

**CQ9-1 (GRADE)**

**P: Septic patients**

**I: Higher SpO<sub>2</sub> target**

**C: Lower SpO<sub>2</sub> target**

**O: Mortality, organ dysfunction, infection**

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
<b>Mortality</b>												
3	randomised trials	not serious	not serious	not serious	serious	none	94/337 (27.9%)	75/336 (22.3%)	RR 1.19 (0.83 to 1.70)	42 more per 1,000 (from 38 fewer to 156 more)	⊕⊕⊕○ Moderate	CRITICAL
<b>Organ dysfunction</b>												
1	randomised trials	not serious	not serious	not serious	serious	none	56/218 (25.7%)	41/216 (19.0%)	RR 1.35 (0.94 to 1.92)	66 more per 1,000 (from 11 fewer to 175 more)	⊕⊕⊕○ Moderate	CRITICAL
<b>Infection</b>												
1	randomised trials	not serious	not serious	not serious	serious	none	50/218 (22.9%)	39/216 (18.1%)	RR 1.27 (0.88 to 1.85)	49 more per 1,000 (from 22 fewer to 153 more)	⊕⊕⊕○ Moderate	CRITICAL

	JUDGEMENT						
<b>PROBLEM</b>	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
<b>DESIRABLE EFFECTS</b>	Trivial	Small	Moderate	Large		Varies	<b>Don't know</b>
<b>UNDESIRABLE EFFECTS</b>	Large	<b>Moderate</b>	Small	Trivial		Varies	Don't know
<b>CERTAINTY OF EVIDENCE</b>	Very low	Low	<b>Moderate</b>	High			No included studies
<b>VALUES</b>	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
<b>BALANCE OF EFFECTS</b>	Favors the comparison	<b>Probably favors the comparison</b>	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
<b>ACCEPTABILITY</b>	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
<b>FEASIBILITY</b>	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know

**CQ9-2 (GRADE)**

**Mortality**

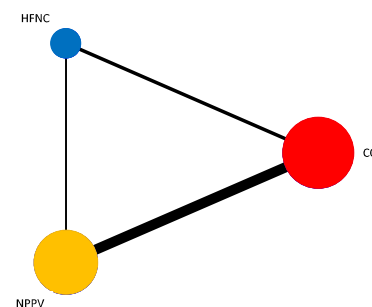
Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy in septic patients with acute respiratory failure.

Frequency NMA-SoF table

**BENEFITS**

Patients or population: Septic patients with acute respiratory failure who need oxygen therapy  
 Interventions: One of the following oxygen therapies: NPPV, HFNC, or COT  
 Comparator (reference): One of the other therapies other than the therapy included in intervention  
 Outcome: Short-term mortality  
 Setting: In-hospital

**Network plot**



	Total studies: 19 Total Patients: 4,837	Relative effect (95% CI) Network estimate	Anticipated absolute effect (95% CI)			Certainly of the evidence	Ranking (SUCRA)	Interpretation of Findings
			Without intervention	With intervention	Difference			
● NPPV (14 RCT; 2,359 participants)		0.88 (0.76 to 1.01) Network estimate	249 per 1000	219 per 1000	30 fewer per 1000 (60 fewer to 3 more)	⊕⊕○○ Low	2 (64.4)	-
● HFNC (5 RCT; 1,463 participants)		0.92 (0.80 to 1.07) Network estimate	306 per 1000	242 per 1000	65 fewer per 1000 (95 fewer to 28 more)	⊕⊕⊕○ Moderate	1 (77.3)	-
● COT		Reference comparator	No estimable	No estimable	No estimable	-	3 (8.3)	-
● NPPV (3 RCT; 338 participants)		0.95 (0.78 to 1.16) Network estimate	157 per 1000	149 per 1000	8 fewer per 1000 (35 fewer to 25 more)	⊕⊕○○ Low	-	-
● HFNC		Reference comparator	No estimable	No estimable	No estimable	-	-	-

## Intubation

Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy in septic patients with acute respiratory failure.

