Supplement: Evidence Profiles

ERS Guidelines: High flow nasal cannula in acute respiratory failure

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Certainty assessment							atients		Effect		
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	сот	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality	(90 day)				•	•	•			•	•
4 RCTs	not serious	not serious	not serious	serious ^a	none	208/659 (31.6%)	208/620 (33.5%)	RR 0.97 (0.83 to 1.13)	10 fewer per 1,000 (from 57 fewer to 44 more)	⊕⊕⊕○ MODERATE	CRITICAL
Mortality	(ICU, hosp	oital, or 28 day)	1			1	1	I			
6 RCTs	not serious	not serious	not serious	serious ^a	none	189/773 (24.5%)	187/734 (25.5%)	RR 0.99 (0.84 to 1.17)	3 fewer per 1,000 (from 41 fewer to 43 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
Intubatio	n		!		1						
11 RCTs	not serious	not serious	not serious	serious ^a	none	231/943 (24.5%)	253/907 (27.9%)	RR 0.89 (0.77 to 1.02)	31 fewer per 1,000 (from 64 fewer to 6 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
Escalatio	n to NIV		!		1	1					!
6 RCTs	not serious	not serious	not serious	serious ^a	none	38/409 (9.3%)	47/388 (12.1%)	RR 0.76 (0.43 to 1.34)	29 fewer per 1,000 (from 69 fewer to 41 more)	⊕⊕⊕○ MODERATE	CRITICAL
Hospital I	ength of s	tay									
5 RCTs	not serious	not serious	not serious	serious ^a	none	683	660	-	MD 0.72 days lower (1.54 lower to 0.1 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
ICU lengt	h of stay		1		1	1	1	I			1
2 RCTs	not serious	not serious	not serious	serious ^b	none	494	482	-	MD 1.97 days higher (1.02 higher to 2.93 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
Patient co	omfort										
6 RCTs	not serious	not serious	not serious	not serious	none	303	293	-	SMD 0.54 lower (0.86 lower to 0.23 lower)		IMPORTANT
Dyspnea											

6 RCTs	not serious	not serious	not serious ^c	serious ^a	none	173	189	-	SMD 0.32 lower (0.66 lower to 0.03 higher)		IMPORTANT
										WODERATE	
PaO2/FiO	2										
4 RCTs	not	serious d	not serious	serious ^a	none	526	514	-	MD 25.01 higher	$\oplus \oplus \bigcirc \bigcirc$	IMPORTANT
	serious								(14.21 lower to 64.24 higher)	LOW	
PaO2			1	!	1	1			1	1	
6 RCTs	not serious	not serious	not serious	not serious	none	202	193	-	MD 16.72 higher (5.74 higher to 27.71 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
PCO2			<u> </u>	1	1	1		<u> </u>			<u> </u>
6 RCTs	not serious	not serious	not serious	not serious	none	202	193	-	MD 0.01 higher (1.17 lower to 1.2 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Respirato	ory rate			1						1	
10 RCTs	not serious	not serious	not serious	not serious	none	713	716	-	MD 2.25 lower (3.24 lower to 1.25 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. Significant imprecision which does not rule out clinically significant benefit nor harm.

b. Though Azoulay 2018 demonstrates statistically significant increase in ICU length of stay, when estimated means and SD are used, they are not statistically significant when median (IQR) are compared.

c. Most studies used the validated Borg dyspnea scale.

d. Very significant heterogeneity between the Frat 2015 RCT and the other trials (I2= 93%) of likely clinical significance.

1. Mortality (90 day)

	HFN	с	CO	г		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M–H, Fixed, 95% Cl	Year	r M–H, Fixed, 95% Cl
1.1.1 Immunocompe	etent							
Frat 2015	9	80	14	64	7.4%	0.51 [0.24, 1.11]	2015	5
Jones 2016 Subtotal (95% CI)	35	165 245	24	138 202	12.4% 19.7%	1.22 [0.76, 1.95] 0.96 [0.65, 1.42]	2016	
Total events	44		38					-
Heterogeneity: $Chi^2 =$	3.53. df	= 1 (P)	= 0.06);	$l^2 = 72$	%			
Test for overall effect	,							
1.1.2 Immunocompr	omised							
Frat 2017	4	26	8	30	3.5%	0.58 [0.20, 1.70]	2017	7
Azoulay 2018 Subtotal (95% CI)	160	388 414	162	388 418	76.7% 80.3%	. , .	2018	3
Total events	164		170					
Heterogeneity: $Chi^2 =$	0.94. df	= 1 (P)	= 0.33):	$l^2 = 0\%$	6			
Test for overall effect	,	,						
Total (95% CI)		659		620	100.0%	0.97 [0.83, 1.13]		•
Total events Heterogeneity: Chi ² = Test for overall effect:	,			l ² = 33	8%			0.2 0.5 1 2 5 Favours HFNC Favours COT
Test for subaroup dif	ferences:	Chi ² =	0.00. df	= 1 (P	= 0.95).	$l^2 = 0\%$		

2. Mortality (early - ICU, hospital, or 28 day)

	HFN	С	CO	Г		Risk Ratio			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year		M-H, Random, 95% Cl
1.3.1 Immunocompt	ent								
Frat 2015	8	80	12	64	3.9%	0.53 [0.23, 1.23]	2015		+
Jones 2016	15	165	11	138	4.9%	1.14 [0.54, 2.40]	2016		_ _
Makdee 2017 Subtotal (95% CI)	1	63 308	0	65 267	0.3% 9.1%		2017		· · · · · · · · · · · · · · · · · · ·
Total events	24		23						
Heterogeneity: $Tau^2 =$	= 0.07; Cł	1i ² = 2.	44, df =	2 (P =	0.29); I ²	= 18%			
Test for overall effect	Z = 0.50	(P = 0)).62)						
1.3.2 Immunocompr	omised								
Frat 2017	4	26	6	30	2.1%	0.77 [0.24, 2.43]	2017		
Azoulay 2018	138	388	140	388	76.8%	0.99 [0.82, 1.19]	2018		
Mendil 2019 Subtotal (95% CI)	23	51 465	18	49 467	12.0% 90.9%		2019		 ◆
Total events	165		164						
Heterogeneity: Tau ² =	,		,	2 (P =	0.63); I ²	= 0%			
Test for overall effect	Z = 0.10	(P = 0)).92)						
Total (95% CI)		773		734	100.0%	0.99 [0.84, 1.17]			•
Total events	189		187						
Heterogeneity: Tau ² =	= 0.00; Cł	1i ² = 3.	73, df =	5 ($P =$	0.59); I ²	= 0%		0.02	0.1 1 10 5
Test for overall effect	Z = 0.08	B (P = 0)).93)					0.02	Favours HFNC Favours COT
Test for subgroup dif	ferences:	Chi ² =	0.26, df	= 1 (P	= 0.61),	$I^2 = 0\%$			

3. Intubation

	HFN	с	co	г		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
1.4.1 Immunocompe	tent							
Frat 2015	32	80	31	64	14.4%	0.83 [0.57, 1.19]	2015	
Bell 2015	0	48	1	52	0.2%	0.36 [0.02, 8.64]	2015	
Rittayamai 2015	0	20	0	20		Not estimable	2015	
Jones 2016	9	165	16	138	3.2%	0.47 [0.21, 1.03]	2016	
Makdee 2017	1	63	0	65	0.2%	3.09 [0.13, 74.55]	2017	
Ko 2020	1	34	1	33	0.3%	0.97 [0.06, 14.88]	2020	
Geng 2020	1	16	1	20	0.3%	1.25 [0.08, 18.46]	2020	
Subtotal (95% CI)		426		392	18.5%	0.76 [0.55, 1.05]		•
Total events	44		50					
1.4.2 Immunocompre Lemaile 2015 Frat 2017 Azoulay 2018 Mendil 2019 Subtotal (95% CI)	omised 4 8 150 24	52 26 388 51 517	2 13 170 16	48 30 388 49 515	0.7% 3.9% 68.9% 7.9% 81.5%	1.85 [0.35, 9.63] 0.71 [0.35, 1.44] 0.88 [0.75, 1.04] 1.44 [0.88, 2.37] 0.99 [0.73, 1.35]	2017 2018	
Total events Heterogeneity: Tau ² = Test for overall effect:				3 (P =	0.21); I ²	= 35%		
Total (95% CI)		943		907	100.0%	0.89 [0.77, 1.02]		•
Total events Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diff	Z = 1.64	4 (P = 0	.10)					0.02 0.1 1 10 50 Favours HFNC Favours COT

4. Escalation to NIV

	HFN	IFNC COT				Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
1.5.1 Immunocompe	tent							
Parke 2011	3	30	12	30	16.6%	0.25 [0.08, 0.80]	2011	
Bell 2015	2	48	2	58	7.5%	1.21 [0.18, 8.26]	2015	
Jones 2016	5	165	7	138	17.3%	0.60 [0.19, 1.84]	2016	
Makdee 2017 Subtotal (95% CI)	1	63 306	3	65 291	5.8% 47.2%		2017	
Total events	11		24					
Heterogeneity: Tau ² =	0.00; Cl	ni ² = 2.	30, df =	3 (P =	0.51); I ²	= 0%		
Test for overall effect:	Z = 2.22	P = 0).03)					
1.5.2 Immunocompre								
Lemaile 2015	6	52	3	48				
Mendil 2019 Subtotal (95% CI)	21	51 103	20	49 97	39.1% 52.8%		2019	
Total events	27		23					
Heterogeneity: Tau ² = Test for overall effect:	,		,	1 (P =	0.39); I ²	= 0%		
rest for overall effect.	2 = 0.5	. (1 – (,,,,,					
Total (95% CI)		409		388	100.0%	0.76 [0.43, 1.34]		
Total events	38		47					
Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diff	Z = 0.96	5 (P = 0)).34)					0.05 0.2 1 5 20 Favours HFNC Favours COT

5. Hospital length of stay

	1	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
1.7.1 Immunocompe	tent									
Jones 2016	5	4.1	165	5.6	4.8	138	46.3%	-0.60 [-1.62, 0.42]	2016	
Makdee 2017	1.1	6.9	63	1.2	4.32	65	15.2%	-0.10 [-2.10, 1.90]	2017	-+-
Geng 2020 Subtotal (95% CI)	6.54	1.85	16 244	7.02	2.32	20 223		,	2020	
Heterogeneity: $Tau^2 =$	0.00; 0	Chi ² =	0.19, d	f = 2 (F	P = 0.9	$(91); I^2 =$	• 0%			
Test for overall effect:	Z = 1.2	28 (P =	• 0.20)			.,				
1.7.2 Immunocompr	omised									
Azoulay 2018	24	19.2	388	27	20	388	8.4%	-3.00 [-5.76, -0.24]	2018	
Mendil 2019	28	30.8	51	36	31.8	49	0.4%	-8.00 [-20.28, 4.28]	2019	
Subtotal (95% CI)			439			437	8.8%	-3.24 [-5.93, -0.55]		\bullet
Heterogeneity: Tau ² =	• 0.00; (Chi² =	0.61, d	f = 1 (F)	P = 0.4	14); I ² =	• 0%			
Test for overall effect:	Z = 2.3	86 (P =	= 0.02)							
Total (95% CI)			683			660	100.0%	-0.72 [-1.54, 0.10]		◆
Heterogeneity: $Tau^2 =$	0.11; 0	Chi ² =	4.51, d	f = 4 (F)	P = 0.3	$(34); I^2 =$: 11%			
Test for overall effect:	,		,							-20 -10 0 10 20
Test for subgroup diff		· _	,	df = 1	(P = 0)).05), l ²	= 73.1%			Favours HFNC Favours COT

