

e-Supplement Table 1: Safety Guidelines for Exercise

Exercise should not be delivered or should cease when:
1. MAP <65 mmHg or below target MAP, MAP >120 mmHg, or MAP ≤10 mmHg lower than normal systolic or diastolic in patients with end stage renal disease
2. HR <50 or >140 beats/minutes, or new arrhythmia develops (including ventricular ectopics or new onset atrial fibrillation)
3. Requires >30 µg/minute of noradrenaline, or comparable dose of other inotrope or vasopressor
4. Patient complains of new onset chest pain
5. Patient becomes pale and sweaty, and/or patient specifically requests to stop due to feeling acutely unwell
6. Presence of femoral ECMO or IABP
7. FiO ₂ >0.8
8. PEEP >15 cmH ₂ O
9. Respiratory rate >35 breaths/minute sustained for >60 seconds
10. SpO ₂ falls >10% below resting level or <85% sustained for >60 seconds
11. Temperature >41°C

Mean Arterial Pressure (MAP); Heart Rate (HR); Extra-corporeal Membrane Oxygenation (ECMO); Intra-aortic balloon pump (IABP); Fraction of inspired Oxygen (FiO₂); Positive End Expiratory Pressure (PEEP); Oxygen saturation (spO₂).

e-Supplement Table 2: Timing of Outcome Assessments

Assessment/Procedure	Initial Measures	ICU Discharge	Hospital Discharge	6 Months	12 Months
Ultrasonography ^a	X		X		
Medical Research Council – Sum Score		X	X	X	X
Hand Grip Dynamometry		X	X	X	X
Hand Held Dynamometry – Quads		X	X		
Physical Function Intensive Care Test Scored		X			
Functional Status Score for the ICU (FSS-ICU)		X			
Short physical performance battery (SPPB)				X	X
6-minute walk test			X	X	X
Lawton IADL	X			X	X
Katz ADL	X			X	X
Cognitive					
Neuropsychological battery of tests				X	X
Psychological					
Hospital Anxiety and Depression Scale (HADS)				X	X
Impact of Events Scale-Revised (IES-R)				X	X
SF-36				X	X
EQ-5D 5L				X	X

^a Performed prior to randomisation;

e-Supplement Table 3: Medications received in ICU from day of enrolment (to maximum of 28 days)

	% of days received in ICU		Mean daily dose ^a (SD)	
	Intervention (n=909)	Control (n=901)	Intervention (n=80)	Control (n=82)
Opiates				
Fentanyl-equivalent ^b (µg)	59.5%	62.9%	933.5 (1208.3)	981.9 (1301.8)
Antipsychotics				
Haloperidol (mg)	3.3%	8.3%	0.8 (2.3)	1.4 (3.5)
Olanzapine (mg)	1.2%	5.4%	0.6 (2.5)	1.0 (3.4)
Quetiapine (mg)	18.9%	30.2%	27.8 (54.5)	34.1 (69.0)
Sedatives				
Dexmedetomidine (µg/kg)	5.4%	9.0%	65.9 (335.5)	34.8 (263.0)
Midazolam-equivalent ^b (mg)	23.4%	23.4%	15.9 (31.3)	10.5 (21.4)
Propofol (mg)	32.9%	36.1%	1424.4 (1311.4)	1472.3 (1312.3)
Neuromuscular Blocking Agent	5.5%	4.2%		
Insulin, cumulative dose (unit)	165 [30-357]	287 [34-351]		

^aMean daily dose calculated only for days when the drug type was administered. ^bSingle variables for benzodiazapine[2] and opiates [3, 4] were created.

e-Supplement Table 4: Nutritional intake in ICU (via enteral or parental route) from day of enrolment (to maximum of 28 days)^a

	Mean (SD) daily intake Intervention Group (n=80)	Mean (SD) daily intake Control Group (n=82)
Protein (g/kg IBW) ^b	1.0 (0.5)	1.0 (0.6)
Fat (g)	54.6 (33.1)	53.6 (34.3)
Carbohydrates (g)	158.9 (77.4)	163.1 (80.2)
Calories	1496.8 (1274.9)	1526.9 (1217.7)

