From Strict Bedrest to Early Mobilization

A History of Physiotherapy in the Intensive Care Unit

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KEYWORDS

• Physiotherapy • Physical therapy • Rehabilitation • Mechanical ventilation • Intensive care units • Post-intensive care syndrome • Early mobility • Clinical trials

KEY POINTS

- Survivors of critical illness are at risk for post-intensive care sequelae including physical and cognitive impairments, mood disorders, fatigue, and frailty.
- Critical care is evolving from a culture of deep sedation and bed rest to one of the proactive strategies to improve long-term outcomes.
- Landmark clinical trials of early mobilization interventions in the late 2000s catalyzed increased awareness of the need for proven physiotherapeutic rehabilitation approaches to mitigate post-intensive care sequelae.
- Physiotherapists are experts in developing targeted, individualized management plans to address physical impairments in critically ill patients, throughout the recovery pathway.
- The evolution of physiotherapy clinician-scientists and their greater engagement and leadership in critical care research, including a specific focus on early mobilization and physical rehabilitation, will continue to change the field.

History is important because it teaches us about the past. And by learning about the past, you come to understand the present, so that you may make educated decisions about the future.

—Richelle Mead[1]

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Crit Care Clin ■ (2023) ■–■
https://doi.org/10.1016/j.ccc.2023.01.003 criticalcare.theclinics.com
0749-0704/23/

INTRODUCTION

Critical care medicine was founded upon principles of interdisciplinary teamwork. Notably, some of the first interdisciplinary interactions occurred between epidemiologists and anesthesiologists in Denmark to study strategies to improve outcomes of people with poliomyelitis and respiratory failure in the early 1950s.[2] Since those early days, physiotherapy as a profession has matured, academically, clinically, and in response to developments in research. In this article, we consider this professional evolution within the specialty of critical care, specifically focused on the context of early mobilization (EM). We examine two perspectives, the clinical and research remits. We explore advancements in these remits that have shaped physiotherapy within the interdisciplinary intensive care unit (ICU) team, moving from past, present, and looking ahead to the future.

CONCEPTS AND DEFINITIONS

Within this article, we will use the term "physiotherapy" and "physical therapy" interchangeably. Both terms refer to regulated health professions involving formalized training qualifications available at undergraduate and postgraduate levels. Traditionally, physiotherapy for critically ill patients within the ICU encompasses the management of both acute and chronic respiratory conditions, as well as the mitigation and treatment of physical deconditioning associated with prolonged immobility, invasive mechanical ventilation, and the deleterious effects of pharmacotherapy including sedation and neuromuscular blocking agents.[3] Within the context of this article, the emphasis will be on physical rehabilitation, although we also recognize the role of physiotherapists in airway clearance and ventilation management in some jurisdictions.

Our use of the concept "early mobility," and related terms, reflects the broad use in the literature. Although there is no universal agreement regarding the exact definition of EM,[4] in clinical practice, EM is typically characterized by a hierarchical progression of increasingly functional activities. In-bed activities such as positioning, assessment, and maintenance of joint range of motion, and bed mobility exercise, progress to out-of-bed activities such as sitting over the edge of the bed, transfers (eg, sit-to-stand or bed-to-chair, standing), and finally ambulation (eg, marching on the spot, gait training, and mobility away from the bed-space). Selection of EM activity depends on the clinical stability and level of active engagement of the patient, and recording of activities often uses established activity codes such as the ICU Mobility Scale.[5] At times, EM activities may be combined with activities of daily living (eg, washing, dressing, and bathing), in coordination with occupational therapy colleagues.

Brief History of Physiotherapy and Critical Care

The academic status and profile of physiotherapy as a profession has developed over the years, emerging around the early 1920s, with origins in therapeutic massage gymnastics, and with strong ties to medicine and nursing. A key driver in shaping modern physiotherapy was as a response to address the rehabilitation of physical impairments in individuals secondary to events such as World War I, and the polio epidemics of the first half of the twentieth century. In the late 1940s physiotherapists were enlisted in acute care to help care for patients with poliomyelitis requiring rehabilitation. Early guidance to physiotherapists included, "*The actual physical therapy measures should be carefully explained. This calls for a consideration of policies on muscle testing, muscle reeducation, preparation of the patient on admission, and for discharge, and limitations on patient activity…. At various times during an epidemic there probably will be* *medically conducted research with special equipment, medications, or statistical surveys. The therapist must cooperate to the fullest extent, and by doing so will find herself (sic) stimulated and be eager to further her knowledge of the disease*."[6]

Clinical education requirements were formalized in the first half of the twentieth century, but at different times in different countries. In the United States, the first Bachelor of Science program for physical therapists was launched in 1927,[7] in Canada, the first physiotherapists graduated with a combined physiotherapy and occupational therapy diploma in 1929,[8] the first physiotherapy degree was offered in Australia in 1950,[9] and in the United Kingdom, the first undergraduate physiotherapy course appeared later, in 1976.[10] Recent times has seen a move towards entry-level practice requiring Masters or Professional Doctorate (eg, DPT) qualification pathways.