6. ICU length of stay

		HFNC			сот			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.6.1 Immunocompt	ent								
Frat 2015 Subtotal (95% CI)	10.7	15.8	106 106	9.1	11.7	94 94		1.60 [-2.23, 5.43] 1.60 [-2.23, 5.43]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.8	32 (P =	0.41)						
1.6.2 Immunocompr	omised								
Azoulay 2018 Subtotal (95% CI)	8	7.4	388 388	6	6.67	388 388	93.7% 93.7%	2.00 [1.01, 2.99] 2.00 [1.01, 2.99]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 3.9	95 (P <	0.000	1)					
Total (95% CI)			494			482	100.0%	1.97 [1.02, 2.93]	
Heterogeneity: $Chi^2 =$	0.04, d	f = 1 (P = 0.8	$(34); I^2 =$	0%			-	
Test for overall effect:									-4 -2 0 2 4 Favours HFNC Favours COT
Test for subgroup diff	ferences	: Chi ² =	= 0.04,	df = 1	(P = 0).84), I ²	= 0%		Favours firme Favours COT

7. Patient comfort (various rating systems)

	н	IFNC			сот			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
1.8.1 Immunocompe	tent									
Schabbauer 2014	2.7	1.8	14	3.1	2.8	14	10.7%	-0.16 [-0.91, 0.58]	2014	
Frat 2015	29	26	106	40	29	94	21.4%	-0.40 [-0.68, -0.12]	2015	
Bell 2015	3	1.5	48	4	0.74	52	18.0%	-0.85 [-1.26, -0.44]	2015	
Rittayamai 2015	1.6	1.7	20	3.7	2.4	20	12.2%	-0.99 [-1.65, -0.33]	2015	_
Makdee 2017 Subtotal (95% CI)	-8.1	2	63 251	-6.4	1.9	65 245	19.2% 81.5%	-0.87 [-1.23, -0.50] -0.66 [-0.94, -0.39]	2017	•
Test for overall effect: 1.8.2 Immunocompresent			< 0.00	001)						
Lemaile 2015 Subtotal (95% CI) Heterogeneity: Not ap	3	3	52 52	3	3.7	48 48	18.5% 18.5%	0.00 [-0.39, 0.39] 0.00 [-0.39, 0.39]	2015	•
Test for overall effect:	Z = 0.0	00 (P	= 1.00)						
Total (95% CI)			303			293	100.0%	-0.54 [-0.86, -0.23]		•
Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diff	Z = 3.3	85 (P	= 0.00	08)					-	-2 -1 0 1 2 Favours HFNC Favours COT

8. Dyspnea (various measures, Borg Dyspnea Scale or visual analog scale)

	1	HFNC			сот			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
1.9.1 Immunocompet	ent									
Schabbauer 2014	2.9	2.1	14	3.3	2.3	14	13.3%	-0.18 [-0.92, 0.57]	2014	
Rittayamai 2015	2	1.8	2	3.8	2.3	20	4.7%	-0.76 [-2.23, 0.71]	2015	
Makdee 2017	3.1	2	63	3.6	2.2	65	25.8%	-0.24 [-0.58, 0.11]	2017	
Ruangsomboon 2019	3.3	2	22	5.6	1.8	22	15.7%	-1.19 [-1.83, -0.54]	2019	
Raeisi 2019	6	1.04	20	6.07	0.88	20	16.4%	-0.07 [-0.69, 0.55]	2019	
Subtotal (95% CI)			121			141	75.9%	-0.42 [-0.84, -0.01]		\bullet
1.9.2 Immunocompro		3	52	3	37	48	24 1%	0 00 [-0 39 0 39]	2015	
Lemaile 2015	3	3	52	3	3.7	48	24.1%	0.00 [-0.39, 0.39]	2015	_ _
Subtotal (95% CI)			52			48	24.1%	0.00 [-0.39, 0.39]		•
Heterogeneity: Not app	licable									
Test for overall effect:	Z = 0.00) (P =	1.00)							
Total (95% CI)			173			189	100.0%	-0.32 [-0.66, 0.03]		•
Heterogeneity: $Tau^2 =$	0.09; Ch	$ni^2 = 1$	0.47, d	f = 5 (F)	P = 0.0)6); I ² =	52%			
Test for overall effect:	Z = 1.81	(P =	0.07)							Favours HFNC Favours COT
Test for subgroup diffe	rences:	Chi ² =	2.11, 0	df = 1 (P = 0.	15), l ² =	= 52.6%			

9. PaO2:FiO2

	н	FNC			сот			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.10.1 Immunocomp	oetent								
Frat 2015	-130	60	106	-161	77	94	26.6%	31.00 [11.69, 50.31]	_ _
Mauri 2016	-184	53	15	-130	35	15	23.9%	-54.00 [-86.14, -21.86]	_
Mauri 2017 Subtotal (95% CI)	-205	61	17 138	-151	60	17 126		-54.00 [-94.67, -13.33] -24.15 [-88.18, 39.88]	
Heterogeneity: $Tau^2 =$	= 2941.8	6; Chi	$^{2} = 27$	51, df =	= 2 (P	< 0.00	001); I ² =	= 93%	
Test for overall effect:	Z = 0.74	4 (P =	0.46)						
1.10.2 Immunocomp	oromised								
Azoulay 2018 Subtotal (95% CI)	-150	93.3	388 388	-119	58.5	388 388		-31.00 [-41.96, -20.04] -31.00 [-41.96, -20.04]	•
Heterogeneity: Not ap Test for overall effect:	•	4 (P <	0.000	01)					
Total (95% CI)			526			514	100.0%	-25.01 [-64.24, 14.21]	
Heterogeneity: Tau ² =	= 1409.7	5; Chi	$^{2} = 37$.64, df =	= 3 (P	< 0.00	001); I ² =	= 92%	-100 -50 0 50 100
Test for overall effect:	Z = 1.25	5 (P =	0.21)						-100 -50 0 50 100 Favours HFNC Favours COT
Test for subaroup diff	ferences:	Chi ² =	= 0.04.	df = 1	(P = 0)	.84). I ²	= 0%		ravours firme ravours cor

10. PaO2

	н	FNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Mauri 2017	-97.4	23	17	-70	9.6	17	17.9%	-27.40 [-39.25, -15.55]		_ - _
Schabbauer 2014	-101	34	14	-85	22	14	12.3%	-16.00 [-37.21, 5.21]	2014	
Frat 2015	-90	35	106	-93	36	94	19.1%	3.00 [-6.87, 12.87]	2015	
Mauri 2016	-98	39	15	-72	5.2	15	13.0%	-26.00 [-45.91, -6.09]	2016	
Geng 2020	-94.73	4.43	16	-86.98	6.42	20	22.1%	-7.75 [-11.30, -4.20]	2020	-
Ko 2020	-107.47	44.15	34	-73.25	13.02	33	15.6%	-34.22 [-49.71, -18.73]	2020	
Total (95% CI)			202			193	100.0%	-16.72 [-27.71, -5.74]		•
Heterogeneity: Tau ² =	= 138.87; 0	$2hi^2 = 2a$	8.63, d	f = 5 (P -	< 0.000	1); I ² =	83%			
Test for overall effect	:: Z = 2.98 (P = 0.0	03)							Favours HFNC Favours COT

11. PCO2 (most commonly PaCO2)

	H	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Mauri 2017	38.3	5.4	17	38.2	5	17	11.5%	0.10 [-3.40, 3.60]		
Schabbauer 2014	37	5	14	37	6	14	8.4%	0.00 [-4.09, 4.09]	2014	
Frat 2015	35	7	106	35	6	94	43.2%	0.00 [-1.80, 1.80]	2015	_
Mauri 2016	41.1	5.9	15	40.7	5.7	15	8.1%	0.40 [-3.75, 4.55]	2016	
Ko 2020	31.54	8.14	34	32.3	6.22	33	11.7%	-0.76 [-4.22, 2.70]	2020	
Geng 2020	40.22	4.37	16	39.87	4.35	20	17.1%	0.35 [-2.52, 3.22]	2020	
Total (95% CI)			202			193	100.0%	0.01 [-1.17, 1.20]		•
Heterogeneity: Tau ² =	= 0.00; C	$Chi^2 = 0$	0.28, d	f = 5 (P	= 1.00	D); $I^2 =$	0%		_	
Test for overall effect	Z = 0.0	2 (P =	0.98)							Favours HFNC Favours COT

12. Respiratory rate

	H	IFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
1.13.1 Immunocompe	tent									
Mauri 2017	18	7	17	24	8	17	3.4%	-6.00 [-11.05, -0.95]		
Schabbauer 2014	26	7	14	28	8	14	2.9%	-2.00 [-7.57, 3.57]	2014	
Frat 2015	27	7	106	29	8	94	12.9%	-2.00 [-4.10, 0.10]	2015	
Rittayamai 2015	26	6.2	2	27.5	4.9	20	1.2%	-1.50 [-10.36, 7.36]	2015	
Mauri 2016	22	5.2	15	24	5.2	15	5.8%	-2.00 [-5.72, 1.72]	2016	
Makdee 2017	23.5	3.6	63	26.5	3.9	65	19.8%	-3.00 [-4.30, -1.70]	2017	
Ruangsomboon 2019	26	3.7	22	31.9	9.3	22	4.8%	-5.90 [-10.08, -1.72]	2019	
Ko 2020	21.32	3.32	34	24.3	3.55	33	16.5%	-2.98 [-4.63, -1.33]	2020	
Subtotal (95% CI)			273			280	67.2%	-2.95 [-3.79, -2.10]		◆
Heterogeneity: $Tau^2 = 0$	0.00; Chi	$^{2} = 4.$	57, df =	= 7 (P =	= 0.71); $I^2 = C$	%			
Test for overall effect: Z	2 = 6.84	(P < 0	0.00001	L)						
1.13.2 Immunocompre	omised									
Lemaile 2015	25	5.2	52	25	7.4	48	10.2%	0.00 [-2.53, 2.53]	2015	
Azoulay 2018	25	7.4	388	26	7.4	388	22.5%	-1.00 [-2.04, 0.04]	2018	
Subtotal (95% CI)			440			436	32.8%	-0.85 [-1.82, 0.11]		\bullet
Heterogeneity: $Tau^2 = 0$	0.00: Chi	$^{2} = 0.$	51. df =	= 1 (P =	= 0.47): $ ^2 = 0$	%			
Test for overall effect: Z	,		,							
Total (95% CI)			713			716	100.0%	-2.25 [-3.24, -1.25]		•
Heterogeneity: $Tau^2 = 0$	0.86: Chi	$^{2} = 15$	5.33. df	= 9 (P)	= 0.0	8): $I^2 =$	41%			
Test for overall effect: Z						-,, .				
Test for subgroup diffe					$(\mathbf{P} = 0)$	001)	$^{2} - 00.2\%$	<u>(</u>		Favours HFNC Favours COT