^a If there was no nutritional intake for a 24 hour period this day was excluded from analysis; ^b IBW=Ideal body weight[5]

e-Supplement Table 5: Fidelity of FES cycling

Total number of scheduled intervention ^a , days	894
Actual number of intervention, days	511
Time from intubation to first FES-cycling, median [IQR] days	3 [2-4]
Number of FES cycling sessions received per participant, median [IQR]	5 [3-9]
Muscle contraction present ^b during intervention n (%)	
Quadriceps	482 (94)
Gastrocnemius	475 (93)
Hamstrings	478 (94)
Gluteals	423 (83)
Electrical energy dose (mean total charge/session/muscle), median [IQR] millicoulombs	
Quadriceps	2483 [1072-4314]
Gastrocnemius	1734 [777-2668]
Hamstrings	2310 [904-3930]
Gluteals	1665 [625-2582]

^aA scheduled FES-cycling day was defined as a day when the intervention either occurred or was attempted based on protocol of delivering intervention ≥ 5 days per week; ^bMuscle contraction was considered present if either visible or palpable

e-Supplement Table 6: Reasons FES cycling not provided (n=383)

Reason	n (%) ^a
Not meeting safety criteria (see eSupp Table 1)	171 (45)
Limited staffing (mainly due to weekend intervention sessions)	57 (15)
Other ^b	45 (12)
Participant declined session	43 (11)
Participant unavailable	28 (7)
Palliation/death	22 (6)
Ward transfer	10 (3)
Equipment malfunction	7 (2)

^aDoes not add to 100% due to rounding; ^bOther includes: not documented, patient fatigue, and interference with renal replacement therapy

e-Supplement Table 7: Reasons usual care rehabilitation not provided in ICU^a

Reason	Both Groups, n (%)	Intervention Group, n (%)	Control Group, n (%)
Patient not responsive to verbal stimulation	632 (54)	335 (56)	297 (53)
Clinical deterioration	145 (12)	67 (11)	78 (14)
Reason not documented	121 (10)	43 (7)	78 (14)
Other ^b	104 (9)	50 (8)	54 (10)
Rehabilitation not indicated	67 (6)	44 (7)	23 (4)
Staffing limitations	44 (4)	20 (3)	24 (4)
Participant fatigue	22 (2)	16 (3)	6 (1)
Hospital transfer	11 (1)	11 (2)	0 (0)
Palliation/Death	8 (1)	7 (1)	1 (0.1)
Medical order for no rehabilitation due to clinical risk	6 (1)	6 (1)	0 (0)
Participant declined	5 (0.4)	1 (0.1)	4 (1)
Totals	1165	600	565

^a Percentages may not add to 100% due to rounding; ^bOther included no physiotherapy order, presence of femoral access devices, active bleeding, scans and theatre

e-Supplement Table 8: Highest level of function mapped to ICU Mobility Scale, during ICU and ward usual care

ICU Mobility Scale ^a	ICU		Ward	
	Intervention Group n (%)	Control Group n (%)	Intervention Group n (%)	Control Group n (%)
10 – Walking independently without a gait aid	5 (2)	0 (0)	49 (12)	57 (13)
9 – Walking independently with gait aid	14 (5)	9 (3)	164 (39)	116 (26)
8 – Walking with assistance of 1 person	39 (13)	41 (12)	84 (20)	100 (22)
7 – Walking with assistance of 2 or more people	22 (7)	18 (5)	18 (4)	29 (6)
6 – Marching in place (at bedside) for short duration	27 (9)	33 (10)	13 (3)	17 (4)
5 – Transferring bed to chair (with standing)	33 (11)	22 (7)	33 (8)	27 (6)
4 – Standing	57 (18)	50 (15)	26 (6)	28 (6)
3 – Sitting over edge of bed	58 (19)	69 (21)	8 (2)	48 (11)
2 – Passively moved to chair (no standing)	5 (2)	11 (3)	2 (0.1)	1 (0.1)
1 – Sitting in bed, exercises in bed	45 (15)	73 (22)	19 (5)	27 (6)
0 – Nothing (lying in bed)	4 (1)	10 (3)	4 (0.1)	3 (0.01)
Total number of usual care rehabilitation sessions	309	336	420	453

