APPENDIX IV: RESULTS OF THE INCLUDED STUDIES

Table 3. Summary of Findings from the included studies

<table>
<tr><th colspan="3">Main Study Findings</th><th>Conclusions</th></tr>
<tr><td colspan="4">Frazer et al. 2013[7] – USA; Systematic review and meta-analysis 1/5</td></tr>
<tr><td colspan="3">The meta-analysis included six trials; two of which evaluated propofol instead of dexmedetomidine. The published results grouped both dexmedetomidine and propofol as one group. CADTH reviewer meta-analyzed dexmedetomidine studies separately. The two sets of results are reported in the table below</td><td rowspan="11">The authors concluded that adult ICU sedation with dexmedetomidine or propofol may reduce ICU length of stay and duration of mechanical ventilation.</td></tr>
<tr><td></td><td>Participants (studies)</td><td>Non-benzodiazepine (or dexmedetomidine)</td></tr>
<tr><td colspan="3">ICU length of stay (days); mean difference (95% CI)</td></tr>
<tr><td>• Non-benzodiazepine versus benzodiazepine</td><td>1,235 (6)</td><td>-1.64 (-2.57, -0.70)</td></tr>
<tr><td>• Dexmedetomidine versus benzodiazepine[a]</td><td>1,026 (4)</td><td>-1.54 (-2.54, -0.54)</td></tr>
<tr><td colspan="3">Duration of mechanical ventilation (days); mean difference (95% CI)</td></tr>
<tr><td>• Non-benzodiazepine versus benzodiazepine</td><td>1,101 (4)</td><td>-1.87 (-2.51, -1.22)</td></tr>
<tr><td>• Dexmedetomidine versus benzodiazepine[a]</td><td>969 (3)</td><td>-1.80 (-2.47, -1.12)</td></tr>
<tr><td colspan="3">Delirium; risk ratio (95% CI)</td></tr>
<tr><td>• Dexmedetomidine versus benzodiazepine</td><td>296 (2)</td><td>0.82 (0.61, 1.11)</td></tr>
<tr><td colspan="3">All-cause mortality; risk ratio (95% CI)</td></tr>
<tr><td>• Non-benzodiazepine versus benzodiazepine</td><td>1,101 (4)</td><td>1.01 (0.78, 1.30)</td></tr>
<tr><td>• Dexmedetomidine versus benzodiazepine[a]</td><td>969 (3)</td><td>0.99 (0.68, 1.43)</td></tr>
<tr><td colspan="3">Studies evaluating dexmedetomidine versus benzodiazepine were meta-analyzed by CADTH reviewer based on the data provided in the reviewed article by Frazer et al.[7]</td></tr>
<tr><td colspan="4">Mo et al. 2013[6] – UK; ; Systematic review 2/5</td></tr>
<tr><td colspan="3"></td><td rowspan="9">The authors concluded that the available evidence showed that dexmedetomidine is useful in the prevention and treatment of delirium in ICU patients.</td></tr>
<tr><td>Study</td><td>Delirium evaluation</td><td>Dexmedetomidine vs. comparator</td></tr>
<tr><td rowspan="2">Jakob 2012</td><td rowspan="3">Incidence of positive CAM-ICU</td><td>Vs. midazolam: difference NS</td></tr>
<tr><td>Vs. propofol: difference NS</td></tr>
<tr><td>Yapici 2011</td><td>No events</td></tr>
<tr><td>Reade 2009</td><td>ICDSC score</td><td>Vs. haloperidol: difference NS</td></tr>
<tr><td>Riker 2009</td><td rowspan="2">Incidence of positive CAM-ICU</td><td>Vs. midazolam: difference NS</td></tr>
<tr><td>Ruokonen 2009</td><td>Vs. midazolam or propofol: difference NS</td></tr>
<tr><td>Shehabi 2009</td><td>CAM-ICU (incidence of delirium)</td><td>Vs. morphine: difference NS</td></tr>
<tr><td>Maldonado 2009</td><td>DSM-IV-TR (incidence of delirium)</td><td>Vs. midazolam or propofol: difference P<0.001</td></tr>
<tr><td>Pandharipande 2007</td><td>CAM-ICU (delirium free days)</td><td>Vs. lorazepam: difference NS</td></tr>
</table>

