SUPPLEMENTARY TABLES: SUMMARY OF FINDINGS

Table SI. Electrical muscle stimulation compared with no intervention/any other type of intervention for preserving muscle mass in patients with multiple organ dysfunction syndrome (MODS): summary of findings

Patient or population: patients with MODS Setting: inpatients Intervention: electrical muscle stimulation Comparison: no intervention/any other type of intervention						
Outcomes	Anticipated absolute effects* (mean±SD)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention/any other type of intervention	Risk with electrical muscle stimulation				
Preservation of muscle mass assessed by ultrasonographic measurement of the cross-sectional diameter (CSD) of the quadriceps muscle	In the control group, from baseline until end of treatment the absolute difference in the CSD of the right rectus femoris was –0.21±0.10 cm. Difference in the CSD of the right vastus intermedius was –0.29±0.28 cm. Difference in the CSD of the left rectus femoris was –0.19±0.16 cm Difference in the CSD of the left vastus intermedius was –0.22±0.26 cm.	In the intervention group, from baseline until the end of treatment, the absolute difference in the CSD of the right rectus femoris was –0.11±0.06 cm. Difference in the CSD of the right vastus intermedius was –0.10±0.05 cm. Difference in the CSD of the left rectus femoris was –0.13±0.10 cm. Difference in the CSD of the left vastus intermedius was –0.09±0.05 cm.	–	26 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]	Authors reported that the difference in the CSD of the right rectus femoris, right vastus intermedius and left vastus intermedius was statistically significant (in the intervention group p=0.009, p=0.034, p=0.018, respectively). However, the difference in the CSD of the left rectus femoris was not statistically significant (p=0.07).
*The risk in the intervention group is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). 95%CI: 95% confidence interval						
GRADE Working Group grades of evidence High certainty: We are confident that the true effect lies close to that of the estimate of the effect Moderate certainty: We are moderately confident in the effect estimate: The true effect is probably close to the estimate of the effect, but there is a possibility that it is substantially different Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect Very low certainty: We have little confidence in the effect estimate: The true effect is probably substantially different from the estimate of the effect						

[a]Downgrade 2 levels due to the high risk of reporting bias (selective reporting), attrition bias (incomplete outcome data) and the unclear risk of selection bias (uncertainty around random sequence generation and allocation concealment). [b]Downgrade 1 level due to small sample size. MODS: Multiple Organ Dysfunction Syndrome; CSD: Cross Sectiomal Diameter; CI: Confidence Interval.

Table SII. Neuromuscular electrical stimulation compared with no intervention/any other type of intervention for preserving muscle strength in patients with multiple organ dysfunction syndrome (MODS): summary of findings

Patient or population: patients with MODS Setting: inpatients Intervention: neuromuscular electrical stimulation Comparison: no intervention/any other type of intervention						
Outcomes	Anticipated absolute effects* (median [IQR])		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention/any other type of intervention	Risk with neuromuscular electrical stimulation				
Quadriceps and biceps muscle strength at awakening assessed with MRC score	In the control group, the MRC median score at awakening was 2 [IQR 2–3] for the quadriceps muscle and 3 [IQR 1–4] for the biceps muscle.	In the intervention group, the MRC median score at awakening was 3 [IQR 2–3] for the quadriceps muscle and 3 [IQR 2–4] for the biceps muscle.	–	28 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was a statistically significant difference (biceps: p=0.014; quadriceps: p=0.025).
Quadriceps and biceps muscle strength on the last day of NMES assessed with MRC score	In the control group, the MRC median score on the last day of NMES was 3 [IQR 2–3] for the quadriceps muscle and 3 [IQR 2–4] for the biceps muscle.	In the intervention group, the MRC median score on the last day of NMES was 3 [3–4] for the quadriceps muscle and 4 [IQR 3–4] for the biceps muscle.	-	28 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was a statistically significant difference (biceps: p=0.005; quadriceps: p=0.034).
Arms circumferences assessed with a 7.5-MHz linear ultrasound transducer	In the control group, from enrolment to the last day of NMES, the median variation was -1.0 cm	In the intervention group, from the enrolment to the last day on NMES, the median variation was –1.3 cm	-	28 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was no statistically significant change in arms circumferences from baseline to the last NMES session. (p=0.615).