The modern specialty of critical care was born during the polio epidemic in the early 1950s, with the demonstration by Dr Bjørn Ibsen of Denmark regarding the utility of positive pressure ventilation outside the operating room.[2] Early ICUs were documented in Canada, the United States, and by the late 1950s and early 1960s.[11] The Society of Critical Care Medicine was established in 1971, and the first world congress of critical care occurred in 1977.[11] Important growth of the critical care field occurred between 1980 and 1989, including the first textbook and establishment of critical care as a specialization.[11] The formation of the Canadian Critical Care Trials Group (CCCTG) in 1989[12] and its first major research output in the New England Journal of Medicine in 1994[13] helped inspire the development of trial groups worldwide. Since 2000, advances in the field of critical care, such as decreased mortality in acute respiratory distress syndrome (ARDS) patients through improved mechanical ventilation strategies,[14] prompted a shift in focus to consideration of life after the ICU, and led to seminal research of long-term outcomes in ARDS survivors.[15] Fig. 1 outlines selected milestones in critical care. In the subsequent sections, we discuss the clinical and research landscapes of critical care and physical therapy—past, present, and future.

THE CLINICAL LANDSCAPE

In this section, we characterize how clinical physiotherapy practice has progressed in critical care, relevant guidance that has driven developments, and suggested areas of future advances (Fig. 2).

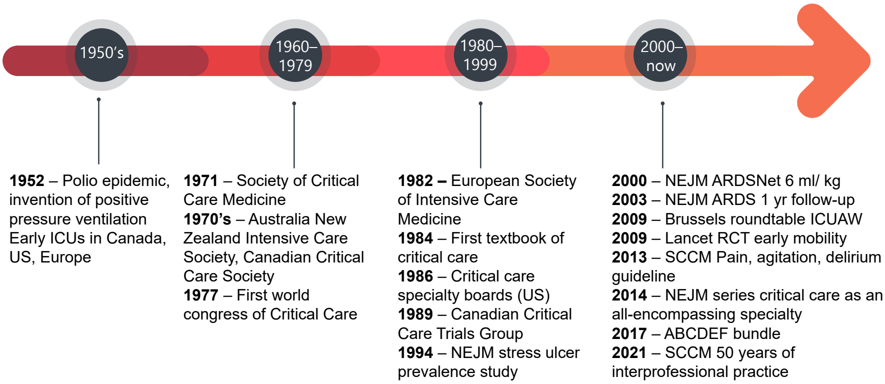

Fig. 1. Selected milestones in critical care. This figure highlights selected milestones in critical care over the last 70 years. ARDS, acute respiratory distress syndrome; ICUAW, ICU-acquired weakness; NEJM, *New England Journal of Medicine*; RCT, randomized clinical trial; SCCM, Society of Critical Care Medicine; US, United States.

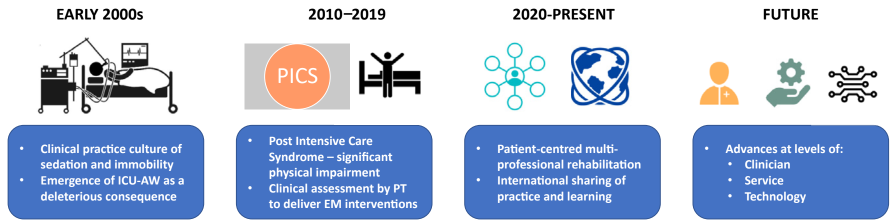

Fig. 2. Schematic representation of developments through the clinical landscape.

PAST

Early 2000s

Reports by Richard Asher, more than 70 years ago, highlighted the negative sequelae across multiple systems of the body associated with consigning acutely ill patients to bed rest.[16] Yet, prolonged immobilization and deep sedation have been characteristic features of critical care medicine for many decades. Traditionally, it had been considered that immobility (achieved through sedation) could preserve metabolic resources for systemic healing and recovery.[17] It was not until the early part of this century that a shift in culture began to appear in the management of critically ill patients in the ICU. One example is the incorporation of daily sedation interruptions (DSI) to potentially improve outcomes such as duration of mechanical ventilation and length of ICU stay.[18] Although subsequent meta-analyses of studies have shown inconsistent findings as a result of DSI,[19,20] the resultant prompt for clinicians to challenge long-standing empirical clinical practices triggered a cascade of further re-evaluation of care practices across multiple domains of patient care.

Alongside changes in the approach to sedation, there was growing recognition of intensive care unit-acquired weakness (ICUAW) as a common and detrimental clinical feature associated with a critical illness.[21] ICUAW is diagnosed clinically, most commonly with the Medical Research Sum-score (MRCSS), a volitional measure that requires the patient to generate muscle force against resistance provided by an examiner. The MRCSS was originally developed to assess critically ill patients with Guillain Barre syndrome,[22] and assesses 6 muscle groups bilaterally (upper extremity: shoulder abduction, elbow flexion, wrist extension; Lower extremity: hip flexion, knee extension, ankle dorsiflexion), rating each muscle group on a scale of 0 to 5 (no contraction, tolerates full resistance), and summing the scores for a minimum score of 0, and maximum score of 60. ICUAW was ascribed to patients scoring <48/60.[23]

Prospective studies showed the estimated prevalence of ICUAW from 24% to 65%.[23–26] Many patients experienced prolonged weaning from mechanical ventilation, which led to delayed rehabilitation, increased hospital length of stay, and mortality in both the ICU and hospital.[23–29] Increasing focus on understanding the biologic, pathophysiologic, and mechanistic nature of ICUAW followed throughout the decade, accompanied by clinical practice position pieces, the 2009 Brussels Roundtable Meeting,[21] and guidelines published by professional bodies such as the European Society of Intensive Care Medicine/European Respiratory Society,[3] and in later years, the American Thoracic Society.[30] With regard to physical rehabilitation, these guidelines recommended a graded approach to EM interventions of escalating intensity based on clinical assessment of patients and consideration of risk.