Table 3. Summary of Findings from the included studies

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<tr><th colspan="3">Main Study Findings</th><th>Conclusions</th></tr>
<tr><td colspan="3">CAM-ICU = Confusion Assessment Method for the ICU; DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders; ICDSC = Intensive Care Delirium Screening Checklist</td><td></td></tr>
<tr><td colspan="4">Xia et al. 2013[8] – China; Systematic review and meta-analysis 3/5</td></tr>
<tr><td></td><td>Participants (studies)</td><td>Dexmedetomidine vs. propofol</td><td rowspan="12">The authors concluded that the use of dexmedetomidine for ICU patients' sedation shortened the length of ICU stay and decreased the incidence of delirium; the author also pointed out that dexmedetomidine was associated with increased incidence of hypertension.</td></tr>
<tr><td>ICU length of stay (days);</td><td></td><td></td></tr>
<tr><td>• mean difference (95% CI)</td><td>655 (5)</td><td>-0.81 (-1.48, -0.15)</td></tr>
<tr><td>Duration of mechanical ventilation (days);</td><td></td><td></td></tr>
<tr><td>• mean difference (95% CI)</td><td>895 (5)</td><td>0.53 (-2.66, 3.72)</td></tr>
<tr><td>Delirium;</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>658 (3)</td><td>0.40 (0.22, 0.74)</td></tr>
<tr><td>All-cause mortality;</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>267 (5)</td><td>0.83 (0.32, 2.12)</td></tr>
<tr><td>Hypotension</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>1015 (6)</td><td>1.12 (0.86, 1.47)</td></tr>
<tr><td>Bradycardia</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>788 (2)</td><td>1.36 (0.85, 2.18)</td></tr>
<tr><td>Hypertension</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>846 (3)</td><td>1.56 (1.11, 2.20)</td></tr>
<tr><td colspan="4">Lin et al. 2012[9] – China; Systematic review and meta-analysis 4/5</td></tr>
<tr><td></td><td>Participants (studies)</td><td>Dexmedetomidine vs. comparator</td><td rowspan="12">The authors concluded that dexmedetomidine was associated with shorter length of mechanical ventilation and fewer incidence of delirium compared with other sedatives; however, dexmedetomidine was associated with a significantly higher incidence of bradycardia.</td></tr>
<tr><td>ICU length of stay (days);</td><td></td><td></td></tr>
<tr><td>• mean difference (95% CI)</td><td>NR</td><td>-3.44 (-11.40, 4.52)</td></tr>
<tr><td>Duration of mechanical ventilation (hours);</td><td></td><td></td></tr>
<tr><td>• mean difference (95% CI)</td><td>16613 (9)</td><td>-2.70 (-5.05, -0.35)</td></tr>
<tr><td>Delirium;</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>10830 (4)</td><td>0.36 (0.21, 0.64)</td></tr>
<tr><td>Hospital mortality;</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>NR</td><td>0.72 (0.37, 1.39)</td></tr>
<tr><td>Hypotension</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>839 (5)</td><td>0.99 (0.72, 1.36)</td></tr>
<tr><td>Bradycardia</td><td></td><td></td></tr>
<tr><td>• risk ratio (95% CI)</td><td>650 (3)</td><td>2.08 (1.16, 3.74)</td></tr>
<tr><td colspan="4">Tan et al. 2010[10] – Australia; Systematic review and meta-analysis 5/5</td></tr>
<tr><td></td><td>Participants (studies)</td><td>Dexmedetomidine vs. comparator</td><td rowspan="8">The authors concluded that the included studies had significant heterogeneity and provided limited evidence that dexmedetomidine might reduce the length of ICU stay. However, it was associated with higher risk of bradycardia.</td></tr>
<tr><td>ICU length of stay (days); mean difference (95% CI)</td><td></td><td></td></tr>
<tr><td>• Overall</td><td>1264 (12)</td><td>-0.48 (0.78, -0.18)</td></tr>
<tr><td>• elective postoperative</td><td>586 (5)</td><td>-0.11 (-0.28, 0.07)</td></tr>
<tr><td>• non-elective critically-ills</td><td>678 (7)</td><td>-1.41 (-2.94, 0.12)</td></tr>
<tr><td>Duration of mechanical ventilation (days); mean difference (95% CI)</td><td></td><td></td></tr>
<tr><td>• Overall</td><td>1901 (12)</td><td>-0.51 (-1.75, 0.73)</td></tr>
<tr><td>• elective postoperative</td><td>1410 (9)</td><td>-0.43 (-1.15, 0.29)</td></tr>
</table>

Table 3. Summary of Findings from the included studies

Main Study Findings			Conclusions
• non-elective critically-ills	491 (3)	-16.96 (-70.55, 36.63)	
Delirium; risk ratio (95% CI)			
• Overall	1754 (8)	0.79 (0.56, 1.11)	
• elective postoperative	1200 (5)	0.54 (0.24, 1.22)	
• non-elective critically-ills	554 (3)	0.95 (0.67, 1.34)	
Mortality; risk ratio (95% CI)			
• Overall	1839 (16)	0.85 (0.64, 1.13)	
• elective postoperative	1145 (9)	0.75 (0.32, 1.76)	
• non-elective critically-ills	694 (7)	0.86 (0.64, 1.17)	
Hypotension; risk ratio (95% CI)			
• Overall	1545 (12)	1.43 (0.78, 2.60)	
• elective postoperative	955 (8)	1.23 (0.50, 2.98)	
• non-elective critically-ills	590 (4)	2.73 (0.40, 18.39)	
Bradycardia[a]; risk ratio (95% CI)			
• Overall	1164 (10)	1.82 (0.66, 5.03)	
• elective postoperative	574 (6)	0.95 (0.39, 2.34)	
• non-elective critically-ills	590 (4)	7.30 (1.73, 30.81)	
Nausea and vomiting; risk ratio (95% CI)			
• Overall	NR	1.03 (0.66, 1.59)	
[a] bradycardia requiring intervention			