Frequency NMA-SoF table

### BENEFITS

Patients or population: Septic patients with acute respiratory failure who need oxygen therapy

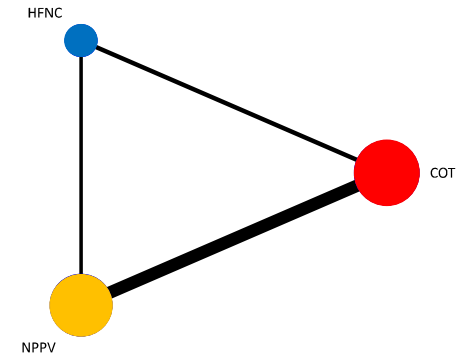
Interventions: One of the following oxygen therapies: NPPV, HFNC, or COT

Comparator (reference): One of the other therapies other than the therapy included in intervention

Outcome: Intubation

Setting: In-hospital

Network plot



Total studies: 24 Total Patients: 4,261	Relative effect (95% CI) Network estimate	Anticipated absolute effect (95% CI)			Certainty of the evidence	Ranking (SUCRA)	Interpretation of Findings
		Without intervention	With intervention	Difference			
● NPPV (17 RCT; 2,506 participants)	0.81 (0.71 to 0.91) Network estimate	317 per 1000	257 per 1000	60 fewer per 1000 (92 fewer to 29 fewer)	⊕⊕○○ Low	2 (74.5)	-
● HFNC (6 RCT; 1,563 participants)	0.79 (0.69 to 0.91) Network estimate	307 per 1000	243 per 1000	65 fewer per 1000 (95 fewer to 28 fewer)	⊕⊕⊕○ Moderate	1 (74.7)	-
● COT	Reference comparator	No estimable	No estimable	No estimable	-	3 (0.8)	-
● NPPV (5 RCT; 584 participants)	1.02 (0.86 to 1.20) Network estimate	230 per 1000	235 per 1000	5 more per 1000 (32 fewer to 46 more)	⊕⊕○○ Low	-	-
● HFNC	Reference comparator	No estimable	No estimable	No estimable	-	-	-

## Time to intubation

Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy in septic patients with acute respiratory failure.

Frequency NMA-SoF table

### BENEFITS

Patients or population: Septic patients with acute respiratory failure who need oxygen therapy

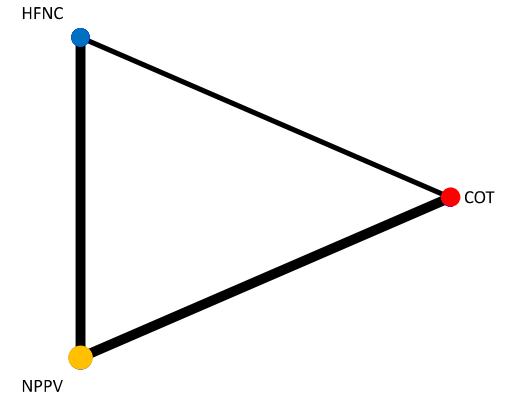
Interventions: One of the following oxygen therapies: NPPV, HFNC, or COT

Comparator (reference): One of the other therapies other than the therapy included in intervention

Outcome: Time to intubation (hours)

Setting: In-hospital

### Network plot



Total studies: 3 Total Patients: 606	Relative effect (95% CI)	Anticipated absolute effect (95% CI)		Certainty of the evidence	Ranking (SUCRA)	Interpretation of Findings
		Without intervention	With intervention			
● NPPV (2 RCT; 284 participants)	-	The mean difference in time to intubation was 0 hours.	The mean difference in time to intubation was 0.53 higher (0.27 lower to 0.80 higher)	⊕⊕⊕⊕ High	2 (40.3)	-
● HFNC (1 RCT; 200 participants)	-	The mean difference in time to intubation was 0 hours.	The mean difference in time to intubation was 1.15 higher (0.21 lower to 2.09 higher)	⊕⊕⊕⊕ High	1 (85.2)	-
● COT	Reference comparator	No estimable	No estimable	-	3 (24.5)	-
● NPPV (2 RCT; 432 participants)	-	The mean difference in time to intubation was 0 hours.	The mean difference in time to intubation was 0.62 lower (1.52 lower to 0.28 higher)	⊕⊕⊕○ Moderate	-	-
● HFNC	Reference comparator	No estimable	No estimable	-	-	-

