ICU.[148] There is an increasing body of evidence indicating that EM is safe, feasible, and potentially ameliorates impairments, limitations, and restrictions.[21,142,147,149,151,153,162,196] However, as in all areas of clinical practice, translating this evidence into practice is problematic.[88,89,140,212]

Most studies that have attempted to elucidate the barriers and facilitators to the implementation of EM[168,171,180,193,198,213,214] have used surveys.[168,180,198,213,214] Unfortunately, surveys often fail to adequately explore the reasons behind the responses given.[215] Focus groups are often used to trace the cognitive and social processes that influence survey responses, deepen the understanding of complex problems, and can add a human dimension to the impersonal data from surveys.[215-217] This is especially important when data is needed for the purpose of program development or implementation.[216] Qualitative data is thus an important complement to quantitative data to inform the design of a knowledge-translation intervention.[218]

To the best of our knowledge, only one study[167] has used a theory-based approach to identify barriers and facilitators of EM. Theory-based approaches can inform the development of an interview topic guide, guide data analysis, and provide an understanding of the underpinning behaviours.[219,220] The Theoretical Domains Framework (TDF) consists of 33 psychological theories and 128 theoretical constructs designed for use in studying the implementation of evidence-based practice and the development of strategies for the effective implementation of this practice.[221,222] The revised validated version of the TDF has 14 domains.[222] The use of the TDF reduces the risk of omitting important factors that may impact decision making regarding the use of evidence-based care in clinical practice.[223]

This qualitative study is a follow-up to a previous quantitative survey conducted by this team.[213] The survey aimed to identify perceived gaps in the clinical practice of EM, as well as the barriers and facilitators of EM in critically ill patients.

The aim of the present study was to deepen our understanding of the barriers to the practice of EM in the ICU from the perspective of ICU clinicians: why these barriers exist, what could be done to ameliorate them, and the facilitators that might enhance the practice of EM.

METHODS

Design

We conducted three heterogeneous focus groups with nurses, respiratory therapists and ICU physiotherapists from three McGill University-affiliated teaching hospitals. We chose heterogeneous groups to capitalize on the interactive nature of focus groups and to explore barriers and facilitators from varying professional angles. We conducted a fourth focus group with ICU physicians from all three hospitals to avoid hierarchical inhibition of the opinions of other ICU professionals.[224,225]

Participants and Context

Participants were licensed ICU clinicians (physicians, nurses, respiratory therapists, and physiotherapists) working in participating hospitals, with at least 6 months experience in the ICU. All had participated in the related survey study.[213]

Procedure and Materials

We purposively targeted all the survey respondents for recruitment via a cover letter included with the survey questionnaire. All clinicians who responded to our invitation were included in one of four focus groups consisting of about 6-10 participants,[226-228] each lasting about 60 minutes.[229,230] To ensure homogeneity in the conduct of the focus groups, the same researcher (DA) who had no prior knowledge of the participants facilitated all the meetings. The focus group topic guide, which was developed by the research team, contained 10 semi-structured open-ended questions (Appendix 1). Specific questions (not included in the guide) were also used to explore a deeper understanding of the findings from the previous survey study[213] such as *'Which specific equipment was lacking in the ICU?'*. All focus group meetings were conducted in English, though participants

were allowed to express themselves in French. Meetings were audio recorded, and two investigators took notes during the discussions. Ethics approval was obtained from McGill University (Montreal, Quebec) and from the participating hospitals.

Analysis

Verbatim transcriptions of audio recordings were anonymized and imported into QDA Miner software (Lite version 2.0, Provalis Research, Montreal, Canada)[231] for coding and analysis. Coding was performed independently by two of the investigators (DA and SM) and disagreements were formally resolved at each step by consensus and in consultation with two other investigators (JS and AB) with expertise in critical care and the TDF framework, respectively.

We performed qualitative content analysis[232] by concurrently classifying quotes into the relevant TDF domains, and then creating specific statements (i.e., barriers or facilitators) summarizing similar quotes under corresponding domains. The naming of the barriers and facilitators was guided by the theoretical constructs associated with each domain of the TDF.[221,222] Quotes that could not be coded within any domain in the TDF were coded under a separate category termed 'Others'.

Several steps were taken to ensure trustworthiness and rigor of the data analysis process. First, one of the two researchers (SM) who analyzed the transcript was not involved in the conducting of the focus groups. Second, the two researchers (DA and SM) independently verified the audio transcription scripts and resolved any differences by referring to a third researcher (JS) if needed. Third, line by line analysis was performed independently and simultaneously by two researchers (DA and SM). Fourth, post analysis, one of the reviewers (DA) read all the scripts again and reviewed all codings, summarized the findings and crosschecked them with the 2nd reviewer (SM). Finally, the final results were also reviewed by both JS and AB.

Finally, three criteria were judged concurrently to identify the key barriers and facilitators.[223,232,233] Criterion 1) Frequency of quotes: Frequency of quotes were based on items judged as 'independent quotes,' implying that items were counted each time they occurred independently. Frequency of quotes was ranked in descending order. Ranks were categorized into 4 quartiles. Barriers and facilitators within the 1st, 2nd, 3rd and 4th quartiles were assigned weights of 2, 1.5. 1 and 0.5,

respectively. Criterion 2) Divergence of opinion: divergence of opinion was assigned a weight of 2 when participants differed on the barrier or facilitator and 1 if there was unanimous agreement. This criterion aimed to capture potential sources of internal conflict when tailoring interventions to address the barriers/facilitators and to capture the salient outliers. Criterion 3) Perceived impact: Perceived impact was given a weight of 2 or 1 based on the investigator's interpretation of the statements of the participants on the barrier or facilitator. Two investigators were involved in this process. All three criteria were weighed equally to judge relevance of the domains as they relate to influencing target behaviour.[223,233] To assess whether or not we had achieved data saturation, concurrent preliminary analysis of data was performed by a single investigator.[234] Barriers and facilitators started reoccurring after the first focus group, and no new themes emerged after the third focus group indicating that we had achieved data saturation: nonetheless, the fourth focus group provided deeper insight into some reoccurring themes.

RESULTS

Focus Groups and Participants

Thirty-three practicing ICU clinicians took part in the four focus group meetings: eighteen nurses, six physiotherapists, three respiratory therapists and six physicians. We omitted the collection of demographic data on age and clinical experience of participants. There was open and uninhibited freedom of expression during the focus groups.

A total of 36 barriers and 25 facilitators with 388 and 237 independent quotes respectively were identified from the focus group discussions (table 1). Thirty-three barriers and 25 facilitators reflected constructs in 13 and 10 domains of the validated version of the TDF,[222] respectively. Four barriers not reflected in the TDF were classified as 'others' (obesity, medical instability, sedation, lack of patient comfort or cooperation). Table 1 also shows the specific barriers and facilitators under each domain. With a cut-off of 4.5 out of 6 for the weights assigned based on our pre-defined criteria, 8 key barriers and 10 key facilitators identified are described below (Figure 1 and 2).

Key Barriers and Their Associated TDF Domains.

Key barriers were identified under the environmental context and resources, belief about consequences, knowledge, as well as the memory, attention and decision processes domains. The barriers and their associated domains, as well as illustrative quotes, are reported below. Quotes are

identified by the type of focus group (PFG: Physicians' Focus Group, MDFG 1: Multidisciplinary Focus Group One, MDFG 2: Multidisciplinary Focus Group Two, MDFG 3: Multidisciplinary Focus Group Three).

Environmental context and resources domain

Key barriers in this domain included limited staffing, lack of time, limited equipment for EM, poor communication among care providers and the unpredictable nature of the ICU environment.

Limited staffing

The limited number of physiotherapists, orderlies, nurses and respiratory therapists was reported as a barrier to EM. However, there was some disagreement among participants regarding the staffing limitations.

"… one physiotherapist, running around the room and dealing with chest regular standard stuffs and is not available to do more time-consuming mobilizations" PFG

"Speaker 1: When you have nurses... I think we are well staffed... Speaker 2: We are not? Speaker 3: We are." MDFG 2

Lack of time

"…sometimes it takes me like an hour to organize. I go like a thousand times around ICU2 and ICU1. I am trying to find the [right] time, but I know the orderly cannot be sure of the time [their availability], so it is hard." MDFG 1

"If you have a double [implying a nurse paired with 2 patients] and you're doing an eight-hour shift, it's very hard to... Or if you've got a patient that has to go down to a test like CT scan, then you can't get it all done in eight hours." MDFG 3

Limited equipment for EM

"We don't have enough [equipment]… it becomes difficult for the nurses and the physiotherapists or anyone who wants to mobilize,…. we don't have enough so that is it." MDFG 1

Poor Communication

"There is no information communication (echo: absolutely!). … the orderlies, they know where is the chair… I [the nurse] don't know how many chairs, what I have available and what I don't have available. There is a gap in the communication 100%." MDFG 1

Unpredictable nature of the ICU

"The level of activity and the unpredictability in the context…, it makes it very complex…" MDFG 1

Belief about consequences domain

The key barrier identified in this domain is the belief, by some clinicians (especially physicians), that there is insufficient conviction regarding the potential benefits of EM or insufficient evidence or data to drive the implementation of EM practice.

Lack of evidence/data/conviction

"But for it to be done consistently people actually have to believe in it. … I think that the lack of conviction, lack of conviction may be the greatest obstacle." PFG

"First of all, the Salt Lake city study was not an RCT. It was an observational prospective study. We do have some RCTs as well, but you don't know whether it's because they had to change their sedation policy so that they could ambulate. Maybe that was the variable and not the ambulation. Maybe once you stop sedating people, all of the effects go away… because they get up themselves and they also pull their own catheters out so that they get out of the ICU faster (waves of laughter)." PFG

Knowledge domain

Limited knowledge on the benefits of EM, the safety parameters for EM, the procedures for EM, and the detrimental consequences of immobility were identified as barriers to EM.

Limited knowledge

"At times the nursing staff doesn't want to mobilize the patient because the patient has a PA catheter in place… although there are no actual contraindication if the patient is hemodynamically stable." PFG

Memory, Attention and Decision Processes domain

The lack of the ability to remember, selectively focus and chose care pathways that will result in optimal health benefits for the patient was identified as a barrier.

Lack of attention to the provision of optimal care

"Like you could have a patient who likes gets up in the chair most of the days, but he has a certain nurse for the whole weekend, ... and the patient doesn't get up in the chair the whole weekend, because they [the nurse] just didn't think of it ... or something like that..." MDFG 2

Key Facilitators and Their Associated TDF Domains.

Key facilitators to EM were identified in the environmental context and resources, social influences, intentions, behavioural regulation, belief about consequences as well as memory, attention and decision processes domains. The key facilitators in these domains, as well as illustrative quotes, are given below.

Environmental context and resources domain

The presence of an organisational culture that encourages EM in the ICU (pro-EM culture), reorganization of the ICU (improved ICU organization), and implementation of a protocol or guideline were key facilitators in this domain. Participants from a certain hospital believed that implementation of a protocol/guideline would not promote the practice of EM.

Pro-EM culture

"And then it [presence of a dedicated team] also takes care of increasing the awareness of the team towards going in favour of early mobilization because if you see a dedicated team ..., you act on it, it is part of our culture, and you are more prone to think about it for your next patient and .... yeah [chorused]." MDFG 1

Improved ICU organization

"If we would have a dedicated team [for EM], like not using the [regular] orderlies, that will take care of all the probabilities and the uncertainties the regular team takes care of. It lessens the

problem of the communication because it is a dedicated team that communicates with you." MDFG 1

Protocol/guideline implementation

"Well if it's protocolized… they should just be done, right? ...looking for contraindications, not for indications. And I think that's the key." PFG

"When I hear the word protocol, the first thing I think of is more paperwork that actually takes away more minutes from our availability to do actual things with the patient. It is something to… a piece of paper to write on that doesn't actually change the care of the patient in any… and more like it takes away from the patient. Speaker 2: Yeah, a guideline would be a better idea than a protocol. Speaker 3: I don't know if a guideline will make a difference though" MDFG 2

Social influences domain

Facilitators under this domain included the influence of having the assistance of clinicians who are highly skilled in facilitating EM (expert support) and the promotion of EM by influential clinicians (influence of champions). Some participants mentioned that the presence of an expert who is both motivated and has the skill to assist them to carry out EM, will have more impact than EM champions who push them to carry out the practice without getting involved.

Expert support

"I think with the physio present; a lot of nurses would feel more comfortable." MDFG 2

Influence of champions

"I said that we need to clone [mentions the name of another nurse] (waves of laughter)… but seriously, she's a champion, and she's motivated and...yeah it's a facilitator" MDFG 3

Intentions domain

Being intrinsically motivated (intrinsic motivation) and taking a conscious decision to implement EM were seen as strong facilitators.

Intrinsic motivation

"Nothing stops me from getting them up if they are able to get up … I will get them up if they can get up… no matter what" MDFG 3

Conscious effort

"Some people [doctors] will stop the proprofol or sedation for two hours, let the patient wake up, it depends. Then you as a nurse, you will have to sort of, "that has to be done, I want my patient awake, so let's do it" MDFG 1

Behavioural regulation domain

One facilitator found under this domain refers to the act of forming a plan or organizing events to facilitate mobilization (action planning and coordination).

Action planning and coordination

"In terms of organizing the planning, I would personally put that higher partly because it's just such low hanging fruit. It's so easy, organizational things we can change almost easily …" PFG

Memory, attention and decision processes domain

Creating a reminder system to remind clinicians about EM was a facilitator that was highly emphasized especially by the physicians.

Reminders

"Speaker 1: The nurses go through their little checklist, they have it all organized and it always has to come in the same order. And if we had just a rehab line that would act as a reminder for us… just saying 'from a rehab point of view, yesterday he stood' – Yeah, yes, yes, easily [responded other participants]. Speaker 2: …trigger yeah, yeah Speaker 3: You go, 'BING!' Speaker 4: Yeah that's a good idea" [the discussion continued about where on the clinical round checklist such a line could fit best]. PFG

Belief about Consequences

Our data showed that clinicians who expect a positive outcome (for the patient or the health care system) from EM were more likely to implement EM.

Positive outcome expectations

"If I knew that every day I got my patient up like twice a day, if I saw that... you know I saw that it cut a week off their stay in ICU, I would be ... pushing that harder to get them up" MDFG 1

DISCUSSION

Our findings are consistent with previous studies that identified barriers and facilitators to EM.[168,171,180,193,198,213,214] A recent systematic review of 40 studies by Dubb et. al[172] identified 28 EM barriers. While barriers in several TDF domains (knowledge, skills, goals, behavioural regulation, social influences, and environmental context and resources domains) were also reported in the Dubb's review,[172] we identified additional domains (belief about capabilities, optimism, intention and memory, attention and decision processes domains). Furthermore, some of the barriers under the social and professional roles (professional identity and teamwork), belief about consequences (negative outcome expectation, lack of evidence/data/conviction) and emotion (fear) domains were uniquely identified for the first time in the current study.

The differences between our findings and those from the 40 studies included in the systematic review by Dubb et. al[172] may be explained primarily by the differences in the design and methods used to identify the barriers. Studies included in the review[172] identified barriers using anecdotal reports (2 studies), identification of predefined medical contraindications (17 studies), surveys (9 studies), data evaluation and/or collection (20 studies), group/staff meetings (7 studies), and interviews (3 studies). Some studies used a combination of these assessment methods. Although many of these methods may reveal objective barriers, they may not unveil attitudinal attributes that may be influencing clinicians' actions. Furthermore, the analysis in the few qualitative studies included in the review were not informed by a theoretical framework. These differences explain the distinct contribution of our study.

All focus groups identified limited resources as a barrier. Interestingly, institutional reorganization has resulted in the movement of two of the ICUs to new locations with larger space, more equipment, and more staffing. It would be interesting to explore how this reorganization could have impacted on EM in these ICUs and on the clinicians' perceptions of barriers and facilitators.

As it is often the case, many of the facilitators identified in this study were the direct opposite of the barriers, but peer modeling was an additional unique item. Enhancement of these facilitators could have the potential to influence EM practice.

Comparison of our focus group and survey findings

We followed up respondents from an initial cross-sectional survey study on EM[213] in the same three ICUs to obtain a deeper understanding of the barriers and facilitators using an exploratory focus group methodology. While both studies agreed that limited staffing and equipment constitute part of the greatest barrier to EM, the survey[213] failed to identify barriers from six of the thirteen domains found in the current study (beliefs about capabilities, optimism, belief about consequences, intentions, emotion, as well as memory, attention and decision processes). Unlike the survey which found primarily physical and organizational barriers, close to 40% of barriers in the current study were related to clinician's attitudes. Finally, contrary to the current study, medical instability, the presence of ICU lines, sedation, and safety concerns of clinicians were the greatest barriers in the survey. These differences highlight limitations associated with survey methodology.[215,235]

Study strengths

Unlike most studies which identified barriers to EM, this study included the perspectives of respiratory therapists, who are particularly important in the mobilization of mechanically ventilated patients but are often excluded from studies exploring barriers to EM. Second, it is the only EM study that has used the TDF to guide its qualitative analysis. The use of the TDF limited our risk of omitting important areas when considering factors that impede implementation of evidence-based practice.[223] Third, two researchers, one not involved in the data collection process, analyzed the results in order to minimize bias. Fourth, the analysis was detailed and in-depth to ensure valid, reliable and credible results. Fifth, data saturation was achieved. Sixth, the barriers and facilitators were derived from practising ICU clinician-generated discussions. Finally, the identification of several attitude-related barriers is therefore a unique contribution. Attitude determines behaviour and the behaviours of health professionals constitute one of the greatest barriers to introducing change in the healthcare system.[236] Theory-based KT interventions are more likely to effect behavioural change, which could result in better health outcomes.[237] The results of

this study could, therefore, be used in the design of theory-based KT interventions by using the TDF to guide the choice of behaviour change techniques and intervention components[238-240] as has been done previously.[218,241,242]

Study Limitations

The frequency counts reported from our analysis involved only items that were judged as 'independent quotes'. An alternative way of counting every quote (including agreements to a previous idea) may have produced some differences in the frequency counts. The results of this study are comprised of the subjective opinions of our focus group participants, which might have varied with different participants. However, 33 of the 36 barriers and 22 of the 25 facilitators were reproduced in more than one focus group, which increases the credibility of our findings. Finally, we acknowledge the fact that volunteers to a focus group meeting are most likely people who are passionate about the subject matter; which is a common limitation of the focus group methodology.[243]

CONCLUSION

This is the first study to examine potential barriers and facilitators to EM in the ICU using the TDF. The study identified 36 barriers and 25 facilitators in 13 and 10 domains of the TDF, respectively. Many of the identified barriers and facilitators were related to clinician behaviour and had not been identified in earlier studies. These findings may be used to inform the design and evaluation of theory-based KT interventions designed to improve EM practice.

Acknowledgment

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Authors Contribution

D. Anekwe was responsible for designing the study, coordinating the overall activities, as well as data collection and analysis and writing of manuscripts. J. Spahija contributed to the study

conception, design, execution, and supervision, as well as proofreading and editing of all the documents as well as the final manuscript. M. de Marchie participated in the design and data collection of the study. S. Milner was involved in the verification of the audio transcript, data analysis, and proofreading and editing of the final manuscript. A. Bussières provided methodological guidance in the analysis, as well as proofreading and editing of the manuscript. All authors critically revised and approved the final manuscript.

TABLE, FIGURES, AND APPENDIX

Table 1: Identified Barriers and Facilitators in the Various Domains of the TDF

Item #	**Domain *(definition)***	**Barrier**	**Frequency**	**Facilitator** *(presence or availability of)*	**Frequency**
1	Knowledge *An awareness of the existence of something*	Limited clinical knowledge	17	Clinical knowledge	19
2		Limited procedural knowledge	8	Procedural knowledge	10
3	Skills *An ability or proficiency acquired through practice*	Limited clinical and organizational skill	9	Clinical and organizational skill	10
4	Social and Professional Role and Identity *A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting*	Lack of teamwork	3	Teamwork	10
5		Unclear professional roles and responsibilities	13	Clear professional roles and responsibilities	5
6		Negative professional identity *(professional self-concept attributes that hinder EM)*	2	Positive professional identity *(professional self-concept attributes that promote EM)*	1
7	Beliefs about Capabilities *Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use*	Low professional confidence	2		
8	Optimism	Lack of optimism	4	Optimism	4

Item #	Domain *(definition)*	Barrier	Frequency	Facilitator *(presence or availability of)*	Frequency
	The confidence that things will happen for the best or that desired goals will be attained				
9	Belief about Consequences *Acceptance of truth, reality, or validity about outcomes of a behaviour in a given situation*	Negative outcome expectations	4	Positive outcome expectations	12
10		Occupational risk	8		
11		Lack of evidence/data/conviction	16	Evidence/data	8
12	Intentions *A conscious decision to perform a behaviour or a resolve to act in a certain way*	Low intrinsic motivation	18	Intrinsic motivation	28
13		Lack of conscious effort	5	Conscious effort	10
14	Goals *Mental representations of outcomes or end states that an individual wants to achieve*	Low prioritization	8		
15	Memory, Attention and Decision Processes *The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives*	No reminders	2	Reminders	10
16		Lack of attention to the provision of optimal care	18	Attention to the provision of optimal care	7
17	Environmental Context and Resources *Any circumstance of a person's situation or environment that discourages or encourages the*	Limited staffing	41	More staffing	7
18		Unpredictable nature of the ICU	14		

Item #	Domain *(definition)*	Barrier	Frequency	Facilitator *(presence or availability of)*	Frequency
19	*development of skills and abilities, independence, social competence and adaptive behaviour*	Lack of time	24		
20		Limited equipment	27	More equipment	6
21		Limited space	2		
22		Poor communication	14	Improved communication	8
23		Cost	1		
24		No EM culture	3	Pro-EM culture	13
25		Poor ICU organization	13	Improved ICU organization	13
26		Doctor's order requirement	8	No doctor's order requirement	4
27		Cumbersome ICU lines and leads	6		
28		Lack of protocol/guideline Implementation	9	Protocol/guideline implementation	9
29	Social Influences	No promotion or support or champion	8	Expert support	13
30	*Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours*			Influence of champions	12
31				Peer modelling	5
32				Peer support	8
33	Emotion	Stress and burnout	13		

Item #	**Domain** ***(definition)***	**Barrier**	**Frequency**	**Facilitator** *(presence or availability of)*	**Frequency**
34	*A complex reaction pattern, involving experiential, behavioural and physiological elements by which the individual attempts to deal with a personally significant matter or event*	Fear	7		
35	Behavioral Regulation *Anything aimed at managing or changing objectively observed or measured actions*	Poor action planning and coordination	13	Good action planning and coordination	9
36	Others	Obesity	11		
37		Medical instability	18		
38		Sedation	9		
39		Lack of patient cooperation or comfort	10		

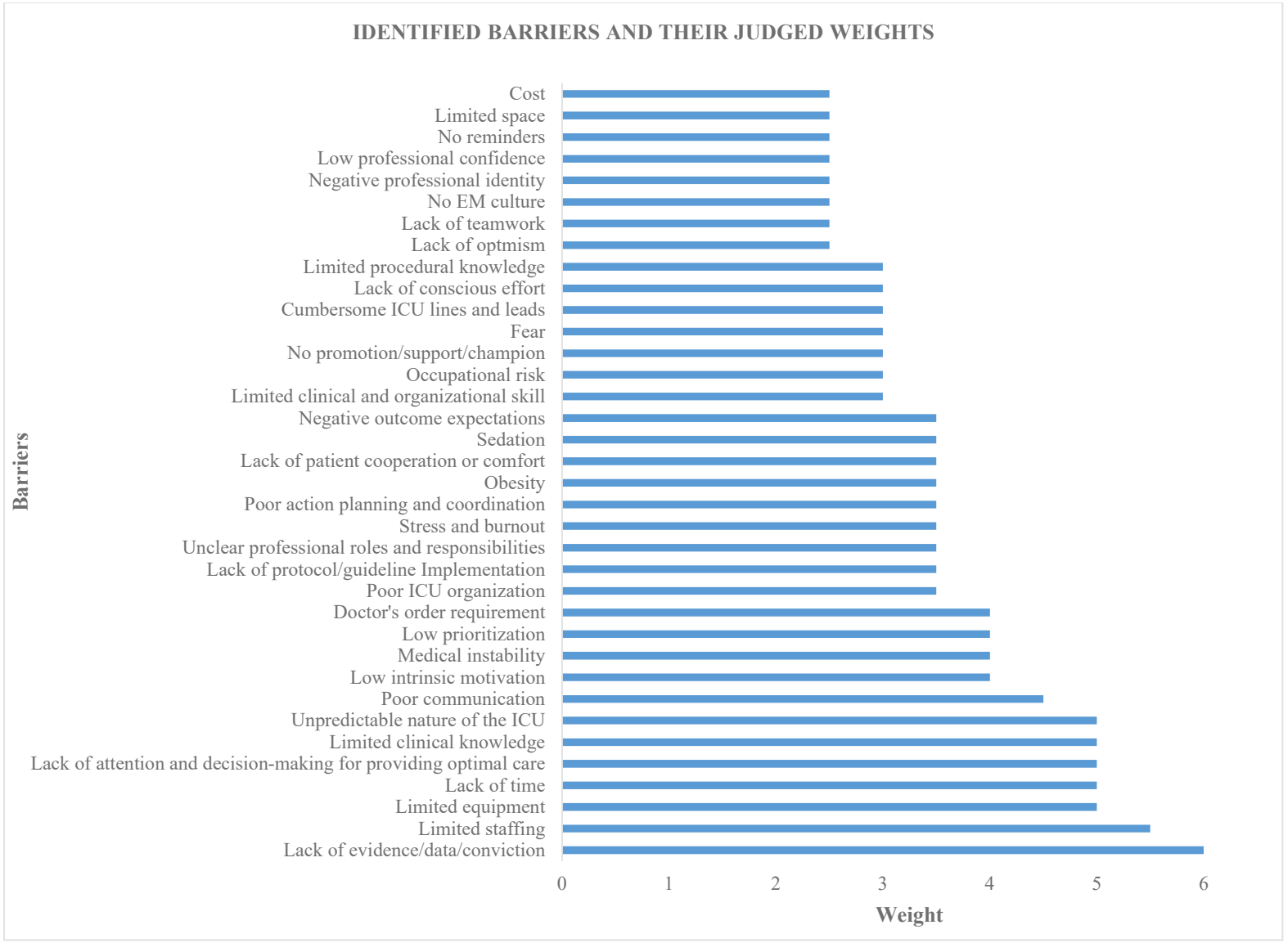

Figure 1: Barriers and their assigned weights. Weights are based on a rating factor of two for each of the following criteria: the (i) frequency of quote, (ii) divergence of opinion and (iii) perceived impact on practice.