		Certa	iinty assessmer	ıt		Nº of p	atients		Effect		
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	NIV	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality	(90 day)										
1 RCT	not serious	not serious	serious ^a	serious ^b	none	13/106 (12.3%)	31/110 (28.2%)	RR 0.43 (0.24 to 0.78)	161 fewer per 1,000 (from 214 fewer to 62 fewer)		CRITICAL
Mortality	/ (ICU, hos	pital or 28 day)			1						1
3 RCTs	not serious	serious ^c	serious ^a	serious ^d	none	35/234 (15.0%)	47/240 (19.6%)	RR 0.77 (0.52 to 1.14)	45 fewer per 1,000 (from 94 fewer to 27 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Intubatio	on	1									1
5 RCTs	not serious	not serious	serious ^a	serious ^d	none	74/352 (21.0%)	92/356 (25.8%)	RR 0.84 (0.61 to 1.16)	41 fewer per 1,000 (from 101 fewer to 41 more)		CRITICAL
Hospital	length of	stay									1
1 RCTs	not serious	not serious	serious ^a	very serious e	none	104	100	-	MD 0.8 days higher (0.59 lower to 2.19 higher)	⊕⊖⊖⊖ VERY LOW	IMPORTANT
ICU leng	th of stay	1	<u> </u>	<u> </u>	1	1					1
2 RCTs	not serious	not serious	serious ^a	serious ^d	none	154	157	-	MD 0.55 days lower (2 lower to 0.89 higher)		IMPORTANT
Patient c	comfort	1	1								
4 RCTs	not serious	not serious	serious ^a	not serious	none	207	208	-	SMD 0.23 lower (0.55 lower to 0.09 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
Dyspnea	1	1	1	1							1
4 RCTs	not serious	very serious ^f	serious ^a	serious ^g	none	193	194	-	SMD 0.19 higher (0.01 lower to 0.40 higher)	⊕⊖⊖⊖ VERY LOW	IMPORTANT

PaO2/FiC	02										
3 RCTs	not serious	not serious	serious ^a	not serious	none	215	219	-	MD 43.26 lower (29.48 lower to 57.04 lower)	$\oplus \oplus \oplus \bigcirc \bigcirc$	IMPORTANT
										MODERATE	
PaO2			•	:					1	!	•
4 RCTs	not	not serious	serious ^a	not serious	none	229	233	-	MD 19.98 mmHg lower	$\oplus \oplus \oplus \bigcirc \bigcirc$	IMPORTANT
	serious								(11.97 lower to 28 lower)	MODERATE	
PCO2			1	1					1		1
4 RCTs	not	serious ^c	serious ^a	not serious	none	209	211	-	MD 0.45 mmHg lower	$\oplus \oplus \bigcirc \bigcirc$	IMPORTANT
	serious								(1.94 lower to 1.05 higher)	LOW	
Respirat	ory rate		1		1		i		1		
5 RCTs	not	serious ^c	serious ^a	not serious	none	302	309	-	MD 0.83 breaths per minute higher	$\oplus \oplus \bigcirc \bigcirc$	IMPORTANT
	serious								(1.04 lower to 2.7 higher)	LOW	

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. Concerns were raised about the short duration of NIV in the study with the largest effects (Frat et al); as well NIV interfaces used (face mask vs. helmet) and use of humidification for secretion clearance during NIV varied between studies. As a result, we rated down for indirectness of the comparator.

b. Optimal information size not met, assuming even a conservative relative risk reduction of 30%; thus we chose to rate down for imprecision, despite a statistically significant reduction in mortality.

c. Substantial heterogeneity (I2>40%) not easily explained by study characteristics.

d. Wide 95% confidence intervals which do not exclude clinically meaningful benefit or harm.

e. Very wide 95% confidence intervals which do not exclude clinically meaningful benefit or harm.

f. Very substantial heterogeneity (I2>80%) with two studies demonstrating opposite effects.

g. We chose not to rate down for imprecision as this was accounted for in considering the very significant inconsistency between the included studies.

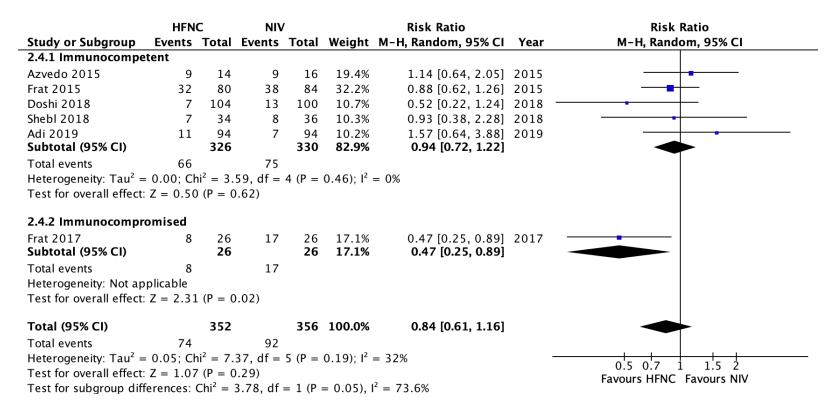
1. Mortality (90 day)

	HFN	с	NIV	,		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M–H, Fixed, 95% Cl
2.1.1 Immunocompe	tent							
Frat 2015 Subtotal (95% CI)	9	80 80	19	84 84	60.7% 60.7%		2015	
Total events	9		19					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 1.87	'(P = 0)	.06)					
2.1.2 Immunocompro	omised							
Frat 2017 Subtotal (95% CI)	4	26 26	12	26 26	39.3% 39.3%	• / •	2017	
Total events	4		12					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 2.17	'(P = 0)	.03)					
Total (95% CI)		106		110	100.0%	0.43 [0.24, 0.78]		
Total events	13		31					
Heterogeneity: $Chi^2 =$	0.40, df	= 1 (P	= 0.52);	$I^2 = 0\%$	6			
Test for overall effect:								0.1 0.2 0.5 1 2 5 10 Favours HFNC Favours NIV
Test for subgroup diff	erences:	Chi ² =	0.40, df	= 1 (P	= 0.52),	$l^2 = 0\%$		FAVOUIS FINC FAVOUIS NIV

2. Mortality (early - ICU, hospital, or 28 day)

	HFN	С	NIV	/		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M–H, Fixed, 95% Cl	Year	M–H, Fixed, 95% Cl
2.3.1 Immunocompe	tent							
Frat 2015	8	80	16	84	33.7%	0.53 [0.24, 1.16]	2015	
Shebl 2018	9	34	11	36	23.1%	0.87 [0.41, 1.83]	2018	
Adi 2019 Subtotal (95% CI)	14	94 208	9	94 214	19.4% 76.2%	. ,	2019	
Total events Heterogeneity: Chi ² = Test for overall effect:	,		.,	$l^2 = 45$	5%			
2.3.2 Immunocompr	omised							
Frat 2017 Subtotal (95% CI)	4	26 26	11	26 26	23.8% 23.8%		2017	
Total events Heterogeneity: Not ap Test for overall effect:	•	7 (P = (11					
Total (95% CI)		234		240	100.0%	0.77 [0.52, 1.14]		
Total events Heterogeneity: Chi ² = Test for overall effect: Test for subgroup diff	Z = 1.32	= 3 (P 2 (P = 0	47 = 0.10);).19)	$l^2 = 52$	2%			0.1 0.2 0.5 1 2 5 10 Favours HFNC Favours NIV

3. Intubation



4. Hospital length of stay

	H	IFNC			NIV			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Doshi 2018	6.8	5.7	104	6	4.4	100	100.0%	0.80 [-0.59, 2.19]	
Total (95% CI)			104			100	100.0%	0.80 [-0.59, 2.19]	
Heterogeneity: Not ap Test for overall effect:	•		= 0.26)					-2 -1 0 1 2 Favours HFNC Favours NIV

5. ICU length of stay

	1	HFNC			NIV			Mean Difference			Mean	Differe	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year		IV, Fix	ed, 95%	6 CI	
Frat 2015	10.7	15.8	106	11	11.6	110	15.2%	-0.30 [-4.01, 3.41]	2015			•		
Doshi 2018	3.3	3.7	48	3.9	4.1	47	84.8%	-0.60 [-2.17, 0.97]	2018				-	
Total (95% CI)			154			157	100.0%	-0.55 [-2.00, 0.89]						
Heterogeneity: Chi ² =					: 0%					 -4	-2	0	2	
Test for overall effect:	Z = 0.7	75 (P =	0.45)							-	Favours HFN	C Favo	urs NIV	

6. Patient comfort (various rating systems)

	F	IFNC			NIV			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Schabbauer 2014	2.7	1.8	14	5.4	3.1	14	12.5%	-1.03 [-1.83, -0.24]	2014	
Frat 2015	38	31	106	46	30	110	38.8%	-0.26 [-0.53, 0.01]	2015	
Doshi 2018	2	3	72	2	3.7	69	34.0%	0.00 [-0.33, 0.33]	2018	_ + _
Grieco 2020	5	3	15	5	3	15	14.7%	0.00 [-0.72, 0.72]	2020	
Total (95% CI)			207			208	100.0%	-0.23 [-0.55, 0.09]		
Heterogeneity: Tau ² =	= 0.05; (Chi² =	6.13,	df = 3	(P =	0.11); I	$^{2} = 51\%$			
Test for overall effect:	Z = 1.4	40 (P	= 0.16)						Favours HFNC Favours NIV

7. Dyspnea (various measures, Borg Dyspnea Scale or visual analog scale)

		HFNC			NIV		:	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Schabbauer 2014	2.9	2.1	13	5	3.3	14	6.7%	-0.73 [-1.51, 0.05]	2014	
Doshi 2018	2.6	2	71	2.2	1.8	71	38.0%	0.21 [-0.12, 0.54]	2018	+=-
Adi 2019	21.7	10.64	94	20.43	11.91	94	50.5%	0.11 [-0.17, 0.40]	2019	
Grieco 2020	8	2.2	15	3	2.2	15	4.7%	2.21 [1.28, 3.15]	2020	
Total (95% CI)			193			194	100.0%	0.19 [-0.01, 0.40]		◆
Heterogeneity: Chi ² = Test for overall effect)001); l ²	² = 87%					-2 -1 0 1 2 Favours HFNC Favours NIV