Incorporation of EM into clinical practice at this time was supported by emerging reports of its feasibility and safety.[31,32] Bailey and colleagues[31] prospectively recorded activity events and adverse events in patients with acute respiratory failure requiring mechanical ventilation > 4 days, including those with endotracheal tubes in situ. Activities that occurred included sitting over the edge of the bed (16%), sitting out in a chair (31%), and ambulation (63%), with a <1% rate of activity-related adverse events reported. Similar data were shown in a separate prospective quasi-randomized study.[32]

Furthermore, in the UK in 2009, the first national guidelines focusing on the rehabilitation of critically ill patients were published.[33] These guidelines advocated a multiprofessional rehabilitation approach across the recovery continuum; for patients in the acute stage of critical illness during ICU admission, this involved an early clinical assessment to determine the risk of physical and nonphysical morbidity, associated rehabilitation requirements, and rehabilitation goal-setting.

Collectively, this decade was witness to the building of momentum of a culture toward embracing mobility as an increasingly important element in the management of patients, and the multiprofessional teamwork needed for its implementation.[33]

2010 to 2019

The landmark event in this decade influencing clinical practice in the field was the consensus roundtable and publication of the term “post-intensive care syndrome” (PICS) to encompass the impairments experienced by critically ill patients, across physical, mental, and cognitive domains, with additional recognition of the impact on families and caregivers.[34] To underpin the PICS concept, there was prolific publication of observational data longitudinally characterizing these impairments. Notably, with regard to the physical domain,[35–38] significant declines in muscle strength, physical function, and exercise capacity were observed in patients, but also in other physical aspects such as swallowing function.[39] For example, in a cohort of 193 survivors of ARDS, 86% experienced a decline in at least 1 physical measure (death, muscle strength [MRCSS], physical function, exercise capacity) at 5-year follow-up with older age, illness severity, and chronic comorbidity influential factors in the decline in physical performance.[36] In another, relatively young, cohort of ARDS survivors, again at 5 years, these patients showed an average walking distance of 76% that of age- and sex-matched predicted comparators (436 m), and physical health-related quality of life fell below average scores (score 41, compared with norm score of 50).[38]

To strengthen the case for early physical rehabilitation as a strategy to mitigate against these impairments, the financial cost savings associated with its implementation were shown, as well as the cost-to-outcome benefit in terms of the modest investment required to potentially improve patient outcomes.[40]

Clinical practice was also supported through further rigorous work detailing the safety of conducting EM interventions when appropriate clinical assessment had been undertaken. Hodgson and colleagues[41] reported the findings of expert multidisciplinary consensus recommendations on the safety criteria for active mobilization of mechanically ventilated critically ill adults. This report used a traffic-light system to indicate the risk associated with active mobilization, with a corresponding approach to the level of activity that could therefore be undertaken. The guidelines incorporated assessments across multiple systems (eg, cardiovascular, respiratory, neurological); clinical parameters according to each system were categorized as to whether they indicated a low risk of an adverse event occurring with mobilization (green = proceed with mobilization according to local policies and procedures), a potential risk/consequence of an adverse event, albeit these may be outweighed by any potential benefits (amber = clarify precautions or contraindications before mobilization and proceed with caution), or a significant potential risk or adverse consequence (red = do not proceed with active mobilization unless authorized by the senior ICU medical, nursing, and physiotherapy staff). From a clinical perspective, this simple-to-follow guidance offered practical support to clinicians in developing and implementing EM programs, in particular those settings where teams may have limited experience, skills, and resources. Furthermore, a large-scale systematic review synthesized safety data regarding patient mobilization rehabilitation in the ICU from 48 studies (7546 patients).[42] Potential safety events totaled 583 out of 22,351 treatment sessions (2.6%), and < 1% of reported interventions incurred a safety event with clinical consequences.

Other drivers of influence over clinical practice included the ABCDEF care bundle, where E reflects early mobilization and exercise.[43] Integrating EM into a composite package of care has increased its profile among clinicians who may have previously paid less attention, and also encouraged the multiprofessional team to collaboratively overcome barriers to implementation. Adoption of care bundles, where components are evidence-based and/or empirically considered valuable to patient management, facilitates the embedding of practices into the daily routine. New clinical practice guidelines recommending EM as a first-line nonpharmacological treatment of delirium,[26] and recommendations for early mobility activities started in the ICU[44] also increased the profile of EM activities.

Present (2020 to Current)

Undoubtedly the COVID-19 pandemic has dominated the shape of critical care rehabilitation over the last 2 to 3 years, both in relation to the clinical workforce (eg, significant additional pressures on ICUs, redeployment of noncritical care staff, development of makeshift critical care areas in alternative hospital settings) and patient demographics (eg, increased illness acuity of the unknown profile, trajectory, and prognosis). The emphasis of clinical care reverted to acute "medical" management to manage the severity of respiratory physiology that was evident in patients. Rehabilitation opportunities became limited. However, the global impact of the pandemic generated an international collaborative response from the clinical physiotherapy community,[45,46] as well as an explosion in the use of focused social media to promote collaboration, experiential learning, information provision, and sharing of practice. Examples such as the #RehabLegend initiative (via Twitter) was already in existence but became a platform for clinicians worldwide to offer peer support in a rapid, inclusive, and responsive manner, providing valuable contact between colleagues.