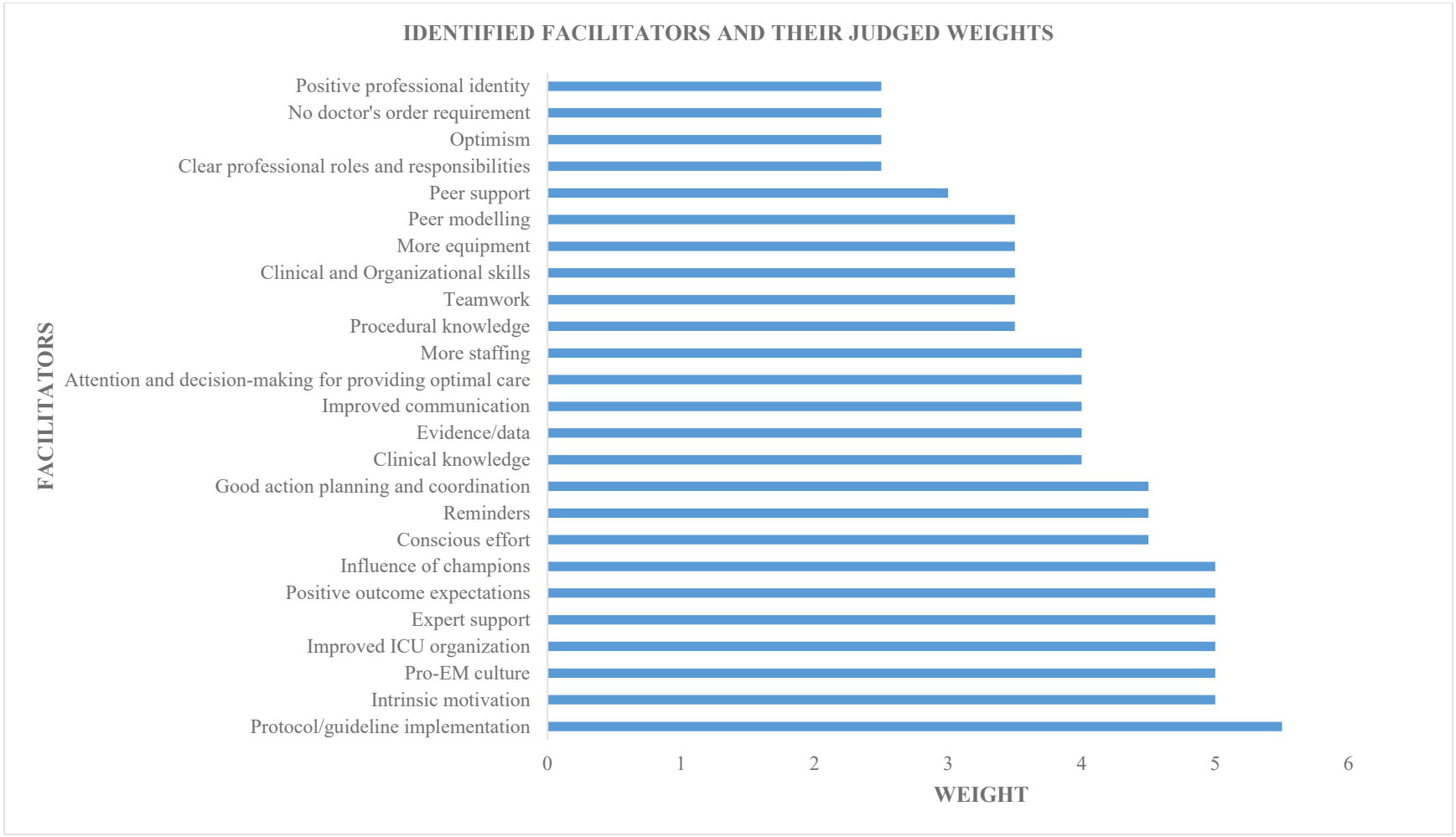

Figure 2: Facilitators and their assigned weights. Weights are based on a rating factor of two for each of the following criteria: the (i) frequency of quote, (ii) divergence of opinion and (iii) perceived impact on practice.

Appendix I

The Focus Group Topic Guide 10 Semi-Structured Questions

10 Semi-Structured Questions (focus-group guiding questions for clinicians)

1. In your ICU, do you often or sometimes have patients that are fit to be mobilized/moved out of bed daily but are not? What possible barriers hinder their early mobilization?
2. What do you think can be done in your ICU to ensure that this patient group is moved daily?
3. What do you think is/are the greatest challenge to getting every patient out of bed early and walking in your ICU?
4. What feasible solution do you think that can be offered to this problem?
5. What are the things you think have helped this practice in your ICU?
6. How do you think that they can be improved?
7. Do you think your ICU team is doing the best presently given the available limited resources?
8. What changes/interventions do you think can be done to the present situation to help ICU patients move more and earlier? What suggestion do you have to improve the present situation in your ICU?
9. How best do you think this can be approached? *(If not answered from 8 above)*
10. Why do you think it is important that we continue to try to find better ways to implement early mobilization? What is important about early mobilization?

Probing clauses: "Well, why is that?" or "Can you tell me more about why that is so?"

CHAPTER 8: PREFACE TO MANUSCRIPT THREE

The first manuscript identified limited awareness of the clinical benefits of EM as a barrier to its implementation into practice. Additionally, the second manuscript showed that one of the reasons behind the low implementation/low priority given to EM was that not all clinicians were convinced of its benefits. The second manuscript showed that this was because the results of some EM studies did not show much benefit with the intervention. Recognizing the limited time and skills of many clinicians in evaluating the available evidence in the published literature, we decided to undertake a project to review the evidence pertaining to the benefits of EM and thereby potentially increase awareness of its clinical benefits when disseminated.

The goal of the third manuscript was therefore to pool the results of all published randomized controlled trials and review the evidence of the impact of EM on ICUAW, which is a very important ICU clinical outcome. Other secondary outcomes that were also addressed in this literature review included ventilator dependency, discharge location, ICU and hospital LOS, and acute mortality.

The specific objective of the manuscript was to estimate the extent to which EM and neuromuscular electrical stimulation interventions, compared to usual care, reduce the incidence of ICUAW among patients in the ICU. The secondary objective was to assess the extent to which EM and NMES interventions impact other outcomes (ventilator dependency, discharge location, ICU and hospital LOS, and acute mortality) that may be associated with ICUAW.

Our findings have increased the strength of the available evidence on the positive impact rehabilitation interventions on a number of ICU outcomes.

CHAPTER 9: MANUSCRIPT THREE

Early Mobilization and Neuromuscular Electrical Stimulation to Reduce Intensive Care Unit-acquired Weakness: A Systematic Review and Meta-Analysis

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Word Count: 3371

LIST OF ABBREVIATIONS

Abbreviation	Meaning
EM	Early mobilization
NMES	Neuromuscular electrical stimulation
ICU	Intensive care unit
ICUAW	Intensive care unit-acquired weakness
LOS	Length of stay
MRC	Medical research council
RCT	Randomized controlled trial

Keywords: Early mobilization, Neuromuscular Electrical Stimulation, Critical Illness, Intensive Care Unit-Acquired Weakness, Length of Stay, Mortality, Ventilator Dependency, Discharge Location.

ABSTRACT

Background: Intensive care unit-acquired weakness (ICUAW) in critically ill patients is associated with significant impairments in body structure and function, activity limitations, and participation restrictions. The etiology and management of ICUAW remain uncertain. We aimed to estimate the extent to which early mobilization (EM) and neuromuscular electrical stimulation (NMES) compared to usual care reduce the incidence of ICUAW and of other secondary outcomes (ventilator dependency, ICU and hospital length of stay, acute mortality, and discharge location) in critically ill patients.

Methods: For this systematic review and meta-analysis, we searched five databases from inception to May 1st, 2017, for randomized controlled trials of EM and NMES interventions in critically ill adults. Data on the incidence of ICUAW were extracted. Both odds and risk ratios for ICUAW were pooled using the random-effects model. PROSPERO registration ID: CRD4201706503.

Findings: We identified 1420 reports after duplicate removal. Eight studies including 791 patients (390 intervention and 401 usual care) were included in the final analysis. The interventions involved EM in four trials, NMES in three trials, and both EM and NMES in one trial. ICU rehabilitation decreased the likelihood of developing ICUAW: odds ratio of 0.658 (95% CI: 0.437-0.990) in the screened population, and 0.723 (95% CI: 0.535-0.976) in the randomized population. Subgroup analysis showed that the impact of rehabilitation was more profound (i) in patients who spent more than seven days in the ICU in both the control or intervention group and (ii) when rehabilitation is started within 2 days of ICU admission. This analysis also showed that the impact of rehabilitation on ICUAW is better assessed at hospital discharge. There was also evidence that rehabilitation increases the likelihood of being discharged home (OR 1.765 [95% CI: 1.005-3.099]), whereas the evidence was inconsistent with regards to ventilator dependency as well as ICU and hospital length of stay.

Interpretation

Early rehabilitation was associated with a decreased likelihood of developing ICUAW. Our findings support early rehabilitation in the ICU. While results were consistent in both the screened and randomized populations, the wide confidence intervals suggest that well-conducted trials are needed to validate our findings.

BACKGROUND

The Problem of ICUAW

Intensive care unit (ICU) survivors often develop muscle weakness which is unrelated to the primary pathology for ICU admission.[1-3] This weakness may progress to a clinical syndrome known as ICU-acquired weakness (ICUAW), a "clinically detected weakness in critically ill patients in whom there is no plausible etiology other than critical illness".[244] This syndrome includes critical illness polyneuropathy, myopathy, and neuromyopathy.[244,245]

ICU-acquired weakness is associated with significant impairments in body structure and function,[85-87] activity limitations,[85,87,125] and participation restrictions.[85] It has a long-lasting impact,[85-87,125] persisting for months or years following ICU discharge with a resultant decline in quality of life for ICU survivors[87,94] and a high burden on the healthcare system.[124]

There is currently no effective treatment for ICUAW.[102,246] It is often recommended that patients with ICUAW be referred for rehabilitation, but a 2015 Cochrane review[247] failed to identify studies able to determine whether physical rehabilitation improve activities of daily living, muscle strength and quality of life in these ICU survivors. Thus, preventing the development of ICUAW through the control of associated risk factors[102] such as immobility[132-134] is key. Immobility predisposes to critical illness myopathy through protein loss resulting from altered protein metabolism[248] and to critical illness polyneuropathy through increased insulin resistance,[248] which leads to hyperglycemia. Therefore, reducing the level of immobility during ICU admission may decrease the likelihood of developing ICUAW.[102,246]

Early mobilization (EM) reduces the duration of immobility, while neuromuscular electrical stimulation (NMES) reduces muscle atrophy[249] which is involved in the pathophysiological process of ICUAW.[100,250] However, few robust studies have evaluated the effectiveness of EM and NMES to reduce the risk of ICUAW. To date, two systematic

reviews[159,162] have evaluated the effectiveness of EM and NMES to reduce the risk of ICUAW with the latest search being in April 1st, 2014.[162] A number of new trials have been published after April 2014 and some computational and methodological limitations exist in the last review.[162] The few trials included in previous reviews also limited exploration of sources of heterogeneity. This review is, therefore, necessary to revise and update the available knowledge.

Intensive care unit-acquired weakness can predict ventilator dependency[122,123,125] (a determinant of the length of stay (LOS) in the ICU and hospital and discharge location.[125] Whether these outcomes are positively impacted by rehabilitation directly or indirectly through possible association with ICUAW is not yet fully known. Some studies have shown early rehabilitation to be safe even in the acute phase of critical illness[21,142,153] which suggests that it may have no positive association with acute mortality, but to date, no study has combined the acute mortality results from RCTs in a meta-analysis to confirm these results.

OBJECTIVES

The aim of this review was to estimate the extent to which EM and NMES interventions compared to usual care, reduce the likelihood of developing ICUAW among patients in the ICU from randomized controlled study designs. Our secondary objectives were to assess the extent to which EM and NMES interventions impact other outcomes (ventilator dependency, discharge location, ICU and hospital LOS, and acute mortality) that may be associated ICUAW.

METHODS

This systematic review and meta-analysis report adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and is registered in PROSPERO (CRD4201706503).

Search Strategy

We searched MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials and Physiotherapy Evidence Database databases from inception to May 1st, 2017 without language restriction (Appendix I). Studies were included if they (i) were done in the ICU (ii) were RCTs or quasi-RCTs (iii) involved adult participants (over 18 years) (iv) evaluated the effect of EM or NMES interventions, and (v) measured ICUAW according to the diagnostic approach published by Stevens et al.,[244] which was adopted in the American Thoracic Society Clinical Practice guideline,[251] or assessed muscle strength using the Medical Research Scale (MRC). Studies that evaluated rehabilitation interventions in patients already diagnosed with ICUAW were excluded.

Study Selection

Two authors (DA and SB) independently screened the titles and abstracts of retrieved articles, and the full texts of potentially eligible articles were obtained and further assessed for final inclusion. Reviewers formally met at each step for consensus, and a senior author (JS) resolved differences if needed.

Data Extraction and Quality Assessment

Two reviewers (DA and SB) participated in data extraction and quality assessment of the individual studies using the Cochrane Risk of Bias Tool.[252] Population characteristics, treatment intervention(s), control/comparators, and outcomes were described for each included study. Quality assessment was performed in duplicate by the reviewers; items were categorized as 'Low, High or Unclear' based on the criteria shown in Appendix II. All disagreements were tracked and resolved by discussions and consensus or by a senior author (JS) if needed. Authors of the primary studies were contacted to request any missing important information. Given the limited number of studies that we expected to find, we planned a priori to include both low, unclear and high-quality

studies, and perform a subgroup analysis by the quality of study design if we identified up to four studies in each category.

Data Analysis

The primary outcome measure was the incidence of ICUAW measured at any time point after the initiation of the intervention. The secondary outcome measures included ventilator duration (ventilator-free days and duration of mechanical ventilation), discharge location, ICU and hospital LOS, and acute mortality (defined as death within the ICU, hospital or 28 days mortality). For binary outcomes, we extracted the number of events and total number in each group. For continuous outcomes, we extracted the mean (standard deviation) or the median (range) values.

Data were analyzed using Stata 14 (StataCorp., 2015). The random-effect model was used to pool the effect sizes from the different studies in a meta-analysis and we performed a sensitivity analysis using the fixed effect model. Only dichotomous data were pooled together and we reported the odds ratios (OR) and risk ratios (RR) (95% confidence intervals) in both the screened and the randomized populations (with the imputation of missing data). Statistical heterogeneity was assessed with the I^2 statistic, while clinical heterogeneity was explored with subgroup analysis based on (i) short vs long ICU LOS (with short ICU LOS defined as > 7 days in either the intervention or control group) (ii) the timing of intervention (iii) the type of rehabilitation intervention (EM or NMES type interventions) (iv) at different time points of ICUAW assessment (ICU awakening, 7^{th} day post-awakening, ICU discharge, hospital discharge). The latest measuring timepoint was used for ICUAW in the main meta-analysis. We assessed publication bias using the funnel plot.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

The searches yielded 1593 articles. After removing 170 duplicates, we screened 1420 articles for eligibility (Figure 1). Of these, 1380 articles did not meet our selection criteria, leaving 40 articles for full-text review. Nine articles[27,32-39] were selected after the full-text review, but only eight studies[27,33-39] were included in the critical appraisal because data could not be obtained for one study.[32] Reasons for the exclusion of studies are given in Appendix III.

Tables 1 and 2 show the characteristics of the included studies, the characteristics of the 791 patients (390 intervention and 401 control) in the studies, and the intervention characteristics, respectively. Most patients received mechanical ventilation during their ICU stay and the primary reason for ICU admission and co-morbidities varied from study to study. A detailed description of tables 1and 2 is given in Appendix IV.

Table 3 shows the number of people with ICUAW in the intervention and in the control groups as reported by the authors, in the screened population, and in the total population randomized (with the imputation of worst values for patients who were not evaluable). Two studies provided data on the incidence of ICUAW at ICU awakening,[253,254] one study at the 7th-day post-awakening,[156] one study at sedation cessation,[255] five studies at ICU discharge[147,253,255-257] and three studies at hospital discharge.[142,253,256] The pooled OR using the random effect model is 0.658 (95% CI: 0.437-0.990) in the screened population and 0.723 (95% CI: 0.535-0.976) in the total population randomized in favor of early rehabilitation (Figure 2). Sensitivity analysis using the fixed effect model showed similar results.

Subgroup analysis showed that the impact of rehabilitation on the odds of developing ICUAW was more profound in a subgroup of studies in which patients had longer ICU LOS (median or mean ICU LOS > 7 days in either the intervention or control group) with OR: 0.529, 95% CI: 0.316-0.885 in the screened and 0.648, 95% CI: 0.453-0.929 in the randomized population

(Figure 3). Sub-analysis by time point of ICUAW assessment favored early rehabilitation at hospital discharge compared to earlier time points (Figure 4). Sub-analysis by the timing of intervention showed a lower OR when early rehabilitation intervention was started about 2 days after ICU admission and/or initiation of mechanical ventilation in comparison to when it was initiated after ~5 days (Figure 5). Similarly, studies with only EM intervention had lower OR compared to studies with only NMES (Figure 6), whereas the OR was similar when studies with EM and NMES alone were compared with usual care.

The fixed effect model of RR analysis showed the same results as the OR analysis, whereas with the random effect model there was only a tendency for a reduced RR in favour of early rehabilitation: 0.776 (95% CI: 0.575-1.046) in the screened population and 0.916 (0.826 – 1.016) in the randomized population. Subgroup analysis using the random effect also showed that the risk of ICUAW was reduced in a subgroup of patients with longer ICU LOS.

Five studies reported ICU mortality,[253-257] four studies reported hospital mortality,[142,147,253,256] while one study reported 28-day[156] (Table 4). There was no difference in the pooled OR for acute mortality between the two groups, 1.165 (95% CI: 0.785-1.729) (Figure 7).

Though ICU LOS was numerically shorter with rehabilitation in five studies,[142,147,254-256] only one involving EM was statistically significant (2 days less for 'LOS until ICU discharge readiness')[147] (Table 5). The same study found a significantly shorter hospital LOS (6.5 days less, p=0.01) in favor of early rehabilitation.[147] Five studies[142,147,156,256,257] reported median changes in LOS, making it impossible to pool the study results in a meta-analysis.

Ventilator duration was reported as 'duration of mechanical ventilation' in seven studies and as 'ventilator-free days' in four studies[142,147,254,257] (Table 6). Duration of mechanical ventilation was statistically shorter in two studies (favoring intervention)[142,254] and was not

different in three studies.[253,255,257] Ventilator-free days, was statistically longer in one study (favoring intervention)[142] and shorter in another study[254] but showed no significant difference in two studies.[147,257] The two studies that showed lesser ventilator dependency began rehabilitation intervention earlier than 48 hours and did not have EM as part of usual care (Table 2).[142,254]

Four studies reported discharge location.[142,147,156,253] Only two studies compared it statistically, favoring discharge home in the intervention group p=0.06[142] and 0.0007.[147] A meta-analysis of discharge location in the randomized population showed a pooled OR of 1.765 (95% CI: 1.005-3.099) in favor of rehabilitation for being discharged home (Figure 8).

Statistical heterogeneity (I^2 statistic) showed values 'that might not be important'[258] ($I^2 <$ 40%) for ICUAW and mortality (Figure 3 and 7), and that represents moderate heterogeneity[258] for discharge location (Figure 8). In contrast, subgroup analysis for ICUAW showed clinical heterogeneity that may be explained by the type and the timing of rehabilitation interventions and by ICU LOS.

The funnel plot analysis (Figure 9) suggests that there is no significant publication bias, which was also confirmed by Egger's test (P = 0.471 for the null hypothesis of 'no small-study effects').

Details of the risk of bias assessment results are shown in table 7. With selection bias, performance bias and detection bias judged as key indicators for our primary outcome,[258] within studies, three studies had high risk of bias, one study unclear risk, and four studies low risk. Across studies, the risk of bias is summarized as unclear.

DISCUSSION

Our study showed that rehabilitation in the ICU is associated with a 34% and 28% reduction in the odds of developing ICUAW in the screened and randomized population,

respectively. This effect is more pronounced in a subgroup of patients with longer ICU LOS. Our study also showed an increased likelihood of being discharged home and inconsistent evidence of shorter ICU and hospital LOS, and lesser ventilator dependency with rehabilitation. It also showed that rehabilitation is not associated with odds of acute mortality.

Contrary to our findings, earlier systematic reviews[159,162] did not find any association (RR) between rehabilitation and ICUAW. This may be attributed to the limited number of publications included in the reviews. Furthermore, the meta-analysis in the second review[162] analyzed patients that were not evaluable as having ICUAW in two of the three included RCTs. In these studies, ICUAW was assessed with the MRC sum score, which is only applicable in awake and cooperative patients. Missing data is therefore common in unconscious, very weak and uncooperative patients. Imputing the best values (= no ICUAW) for this group of patients in the intention to treat analysis does not seem optimal given the clinical context and the possible reasons for missing data. This current study conservatively erred on the side of inclusion and imputed the worst values for patients who were not evaluable.

Our analysis further showed that a subgroup of studies in which patients spent a long time in the ICU had 47% and 35% lower odds (screened and randomized population, respectively) of developing ICUAW with rehabilitation. This finding is supported by a previous study which showed benefit with exercise in patients who were expected to stay at least seven days in the ICU.[153] Most of the patients included in this previous study[153] were ventilated, and it has been shown that ventilated patients who stayed five days or more in the ICU had more than a twofold increase in the likelihood of developing ICUAW.[156]

Our results also showed that the effect of rehabilitation on ICUAW is best assessed at hospital discharge. This finding agrees with an earlier study which found increased quadriceps

force at hospital discharge and not at ICU discharge after an exercise intervention in the ICU.[153] Unlike drugs, exercise improves health through neurological, metabolic and morphological adaptation mechanisms[259-262] which yield measurable effects at a distant time past the point of administration. Assessment at earlier time points may therefore not accurately reflect the effect of rehabilitation. Moreover, the MRC sum score, which was used to assess ICUAW in these studies, is known to have some biases and measurements challenges that can lead to false positive results when used within the ICU.[251,263,264]

Our results suggest that early compared to late onset of rehabilitation (≤ 48 hours versus > 48 hours after ICU admission) may be more protective against ICUAW. This finding should be viewed with caution given that only two studies began rehabilitation later, and the OR from the subgroup analysis did not reach the level of significance. Nonetheless, studies have shown decreased skeletal muscle synthesis and thickness loss within the first 72 hours of critical illness.[265,266] The timing of the intervention appears to be an important variable to consider when providing rehabilitation in the ICU.

This review suggests that EM has a greater impact compared to NMES, perhaps because of EM's greater potential to affect all the muscles of the body. More studies are needed in each subgroup to further explore this effect. The results for the random effect model of the RR for ICUAW were not consistent with the OR. This may be attributed to the mathematical attributes of the two measures. Risk ratios are bounded by the control group risk.[267,268] In our analysis, the control group (without exposure to the intervention) risk is unknown as the control group in five studies had EM as part of standard care, which makes OR mathematically superior for this meta-analysis.[267-269]

Importantly, findings from this review show that rehabilitation is not associated with acute mortality. This review agrees with the findings of the primary studies included in this review, other primary studies[21,138,153,157,158] and systematic reviews[150,151,159-161,270,271] that rehabilitation is safe even at the early stage of critical illness.

Our study showed some evidence of shorter ICU and hospital LOS with EM but not with NMES. This result is consistent with the results of previous non-RCT studies.[138-141,158] and systematic reviews.[151,271,272] No RCT included in this review was powered to detect a difference in ICU or hospital LOS. A previous systematic review,[151] pooled the results of six and five studies for ICU and hospital LOS, respectively, using the Hedges' g statistic and reported shorter ICU and hospital LOS in favor of rehabilitation; however, clinical interpretation of the Hedges' g statistic in relation to LOS is unknown. The review from Zhang et. al[271] showed evidence of shorter ICU LOS, and a tendency to shorter hospital LOS with rehabilitation. But it is unclear how the authors pooled means and medians together in the meta-analysis.

This review found some evidence indicating that rehabilitation favors lesser ventilator dependency. Four studies[142,253,255,257] in which the control group received EM as part of usual care found no difference in ventilator dependency but two studies in which EM was not part of usual care reported lesser ventilator dependency in favor of rehabilitation. In the studies, where all patients typically received rehabilitation, the only difference between the intervention and control groups is the administered dosages of the rehabilitation. A higher dosage of exercise in the critically ill may not be beneficial, as ICU patients may be prone to early fatigue, which can predispose to negative outcomes. Evidence from stroke patients suggests that higher frequency of very early rehabilitation with lower-dose intensity is associated with more favorable outcomes.[273] The higher dosage of exercise in the EM group and the presence of EM in both the intervention

and control groups may be possible confounders differentiating studies with a positive outcome[142,254] from those without.[147,156,255,257] These results show that in comparison to a usual care group without EM, rehabilitation may reduce ventilator dependency during ICU stay.

Expectedly, rehabilitation also showed higher odds of patients being discharged home in comparison to usual care in this review. This finding is contrary to the finding of a previous systematic review which only showed a tendency towards being discharged home.[270] This difference can be explained by the differences in the types of included studies and the type of interventions evaluated. Contrary to the current review, the previous review[270] included both RCTs and controlled study designs and evaluated only active mobilization interventions.

The rigorous nature of the search strategy, the inclusion of only RCTs, the conservative nature of data imputation, the consistency of results (in the screened and the randomized population, and with fixed and random effect models for OR) and the 'no evidence of statistical heterogeneity' support the strength of the evidence generated in this review. Nonetheless, a number of limitations exist. First, our search strategy identified only RCTs which provided information on our primary outcome. Second, sub-analyses may be subject to limitations of observational investigations, therefore the interpretations of the results of the sub-analysis are limited. Third, the upper boundary of the confidence interval for ICUAW suggests that more RCTs are needed to verify the results. Fourth, control group intervention varied across studies (with and without EM). We limited the effect of this by focusing on the results of our OR analysis. Finally, ICUAW was measured with the MRC sum score in all the primary studies which may have underestimated the real incidence of ICUAW as compared to electrophysiological studies.[97]

This is the first systematic review to show that rehabilitation in the ICU reduces the odds of developing ICUAW. Our results imply that beginning rehabilitation early in the course of

critical illness may reduce the odds of developing ICUAW, reduce ICU and hospital LOS, and ventilator dependency. Wide-scale adoption of rehabilitation in the ICU is therefore encouraged. Though such adoption may involve extra cost, potential savings associated with the prevention of ICUAW may imply net savings for the health care system and improved quality of life for ICU survivors.[138,141,274] Studies exploring the return on such investments are needed. Future studies should also assess ICUAW at hospital discharge, be adequately powered to detect differences in ICUAW, ventilator dependency, discharge location, and ICU and hospital LOS.

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Authors Contribution

DA conceived and designed the study and did the data searches. DA and SB did the study selection, data extraction, and quality assessment. DA did the statistical analyses, created the tables and figures, prepared the supplementary materials, and drafted the manuscript. SB verified and edited all the tables, as well as proofreading and editing of the manuscript. JS contributed to the study conception, design, execution, and supervision, as well as proofreading and editing of all the documents as well as the final manuscript. AB provided methodological guidance in the design and analysis, as well as proofreading and editing of the manuscript. All authors critically revised and approved the final manuscript.

