# Question #1: Should NIV be used in acute hypercapnic respiratory failure due to an acute exacerbation of COPD (AECOPD)?

# Mortality (1.1.1 & 1.1.2 in acidotic patients)

	NIV		Standard Medical	Care		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 Compared to s	tandard o	f care					
Avdeev 1998	3	26	9	29	9.7%	0.37 [0.11, 1.23]	<del></del>
Bardi 2000	0	15	1	15	1.7%	0.33 [0.01, 7.58]	
Bott 1993	3	26	9	30	9.5%	0.38 [0.12, 1.27]	<del></del>
Brochard 1995	4	43	12	42	13.8%	0.33 [0.11, 0.93]	<del></del>
Celikel 1998	0	15	1	15	1.7%	0.33 [0.01, 7.58]	<del></del>
Chen 2005	12	171	7	71	11.3%	0.71 [0.29, 1.73]	<del></del>
Dikensoy 2002	1	17	2	17	2.3%	0.50 [0.05, 5.01]	<del></del>
Khilnani 2010	3	20	2	20	2.3%	1.50 [0.28, 8.04]	<del></del>
Martin 2000	3	12	6	11	7.1%	0.46 [0.15, 1.40]	<del></del>
Plant 2000	12	118	24	118	27.3%	0.50 [0.26, 0.95]	<del></del>
Subtotal (95% CI)		463		368	86.8%	0.49 [0.34, 0.70]	<b>◆</b>
Total events	41		73				
Heterogeneity: Chi2 =	3.46, df	= 9 (P	$= 0.94$ ); $I^2 = 0\%$				
Test for overall effect	Z = 3.89	(P = 0)	.0001)				
1.1.2 Compared to M	IV						
Conti 2002	6	23	5	26	5.3%	1.36 [0.48, 3.86]	<del></del>
Jurjevic 2009	4	78	5	78	5.7%	0.80 [0.22, 2.87]	<del></del>
Subtotal (95% CI)		101		104	11.0%	1.07 [0.48, 2.39]	<b>*</b>
Total events	10		10				
Heterogeneity: Chi <sup>2</sup> =							
Test for overall effect	Z = 0.16	(P = 0)	.87)				
1.1.3 Patients with A							
Barbe 1996	0	10	0	10		Not estimable	
Keenan 2005	1	25	2	27	2.2%	0.54 [0.05, 5.59]	•
Subtotal (95% CI)		35		37	2.2%	0.54 [0.05, 5.59]	
Total events	1		2				
Heterogeneity: Not ap							
Test for overall effect	Z = 0.52	(P = 0)	.61)				
Total (95% CI)		599		509	100.0%	0.55 [0.40, 0.77]	•
Total events	52		85				•
Heterogeneity: Chi <sup>2</sup> =		= 12 (F					
Test for overall effect							0.01 0.1 1 10 100
Test for subgroup diff				.22). I <sup>2</sup> :	= 33.7%		Favours NIV Favours Control
rest for subgroup un	erences.	-	3.02, di = 2 (r = 0.	,, .	- 33.770		