Separate to the pandemic, the wider clinical community has continued to explore and understand PICS in greater detail, expanding our previous knowledge by understanding the complex depth and breadth of impairments experienced by patients.[47] Examples of further domains requiring rehabilitation attention include sleep disorders, fatigue, occupational limitations (return to work),[48] chronic pain, and frailty.[49] The continued growth of interest in post-critical illness recovery and rehabilitation services highlights the need for a truly multiprofessional and multidisciplinary approach to following up with these patients and intervening accordingly.[50]

FUTURE

So where does the future lie for physiotherapy practice in the ICU? Areas for consideration include at the clinician, service, and technology levels.

- *Clinician*: Clinical physiotherapy teams will need to develop local approaches to ensure the rapid and efficient implementation of evidence to guide the delivery of EM interventions; this is likely to center on identifying patients who benefit most from interventions. EM interventions will continue to evolve as just one component of the multidomain rehabilitation required by critically ill patients. This will necessitate adaptive and flexible models of therapy delivery, integration with multiprofessional colleagues, and identifying areas of commonality in therapy delivery to maximize resources while retaining the delivery of interventions of unique physiotherapeutic value, and requiring bespoke physiotherapy skills. Rehabilitation, including EM and other physical rehabilitation interventions, will increase patient-centeredness to build a personalized rehabilitation approach.

- *Service*: At a service level, a detailed workforce review provides the opportunity for evaluating the profile of teams for skill-mix, experience, resources, relevant performance metrics, and innovative approaches to using support staff to complement qualified clinicians. Addressing these aspects can help to ensure the robustness and "fitness for purpose" of clinical teams for optimizing patient services.[51] Development of rehabilitation-focused competency frameworks may be valuable for building consistent and standardized quality of service. Such competency frameworks have been developed for critical care physiotherapy,[52,53] but with relatively little emphasis on mobilization; less than 5% of items deemed essential for competency reflected EM treatments (eg, competency with mobilization of nonventilated patients, competency of mobilization of ventilated patients, and delivery of bed exercise), with one other item addressing the performance of musculoskeletal and/or functional assessments. Furthermore, given the holistic approach to the delivery of rehabilitation to critically ill patients, competency frameworks may be beneficial across the multiprofessional team. Service managers should also be encouraged to explore opportunities around the use of "big data" to harness the value of routinely collected clinical data to inform service provision, team staffing profiles, and business cases.
- *Technology*: Advances in technology will undoubtedly shape future physiotherapy practice, especially in the context of EM interventions. Increasingly sophisticated assistive devices can provide practical support to rehabilitation practice and facilitate patient participation. Colleagues collaborating with clinical, engineering, computer, and robotics/automated intelligence experts are already exploring use of robotics in addition to in-person delivery of therapy. It is likely that carryover will be seen from enhanced technology supporting other domains of rehabilitation that may then improve physical interventions. For example, it is important to be able to effectively communicate with these patients to safely and accurately deliver interventions and maximize engagement from patients. New communication applications can support patients with impaired vocalization.

The Research Landscape: From Muscle Weakness to Post-Intensive Care Unit Sequelae

In this section, we summarize the evolution of evidence and inquiry for physiotherapy interventions in the ICU. We identify milestones of original research (including those led by physical therapists), knowledge synthesis, and propose areas for further inquiry. **Table 1** juxtaposes the clinical and research landscapes.

Past

Early 2000s: focus on muscle weakness and early randomized clinical trials

We highlight two landmark studies in this era. Herridge and colleagues[15,38] identified 1- and 5-year long-term sequelae in ARDS survivors, published in the New England Journal of Medicine. These articles raised awareness of post-ICU sequelae and paved

Table 1
Clinical and research landscape

	Past		Present	Future
	Pre-2010	**2010 to 2019**	**2020 to Now**	
Clinical Landscape				
Clinical events	Bedrest,[17] deep sedation Brussels Round Table Conference—ICU-acquired weakness[21] ERS and ESICM,[3] NICE guidelines[33] Feasibility of early activity[31,32]	Post-intensive care syndrome[34] SCCM guidelines[26,44] Safety of rehabilitation activities[41,42] Financial impact of early mobility[40] ABCDEF bundle[43] Frailty[49,61]	Post-intensive care syndrome-extended[47] COVID-19[46] Patient engagement ECLS Social media and sharing international practice	Clinical Service models Technology
Original Research - Outcomes	ICU-acquired weakness[23] Long-term follow-up of ARDS Survivors[15]	Rapid skeletal muscle atrophy in patients receiving mechanical ventilation[62] Cognitive and functional outcomes[63,64]	COVID-19	
Research Landscape				
Research Synthesis - Interventions	Narrative reviews[55–60]	Systematic reviews,[65–67] scoping reviews,[68] and overview of reviews[69]	Bibliometric analysis Network meta-analysis[70]	Integrated mixed-methods syntheses
RCT intervention focus	Early mobility In-bed cycling	Neuromuscular electrical stimulation In-bed cycling and adjuncts Early in-bed cycling	Early mobility extended to other areas of critical care Progressive mobility	Multidisciplinary rehabilitation
Published RCTs	Early mobility[54] Mobility team[32] (quasi-randomized) In-bed cycling[71] Neuromuscular electrical stimulation[72]	Goal-directed mobility (surgical)[73] Mobility "dose"[74] Exercise intervention from ICU to community[75] Multicenter pilot studies[76,77]	International multicenter trials in progress	
Methodological advancements	Focus on muscle strength	Use of ICF framework[78] Outcome measure psychometrics[79,80] Core outcome sets[81]	Factorial trials[82]	Platform trials Research process

the way for subsequent multicenter outcome studies. The second landmark study, led by Schweickert and colleagues,[54] was a multicenter RCT of early occupational and physical therapy started within the first 72 h of intubation versus the usual timing of therapy and was published in The Lancet. Narrative reviews identified treatments to proactively address immobility and muscle weakness, with interventions started in the ICU.[55–60]