TABLES OF RESULTS

Table 1. Characteristics of Included Studies and Patients included in the Primary Studies included in the Systematic Review

Study	Design [Clinical setting]	Population description [% on MV]	Intervention	Comparison		Group [Sample size (n)]	Age, Mean (SD)* or Median (IQR) **	Sex, n (%) females	Illness Severity (APACHE II) Mean (SD) * or Median (IQR) **	Primary ICU admission Diagnosis, n (%)		
				Usual care with EM	Usual care without EM							
Schweickert 2009	Parallel RCT [ICUs in the University of Chicago and the University of IOWA medical]	Medical ICU patients (MV < 72 hours) [100%]	PT & OT		√	Intervention (49)	57.7 (36.3-69.1) **	29 (59%)	20.8 (15.8-24.0) **	Condition	Intervention.	Usual Care
										ALI	27(55)	31(56)
										COPD exacer.	4(8)	6(11)
										Asthma exacer.	5 (10)	4 (7)
										Sepsis	7 (14)	9 (16)
										Haemorrhage	1 (2)	2 (4)
										Malignancy	2 (4)	1 (2)
						Usual care (55)	54.4 (46.5-66.4) **	23 (41.9%)	19.0 (13.3-23.0) **	Others	3 (6)	2 (4)
Routsi 2010	Parallel RCT [Multidisciplinary 28-bed University ICU in Evangelismos hospital, a 1000-bed medical centre]	All ICU patients [3%]	NMES		√	EMS (68)	61 (19) *	22 (32%)	18 (4) *	Diagnosis	EMS	Control
										Sepsis	11(16.2)	14(19.4)
										Trauma	12(17.6)	14(19.4)
										Post-surgical	13 (19.1)	12 (16.7)
										Brain injury	24 (25.3)	23 (31.9)
										Resp. failure	2 (2.9)	4 (5.6)
										Other	6 (8.8)	5(6.9)
						Control (72)	58 (18) *	23 (32%)	18 (5) *			
Dantas 2012	Parallel RCT Single blinded [General ICU of the Hospital Agamenon Magalhães]	ICU patients on MV [100%]	PT interventions	√		EMG (26)	59.1† (15.2) *	7† (50%)	23.7 † (8.5) *	Condition	EMG†	CPTG†
										ARF	7 (50)	6 (43)
										Pneumonia	3 (21.4)	1 (7)
										Collagenosis	1 (7.1)	0 (0)
										Post-operation	1 (7.1)	2 (14.3)
										Acute MI	1 (7.1)	1 (7.1)

Study	Design [Clinical setting]	Population description [% on MV]	Intervention	Comparison		Group [Sample size (n)]	Age, Mean (SD)* or Median (IQR) **	Sex, n (%) females	Illness Severity (APACHE II) Mean (SD) * or Median (IQR) **	Primary ICU admission Diagnosis, n (%)		
				Usual care with EM	Usual care without EM					Leptospirosis	0 (0)	1 (7.1)
										Renal insuff.	0 (0)	1 (7.1)
										Pulmonary TB	1 (7.1)	1(7.1)
						CPTG (33)	50.4 (20.5) *	10† (71.4%)	21.1 (7.2) *	Neoplasia	0 (0)	1 (7.1)
Denehy 2013	Parallel RCT [20-bed tertiary ICU in Melbourne, Australia]	Medical & Surgical ICU patients [55.4% (Intervention) & 55.3% (Usual Care) on MV at day5]	PT interventions	√		Intervention (74)	61.4 (15.9) *	31 (42%)	19 (6) *	Condition	Intervention	Usual Care
										Pneumonia	17(23.0)	17(22.4)
										Cardiac cond	20(27.0)	14(18.4)
										Surgery	38(51.4)	38(50.0)
										Liver	7(9.5)	14(18.4)
										Sepsis	7(9.5)	10(13.2)
										Renal	4(5.4)	3(3.9)
						Usual care (76)	60.1 (15.8) *	24 (31.5%)	20.7 (7.7) *			
Kho 2015	Parallel RCT [3 Medical and surgical ICUs at John Hopkins Hospital]	Patients on MV [100%]	NMES	√		NMES (16)	54 (16) *	9 (56.3%)	25 (8) *	Condition	Intervention	Usual Care
										Sepsis	9 (56)	12 (67)
										Resp failure	3 (19)	2 (11)
										GIT	1 (6)	2 (11)
										Others	3 (19)	2 (11)
						Sham (18)	56 (18) *	8 (44.4%)	25 (6) *			
Kayambu 2015	Parallel RCT Double blinded [Single quaternary university-affiliated general ICU – Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia]	ICU patients on MV with Sepsis [100%]	NMES and PT interventions	√		Intervention (26)	62.5 (30-83) **	8 (30.1%)	28 (7.6) *	Condition	Intervention	Usual Care
										Sepsis	1(3.8)	1 (4.2)
										Severe sepsis	6(23.1)	6 (25)
										Septic shock	19 (73.1)	17 (70.8)
						Standard care (24)	65.5 (37-85) **	10 (41.7%)	27 (6.8) *			

Study	Design [Clinical setting]	Population description [% on MV]	Intervention	Comparison: Usual care with EM	Comparison: Usual care without EM	Group [Sample size (n)]	Age, Mean (SD)* or Median (IQR) **	Sex, n (%) females	Illness Severity (APACHE II) Mean (SD) * or Median (IQR) **	Primary ICU admission Diagnosis, n (%)
Fischer 2016	Parallel RCT Single-blinded [General Hospital affiliated to the Medical University Vienna]	Cardiac surgery patients [100%]	NMES		√	NMES (27)	63.3 (15.5) *	9 (33%)	SAP II 26 (7-46) ** SOFA score (POD 1) 9.0 (1-15) **	Surgery type: NMES / Sham Aortic valve replacement: 9(23) / 11(28) Coronary artery bypass grafting: 11(28) / 8(20) Heart transplantation: 6(15) / 5(13) Other cardiothoracic surgery: 4(10) / 4(10) Mitral valve replacement: 2(5) / 5(13) Mitral valve reconstruction: 4(10) / 3(8) Tricuspid valve reconstruction: 3(8) / 2(5) Bentall procedure: 1(2.5) / 2(5)
						Sham (27)	69.7 (13.1) *	7 (26%)	SAP II 24 (7-47) ** SOFA score (POD 1) 7.0 (1-11) **	
Schaller 2016	Parallel RCT [Surgical ICUs of five university hospitals: Austria (Landeskrankenhaus Salzburg), Germany (Klinikum Rechts der Isar der Technischen Universität München), and the USA (Beth Israel Deaconess Medical Center, Massachusetts General Hospital, and University of Massachusetts Medical Center)]	Surgical adult ICU patients [100%]	PT interventions	√		Intervention (104)	66 (48-73) **	39 (37.5%)	16 (12-22) **	Condition: Interv. / Control Visceral: 26 (25) / 28 (29) Vascular: 19 (18) / 14 (15) Eye, ear, nose, throat: 12 (12) / 8 (8) Transplant: 4 (4) / 3 (3) Neurosurgical: 4 (4) / 2 (2) Orthopaedic: 2 (2) / 3 (3) Thoracic: 4 (4) / 1 (1) Gynaecology: 3 (3) / 0 Urology: 1 (1) / 1 (1) Plastic surgery: 1 (1) / 0 Medical or neurological: 7 (7) / 5 (5) Trauma: 21 (20) / 31 (32)
						Control (96)	64 (45-76) **	35 (36.5%)	17 (11-22) **	

† Refers to values in the screened population only. The authors did not report data for the total randomized population. *EMG: early mobilization group. CPTG: conventional physical therapy group*.

Table 2. Characteristics of Physical Therapy Interventions

Study	Group	Time to 1st intervention mean (SD)*/ median (IQR)** or range***	Type of intervention	Intervention period	Frequency	Duration mins/day	Intensity	Integrity of intervention delivery	Co-interventions [α]
Schweickert 2009	Intervention	1.5 (1.0-2.1) ** days after intubation	Progressively: prom ex, aarom/arom, supine ex, bed mobility, sitting balance, transfers, ADLs, pre-gait activities, walking	ICU & hospital stay Or till previous functional level	Daily	During MV: 0.32 (0.17-0.48) ** Post weaning: 0.21 (0.08-0.33)	To patients' tolerance	94% of patients received the intervention Delivered 87% of days	Daily interruption of sedation
	Control	7.4 (6.0-10.9) ** days after intubation	Not reported	After weaning from mechanical ventilation	Not reported	During MV: 0.00 (0.00-0.00) ** Post weaning: 0.19 (0.00-0.38)	Not reported	Not reported	Daily interruption of sedation
Routsi 2010	EMS	1.0-2.0*** days	Biphasic symmetric ES (45hz, 400μsec, 12sec on, 6 secs off) to Quads (medialis & lateralis) and peroneus muscles	Till ICU discharge	Daily	55 mins (including 5min warm-up & 5mins recovery)	Till visible or palpable contractions	Not reported	Not reported
	Control	None	None	N/A	N/A	N/A	N/A	N/A	N/A

Study	Group	Time to 1st intervention mean (SD)*/ median (IQR)** or range***	Type of intervention	Intervention period	Frequency	Duration mins/day	Intensity	Integrity of intervention delivery	Co-interventions [α]
Dantas 2012	EMG	2.6 days (mean)	Progressive exercises via protocol Passive stretching Passive mobilizations AA exercises Resisted ex Transfers Balance ex Leg ergometry Ambulation	ICU admission to ICU discharge	2x/day for 7 days each week	Average duration of 40 mins daily	Not reported	Not reported	None reported
	CPTG	Not reported	Passive mobilizations AA exercises	Same	5 days/week				
Denehy 2013	Intervention	≥ 5 days	Cardiovascular (marching in place) Functional (moving from sitting to standing) Resistance (AAE, AE, and resisted ex)	Admission to 8 weeks post-hospital discharge	During Admission: 6 days per week Outpatient: 2x per week	ICU: Mech vent: 15min/day Weaned: 2 X 15min/day Ward: 60 mins per day Outpatient: 60 minutes per session	Cardiovascular: RPE 3-5 (modified Borg) 3 Reps of 70% of PFIT marching time (including rests) Resistance: 5Reps X 3sets (all as tolerated)	Not all patients in the intervention arm received at least one treatment at the point of primary outcome assessment	Nil

Study	Group	Time to 1st intervention mean (SD)*/ median (IQR)** or range***	Type of intervention	Intervention period	Frequency	Duration mins/day	Intensity	Integrity of intervention delivery	Co-interventions α
	Usual care	N/A	Not reported. Unit protocols include bed ex, sitting out of bed, marching, walking	During ICU and ward	Not reported. Usually 12 hours 7days/week	Not reported	Not reported	Not reported	Not reported
Kho 2015	NMES	4.6 (1.8) * days	Biphasic asymmetric ES @ 50hz, to Quads (medialis & lateralis) - 400µsec, 5sec on, 10 secs off), Tibialis ant. & gastroc. (alternatively); 250 µs, on-time 5s/off-time 5s	During ICU stay to max of 45 days	Daily	60 minutes	Till visible contraction or max intensity	100%	EM which is part of usual care
	Sham	4.4 (1.6) * days	As above with amplitude set to zero	As above	As above	As above	Sham – no contractions	As above	EM
Kayambu 2015	Intervention	About 2 days from diagnosis of sepsis	EMS, PROM, AROM, AAE, SOEB/SOB, Sit-Stand, marching on the spot, balance ex, arm/leg	Within 48 hours of diagnosis to ICU discharge	1-2 sessions daily	30 minutes per session	Higher duration and frequency reported compared to standard care	No withdrawals All participants remained around for an average of 11.4 days	

Study	Group	Time to 1st intervention mean (SD)*/ median (IQR)** or range***	Type of intervention	Intervention period	Frequency	Duration mins/day	Intensity	Integrity of intervention delivery	Co-interventions [α]
			ergometry, tilt table therapy, ambulation						
	Standard care	Not reported	PROM, AROM, AAE, SOEB/SOB, Sit-Stand, marching on the spot, balance ex, ambulation	Not reported	Not reported	Not reported	Lower duration and frequency reported compared to the intervention group	As above	
Fischer 2016	NMES	Post op. day 1	Pulsed, biphasic, rectangular ES at 66hz to quadriceps (all 4 muscle groups) - 400µsec, 3.5sec on, 4.5 secs off (ramp up/down 5sec each)	Post op. day 1 to 14days post op (14 days at the max)	Daily	60 mins (30mins X 2 – separated with 30 mins rest period)	Median intensities: 40.5 mA (range, 2–100 mA) for the right thigh & 40 mA (range, 5–120 mA) for the left thigh	Only 9 out of 145 NMES sessions could not be administered	None
	Sham	Post op. day 1	Electrodes with no electrical current	As above	As above	As above	None	Only 6 out of 154 NMES sessions could not be administered	None
Schaller 2016	Intervention	1.8 (1.6) * days	PROM ex Sitting Standing	Enrolment to ICU discharge	Daily	Not reported	Not reported	817 (89%) of 918 study days	None reported

Study	Group	Time to 1st intervention mean (SD)*/ median (IQR)** or range***	Type of intervention	Intervention period	Frequency	Duration mins/day	Intensity	Integrity of intervention delivery	Co-interventions α
			Ambulation						
	Control	1.7 (1.5) * days	Individual centres' usual practice	Enrolment to ICU discharge	Individual centres' usual practice	Not reported	Not reported	Not reported	None reported

α Any other treatment that may potentially reduce the rate of muscle deconditioning and affect the incidence of ICUAW. *N/A= not applicable*
**median (IQR)

Table 3. Summary of Results for Primary Outcome: ICUAW

		Proportion of events reported			Proportion of events in screened population		Proportion of events in total population randomized (reanalysis*)	
Study	**Time Point**	**Intervention**	**Control**	**p-value**	**Intervention**	**Control**	**Intervention**	**Control**
Schweickert 2009	Hospital Discharge	15/49	27/55	0.09	6/40	13/41	Same as reported	Same as reported
Routsi 2010	ICU awakening	3/24	11/28	0.04	3/24	11/28	47/68	55/72
Dantas 2012	Sedation cessation	Not reported	Not reported	Not reported	7/14	8/14	19/26	27/33
	ICU discharge	Not reported	Not reported	Not reported	4/14	7/14	16/26	26/33
Denehy 2013	7^{th}-day post-awakening	16/74	13/76	Not reported	16/57	13/49	33/74	40/76
Kho 2015	ICU awakening	8/12	5/15	0.128	8/12	5/15	12/16	8/18
	ICU discharge	3/12	4/16	1	3/12	4/16	7/16	6/18
	Hospital discharge	1/12	5/17	0.354	1/12	5/17	5/16	6/18
Kayambu 2015	ICU discharge	Not reported	Not reported	Not reported	9/19	14/23	16/26	15/24
Fischer 2016	ICU awakening	Not reported	Not reported	Not reported				
	ICU discharge	Not reported	Not reported	Not reported	6/21	4/20	12/27	11/27
	Hospital discharge	Not reported	Not reported	Not reported	1/14	1/10	14/27	18/27
Schaller 2016	ICU Discharge	50/104	51/96	0.95	50/76	51/77	78/104	70/96

Reanalysis was performed with imputation of worst values for patients who were not evaluable*

Table 4. Summary of Results for Secondary Outcomes: Mortality

		Proportion of events reported		
Study	**Time Point**	**Intervention**	**Control**	**p-value**
Schweickert 2009	Hospital mortality	9/49	14/55	0.53
Routsi 2010	ICU mortality	28/68	22/72	Not reported
Dantas 2012	ICU mortality	12/26	19/33	Not reported
Denehy 2013	28-day mortality	6/74	6/76	Not reported
	12-months mortality	13/74	19/76	Not reported
Kho 2015	ICU mortality	3/16	1/18	0.32
	Hospital mortality	3/16	3/18	1.00
Kayambu 2015	ICU mortality	3/26	1/24	0.34
	90-day mortality	8/26	2/24	0.08
Fischer 2016	ICU mortality	1/27	3/27	Not reported
	Hospital mortality*	1/27	3/27	Not reported
Schaller 2016	In hospital mortality	17/104	8/96	0.09
	3-months mortality	21/104	15/96	0.35

** The hospital mortality consists only of the people who died during ICU stay*

Table 5. Summary of Results for Secondary Outcomes: Length of stay

	Length of stay ICU, days			Length of stay hospital, days		
Study	**Intervention**	**Control**	**p-value**	**Intervention**	**Control**	**p-value**
Schweickert 2009	5.9 (4.5-13.2) †	7.9 (6.1-12.9) †	0.08	13.5 (8.0-23.1) †	12.9 (8.9-19.8) †	0.93
Routsi 2010	14 (4-62) ‡	22 (2-92) ‡	0.11	Not reported	Not reported	Not reported
Dantas 2012	19.41 (10.76) *	21.43 (17.14) *	0.77	25.12 (23.54) *	21.59 (25.25) *	0.25
Denehy 2013	8 (6-12) †	7 (6-11) †	Not reported	23.54 (16.0-41.5) †	20.0 (13.0-30.8) †	Not reported
Kho 2015	22 (17) *	20 (17) *	0.72	36 (22) *	35 (20) *	0.85
Kayambu 2015	12 (4.0-45.0) †	8.5 (3.0-36.0) †	0.43	41 (9-158) †	45 (14-308) †	0.80
Fischer 2016	6 (3-23) ∫	7 (3-213) ∫	0.46	22 (4-84) ∫	19 (9-213) ∫	d = 0.60
Schaller 2016 ICU LOS:	7 (5-12) ∫	10 (6-15) ∫	0.0054	15 (11-27) ∫	21.5 (15.0-30.0) ∫	0.01
Schaller 2016 ICU LOS until discharge readiness:	5 (3-8) ∫	7 (5-13) ∫	0.0006			

*Mean (SD); ‡Mean (range); †Median (IQR); ∫Median (range)

Table 6. Summary of Results for Secondary Outcomes: Ventilator duration

	Duration of Mechanical Ventilation			Ventilator Free Days		
Study	**Intervention**	**Control**	**p-value**	**Intervention**	**Control**	**p-value**
Schweickert 2009	3.4 days (2.3-7.3) †	6.1 days (4.0-9.6) †	0.002	23.5¶ (7.4-25.6) †	21.1¶ (0.0-23.8) †	0.05
Routsi 2010	7 days (2-41) ∫	10 days (1-62) ∫	0.07	4.0 (0.0-16.0) ∫	6.0 (0.0-0.41) ∫	0.003
Dantas 2012	10.24 (8.89) *	11.36 (13.32) *	0.60	Not reported	Not reported	Not reported
Denehy 2013	105.0 hrs (52.0-216.5) †	98.0 hrs (47.5-160.5) †	Not reported	Not reported	Not reported	Not reported
Kho 2015	20 days (18) *	16 days (15) *	0.492	Not reported	Not reported	Not reported
Kayambu 2015	8 (4-64) †	7 (2-30) †	0.22	20 (0-24) †	21 (0-26) †	0.71
Fischer 2016	2 (1-7) ∫	2 (1-15) ∫	Not reported	Not reported	Not reported	Not reported
Schaller 2016	Not reported	Not reported	Not reported	23.0 (18.0-25.0) ∫	22.5 (16.0-25.0) ∫	0.31

*Mean (SD); ‡Mean (range); †Median (IQR); ∫Median (range); ¶ Day 1-28

Table 7. Methodological Quality of Included Studies

Study	Random sequence generation *(selection bias)*	Allocation concealment *(selection bias)*	Blinding of participants§ *(performance bias)*	Blinding of personnel§ *(performance bias)*	Blinding of outcome assessment *(detection bias)*: **ICUAW**	Blinding of outcome assessment *(detection bias)*: **Mortality**	Blinding of outcome assessment *(detection bias)*: **ICU & Hospital LOS‡**	Incomplete outcome data† *(attrition bias)*: **ICUAW**	Incomplete outcome data† *(attrition bias)*: **Other Outcomes**	Selective outcome reporting? *(reporting bias)*	Other bias
Schweickert 2009	Low	Low	Low *	Low *	Low	Low	High	Low	Low	Low	Low
Routsi 2010	High	High	Low *	High	High	Low	High	High	Low	Unclear [a]	Low
Dantas 2012	Low	Low	Low	High	High	Low	High	High	High	Low [b]	Unclear [f]
Denehy 2013	Low	Low	Low *	Low *	Low	Low	High	High	Low	Low [c]	Low
Kho 2015	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Kayambu 2015	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low [d]	Low
Fischer 2016	Low	Low	Low	Low *	High	Low	High	High	Low	Unclear [e]	Low
Schaller 2016	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Low

*: We judged that though the personnel were not blinded, this was unlikely to have affected the primary outcome since the assessor was blinded.

§ These items (blinding of participants and personnel) were judged based on their impact on the primary outcome only.

‡ = We judged this as high if personnel were not blinded to allocation assignment as this may have affected the patient's discharge readiness versus the actual discharge; hence introducing bias. We judged it as low if both outcome assessor and personnel were blinded or if both discharge readiness and actual LOS were reported.

†=This item was judged based on the primary outcome only. It was judged 'Low' when 80% of participants were followed up or authors statistically adjusted for missing data with patients who were not evaluable treated as '+' for ICUAW.

[a] Registered protocol shows 'muscle biopsy and electromyography' among other outcomes, which were not reported in the final paper. It is unclear if these measures were also used to assess ICUAW.

[b] Trial registration was not reported in the publication and no published protocol was found. It is therefore unclear if selective outcome reporting exists.

[c] The registered and published protocols indicated that cost-effectiveness and cost-utility analysis would be done, but these were not reported. Nonetheless, this does not imply a bias for our review.

[d] Some outcomes (mitochondrial DNA, muscle oxygenation, and microcirculation) shown in the trial registration were not reported in the publication. The authors stated that these outcomes would be reported in future manuscripts. The outcomes do not imply a bias for our review.

[e] In the registered protocol, the authors reported that they would include JAGS score as an outcome. What this refers to is unclear and there is no mention of this outcome in the final publication. It is, therefore, unclear to us if reporting bias exists.

[f] Trial registration and details of the 'randomization sequence generation, allocation concealment, and blinding' were not reported in the original publication.

FIGURES

List of Figures

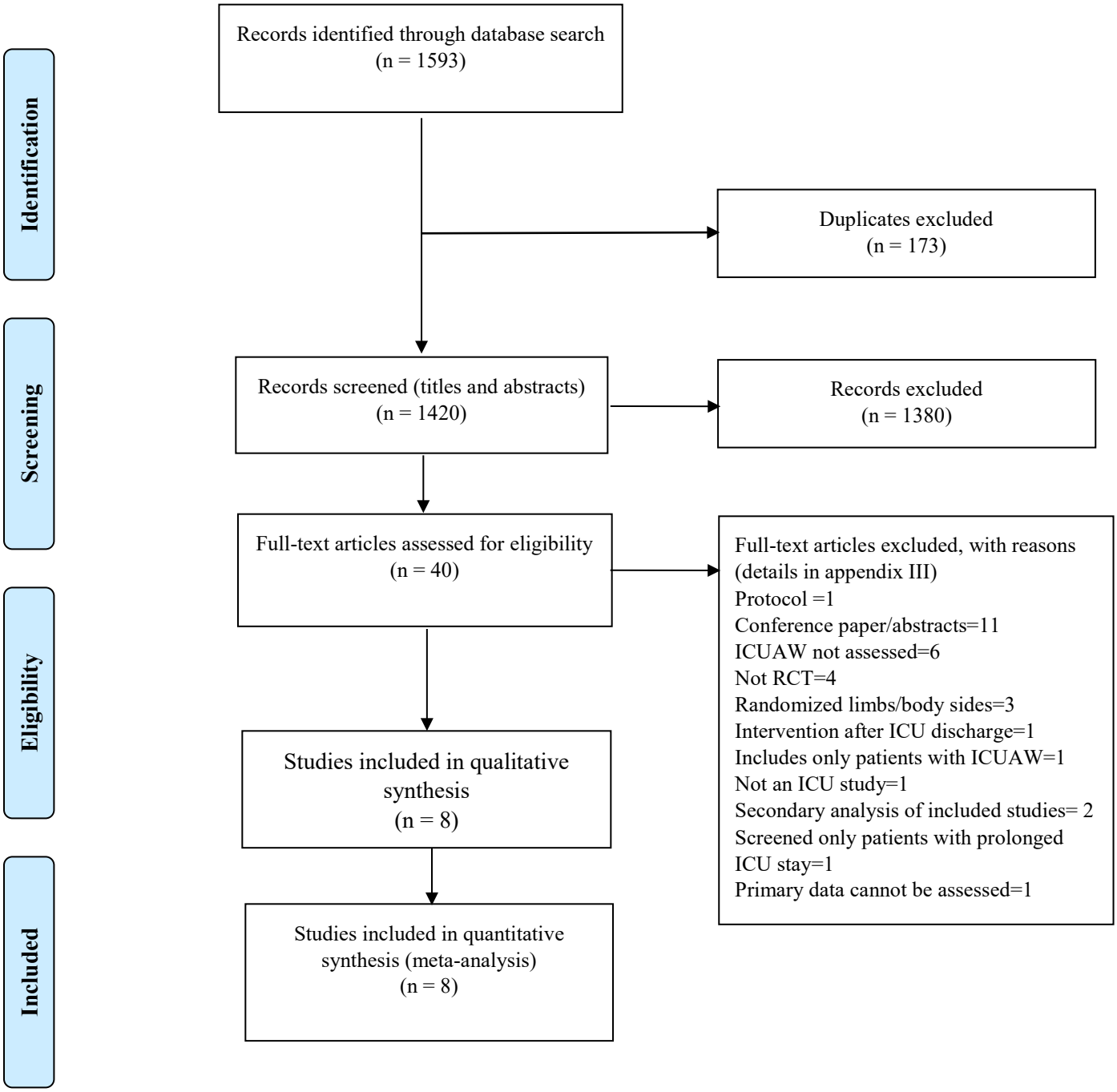
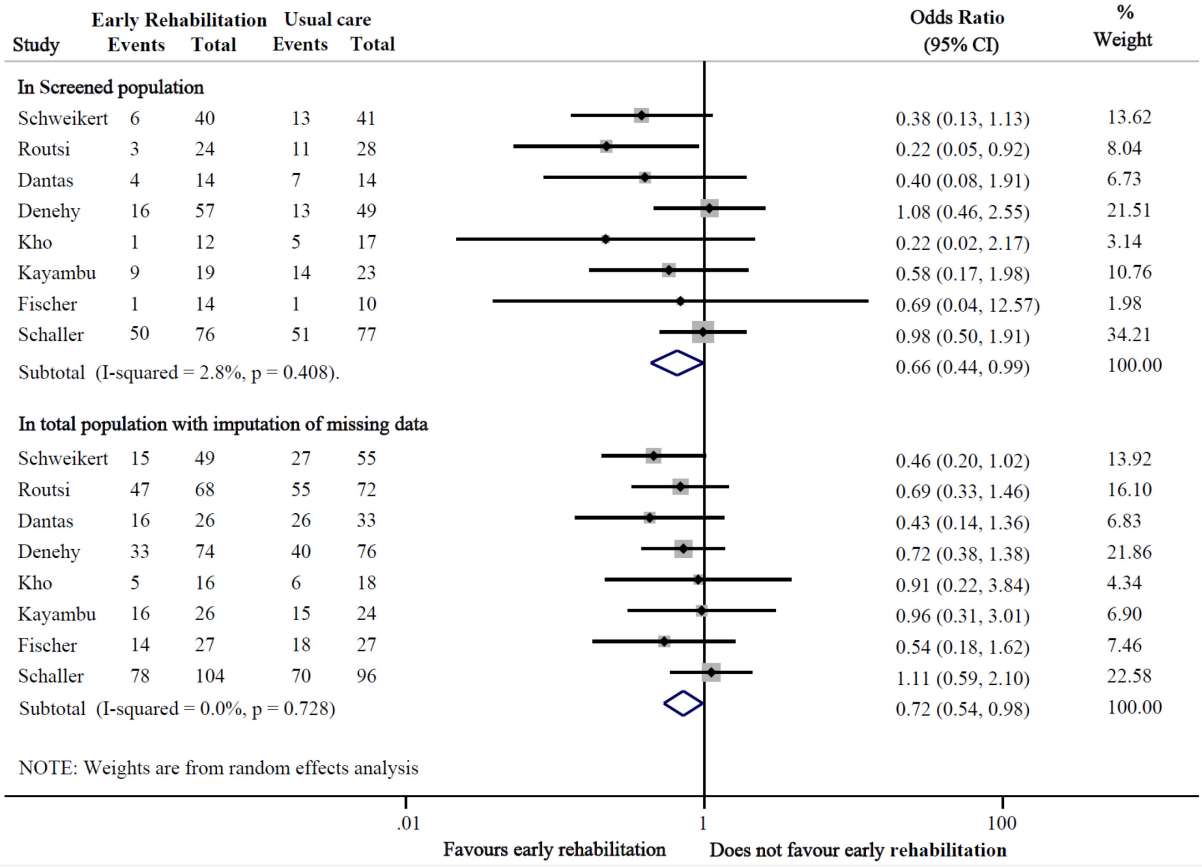