8. PaO2:FiO2

	н	FNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Frat 2015	-130	60	106	-186	85	110	49.6%	56.00 [36.44, 75.56]	2015	
Adi 2019	-271.83	73.63	94	-294.19	68.52	94	45.9%	22.36 [2.03, 42.69]	2019	
Grieco 2020	-138	52.6	15	-255	118	15	4.4%	117.00 [51.62, 182.38]	2020	
Total (95% CI)			215			219	100.0%	43.26 [29.48, 57.04]		•
Heterogeneity: Chi ² = Test for overall effect	,); $I^2 = 81\%$	6				_	-100 -50 0 50 100 Favours HFNC Favours NIV

9. PaO2

	ŀ	HFNC			NIV			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Adi 2019	-163.1	44.18	94	-176.52	41.11	94	43.2%	13.42 [1.22, 25.62]	
Frat 2015	-90	35	106	-111	59	110	38.7%	21.00 [8.12, 33.88]	— ∎ —
Grieco 2020	-69	21.5	15	-108	48.1	15	9.0%	39.00 [12.34, 65.66]	
Schabbauer 2014	-101	34	14	-129	38	14	9.0%	28.00 [1.29, 54.71]	
Total (95% CI)			229			233	100.0%	19.98 [11.97, 28.00]	•
Heterogeneity: Chi ² = Test for overall effect								-	-50 -25 0 25 50 Favours HFNC Favours NIV

10. PCO2 (most commonly PaCO2)

	I	HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Schabbauer 2014	37	5	14	39	7	14	11.0%	-2.00 [-6.51, 2.51]	2014	
Frat 2015	35	7	106	35	7	110	64.1%	0.00 [-1.87, 1.87]	2015	
Doshi 2018	46.3	12.7	74	52.5	17.8	72	8.8%	-6.20 [-11.23, -1.17]	2018	
Grieco 2020	33	4.4	15	31	5.9	15	16.1%	2.00 [-1.72, 5.72]	2020	
Total (95% CI)			209			211	100.0%	-0.45 [-1.94, 1.05]		•
Heterogeneity: Chi ² = Test for overall effect					= 59%					-10 -5 0 5 10 Favours HFNC Favours NIV

11. Respiratory rate

	H	HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Schabbauer 2014	26	7	14	24	9	14	7.5%	2.00 [-3.97, 7.97]	2014	
Frat 2015	27	7	106	29	7	110	23.9%	-2.00 [-3.87, -0.13]	2015	_
Doshi 2018	22.2	4.7	73	22.1	4.8	76	26.0%	0.10 [-1.43, 1.63]	2018	_
Adi 2019	24.51	3.69	94	23	3.61	94	28.6%	1.51 [0.47, 2.55]	2019	
Grieco 2020	29	4.4	15	24	5.9	15	14.0%	5.00 [1.28, 8.72]	2020	
Total (95% CI)			302			309	100.0%	0.83 [-1.04, 2.70]		
Heterogeneity: Tau ² =	= 2.92; C	: 2hi ² = 2	16.23,	df = 4 ((P = 0.	003); l ²	² = 75%			
Test for overall effect	: Z = 0.8	7 (P =	0.39)							-4 -2 0 2 4 Favours HFNC Favours NIV

Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

		Certainty a	issessment			№ of pa	tients		Effect		
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	СОТ	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality ·	- Post-opera	ative	!		· · · · · ·		I		1	-	
7 RCTs	not serious	not serious	not serious	serious ^a	none	4/526 (0.8%)	7/523 (1.3%)	RR 0.64 (0.19 to 2.14)	5 fewer per 1,000 (from 11 fewer to 15 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
Re-intuba	tion - Post-	operative									
8 RCTs	serious ^b	not serious	not serious	serious ^a	none	14/609 (2.3%)	22/601 (3.7%)	RR 0.66 (0.23 to 1.91)	12 fewer per 1,000 (from 28 fewer to 33 more)		CRITICAL
Escalate t	to NIV - Pos	t-op	1		II		I				1
7 RCTs	serious ^b	serious ^c	not serious	serious ^a	none	52/558 (9.3%)	65/552 (11.8%)	RR 0.77 (0.42 to 1.40)	27 fewer per 1,000 (from 68 fewer to 47 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
ICU Lengt	th of Stay - I	Post-op								_	
10 RCTs	not serious	not serious	not serious	not serious	none	707	709	-	MD 0.02 higher (0.09 lower to 0.13 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospital L	_ength of St	ay - Post-op									
11 RCTs	not serious	not serious	not serious	not serious	none	639	655	-	MD 0.47 lower (0.83 lower to 0.11 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
Comfort -	Post-op										
6 RCTs	not serious	very serious ^d	not serious	not serious ^e	none	413	415	-	SMD 0.54 lower (1.12 lower to 0.05 higher)		IMPORTANT
PaO2 - Po	ost-op								1		
2 RCTs	not serious	not serious	not serious	not serious	none	158	162	-	MD 6.2 lower (8.82 lower to 3.58 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PCO2 - Po	ost-Op										

Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

5 RCTs	not serious	not serious ^f	not serious	not serious	none	284	285	-	MD 1.9 lower (4.18 lower to 0.38 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
PaO2:FiO	2 - Post-op										
4 RCTs	not serious	not serious ^f	not serious	not serious	none	159	142	-	MD 34.89 lower (84.96 lower to 15.19 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
Respirato	ry Rate - Po	st-op	1								
3 RCTs	not serious	serious °	not serious	not serious	none	178	167	-	MD 0.14 lower (0.83 lower to 0.54 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. Wide 95% confidence intervals which do not exclude clinically important benefit or harm.

b. Lack of blinding may have resulted in bias from co-intervention as many trials did not have protocols for escalation of respiratory support.

c. Significant heterogeneity (I2 >50%) with point estimates on both sides of the line of no effect and limited overlap of 95% confidence intervals.

d. Very significant heterogeneity (12 >90%) with point estimates on both sides of the line of no effect and limited overlap of 95% confidence intervals.

e. We did not rate down for imprecision as this is accounted for in rating down twice for inconsistency.

f. Although there is significant heterogeneity (I2 >90%) the discrepancies in absolute effect sizes are of questionable significance

1. Mortality

	HFN	С	CO	г		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M–H, Random, 95% Cl	
Futier 2016	2	108	3	112	46.0%	0.69 [0.12, 4.06]			
Parke 2013	1	169	1	171	18.9%	1.01 [0.06, 16.05]			
Pennisi 2019	0	47	0	48		Not estimable			
Sahin 2018	0	50	2	50	15.9%	0.20 [0.01, 4.06]			
Vourc'h 2020	0	47	0	43		Not estimable			
Yu 2017	0	56	0	54		Not estimable			
Zochios 2018	1	49	1	45	19.2%	0.92 [0.06, 14.25]			
Total (95% CI)		526		523	100.0%	0.64 [0.19, 2.14]			
Total events	4		7					_	
Heterogeneity: Tau ² =	= 0.00; Cl	$ni^2 = 0.$	76, df =	3 (P =	0.86); I ²	= 0%			100
Test for overall effect	Z = 0.72	2 (P = 0)).47)				0.01	0.1 1 10 Favours HFNC Favours COT	100

2. Re-intubation

	HFN	С	co	Г		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
Parke 2013	2	169	0	171	9.1%	5.06 [0.24, 104.59]	2013	
Corley 2015	0	81	2	74	9.1%	0.18 [0.01, 3.75]	2015	
Futier 2016	7	108	4	112	23.7%	1.81 [0.55, 6.02]	2016	
Yu 2017	0	56	5	54	9.8%	0.09 [0.00, 1.55]	2017	
Sahin 2018	0	50	4	50	9.7%	0.11 [0.01, 2.01]	2018	
Zochios 2018	1	51	5	49	14.5%	0.19 [0.02, 1.59]	2018	
Pennisi 2019	1	47	1	48	10.5%	1.02 [0.07, 15.86]	2019	
Vourc'h 2020	3	47	1	43	13.7%	2.74 [0.30, 25.40]	2020	
Total (95% CI)		609		601	100.0%	0.66 [0.23, 1.91]		
Total events	14		22					
Heterogeneity: Tau ² =	0.88; Cl	$hi^2 = 11$	L.51, df =	= 7 (P =	= 0.12); I	$^{2} = 39\%$		0.005 0.1 1 10 200
Test for overall effect:	Z = 0.77	7 (P = 0)).44)					Favours HFNC Favours COT

Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

3. Escalation to NIV

	HFN	с	CO	г		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Corley 2015	3	81	2	74	8.3%	1.37 [0.24, 7.97]	
Futier 2016	18	108	11	112	20.4%	1.70 [0.84, 3.42]	+
Parke 2013	9	169	5	171	14.9%	1.82 [0.62, 5.32]	
Pennisi 2019	1	47	3	48	5.8%	0.34 [0.04, 3.16]	
Sahin 2018	6	50	11	50	17.1%	0.55 [0.22, 1.36]	
Vourc'h 2020	13	47	24	43	23.0%	0.50 [0.29, 0.84]	
Yu 2017	2	56	9	54	10.4%	0.21 [0.05, 0.95]	
Total (95% CI)		558		552	100.0%	0.77 [0.42, 1.40]	
Total events	52		65				
Heterogeneity: Tau ² =	= 0.34; Cł	$ni^2 = 14$	4.31, df =	= 6 (P =	= 0.03); I	$^{2} = 58\%$	0.05 0.2 1 5 20
Test for overall effect	z = 0.86	5 (P = 0)).39)				Favours HFNC Favours COT

4. ICU length of stay

		HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Parke 2013	1.39	0.95	169	1.2	1	171	24.8%	0.19 [-0.02, 0.40]	2013	
Corley 2015	1.61	1.47	81	1.61	0.995	74	7.4%	0.00 [-0.39, 0.39]	2015	
Futier 2016	6	8.9	108	5	7.4	112	0.2%	1.00 [-1.17, 3.17]	2016	
Yu 2017	3.72	0.56	56	3.64	0.83	54	15.7%	0.08 [-0.19, 0.35]	2017	- - -
Brainard 2017	2	1.2	18	3.2	3.8	26	0.5%	-1.20 [-2.76, 0.36]	2017	
Zochios 2018	1	0.74	49	1	0.74	45	12.5%	0.00 [-0.30, 0.30]	2018	_ + _
Sahin 2018	2.4	0.5	50	2.8	1.7	50	4.8%	-0.40 [-0.89, 0.09]	2018	
Pennisi 2019	1	1.48	47	1	1.48	48	3.3%	0.00 [-0.60, 0.60]	2019	
Twose 2019	1.04	0.34	10	1.22	0.42	10	10.1%	-0.18 [-0.51, 0.15]	2019	
Tatsuishi 2020	1	0.74	72	1	0.74	76	19.2%	0.00 [-0.24, 0.24]	2020	+
Vourc'h 2020	3.3	2.4	47	3.1	1.6	43	1.7%	0.20 [-0.64, 1.04]	2020	
Total (95% CI)			707			709	100.0%	0.02 [-0.09, 0.13]		•
Heterogeneity: Tau ² =	= 0.00; 0	Chi ² =	10.31,	df = 10	0 (P = 0)	.41); I ²	= 3%		_	<u> </u>
Test for overall effect	Z = 0.4	41 (P =	0.68)							-2 -1 U I 2
Test for overall effect	Z = 0.4	41 (P =	= 0.68)							Favours HFNC Favours C