RCTs focused on interventions started in the ICU, with some interventions occurring while patients received life support therapies such as mechanical ventilation or vasoactive agents. These approaches challenged commonly held beliefs that patients in the ICU were "too sick" for activity. One of the earliest clinical RCTs led by a physical therapist from Canada examined incentive spirometry and usual physiotherapy, which involved early mobility, versus usual PT alone.[83] Another RCT led by a physical therapist and team from Belgium evaluated in-bed cycling and routine PT versus routine PT alone, started after ICU day 14 in 90 patients, noting a clinically and statistically important improvement in 6-min walk test at hospital discharge (in-bed cycling median [interquartile range] = 196 [126 to 329] vs control 143 [37 to 226] m; 29 [19 to 43] vs 25 [8 to 36]% predicted, $p < 0.05$).[71]

Other studies evaluated neuromuscular electrical stimulation (NMES), an intervention that applies surface electrodes to muscles, initiating visible muscle contractions using a small device that sends a small electrical current to activate the muscle.[84] NMES focused on preserving muscle strength, is noninvasive, and can activate muscles without volitional control, thus it was very attractive to the ICU setting because it could be used with patients who were sedated or unable to follow commands. NMES is an intervention used by physical therapists with other patient populations, such as people with chronic obstructive pulmonary disease, to improve muscle strength.[85] An early RCT with 49 critically ill patients, noted better preservation of quadriceps muscle cross-sectional area measured by ultrasound at ICU day 10 in those receiving NMES within 2 days of ICU admission versus the control group.[72] A subsequent systematic review and meta-analysis of 6 RCTs from 2003 to 2018 enrolling 718 patients identified no difference in muscle strength at ICU discharge, duration of mechanical ventilation, ICU length of stay or mortality; however, included trials were heterogeneous.[86] Important considerations for implementation of NMES exist. Segers and colleagues[87] documented challenges consistently achieving muscle contractions. NMES requires continuous supervision and titration to ensure ongoing muscle contractions during ICU sessions which lasted from 30 to 60 min daily (excluding preparation and cleanup). Considerations for which ICU health care personnel administer this intervention are required, which could come at the opportunity cost of conducting other functional activities.

This period heralded the start of "early mobility" activities in the ICU. A quasi-randomized study evaluated whether a standard early mobility protocol increased the proportion of patients receiving physical therapy compared with usual care in 330 medical ICU patients with acute respiratory failure.[32] The premise of this study was elegant and simple–can an automatic physician order triggering the involvement of a mobility team including a nurse, nurse assistant, and physical therapist, increase the number of patients receiving at least one physical therapy session? Results were highly encouraging. More patients managed using the protocol received at least one physical therapy session than those not managed using the protocol (80% vs 47%, $p \leq 0.001$), with physical therapy commencing more frequently during ICU stay (91% vs 13%, $p \leq 0.001$). In addition, compared with usual care, protocol patients were out of bed earlier (5 vs 11 days, $p \leq .001$), had reduced ICU and hospital length of stay (5.5 vs 6.9 days, $p = 0.025$, and 11.2 vs 14.5 days, $p = 0.006$, respectively), and similar low complication rates with no adverse events during protocol-based mobility sessions. Together, with the landmark RCT of early physical and occupational therapy,[54] interest in physical therapy and engagement of physical therapists in the ICU increased substantially. **Table 2** summarizes selected clinical trials by population, intervention, comparison, and primary outcome.

2010 to 2019: early mobility, safety, and feasibility

Many activities in this decade advanced the field. ICU survivorship assumed a more prominent role with the publication of nomenclature for PICS, as described earlier.[34] This publication, with international multidisciplinary input, raised awareness about outcomes beyond muscle strength for clinical trials. In addition to PICS, the World Health Organization International Classification of Function, Disability, and Health provided a framework for ICU outcomes, considering a continuum from body structure and body function, to activities, and participation.[78,93] This era also saw an expansion of physiotherapist-led clinical research programs, including preparatory work culminating in randomized clinical trials,[75–77] and publications led by trainees from the next generation of research physiotherapists in graduate programs.[66,94,95]

The first systematic reviews of interventions started in the ICU identified few RCTs, mostly relying on observational studies.[65–67,96] Typical interventions assessed included NMES, "EM," "general physiotherapy," limb strengthening, active mobilization, and exercise training. However, reviewers identified important weaknesses in intervention descriptions. The systematic reviews also documented variable outcome measures across studies, with measurements occurring primarily at short-term timepoints (eg, ICU discharge, hospital discharge), and few studies reporting longer-term follow-up. Overall, the systematic reviews determined physical interventions initiated in the ICU were safe, with small effects favoring the intervention groups for muscle strength, function, ICU and hospital length of stay, and health-related quality of life.[65–67,96] However, new original research published during this decade began to question the efficacy of physical interventions started in the ICU.