Aydogan et al. 2013[11] – Turkey; Randomized-controlled trial 1/5

	Dexmedetomidine (N = 16)	Midazolam (N = 16)	Difference (P-value)	Conclusions
ICU length of stay				The authors concluded that dexmedetomidine may be beneficial for managing sedation in adolescents who have undergone scoliosis surgery.
• Days	2	2	(0.421)	
Duration of mechanical ventilation				
• Minutes	107	225	(0.035)	
Delirium;				
• Incidence rate	12.5%	31.3%	(<0.05)	
Use of fentanyl				
• µg (at 24 hours)	124.1	165.8	(0.002)	
Bradycardia;				
• Incidence rate	25%	6.25%	NR	

MacLaren et al. 2013[12] – USA; Randomized-controlled trial 2/5

	Dexmedetomidine (N = 11)	Midazolam (N = 12)	Difference (P-value)	Conclusions
HADS, mean score (SD)				The authors concluded that dexmedetomidine didn't reduce the mechanical ventilation time, and it was associated with more hypotension, less delirium and greater recall of the ICU experience.
• Anxiety	6 (7.6), n=8	3 (3.1), n=8	NS	
• Depression	4 (5.3) , n=8	6 (6.7) , n=8	NS	
ASD; mean score (SD)				
• Intrusion	16 (6.3), n=8	4 (5.2), n=8	(0.007)	
• Avoidance	18 (4), n=8	6 (7), n=8	(0.066)	
• Hyperarousal	6 (2.3), n=8	3 (1.6), n=8	(0.013)	
• Cumulative	36 (12), n=8	13 (12), n=8	(0.029)	
Delirium;				
• Incidence rate	36.4%	66.7%	(0.07)	
Tachycardia;				
• Incidence rate	63.6%	41.7%	NS	
Hypotension;				
• Incidence rate	90.9%	50%	(0.069)	

Table 3. Summary of Findings from the included studies

Main Study Findings				Conclusions
Bradycardia; risk ratio (95% CI)				
• Incidence rate	63.6%	58.3%	NS	
HADS = hospital anxiety and depression scale; NS = not significant				
Prasad et al. 2012[13] – India; Randomized-controlled trial 3/5				
	Dexmedetomidine (N = 30)	**Fentanyl (N = 30)**	**Difference (P-value)**	The authors concluded that dexmedetomidine was associated with earlier extubation than fentanyl, and it was associated with minimal depression of respiratory drive.
Time to extubation;				
• Mean minutes (SD)	131 (51.06)	373 (121.4)	(<0.001)	
Ramsay sedation score				
• Mean	NR	NR	NS	
NR = not reported; NS = not significant				
Huang et al. 2012[14] – China; Randomized-controlled trial 4/5				
	Dexmedetomidine (N = 33)	**Midazolam (N = 29)**	**Difference (P-value)**	The authors concluded that dexmedetomidine reduced the failure of non-invasive ventilation in patients with acute cardiogenic pulmonary edema.
Endotracheal intubation;				
• Incidence rate	21.2%	44.8%	(0.043)	
Time to intubation				
• Mean time (hours)	27.6	17.8	(0.024)	
ICU length of stay				
• Mean (days)	4.9	8.5	(0.042)	
ICU mortality;				
• Incidence rate	6.1%	10.3%	(0.658)	
Delirium;				
• Incidence rate	3.0%	13.8%	0.089	
Hypotension;				
• Incidence rate	12.1%	17.2%	0.772	
Bradycardia; risk ratio (95% CI)				
• Incidence rate	18.2%	0	0.016	
Mirski et al. 2010[15] and Goodwin et al. 2013[16] – USA ; Randomized-controlled trial 5/5				
	Dexmedetomidine	**Propofol**	**Difference (P-value)**	The authors concluded that dexmedetomidine ameliorate the cognitive functions when used for sedation of selected ICU patients.
Cognitive function (Adaptive cognitive exam: Overall)				
• Change from baseline	6.81	-12.38	19.19 (0.001)	
Cognitive function (Adaptive cognitive exam: Orientation)				
• Change from baseline	1.15	-3.04	4.19 (0.002)	
Cognitive function (Adaptive cognitive exam: Language)				
• Change from baseline	-0.23	-3.4	3.17 (0.007)	
Cognitive function (Adaptive cognitive exam: Registration)				
• Change from baseline	0.46	-1.11	1.58 (<0.001)	
Cognitive function (Adaptive cognitive exam: Attention/calculation)				

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Main Study Findings				Conclusions
• Change from baseline	3.55	-1.97	5.52 (<0.001)	
Cognitive function (Adaptive cognitive exam: Recall)				
• Change from baseline	2.02	-2.86	4.87 (<0.001)	
Delirium; risk ratio (95% CI)				
• Number of cases	1		NR	