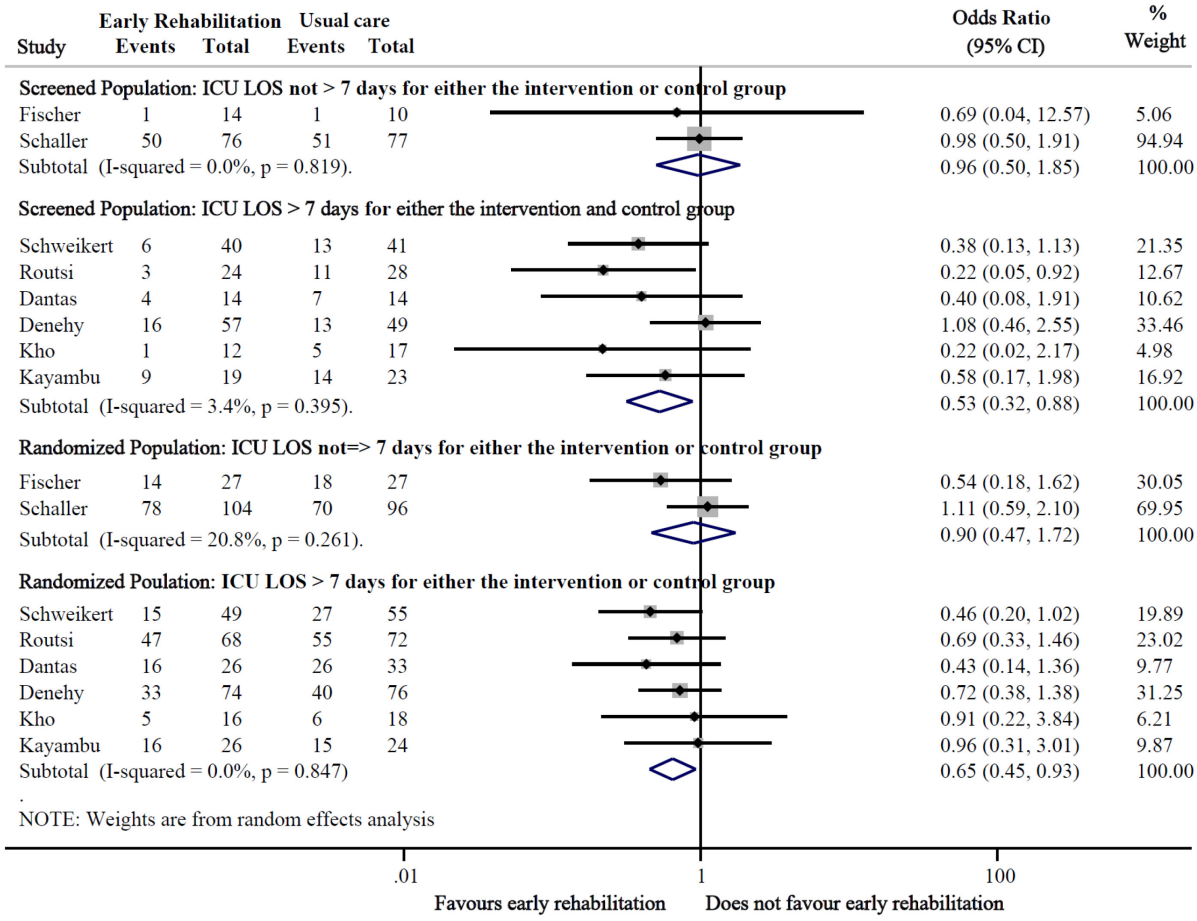
Figure 1. PRISMA Flow Diagram

Figure 2: Forest Plot of Comparison: Incidence of ICUAW between Early Rehabilitation versus Usual Care in both the Screened Population and the Randomized Population *(timepoint: last ICUAW assessment)*



```
           Study     |     OR    [95% Conf. Interval]
---------------------+-------------------------------------------------
     In screened populati
Schweikert           |    0.380     0.128     1.129
Routsi               |    0.221     0.053     0.921
Dantas               |    0.400     0.084     1.909
Denehy               |    1.081     0.458     2.548
Kho                  |    0.218     0.022     2.171
Kayambu              |    0.579     0.169     1.979
Fischer              |    0.692     0.038    12.572
Schaller             |    0.980     0.502     1.914
 Sub-total           |
  D+L pooled OR      |    0.658     0.437     0.990
---------------------+-------------------------------------------------
     In total population
Schweikert           |    0.458     0.204     1.024
Routsi               |    0.692     0.327     1.463
Dantas               |    0.431     0.137     1.359
Denehy               |    0.724     0.381     1.377
Kho                  |    0.909     0.215     3.843
Kayambu              |    0.960     0.306     3.012
Fischer              |    0.538     0.179     1.618
Schaller             |    1.114     0.592     2.097
 Sub-total           |
  D+L pooled OR      |    0.723     0.535     0.976
---------------------+-------------------------------------------------

Test(s) of heterogeneity:
               Heterogeneity  degrees of
                 statistic     freedom      P    I-squared**   Tau-squared

In screened populati  7.20         7      0.408      2.8%       0.0106
In total population   4.44         7      0.728      0.0%       0.0000
** I-squared: the variation in OR attributable to heterogeneity)


Significance test(s) of OR=1

In screened populati  z=  2.01     p = 0.045
In total population   z=  2.12     p = 0.034
-------------------------------------------------------------------------
```

Figure 3: Forest Plot of Comparison: Incidence of ICUAW between Early Rehabilitation versus Usual Care in both the Screened Population and the Randomized Population (*subanalysis by ICU LOS)*



Study	OR	[95% Conf.	Interval]
Screened Population:			
Fischer	0.692	0.038	12.572
Schaller	0.980	0.502	1.914
Sub-total			
D+L pooled OR	0.963	0.502	1.849
Screened Population:			
Schweikert	0.380	0.128	1.129
Routsi	0.221	0.053	0.921
Dantas	0.400	0.084	1.909
Denehy	1.081	0.458	2.548
Kho	0.218	0.022	2.171
Kayambu	0.579	0.169	1.979
Sub-total			
D+L pooled OR	0.529	0.316	0.885
Randomized Poulation			
Fischer	0.538	0.179	1.618
Schaller	1.114	0.592	2.097
Sub-total			
D+L pooled OR	0.896	0.466	1.721
Randomized Poulation			
Schweikert	0.458	0.204	1.024
Routsi	0.692	0.327	1.463
Dantas	0.431	0.137	1.359
Denehy	0.724	0.381	1.377
Kho	0.909	0.215	3.843
Kayambu	0.960	0.306	3.012
Sub-total			
D+L pooled OR	0.648	0.453	0.929

Test(s) of heterogeneity:

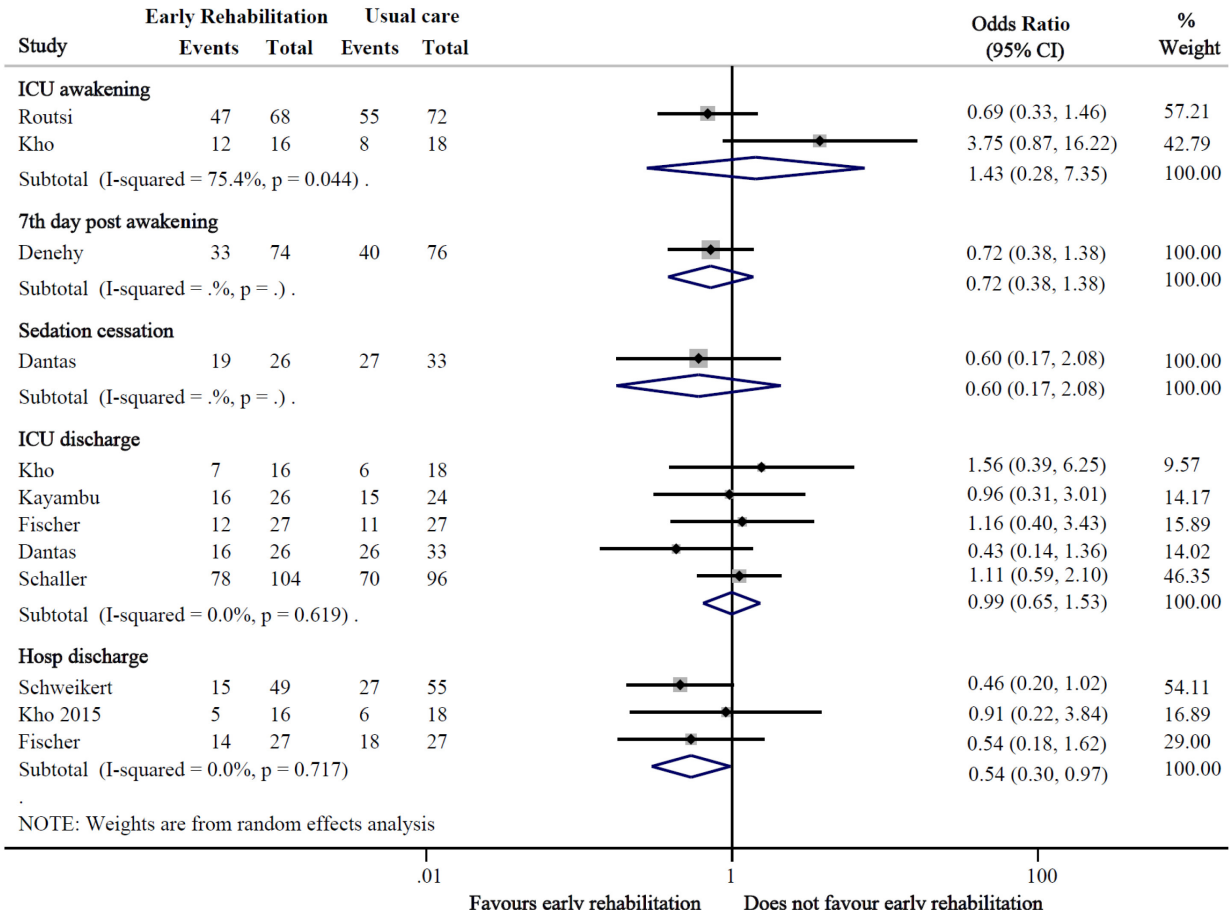
	Heterogeneity statistic	degrees of freedom	P	I-squared**	Tau-squared
Screened Population:	0.05	1	0.819	0.0%	0.0000
Screened Population:	5.18	5	0.395	3.4%	0.0149
Randomized Poulation	1.26	1	0.261	20.8%	0.0549
Randomized Poulation	2.01	5	0.847	0.0%	0.0000

** I-squared: the variation in OR attributable to heterogeneity)

Significance test(s) of OR=1

Screened Population:	z= 0.11	p = 0.910
Screened Population:	z= 2.43	p = 0.015
Randomized Poulation	z= 0.33	p = 0.741
Randomized Poulation	z= 2.36	p = 0.018

Figure 4: Forest Plot of Comparison: Incidence of ICUAW between Early Rehabilitation versus Usual Care in Total Randomized Population (*subgroup analysis at different assessment timepoints)*



Study	OR	[95% Conf.	Interval]
ICU awakening			
Routsi	0.692	0.327	1.463
Kho	3.750	0.867	16.220
Sub-total			
D+L pooled OR	1.426	0.277	7.351
7th day post awakein			
Denehy	0.724	0.381	1.377
Sub-total			
D+L pooled OR	0.724	0.381	1.377
Sedation cessation			
Dantas	0.603	0.175	2.081
Sub-total			
D+L pooled OR	0.603	0.175	2.081
ICU discharge			
Kho	1.556	0.387	6.254
Kayambu	0.960	0.306	3.012
Fischer	1.164	0.395	3.425
Dantas	0.431	0.137	1.359
Schaller	1.114	0.592	2.097
Sub-total			
D+L pooled OR	0.993	0.645	1.527
Hosp discharge			
Schweikert 2009	0.458	0.204	1.024
Kho 2015	0.909	0.215	3.843
Fischer	0.538	0.179	1.618
Sub-total			
D+L pooled OR	0.539	0.298	0.974

Test(s) of heterogeneity:

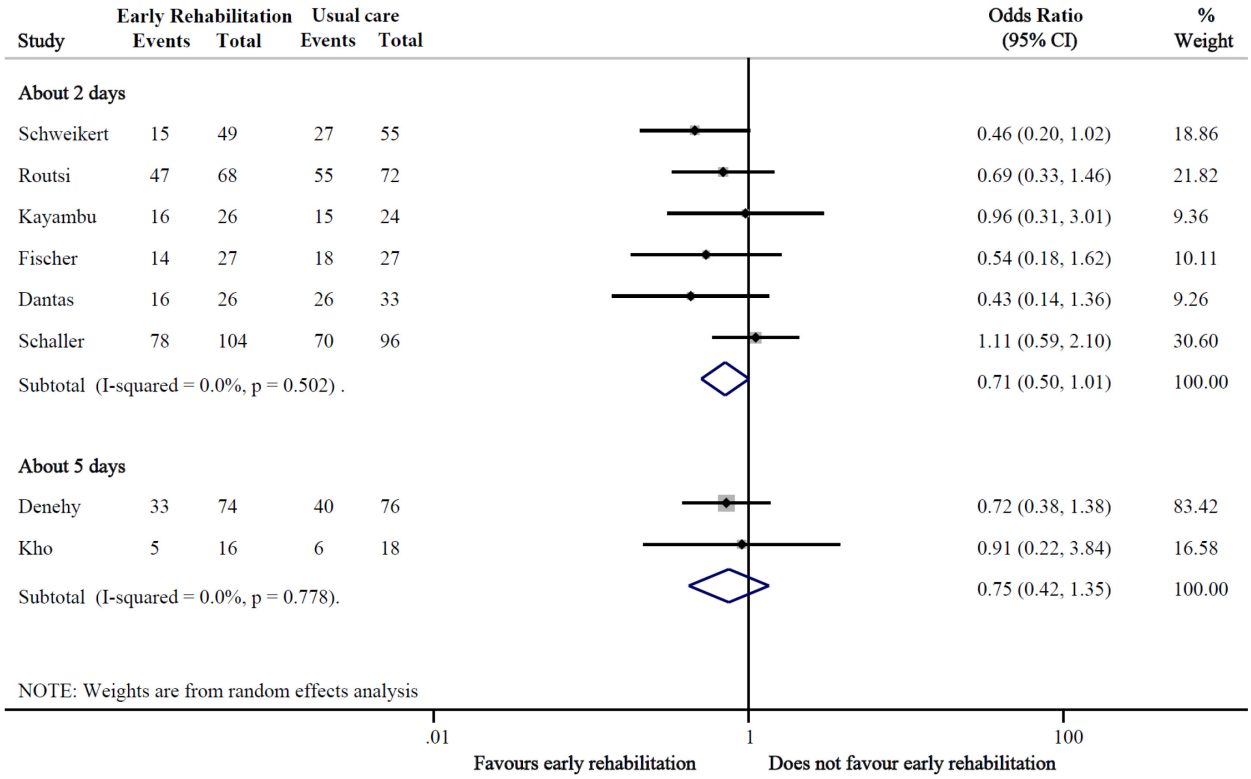
	Heterogeneity statistic	degrees of freedom	P	I-squared**	Tau-squared
ICU awakening	4.06	1	0.044	75.4%	1.0780
7th day post awakein	0.00	0	.	.%	1.0780
Sedation cessation	0.00	0	.	.%	1.0780
ICU discharge	2.64	4	0.619	0.0%	0.0000
Hosp discharge	0.66	2	0.717	0.0%	0.0000

** I-squared: the variation in OR attributable to heterogeneity)

Significance test(s) of OR=1

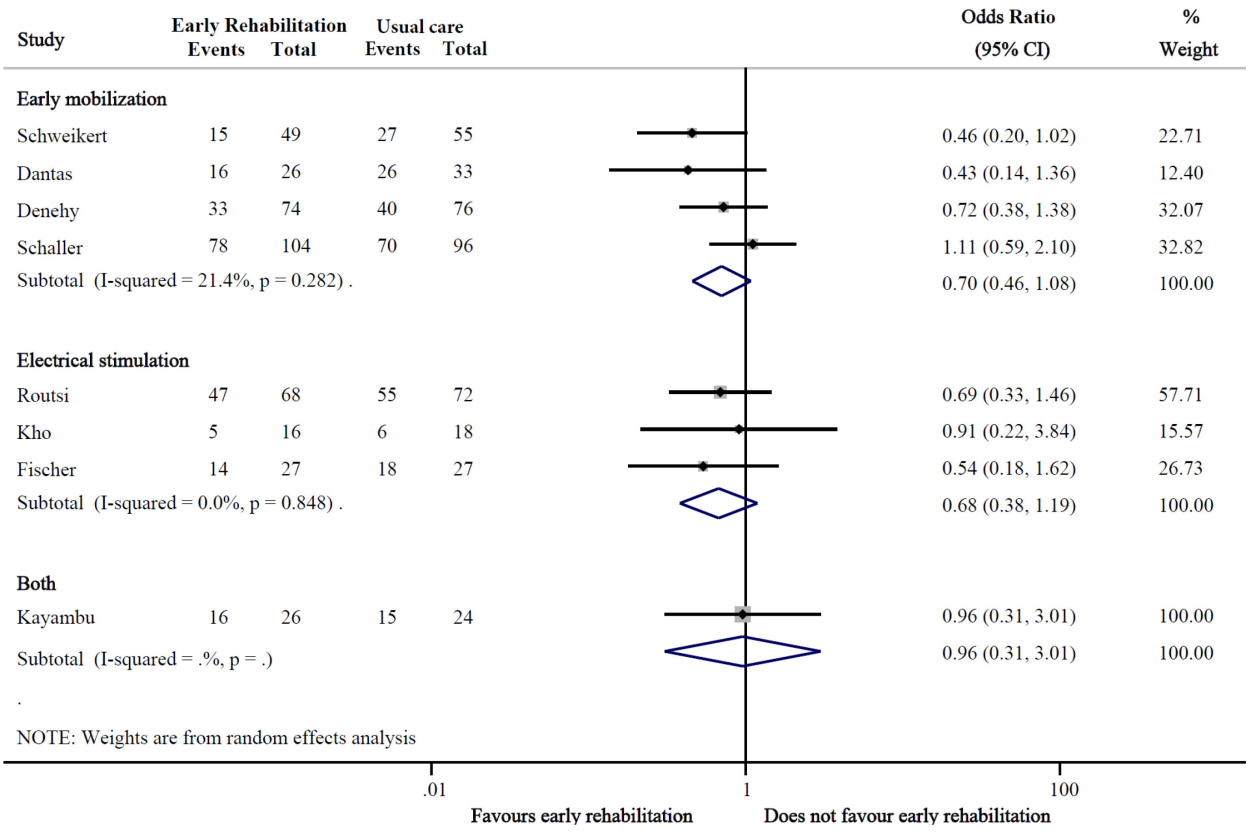
ICU awakening	z= 0.42	p = 0.672
7th day post awakein	z= 0.98	p = 0.325
Sedation cessation	z= 0.80	p = 0.424
ICU discharge	z= 0.03	p = 0.973
Hosp discharge	z= 2.05	p = 0.041

Figure 5: Forest Plot of Comparison: Incidence of ICUAW between Early Rehabilitation versus Usual Care in Total Randomized Population (*subgroup analysis by the timing of rehabilitation intervention)*



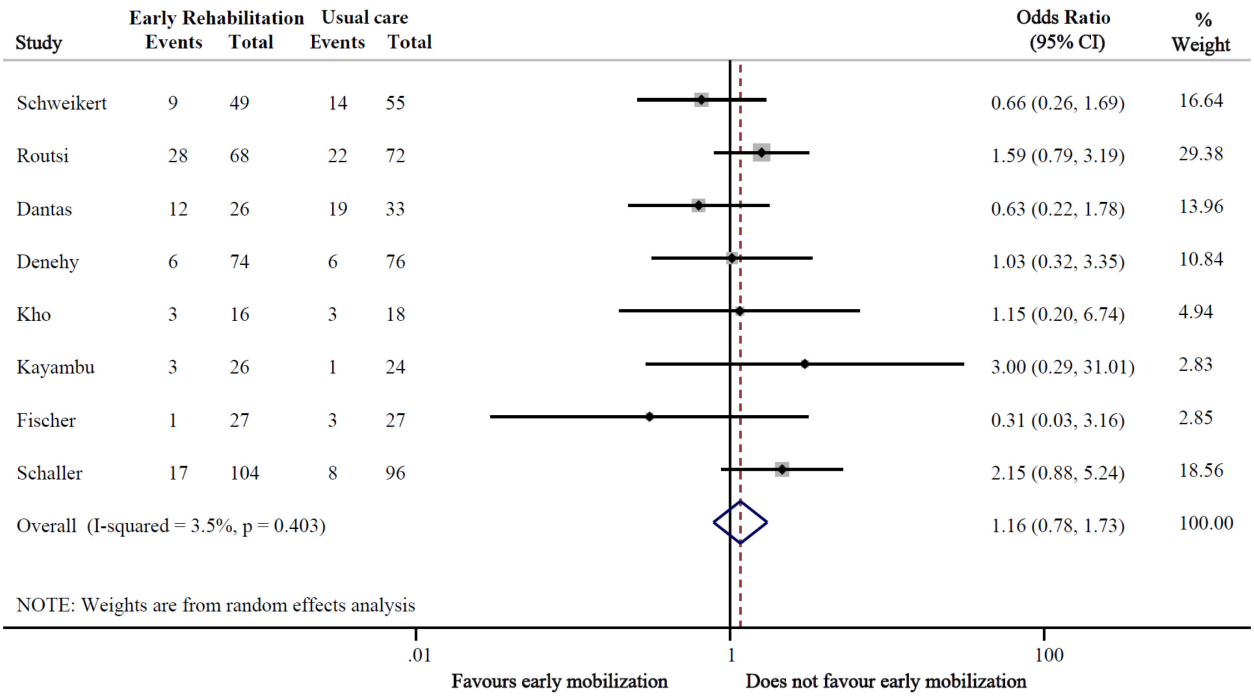

```
          Study      |      OR    [95% Conf. Interval]
---------------------+---------------------------------------------------
     About 2 days
Schweikert            |    0.458     0.204     1.024
Routsi                |    0.692     0.327     1.463
Kayambu               |    0.960     0.306     3.012
Fischer               |    0.538     0.179     1.618
Dantas                |    0.431     0.137     1.359
Schaller              |    1.114     0.592     2.097
 Sub-total            |
  D+L pooled OR       |    0.712     0.502     1.011
---------------------+---------------------------------------------------
     About 5 days
Denehy                |    0.724     0.381     1.377
Kho                   |    0.909     0.215     3.843
 Sub-total            |
  D+L pooled OR       |    0.752     0.418     1.353
---------------------+---------------------------------------------------

Test(s) of heterogeneity:
               Heterogeneity  degrees of
                 statistic     freedom      P    I-squared**   Tau-squared

About 2 days         4.34          5      0.502      0.0%       0.0000
About 5 days         0.08          1      0.778      0.0%       0.0000
** I-squared: the variation in OR attributable to heterogeneity)


Significance test(s) of OR=1

About 2 days          z=  1.90     p = 0.057
About 5 days          z=  0.95     p = 0.342
---------------------------------------------------------------------------
```

Figure 6: Forest Plot of Comparison: Incidence of ICUAW between Early Rehabilitation versus Usual Care in Total Randomized Population (*subgroup analysis by type of rehabilitation intervention— Early Mobilization vs Neuromuscular electrical stimulation)*



```
           Study     |     OR    [95% Conf. Interval]
---------------------+-------------------------------------------------
     Early mobilization
Schweikert           |    0.458     0.204     1.024
Dantas               |    0.431     0.137     1.359
Denehy               |    0.724     0.381     1.377
Schaller             |    1.114     0.592     2.097
 Sub-total           |
  D+L pooled OR      |    0.705     0.459     1.082
---------------------+-------------------------------------------------
     Electrical stimulati
Routsi               |    0.692     0.327     1.463
Kho                  |    0.909     0.215     3.843
Fischer              |    0.538     0.179     1.618
 Sub-total           |
  D+L pooled OR      |    0.675     0.382     1.192
---------------------+-------------------------------------------------
     Both
Kayambu              |    0.960     0.306     3.012
 Sub-total           |
  D+L pooled OR      |    0.960     0.306     3.012
---------------------+-------------------------------------------------

Test(s) of heterogeneity:
               Heterogeneity  degrees of
                 statistic     freedom      P    I-squared**   Tau-squared

Early mobilization   3.82          3      0.282     21.4%       0.0415
Electrical stimulati  0.33         2      0.848      0.0%       0.0000
Both                 0.00          0         .         .%       0.0000
** I-squared: the variation in OR attributable to heterogeneity)


Significance test(s) of OR=1

Early mobilization    z=  1.60     p = 0.109
Electrical stimulati  z=  1.35     p = 0.176
Both                  z=  0.07     p = 0.944
------------------------------------------------------------------------------
```

Figure 7: Forest Plot of Comparison of Mortality between Early Rehabilitation and Usual Care

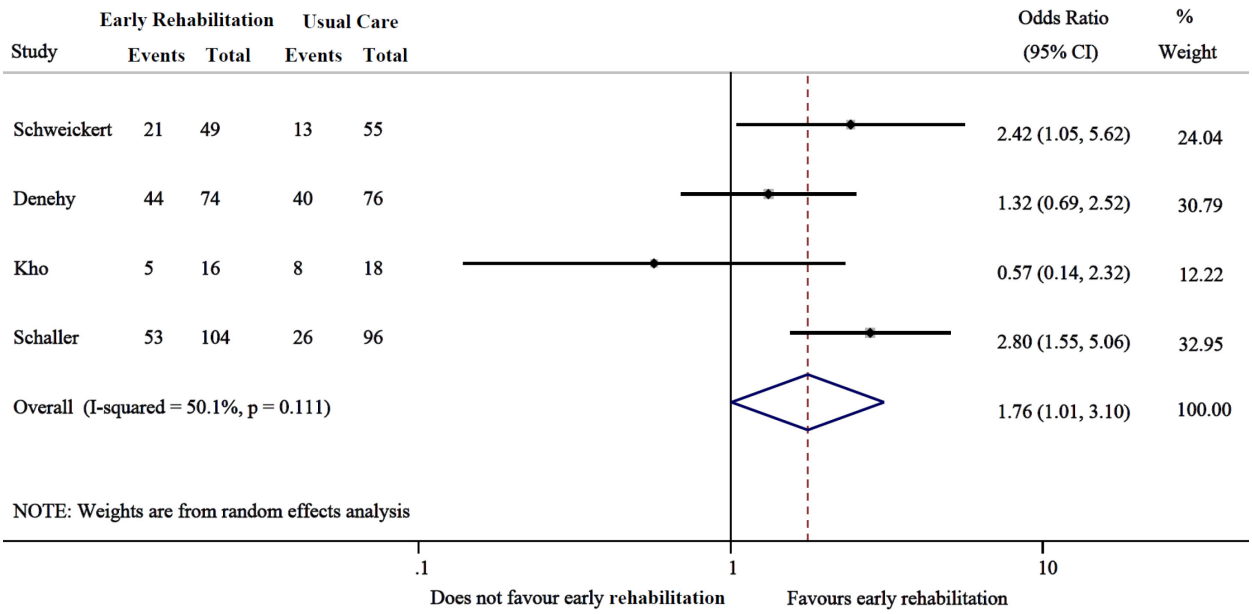


Study	OR	[95% Conf.	Interval]	% Weight
Schweikert	0.659	0.256	1.693	16.64
Routsi	1.591	0.793	3.191	29.38
Dantas	0.632	0.224	1.778	13.96
Denehy	1.029	0.316	3.349	10.84
Kho	1.154	0.198	6.735	4.94
Kayambu	3.000	0.290	31.013	2.83
Fischer	0.308	0.030	3.163	2.85
Schaller	2.149	0.882	5.240	18.56
D+L pooled OR	1.165	0.785	1.729	100.00

Heterogeneity chi-squared = 7.25 (d.f. = 7) p = 0.403
I-squared (variation in OR attributable to heterogeneity) = 3.5%
Estimate of between-study variance Tau-squared = 0.0120

Test of OR=1 : z= 0.76 p = 0.449

Figure 8: Forest Plot of Discharge Location



Study	OR	[95% Conf.	Interval]	% Weight
Schweickert	2.423	1.045	5.618	24.04
Denehy	1.320	0.691	2.520	30.79
Kho	0.568	0.139	2.322	12.22
Schaller	2.798	1.548	5.057	32.95
D+L pooled OR	1.765	1.005	3.099	100.00

Heterogeneity chi-squared = 6.01 (d.f. = 3) p = 0.111
I-squared (variation in OR attributable to heterogeneity) = 50.1%
Estimate of between-study variance Tau-squared = 0.1593