## Intubation

	NIV	,	Standard Medical	Care		Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.2.1 Patients with A	ARF who a	are aci	dotic				
Avdeev 1998	5	26	8	29	3.9%	0.70 [0.26, 1.86]	<del></del>
Bardi 2000	1	15	2	15	1.0%	0.50 [0.05, 4.94]	<del></del>
Bott 1993	0	30	2	30	1.3%	0.20 [0.01, 4.00]	<del></del>
Brochard 1995	11	43	31	42	16.3%	0.35 [0.20, 0.60]	<del></del>
Carrera 2009	5	37	13	38	6.7%	0.40 [0.16, 1.00]	
Celikel 1998	1	15	2	15	1.0%	0.50 [0.05, 4.94]	<del></del>
Chen 2005	8	171	26	71	19.1%	0.13 [0.06, 0.27]	
Conti 2002	12	23	26	26	12.9%	0.53 [0.36, 0.78]	- <del></del>
Del Castillo 2003	1	20	3	21	1.5%	0.35 [0.04, 3.09]	<del></del>
Dikensoy 2002	2	17	7	17	3.6%	0.29 [0.07, 1.18]	<del></del>
Khilnani 2010	3	20	12	20	6.2%	0.25 [0.08, 0.75]	
Kramer 1995	1	11	8	12	4.0%	0.14 [0.02, 0.92]	<del></del>
Martin 2000	3	12	5	11	2.7%	0.55 [0.17, 1.78]	<del></del>
Plant 2000	18	118	32	118	16.6%	0.56 [0.34, 0.94]	-
Thys 2002	0	7	3	5	2.1%	0.11 [0.01, 1.71]	<del></del>
Subtotal (95% CI)		565		470	99.0%	0.37 [0.29, 0.46]	<b>•</b>
Total events	71		180				
Heterogeneity: Chi <sup>2</sup> =	= 18.68, d	f = 14	$(P = 0.18); I^2 = 259$	6			
Test for overall effect	:: Z = 8.74	1 (P < 0	0.00001)				
1.2.2 Patients with A	ARF who a	re not	acidotic				
Barbe 1996	0	10	0	10		Not estimable	
Keenan 2005	2	25	2	27	1.0%	1.08 [0.16, 7.10]	
Subtotal (95% CI)		35		37	1.0%	1.08 [0.16, 7.10]	
Total events	2		2				
Heterogeneity: Not a	pplicable						
Test for overall effect		B (P = 0	0.94)				
Total (95% CI)		600		507	100.0%	0.37 [0.30, 0.47]	•
Total events	73		182				-
Heterogeneity: Chi <sup>2</sup> =	= 19.61, d	f = 15	$(P = 0.19); I^2 = 249$	6			
Test for overall effect							0.01 0.1 1 10 100 Favours NIV Favours Control
Test for subgroup dif				.26), I <sup>2</sup> :	= 19.6%		ravours NIV Favours Control
			, , ,	,,			

### Nosocomial Pneumonia

	NIV		Standard Medical	Care		Risk Ratio	Risk Ratio
Study or Subgroup	Events T	otal	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.3.1 Patients with	ARF who are	e acid	otic				
Brochard 1995	2	43	7	42	52.5%	0.28 [0.06, 1.27]	<del></del>
Khilnani 2010	1	20	4	20	29.7%	0.25 [0.03, 2.05]	<del></del>
Subtotal (95% CI)		63		62	82.2%	0.27 [0.08, 0.92]	•
Total events	3		11				
Heterogeneity: Chi2 =	= 0.01, df =	1 (P =	$= 0.93$ ); $I^2 = 0\%$				
Test for overall effec	t: Z = 2.10 (	(P=0.	.04)				
1.3.2 Patients with	ARF who are	e not	acidotic				
Keenan 2005	0	25	2	27	17.8%	0.22 [0.01, 4.28]	
Subtotal (95% CI)		25		27	17.8%	0.22 [0.01, 4.28]	
Total events	0		2				
Heterogeneity: Not a	pplicable						
Test for overall effec	t: Z = 1.01 (	(P=0.	31)				
Total (95% CI)		88		89	100.0%	0.26 [0.08, 0.81]	-
Total events	3		13				
Heterogeneity: Chi2 =	= 0.03, df =	2 (P =	$= 0.99$ ); $I^2 = 0\%$				0.01 0.1 1 10 100
Test for overall effect	t: Z = 2.33 (	(P = 0.	.02)				Favours NIV Favours Control
Test for subgroup di	fferences: Cl	$hi^2 = 0$	0.02, $df = 1$ ( $P = 0$ .	89), I2 :	= 0%		TAVOUTS THIS PAVOUTS CONTION

