APPENDIX III: CRITICAL APPRAISAL OF THE INCLUDED STUDIES

Strengths	Limitations
Frazer et al. 2013[7] – USA; Systematic review and meta-analysis 1/5	
• Literature selection and data extraction were conducted by two reviewers independently. • The risk of bias and the methodological quality were evaluated systematically by the two reviewers using the Cochrane risk of bias tool.	• The review excluded trials on cardiac and critically ill ICU patients; the results of the review may not be generalizable to these two categories of patients. • The meta-analysis evaluated heterogeneity using statistical methods only; the clinical heterogeneity (e.g. the use of different sedation regimens and protocols) were not taken into consideration. • The exclusion criteria in each of the included studies were not reported; therefore, the generalizability of the study finding could not be ascertained.
Mo et al. 2013[6] – UK; Systematic review 2/5	
• The review included studies that evaluated delirium using objective monitoring tools; this was done to minimize bias in the outcome evaluation	• The article did not report who conducted the literature search and data selection; double selection and extraction could not verified. • The quality of the included studies was not evaluated. • The exclusion criteria in each of the included studies were not reported; therefore, the generalizability of the study finding could not be ascertained.
Xia et al. 2013[8] – China; Systematic review and meta-analysis 3/5	
• Literature selection and data extraction were conducted by two reviewers independently. • The article reported that the methodological quality was evaluated using the Cochrane Collaboration tool; however, the results of this evaluation wasn't reported.	• The meta-analysis evaluated heterogeneity using statistical methods only; the clinical heterogeneity (e.g. the use of different sedation regimens and protocols) were not taken into consideration. • The exclusion criteria in each of the included studies were not reported; therefore, the generalizability of the study finding could not be ascertained.
Lin et al. 2012[9] – China; Systematic review and meta-analysis 4/5	
• Literature selection and data extraction were conducted by two reviewers independently. • The risk of bias and the methodological quality were evaluated systematically by the two reviewers using the Newcastle-Ottawa scale.	• The meta-analysis evaluated heterogeneity using statistical methods only; the clinical heterogeneity (e.g. the infusion rate) were not taken into consideration. • The exclusion criteria in each of the included studies were not reported; therefore, the generalizability of the study finding could not be ascertained.
Tan et al. 2010[10] – Australia; Systematic review and meta-analysis 5/5	
• Literature selection and data extraction were conducted by two reviewers independently. • The methodological quality of the included studies were evaluated and reported; the article did not specify the method used or who conducted this evaluation • The review conducted subgroup analysis for studies that included elective surgery, and those that included	• The meta-analysis included studies that allowed rescue medications; the analysis did not consider the differences in the used rescue medications or their amount, dosage and regimens.

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non-elective critically ill patients; this was done as complement for the statistical heterogeneity assessment	
• Literature selection and data extraction were conducted by two reviewers independently. • The methodological quality of the included studies were evaluated and reported; the article did not specify the method used or who conducted this evaluation • The review conducted subgroup analysis for studies that included elective surgery, and those that included non-elective critically ill patients; this was done as complement for the statistical heterogeneity assessment	• The meta-analysis included studies that allowed rescue medications; the analysis did not consider the differences in the used rescue medications or their amount, dosage and regimens.
Aydogan et al. 2013[11] – Turkey; Randomized-controlled trial 1/5	
• The study was double blinded • The sample size was estimated based on power calculation. The trial was powered to detect 30% difference in fentanyl consumption. • All randomized patients completed the study	• Randomization method and allocation concealment were not described. • The article did not precise if the analysis was based on the intention to treat or per-protocol dataset. • The trial excluded several medical condition that may affect the reaction to sedative agents. Therefore, the finding form this study might not be generalizable to the excluded patients.
MacLaren et al. 2013[12] – USA; Randomized-controlled trial 2/5	
• The study was double blinded • Allocation concealment was assured by indistinguishable infusion bags and same dose adjustment increments (2 mL/h) • The sample size was based on power calculation to detect 30% difference in the occurrence of anxiety, depression and ASD manifestations. However, the study was stopped before including the estimated sample size.	• Primary outcome was reported for 70% of the randomized patients • The article did not precise if the analysis was based on the intention to treat or per-protocol dataset. • Exclusion criteria were extensive and eliminated several medical condition that cause patients' admission to ICU. Therefore, the finding form this study might not be generalizable to the excluded patients.
Prasad et al. 2012[13] – India; Randomized-controlled trial 3/5	
• The study was double blinded • The sample size was based on power calculation to detect 180 minutes difference in time to extubation; another calculation was based on power estimation to detect 0.6 RSS difference.	• Methods used for allocation concealment were not described in the report • The article did not precise if the analysis was based on the intention to treat or per-protocol dataset. • The study excluded several medication conditions that require ICU admission; results might not be generalizable to other than the included patients.

Strengths	Limitations
Huang et al. 2012[14] – China; Randomized-controlled trial 4/5	
• The study was double blinded • All randomized patients completed the study and were included in outcome analysis	• The sample size was based on convenience rather than power analysis • The article did not precise if the analysis was based on the intention to treat or per-protocol dataset. • Concealment of treatment allocation was not clear. The trial interventions could be adjusted; the adjustment rates are different. And therefore, the allocated treatment could be unconcealed. • The trial excluded many clinical conditions that require patients' admission to ICU. The trial findings could not be applied to the excluded patients.
Mirski et al. 2010[15] and Goodwin et al. 2013[16] – USA ; Randomized-controlled trial 5/5	
• The study was double blinded • Sample size was based on power calculation	• The article did not precise if the analysis was based on the intention to treat or per-protocol dataset. • Of the 35 randomized patients, 33 received at least one treatment, and 30 patients completed the trial. • Concealment of treatment allocation was not clear. Treatment allocation could be breached by the differences in solution texture and the titration regimens of the compared interventions. • The article did not report any exclusion criteria, and it did not specify that there weren't any.