Test of OR=1 : z= 1.98 p = 0.048

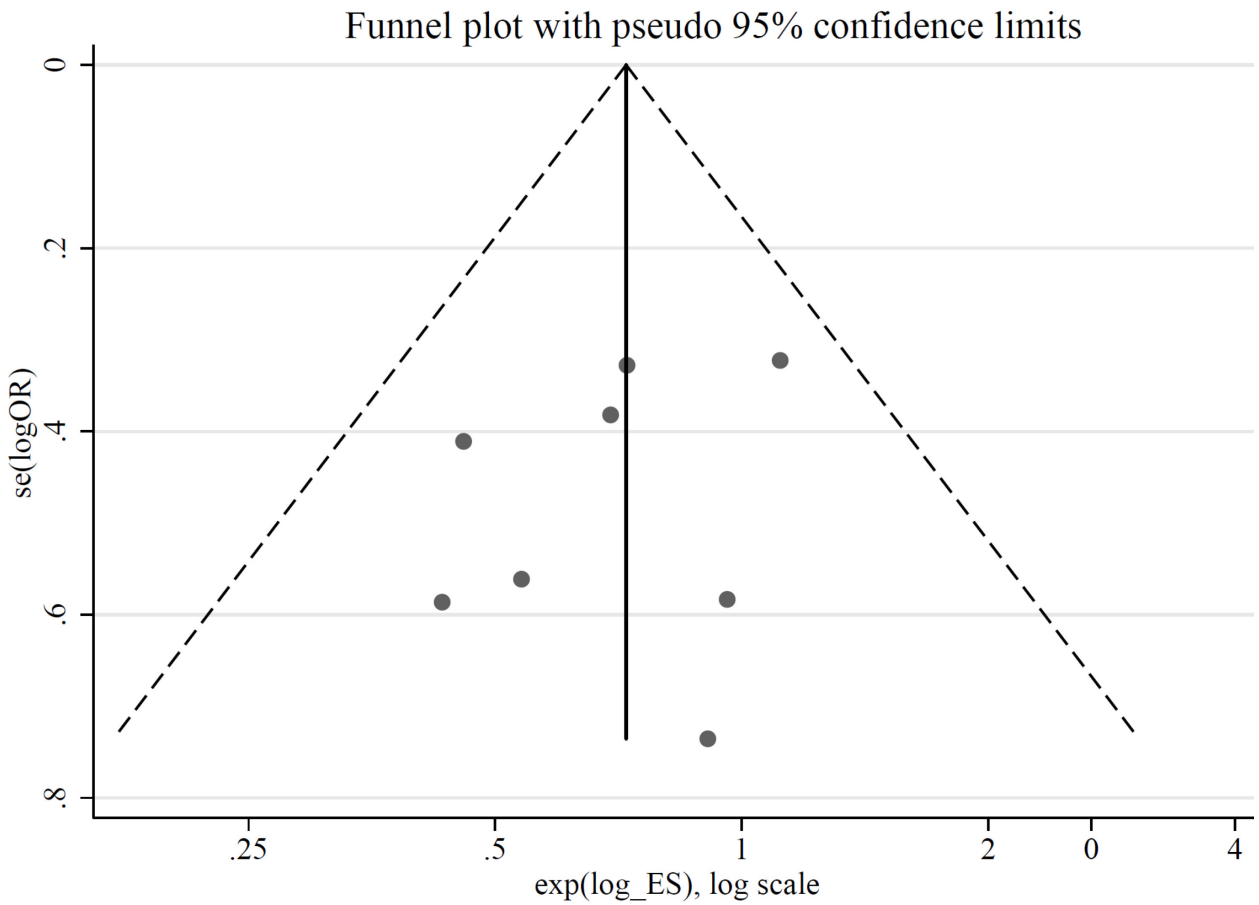


Figure 9: Funnel Plot Analysis of Included Studies

APPENDICES

APPENDIX I

Details of Search Strategy

MEDLINE SEARCH STRATEGY

1. critical illness/
2. critically ill.tw.
3. critical illness*.tw.
4. intensive care/
5. intensive care units/
6. icu.tw.
7. intensive care.tw.
8. respiratory care units/
9. respiratory care unit*.tw.
10. critical care/
11. critical care.tw.
12. or/1-11
13. exercise therapy/
14. exerci*.tw.
15. motion therapy, continuous passive/
16. continuous passive motion.tw.
17. passive movement*.tw.
18. cprom.tw.
19. passive range of motion.tw.
20. muscle strengthening.tw.
21. resistance training/
22. resistance training.tw.
23. strength training.tw.
24. weight training.tw.
25. walking/
26. dependent ambulation/
27. walking.tw.
28. electric stimulation therapy/
29. transcutaneous electric nerve stimulation/
30. electric* stimulation.tw.
31. tens.tw.
32. exercise movement techniques/
33. therapy, soft tissue/
34. soft tissue manipulation.tw.
35. massage/
36. massage.tw.
37. rehabilitation/
38. rehabilitat*.tw.
39. physical therapy modalities/

40. physical therap*.tw.
41. physiotherapy.tw.
42. "physical and rehabilitation medicine"/
43. physical medicine.tw.
44. functional training.tw.
45. occupational therapy/
46. occupational therap*.tw.
47. early ambulation/
48. ambulation.tw.
49. mobilisation.tw.
50. mobilization.t
w. 51. or/13-50
52. muscle weakness/
53. muscle weakness.tw.
54. neuromuscular manifestation*.tw.
55. muscular atrophy/
56. musc* atrophy.tw.
57. sarcopenia/
58. sarcopenia.tw.
59. polyneuropathies/
60. polyneuropath*.tw.
61. myopath*.tw.
62. polyneuromyopath*.tw.
63. neuromuscular disorder*.tw.
64. neuromuscular disease*.tw.
65. paresis/
66. paresis.tw.
67. quadriplegia/
68. quadriplegi*.tw.
69. weakness*.tw.
70. neuromyopath*.tw.
71. motor syndrome*.tw.
72. musc* funct*.tw.
73. musc* dysfunct*.tw.
74. neuromusc* dysfunct*.tw.
75. neuromusc* funct*.tw.
76. muscle strength/
77. musc* strength*.tw.
78. intensive care unit acquired weakness*.tw.
79. (icuaw or icu-aw).tw.
80. 80. or/52-79
81. 12 and 51 and 80
82. limit 81 to (controlled clinical trial or randomized controlled trial)
83. (randomized or placebo or randomly or trial or groups or randomised).ti,ab.
84. 81 and 83

85. 82 or 84

EMBASE SEARCH STRATEGY

1. critical illness/
2. critically ill.tw.
3. critical illness*.tw.
4. intensive care/
5. intensive care unit/
6. icu.tw.
7. intensive care.tw.
8. respiratory care units.mp.
9. respiratory care unit*.tw.
10. recovery room/
11. recovery room*.tw.
12. critical care.mp.
13. critical care.tw.
14. or/1-13
15. kinesiotherapy/
16. exerci*.tw.
17. passive movement/
18. continuous passive motion therap*.tw.
19. passive movement.tw.
20. cprom.tw.
21. passive range of motion.tw.
22. stretching exercise/
23. muscle stretching.tw.
24. resistance training/
25. resistance training.tw.
26. strength training.tw.
27. weight training.tw.
28. walking/
29. walking difficulty/
30. walking.tw.
31. electrostimulation therapy/
32. transcutaneous nerve stimulation/
33. electric* stimulation.tw.
34. tens.tw.
35. electroacupuncture/
36. electroacupunture.tw.
37. exercise movement techniques.mp.
38. soft tissue therapy/
39. soft tissue manipulation.tw.
40. massage/
41. massage.tw.
42. rehabilitation/
43. rehabilitat*.tw.
44. physical therapy modalities.mp.

45. physical therap*.tw.
46. physiotherapy.tw.
47. rehabilitation medicine/
48. physical medicine.tw.
49. functional training.tw.
50. occupational therapy/
51. occupational therap*.tw.
52. mobilization/
53. ambulation.tw.
54. mobilization.tw.
55. mobilisation.tw.
56. or/15-55
57. muscle weakness/
58. muscle weakness.tw.
59. neuromuscular manifestation*.tw.
60. muscle atrophy/
61. musc* atrophy.tw.
62. sarcopenia/
63. sarcopenia.tw.
64. polyneuropathy/
65. polyneuropath*.tw.
66. myopath*.tw.
67. polyneuromyopath*.tw.
68. neuromuscular disorder*.tw.
69. neuromuscular disease*.tw.
70. paresis/
71. paresis.tw.
72. quadriplegia/
73. quadriplegi*.tw.
74. weakness*.tw.
75. neuromyopath*.tw.
76. motor syndrome*.tw.
77. muscle function*.tw.
78. muscular function*.tw.
79. muscle dysfunction*.tw.
80. musc* dysfunct*.tw.
81. neuromusc* dysfunct*.tw.
82. neuromusc* funct*.tw.
83. muscle strength/
84. muscle strength.tw.
85. muscular strength.tw.
86. intensive care unit acquired weakness.tw.
87. (icuaw or icu-aw).tw.
88. or/57-87
89. 14 and 56 and 88

90. ('clinical':ti,ab and 'trial':ti,ab).mp. or 'clinical trial'/exp or random*.mp. or 'drug therapy':lnk.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
91. 89 and 90
92. limit 89 to randomized controlled trial
93. 91 or 92

CINAHL SEARCH STRATEGY

Search ID#	Search Terms
S94	S90 AND S92
S93	S90 AND S91
S92	EM 20150901-
S91	EM -20150901
S90	S88 OR S89
S89	S83 AND S87
S88	S83 AND S84
S87	S85 OR S86
S86	AB (randomized or placebo or randomly or trial or groups or randomised)
S85	TI (randomized or placebo or randomly or trial or groups or randomised)
S84	Limiters - Randomized Controlled Trials
S83	S13 AND S53 AND S82
S82	S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81
S81	TX (ICUAW or ICU-aw)
S80	TX intensive care unit acquired weakness*
S79	TX musc* strength*
S78	(MH "muscle strength")
S77	TX neuromusc* funct*
S76	TX neuromusc* dysfunct*
S75	TX musc* dysfunct*
S74	TX musc* funct*
S73	TX motor syndrome*
S72	TX neuromyopath*
S71	TX weakness*
S70	TX quadriplegi*
S69	(MH "quadriplegia")
S68	TX paresis
S67	"paresis"
S66	TX neuromuscular disease*
S65	TX neuromuscular disorder*
S64	TX polyneuromyopath*
S63	TX myopath*
S62	TX polyneuropath*
S61	(MH "polyneuropathies")
S60	TX sarcopenia
S59	(MH "sarcopenia")
S58	TX musc* atrophy
S57	(MH "muscular atrophy")
S56	TX neuromuscular manifestation*
S55	TX muscle weakness
S54	(MH "muscle weakness")

S53 S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52

S52 TX mobilisation

S51 TX mobilization

S50 TX ambulation

S49 (MH "early ambulation")

S48 TX occupational therap*

S47 (MH "occupational therapy")

S46 TX functional training

S45 TX physical medicine

S44 (MH "physical medicine")

S43 TX physiotherapy

S42 TX physical therap*

S41 (MH "physical therapy")

S40 TX rehabilitat*

S39 (MH "rehabilitation")

S38 TX massage

S37 (MH "massage")

S36 TX soft tissue manipulation

S35 "therapy, soft tissue"

S34 (MH "therapeutic exercise")

S33 TX tens

S32 TX electric* stimulation

S31 (MH "electrical stimulation, neuromuscular")

S30 (MH "transcutaneous electric nerve stimulation")

S29 TX walking

S28 "dependent ambulation"

S27 (MH "walking")

S26 TX weight training

S25 TX strength Training

S24 TX resistance training

S23 (MH "resistance training")

S22 TX muscle strengthening

S21 (MH "muscle strengthening")

S20 TX passive range of motion

S19 TX cprom

S18 TX passive movement

S17 TX continuous passive motion

S16 (MH "motion therapy, continuous passive")

S15 TX exerci*

S14 (MH "therapeutic exercise")

S13 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12

S12 TX critical care

S11 "intensive care"
S10 TX respiratory care unit*
S9 (MH "respiratory care units")
S8 TX intensive care
S7 TX icu
S6 (MH "intensive care units")
S5 TX critically ill
S4 (MH "critical care")
S3 TX critical illness
S2 (MH "critically ill patients")
S1 (MH "critical illness")

COCHRANE CENTRAL REGISTER OF CONTROLLED TRIALS SEARCH STRATEGY

ID	Search
#1	MeSH descriptor: [Critical Illness]
#2	"critically ill"
#3	"critical illness*"
#4	MeSH descriptor: [Intensive Care]
#5	MeSH descriptor: [Intensive Care Units]
#6	"icu"
#7	"intensive care"
#8	MeSH descriptor: [Respiratory Care Units]
#9	"respiratory care unit*"
#10	MeSH descriptor: [Critical Care]
#11	"critical care"
#12	or #1-#11
#13	MeSH descriptor: [Exercise Therapy]
#14	"exerci*"
#15	MeSH descriptor: [Motion Therapy, Continuous Passive]
#16	"continuous passive motion"
#17	"passive movement"
#18	CPROM
#19	"passive range of motion"
#20	"muscle strengthening"
#21	MeSH descriptor: [Resistance Training]
#22	"resistance training"
#23	"strength training"
#24	"weight training"
#25	MeSH descriptor: [Walking]
#26	MeSH descriptor: [Dependent Ambulation]
#27	walking
#28	MeSH descriptor: [Electric Stimulation Therapy]
#29	MeSH descriptor: [Transcutaneous Electric Nerve Stimulation]
#30	"electric* stimulation" or "electric* nerve stimulation"
#31	tens
#32	MeSH descriptor: [Exercise Movement Techniques]
#33	MeSH descriptor: [Therapy, Soft Tissue]
#34	"soft tissue manipulation"
#35	MeSH descriptor: [Massage]
#36	massage
#37	MeSH descriptor: [Rehabilitation]
#38	rehabilitat*
#39	MeSH descriptor: [Physical Therapy Modalities]
#40	"physical therap*"

#41 physiotherapy
#42 MeSH descriptor: [Physical and Rehabilitation Medicine]
#43 "physical medicine"
#44 "functional training"
#45 MeSH descriptor: [Occupational Therapy]
#46 "occupational therap*"
#47 MeSH descriptor: [Early Ambulation]
#48 ambulation
#49 mobilisation
#50 mobilization
#51 or #13-#50
#52 MeSH descriptor: [Muscle Weakness]
#53 "muscle weakness"
#54 "neuromuscular manifestation*"
#55 MeSH descriptor: [Muscular Atrophy]
#56 "musc* atrophy"
#57 MeSH descriptor: [Sarcopenia]
#58 sarcopenia
#59 MeSH descriptor: [Polyneuropathies]
#60 polyneuropath*
#61 myopath*
#62 polyneuromyopath*
#63 "neuromuscular disorder*"
#64 "neuromuscular disease*"
#65 MeSH descriptor: [Paresis]
#66 paresis
#67 MeSH descriptor: [Quadriplegia]
#68 quadriplegi*
#69 weakness*
#70 neuromyopath*
#71 "motor syndrome*"
#72 "musc* funct*"
#73 "musc* dysfunct*"
#74 "neuromusc* dysfunct*"
#75 "neuromusc* funct*"
#76 MeSH descriptor: [Muscle Strength]
#77 "musc* strength"
#78 "intensive care unit acquired weakness*"
#79 icuaw or icu-aw
#80 51-#79
#81 #12 and #51 and #80

APPENDIX II
Criteria for Risk of Bias Assessment

Quality of each trial was evaluated using the items below. Items below were categorized as 'Low, High or Unclear' based on the criteria below

i. Adequate sequence generation: 'Low' when the allocation sequence protects against biased allocation to the comparison groups.

ii. Allocation concealment: 'Low' when clinicians and participants are unaware of future allocations.

iii. Blinding of participants, personnel and outcome assessors - 'Low' when participants and personnel are unaware of the allocation, or when the awareness of participants and/or personnel is unlikely to influence the outcome (performed at an outcome level).

iv. Incomplete outcome data (adequate/addressed) - 'Low' when 80% of participants are followed up or authors statistically adjusted for missing data (performed at an outcome level).

v. Selective reporting: 'Low' when reports of the study are free of suggestions of selective reporting.

vi. Other sources of bias: 'Low' when the study is apparently free of other problems that could put it at a high risk of bias.

APPENDIX III

List of Excluded Papers and Rationale for Exclusion

S/N	First Author (Year)	Reason for Exclusion
1	Dall[275] (2017)	No ICUAW outcome
2	Fossat[276] (2017)	Conference paper (author contacted to know if paper has been published; no response yet)
3	Sarfati[277] (2017)	Conference paper (author contacted to know if paper has been published; no response yet)
4	Morris [154] (2016)	ICUAW not assessed
5	Pinto[278] (2016)	Conference paper (author contacted to know if paper has been published; no response yet)
6	Connolly [279] (2015)	Exercise intervention was initiated after ICU discharge Intervention was on patients already diagnosed with ICUAW
7	Yosef-Brauner [280] (2015)	Intervention was on patients already diagnosed with ICUAW
8	Borges [281] (2015)	Not RCT ICUAW not assessed
9	Team Study Investigators [212] (2015)	Not RCT Reported ICUAW for only a subset of observed patients
10	Dirks [282] (2015)	Randomized limbs ICUAW not assessed
11	Patel [283] (2014)	Conference paper Abstract only
12	Elbouhy [284] (2014)	ICUAW not assessed
13	Patel [285] (2014)	Secondary analysis of an included study (Schweickert 2009)
14	Connolly[286] (2013)	Conference paper Abstract only
15	Pandey [287] (2013)	ICUAW not assessed
16	Hirose [288] (2013)	Not RCT ICUAW not assessed
17	Abu-Khaber[289] (2013)	First author has passed on and second author could not retrieve additional data that was needed
18	Brummel [290] (2012)	A Protocol
19	Paternostro-Sluga [291] (2012)	Conference paper Abstract only
20	Chen [292] (2012)	Not an ICU setting (Respiratory Care Centre) No ICUAW Outcome

21	Karatzanos [293] (2012)	Secondary analysis of an included study (Routsi 2010)
22	Rodriguez [294] (2012)	Sides of the body were randomized to the intervention, rather than individuals
23	Devost [295] (2011)	Conference paper Abstract only
24	Gerovasili [296] (2011)	Conference paper Abstract only
25	Chang [297] (2011)	ICUAW not assessed
26	Poulsen [298] (2011)	Randomized limbs ICUAW not assessed
27	Karatzanos [299] (2010)	Conference paper Abstract only
28	Rodriguez [300] (2009)	Conference paper Abstract only
29	Gerovasili [301] (2009)	ICUAW not assessed
30	Burtin [153] (2009)	Screening for ICUAW was only performed in patients with prolonged ICU stay
31	Morris [138] (2008)	Not RCT ICUAW not assessed
32	Griffiths [302] (1996)	Only abstract found, actual study not located

APPENDIX IV

Description and Risk of Bias Assessment of Included Studies

Description of Included Studies

Table 1 shows the characteristics of the eight included studies. Study publication dates ranged from 2005 to 2015. The population consisted of mechanically ventilated patients in four studies,[142,253,257] cardiac surgery patients in one study,[256] medical and surgical ICU patients in two studies,[156,254] and surgical ICU patients in one study.[147] Most studies were done in university-affiliated hospitals. Table 2 shows the characteristics of patients included in the primary studies with a total of about 791 patients (390 intervention and 401 control). Most patients received mechanical ventilation during their ICU stay (all patients were ventilated patients in six studies,[142,147,253,255-257] with about 55% in one study[156] and less than 1% in one study.[156]). The primary reason for ICU admission and co-morbidities varied from study to study.

Table 3 shows the intervention characteristics of the studies. The intervention was only NMES in three studies,[253,254,256] progressive EM exercises in four studies[142,147,156,255] and a combination of NMES with EM in one study.[257] The control group received EM interventions as part of usual care in five studies.[147,156,253,255,257] Time to first intervention was about two days or less from ICU admission or initiation of mechanical ventilation in six studies,[142,147,254-257] while it was about 4.6 and ≥ 5 days in two studies.[156,253] Two of the studies, which began rehabilitation interventions in about two days, consisted of only NMES;[254,256] three were only EM[142,147,255] and the last consisted of both.[257] The two studies that began intervention in about 5 days consisted of one EM study[156] and one NMES study.[253] The intervention period was limited to the ICU stay in five studies,[253-257] while it extended to hospital stay in one study[142] and up to 12 months post-hospital discharge in one study.[156] The frequency of treatment was daily in most studies, though in one study it was 6x/week.[156] In studies that reported the duration of treatment per day, it was higher in NMES

studies (about 60mins per day)[253,254,256] compared to about 15-20[33,36] and 40[255] mins in EM studies. The study that combined both NMES and EM reported 30 mins per session treatment with a frequency of 1-2 times daily. Intensity was limited to visible contraction in most NMES studies[253,254] with the exception of Fischer et al.[256], who reported intensity of about 40mA. Two studies with EM[142,156] limited intensity to patients' tolerance. Dantas et al.[255] and Schaller et. al[147] did not report the intensity of the EM interventions. One NMES study[253] reported 100% delivery integrity, while two studies reported over 85% delivery integrity,[142,256] and four studies did not report the percentage of delivery integrity,[156,254,255,257] though one of the three stated through personal communication that not all patients in the intervention group received the intervention.[156] Co-intervention, which could affect the incidence of ICUAW, included EM in one NMES study[253] and daily interruption of sedation,[142] which were offered to both groups as part of usual care.

Risk of bias in the included studies

The risk of bias assessment results are shown in table 4. Selection bias (random sequence generation) was low in six studies,[142,147,156,255-257] high in one[254] and unclear in one.[253] Selection bias (allocation concealment) was high in one study[254] and low in seven studies.[142,147,156,253,255-257] Performance bias for blinding of participants was judged low in all studies, while performance bias for blinding of personnel was high in two studies[254,255] and low in six studies.[142,147,156,253,256,257] Detection bias varied by outcome. For the primary outcome, ICUAW detection, bias was high in three studies[254-256] and low in five studies.[142,147,156,253,257] For mortality, detection bias was low in all eight studies, while for other secondary outcomes, detection bias was high in five studies[142,156,254-256] and low in three studies.[147,253,257] About 85%,[253] 84%,[257] 78%,[142] 77%,[147] 71%,[156] 44%,[256] 37%,[254] and 24%,[255] of participants were screened for ICUAW in the studies. One study (78% evaluated),[142] statistically adjusted for missing data with patients who were not evaluable analyzed as having ICUAW. Therefore, attrition bias for ICUAW was judged to be high

in five studies[147,156,254-256] and low in three studies.[142,253,257] Attrition bias for secondary outcomes (except mortality) is low in all studies with the exception of one study[255] in which it is high. Reporting bias was judged to be high in one study,[254] unclear in three studies[156,255,256] and low in four studies.[142,147,253,257] 'Other bias' was unclear in only one study.[255]

CHAPTER 10: PREFACE TO MANUSCRIPT FOUR

Limited knowledge, limited skills and the lack of confidence to implement EM intervention are among the barriers to EM identified in the first two manuscripts. The focus group studies also found that these barriers cut across various ICU professions, including physiotherapists who are deemed to be the experts in this area of EM. There is, therefore, a need to bridge the knowledge/skill gaps of physiotherapists working in the ICU. To achieve this goal, it is essential to first identify these gaps. There is currently no existing critical care learning needs assessment tool for physiotherapists aiming to work in the ICU. The fourth manuscript describes the initial process involved in the development of the first Physical Therapy Critical Care Learning Needs Assessment Tool.

The specific objective of this study was to identify the theoretical and practical knowledge as well as skills required for physiotherapy practice in the ICU, and select the topic areas that would inform the development of a learning needs assessment tool.

This information will in the future be used to develop the Critical Care Learning Needs Assessment Tool for physiotherapists who intend to work in the ICU. The results will also inform and direct the development of educational modules that will be helpful in bridging the knowledge and skill gaps of physiotherapists working in the ICU.

CHAPTER 11: MANUSCRIPT FOUR

The Identification and Selection of Topic Areas for a Physiotherapy Critical Care Learning Needs Assessment Tool

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
ICU	Intensive care unit

Keywords: skills, knowledge, physiotherapists, critical care, learning needs assessment, intensive care unit.

ABSTRACT

Background

Physiotherapists are increasingly expected to provide rehabilitation interventions to critically ill patients in the ICU. However, inadequate knowledge and skills can be a barrier to practice in this milieu. In order to upgrade any expertise, it would first be necessary to identify the existing gaps in such knowledge and skills. We describe the methodological approach used, and the items identified and selected for inclusion in a critical care learning need assessment tool.

Methods

We conducted a scoping review of the literature to identify knowledge/skill areas relevant to physiotherapy ICU practice. Findings from this review were used to develop a survey questionnaire which was administered to 22 physiotherapists (with an average of 13 years' experience) working in an acute hospital. Physiotherapists rated the relevance of each of the included items for practice in the ICU, as well as their knowledge pertaining to each item. Descriptive statistics summarized the responses. A statistically-based algorithm was used to identify highly relevant items where the level of knowledge/skill was relatively low. Senior and experienced physiotherapists were consulted to confer and agree on the items or topics that should be included in the future tool.

Main Results

A total of 238 knowledge/skill topics, identified from 40 articles, were included in the survey questionnaire and rated by physiotherapists on a 5 point Likert scale with 1 being "not at all" and 5 being "a great deal". The survey questionnaire included the foundational knowledge domain with subdomains of anatomy, physiology, exercise physiology, pathophysiology and presenting features of common ICU conditions, pharmacology, medical therapies and procedures, lines, leads and/or ICU equipment. Other domains were tests and laboratory findings, assessment, clinical reasoning, evaluation skills, physiotherapy interventions, as well as professional and ethical practice. From the rating results, the statistical-based algorithm identified 113 important topic areas for inclusion (47.48%). Expert consensus further refined the selected areas to 90 topics. Areas excluded by the experienced physiotherapists were deemed either not relevant for the hospital's patient population or outside the physiotherapists' roles in that hospital.

Conclusion: Topics identified in this study will be used to develop a physiotherapy critical care learning needs assessment tool. Our survey tool and methodological approach could also guide the development of a hospital-specific learning needs assessment tool in other clinical settings.

1. BACKGROUND

The intensive care unit (ICU) is a complex and dynamic interdisciplinary environment[303] that provides life-sustaining and life-saving care for critically ill patients. Clinical practice in this environment requires specialization and familiarity with the specifics of this setting. Traditionally, physiotherapists in the ICU were involved mainly in the management of respiratory conditions. More recently, however, the provision of mobilization and other rehabilitation interventions early in the course of critical illness has gained prominence.[88,89,142,149-153] As a result, there is greater involvement of physiotherapists in the ICU setting.

Previous studies have shown limited training,[168,180,213] staff knowledge[172,213] and availability of ICU-competent physiotherapists to be barriers to the provision of physiotherapy interventions in this milieu.[168,177,193,213] Most ICU physiotherapists have either received no ICU training or received only hospital-based informal training.[180,181,183,304] Consequently, physiotherapy competencies and practices vary widely from one hospital to another and from one region to another. Furthermore, factors such as weekend calls, absences, maternity and sick leaves often cause the replacement of ICU physiotherapists with other physiotherapists regardless of experience, competence or confidence in the assessment and treatment of critically ill patients. As a result, some physiotherapists may lack necessary knowledge and skills to provide safe and appropriate interventions for patients with critical illnesses.[183] Patients, thus, may not always receive the optimal intervention for their condition because treatment administered may depend on the skills and competencies of the treating therapist.[213] Hanekom et al.[304] postulated that "the lack of consistency in professional standards and dedicated training poses a substantial threat to the practice of physiotherapy, the credibility of the profession within ICU and patient outcome." It appears timely to identify the knowledge and skill gaps of physiotherapists who work in the ICU

in order to design tailored knowledge translation interventions to reduce such gaps. This study aimed to generate an agreed upon list of critical care related knowledge and skill topic areas to be incorporated into a prototype learning needs assessment tool for physiotherapists aiming to work in the ICU.

The specific objective of this study was to identify the theoretical and practical knowledge and skill topic areas required for physiotherapy practice in the ICU, and select topics that could inform future development of a learning need assessment tool.

2. METHODS

Mixed methodology[305] involving a combination of statistical approach and end-user participation was used to generate and select topic areas for the tool. The process involved five phases: 1) a scoping review of the literature; 2) development of a survey questionnaire; 3) administration of the survey questionnaire to physiotherapists with experience in the ICU; 4) focus group meeting with survey respondents; and 5) triangulation of all data sources using a team of senior and experienced physiotherapists.

2.1. Scoping Review

A scoping literature review was conducted to identify the knowledge and practical skills that physiotherapists require for practice in the ICU. The review was based on the five-stage framework outlined by Arksey and O'Malley[306] and identified the key concepts pertaining to physiotherapy practice in the ICU, as well as the sources of such concepts.[307] The research question was: What are the theoretical and practical knowledge and clinical skills (practice standards) required for physiotherapists to work in the ICU?

Five databases (MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials [CENTRAL], and Physiotherapy Evidence Database [PEDro]) were searched from inception to July 29th, 2017. A Combination of MeSH terms and keywords related to (*physiotherapists or physical therapists*) and (*intensive care or critical care unit*) and (*knowledge or skills or practice or standards or professional competence or clinical competence education*) were used for the search. The strategy was first designed in MEDLINE (Appendix I) with the participation of a medical librarian (J.B.) and adapted to other databases. There was no language restriction. In addition, on September 7th, 2017, we searched the Early Mobilization/Physiotherapy & Occupational Therapy section of the ICU Mobilization Network reference list. We also reviewed the bibliographies of identified studies.

Studies were selected based on the following inclusion criteria: i) type of studies: research publications, guidelines, expert opinions and reviews as well as recommendation and consensus papers, ii) studies involving physiotherapists or physiotherapy students, and iii) studies that elicited information on knowledge or skills related to physiotherapy practice in the ICU. The following categories were excluded: i) studies that focused on the pediatric population, ii) study protocols, iii) trials providing no clear distinction between rehabilitation interventions delivered by physiotherapists and other members of the critical care team, iv) studies published in languages other than English or French, and v) non-human studies. A single assessor screened the titles and abstracts of retrieved articles, and the full texts of potentially eligible articles were obtained and further assessed for final inclusion.