Favours HFNC Favours COT

Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

5. Hospital length of stay

	I	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	r IV, Random, 95% CI
Parke 2013	11.6	6.6	169	11.4	6.7	171	5.3%	0.20 [-1.21, 1.61]	2013	·
Ansari 2016	2.5	7.4	28	4	12.6	31	0.5%	-1.50 [-6.71, 3.71]	2016	;
Futier 2016	12	9.6	108	11	8.1	112	2.2%	1.00 [-1.35, 3.35]	2016	;
Brainard 2017	6.6	2.1	18	9.5	7	26	1.5%	-2.90 [-5.76, -0.04]	2017	·
Yu 2017	7.41	0.82	56	7.54	0.91	54	22.7%	-0.13 [-0.45, 0.19]	2017	' +
Sahin 2018	6.5	0.7	50	6.9	1.1	50	21.7%	-0.40 [-0.76, -0.04]	2018	; 🗕
Zochios 2018	7	2.2	49	9	6.7	45	2.8%	-2.00 [-4.05, 0.05]	2018	;
Pennisi 2019	6	1.48	47	6	1.48	48	15.8%	0.00 [-0.60, 0.60]	2019) +
Ferrando 2019	3	1	32	4	1	32	18.3%	-1.00 [-1.49, -0.51]	2019) -
Twose 2019	14.5	12.4	10	16	5.2	10	0.2%	-1.50 [-9.83, 6.83]	2019	•
Tatsuishi 2020	8	2.2	72	9	3.7	76	9.1%	-1.00 [-1.97, -0.03]	2020)
Total (95% CI)			639			655	100.0%	-0.47 [-0.83, -0.11]		◆
Heterogeneity: Tau ² = Test for overall effect:				df = 10) (P =	0.04); I	$^{2} = 48\%$			
i est isi sverali elleet.			0.01)							Favours HFNC Favours COT

6. Comfort

	H	IFNC			сот			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Tiruvoipati 2010	0.53	1.04	42	0.96	1.42	42	16.9%	-0.34 [-0.77, 0.09]	2010	- -+
Parke 2013	-6.94	2.5	169	-7.78	1.9	171	18.1%	0.38 [0.16, 0.59]	2013	
Rittayamai 2014	1.4	0.9	17	1.9	1.1	17	14.8%	-0.49 [-1.17, 0.20]	2014	
Futier 2016	7.9	2.1	108	8.1	2.4	112	17.9%	-0.09 [-0.35, 0.18]	2016	
Song 2017	3	1.1	30	5	1.5	30	15.7%	-1.50 [-2.08, -0.92]	2017	_
Vourc'h 2020	-4	0.74	47	-3	0.74	43	16.6%	-1.34 [-1.80, -0.88]	2020	_ - _
Total (95% CI)			413			415	100.0%	-0.54 [-1.12, 0.05]		
Heterogeneity: Tau ² =	= 0.47; 0	2hi ² = 2	71.88,	df = 5 (P < 0.	00001)); $I^2 = 93\%$	6		
Test for overall effect	: Z = 1.8	1 (P =	0.07)							Favours HFNC Favours COT

7. PaO2

	н	IFNC		C	сот			Mean Difference		Mean Differen	ce
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 959	% CI
Futier 2016	-89	35	108	-87	32	112	8.7%	-2.00 [-10.87, 6.87]	2016	· · · · · · · · · · · · · · · · · · ·	
Sahin 2018	-106	6.9	50	-99.4	7.1	50	91.3%	-6.60 [-9.34, -3.86]	2018		
Total (95% CI)			158			162	100.0%	-6.20 [-8.82, -3.58]			
Heterogeneity: Tau ² =					(P =)	0.33); I	$^{2} = 0\%$			-10 -5 0	5 10
Test for overall effect:	Z = 4.6	53 (P	< 0.00	001)						Favours HFNC Favou	irs COT

8. PCO2

	1	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Futier 2016	41	7	108	41	6	112	19.9%	0.00 [-1.73, 1.73]	2016	
Sahin 2018	37.9	2.6	50	42.3	2.2	50	21.6%	-4.40 [-5.34, -3.46]	2018	_ _
Pennisi 2019	38.9	3.15	47	40.6	3.89	48	20.6%	-1.70 [-3.12, -0.28]	2019	
Ferrando 2019	37.9	5.6	32	42.3	5.1	32	17.3%	-4.40 [-7.02, -1.78]	2019	
Vourc'h 2020	39.8	3	47	39	3.8	43	20.6%	0.80 [-0.62, 2.22]	2020	
Total (95% CI)			284			285	100.0%	-1.90 [-4.18, 0.38]		
Heterogeneity: Tau ² =	= 6.03; 0	Chi ² =	47.20,	df = 4	(P < 0	.00001); $I^2 = 92$	%		
Test for overall effect	: Z = 1.6	63 (P =	0.10)							Favours HFNC Favours COT

9. PaO2/FiO2

		HFNC			СОТ			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Ye	ar IV, Random, 95% CI
Corley 2015	-175.8	96.3791	33	-159.3	96.3791	19	22.0%	-16.50 [-70.90, 37.90] 202	15
Ferrando 2019	-344	104.8	32	-226	66.3	32	24.3%	-118.00 [-160.97, -75.03] 202	19 —
Pennisi 2019	-300	75.2	47	-299	81.3	48	26.5%	-1.00 [-32.48, 30.48] 201	19 —
Vourc'h 2020	-136.5	47	47	-128.1	81.3	43	27.2%	-8.40 [-36.17, 19.37] 202	20
Total (95% CI)			159			142	100.0%	-34.89 [-84.96, 15.19]	
Heterogeneity: Tau ² = Test for overall effect				f = 3 (P -	< 0.0001);	$l^2 = 86$	5%		-100 -50 0 50 100 Favours HFNC Favours COT

10. Respiratory rate

		HFNC			СОТ			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Corley 2015	18.29	2.6017	81	17.85	2.6017	74	33.5%	0.44 [-0.38, 1.26]	2015	
Sahin 2018	19.3	0.9	50	19.5	1.1	50	53.2%	-0.20 [-0.59, 0.19]	2018	
Vourc'h 2020	19.2	4	47	20.6	4.1	43	13.3%	-1.40 [-3.08, 0.28]	2020	
Total (95% CI)			178			167	100.0%	-0.14 [-0.83, 0.54]		-
Heterogeneity: Tau ² =	= 0.19; C	$2hi^2 = 4.1$	8, df =	2 (P =	0.12); I ²	= 52%				
Test for overall effect:	Z = 0.4	1 (P = 0.	68)							Favours HFNC Favours COT

		Certainty as	sessment			Nº of p	atients		Effect		
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	NIV	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality	- Post-op										1
1 RCT	not serious	not serious	not serious ^a	very serious b	none	28/414 (6.8%)	23/416 (5.5%)	RR 1.22 (0.72 to 2.09)	12 more per 1,000 (from 15 fewer to 60 more)		CRITICAL
Re-intuba	ation - Post-op										
1 RCT	not serious ^c	not serious	not serious ^a	serious ^d	none	58/414 (14.0%)	57/416 (13.7%)	RR 1.02 (0.73 to 1.44)	3 more per 1,000 (from 37 fewer to 60 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
ICU lengt	th of stay - Post	-ор									
1 RCT	not serious	not serious	not serious ^a	not serious ^e	none	414	416	-	MD 0 days (0.6 lower to 0.6 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Hospital	length of stay -	Post-op									
1 RCT	not serious	not serious	not serious ^a	serious ^d	none	414	416	-	MD 1 lower (2.21 lower to 0.21 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
PCO2 - P	ost-op										
1 RCT	not serious	not serious	not serious ^a	not serious	none	414	416	-	MD 1.1 mmHg lower (2.02 lower to 0.18 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PaO2:FIC	02 - Post-op										
1 RCT	not serious	not serious	not serious ^a	not serious	none	414	416	-	MD 63 lower (80 lower to 46 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
Respirate	ory Rate - Post-	ор									
1 RCT	not serious	not serious	not serious ^a	not serious	none	414	416	-	MD 0.9 RPM lower (1.81 lower to 0.01 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference

Explanations

a. Single trial recruited patients after cardiothoracic surgery only; patients with other types of surgery are not represented in this evidence.

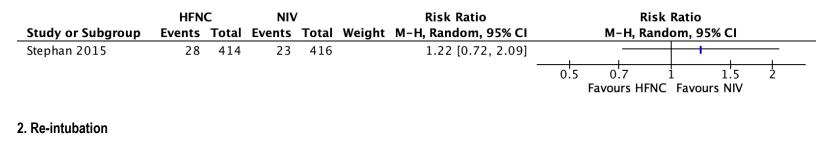
b. Very wide 95% confidence interval does not exclude moderate harm or small benefit of HFNC.

c. Single included trial used pre-specified criteria for escalation of respiratory support, including intubation.

d. Wide 95% confidence interval does not exclude clinically meaningful benefit or harm.

e. Though not statistically significant, the 95% confidence intervals likely exclude a meaningful benefit (less than 1 day difference).

1. Mortality



	HFN	С	NIV	/		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M–H, I	Random, 9	5% CI	
Stephan 2015	58	414	57	416		1.02 [0.73, 1.44]					
							L				
							0.5	0.7	1	1.5	2
								Favours H	IFNC Favou	ırs NIV	

3. ICU length of stay

	н	IFNC			NIV			Mean Difference		Mea	an Differe	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ra	andom, 95	% CI	
Stephan 2015	6	4.4	414	6	4.4	416		0.00 [-0.60, 0.60]					
									-1	-0.5	0	0.5	1
										Favours H	FNC Favo	urs NIV	

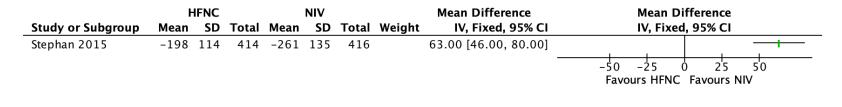
4. Hospital length of stay

	н	IFNC			NIV			Mean Difference			Mea	n Differe	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year		IV, F	ixed, 95%	6 CI	
Stephan 2015	13	9.6	414	14	8.1	416		-1.00 [-2.21, 0.21]	2015					
									-	-2	-1	0	i	2
											Favours HI	NC Favo	urs NIV	

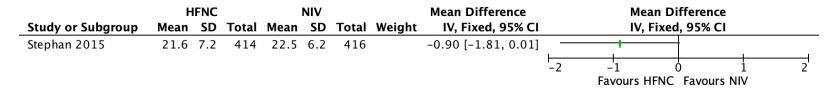
5. PCO2

	н	IFNC			NIV			Mean Difference		Mean	Differ	ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fi	xed, 95	% CI	
Stephan 2015	38.2	6.2	414	39.3	7.3	416		-1.10 [-2.02, -0.18]			-		1
									-2	-1	Ó	1	2
										Favours HF	NC Fav	ours NIV	