As the field matured, investigators received national research funding to study ICU physical rehabilitation interventions in larger multicenter trials.[74,89] These novel RCTs explored different ways of implementing ICU physical rehabilitation. But study interventions and results for primary outcomes varied, introducing confusion to the field. Several larger studies of physical rehabilitation published during this decade reported variable results for their primary outcomes (see **Table 2**).[73–75,89,90] However, similar to the systematic reviews, these trials studied different interventions, for different duration, and measured different outcomes, a nuance that may have been underappreciated by the wider ICU community. For example, outcomes were heterogeneous in terms of both type and measurement time points (see **Table 2**). This heterogeneity of the primary outcome and results, and differences in secondary outcomes, made things unclear for the ICU community. A systematic review evaluating mortality outcomes raised concerns for possible harms with active mobilization activities in the ICU.[66] However, the small number of studies assessed, the small number of enrolled patients, as well as the overall low event rate (active mobility 12.3% (34/275) vs standard care 11.6% (32/276)) limits the certainty of currently available evidence.[97]

Other methodological advancements included the publication of quality improvement studies, and case series of the safety and feasibility of novel physical rehabilitation interventions in the ICU.[68] Building on clinical data, a systematic review documented a low adverse safety event rate (2.6%) in physical rehabilitation activities.[42] A scoping review identified reporting important gaps in key intervention attributes among ICU rehabilitation studies, notably protocol adherence and protocol

Table 2
Selected clinical rehabilitation trials

Author	Study Design	Population	Intervention	Comparison	Primary Outcome Results (Intervention vs Comparison)
			Pre-2009		
Schweickert et al,[54] 2009	RCT; 2 centers, 1 country (United States)	Medical patients mechanically ventilated <72 h (N = 104)	Order for early exercise and mobilization during daily interruption of sedation beginning on day of enrolment (n = 49)	Daily interruption of sedation and therapy as ordered by primary care team (n = 55)	*Return to independent functional status* a hospital discharge (29 [59%] vs 19 [35%]; odd ratio [95% CI] 2.7 [1.2 to 6.1]) (blinded) ✓
Morris et al,[32] 2008	Quasi-randomized study; 1 center (United States)	Medical patients with acute respiratory failure requiring mechanical ventilation (N = 330)	Automatic order for ICU mobility team (critical care nurse, nursing assistant, physical therapist) (n = 165)	Patient-specific order for physical therapy (n = 165)	*% patients receiving physical therapy* of patients surviving to hospital discharge (80% vs 47%; $p \leq 0.001$) (blinding not relevant for this objective outcome) ✓
Burtin et al,[71] 2009	RCT; 1 center (Belgium)	Medical or surgical patients with expected prolonged ICU stay (N = 90)	20 min of in-bed cycling and respiratory physiotherapy and daily active motion of upper and lower limbs (n = 45)	Respiratory physiotherapy and daily active motion of upper and lower limbs (n = 45)	*6-min walk distance* at hospital discharge median (interquartile range)[88] (196 [126 to 329] vs 143 [37 to 226] m; 29 [19 to 43] vs 25 [8 to 36]% predicted, $p < 0.05$]) (blinding unclear) ✓

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Table 2
(*continued*)

Author	Study Design	Population	Intervention	Comparison	Primary Outcome Results (Intervention vs Comparison)	
			Pre-2009			
Gerovasilli et al,[72] 2009	RCT; 1 center (Greece)	Multidisciplinary ICU ($N = 49$)	60 min of neuromuscular electrical stimulation on quadriceps and peroneus longus x 7 days starting ICU day 2 ($n = 24$)	Not reported ($n = 25$)	Change in *quadriceps muscle cross-sectional diameter* at 7 to 8 days after randomization measured by ultrasound; R and L rectus femoris and vastus intermedius; both decreased significantly less for absolute difference (13 evaluated in each group; blinded)	✓
2010 to 2019						
Denehy et al,[75] 2013	RCT; 1 center (Australia)	Medical or surgical patients ($N = 150$ enrolled out of planned 200)	Intensive exercises in the ICU, ward, and as outpatients ($n = 74$)	Usual care ($n = 76$)	*6-min walk distance* at 6 months (402.4 [166.6] vs 394.2 [156.2] m; −4.9 [−68.0 to 58.3] 0.879) (blinded)	✗
Moss et al,[74] 2015	RCT; 5 centers (United States)	Patients requiring mechanical ventilation for at least 4 days ($N = 120$)	Intensive PT up to 28 days (7 days per week as an inpatient; 3 days per week at home or outpatient); 30 min in ICU; up to 60 min in on-ward and other settings) ($n = 59$)	Standard of care (3 days per week as an inpatient; no home or outpatient therapy) ($n = 61$)	*Continuous scale physical functional performance test short form* at 1 month (19.0 [3.7] vs 20.9 [4.1]; $p = 0.73$) (blinded)	✗

Morris et al,[89] 2016	RCT; 1 center (United States)	Medical patients with acute respiratory failure requiring mechanical ventilation (N = 300)	Standardized rehabilitation therapy protocol including passive range of motion, physical therapy, and progressive resistance exercises by a rehabilitation team from enrolment to hospital discharge 7 days per week (n = 150)	Physical therapy (unprotocolized) Monday to Friday (n = 150)	*Hospital length of stay* (median 10 [6 to 17] vs 10 [7 to 16]; median difference [95% CI] 0 [−1.5 to 3] days, p = 0.41) (blinding not relevant for this objective outcome)	✗
Schaller et al,[73] 2016	RCT; five centers and three countries (Austria, Germany, United States)	Surgical patients mechanically ventilated <48 h (N = 200)	Early goal-directed mobilization facilitated by interprofessional closed-loop communication (n = 104)	Standard treatment (n = 96)	Mean (SD) SICU optimal mobilization score achieved during SICU stay (2.2 [1.0] vs [1.5 0.8]; mean difference [95% CI] 0.7 [0.4 to 1.0, p < 0.0001]) (blinded)	✓
Wright et al,[90] 2017	RCT; four centers, one country (United Kingdom)	Medical and surgical patients mechanically ventilated (invasive or noninvasive) >48 h (N = 308)	90 min of physical rehabilitation per day (Monday to Friday), split between at least 2 sessions (n = 150)	Standard care—30 min of physical rehabilitation per day (Monday to Friday) (n = 158)	*Physical Component Summary measure of Short Form 36 (Version 2)* Quality of Life questionnaire at 6 months (37[12.2] vs 37 [11.3]; the adjusted difference in means [95% CI] −1.1 [−7.1 to 5.0]) (blinded)	✗