	JUDGEMENT						
PROBLEM	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	<b>Moderate</b>	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	<b>Don't know</b>
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	<b>High</b>			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	<b>Probably favors the intervention</b>	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know





**CQ9-3 (GRADE)**

**P: Septic patients**

**I: Lung protective ventilation**

**C: Conventional ventilation**

**O: Mortality, ventilator free days, barotrauma, ventilator associated pneumonia**

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
<b>Mortality</b>												
9	randomised trials	not serious	not serious	serious	not serious	none	446/1217 (36.6%)	482/1205 (40.0%)	<b>RR 0.91</b> (0.78 to 1.06)	<b>36 fewer per 1,000</b> (from 88 fewer to 24 more)	 Moderate	CRITICAL
<b>Ventilator free days</b>												
3	randomised trials	not serious	serious	serious	serious	none	958	953	-	<b>MD 1.79 day higher</b> (from 0.62 lower to 4.2 higher)	 Very low	CRITICAL
<b>Barotrauma</b>												
7	randomised trials	not serious	not serious	serious	very serious	none	71/1093 (6.5%)	79/1089 (7.3%)	<b>RR 0.89</b> (0.57 to 1.38)	<b>8 fewer per 1,000</b> (from 31 fewer to 28 more)	 Very low	CRITICAL
<b>Ventilator associated pneumonia</b>												
1	randomised trials	serious	not serious	very serious	very serious	none	9/15 (60.0%)	6/13 (46.2%)	<b>RR 1.30</b> (0.63 to 2.67)	<b>138 more per 1,000</b> (from 171 fewer to 771 more)	 Very low	IMPORTANT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
DESIRABLE EFFECTS	Trivial	<b>Small</b>	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	<b>Trivial</b>		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	<b>Moderate</b>	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	<b>Probably favors the intervention</b>	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know

**CQ9-4 (GRADE)**

**P: Septic critically ill patients who need mechanical ventilation**

**I: High PEEP**

**C: Low PEEP**

**O: Mortality, ventilator free days, barotrauma, PaO<sub>2</sub>/FiO<sub>2</sub> (Day 1 to 3), circulatory insufficient due to PEEP**

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
<b>Mortality</b>												
7	randomised trials	not serious	not serious	serious	not serious	none	706/1815 (38.9%)	717/1842 (38.9%)	<b>RR 0.98</b> (0.86 to 1.12)	<b>8 fewer per 1,000</b> (from 54 fewer to 47 more)	⊕⊕⊕○ Moderate	CRITICAL
<b>Ventilator free days</b>												
3	randomised trials	not serious	very serious	serious	not serious	none	827	827	-	<b>MD 0.45 day higher</b> (from 2.02 lower to 2.92 higher)	⊕○○○ Very low	CRITICAL
<b>Barotrauma</b>												
6	randomised trials	not serious	serious	serious	very serious	none	122/1716 (7.1%)	101/1741 (5.8%)	<b>RR 1.08</b> (0.61 to 1.91)	<b>5 more per 1,000</b> (from 23 fewer to 53 more)	⊕○○○ Very low	CRITICAL
<b>PaO<sub>2</sub>/FiO<sub>2</sub></b>												
6	randomised trials	not serious	not serious	serious	not serious	none	1135	1174	-	<b>MD 57.71 higher</b> (from 35.13 higher to 80.3 higher)	⊕⊕⊕○ Moderate	IMPORTANT
<b>Circulatory insufficient due to PEEP</b>												
1	randomised trials	serious	not serious	serious	not serious	none	174/501 (34.7%)	144/509 (28.3%)	<b>RR 1.23</b> (1.02 to 1.47)	<b>65 more per 1,000</b> (from 6 more to 133 more)	⊕⊕○○ Low	CRITICAL



	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
DESIRABLE EFFECTS	<b>Trivial</b>	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	<b>Small</b>	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	<b>Very low</b>	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	<b>Probably favors the comparison</b>	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know