A single investigator used the data extraction form to extract the relevant data. Data regarding the characteristics of the papers were extracted including the: name of the first author, type of paper, number of participants, the identity of the participants, study design, the country where the study

was conducted and a comments section and the extracted knowledge and skill. Similar topic areas from different papers were collapsed into single topic areas during the analysis and classification. The Curriculum Content Framework[308] of the Council of Canadian Physiotherapy University Programs informed the extraction, analysis, and classification of topic areas from the literature.

2.2. Development of the Survey Questionnaire

A survey questionnaire was developed to assess the perceived relevance of each topic area to physiotherapy practice in the ICU and the perceived personal knowledge/skill of respondents. Each topic from the literature review was used to form a question item on the questionnaire. A Likert scale (from 1-5) was used for responses with '1' meaning 'Not at all' and '5' meaning 'A great deal'. Participants were also asked to indicate items for which they were unable to rate relevance or their knowledge. The research team worked together on evaluating the face content validity and refining the questionnaire through an iterative process until the final tool was deemed fit for administration.

2.3. Administration of the Survey Questionnaire to Physiotherapists

2.3.1. Population and Procedures

We targeted all physiotherapists working at a local area general hospital in Montreal, Canada. Potential respondents were recruited through a mini-presentation at the clinical meeting of the physiotherapy department and through email communications. Clinicians were eligible if they had worked in the ICU or covered the ICU on weekend call, evening duties or as a replacement. There was no limit on years of experience for the survey respondents. With a total population of 27 eligible participants in the local hospital, a confidence level of 95% and a confidence interval (margin of error)[309,310] of 10, a minimum sample size of 21 respondents was estimated for the survey. Surveys were paper administered and completed independently at the time of

administration. Ethics approval was obtained from the responsible regional Research Ethics Review Board.

2.3.3. Data Analysis

Descriptive statistics were used to summarize the responses on relevance and knowledge/skill for each topic area. A statistical-based algorithm was used to select topic areas with potential knowledge/skill gaps. A scatter plot of relevance (predictor variable - x-axis) and knowledge/skill level (dependent variable - y-axis) with a line of best fit as well as the associated confidence intervals was plotted. For the scatter plot regression line, we estimated a minimum sample size of 58 data points based on the rule of the thumb $N \geq 50 + 8m$ for multiple regression (where m is the number of predictors).[311] Topic areas below the line of best fit were identified as areas where the perceived knowledge/skill was less than the knowledge/skill expected for that relevance level. As clinicians' perceived knowledge/skill was often higher than actual knowledge,[168,213,312] we chose all topic areas below the upper confidence interval for the line of best fit to represent areas with potential knowledge/skill gaps. All topics with potential knowledge/skill gaps and an average relevance rating above 3.75 of 5 (upper quartile of the relevance range) were selected for potential inclusion in the future assessment tool.

2.4. Focus Group with Survey Respondents

All clinicians who completed the survey participated in a post-survey focus group meeting. Participants were asked to provide feedback with regards to the items included in the survey questionnaire and whether they felt any items were missing. They were also asked for their perception on the potential inclusion or exclusion of items from the future learning needs assessment tool.

2.5. Triangulation of All Data Sources

All data sources were triangulated by consulting a team of four senior and experienced physiotherapists for consensus using a modified Triage technique.[313,314] Two physical meetings were held with the team. Prior to the meetings, the team was sent the summaries of the survey results, focus group discussions and the items included and excluded by the statistical-based algorithm via email. Members were asked to review the items and the results, and to select items for inclusion into the future learning needs assessment tool. Items with unanimous agreement were included while the rest moved to the interactive phase of the TRIAGE technique for discussion. After an interactive discussion on an item, it was included or excluded by a unanimous consent.

3. RESULTS

3.1. Scoping Review Results

The literature search identified 293 potentially relevant articles. After removal of duplicates, 263 articles were screened for eligibility (Figure 1). We identified 190 articles that did not meet our selection criteria, leaving 73 articles for full-text review of which 40 were retained.[146,174,181,183,204,206,211,304,315-346] The reasons for the exclusions are provided in Appendix II. The characteristics of the 40 included studies are shown in Table 1. A total of 238 knowledge and skill topics were extracted from the literature.

3.2. The Survey Questionnaire

The resulting questionnaire had 238 question items in six domains: foundational knowledge, tests and laboratory findings, assessment, critical reasoning and evaluation skills, physiotherapy interventions, and professional and ethical practice. Foundational knowledge items had seven subdomains: anatomy and/or physiology, exercise physiology, pathophysiology and presenting features of a number of common ICU conditions, pharmacology, common medical therapies and

procedures, knowledge of common ICU lines, leads and/or equipment, and others. The questionnaire is shown in Appendix III.

3.3. Survey Results and the Analysis Results

Twenty-two physiotherapists took part in the survey. On average, they had 13 years of clinical experience (median 13 years, range 0-33 years) and had worked in the ICU on average for about 8.8 years (median 8 years, range 0-32 years).

Table 2a and 2b show the average relevance and personal knowledge ratings for the various knowledge and skill items. Missing items were very negligible: participants reported an inability to rate their perceived knowledge or relevance on a small proportion of the items in each domain (1.14% for foundational knowledge, 1.57% for tests and laboratory findings, 1.55% for assessment, 0.68% for critical reasoning and evaluation skills, 1.52% for physiotherapy interventions, and 0.00% for professional and ethical practice). Figure 2 shows the scatter plot of relevance versus knowledge with the associated line of best fit and its 95% confidence interval. The line of best fit ($y = 1.022x - 0.9904$) had a Coefficient of Correlation of (r) of 0.672 and coefficient of determination (R^2) of 0.452. There was a positive correlation between relevance and knowledge. A total of 113 topic areas with potential knowledge/skill gaps were selected by the statistical-based algorithm (Annex 4a).

3.4. Focus Group Results

The 22 physiotherapists who took part in the survey participated in the focus group discussions. Overall, they felt that the content of the survey tool was comprehensive, detailed, and did not omit any important area of knowledge. Nonetheless, in the pharmacology section, some physiotherapists were of the view that apart from the general classes of medication in the tool,

there were some medications that were highly specific to the ICU that should be emphasized. Others were of the opinion that general knowledge of the classes of the drugs was sufficient, as they have the guidance of the nurses or physicians for any extra information related to the medications. In addition, a participant mentioned that it may be important to include ethical issues such as coping with the psychological trauma that is involved with managing critically ill patient (though this may not be specific to physiotherapy practice or the ICU).

3.5. Data Triangulation Results

The team of four senior and experienced physiotherapists had a median of 29.5 (range: 25-40) years of experience working as physiotherapists and 19.5 (range: 14-25) years of clinical and administrative work in the ICU. The consultation of experienced physiotherapists for triangulation of the results of the survey, the statistical-based analysis, and the focus group further refined the topic areas in the list that were selected by the statistical method. The TRIAGE technique consensus methodology resulted in the exclusion of 32 topics and inclusion of 9 topics which were earlier included and excluded, respectively, by the statistical approach. Annex 4b and 4c show the list of 32 and 9 topics, respectively. Topics that were not relevant to the hospital's patient population or that were outside the physiotherapists' roles in that hospital were excluded (Annex 4b). Topics that the experts judged important to include despite high knowledge were also included (Annex 4c). Table 2a and 2b show the final 90 included topics and 148 excluded topics, respectively. Figure 3a shows the percentage of items selected in each domain/subdomain. A median of 78% (range 61-91%) of all items in the pathophysiology/clinical features, pharmacology, medical therapies and procedures, ICU lines, leads and/or equipment, tests and laboratory findings domains/subdomains were selected for inclusion. Overall, items in domains/subdomains of pathophysiology/clinical features, pharmacology, medical therapies and

procedures, ICU lines, leads and/or equipment, tests and laboratory findings, and assessment made up 84% of all selected items (Figure 3b shows the proportion of selected items by domains/subdomains)

4. DISCUSSION

This study identified and selected specific knowledge and skills topics for potential inclusion in a critical care learning needs assessment tool for physiotherapists aiming to work in the ICU. Selected items were concentrated around the following domains/subdomains: test and laboratory findings, ICU lines, leads and/or equipment, medical therapies and procedures, pharmacology and assessment. The methodology involved in the study also resulted in the development of a questionnaire that could be used to adapt the item selection process to the clinical setting of other local facilities in Canada or elsewhere.

The use of a scoping review enabled the identification of relevant literature in the item generation phase of the study. The identified studies included some research studies exploring the scope of physiotherapy practice and studies involving the training of physiotherapy students, observational studies, clinical practice guidelines, review papers and expert recommendations. The survey contained an exhaustive list of categorized items and was judged by our survey respondents as not missing any important item. There have been earlier efforts to identify the knowledge and skills that physiotherapists need for practice in the ICU. Skinner et. al[347] used a modified Delphi technique involving 45 experts to define the minimum standards of clinical practice for physiotherapists working in critical care settings in Australia and New Zealand. While that study made a significant contribution towards defining relevant physiotherapy critical care knowledge and skills, it focused primarily on Australia and New Zealand's scope of practice and on skills

required for entry-level practice. In contrast, our study generated information from the literature that emanated from several countries, which was then used to develop a questionnaire. This makes the content of our questionnaire applicable in the clinical settings of other countries. Furthermore, the paper by Skinner et. al[347] did cover some foundational knowledge domains that influence advanced-level skills in the ICU, as well as non-technical skills related to professionalism and ethical practice. However, it could be argued that some of these areas do not pertain solely to practice in the ICU. Hanekom et. al[304] and van Aswegen et. al[183] also published studies that identified the minimum standards of clinical practice needed by physiotherapists to ensure safe and independent practice in South African ICUs. These studies used a qualitative approach and only generated information regarding broad areas of practice, without eliciting details on the specific content in those areas. In contrast, the results of the current study provide a comprehensive summary of the specific knowledge and skill areas that fall within the physiotherapy area of practice in the ICU. Therefore, we consider the developed questionnaire to be applicable to a wider clinical setting.

The methodology used to select the topic areas for inclusion in this study involved end-user participation. The active involvement of frontline physiotherapists, who are faced with the daily challenges in the ICU environment, helped us to select items that are very relevant to the end-users (the physiotherapists). The use of both quantitative and qualitative methods to select items resulted in the selection of critical care topics where the end users felt they needed to update their skills and knowledge.

Items selected for inclusion were mostly in the pathophysiology/clinical features, pharmacology, medical therapies and procedures, ICU lines, leads and/or equipment, and tests and laboratory findings domains. Understandably, the patient population in the ICU, the medical procedures and

therapies, and equipment being used are not common in daily physiotherapy practice. Furthermore, lines and leads connected to life-sustaining machines could create an intimidating environment for someone who wants to administer exercise in the ICU. Knowledge and understanding of the pathophysiology of the patient's condition, the effect of medications, the medical therapies and procedures, the lines, leads and/or equipment and the implication of these factors are fundamental to safe physiotherapy practice in the ICU. These knowledge areas may not have been included in the academic training curriculum of many older licensed physiotherapists. Two other domains with a high percentage of selected items were the tests and laboratory findings domain, and the assessment domain. While most of the items in the tests and laboratory findings domain were selected, only about 34% were selected from the assessment domain. The domains and subdomains with a higher percentage of selected items may reflect the topics that need to be emphasized in a continuing education program developed for the physiotherapists at this specific hospital in order to bridge the potential knowledge/skill gaps.

In the next step of the tool development process, the selected topics from this study will need to be further delineated and converted into either questions or integrated into clinical vignettes. This process should also involve the end users to make the final tool more usable by them.

This study is not without limitations. First, the literature review and data extraction process was not conducted in duplicate. Second, all end-users who participated in the study were from a single hospital facility. Therefore the tool in development will be specific to that hospital. Finally, as this study used a scoping review, we did not explore the available evidence on the effectiveness of the physiotherapy skills or interventions that have been identified in the literature. Future studies are needed to explore such evidence.

5. CONCLUSION

This study has identified and selected the theoretical and practical knowledge as well as skill areas would be integrated into a learning needs assessment tool for physiotherapists aiming to work in the intensive care. This forms part of a larger project which aims to identify and bridge the knowledge and skill gaps of physiotherapists in critical care.

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Authors Contribution

D. Anekwe, was responsible for designing the study, coordinating the overall activities as well as collecting and analyzing data, and writing of the manuscript. J. Spahija contributed to the study's conception, design, execution, and supervision as well as proofreading and editing of all the documents and the final manuscript. S. Katz and L. Gillespie contributed to the study's conception and facilitated data collection. A. Bussières provided methodological guidance in the analysis, as well as proofreading and editing of the manuscript. G. Moullec was a collaborator in the study.

TABLES

Table 1: Characteristics of Included Studies

Article ID	First author	Type of paper	Number of Participants	Professional Involved	Design	Country	Comments
1	Skinner[181]	Research paper	61 invited 45 completed	PTs	Delphi Technique Consensus	Australia and New Zealand	From the list of items presented to the Delphi panel
2	Hanekom[304]	Research paper	25	PTs	Nominal Group Technique	South Africa	From the list of items emanating from the focus groups
3	van Aswegen[183]	Research paper	25	PTs	Focus group	South Africa	From the list of items emanating from the focus groups (same study as above)
4	Bishop[316]	Research paper	N/A	PT students	Course design case report	USA	The reported content area/focus of the designed course
5	Taito[333]	Research paper	318	PTs and others	Survey	Japan	Survey results: PT treatment interventions
6	Sigera[332]	Research paper	213	PTs	Interview-administered survey	Sri Lanka	Survey results: Treatment and equipment
7	Nithman[328]	Research paper	N/A	PT students	Case report: ICU stimulation	USA	The reported content area/focus of the stimulation
8	Bisset[343]	Conf Abstract	N/A	PT students	Case report: Clinical visit	Australia	Learning outcomes for the visit
9	Stockert[345]	Conf Abstract	N/A	PT students	Case report: ICU stimulation	USA	The reported content area/focus of the stimulation
10	Sommers[204]	Research paper	N/A	N/A	Guideline development	Netherlands	The guideline focused on the musculoskeletal system, based on the local context of Dutch PTs
11	Lewko[326]	Conf Abstract	15	Academicians (respiratory PT education)	Survey	Europe	Information from the reported areas of education in respiratory physiotherapy across Europe
12	Clark[319]	Conf Abstract	N/A	N/A	Course design case report	USA	The reported content area/focus of the designed course
13	Castro Avila[317]	Conf Abstract	19	PT	Direct observation	Chile	Treatment techniques observed (3 hospitals)
14	Pawlik[331]	Review paper	NA	NA	Review	USA	The review extracted information from other sources e.g. APTA
15	Pathmanathan[330]	Abstract	N/A	N/A	Course design	Unknown	Multi-disciplinary course. Information from course aims

Article ID	First author	Type of paper	Number of Participants	Professional Involved	Design	Country	Comments
16	Ohtake[329]	Research paper	N/A	PT students	Course design case report	USA	The reported content area/focus of the designed course
17	Gough[321]	Research paper		PT service leads	Survey	England, Northern Ireland, Scotland, Wales	Information extracted from the survey
18	Webster[336]	Conf Abstract	N/A	N/A	Case report of an educational program	USA	Educational content focus for the PTs
19	Palmieri[315]	Paper	N/A	N/A	Case report of QIP	USA	Data extracted from the plan and algorithm resulting from a QIP
20	Havrilla[323]	Conf Abstract	N/A	PT students	Case report: ICU stimulation	USA	The reported content area/focus of the stimulation
21	Hopkins-Rosseel[344]	Conf Abstract	N/A	PT students and others (nursing and medical)	Case report: ICU stimulation	Not stated. First and last author suggests Canada	The reported content area/focus of the stimulation
22	Grandet[322]	Paper	N/A	N/A	Paper (in French)	France	The areas of skills highlighted in the paper
23	Thomas[346]	Conf Abstract	Not given	PTs	Case report of an intensive care course for PTs	Australia	The reported content area/focus of the stimulation
24	Hiner[324]	Research Paper	N/A	N/A	Survey	USA	The study evaluated clinicians perception and knowledge of the correct head of elevation to reduced VAP in critically ill patients.
25	Dennis[320]	Research paper	64 Australian hospitals	Senior PTs	Survey	Australia	Background and focus of the survey
26	Perme[206]	Expert opinion	N/A	N/A	Opinion paper	Brazil	Information extracted from the expert's recommendation
27	Jham[325]	Conf abstract	N/A	N/A	Review paper	N/A	Information given on the role of the physiotherapist in the ICU
28	Hodgin[174]	Research paper	N/A	N/A	Survey	USA	Information from PT practices surveyed
29	Stiller[211]	Review	N/A	N/A	Review and expert opinion paper	N/A	Information extracted from the expert's recommendation

Article ID	First author	Type of paper	Number of Participants	Professional Involved	Design	Country	Comments
30	Thomas[334]	Research paper	PTs= 36 Nurses=35	ICU experienced PTs & Nurses	Survey	Australia	Information extracted from the focus of the survey
31	Napolis[327]	Research paper		PTs, Nurses, Physicians	Survey	Brazil	Information extracted from the survey results
32	Chang[318]	Research paper	86 Australian hospitals	PTs	Survey	Australia	Information extracted from the survey content and results
33	van de Mortel[335]	Research paper	N/A	ICU staff (including PTs)	Observational study	Australia	Study focused on an important clinical habit
34	Masley[342]	Research paper	18	PTs	Interview	USA	Data emanating from the qualitative interview
35	Gorman[339]	Research paper	254	PTs	Survey and consensus methodology	USA	From the survey results and subject matter experts consensus
36	Flanders[338]	Paper	N/A	N/A	Literature review	N/A	Extracted from the summary of factors to consider before mobilizing critical care patients
37	APTA & Greenwood[340]	APTA document	N/A	N/A	Literature review, task force consensus and experts' review	USA	Extracted from APTA document - Core Competencies for Entry-Level Practice in Acute Care ...
38	Gosselink[146]	Recommendation paper	N/A	N/A	Literature review and recommendation	Europe	Recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients
39	Hodgson[341]	Consensus paper	23	ICU experts:	Literature review and consensus meeting	International Australia (n = 19) United States (n = 2) New Zealand (n = 1) Finland (n = 1)	Safety consensus provided in the paper
40	Berry[337]	Guideline	N/A	N/A	Literature review and consensus derived clinical guideline	Australia	Information on safety guidelines and progression guidelines.

***** *Survey study information was extracted from the survey content area and/or respondents' report of their practice (survey results)*

TABLE 2A: LIST OF SELECTED TOPIC AREAS

#	Items	Domain/Subdomain	Relevance	Knowledge
1	Respiratory system	Anatomy and/or physiology	4.95	3.95
2	Cardiovascular system	Anatomy and/or physiology	4.91	3.95
3	Physiological monitoring	Exercise physiology	5.00	4.23
4	ICU-acquired weakness (ICU-AW)	Underlying pathophysiology and presenting features	4.91	3.67
5	Cardiac surgery (e.g. coronary artery bypass graft etc.)	Underlying pathophysiology and presenting features	4.91	4.09
6	Heart failure	Underlying pathophysiology and presenting features	4.86	3.64
7	Thoracic surgery	Underlying pathophysiology and presenting features	4.86	3.64
8	Other cardiac conditions (e.g. cardiomyopathy, pericarditis, pericardial effusion, tamponade, endocarditis, valvular heart disease, aortic stenosis, myocarditis etc.)	Underlying pathophysiology and presenting features	4.82	3.59
9	Pleural conditions (e.g. pleural effusions)	Underlying pathophysiology and presenting features	4.77	3.77
10	Acute coronary syndrome (e.g. angina, STEMI/non-STEMI)	Underlying pathophysiology and presenting features	4.77	3.82
11	Vascular surgery	Underlying pathophysiology and presenting features	4.73	3.41
12	Acute lung injury/acute respiratory distress syndrome (ARDS)	Underlying pathophysiology and presenting features	4.73	3.45
13	Guillain–Barre Syndrome	Underlying pathophysiology and presenting features	4.73	3.73
14	Restrictive respiratory disease	Underlying pathophysiology and presenting features	4.68	3.77

15	Spinal cord injury	Underlying pathophysiology and presenting features	4.64	3.64
16	Abdominal surgery	Underlying pathophysiology and presenting features	4.64	3.77
17	Shock (cardiogenic, neurogenic, allergic etc.)	Underlying pathophysiology and presenting features	4.50	3.09
18	Renal failure (acute / chronic)	Underlying pathophysiology and presenting features	4.14	3.23
19	Chest trauma	Underlying pathophysiology and presenting features	3.91	2.95
20	Systemic inflammatory response syndrome (SIRS)	Underlying pathophysiology and presenting features	3.77	2.36
21	Multi-organ dysfunction syndrome (MODS)	Underlying pathophysiology and presenting features	3.77	2.41
22	Brain death, organ procurement	Underlying pathophysiology and presenting features	3.05	2.23
23	Analgesics	Pharmacology	4.68	3.77
24	Sedatives	Pharmacology	4.55	3.05
25	Beta blockers	Pharmacology	4.50	2.64
26	Bronchodilators	Pharmacology	4.50	3.50
27	Neuromuscular paralyzing agents	Pharmacology	4.41	2.82
28	Diuretics	Pharmacology	4.32	3.27
29	Ventilator weaning	Medical therapies and procedures	4.86	2.64
30	Pacemakers (temporary, automated external defibrillators etc.)	Medical therapies and procedures	4.86	3.59
31	Supplemental oxygen (including delivery devices)	Medical therapies and procedures	4.82	3.73
32	Intra-aortic balloon pump (IABP)	Medical therapies and procedures	4.73	2.82

33	Endotracheal tube and tracheostomy management	Medical therapies and procedures	4.73	3.41
34	Sedation vacation	Medical therapies and procedures	4.64	2.55
35	Epidural	Medical therapies and procedures	4.64	3.73
36	Cardiac catheterization (e.g. angioplasty etc.)	Medical therapies and procedures	4.50	3.36
37	Renal replacement therapy (peritoneal dialysis, hemodialysis, arteriovenous / venovenous hemodialysis etc.)	Medical therapies and procedures	4.27	3.00
38	Pericardial drains	ICU lines, leads and/or equipment	4.91	3.05
39	Arterial lines (including pulmonary artery catheter)	ICU lines, leads and/or equipment	4.91	3.55
40	Chest tubes	ICU lines, leads and/or equipment	4.91	3.73
41	Intravenous lines	ICU lines, leads and/or equipment	4.91	4.09
42	Wound drains	ICU lines, leads and/or equipment	4.77	3.36
43	Intracranial pressure monitors	ICU lines, leads and/or equipment	4.73	2.50
44	Implantable central venous device (Port-a-cath)	ICU lines, leads and/or equipment	4.73	3.05
45	Nasogastric tubes	ICU lines, leads and/or equipment	4.73	3.77
46	Rectal pouch/tube	ICU lines, leads and/or equipment	4.50	2.73
47	Extra-ventricular drains (for hydrocephalus)	ICU lines, leads and/or equipment	4.41	2.77
48	Ambu bags	ICU lines, leads and/or equipment	3.77	2.23
49	Cardiac output/Ejection fraction/Cardiac index	Tests and Laboratory Findings	4.86	3.29
50	ECGs (e.g. tachycardia/bradycardia, atrial / ventricular tachy-dysrhythmias, premature contractions, heart blocks etc.)	Tests and Laboratory Findings	4.57	2.90
51	Cardiac pressures (central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure etc.)	Tests and Laboratory Findings	4.50	2.45
52	Common hematology (complete blood count, platelet count, Prothrombin time, APTT (activated partial thromboplastin time), INR (international normalized ratio)	Tests and Laboratory Findings	4.41	2.91

53	Arterial blood gases (pH, PaCO2, PaO2, PaO2/FiO2 ratio, HCO3-, base excess)	Tests and Laboratory Findings	4.33	2.90
54	Cerebral pressures (e.g. Intra-cranial pressure and cerebral perfusion pressure)	Tests and Laboratory Findings	4.32	2.45
55	Chest radiographs (without report)	Tests and Laboratory Findings	4.32	2.77
56	Blood glucose levels	Tests and Laboratory Findings	4.23	3.18
57	Fluid intake and output	Tests and Laboratory Findings	4.09	2.95
58	Presence of delirium	Assessment	4.95	3.41
59	Signs of respiratory distress (e.g. cyanosis, nasal flaring, intercostal indrawing, accessory muscle use, etc.)	Assessment	4.95	4.14
60	Cognitive function	Assessment	4.82	4.00
61	Physical function (e.g. Physical Function ICU Test, Functional Status Score-ICU)	Assessment	4.73	2.64
62	Level of consciousness (e.g. Glasgow Coma Score)	Assessment	4.68	3.55
63	Exercise tolerance	Assessment	4.59	4.32
64	Sedation level (e.g. Ramsey Sedation Scale, Richmond Agitation-Sedation Scale)	Assessment	4.55	2.64
65	Modified manual muscle testing: Medical Research Council sum score	Assessment	4.50	3.55
66	Mode of mechanical ventilation	Assessment	4.45	2.64
67	Ventilator alarms	Assessment	4.38	2.05
68	Level of assist (inspiratory pressure)/PEEP	Assessment	4.32	2.41
69	FiO_2 level	Assessment	4.32	2.59
70	Ventilator waveforms	Assessment	4.24	1.95
71	Cuff volume and/or pressure (cuff leaks)	Assessment	4.05	1.86
72	Screen for contraindications to exercise intervention	Critical Reasoning and Evaluation Skills	4.95	4.14
73	Integrate multiple sources of information (background information, assessment/evaluation tools, test results)	Critical Reasoning and Evaluation Skills	4.91	3.95

74	Evaluate and identify the mechanisms that result in the impaired lung ventilation	Critical Reasoning and Evaluation Skills	4.86	3.50
75	Evaluate and identify the mechanisms that result in the impaired airway clearance	Critical Reasoning and Evaluation Skills	4.86	3.82
76	Implement PT therapeutic interventions using appropriate dosage parameters	Critical Reasoning and Evaluation Skills	4.86	4.00
77	Select assessment/evaluation tools and techniques	Critical Reasoning and Evaluation Skills	4.86	4.00
78	Evaluate and identify the mechanisms that result in the impaired respiratory insufficiency	Critical Reasoning and Evaluation Skills	4.50	3.45
79	Evaluate and identify the mechanisms that result in the impaired gas exchange	Critical Reasoning and Evaluation Skills	4.27	2.95
80	Walking (while on a mechanical ventilator)	Physiotherapy Interventions	5.00	2.82
81	Walking (with lines and leads but no mechanical ventilator)	Physiotherapy Interventions	5.00	4.50
82	Cycling in or out of bed—passive & active	Physiotherapy Interventions	4.77	4.64
83	Positioning (for dyspnea, optimization of V/Q matching)	Physiotherapy Interventions	4.73	3.32
84	Standing with the assistance of a tilt table	Physiotherapy Interventions	4.59	4.09
85	End-inspiratory hold manoeuvres	Physiotherapy Interventions	4.45	3.32
86	Use of abdominal belts (spinal cord injury)	Physiotherapy Interventions	4.32	3.00
87	Manually assisted coughing techniques	Physiotherapy Interventions	4.27	3.73
88	Suctioning (tracheal / nasopharyngeal / oropharyngeal / closed suction)	Physiotherapy Interventions	3.73	2.68
89	Neuromuscular electrical stimulation (including indications, selection of appropriate dosage and contraindications in the critically ill)	Physiotherapy Interventions	3.18	2.50
90	Time and resource management in challenging situations e.g. caseload prioritization	Professional and Ethical practice	4.91	4.32

TABLE 2B: LIST OF EXCLUDED TOPIC AREAS

#	Items	Domain/Subdomain	Relevance	Knowledge
1	Musculoskeletal system (including muscle physiology, deconditioning & soft tissue healing)	Anatomy and/or physiology	4.86	4.64
2	Nervous system	Anatomy and/or physiology	4.64	4.14
3	Renal system	Anatomy and/or physiology	3.59	2.55
4	Immune system	Anatomy and/or physiology	3.32	2.45
5	Integumentary system (skin, hair, nails, and glands)	Anatomy and/or physiology	3.32	3.09
6	Endocrine system (hypothalamus, thyroid, pituitary, pineal, thyroid, parathyroid)	Anatomy and/or physiology	3.27	2.32
7	Lymphatic system	Anatomy and/or physiology	3.05	2.41
8	Hepatic & biliary systems	Anatomy and/or physiology	3.00	2.41
9	Hematopoietic system (bone marrow, spleen, tonsils, and lymph nodes— production of blood cellular elements)	Anatomy and/or physiology	2.91	2.27
10	Normal/abnormal responses to exercise	Exercise physiology	5.00	4.45
11	Effect of bedrest and inactivity	Exercise physiology	5.00	4.68
12	Principles of exercise prescription	Exercise physiology	4.77	4.41
13	Respiratory failure	Underlying pathophysiology and presenting features	4.86	4.18
14	Pneumonia	Underlying pathophysiology and presenting features	4.82	4.27
15	Thromboembolic disease	Underlying pathophysiology and presenting features	4.77	4.09
16	Obstructive respiratory disease	Underlying pathophysiology and presenting features	4.73	4.00