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Table 2
(*continued*)

Author	Study Design	Population	Intervention	Comparison	Primary Outcome Results (Intervention vs Comparison)	
			Pre-2009			
2020 to present						
Berney et al,[91] 2021	RCT; four centers, two countries (Australia, United States)	Mechanically ventilated patients with sepsis ($N = 162$)	Up to 60 min of functional electrical stimulation-assisted in-bed leg cycling (applied to 1 leg) and usual care rehabilitation $\geq$ 5 days per week ($n = 80$)	Usual care rehabilitation ($n = 82$)	*2 Primary outcomes* (blinded): *1. Muscle strength at hospital discharge measured by hand-held dynamometry* Adjusted mean difference (95% CI) 3.3 (−5.0 to 12.1 Nm; $p = 0.460$) *2. Cognitive impairment at 6 months (one test >2 SD below population norms or 2 tests > 1.5 SD population norms)* (41% [9/22] vs 40% [6/15]; odds ratio [95% CI] 1.1 [0.30 to 3.8; $p = 0.929$]; [22/46 and 15/46 of planned 92])	✗
Waldauf et al,[92] 2021	RCT; 1 center (Czech Republic)	Multidisciplinary ICU; mechanically ventilated patients <72 h and predicted to need ICU > 1 week ($N = 150$)	Progressive tailored 90-min mobility program including functional electrical stimulation in-bed leg cycling initiated 1 day post-randomization up to 28 days ($n = 75$)	Standard physiotherapy 2 times per day, 6 days per week (nonprotocolized, initiated at request of treating physician) ($n = 75$)	*Physical Component Summary measure of Short Form 36 (Version 1)* Quality of Life questionnaire at 6 months median (IQR) (50 [21 to 69] vs 49 [26 to 77]; $p = 0.261$]) (blinded)	✗

fidelity.[68] Clinical trialists started publishing trial protocols[82,98] highlighting ongoing studies, and conducted pilot and feasibility studies in preparation for future large multicentre trials.[76,77,99] Finally, given the increase in the number of clinical studies across many disciplines, several groups developed core outcome sets to improve the standardization across studies,[81,100] including those extending to sub-specialty populations such as extra-corporeal membrane oxygenation.[101]

Present

2020 to now: coronavirus disease-2019

Systematic reviews have identified over 60 RCTs focused on physical rehabilitation in the ICU.[102] Multiple systematic reviews identified that in RCT intervention groups, there were no differences in mortality[102,103] or muscle strength,[102] but lower ICU length of stay,[102,103] small improvements in physical function at hospital discharge,[102] and no adverse safety events.[103] Inconsistency in pooled results for hospital length of stay occurred across reviews.[102,103] Authors identified ongoing gaps in primary study reporting, and opportunities to improve documentation of protocol adherence and intervention dose. Amidst the pandemic, two RCTs of in-bed cycling and electrical stimulation were published (see **Table 2**).[91,92] At the time of writing, results are pending for at least 2 international multicenter trials.[76,104]

The COVID-19 pandemic had devastating effects on ICUs worldwide. First, the overwhelming influx of patients into ICUs required immediate prioritization of clinical care of patients, with many research studies halted,[105] and ICUs focused on research identifying treatments for COVID-19. International ICU physiotherapists quickly mobilized to provide clinical guidance for the acute management of patients with COVID-19.[46] Ongoing ICU rehabilitation research studies were also interrupted,[104] and guidance to resume non-COVID ICU research emerged.[106] Processes of ICU care for COVID-19 patients reverted back to earlier paradigms, including deep sedation, neuromuscular blockade, and prolonged immobility.[107–109] Proning, both with and without invasive mechanical ventilation was common in patients with COVID-19.[109] All of these factors raise concerns for severe long-term post-ICU outcomes in COVID-19 survivors, and highlight the need to identify additional impairments caused by COVID-19. A core set of COVID-19 outcomes was recently published,[110] and information about Long COVID and outcomes post-COVID is of global concern.[111,112] Rehabilitation interventions within and beyond ICU will be required for COVID-19 survivors.

Future

In anticipation of more survivors of ICU, we urgently need innovative research to improve the outcomes of critically ill patients. Innovation may occur in research designs, research processes, or research personnel.

Innovation in research designs includes consideration of novel approaches such as platform trials and embedded studies within health care systems. A platform trial design provides the scaffolding to study multiple interventions for a disease or problem, rather than a single intervention.[113] Studies embedded in health care systems could allow the development of patient cohorts from ICU admission to hospital discharge, and also include post-hospital rehabilitation to home, facilitated by long-term longitudinal follow-up using health administrative databases.

Innovation in research processes includes careful and proactive study of research conduct from inception to completion. Rehabilitation interventions are complex,[114] and require ongoing monitoring to ensure the intervention is implemented as intended. Universal strategies to monitor protocol fidelity and adherence, improve enrolment, and optimize participant retention to minimize missing outcome data are needed.