**CQ9-5 (GRADE)**

**P: Patients who need mechanical ventilation**

**I: Protocol-directed weaning**

**C: Physician-directed weaning**

**O: Mortality, re-intubation (within 48-72 hours), ventilator free days, length of ICU stay**

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Placebo	Relative (95% CI)	Absolute (95% CI)		
<b>Mortality</b>												
8	randomised trials	serious	not serious	not serious	very serious	none	104/640 (16.3%)	111/642 (17.3%)	RR 0.94 (0.70 to 1.26)	10 fewer per 1,000 (from 52 fewer to 45 more)	⊕○○○ Very low	CRITICAL
<b>Re-intubation</b>												
7	randomised trials	serious	not serious	not serious	very serious	none	50/542 (11.1%)	59/539 (11.0%)	RR 0.78 (0.45 to 1.37)	24 fewer per 1,000 (from 61 fewer to 41 more)	⊕○○○ Very low	CRITICAL
<b>Length of ICU stay</b>												
5	randomised trials	serious	not serious	not serious	serious	none	348	354	-	MD 0.89 day lower (from 2.73 lower to 0.95 higher)	⊕⊕○○ Low	IMPORTANT

	JUDGEMENT						
<b>PROBLEM</b>	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
<b>DESIRABLE EFFECTS</b>	Trivial	<b>Small</b>	Moderate	Large		Varies	Don't know
<b>UNDESIRABLE EFFECTS</b>	Large	Moderate	Small	Trivial		Varies	<b>Don't know</b>
<b>CERTAINTY OF EVIDENCE</b>	<b>Very low</b>	Low	Moderate	High			No included studies
<b>VALUES</b>	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
<b>BALANCE OF EFFECTS</b>	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	<b>Probably favors the intervention</b>	Favors the intervention	Varies	Don't know
<b>ACCEPTABILITY</b>	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
<b>FEASIBILITY</b>	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know

**CQ9-6 (GRADE)**

**Mortality**

Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy after extubation in patients recovering from sepsis

Frequency NMA-SoF table

**BENEFITS**

Patients or population: septic patients after extubation

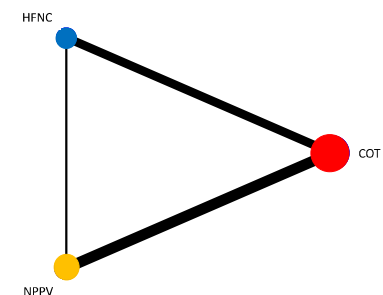
Interventions: One of the following oxygen therapies: NPPV, HFNT, or COT

Comparator (reference): One of the other therapies other than the therapy included in intervention

Outcome: Short-term mortality

Setting: In-hospital

**Network plot**



	Total studies: 10 Total Patients: 2,190	Relative effect (95% CI) Network estimate	Anticipated absolute effect (95% CI)			Certainty of the evidence	Ranking (SUCRA)	Interpretation of Findings
			Without intervention	With intervention	Difference			
● NPPV (5 RCT; 784 participants)		0.70 (0.49 to 1.01) Network estimate	104 per 1000	73 per 1000	31 fewer per 1000 (53 fewer to 1 more)	⊕⊕⊕○ Moderate	1 (91.8)	-
● HFNT (4 RCT; 802 participants)		0.84 (0.58 to 1.21) Network estimate	75 per 1000	63 per 1000	12 fewer per 1000 (32 fewer to 16 more)	⊕⊕⊕○ Moderate	2 (46.3)	-
● COT		Reference comparator	No estimable	No estimable	No estimable	-	3 (11.8)	-
● NPPV (1 RCT; 604 participants)		0.84 (0.62 to 1.12) Network estimate	269 per 1000	226 per 1000	43 fewer per 1000 (102 fewer to 32 more)	⊕⊕⊕○ Moderate	-	-
● HFNC		Reference comparator	No estimable	No estimable	No estimable	-	-	-

## Re-intubation

Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy after extubation in patients recovering from sepsis

Frequency NMA-SoF table

### BENEFITS

Patients or population: septic patients after extubation

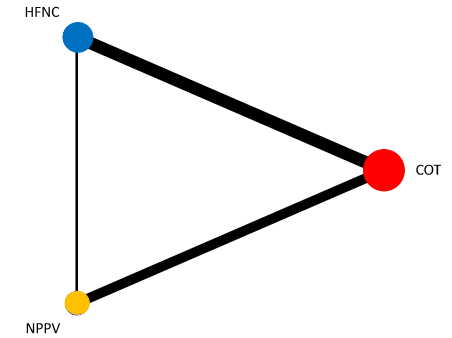
Interventions: One of the following oxygen therapies: NPPV, HFNT, or COT