	[IQR –2.5 to 0] cm.	[IQR –1.9 to 0] cm.				
Thigh circumference assessed with a 7.5-MHz linear ultrasound transducer	In the control group, from the enrolment to the last day of NMES, the median variation was 0.9 cm [IQR –1.0 to 1.9] cm.	In the intervention group, from the enrolment to the last day on NMES, the median variation was –0.4 cm [IQR –1.5 to 1.8] cm.	–	28 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was no statistically significant change in tights circumferences from baseline to the last NMES session. (p=0.979).
Biceps thickness assessed with a 7.5-MHz linear ultrasound transducer	In the control group, from the enrolment to the last day of NMES, the median variation was 0 cm [IQR −2 to 2] cm.	In the control group, from the enrolment to the last day of NMES, the median variation was 0 cm [IQR −3 to 0] cm.	–	28 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that biceps thickness did not change during the whole NMES session. There was no statistically significant difference (p=0.290).
*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).						
GRADE Working Group grades of evidence. High certainty: We are confident that the true effect lies close to that of the estimate of the effect Moderate certainty: We are moderately confident in the effect estimate: The true effect is probably close to the estimate of the effect, but there is a possibility that it is substantially different Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect Very low certainty: We have little confidence in the effect estimate: The true effect is probably substantially different from the estimate of the effect						

[a]Downgrade 1 level due to the unclear risk of selection bias (random sequence generation and selective reporting) and due to the high risk of reporting bias for incomplete outcome data. [b]Downgrade 1 level due to the small sample size. MODS: Multiple Organ Dysfunction Syndrome; MRC score: Medical Research Council score; NMES: Neuro-Muscolar Electrical Stimulation; CI: Confidence Interval.

Table SIII. Muscle activating measures in addition to an early protocol-based physiotherapy compared with early protocol-based physiotherapy alone for improving muscle strength and functional independency in patients with sepsis-related multiple organ dysfunction syndrome (MODS): summary of findings

Patient or population: patients with MODS Setting: inpatients, outpatients Intervention: muscle-activating measures in addition to an early protocol-based physiotherapy Comparison: early protocol-based physiotherapy alone						
Outcomes	Anticipated absolute effects* (median [IQR])		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with early protocol-based physiotherapy alone	Risk with muscle-activating measures in addition to an early protocol-based physiotherapy				
Muscle strength (at awakening) assessed with MRC score	In the control group, the MRC median score at awakening was 3.0. [IQR 2.7–3.4]	In the intervention group, the MRC median score at awakening was 3.0. [IQR 2.1–3.8]	–	50 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was no statistically significant difference between groups (p>0.05).
Muscle strength (at ICU discharge) assessed with MRC score	In the control group, the MRC median score at ICU discharge was 3.9. [IQR 3.3–4.0]	In the intervention group, the MRC median score at ICU discharge was 3.6. [IQR 2.8–4.0]	–	50 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was no statistically significant difference between groups (p>0.05).
Muscle strength (at 12 months follow-up) assessed with MRC score	In the control group, the MRC median score at 12 months follow-up was 5.0. [IQR 4.3–5.0]	In the intervention group, the MRC median score at 12 months follow-up was 4.8. [IQR 4.3–5.0]	–	50 (1 RCT)	⨁⨁◯◯ LOW [a,b]	Authors reported that there was no statistically significant difference between groups (p>0.05).
Muscle strength assessed with handgrip dynamometry	NR	NR	–	50 (1 RCT)	⨁⨁◯◯ LOW [a,b]	The results among groups are not reported, nevertheless authors reported that muscle strength did not present any statistically significant differences

						between the intervention and control groups (p>0.05).
Muscle strength assessed with 6-min walking test	NR	NR	–	50 (1 RCT)	⊕⊕◯◯ LOW [a,b]	At the 12-month follow-up visit the 6-month walking test revealed significant muscle fatigue with no difference between the intervention and control groups.
Physical ability assessed with minimal modified FIM	In the control group, the mmFIM median score was 0.5 [IQR 0.5-2.0].	In the intervention group, the mmFIM median score was 0.5 [IQR 0.25-2.0].	–	50 (1 RCT)	⊕⊕◯◯ LOW [a,b]	Authors reported that there was no statistically significant difference between groups (p=0.842).

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
95% CI: 95% confidence interval.

GRADE Working Group grades of evidence
High certainty: We are confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is probably close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have little confidence in the effect estimate: The true effect is probably substantially different from the estimate of the effect

[a]Downgrade 1 level due to the unclear risk of selection bias (allocation concealment) and of reporting bias (selective reporting).
[b]Downgrade 1 level due to small sample size. MODS: Multiple Organ Dysfunction Syndrome; MRC score: Medical Research Council score; ICU: Intensive Care Unit; NR: Not Reported; CI: Confidence Interval.