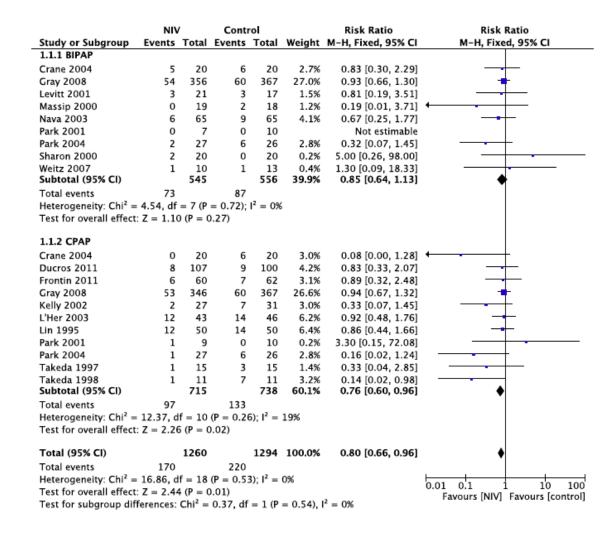
			Quality assess	ment				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality	Mortality											
14 [1-14]	randomised trials	not serious	not serious	not serious	not serious	strong association	52/599 (8.7%)	85/609 (14.0%)	RR 0.63 (0.46 to 0.87)	52 fewer per 1000 (from 18 fewer to 75 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Intubation					•							
17 [1-9, 11- 18]	randomised trials	serious 1	not serious	not serious	not serious	strong association	73/600 (12.2%)	182/607 (30.0%)	RR 0.41 (0.33 to 0.52)	177 fewer per 1000 (from 144 fewer to 201 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Nosocomial	Pneumonia											
3 [6, 11, 12]	randomised trials	serious 1	not serious	serious <sup>2</sup>	not serious	none	3/88 (3.4%)	13/89 (14.6%)	RR 0.26 (0.08 to 0.81)	108 fewer per 1000 (from 28 fewer to 134 fewer)	⊕⊕○ LOW	CRITICAL

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

- Lack of blinding of intervention in all included trials.
   Variable definition of nosocomial pneumonia used across studies with variable severity and perceived importance to patients.

#### Question #2a: Should NIV be used in acute respiratory failure due cardiogenic pulmonary edema (CPE)?

#### Mortality



Intubation

Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.2.1 BIPAP							
Crane 2004	1	20	0	20	0.4%	3.15 [0.12, 82.16]	
Gray 2008	13	356	10	367	8.4%	1.35 [0.59, 3.13]	<del> -</del>
Levitt 2001	5	21	7	17	5.2%	0.45 [0.11, 1.80]	<del></del>
Massip 2000	1	19	6	18	5.2%	0.11 [0.01, 1.04]	-
Nava 2003	13	65	16	65	11.3%	0.77 [0.33, 1.75]	<del></del>
Park 2001	0	7	4	10	3.1%	0.10 [0.00, 2.15]	<del></del>
Park 2004	2	27	11	26	9.2%	0.11 [0.02, 0.56]	<del></del>
Sharon 2000	16	20	4	20	0.7%		
Subtotal (95% CI)		535		543	43.4%	0.85 [0.56, 1.28]	•
Total events	51		58				
Heterogeneity: Chi <sup>2</sup> =	= 27.58, d	f = 7 (1)	P = 0.00	03); I <sup>2</sup> =	= 75%		
Test for overall effect	z = 0.79	P = 0	).43)				
1.2.2 CPAP							
Crane 2004	1	20	0	20	0.4%	3.15 [0.12, 82.16]	<del> </del>
Ducros 2011	3	107	6	100	5.3%	0.45 [0.11, 1.86]	<del></del>
Frontin 2011	2	60	3	62	2.5%	0.68 [0.11, 4.21]	
Gray 2008	8	346	10	367	8.4%	0.84 [0.33, 2.17]	<del></del>
Kelly 2002	0	27	1	31	1.2%	0.37 [0.01, 9.46]	<del></del>
L'Her 2003	2	43	4	46	3.3%	0.51 [0.09, 2.95]	<del></del>
Lin 1995	8	50	18	50	13.3%	0.34 [0.13, 0.88]	-
Park 2001	3	9	4	10	2.2%	0.75 [0.11, 4.90]	<del></del>
Park 2004	2	27	11	26	9.2%	0.11 [0.02, 0.56]	<del></del>
Takeda 1997	1	15	6	15	4.9%	0.11 [0.01, 1.04]	<del></del>
Takeda 1998	2	11	8	11	5.8%		<del></del>
Subtotal (95% CI)		715		738	56.6%	0.40 [0.26, 0.63]	•
Total events	32		71				
Heterogeneity: Chi <sup>2</sup> =			•	$6); I^2 =$	9%		
Test for overall effect	z = 4.0	L (P < (	0.0001)				
Total (95% CI)		1250		1281	100.0%	0.60 [0.44, 0.80]	<b>♦</b>
Total events	83		129				
Heterogeneity: Chi <sup>2</sup> =	= 43.30, d	f = 18	(P = 0.0)	007); I <sup>2</sup>	= 58%		0.01 0.1 1 10 100
Test for overall effect	t: Z = 3.39	) (P = 0	0.0007)				Favours [NIV] Favours [control]
Test for subgroup dif	ferences:	Chi <sup>2</sup> =	5.76, df	= 1 (P	= 0.02),	$I^2 = 82.6\%$	ravours [NIV] ravours [Control]