Comparator (reference): One of the other therapies other than the therapy included in intervention

Outcome: Reintubation

Setting: In-hospital

### Network plot



	Total studies: 10 Total Patients: 2,130	Relative effect (95% CI) Network estimate	Anticipated absolute effect (95% CI)			Certainly of the evidence	Ranking (SUCRA)	Interpretation of Findings
			Without intervention	With intervention	Difference			
● NPPV (4 RCT; 664 participants)		0.52 (0.28 to 0.99) Network estimate	138 per 1000	72 per 1000	66 fewer per 1000 (99 fewer to 1 fewer)	⊕⊕⊕○ Moderate	2 (69.8)	-
● HFNT (5 RCT; 862 participants)		0.49 (0.27 to 0.91) Network estimate	135 per 1000	66 per 1000	69 fewer per 1000 (99 fewer to 12 fewer)	⊕⊕○○ Low	1 (77.8)	-
● COT		Reference comparator	No estimable	No estimable	No estimable	-	3 (2.8)	-
● NPPV (1 RCT; 604 participants)		1.07 (0.52 to 2.19) Network estimate	228 per 1000	244 per 1000	16 more per 1000 (109 fewer to 271 more)	⊕○○○ Very low	-	-
● HFNC		Reference comparator	No estimable	No estimable	No estimable	-	-	-

## Respiratory failure

Estimates of effects, confidence intervals, and certainty of the evidence for oxygen therapy after extubation in patients recovering from sepsis

Frequency NMA-SoF table

### BENEFITS

Patients or population: septic patients after extubation

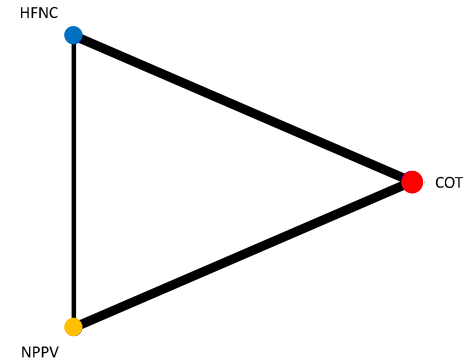
Interventions: One of the following oxygen therapies: NPPV, HFNT, or COT

Comparator (reference): One of the other therapies other than the therapy included in intervention

Outcome: Respiratory failure

Setting: In-hospital

### Network plot



	Total studies: 5 Total Patients: 1, 854	Relative effect (95% CI) Network estimate	Anticipated absolute effect (95% CI)			Certainly of the evidence	Ranking (SUCRA)	Interpretation of Findings
			Without intervention	With intervention	Difference			
<span style="color: yellow;">●</span> NPPV (2 RCT; 568 participants)		0.85 (0.58 to 1.24) Network estimate	188 per 1000	160 per 1000	28 fewer per 1000 (79 fewer to 45 more)	⊕⊕⊕○ Moderate	1 (97.1)	-
<span style="color: blue;">●</span> HFNT (2 RCT; 682 participants)		0.61 (0.42 to 0.89) Network estimate	174 per 1000	106 per 1000	68 fewer per 1000 (101 fewer to 19 fewer)	⊕⊕⊕○ Moderate	2 (42.1)	-
<span style="color: red;">●</span> COT		Reference comparator	No estimable	No estimable	No estimable	-	3 (10.6)	-
<span style="color: yellow;">●</span> NPPV (1 RCT; 604 participants)		1.39 (0.95 to 2.02) Network estimate	269 per 1000	374 per 1000	105 more per 1000 (13 fewer to 274 more)	⊕⊕⊕○ Moderate	-	-
<span style="color: blue;">●</span> HFNC		Reference comparator	No estimable	No estimable	No estimable	-	-	-

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	<b>Moderate</b>	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	<b>Don't know</b>
CERTAINTY OF EVIDENCE	Very low	Low	<b>Moderate</b>	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	<b>Probably no important uncertainty or variability</b>	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	<b>Probably favors the intervention</b>	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know