6. PaO2/FiO2



7. Respiratory rate



		Certainty a	ssessment			Nº of p	atients		Effect		
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	СОТ	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality											
9 RCTs	not serious	not serious	not serious	serious ^a	none	42/503 (8.3%)	41/495 (8.3%)	RR 1.01 (0.68 to 1.52)	1 more per 1,000 (from 27 fewer to 43 more)		CRITICAL
Re-intuba	tion	1	1	!				1	1		
10 RCTs	serious ^b	not serious	not serious	not serious ^c	none	42/563 (7.5%)	75/564 (13.3%)	RR 0.62 (0.38 to 1.01)	51 fewer per 1,000 (from 82 fewer to 1 more)		CRITICAL
Escalate t	to NIV	1		1				1			
6 RCTs	serious ^b	not serious	not serious	not serious	none	15/260 (5.8%)	40/265 (15.1%)	RR 0.38 (0.17 to 0.85)	94 fewer per 1,000 (from 125 fewer to 23 fewer)		CRITICAL
ICU Lengt	th of Stay	1	<u> </u>					1			
6 RCTs	not serious	not serious	not serious	not serious ^c	none	485	487	-	MD 0.29 higher (0.27 lower to 0.85 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Hospital L	_ength of St	tay	<u> </u>					1			
4 RCTs	not serious	serious ^d	not serious	serious ^a	none	424	417	-	MD 1.08 lower (4.83 lower to 2.66 higher)		IMPORTANT
Comfort	1										
3 RCTs	not serious	not serious ^e	not serious	not serious	none	89	89	-	SMD 0.77 lower (1.5 lower to 0.03 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PaO2											
5 RCTs	not serious	not serious	not serious	not serious	none	165	154	-	MD 7.57 higher (2.68 higher to 12.46 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
PCO2											

7 RCTs	not serious	not serious	not serious	not serious	none	460	446	-	MD 0.15 lower (1.89 lower to 1.58 higher)	⊕⊕⊕ HIGH	IMPORTANT
PaO2:FiO	2										
4 RCTs	not serious	serious ^d	not serious	serious ^a	none	378	383	-	MD 14.13 higher (20.48 lower to 48.75 higher)		IMPORTANT
Respirato	ory Rate										
7 RCTs	not serious	not serious ^f	not serious	not serious	none	213	200	-	MD 1.98 lower (3.9 lower to 0.06 lower)	⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. Wide 95% confidence intervals do not exclude clinically significant benefit nor harm.

b. Lack of blinding may have resulted in bias from co-intervention, though several trials did have specific criteria for escalation of respiratory support.

c. Though not statistically significant, 95% confidence interval likely excludes a significant differences.

d. Large values of I2 (>70%) with point estimates on both sides of the line of no effect.

e. Significant statistical heterogeneity, however all estimates of effect favour HFNC.

f. Although significant statistical heterogeneity, the absolute differences are of questionable clinical significance.

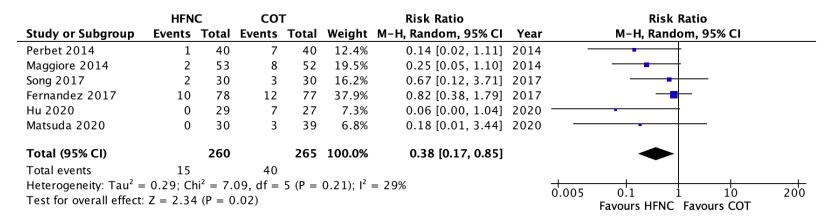
1. Mortality

	HFN	с	CO	г		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Maggiore 2014	6	53	5	52	13.0%	1.18 [0.38, 3.62]	2014	
Perbet 2014	3	40	4	40	8.0%	0.75 [0.18, 3.14]	2014	
Hernandez (low risk) 2016	10	264	13	263	25.3%	0.77 [0.34, 1.72]	2016	
Fernandez 2017	12	78	12	77	30.4%	0.99 [0.47, 2.06]	2017	+
Arman 2017	0	8	0	7		Not estimable	2017	
Hu 2020	2	29	1	27	3.0%	1.86 [0.18, 19.38]	2020	
Cho 2020	9	31	6	29	20.3%	1.40 [0.57, 3.45]	2020	
Total (95% CI)		503		495	100.0%	1.01 [0.68, 1.52]		•
Total events	42		41					
Heterogeneity: $Tau^2 = 0.00$;	$Chi^2 = 1.$	47, df	= 5 (P =	0.92);	$l^2 = 0\%$			
Test for overall effect: $Z = 0$.		-						0.1 0.2 0.5 1 2 5 10 Favours HFNC Favours COT

2. Re-intubation

	HFN	С	co	г		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
Perbet 2014	9	40	10	40	21.1%	0.90 [0.41, 1.98]	2014	
Maggiore 2014	2	53	11	52	9.0%	0.18 [0.04, 0.77]	2014	
Hernandez (low risk) 2016	13	264	32	263	26.6%	0.40 [0.22, 0.75]	2016	_
Song 2017	1	30	3	30	4.4%	0.33 [0.04, 3.03]	2017	· · · · · · · · · · · · · · · · · · ·
Fernandez 2017	9	78	12	77	20.5%	0.74 [0.33, 1.66]	2017	
Arman 2017	0	8	0	7		Not estimable	2017	
Hu 2020	0	29	0	27		Not estimable	2020	
Matsuda 2020	5	30	6	39	14.0%	1.08 [0.37, 3.21]	2020	
Cho 2020	3	31	1	29	4.4%	2.81 [0.31, 25.48]	2020	
Total (95% CI)		563		564	100.0%	0.62 [0.38, 1.01]		•
Total events	42		75					
Heterogeneity: $Tau^2 = 0.13$;	$Chi^2 = 8$.88, df	= 6 (P =	0.18);	$I^2 = 32\%$			
Test for overall effect: $Z = 1$.								0.05 0.2 İ 5 20 Favours HFNC Favours COT

3. Escalation to NIV



4. ICU length of stay

	1	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Maggiore 2014	11.7	10.2	53	10.4	8.5	52	2.4%	1.30 [-2.29, 4.89]	2014	
Hernandez (low risk) 2016	6	4.4	264	6	5.2	263	45.8%	0.00 [-0.82, 0.82]	2016	
Fernandez 2017	12	13.3	78	14	5.9	77	3.0%	-2.00 [-5.23, 1.23]	2017	
Matsuda 2020	4.4	1.8	30	3.8	1.8	39	42.3%	0.60 [-0.26, 1.46]	2020	+=-
Hu 2020	10	4.4	29	9	4.4	27	5.8%	1.00 [-1.31, 3.31]	2020	
Cho 2020	14.7	9.6	31	13.8	15.7	29	0.7%	0.90 [-5.74, 7.54]	2020	
Total (95% CI)			485			487	100.0%	0.29 [-0.27, 0.85]		•
Heterogeneity: $Tau^2 = 0.00$;	$Chi^2 = 3$	3.61, d	df = 5 (P = 0.6	51); I ² =	= 0%				
Test for overall effect: $Z = 1$.02 (P =	0.31)								Favours HFNC Favours COT

5. Hospital length of stay

	I	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Hernandez (low risk) 2016	11	6.7	264	12	7.4	263	42.2%	-1.00 [-2.21, 0.21]	2016	
Fernandez 2017	27	26.7	78	27	21.5	77	15.6%	0.00 [-7.63, 7.63]	2017	
Blaudszun 2017	8.6	4.3	51	13.4	9.9	48	34.1%	-4.80 [-7.84, -1.76]	2017	
Cho 2020	37.7	25.8	31	25.7	20.9	29	8.1%	12.00 [0.15, 23.85]	2020	
Total (95% CI)			424			417	100.0%	-1.08 [-4.83, 2.66]		-
Heterogeneity: $Tau^2 = 8.26$;				(P = 0)	.02); I ²	= 71%			-	-20 -10 0 10 20
Test for overall effect: $Z = 0$.57 (P =	0.57)								Favours HFNC Favours COT

6. Comfort

	I	HFNC			сот			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Tiruvoipati 2010	0.53	1.04	42	0.96	1.42	42	36.4%	-0.34 [-0.77, 0.09]	2010	
Rittayamai 2014	1.4	0.9	17	1.9	1.1	17	30.6%	-0.49 [-1.17, 0.20]	2014	
Song 2017	3	1.1	30	5	1.5	30	33.1%	-1.50 [-2.08, -0.92]	2017	_
Total (95% CI)			89			89	100.0%	-0.77 [-1.50, -0.03]		
Heterogeneity: Tau ² = Test for overall effect				df = 2	(P = 0	.005); I	$^{2} = 81\%$			-2 -1 0 1 2 Favours HFNC Favours COT

7. PaO2

	Н	IFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Tiruvoipati 2010	-102.14	40.25	42	-98.35	38.54	42	7.5%	-3.79 [-20.64, 13.06]	2010	
Maggiore 2014	-97.5	29.2	53	-85.4	16.3	52	20.2%	-12.10 [-21.12, -3.08]	2014	
Song 2017	-83.2	10.5	27	-74.5	13.1	19	27.4%	-8.70 [-15.80, -1.60]	2017	
DiMussi 2018	-75.1	6.9	14	-72.9	8.6	14	34.1%	-2.20 [-7.98, 3.58]	2018	
Hu 2020	-102.4	25.4	29	-86.6	26.4	27	10.8%	-15.80 [-29.39, -2.21]	2020	
Total (95% CI)			165			154	100.0%	-7.57 [-12.46, -2.68]		•
Heterogeneity: Tau ² =	,		,	4 (P = 0.	21); $I^2 =$	32%				-20 -10 0 10 20
Test for overall effect:	Z = 3.04	(P = 0.0)	02)							Favours HFNC Favours COT

8. PCO2

	I	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Tiruvoipati 2010	37.53	6.23	42	37.91	6.22	42	20.2%	-0.38 [-3.04, 2.28]	2010	
Maggiore 2014	32.3	7.1	53	36.2	11	52	14.7%	-3.90 [-7.45, -0.35]	2014	_
Hernandez (low risk) 2016	37	8	264	36	6	263	32.5%	1.00 [-0.21, 2.21]	2016	+=-
Song 2017	41.4	6.5	27	42.2	13.1	19	6.2%	-0.80 [-7.18, 5.58]	2017	
DiMussi 2018	49.9	11.9	14	51.8	12.7	14	3.3%	-1.90 [-11.02, 7.22]	2018	
Hu 2020	41.3	7.5	29	37.2	9.6	27	10.6%	4.10 [-0.43, 8.63]	2020	
Cho 2020	35.9	7	31	37.1	8.8	29	12.4%	-1.20 [-5.24, 2.84]	2020	
Total (95% CI)			460			446	100.0%	-0.15 [-1.89, 1.58]		•
Heterogeneity: $Tau^2 = 2.02$;	$Chi^2 = 1$	0.46,	df = 6	(P = 0.2)	11); I ²	= 43%				
Test for overall effect: $Z = 0$.17 (P =	0.86)								-10 -5 0 5 10 Favours HFNC Favours COT

