Supplementary Table 9. Certainty of evidence

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No. of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **protocolized sedation** | **conventional sedation** | **Relative (95% CI)** | **Absolute (95% CI)** | | |
| **Duration of invasive mechanical ventilation (follow-up: mean 1 months; assessed with: hours; Scale from: 0 to 1200)** | | | | | | | | | | | | |
| 20 | observational studies | serious[a] | serious[b] | not serious | not serious | none | 6787 | 6245 | - | MD **13.88 hours shorter** (25.46 to 2.29 shorter) | ⊕⊕◯◯ Low | CRITICAL |
| **ICU length of stay (follow-up: mean 1 months; assessed with: days; Scale from: 0 to 100)** | | | | | | | | | | | | |
| 14 | observational studies | serious[a] | serious[c] | not serious | not serious | none | 6756 | 6206 | - | MD **0.6 days lower** (1.72 lower to 0.51 higher) | ⊕⊕◯◯ Low | CRITICAL |
| **Hospital length of stay (follow-up: mean 1 months; assessed with: days; Scale from: 0 to 100)** | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | observational studies | serious[a] | serious[d] | not serious | not serious | none | 5577 | 5166 | - | MD **1.04 days lower** (3 lower to 0.92 higher) | ⊕⊕◯◯ Low | CRITICAL |
| **Withdrawal syndrome (follow-up: median 1 months; assessed with: clinical evaluation)** | | | | | | | | | | | | |
| 8 | observational studies | not serious | serious[e] | serious[f] | not serious | all plausible residual confounding would suggest spurious effect, while no effect was observed | 568/1921 (29.6%) | 486/1898 (25.6%) | **OR 0.79** (0.39 to 1.61) | **42 fewer per 1,000** (from 138 fewer to 101 more) | ⊕⊕⊕◯ Moderate | IMPORTANT |
| **unplanned extubation (follow-up: median 1 months; assessed with: clinical assessment)** | | | | | | | | | | | | |
| 7 | observational studies | serious[a] | not serious | not serious | not serious | all plausible residual confounding would reduce the demonstrated effect | 150/4993 (3.0%) | 118/4501 (2.6%) | **OR 1.15** (0.98 to 1.34) | **4 more per 1,000** (from 1 fewer to 9 more) | ⊕⊕⊕⊕ High | IMPORTANT |
| **ICU mortality (follow-up: median 3 months; assessed with: report based on follow-up)** | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | observational studies | not serious | not serious | not serious | not serious | all plausible residual confounding would reduce the demonstrated effect | 233/4496 (5.2%) | 185/3995 (4.6%) | **OR 1.13** (0.92 to 1.37) | **6 more per 1,000** (from 4 fewer to 16 more) | ⊕⊕⊕⊕ High | IMPORTANT |
| **Duration of intravenous sedation (follow-up: median 1 months; assessed with: days; Scale from: 0 to 100)** | | | | | | | | | | | | |
| 3 | observational studies | serious[a] | serious[g] | not serious | not serious | none | 199 | 189 | - | MD **3.29 days lower** (8.16 lower to 1.58 higher) | ⊕⊕◯◯ Low | IMPORTANT |

CI, confidence interval; MD, mean difference; OR, odds ratio.

[a)]Downgraded one level due to potential serious risk of bias. [b)]We observed inconsistency between the results of the included studies, Deeter 2011 found significantly shorter, Chomat 2021 significantly longer duration of IMV in the experimental group, causing substantial heterogeneity. Two included studies (Gaillard Le-Roux 2017, Kozin 2015) were assessed as having serious risk of bias. [c)]We observed inconsistency between the results of the included studies, Verlaat 2013, Hanser 2020, Deeter 2011 found significantly shorter ICU length of stay (LOS) in the experimental group, causing substantial heterogeneity. Two included studies (Gaillard Le-Roux 2017, Kozin 2015) were assessed as having serious risk of bias. [d)]We observed inconsistency between the results of the included studies. Only Curley 2015 found significantly shorter in-hospital LOS in the experimental group. Mean in-hospital LOS varied across the included studies due to different clinical settings causing substantial heterogeneity. Kozin 2015 was assessed as having serious risk of bias. [e)]Large difference in ORs and CIs, heterogeneity 82% caused by different measurement of withdrawal syndrome. [f)]The incidence of withdrawal was measured with validated

assessment tools (WAT-1, SOS, modified Finnegan score), or defined as clinically significant by the necessity of benzodiazepine or opiate rescue therapy.
[g)]We observed inconsistency between the results of the included studies. In the protocolized sedation subgroup Deeter 2011 and Jin 2007 found significantly shorter duration of sedation causing substantial heterogeneity. Kozin 2015 were assessed as having serious risk of bias.