# Acute myocardial infarction

	NIV	/	Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.3.1 BIPAP							
Crane 2004	9	20	6	20	2.3%	1.91 [0.52, 7.01]	+
Gray 2008	95	356	91	367	45.7%	1.10 [0.79, 1.54]	#
Levitt 2001	0	21	0	17		Not estimable	
Nava 2003	7	65	5	65	3.1%	1.45 [0.43, 4.82]	<del></del>
Sharon 2000 Subtotal (95% CI)	11	20 <b>482</b>	2	20 <b>489</b>	0.6% <b>51.7%</b>	11.00 [2.00, 60.57] 1.28 [0.95, 1.73]	<u> </u>
		402		409	31.7%	1.26 [0.93, 1.73]	<b>Y</b>
Total events	122		104				
Heterogeneity: Chi <sup>2</sup> =				$I^2 = 59$	%		
Test for overall effect:	Z = 1.60	0 (P = 0	0.11)				
1.3.2 CPAP							
Crane 2004	3	20	6	20	3.5%	0.41 [0.09, 1.95]	<del></del>
Gray 2008	94	346	91	367	44.7%	1.13 [0.81, 1.58]	<b>+</b>
Subtotal (95% CI)		366		387	48.3%	1.08 [0.78, 1.49]	<b>*</b>
Total events	97		97				
Heterogeneity: Chi2 =	1.55, df	= 1 (P	= 0.21);	$I^2 = 35$	%		
Test for overall effect:	Z = 0.4	5 (P = 0	0.65)				
Total (95% CI)		848		876	100.0%	1.18 [0.95, 1.48]	•
Total events	219		201				ĺ
Heterogeneity: Chi <sup>2</sup> =		= 5 (P	= 0.10):	$I^2 = 46$	%		<del> </del>
Test for overall effect:							0.01 0.1 1 10 100
Test for subgroup diff				= 1 (P	= 0.45),	<sup>2</sup> = 0%	Favours [NIV] Favours [control]

			Quality assessm	ent				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality (asse	Mortality (assessed with: longest available)											
16 [19-34]	randomised trials	serious 1	not serious	not serious	not serious	none	170/1260 (13.5%)	220/1294 (17.0%)	RR 0.80 (0.66 to 0.96)	34 fewer per 1000 (from 7 fewer to 58 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Intubation												
15 [19-33]	randomised trials	serious 1	serious <sup>2</sup>	not serious	not serious	none	83/1250 (6.6%)	129/1281 (10.1%)	RR 0.60 (0.44 to 0.80)	40 fewer per 1000 (from 20 fewer to 56 fewer)	⊕⊕© LOW	CRITICAL
Acute Myocard	lial infarction (ass	essed with: c	riteria reported in	individual stud	ly)							
5 [19, 22, 25, 28, 31]	randomised trials	serious 1	not serious	serious 3	serious <sup>4</sup>	none	219/848 (25.8%)	201/876 (22.9%)	OR 1.18 (0.95 to 1.48)	41 more per 1000 (from 11 fewer to 110 more)	⊕∭ VERY LOW	IMPORTANT

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

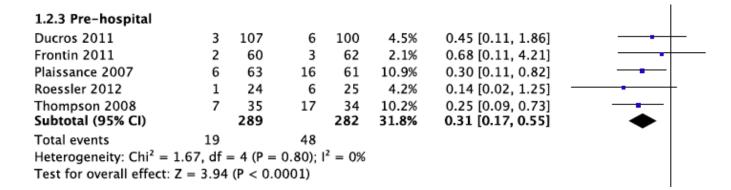
- Included study stopped early for harm.
   Isquared = 60%, visually evident statistical heterogeneity
   Variable diagnostic criteria for AMI used between studies.
   Wide confidence intervals that do not exclude benefit.

# Question #2b: Should patients with acute respiratory failure due to cardiogenic pulmonary edema receive a trial of CPAP to prevent deterioration prior to hospitalization?