9. PaO2/FiO2

	I	HFNC			сот			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Maggiore 2014	-313.3	83.8	53	-259.2	110.1	52	24.2%	-54.10 [-91.58, -16.62]	2014	
Hernandez (low risk) 2016	-105	32	264	-108	34	263	33.6%	3.00 [-2.64, 8.64]	2016	-
Cho 2020	-277.1	102.5	31	-314.2	102.1	29	19.3%	37.10 [-14.70, 88.90]	2020	
Matsuda 2020	-264	105	30	-224	53	39	22.9%	-40.00 [-81.09, 1.09]	2020	
Total (95% CI)			378			383	100.0%	-14.13 [-48.75, 20.48]		
Heterogeneity: $Tau^2 = 920.9$ Test for overall effect: $Z = 0$			df = 3	(P = 0.0)	02); I ² =	79%				-100 -50 0 50 100 Favours HFNC Favours COT

10. Respiratory rate

	HFNC COT					Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Tiruvoipati 2010	18.68	5.51	42	19.68	6.5	42	14.0%	-1.00 [-3.58, 1.58]	2010	
Maggiore 2014	21	4	53	26	4.3	52	16.6%	-5.00 [-6.59, -3.41]	2014	_
Rittayamai 2014	19.8	3.2	17	23.1	4.4	17	14.0%	-3.30 [-5.89, -0.71]	2014	
Song 2017	22	4	27	26	4	19	14.6%	-4.00 [-6.35, -1.65]	2017	
DiMussi 2018	20.5	2.9	14	21.4	4	14	14.0%	-0.90 [-3.49, 1.69]	2018	
Hu 2020	21	5	29	22	6	27	13.1%	-1.00 [-3.90, 1.90]	2020	
Cho 2020	22.8	5.9	31	20.7	4.5	29	13.8%	2.10 [-0.54, 4.74]	2020	
Total (95% CI)			213			200	100.0%	-1.98 [-3.90, -0.06]		
Heterogeneity: Tau ² =	= 5.11; C	$hi^2 = 2$	26.84,	df = 6 (P = 0	.0002)	; $I^2 = 78\%$			
Test for overall effect:	Z = 2.0	3 (P =	0.04)							Favours HFNC Favours COT

		Certainty a	ssessment			Nº of p	atients		Effect		
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	NIV	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality	- General IC	CU		4		•					-
5 RCTs	not serious	not serious	not serious	serious ^a	none	111/729 (15.2%)	112/784 (14.3%)	RR 1.07 (0.84 to 1.36)	10 more per 1,000 (from 23 fewer to 51 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
Re-intuba	ation - Gene	ral ICU		1		1					
5 RCTs	not serious ^b	not serious	not serious	serious	none	139/746 (18.6%)	115/803 (14.3%)	RR 1.31 (1.04 to 1.64)	44 more per 1,000 (from 6 more to 92 more)	⊕⊕⊕⊕ HIGH	CRITICAL
ICU lengt	th of stay - (General ICU		1		1			1		_
4 RCTs	not serious	not serious	not serious	not serious	none	658	705	-	MD 1.0 days lower (1.52 lower to 0.47 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
Hospital	length of st	ay - General ICU		1		1			1		
3 RCTs	not serious	not serious	not serious	not serious	none	636	695	-	MD 1.44 days lower (2.63 lower to 0.25 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
Comfort	- General IC	U	1								_
4 RCTs	not serious	not serious	not serious	not serious	none	85	79	-	SMD 0.73 SD lower (0.98 lower to 0.49 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PCO2 - G	eneral ICU			I		1					
3 RCTs	not serious	not serious	not serious	not serious	none	356	376	-	MD 1.01 mmHg lower (1.47 lower to 0.55 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PaO2:FIC)2 - General	ICU									
3 RCTs	not serious	not serious	not serious	not serious ^c	none	356	376	-	MD 3.86 higher (0.39 higher to 7.34 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Respirate	ory Rate - G	eneral ICU									
2 RCTs	not serious	not serious ^d	not serious	not serious ^c	none	66	62	-	MD 0.59 respirations per minute lower (2.48 lower to 1.29 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

- a. Wide 95% confidence intervals do not exclude the possibility of meaningful benefit nor harm.
- b. Lack of blinding may have resulted in bias from co-intervention, though most trials did have specific criteria for escalation of respiratory support, including intubation.
- c. Though not statistically significant, 95% confidence interval likely excludes a meaningful difference.
- d. Statistically significant statistical heterogeneity, but considerable overlap of confidence intervals.

1. Mortality

	HFN	С	NIV	/		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
Hernandez (high risk) 2016	59	290	56	314	53.6%	1.14 [0.82, 1.59]	2016	
Theerawit 2020	7	71	7	69	5.9%	0.97 [0.36, 2.63]	2017	
Jing 2018	5	22	5	20	5.0%	0.91 [0.31, 2.68]	2018	
Thille 2019	33	302	39	339	30.4%	0.95 [0.61, 1.47]	2019	
Tan 2020	7	44	5	42	5.1%	1.34 [0.46, 3.88]	2020	
Total (95% CI)		729		784	100.0%	1.07 [0.84, 1.36]		
Total events	111		112					
Heterogeneity: $Tau^2 = 0.00$; 0	$Chi^2 = 0.7$	72, df =	= 4 (P =	0.95); I	$^{2} = 0\%$		_	
Test for overall effect: $Z = 0.5$	52 (P = 0)	.61)						0.5 0.7 1 1.5 2 Favours HFNC Favours NIV

2. Re-intubation

	HFN	С	NIV	/		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Hernandez (high risk) 2016	66	290	60	314	52.3%	1.19 [0.87, 1.63]	2016	
Theerawit 2020	5	71	6	69	3.9%	0.81 [0.26, 2.53]	2017	
Guoqiang 2018	1	17	1	19	0.7%	1.12 [0.08, 16.52]	2018	· · · · · · · · · · · · · · · · · · ·
Jing 2018	2	22	1	20	0.9%	1.82 [0.18, 18.55]	2018	· · · · · · · · · · · · · · · · · · ·
Thille 2019	59	302	41	339	37.6%	1.62 [1.12, 2.33]	2019	- -
Tan 2020	6	44	6	42	4.6%	0.95 [0.33, 2.73]	2020	
Total (95% CI)		746		803	100.0%	1.31 [1.04, 1.64]		◆
Total events	139		115					
Heterogeneity: $Tau^2 = 0.00$;	$Chi^2 = 2.7$	73, df =	= 5 (P =	0.74); I	$^{2} = 0\%$			0.05 0.2 1 5 20
Test for overall effect: $Z = 2.3$	33 (P = 0)	.02)						Favours HFNC Favours NIV

3. ICU length of stay

	F	IFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Hernandez (high risk) 2016	3	3.7	290	4	5.2	314	54.4%	-1.00 [-1.72, -0.28]	2016	
Jing 2018	8.5	3.5	22	9.4	4.8	20	4.2%	-0.90 [-3.46, 1.66]	2018	
Thille 2019	11	5.9	302	12	5.9	339	33.3%	-1.00 [-1.92, -0.08]	2019	
Tan 2020	7.5	3	44	8.5	4.7	32	8.1%	-1.00 [-2.85, 0.85]	2020	
Total (95% CI)			658			705	100.0%	-1.00 [-1.52, -0.47]		•
Heterogeneity: Tau ² = 0.00; Test for overall effect: Z = 3.				(P = 1.0	00); I	$^{2} = 0\%$				-2 -1 0 1 2 Favours HFNC Favours NIV

4. Hospital length of stay

	I	HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Hernandez (high risk) 2016	23	23.7	290	26	15.6	314	13.6%	-3.00 [-6.23, 0.23]	2016	
Thille 2019	23	17.8	302	25	20	339	16.5%	-2.00 [-4.93, 0.93]	2019	
Tan 2020	10	2.7	44	11	3.9	42	69.9%	-1.00 [-2.42, 0.42]	2020	
Total (95% CI)			636			695	100.0%	-1.44 [-2.63, -0.25]		•
Heterogeneity: Chi ² = 1.40, c Test for overall effect: Z = 2.2			0); I ² =	0%						-4 -2 0 2 4 Favours HFNC Favours NIV

5. Comfort

	н	IFNC			NIV			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Guoqiang 2018	-6	3	19	-4	2.2	17	12.7%	-0.74 [-1.42, -0.06]	
Jing 2018	3.6	1.9	22	5.2	2.3	20	14.7%	-0.75 [-1.38, -0.12]	
Tan 2020	-7	1.5	44	-5	2.2	42	27.1%	-1.06 [-1.51, -0.60]	-
Theerawit 2020	2.8	1.8	71	3.8	1.9	69	45.4%	-0.54 [-0.88, -0.20]	
Total (95% CI)			156			148	100.0%	-0.73 [-0.98, -0.49]	◆
Heterogeneity: Tau ² =	= 0.01; 0	Chi² =	= 3.26,	df = 3	(P =	0.35); I	$ ^2 = 8\%$		
Test for overall effect	Z = 5.8	32 (P	< 0.00	001)					Favours HFNC Favours NIV

6. Dyspnea

	н	FNC			NIV			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Tan 2020	3	1.5	44	2	0.74	42		1.00 [0.50, 1.50]	-1 -0.5 0 0.5 1 Favours HFNC Favours NIV

8. PCO2

	н	IFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Hernandez (high risk) 2016	46	3.1	290	47	2.8	314	96.2%	-1.00 [-1.47, -0.53]	2016	
Jing 2018	56.9	10	22	61.5	16.3	20	0.3%	-4.60 [-12.88, 3.68]	2018	
Tan 2020	51	6.5	44	52	5.2	42	3.5%	-1.00 [-3.48, 1.48]	2020	
Total (95% CI)			356			376	100.0%	-1.01 [-1.47, -0.55]		•
Heterogeneity: $Chi^2 = 0.72$, c Test for overall effect: $Z = 4.2$				= 0%					-	-10 -5 0 5 10 Favours HFNC Favours NIV

9. PaO2/FiO2

	н	FNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Hernandez (high risk) 2016	-99	2	290	-103	32	314	96.0%	4.00 [0.45, 7.55]	2016	
Jing 2018	-201.2	92.4	22	-257.5	130.7	20	0.3%	56.30 [-12.78, 125.38]	2018	
Tan 2020	-230.3	44	44	-227.2	40.5	42	3.8%	-3.10 [-20.96, 14.76]	2020	
Total (95% CI)			356			376	100.0%	3.86 [0.39, 7.34]		•
Heterogeneity: $Chi^2 = 2.80$, or Test for overall effect: $Z = 2$.); $I^2 = 2$	9%					-	-100 -50 0 50 100 Favours HFNC Favours NIV