^aEach level of scale is mutually exclusive for every daily usual care rehabilitation session performed in ICU; percentages do not add to 100% due to rounding

e-Supplement Table 9: Reasons usual care rehabilitation not provided on the ward^a

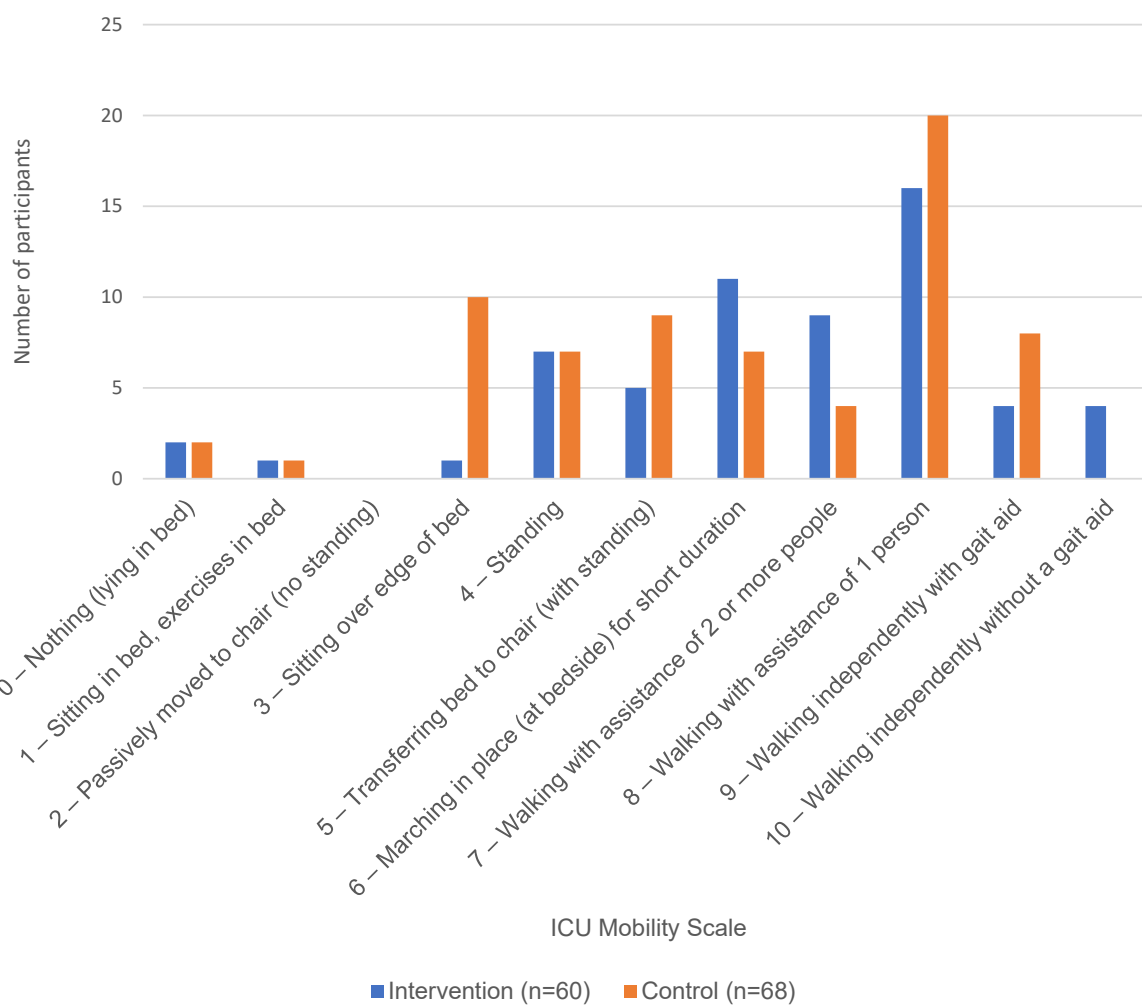
Reasons	Both Group, n (%)	Intervention Group, n (%)	Control Group, n (%)
Staffing limitations	271 (41)	111 (40)	160 (42)
Physiotherapy not indicated ^b	105 (16)	63 (23)	42 (11)
Participant unavailable	75 (11)	21 (8)	54 (14)
Other	58 (9)	22 (8)	36 (9)
Not documented	43 (7)	15 (5)	28 (7)
Participant declined	38 (6)	19 (7)	19 (5)
Clinical deterioration	32 (5)	12 (4)	20 (5)
Medical order for no rehabilitation due to clinical risk	12 (2)	3 (1)	9 (2)
Hospital transfer	12 (2)	4 (1)	8 (2)
Participant fatigue	7 (1)	3 (1)	4 (1)
Participant unresponsive	5 (1)	3 (1)	2 (1)
Palliation/death	4 (1)	4 (1)	0 (0)
Totals for reasons usual care not provided	662	280	382