#### Mortality

#### 1.1.3 Pre-hospital Ducros 2011 107 100 0.83 [0.33, 2.07] 4.5% Frontin 2011 60 62 3.3% 0.89 [0.32, 2.48] Weitz 2007 10 1.30 [0.09, 18.33] 13 0.4% Subtotal (95% CI) 175 8.2% 0.88 [0.45, 1.70] 177 15 Total events 17 Heterogeneity: $Chi^2 = 0.10$ , df = 2 (P = 0.95); $I^2 = 0\%$ Test for overall effect: Z = 0.39 (P = 0.70)

#### Intubation



			Quality assessi	ment				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative Absolute (95% CI) (95% CI)		Quality	Importance
Mortality												
3 [20, 21, 34]	randomised trials	not serious <sup>1</sup>	not serious	not serious	serious <sup>2</sup>	none	15/177 (8.5%)	17/175 (9.7%)	<b>RR 0.88</b> (0.45 to 1.70)	12 fewer per 1000 (from 53 fewer to 68 more)	⊕⊕⊕○ MODERATE	CRITICAL
Intubation												
5 [20, 21, 35-37]	randomised trials	serious <sup>3</sup>	not serious	not serious	serious <sup>4</sup>	none	19/289 (6.6%)	48/282 (17.0%)	<b>RR 0.31</b> (0.17 to 0.55)	117 fewer per 1000 (from 77 fewer to 141 fewer)	⊕⊕© LOW	CRITICAL

 $\label{eq:md-mono} \mbox{MD-mean difference, RR-relative risk} \ , \mbox{NIV-noninvasive ventilation, CI-Confidence interval} \ .$ 

- Lack of blinding but not lowered for ROB given objective nature of outcome.
   Wide confidence intervals do not exclude harm or benefit and low number of events.
   Lack of blinding for all studies.
   Although point estimate and confidence interval suggest benefit there is a low number of events lowering overall certainty.

#### Question #3: Should NIV be used in acute respiratory failure due to an acute exacerbation of asthma?

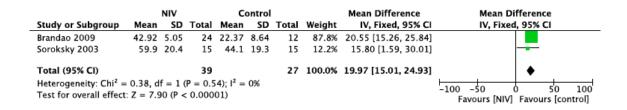
#### Intubation

	NIV	,	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Gupta 2010	2	28	0	25	100.0%	4.48 [0.23, 89.13]	
Soroksky 2003	0	17	0	16		Not estimable	_
Total (95% CI)		45		41	100.0%	4.48 [0.23, 89.13]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.98	3 (P = 0	).33)				0.01 0.1 1 10 100 Favours [NIV] Favours [control]

#### FEV1 Change

	NIV Control							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Brandao 2009	49.72	5.91	24	35.51	12.26	12	4.6%	14.21 [6.88, 21.54]	~
Gupta 2010	54	3	28	58	3	25	93.8%	-4.00 [-5.62, -2.38]	•
Soroksky 2003	57.4	17.7	15	43.9	16.7	15	1.6%	13.50 [1.19, 25.81]	<del></del>
Total (95% CI)			67				100.0%	-2.88 [-4.45, -1.32]	•
Heterogeneity: Chi <sup>2</sup> = Test for overall effect						3%			-100 -50 0 50 100 Favours [NIV] Favours [control]

## **Peak Expiratory Flow**



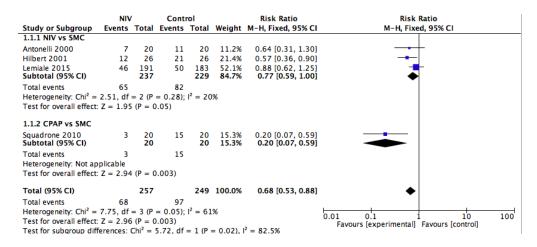
			Quality assess	ment				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Hospital Mo	rtality											
2 [38, 39]	randomised trials	serious 1	not serious	not serious	very serious <sup>2</sup>	none	0/45 (0.0%)	0/41 (0.0%)	not estimable	not estimable	⊕∭ VERY LOW	CRITICAL
Intubation												
2 [38, 39]	randomised trials	serious 1	not serious	not serious	very serious 3	none	2/45 (4.4%)	0/41 (0.0%)	<b>RR 4.48</b> (0.23 to 89.13)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕∭ VERY LOW	CRITICAL
Forced Expi	ratory Volume in 1	second Chan	ge (measured wit	h % predicted, h	nigher being bett	ter)						
3 [38-40]	randomised trials	serious 1	not serious	serious 4	not serious	none	39	27	-	MD <b>14.02 higher</b> (7.73 higher to 20.32 higher)	⊕⊕∭ LOW	IMPORTANT
Peak Expira	tory Flow (measure	ed with % pred	dicted, higher beir	ng better)								
2 [39, 40]	randomised trials	serious 1	not serious	serious 4	not serious	none	39	27	-	MD <b>19.97 higher</b> (15.01 higher to 24.93 higher)	⊕⊕∭ LOW	IMPORTANT
ICU Length	of Stay											
1 [39]	randomised trials	serious 5	not serious	serious 4	serious <sup>6</sup>	none	15	15	-	MD <b>0.3 higher</b> (0.63 lower to 1.23 higher)	⊕∭ VERY LOW	IMPORTANT