17	Stroke (thrombotic cerebrovascular accident, intracerebral hemorrhage)	Underlying pathophysiology and presenting features	4.64	4.32
18	Amyotrophic lateral sclerosis (ALS)	Underlying pathophysiology and presenting features	4.59	3.23
19	Multiple Sclerosis (MS)	Underlying pathophysiology and presenting features	4.59	3.68
20	Orthopaedic surgery	Underlying pathophysiology and presenting features	4.50	4.36
21	Traumatic brain injury	Underlying pathophysiology and presenting features	4.36	3.45
22	Lung abscess	Underlying pathophysiology and presenting features	4.23	3.14
23	Diabetes	Underlying pathophysiology and presenting features	4.23	3.77
24	Electrolyte imbalances (e.g. hypo/hypernatremia)	Underlying pathophysiology and presenting features	4.14	3.41
25	Cancer	Underlying pathophysiology and presenting features	3.95	3.64
26	Fat embolism	Underlying pathophysiology and presenting features	3.82	2.45
27	Immune deficiency	Underlying pathophysiology and presenting features	3.59	2.59
28	Burns (inhalational and/or cutaneous)	Underlying pathophysiology and presenting features	3.55	2.41
29	Pancreatitis	Underlying pathophysiology and presenting features	3.45	2.91
30	Hepatitis	Underlying pathophysiology and presenting features	3.09	2.73

31	Transplantation	Underlying pathophysiology and presenting features	3.05	2.32
32	Nitrates	Pharmacology	4.18	2.41
33	Calcium channel blockers	Pharmacology	4.09	2.36
34	ACE inhibitors	Pharmacology	4.05	2.36
35	Antiplatelets medications	Pharmacology	3.91	2.86
36	Mucolytics	Pharmacology	3.86	2.55
37	Cardiac glycosides	Pharmacology	3.36	2.00
38	Patient controlled analgesia (PCA)	Medical therapies and procedures	4.59	4.14
39	Extra Corporeal Membrane Oxygenation (ECMO)	Medical therapies and procedures	4.55	2.27
40	Ventricular assist device (e.g. LVAD)	Medical therapies and procedures	4.27	2.45
41	Bronchoscopy	Medical therapies and procedures	4.27	3.36
42	Whole body hypothermia or cooling	Medical therapies and procedures	4.18	2.27
43	Bronchial lavage	Medical therapies and procedures	3.77	2.59
44	Biopsy	Medical therapies and procedures	3.68	3.27
45	Abdominal tap	Medical therapies and procedures	3.59	2.82
46	Thoracentesis	Medical therapies and procedures	3.27	2.45
47	Foley catheters	ICU lines, leads and/or equipment	4.86	4.41
48	Infection control principles	ICU lines, leads and/or equipment	4.77	4.36
49	Transcutaneous oxygen saturation (SpO2)	Tests and Laboratory Findings	4.91	4.64
50	CT – Chest	Tests and Laboratory Findings	4.36	2.86
51	Cardiac markers (e.g. Troponin, Creatinine kinase)	Tests and Laboratory Findings	4.32	2.59
52	Ventilation-perfusion scan (V/Q scan)	Tests and Laboratory Findings	4.27	2.41

53	Skeletal X-rays (without report)	Tests and Laboratory Findings	4.27	3.09
54	MRI – Chest	Tests and Laboratory Findings	4.18	2.64
55	Ultrasound – Chest	Tests and Laboratory Findings	4.09	2.50
56	Electroencephalograms (EEG)	Tests and Laboratory Findings	4.05	2.59
57	Lung PET scan	Tests and Laboratory Findings	3.95	2.16
58	Renal function (e.g. urea, creatinine)	Tests and Laboratory Findings	3.86	2.45
59	Electrolytes levels (e.g. Na+, K+, CL-, Ca2+, Mg2+)	Tests and Laboratory Findings	3.82	2.59
60	Bone scan	Tests and Laboratory Findings	3.82	2.68
61	Oxygen content (CaO2)	Tests and Laboratory Findings	3.75	2.10
62	Venous blood gas interpretation (including SvO2)	Tests and Laboratory Findings	3.71	1.86
63	End-tidal carbon dioxide (PETCO2)	Tests and Laboratory Findings	3.67	1.94
64	Blood lactate	Tests and Laboratory Findings	3.45	2.05
65	Liver function tests (e.g. ALT, LDH, Bilirubin)	Tests and Laboratory Findings	3.27	2.05
66	Signs of vascular disorder	Assessment	4.95	4.45
67	Blood pressure (systolic, diastolic, mean arterial pressure)	Assessment	4.95	4.55
68	Dyspnea (e.g. VAS, Borg etc.)	Assessment	4.95	4.55
69	Pain	Assessment	4.95	4.73
70	Muscle strength	Assessment	4.95	4.82
71	Breath sounds (auscultation)	Assessment	4.91	4.27
72	Breathing pattern (e.g. rate, depth, paradox etc.)	Assessment	4.91	4.50
73	Fatigue	Assessment	4.91	4.59
74	Cough strength - quality and effectiveness	Assessment	4.91	4.59

75	Muscle atrophy	Assessment	4.91	4.73
76	Heart rate/pulse rate	Assessment	4.91	4.77
77	Functional mobility (e.g. rolling, transfers, ambulation)	Assessment	4.90	4.81
78	Muscle tone	Assessment	4.86	4.45
79	Neurological level impairment (e.g. dermatomes, myotomes and reflexes)	Assessment	4.86	4.59
80	Sensation	Assessment	4.82	4.59
81	Joint range of motion (ROM)	Assessment	4.82	4.86
82	Sputum assessment (colour, quantity, quality)	Assessment	4.77	4.41
83	Emotional state	Assessment	4.73	3.95
84	Anxiety level	Assessment	4.73	4.09
85	Skin integrity	Assessment	4.64	4.18
86	Balance assessment	Assessment	4.59	4.45
87	Cranial nerve function	Assessment	4.45	3.41
88	Patient cooperation [e.g. Standardized Five Questions (S5Q)]	Assessment	4.45	2.60
89	Body temperature	Assessment	4.41	4.41
90	Homan's sign	Assessment	4.25	4.00
91	Sit to stand test	Assessment	4.14	4.77
92	Ankle-brachial index	Assessment	3.67	2.72
93	Limb girth	Assessment	3.62	3.81
94	Hand grip strength (Jamar) for MRC >= 3	Assessment	3.53	4.00
95	Muscle strength assessment using a hand-held dynamometer	Assessment	3.23	4.18
96	Timed up and go test	Assessment	2.95	4.77

97	Mediate percussion	Assessment	2.78	2.44
98	6-minute walk test	Assessment	2.59	4.73
99	Develop a prioritized problem list	Critical Reasoning and Evaluation Skills	4.91	4.32
100	Chose physiological parameters to monitor during exercise	Critical Reasoning and Evaluation Skills	4.86	4.09
101	Evaluate the effectiveness of PT interventions and makes appropriate adjustments	Critical Reasoning and Evaluation Skills	4.86	4.14
102	Integrate clinical and physiological parameters during exercise to determine exercise safety, risk, and termination	Critical Reasoning and Evaluation Skills	4.86	4.18
103	Formulate a treatment plan	Critical Reasoning and Evaluation Skills	4.86	4.27
104	Identify the need for referral to other healthcare professionals	Critical Reasoning and Evaluation Skills	4.86	4.27
105	Determine an appropriate patient reassessment schedule	Critical Reasoning and Evaluation Skills	4.82	4.09
106	Establish a physiotherapy prognosis	Critical Reasoning and Evaluation Skills	4.77	4.00
107	Make a differential physiotherapy diagnosis (or clinical impression)	Critical Reasoning and Evaluation Skills	4.68	4.09
108	Identify the need for further information/data	Critical Reasoning and Evaluation Skills	4.68	4.14
109	Evaluated and identify the mechanisms that result in the impaired muscle weakness	Critical Reasoning and Evaluation Skills	4.68	4.27
110	Evaluate and identify the mechanisms that result in the impaired functional limitations	Critical Reasoning and Evaluation Skills	4.68	4.36
111	Upright sitting a chair	Physiotherapy Interventions	5.00	4.77

112	Standing	Physiotherapy Interventions	5.00	4.82
113	Transferring from the bed or chair (use of hoist, use of slide, sit-stand-pivot transfer)	Physiotherapy Interventions	4.95	4.50
114	Stepping in place	Physiotherapy Interventions	4.95	4.82
115	Chair exercises	Physiotherapy Interventions	4.95	4.86
116	Coughing manoeuvres	Physiotherapy Interventions	4.91	4.41
117	Use of walking and standing aids/frames	Physiotherapy Interventions	4.91	4.50
118	Incentive spirometry	Physiotherapy Interventions	4.91	4.91
119	Active-assisted and active exercise	Physiotherapy Interventions	4.91	4.91
120	Sitting over the edge of the bed	Physiotherapy Interventions	4.91	4.91
121	Instructing the patient on how to cough effectively	Physiotherapy Interventions	4.86	4.45
122	Bed exercises	Physiotherapy Interventions	4.82	4.91
123	Forced expiratory techniques (huffing)	Physiotherapy Interventions	4.77	4.41
124	Joint range of motion exercises	Physiotherapy Interventions	4.77	4.86
125	Breathing exercises (e.g. pursed-lip breathing, breathing control/relaxed diaphragmatic, segmental)	Physiotherapy Interventions	4.64	4.45
126	Percussion (clapping)	Physiotherapy Interventions	4.59	4.36
127	Chest vibration/ shaking (fine and coarse)	Physiotherapy Interventions	4.55	4.23
128	Respiratory muscle training	Physiotherapy Interventions	4.50	3.27
129	Active cycle breathing	Physiotherapy Interventions	4.45	3.95
130	Splinting for pain	Physiotherapy Interventions	4.36	3.68
131	Stretching	Physiotherapy Interventions	4.36	4.50
132	Relaxation training	Physiotherapy Interventions	4.32	3.95
133	Tracheal stimulation, tickle etc.	Physiotherapy Interventions	4.27	2.91

134	Postural drainage or modified drainage	Physiotherapy Interventions	3.91	3.45
135	Use of PEP devices	Physiotherapy Interventions	3.59	2.41
136	Intermittent, short-term application of NIV/BiPAP during physiotherapy to assist secretion mobilization techniques	Physiotherapy Interventions	3.36	1.82
137	Secretion mobilization during bronchoscopy	Physiotherapy Interventions	3.23	1.95
138	Aerosol therapy	Physiotherapy Interventions	3.14	2.18
139	Manual hyperinflation	Physiotherapy Interventions	3.09	2.00
140	Use of high-frequency chest wall oscillators (Vest)	Physiotherapy Interventions	2.95	1.86
141	Use of oscillating PEP devices (e.g. Acapella, Flutter, intrapulmonary percussive ventilation)	Physiotherapy Interventions	2.82	1.77
142	Ventilator hyperinflation	Physiotherapy Interventions	2.77	1.68
143	Advocate for patient early mobilization (or quality of care)	Professional and Ethical practice	4.95	4.59
144	Practice in a safe and secure manner that minimizes risk to clients, self, and others	Professional and Ethical practice	4.95	4.73
145	Respect the rights of the patient (information privacy/confidentiality)	Professional and Ethical practice	4.95	4.95
146	Critically evaluate and apply research relevant to practice (best evidence)	Professional and Ethical practice	4.91	4.00
147	Demonstrate effective communication skills (with patients and other ICU professionals)	Professional and Ethical practice	4.91	4.64
148	Take professional, clinical, resource and economic factors into consideration	Professional and Ethical practice	4.82	4.41

FIGURES

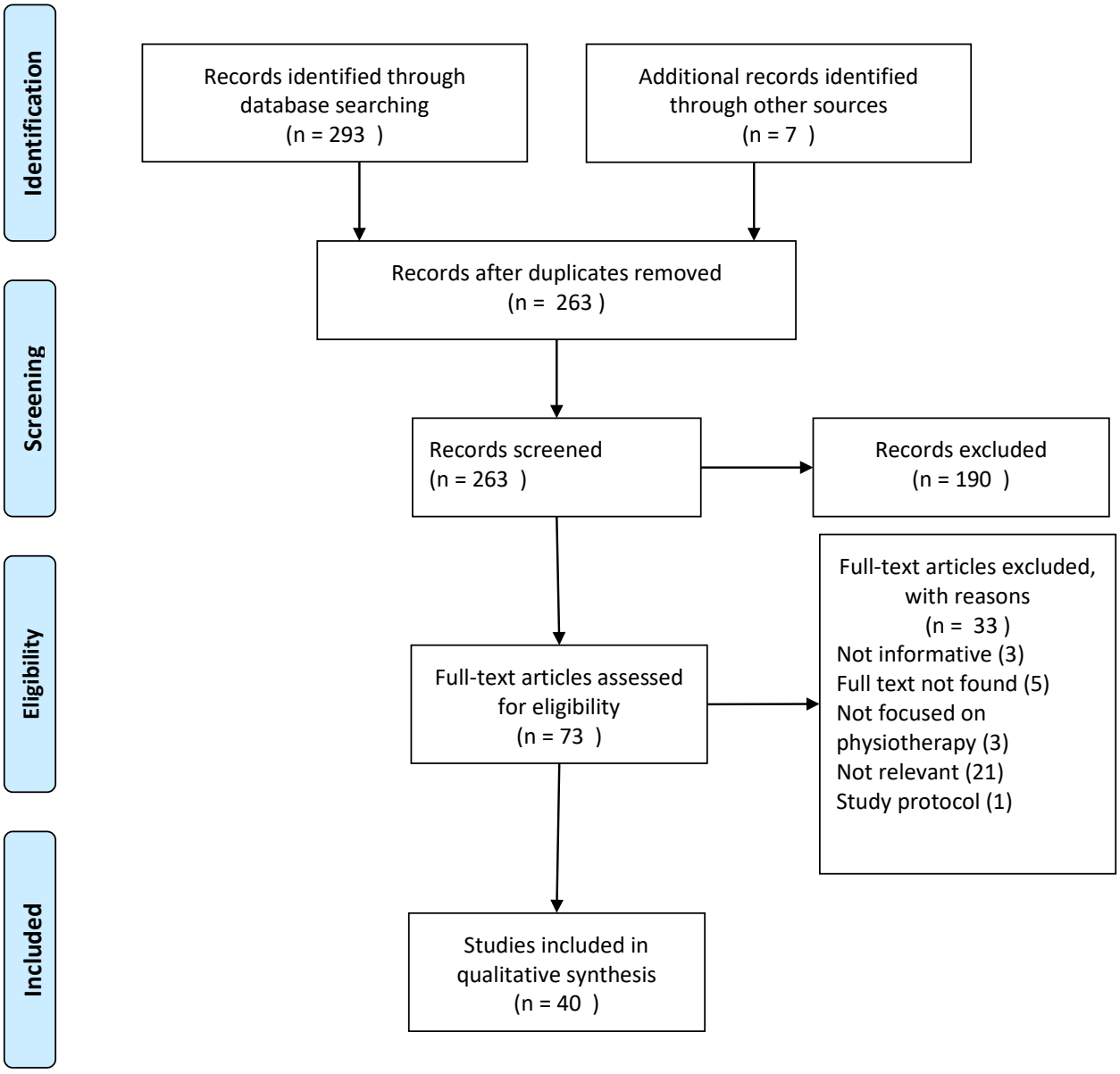

Figure 1 PRISMA Flow Diagram

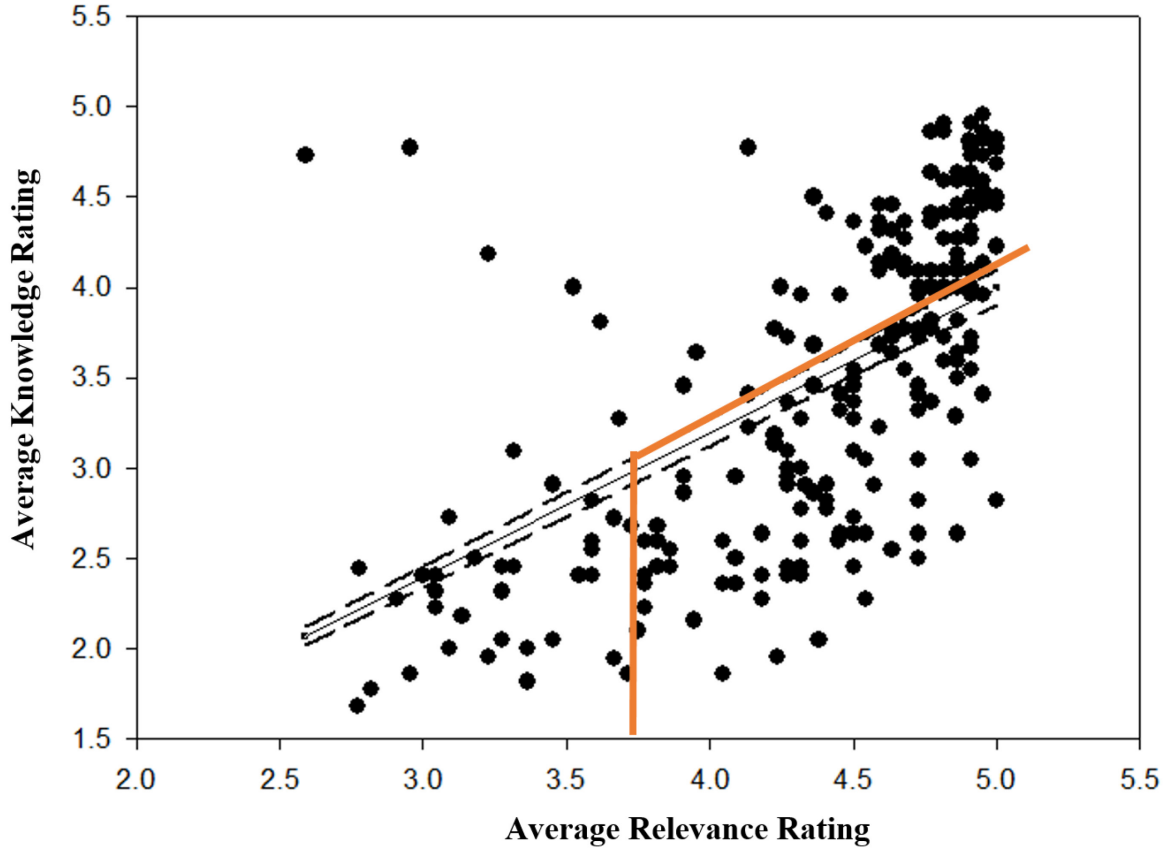

Figure 2: Scatter plot with regression line and the regression line confidence interval. The data points represent the average of the 238 topic areas rated by the study respondents. The statistical method applied identified 113 topic areas which fell below the upper confidence interval for the line of best fit and which had an average relevance rating greater than 3.75 (upper quartile of relevance range), corresponding to the points under and to the right of the orange lines, respectively.

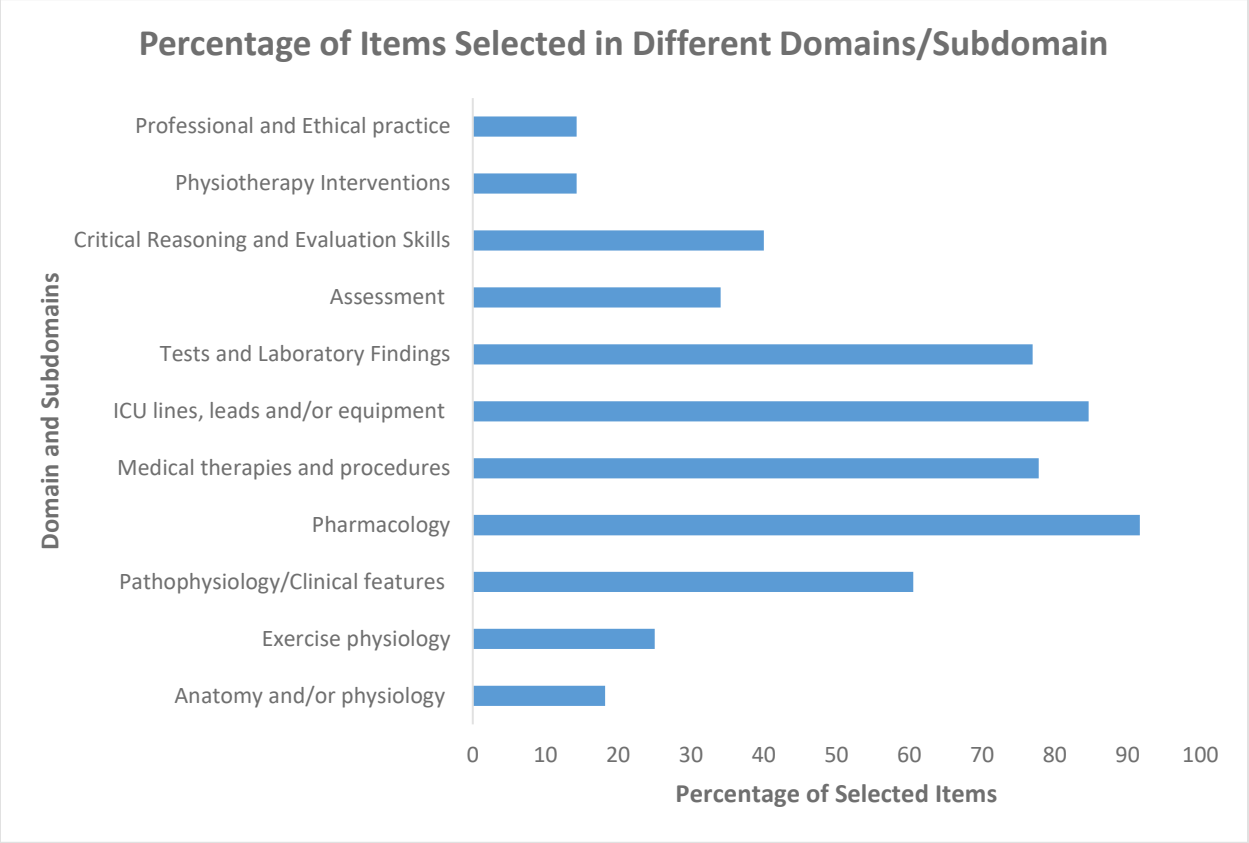

Figure 3a: Percentage of Items Selected within Each Domain/Subdomain

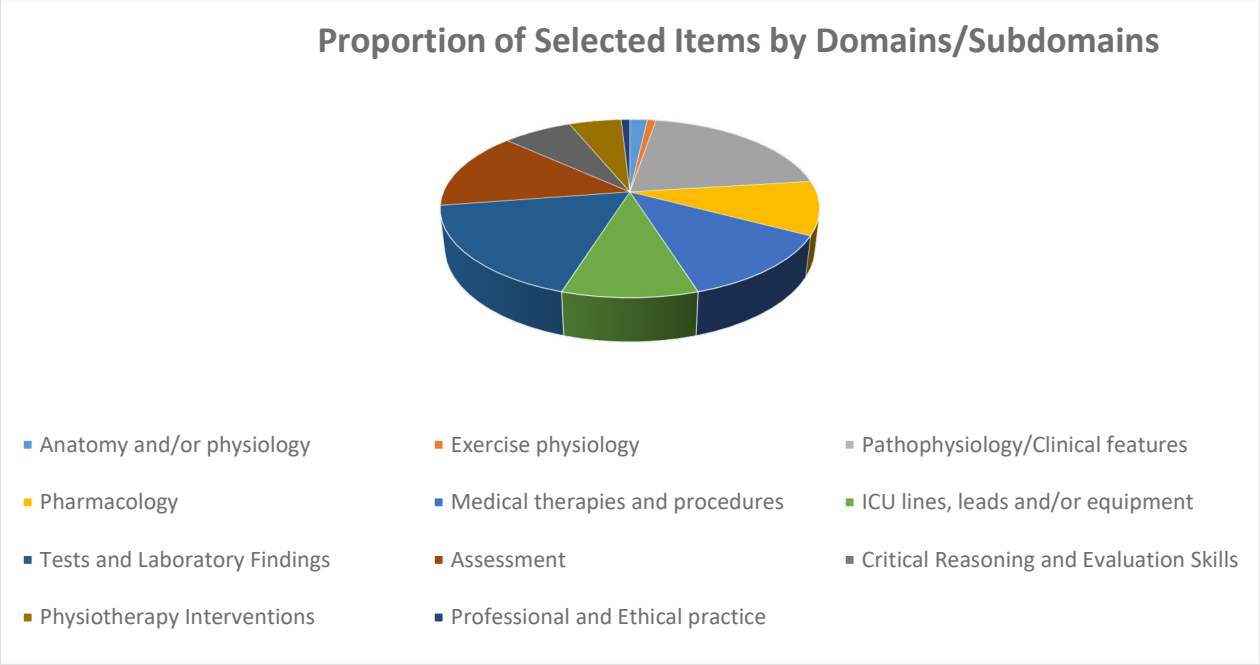

Figure 3b: Proportion of All Selected Items by Domain/Subdomain

APPENDICES

Appendix I: Search Strategy

Ovid Medline 1946-

1. Physical Therapy Specialty/
2. Physical Therapists/
3. physiotherap*
4. physical therap*
5. Critical Care/
6. Intensive Care Units/
7. Respiratory Care Units/
8. intensive care unit*
9. Knowledge/
10. Health Knowledge, Attitudes, Practice/
11. Knowledge Bases/
12. Clinical Competence/
13. Social Skills/
14. "Standard of Care"/
15. Professional Practice/
16. Reference Standards/
17. Education/
18. Competency-Based Education/
19. Education, Continuing/
20. Education, Professional/
21. Education, Medical/
22. Education, Professional, Retraining/
23. Education, Medical, Continuing/
24. Practice Guideline/
25. Practice Guidelines as Topic/
26. Professional Competence/
27. clinical skill*
28. OR/Lines 1-4
29. OR/Lines 5-8
30. OR/Lines 9-27
31. AND/Lines 28,29,30

Appendix II: Reasons for Exclusions

Not informative abstracts

1. Breeding J, Buscher H, Nair P, et al. Evaluating learning in an ECMO workshop. Anaesthesia and Intensive Care. 2016;44 (2):315-316.
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Full text not found

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Not focused on physiotherapy

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Not relevant

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19. Dinh TA. Measuring the impact of a caregiver education and awareness campaign on hand-hygiene in an adult critical care unit. American Journal of Infection Control. 2014;1): S76-S77.
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Study protocol

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Appendix III

The Survey Questionnaire

Foundational Knowledge Items

*Please rate the relevance for PT practice in the ICU and your personal knowledge for each of the following topics with **'1' meaning 'Not at all'** and **'5' meaning 'A great deal'***

Knowledge	Perceived Relevance					Personal knowledge				
1. Anatomy and/or physiology of the following systems	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Respiratory system										
b. Cardiovascular system										
c. Lymphatic system										
d. Renal system										
e. Immune system										
f. Endocrine system (hypothalamus, thyroid, pituitary, pineal, thyroid, parathyroid)										
g. Hematopoietic system (bone marrow, spleen, tonsils, and lymph nodes— production of blood cellular elements)										
h. Hepatic system and biliary systems										
i. Musculoskeletal system (including muscle physiology, deconditioning & soft tissue healing)										
j. Nervous system										
k. Integumentary system (skin, hair, nails, and glands)										
2. Exercise physiology	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Normal and abnormal responses										
b. Effect of bedrest and inactivity										
c. Physiological monitoring										
d. Principles of exercise prescription										
3. Underlying pathophysiology and presenting features of the following conditions										
Respiratory Conditions	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Pneumonia										
b. Respiratory failure										
c. Lung abscess										
d. Obstructive respiratory disease										
e. Restrictive respiratory disease										
f. Acute lung injury/acute respiratory distress syndrome (ARDS)										
g. Pleural conditions (e.g. pleural effusions)										
h. Chest trauma										
i. Burns (inhalational and/or cutaneous)										
Cardiovascular Conditions	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Acute coronary syndrome (e.g. angina, STEMI/non-STEMI)										
b. Heart failure										
c. Other cardiac conditions (e.g. cardiomyopathy, pericarditis, pericardial effusion, tamponade, endocarditis, valvular heart disease, aortic stenosis, myocarditis etc.)										