Explicit description of rehabilitation interventions using an approach like the Rehabilitation Treatment Specification System[115] would help advance a multidisciplinary understanding of the “active ingredients” of treatments. Ideally, all research studies include an embedded process evaluation to improve the design and conduct of future research.[114]

Finally, we need innovations to build research personnel. Women, visible minorities, and nonphysicians are all underrepresented in critical care research.[116] Research by individuals in allied health and nursing represented only 10% of conference presentations at national or international meetings between 2010 and 2016.[116] Fig. 3 is a schematic of the roles, training, and infrastructure required to develop research personnel. Students need exposure to research careers and practical opportunities to conduct clinical research. One model exposes students to the role of a clinician-scientist through a novel clinical placement of 50% clinical training and 50% embedded in a research team led by a physiotherapist as part of the entry-level university curriculum.[117] Clinicians need opportunities to contribute to research and learn about research career opportunities such as research physiotherapist or trial managers. One novel training opportunity by Sepsis Canada offers research methods modules and interactive sessions for clinicians.[118] Positions for clinician-scientists in health systems, and partnerships between universities and health systems will advance the field. Contemporary examples of clinical research leadership positions held by physiotherapists will help expand representation in the complex trials needed to improve patient outcomes.

DISCUSSION

In this article, we reflected on the clinical and research aspects of critical care and physiotherapy. As the critical care field evolved from a culture of bed rest, deep

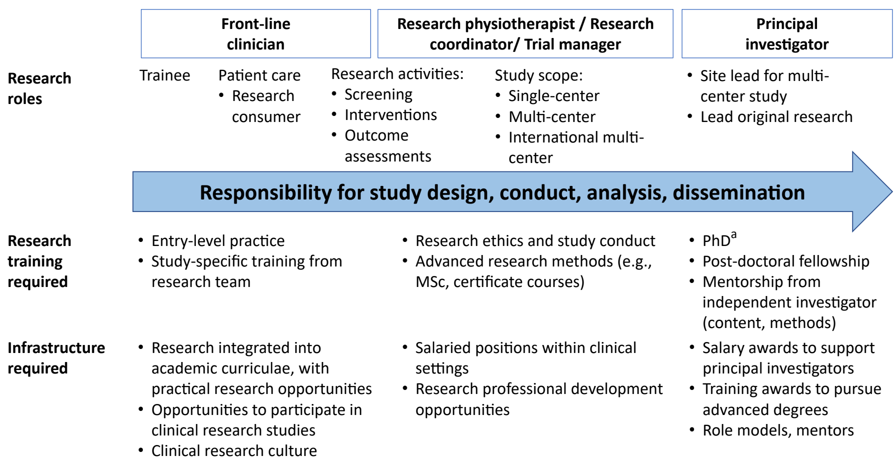

Fig. 3. Schematic of roles, training, and infrastructure required to develop research personnel. This figure summarizes a continuum of research roles, training, and infrastructure required to increase capacity of research personnel. The far left of the continuum represents trainees, and the far right represents independent investigators. The arrow represents increasing responsibility for design, conduct, and oversight of research. [a]PhD training is typically required to lead larger-scale research studies. For healthcare professionals without a PhD or research training to lead research activities, we recommend seeking a research mentor with content and methodological expertise.

sedation, treatments to improve ICU outcomes also evolved from those solely focused on muscles to complex physical interventions. These complex interventions could impact many outcomes including physical function, cognition, mood, and the development of frailty. Thus, expanding the multidisciplinary team and patient and caregiver input to design new interventions is critical. As we plan future interventions, we need to consider implementability and generalizability across different settings, including academic and community settings, and different income settings and health care systems.

As critical care matures, we also anticipate a shift in terminology, progressing from early mobility to rehabilitation. "Early mobility" reflects an initial focus on muscle weakness, whereas "rehabilitation" reflects an anticipation of the future needs of ICU survivors and recognition of the need to start interventions in the ICU to address long-term outcomes.[93] For physiotherapists, we encourage our colleagues to seek broader exposure to developments in research methodology and critical care to inform clinical practice and research. The most clinically relevant interventions will represent the convergence of developments in clinical critical care and research methodology.

SUMMARY

Over the last century, the profession of physiotherapy has evolved tremendously. In this article, we have highlighted the journey of physiotherapists and their contributions to improving the outcomes of critical illness survivors. We witnessed a transition from bed rest to early mobility, and now to rehabilitation. And a focus from muscle weakness to returning to life participation. Clinical and research leadership are now key features of the profession, with an emphasis on interdisciplinary and interprofessional collaboration within the specialty.

CLINICS CARE POINTS

- Critical care clinicians should consider the depth, breadth, and complex inter-relationships of post-critical illness impairments that patients experience, during critical illness and recovery
- Physiotherapists can focus on bespoke restorative interventions to target muscle weaknesses, deficits in physical function, and limitations in exercise capacity
- Physiotherapists should undertake assessments of patients to determine clinical safety and appropriateness for delivering early mobilization and physical rehabilitation interventions
- Research has supported developments in clinical practice, and the future direction for the profession in the specialty of critical care should be greater convergence between research and clinical contexts

DISCLOSURE

M.E. Kho is funded by a Canada Research Chair in Critical Care Rehabilitation and Knowledge Translation. She currently holds grants from the Canadian Institutes of Health Research, the Canada Foundation for Innovation, and the Ontario Research Fund. She leads CYCLE, an international, multicenter randomized clinical trial of early in-bed cycling. Restorative Therapies (Baltimore, MD, United States) loaned Dr Kho 3 RT300 in-bed cycle ergometers to conduct her research. B. Connolly currently receives project grant funding from the National Institute for Health and Care Research (United Kingdom).

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