^a Percentages may not add to 100% due to rounding ^bPhysiotherapy not indicated when either no order was placed for treatment or participants were discharged from physiotherapy care

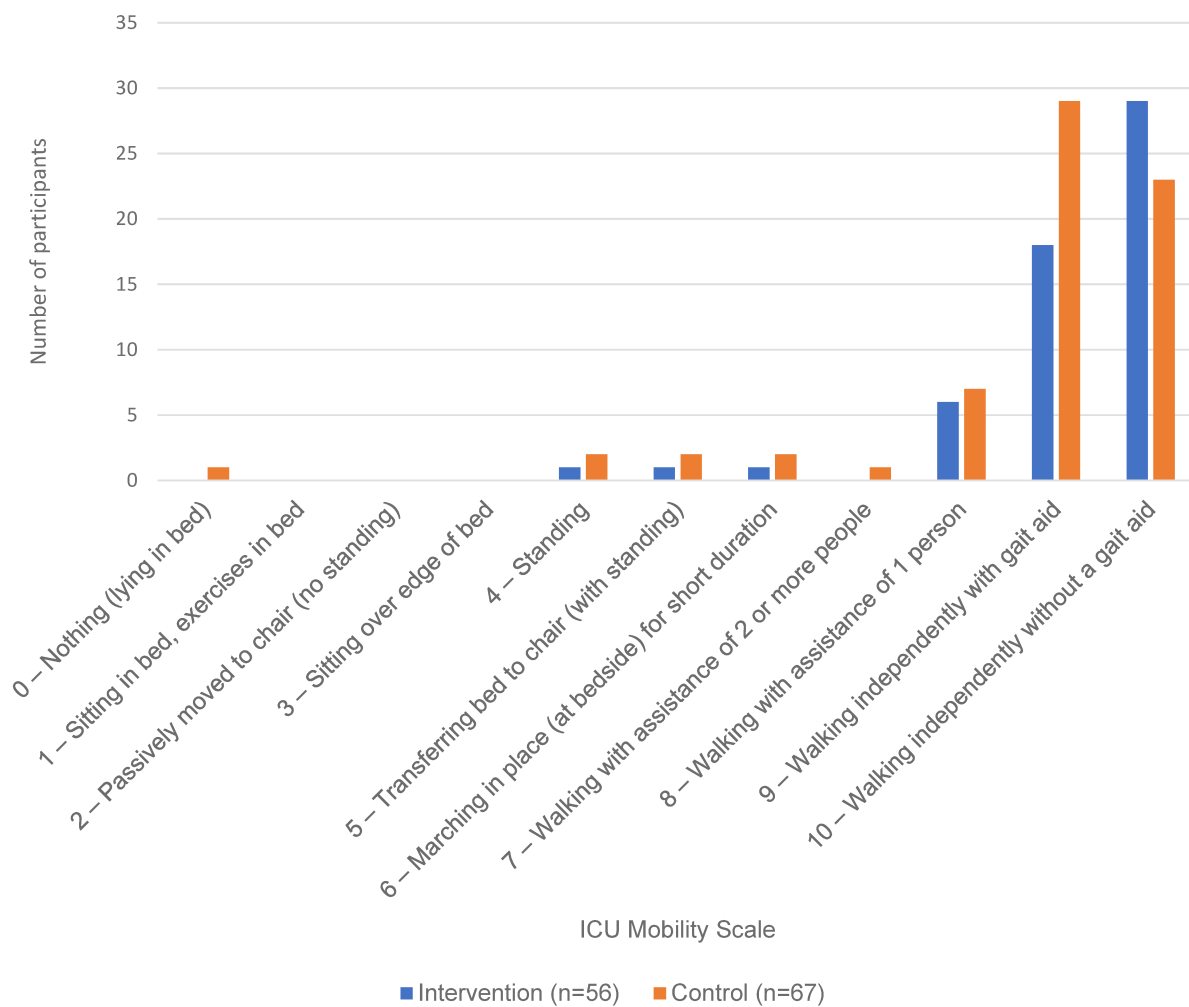
e-Supplement Table 10: Study secondary and clinical outcomes (in-hospital) FES-cycle and cycle only leg