Knowledge	Perceived Relevance					Personal knowledge				
d. Fat embolism										
e. Thromboembolic disease (e.g. deep vein thrombosis, pulmonary embolus etc.)										
Surgical conditions including approaches, incisions and associated complications	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Cardiac surgery (e.g. coronary artery bypass graft etc.)										
b. Thoracic surgery										
c. Abdominal surgery										
d. Orthopaedic surgery										
e. Vascular surgery										
Other Medical Conditions	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Renal failure (acute / chronic)										
b. Pancreatitis										
c. Shock (cardiogenic, neurogenic, allergic etc.)										
d. Immune deficiency										
e. Systemic inflammatory response syndrome (SIRS)										
f. Multi-organ dysfunction syndrome (MODS)										
g. ICU-acquired weakness (ICU-AW)										
h. Hepatitis										
i. Brain death, organ procurement										
j. Transplantation										
k. Diabetes										
l. Electrolyte imbalances (e.g. hypo/hypernatremia)										
m. Cancer										
Neurological Conditions	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Guillain–Barre Syndrome										
b. Stroke (thrombotic cerebrovascular accident, intracerebral hemorrhage)										
c. Traumatic brain injury										
d. Spinal cord injury										
e. Multiple Sclerosis (MS)										
f. Amyotrophic lateral sclerosis (ALS)										
4. Pharmacology: The following medications (including their actions and implication for PT interventions)	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Nitrates										
b. Beta blockers										
c. Calcium channel blockers										
d. Sedatives										
e. Neuromuscular paralyzing agents										
f. Bronchodilators										
g. Mucolytics										
h. Analgesics										
i. Antiplatelets medications										
j. Diuretics										
k. Cardiac glycosides										
l. ACE inhibitors										

Knowledge	Perceived Relevance					Personal knowledge				
5. The following medical therapies and procedures	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Bronchoscopy										
b. Bronchial lavage										
c. Thoracentesis										
d. Biopsy										
e. Abdominal tap										
f. Ventricular assist device (e.g. LVAD)										
g. Intra-aortic balloon pump (IABP)										
h. Extra Corporeal Membrane Oxygenation (ECMO)										
i. Whole body hypothermia or cooling										
j. Cardiac catheterization (e.g. angioplasty etc.)										
k. Epidural										
l. Patient controlled analgesia (PCA)										
m. Renal replacement therapy (peritoneal dialysis, hemodialysis, arteriovenous / venovenous hemodialysis etc.)										
n. Pacemakers (temporary, automated external defibrillators etc.)										
o. Endotracheal tube and tracheostomy management										
p. Ventilator weaning										
q. Sedation vacation										
r. Supplemental oxygen (including delivery devices)										
6. The following ICU lines, leads and/or equipment	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Arterial lines (including pulmonary artery catheter)										
b. Intravenous lines										
c. Implantable central venous device (Port-a-cath)										
d. Wound drains										
e. Nasogastric tubes										
f. Chest tubes										
g. Pericardial drains										
h. Rectal pouch/tube										
i. Extra-ventricular drains (for hydrocephalus)										
j. Intracranial pressure monitors										
k. Ambu bags										
l. Foley catheters										
7. Others	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Infection control principles (standard and isolation precautions)										

Tests and Laboratory Findings

Please rate the relevance for PT practice in the ICU and your personal knowledge for each of the following topics with ***'1' meaning 'Not at all'*** *and* ***'5' meaning 'A great deal'***

Knowledge	Perceived Relevance					Personal Knowledge				
	1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
1. **Knowledge/interpretation of the following tests and laboratory findings**										
a. Arterial blood gases (pH, $PaCO_2$, PaO_2, PaO_2/FiO_2 ratio, HCO_3^-, base excess)										
b. Transcutaneous oxygen saturation (SpO_2)										
c. End-tidal carbon dioxide ($P_{ET}CO_2$)										
d. Oxygen content (CaO_2)										
e. Venous blood gas interpretation [including SvO_2])										
f. Cardiac pressures (central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure etc.)										
g. Cardiac output/Ejection fraction/Cardiac index										
h. ECGs (e.g. tachycardia/bradycardia, atrial / ventricular tachy-dysrhythmias, premature contractions, heart blocks etc.)										
i. Fluid intake and output										
j. Cerebral pressures (e.g. Intra-cranial pressure and cerebral perfusion pressure)										
k. Common hematology (complete blood count, platelet count, Prothrombin time, APTT (activated partial thromboplastin time), INR (international normalized ratio)										
l. Renal function (e.g. urea, creatinine)										
m. Blood glucose levels										
n. Electrolytes levels (e.g. Na+, K+, CL-, Ca2+, Mg2+)										
o. Liver function tests (e.g. ALT, LDH, Bilirubin)										
p. Cardiac markers (e.g. Troponin, Creatinine kinase)										
q. Blood lactate										
r. Chest radiographs (without report)										
s. Skeletal X-rays (without report)										
t. Ventilation-perfusion scan (V/Q scan)										
u. Lung PET scan										
v. Bone scan										
w. CT – Chest										
x. MRI – Chest										
y. Ultrasound – Chest										
z. Electroencephalograms (EEG)										

Assessment

*Please rate the relevance for PT practice in the ICU and your personal knowledge/skill for each of the following topics with **'1' meaning 'Not at all'** and **'5' meaning 'A great deal'***

	Perceived Relevance					**Personal Knowledge/Skill**				
	1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
1. **Knowledge and ability to assess and/or interpret the following are essential to PT practice in the ICU?**										
a. Body temperature										
b. Heart rate/pulse rate										
c. Breathing pattern (e.g. rate, depth, paradox etc.)										
d. Blood pressure (systolic, diastolic, mean arterial pressure)										
e. Pain										
f. Dyspnea (e.g. VAS, Borg etc.)										
g. Fatigue										
h. Presence of delirium (e.g. CAM-ICU)										
i. Sedation level (e.g. Ramsey Sedation Scale, Richmond Agitation-Sedation Scale)										
j. Level of consciousness (e.g. Glasgow Coma Score)										
k. Patient cooperation [e.g. Standardized Five Questions (S5Q)]										
l. Cognitive function										
m. Emotional state										
n. Anxiety level										
o. Signs of respiratory distress (e.g. cyanosis, nasal flaring, intercostal indrawing, accessory muscle use, etc.)										
p. Signs of vascular disorder (e.g. limb redness, swelling etc.)										
q. Skin integrity										
r. Cough strength - quality and effectiveness										
s. Sputum assessment (colour, quantity, quality)										
t. Breath sounds (auscultation)										
u. Joint range of motion (ROM)										
v. Muscle atrophy										
w. Muscle strength										
x. Neurological level impairment (e.g. dermatomes, myotomes and reflexes)										
y. Sensation										
z. Cranial nerve function										
aa. Muscle tone										
bb. Functional mobility (e.g. rolling, transfers, ambulation)										
cc. Physical function (e.g. Physical Function ICU Test, Functional Status Score-ICU)										
dd. Balance assessment										
ee. Exercise tolerance										

	Perceived Relevance					Personal Knowledge/Skill				
2. **Knowledge and ability to perform and interpret the following are essential to PT practice in the ICU?**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Homan's sign										
b. Limb girth										
c. Ankle-brachial index										
d. Mediate percussion										
e. Modified manual muscle testing: Medical Research Council (MRC) sum score										
f. Muscle strength assessment using a hand-held dynamometer										
g. Hand grip strength (Jamar) for MRC >= 3										
h. Sit to stand test										
i. Timed up and go test										
j. 6-minute walk test										
3. Assess mechanical ventilation settings/integrity	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Mode of mechanical ventilation										
b. FiO_2 level										
c. Level of assist (inspiratory pressure)/PEEP										
d. Ventilator alarms										
e. Ventilator waveforms										
f. Cuff volume and/or pressure (cuff leaks)										

Critical Reasoning and Evaluation Skills

*Please rate the relevance for PT practice in the ICU and your personal competence for each of the following with '**1' meaning 'Not at all'** and **'5' meaning 'A great deal'***

	Perceived Relevance					**Personal Competence**				
1. The following critical reasoning and evaluation skills	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Ability to:										
a. Select appropriate assessment/evaluation tools and techniques.										
b. Integrate multiple sources of information (background information, assessment/evaluation tools, test results)										
c. Identify the need for further information/data										
d. Evaluate and identify the mechanisms that result in the impaired	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
i. airway clearance										
ii. lung ventilation										
iii. gas exchange										
iv. respiratory insufficiency										
v. muscle weakness										
vi. functional limitations										
e. Make a differential physiotherapy diagnosis										
f. Develop a prioritized problem list										
g. Establish a physiotherapy prognosis										
h. Screen for contraindications to exercise intervention										
i. Formulate a treatment plan										
j. Identify the need for referral to other healthcare professionals										
k. Determine an appropriate patient reassessment schedule										
l. Chose physiological parameters to monitor during exercise										
m. Integrate clinical and physiological parameters during exercise to determine exercise safety, risk and termination										
n. Implement PT therapeutic interventions using appropriate dosage parameters										
o. Evaluate the effectiveness of PT interventions and makes appropriate adjustments										

Physiotherapy Interventions

Please rate the relevance for PT practice in the ICU and your personal knowledge/skill for each of the following topics with ***'1' meaning 'Not at all'*** *and* ***'5' meaning 'A great deal'***

	Perceived Relevance					**Personal Knowledge/Skill**				
	1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
1. Knowledge of the physiological basis, contraindications and how to perform:										
a. Airway clearance techniques										
i. Coughing manoeuvres										
ii. Instructing the patient on how to cough effectively										
iii. Tracheal stimulation, tickle etc.										
iv. Manually assisted coughing techniques										
v. Forced expiratory techniques (huffing)										
vi. Active cycle breathing										
vii. Percussion (clapping)										
viii. Chest vibration/ shaking (fine and coarse)										
ix. Postural drainage or modified drainage										
x. Use of PEP devices										
xi. Use of high-frequency chest wall oscillators (Vest)										
xii. Use of oscillating PEP devices (e.g. Acapella, Flutter, intrapulmonary percussive ventilation)										
xiii. Suctioning (tracheal / nasopharyngeal / oropharyngeal / closed suction)										
xiv. Aerosol therapy (nebulization and humidification)										
xv. Assisting bronchoscopy via delivery of secretion mobilization techniques (e.g. vibrations, assisted coughing)										
xvi. Intermittent, short-term application of NIV/BiPAP during physiotherapy to assist secretion mobilization techniques										
b. Positioning (for dyspnea, optimization of V/Q matching)										
c. End-inspiratory hold manoeuvres										
d. Manual hyperinflation										
e. Ventilator hyperinflation										
f. Breathing exercises (e.g. pursed-lip breathing, breathing control/relaxed diaphragmatic, segmental)										
g. Incentive spirometry										
h. Relaxation training										
i. Joint range of motion exercises										
j. Bed exercises										
k. Active-assisted and active exercise										
l. Cycling in or out of bed—passive & active										
m. Sitting over the edge of the bed										

	Perceived Relevance					Personal Knowledge/Skill				
n. Transferring from the bed or chair (use of hoist, use of slide, sit-stand-pivot transfer)										
o. Upright sitting a chair										
p. Chair exercises										
q. Standing with the assistance of a tilt table										
r. Standing										
s. Stepping in place										
t. Walking (with lines and leads but no mechanical ventilator)										
u. Walking (while on a mechanical ventilator)										
v. Stretching										
w. Splinting for pain										
x. Use of walking and standing aids/frames										
y. Use of abdominal belts (spinal cord injury)										
z. Respiratory muscle training										
aa. Neuromuscular electrical stimulation (including indications, selection of appropriate dosage and contraindications in the critically ill)										

Professional and Ethical practice

*Please rate the relevance for PT practice in the ICU and your personal ability for each of the following with '**1' meaning 'Not at all'** and **'5' meaning 'A great deal'***

	Perceived Relevance					**Personal Ability**				
1. **Ability to**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
a. Advocate for patient early mobilization (or quality of care)										
b. Respect the rights of the patient (information privacy/confidentiality)										
c. Take professional, clinical, resource and economic factors into consideration										
d. Critically evaluate and apply research relevant to practice (best evidence)										
e. Time and resource management in challenging situations e.g. caseload prioritization										
f. Practice in a safe and secure manner that minimizes risk to clients, self and others										
g. Demonstrate effective communication skills (with patients and other ICU professionals)										

Demographics

1. How many years have you been practising as a PT? _____
2. Do you work part time or full time?
    a. Part time
    b. Full time
3. On the average, how many days do you work as a PT per week? _____
4. Have you ever treated patients in the ICU?
    a. Yes
    b. No
5. If yes, what year did you start treating patients in the ICU? _____
6. On the average, how frequently do you work in the ICU?
    a. Daily
    b. Few times in a week
    c. Few times in a month
    d. Few times in a year
    e. Others: please specify _____

Appendix 4A: 113 Topics Selected by the Statistical Approach

1. Respiratory system
2. Cardiovascular system
3. Physiological monitoring
4. ICU-acquired weakness (ICU-AW)
5. Cardiac surgery (e.g. coronary artery bypass graft etc.)
6. Heart failure
7. Thoracic surgery
8. Other cardiac conditions (e.g. cardiomyopathy, pericarditis, pericardial effusion, tamponade, endocarditis, valvular heart disease, aortic stenosis, myocarditis etc.)
9. Pleural conditions (e.g. pleural effusions)
10. Acute coronary syndrome (e.g. angina, STEMI/non-STEMI)
11. Vascular surgery
12. Acute lung injury/acute respiratory distress syndrome (ARDS)
13. Guillain–Barre Syndrome
14. Restrictive respiratory disease
15. Spinal cord injury
16. Abdominal surgery
17. Amyotrophic lateral sclerosis (ALS)
18. Multiple Sclerosis (MS)
19. Shock (cardiogenic, neurogenic, allergic etc.)
20. Traumatic brain injury
21. Lung abscess
22. Renal failure (acute / chronic)
23. Chest trauma
24. Fat embolism
25. Systemic inflammatory response syndrome (SIRS)
26. Multi-organ dysfunction syndrome (MODS)
27. Analgesics
28. Sedatives
29. Beta blockers
30. Bronchodilators
31. Neuromuscular paralyzing agents
32. Diuretics
33. Nitrates
34. Calcium channel blockers
35. ACE inhibitors
36. Antiplatelets medications
37. Mucolytics
38. Ventilator weaning
39. Pacemakers (temporary, automated external defibrillators etc.)
40. Supplemental oxygen (including delivery devices)
41. Intra-aortic balloon pump (IABP)
42. Endotracheal tube and tracheostomy management
43. Sedation vacation
44. Epidural
45. Extra Corporeal Membrane Oxygenation (ECMO)
46. Cardiac catheterization (e.g. angioplasty etc.)

47. Ventricular assist device (e.g. LVAD)
48. Renal replacement therapy (peritoneal dialysis, hemodialysis, arteriovenous / venovenous hemodialysis etc.)
49. Bronchoscopy
50. Whole body hypothermia or cooling
51. Bronchial lavage
52. Pericardial drains
53. Arterial lines (including pulmonary artery catheter)
54. Chest tubes
55. Intravenous lines
56. Wound drains
57. Intracranial pressure monitors
58. Implantable central venous device (Port-a-cath)
59. Nasogastric tubes
60. Rectal pouch/tube
61. Extra-ventricular drains (for hydrocephalus)
62. Ambu bags
63. Cardiac output/Ejection fraction/Cardiac index
64. ECGs (e.g. tachycardia/bradycardia, atrial / ventricular tachy-dysrhythmias, premature contractions, heart blocks etc.)
65. Cardiac pressures (central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure etc.)
66. Common hematology (complete blood count, platelet count, Prothrombin time, APTT (activated partial thromboplastin time), INR (international normalized ratio)
67. CT – Chest
68. Arterial blood gases (pH, PaCO2, PaO2, PaO2/FiO2 ratio, HCO3-, base excess)
69. Cerebral pressures (e.g. Intra-cranial pressure and cerebral perfusion pressure)
70. Cardiac markers (e.g. Troponin, Creatinine kinase)
71. Chest radiographs (without report)
72. Ventilation-perfusion scan (V/Q scan)
73. Skeletal X-rays (without report)
74. Blood glucose levels
75. MRI – Chest
76. Ultrasound – Chest
77. Fluid intake and output
78. Electroencephalograms (EEG)
79. Lung PET scan
80. Renal function (e.g. urea, creatinine)
81. Electrolytes levels (e.g. Na+, K+, CL-, Ca2+, Mg2+)
82. Bone scan
83. Presence of delirium
84. Signs of respiratory distress (e.g. cyanosis, nasal flaring, intercostal indrawing, accessory muscle use, etc.)
85. Cognitive function
86. Physical function (e.g. Physical Function ICU Test, Functional Status Score-ICU)
87. Level of consciousness (e.g. Glasgow Coma Score)
88. Sedation level (e.g. Ramsey Sedation Scale, Richmond Agitation-Sedation Scale)
89. Modified manual muscle testing: Medical Research Council sum score
90. Mode of mechanical ventilation

91. Cranial nerve function
92. Patient cooperation [e.g. Standardized Five Questions (S5Q)]
93. Body temperature
94. Ventilator alarms
95. Level of assist (inspiratory pressure)/PEEP
96. FiO2 level
97. Ventilator waveforms
98. Cuff volume and/or pressure (cuff leaks)
99. Screen for contraindications to exercise intervention
100. Integrate multiple sources of information (background information, assessment/evaluation tools, test results)
101. Evaluate and identify the mechanisms that result in the impaired lung ventilation
102. Evaluate and identify the mechanisms that result in the impaired airway clearance
103. Implement PT therapeutic interventions using appropriate dosage parameters
104. Select assessment/evaluation tools and techniques
105. Evaluate and identify the mechanisms that result in the impaired respiratory insufficiency
106. Evaluate and identify the mechanisms that result in the impaired gas exchange
107. Walking (while on a mechanical ventilator)
108. Positioning (for dyspnea, optimization of V/Q matching)
109. Respiratory muscle training
110. End-inspiratory hold manoeuvres
111. Use of abdominal belts (spinal cord injury)
112. Tracheal stimulation, tickle etc.
113. Critically evaluate and apply research relevant to practice (best evidence)

Appendix 4B: Topics Included by the Statistical Approach but Excluded by Expert Consensuses

1. Amyotrophic lateral sclerosis (ALS)
2. Multiple Sclerosis (MS)
3. Traumatic brain injury
4. Lung abscess
5. Fat embolism
6. Nitrates
7. Calcium channel blockers
8. ACE inhibitors
9. Antiplatelets medications
10. Mucolytics
11. Extra Corporeal Membrane Oxygenation (ECMO)
12. Ventricular assist device (e.g. LVAD)
13. Bronchoscopy
14. Whole body hypothermia or cooling
15. Bronchial lavage
16. CT – Chest
17. Cardiac markers (e.g. Troponin, Creatinine kinase)
18. Ventilation-perfusion scan (V/Q scan)
19. Skeletal X-rays (without report)
20. MRI – Chest
21. Ultrasound – Chest
22. Electroencephalograms (EEG)
23. Lung PET scan
24. Renal function (e.g. urea, creatinine)
25. Electrolytes levels (e.g. Na+, K+, CL-, Ca2+, Mg2+)
26. Bone scan
27. Cranial nerve function
28. Patient cooperation [e.g. Standardized Five Questions (S5Q)]
29. Body temperature
30. Respiratory muscle training
31. Tracheal stimulation, tickle etc.
32. Critically evaluate and apply research relevant to practice (best evidence)

Annex 4C: Items Excluded by the Statistical Approach but Added by Expert Consensuses

1. Brain death, organ procurement
2. Exercise tolerance
3. Walking (with lines and leads but no mechanical ventilator)
4. Cycling in or out of bed—passive & active
5. Standing with the assistance of a tilt table
6. Manually assisted coughing techniques
7. Suctioning (tracheal / nasopharyngeal / oropharyngeal / closed suction)
8. Neuromuscular electrical stimulation (including indications, selection of appropriate dosage and contraindications in the critically ill)
9. Time and resource management in challenging situations e.g. caseload prioritization

CHAPTER 12: SUMMARY AND CONCLUSIONS

Early mobilization of critically ill patients has been shown to be a promising intervention in the ICU. There is evidence that it may reduce muscle weakness, functional decline, ICU and hospital LOS, as well as increase ventilator-free days, the proportion of patients to be discharged home, and improve quality of life.[142,147,153,162,255] Nonetheless, a number of barriers hinder its implementation into daily clinical practice. Little was known about the practice of EM in Montreal area ICUs, the barriers encountered, or the facilitators that could improve the implementation of EM practice. The research studies presented in the preceding chapters provided a picture of the current practice of EM in Montreal area ICUs, identified the barriers and facilitators being encountered, and begun the process of addressing some of the identified barriers.

Findings from the first manuscript showed that in the Montreal area, EM was not perceived as a top priority among many ICU clinicians and that many clinicians were not fully aware of the benefits of EM. The study also showed that many clinicians did not feel well trained and informed enough to mobilize mechanically ventilated patients. The study identified medical instability, nurse safety concerns, and a limited number of physiotherapists/nurses as well as insufficient equipment as the greatest perceived barriers to EM. Other highly perceived barriers were the risk of dislodgement of devices or lines, excessive sedation, and the lack of coordination among providers. Moreover, the slow recognition of when patients should begin EM, the inadequate training to facilitate EM, conflicting perceptions among physicians about the suitability of EM in some patients, and the lack of communication were also identified as barriers. The study also showed that perceptions of patient-level barriers varied with clinicians' professional training, and there was a high degree of inter- and intra-professional disagreement on the permissible maximal level of activity in different critically ill patients. The results of the study further revealed that most ICUs require a physician order for a PT initiation of EM and that some ICUs have a champion for EM. Finally, they showed that PT services in the ICU were not available and were limited in the evening hours and on weekends, respectively.

From these findings, we concluded that there is a need for knowledge translation (KT) interventions. These interventions would augment the clinicians' knowledge of the potential benefits of EM. They would also have the potential to enhance skills for the safe and effective mobilization of mechanically ventilated critically ill patients. Knowledge translation interventions could also promote the standardization of care in the clinical practice of EM.

The second manuscript explored the perspectives of ICU clinicians regarding the barriers, facilitators, and potential solutions for improving the practice of EM using qualitative data.

The data analyzed with the TDF framework showed lack of conviction or knowledge regarding the available evidence on early mobilization, lack of attention to the provision of optimal care, poor communication and the unpredictable nature of the intensive care unit as barriers to EM. Furthermore, limited staffing, equipment, time and clinical knowledge were found to be other key barriers. The study also identified the presence of a physiotherapist in the ICU (expert support), intrinsic motivation, conscious effort to mobilize early, and positive outcome expectation as strong facilitators. The presence of pro-EM culture, ICU champions, and EM reminder systems were also identified as strong facilitators. Other key facilitators were implementation of an early mobilization protocol, improved ICU organization, and planning and coordinating actions that will improve EM practice. Interestingly, many of the identified barriers and facilitators may be reduced or enhanced, respectively by KT-interventions. The unique findings in the various domains of the TDF provide a framework for the design of theory-based knowledge translation interventions that may improve EM practice in the ICU.

The third manuscript evaluated the available evidence on the beneficial impact of EM. The manuscript systematically summarized the evidence on the effectiveness of rehabilitation interventions of EM and NMES in reducing the incidence of ICUAW which is a very important clinical outcome in ICU survivors. It also summarized the available evidence of the impact of rehabilitation on ventilator dependency, ICU and hospital LOS, mortality, and discharge locations. The results of the manuscript showed that rehabilitation in the ICU is associated with a reduction in the odds of developing ICUAW especially in a subgroup of patients with longer ICU LOS. The study also indicated that rehabilitation in the ICU is associated with an increased likelihood of being discharged home. There was also moderate but inconsistent evidence that rehabilitation is associated with shorter ICU and hospital LOS, and reduced ventilator dependency. Furthermore, it showed that rehabilitation was not associated with odds of acute mortality. We anticipate that disseminating these findings would increase the knowledge and conviction of ICU clinicians on the beneficial impact of EM.

Finally, the last manuscript identified specific knowledge and practice topics to be included in a critical care learning needs assessment tool for physiotherapists aiming to work in the ICU of a local hospital. Following a thorough literature review, a questionnaire was developed to survey

physiotherapists on the relevance of the various topics relative to practice in the ICU. Physiotherapists were also asked to rate their personal knowledge of the topics. The ultimate objective was to identify and select topics to be integrated into a learning needs assessment tool for physiotherapists at that local hospital, but as such, this project also presents the methodology that may be used to tailor the identified topic areas to the needs of physiotherapists working at other hospitals. The initial process presented is part of a larger project that could help bridge the knowledge-to-practice gaps that would be identified with the learning needs assessment tool.

STRENGTHS AND LIMITATIONS

The novelty of this thesis lies not just in the results it has generated, but in the unique methodological approaches that were used in the included studies. The identification of barriers was first done quantitatively and then followed up with a qualitative exploration for a deeper and better understanding of factors underlying the barriers. Furthermore, the analysis of the qualitative data was done using the TDF framework, which minimized the risk of our omitting important concepts. The theory-based analysis also revealed a number of behavioural barriers that had not been captured in earlier studies. The systematic review and meta-analysis also followed a thorough methodology and explored several sources of heterogeneity that could explain the differences in the results of various RCTs that explored the impact of EM and NMES on ICUAW. The last manuscript also detailed a methodological approach that ensured that important concepts were captured in the prospective critical care learning needs assessment tool in development.

Nonetheless, certain limitations exist, which have been discussed in the relevant sections of the various manuscripts. A general limitation of the studies included in manuscript one, two and four is that the results emanated from the same geographical locality. The identified barriers may not be directly applicable to a different setting because ICU barriers may vary from one local unit to another. Furthermore, the knowledge and skill topic areas that were selected for the development of the learning needs assessment tool are specific to the hospital where the study was conducted. However, the methodological processes can easily be adapted to other local settings to reproduce the results in those specific settings.

IMPLICATION OF RESULTS

The findings of the various manuscripts included in this thesis could have implications for the patient, clinician, and policymaker.

Patient-level implications

The first two manuscripts identified barriers, which if reduced, could result in an increased EM of critically ill patients. The second study also identified facilitators which could enhance EM. The third study showed that if EM was implemented, there was a lower likelihood that patients would develop ICUAW which is a very important clinical outcome. There was also an increased likelihood of patients being discharged back home, as well as spending less time on the ventilator, in the ICU or in the hospital in general. Overall, these would be expected to result in better outcomes and improved quality of life for ICU survivors.

Clinician level implications

At the clinician level, the studies in this dissertation reveal a number of provider-level barriers. Reduction of these barriers could result in improved implementation of EM by ICU clinicians. One of the studies is also developing a learning needs assessment tool that could be useful in identifying the knowledge and practice gaps of physiotherapists who may work in the ICU. Identification of these gaps forms the first process towards increased competency to provide care in the ICU environment.

Policymaker level implications

The findings from the projects included in this thesis also show a number of barriers that need the attention of decision-makers at the policy level. The evidence provided in this thesis shows that EM reduces the likelihood of developing ICUAW and may improve other secondary outcomes. These results could imply potential cost savings for the healthcare system. This should encourage policymakers to invest in the implementation of EM and follow-up such investments with cost-benefit analysis.

FUTURE DIRECTIONS

For the first two studies, future work should consider exploring barriers to EM in the ICUs of French-speaking hospitals of Montreal and in the province of Quebec. Future studies should also explore the influence of the changes associated with the modernized new ICU environment (organizational intervention) on the clinical practice of EM and on perceived barriers and facilitators. For the final manuscript, future work should focus on completion of the development of the learning needs assessment tool, testing and validating the tool, and the development of educational materials that would bridge the potential knowledge-practice gaps.

CONCLUSION

In conclusion, the studies included in this thesis have provided a unique insight into the barriers that hinder the implementation of EM in selective Montreal area ICUs, and has created the groundwork for the development of future KT interventions that could improve the practice of EM in these hospitals. This thesis also contributes to the existing body of knowledge on EM and provides evidence that EM reduces the likelihood of developing ICUAW.

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