9. Respiratory rate

	Н	IFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Jing 2018	22.4	4.4	22	21	4.5	20	48.9%	1.40 [-1.30, 4.10]	2018	
Tan 2020	19	5.6	44	21.5	6.8	42	51.1%	-2.50 [-5.14, 0.14]	2020	
Total (95% CI)			66			62	100.0%	-0.59 [-2.48, 1.29]		
Heterogeneity: Chi ² =	4.10, d	f = 1	(P = 0)	.04); I ²	= 76	%				
Test for overall effect:	Z = 0.6	61 (P	= 0.54)						Favours HFNC Favours NIV

Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

		Certai	nty assessment	t		Nº of p	atients		Effect		
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	NIV	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Mortality	- RCTs	!	1	1		1					
4 RCTs	not serious	not serious	not serious ^a	very serious b	none	18/127 (14.2%)	21/123 (17.1%)	RR 0.82 (0.46 to 1.47)	31 fewer per 1,000 (from 92 fewer to 80 more)		CRITICAL
Intubatio	n - RCTs	1	1	1							1
4 RCTs	not serious	not serious	not serious ^a	very serious b	none	19/141 (13.5%)	23/134 (17.2%)	RR 0.79 (0.46 to 1.35)	36 fewer per 1,000 (from 93 fewer to 60 more)		CRITICAL
ICU lengt	th of stay - I	RCTs	l			1					
3 RCTs	not serious	not serious	not serious	serious ^c	none	118	117	-	MD 0.1 higher (0.73 lower to 0.94 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
Hospital	length of st	ay - RCTs	1	1							1
4 RCTs	not serious	not serious	not serious	serious ^c	none	178	174	-	MD 0.82 days lower (1.83 lower to 0.2 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
Comfort	(lower is be	tter) (Scale from:	0 to 10)								
2 RCTs	not serious ^d	serious ^e	not serious	serious ^f	none	49	52	-	SMD 0.57 SD lower (0.98 lower to 0.16 lower)		IMPORTANT
Dyspnea					1						
3 RCTs	not serious ^d	not serious	not serious	serious ^c	none	77	76	-	MD 0.31 lower (0.94 lower to 0.33 higher)	⊕⊕⊕⊖ MODERATE	IMPORTANT
PaO2/FiC	02 - RCTs (fe	ollow up: mean 6	hours)								

Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

2 RCTs	not serious	not serious	not serious ^a	not serious	none	44	44	-	MD 0.52 lower (3.59 lower to 2.56 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
PO2 - RC	Ts		1								
3 RCTs	not serious	not serious	not serious	not serious	none	151	109	-	MD 0.32 higher (3.83 lower to 4.47 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
PCO2 - R	CTs										
6 RCTs	not serious	serious ^e	not serious	serious ^c	none	230	227	-	MD 0.79 mmHg lower (5.19 lower to 3.61 higher)		IMPORTANT
Respirate	ory rate - RC	CTs	1								
5 RCTs	not serious	not serious	not serious	not serious	none	148	144	-	MD 0.40 lower (1.60 lower to 0.8 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. NIV settings in comparison group appear to have been reasonable and titrated to patient need in most studies.

b. Very wide 95% confidence intervals resulting in very serious imprecision.

c. Wide 95% confidence intervals which do not rule out significant benefit nor harm.

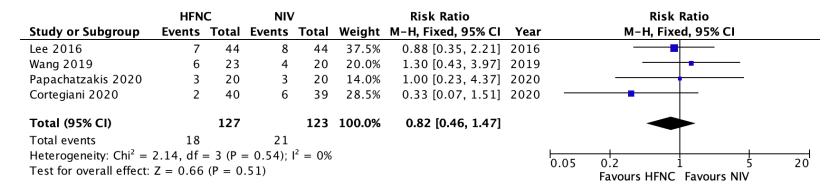
d. High statistical heterogeneity with study point estimates on opposite sides of the line of no effect.

e. Lack of blinding of patients may result in bias, but given the immediacy of the comfort/discomfort using NIV/HFNC we judge patient assessments of comfort and dyspnea to be of lower risk of bias.

f. Statistically significant but optimal information size not met.

Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercaphic respiratory failure

1. Mortality



2. Intubation

	HFN	С	NIV	/		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M–H, Fixed, 95% Cl	Year		M–H, Fixed, 95% CI		
Lee 2016	11	44	12	44	50.9%	0.92 [0.45, 1.85]	2016				
Wang 2019	4	23	5	20	22.7%	0.70 [0.22, 2.24]	2019				
Doshi 2020	2	34	5	31	22.2%	0.36 [0.08, 1.75]	2020				
Cortegiani 2020	2	40	1	39	4.3%	1.95 [0.18, 20.64]	2020				
Total (95% CI)		141		134	100.0%	0.79 [0.46, 1.35]					
Total events	19		23						_		
Heterogeneity: Chi ² =	1.72, df	= 3 (P	= 0.63);	$l^2 = 0\%$	6					<u> </u>	- 20
Test for overall effect	Z = 0.86	5 (P = C)).39)					0.05	0.2 1 Favours HFNC Favours N	1IV 2	20

Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

3. ICU length of stay

	H	HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Wang 2019	9.09	1.56	23	8.5	1.32	20	57.1%	0.59 [-0.27, 1.45]	2019	
Cong 2019	18.04	6.15	84	18.31	7.01	84	15.6%	-0.27 [-2.26, 1.72]	2019	
Doshi 2020	1.8	1.2	11	2.5	2.3	13	27.3%	-0.70 [-2.14, 0.74]	2020	
Total (95% CI)			118			117	100.0%	0.10 [-0.73, 0.94]		
Heterogeneity: Tau ² = Test for overall effect				f = 2 (P	= 0.29	9); I ² =	20%			-2 -1 0 1 2 Favours HFNC Favours NIV

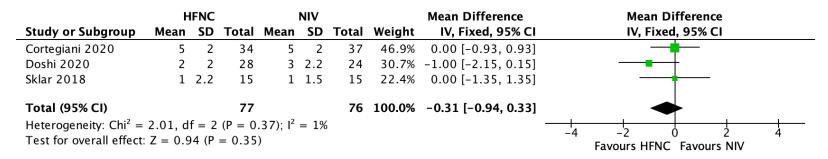
4. Hospital length of stay

	I	HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Cong 2019	18.04	6.15	84	18.31	7.01	84	26.0%	-0.27 [-2.26, 1.72]	2019	
Doshi 2020	4.37	3.08	34	5.01	2.39	31	58.0%	-0.64 [-1.97, 0.69]	2020	
Papachatzakis 2020	11.5	8.5	20	11	10.5	20	2.9%	0.50 [-5.42, 6.42]	2020	
Cortegiani 2020	10	7.4	40	13	5.2	39	13.0%	-3.00 [-5.81, -0.19]	2020	
Total (95% CI)			178			174	100.0%	-0.82 [-1.83, 0.20]		•
Heterogeneity: Chi ² =	2.86, df	= 3 (P	P = 0.42	1); $I^2 = 0$	0%				-	
Test for overall effect:	Z = 1.5	8 (P =	0.11)							Favours HFNC Favours NIV

5. Comfort

	ŀ	IFNC			NIV			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Sklar 2018	-6	2.2	15	-7	2.2	15	32.0%	0.44 [-0.28, 1.17]	2018	
Cortegiani 2020	0	1.5	34	2	2.2	37	68.0%	-1.04 [-1.54, -0.54]	2020	
Total (95% CI)			49			52	100.0%	-0.57 [-0.98, -0.16]		•
Heterogeneity: Chi ² =); ² =	= 91%				
Test for overall effect	Z = 2.7	71 (P	= 0.00	7)						Favours HFNC Favours NIV

6. Dyspnea



7. PaO2/FiO2

	н	FNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Lee 2016	-134.8	7.3	44	-134.5	7.5	44	98.9%	-0.30 [-3.39, 2.79]	2016	
Cortegiani 2020	-2.2	62.3	40	17.8	70.8	39	1.1%	-20.00 [-49.44, 9.44]	2020 🕂	<u>_</u>
Total (95% CI)			84			83	100.0%	-0.52 [-3.59, 2.56]		•
Heterogeneity: Chi ² = Test for overall effect	,	,); $I^2 = 41$.%				_	-20 -10 0 10 20 Favours HFNC Favours NIV

8. PO2

		HFNC			NIV			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Cong 2019	81.87	15.27	84	82.22	15.64	84	78.7%	-0.35 [-5.02, 4.32]	2019	
Doshi 2020	83	43	27	88	14.8	25	5.8%	-5.00 [-22.23, 12.23]	2020	
Cortegiani 2020	3.1	20.7	40	-2.6	26.6	39	15.5%	5.70 [-4.83, 16.23]	2020	- +
Total (95% CI)			151			148	100.0%	0.32 [-3.83, 4.47]		•
Heterogeneity: Chi ² = Test for overall effect:				b); $I^2 = 0$	%					-50 -25 0 25 50 Favours HFNC Favours NIV

9. PCO2

	HFNC			NIV				Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	r IV, Random, 95% CI
Lee 2016	56.4	10.1	44	52.6	8.8	44	21.5%	3.80 [-0.16, 7.76]	2016	5
Sklar 2018	53	14	15	54	14	15	11.1%	-1.00 [-11.02, 9.02]	2018	3
Cong 2019	58.87	14.42	84	59.95	13.56	84	21.0%	-1.08 [-5.31, 3.15]	2019)
Doshi 2020	50	11.9	27	57	17	25	13.9%	-7.00 [-15.03, 1.03]	2020)
Cortegiani 2020	64	14.9	40	58.1	12.4	39	17.5%	5.90 [-0.14, 11.94]	2020)
Papachatzakis 2020	50.8	9.4	20	59.6	13.9	20	15.1%	-8.80 [-16.15, -1.45]	2020)
Total (95% CI)			230			227	100.0%	-0.79 [-5.19, 3.61]		
Heterogeneity: Tau ² = 19.33; Chi ² = 15.83, df = 5 (P = 0.007); l ² = 68%										
Test for overall effect: $Z = 0.35$ (P = 0.72) Test for overall effect: $Z = 0.35$ (P = 0.72) Test for overall effect: $Z = 0.35$ (P = 0.72)										

10. Respiratory rate

	HFNC			NIV				Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	r IV, Random, 95% CI		
Lee 2016	24	5.9	44	24	5.4	44	25.8%	0.00 [-2.36, 2.36]	2016	;		
Sklar 2018	18	5.2	15	19	5.9	15	9.1%	-1.00 [-4.98, 2.98]	2018	;		
Papachatzakis 2020	15.7	3.5	20	17.3	4.6	20	22.5%	-1.60 [-4.13, 0.93]	2020)		
Doshi 2020	21	3.7	29	22	5.2	26	24.8%	-1.00 [-3.41, 1.41]	2020)		
Cortegiani 2020	-6	6	40	-7.7	6.9	39	17.7%	1.70 [-1.15, 4.55]	2020)		
Total (95% CI)			148			144	100.0%	-0.40 [-1.60, 0.80]		•		
Heterogeneity: Tau ² = 0.00; Chi ² = 3.38, df = 4 (P = 0.50); $l^2 = 0\%$												
Test for overall effect: $7 = 0.65$ (P = 0.52)										-10 -5 0 5 10 Favours HFNC Favours NIV		

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