	Cycling only n=80	Mean difference ^a (intervention minus control) with 95% CI ^b
Ultrasound cross sectional area of rectus femoris (baseline to hospital discharge), % change (95% CI)		
Cycling only leg ^c	-8.7 (-19.7 to 2.4)	
Cycling only vs FES cycling		2.1 (-33.1 to 37.4) ^a
Cycling only vs control group		-5.1 (-40.1 to 29.8) ^a
Strength at Hospital Discharge		
Quadriceps strength (Nm), mean (SD) Cycle ^d	57.4 (24.1)	
MRC at hospital discharge: Cycling only vs. control ^e		0.0 (0.4 to 0.5) ^a

^a Mean differences calculated on imputed data set; ^b CI = confidence interval; ^c For ultrasound CSA n=31 cycle only leg; ^d For quadriceps strength (complete cases) at hospital discharge n=49 (cycle only leg); ^e Medical Research Council sum score (0-60) higher values indicate better strength



e-Supplement Fig 1 Highest ICU Mobility Scale score in ICU during usual care rehabilitation



e-Supplement Fig 2: Highest ICU mobility scale score in ward setting during usual care rehabilitation

References

1. Hodgson CL, Berney S, Haines K, Harrold M, Young P, Buhr H, Needham DM, (2013) Development of a mobility scale for use in a multicentre Australia and New Zealand: Trial of Early Activity and Mobilisation in ICU. *American Journal of Respiratory & Critical Care Medicine* 187: A1323
2. Wilson E, Seymour J, Aubeeluck A, (2011) Perspectives of staff providing care at the end of life for people with progressive long-term neurological conditions. *Palliat Support Care* 9: 377-385
3. Barr JMDF, Kishman CPJM, Jaeschke RMD, (2013) The Methodological Approach Used to Develop the 2013 Pain, Agitation, and Delirium Clinical Practice Guidelines for Adult ICU Patients. *Critical Care Medicine* 41(9) Supplement: S1-S15
4. Brunton LL, Lazo JS, Parker KL (2006) *Goodman and Gilman's the pharmacological basis of therapeutics*. McGraw-Hill, New York
5. ARDS Network, (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory disease syndrome *New England Journal of Medicine* 342: 1301-1308