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

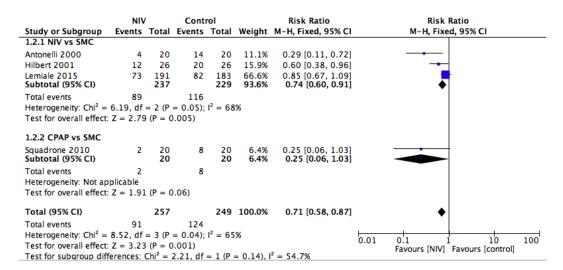
- 1. individual study low ROB in 1 study, moderate in the other
- 2. Point estimate not estimable due to no events in included studies.
- 3. Very wide confidence intervals with low number of events.
- Surrogate outcome with unclear clinical implications to patients.
   Moderate ROB in individual study.
   Very wide confidence intervals.

#### Question #4: Should NIV be used in acute respiratory failure in immunecompromised patients?

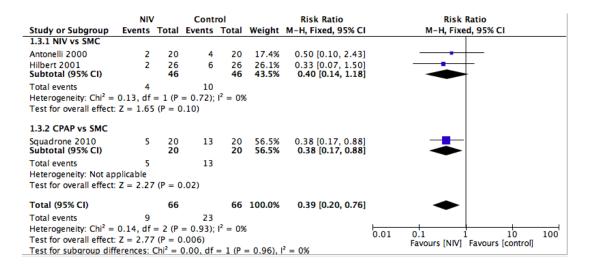
#### Mortality



#### Intubation



#### Nosocomial Pneumonia



SMC = standard medical care

			Quality assess	ment				№ of patients		Effect		Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	
Mortality												
4 [41-44]	randomised trials	not serious <sup>1</sup>	serious <sup>2</sup>	not serious	not serious	none	68/257 (26.5%)	97/249 (39.0%)	<b>RR 0.68</b> (0.53 to 0.88)	<b>125 fewer per 1,000</b> (from 47 fewer to 183 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Intubation												
4 [41-44]	randomised trials	serious <sup>3</sup>	not serious	not serious	not serious	none	91/257 (35.4%)	124/249 (49.8%)	<b>RR 0.71</b> (0.58 to 0.87)	<b>144 fewer per 1,000</b> (from 65 fewer to 209 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Nosocomial	Pneumonia											
3 [41, 42, 44]	randomised trials	serious <sup>3</sup>	not serious	serious <sup>4</sup>	not serious	none	9/66 (13.6%)	23/66 (34.8%)	RR 0.39 (0.20 to 0.76)	<b>213 fewer per 1,000</b> (from 84 fewer to 279 fewer)	⊕⊕◯◯ LOW	CRITICAL

 $\textbf{CI:} \ \ \text{Confidence interval;} \ \ \textbf{RR:} \ \ \text{Risk ratio, NIV-noninvasive ventilation, CI-Confidence interval}$ 

- Intervention was not blinded but felt to be less important for objective outcome of mortality.
   High Isquared value >80%.
   Intervention was not blinded.
   Variability in diagnosing nosocomial pneumonia.

# **Question #5: Should NIV be used in de novo acute respiratory failure?**

# Mortality

	NIV Control					Risk Ratio	Risk Ratio
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 NPPV							
Antonelli 1998	3	8	4	7	4.2%	0.66 [0.22, 1.97]	<del></del>
Confalonieri 1999	7	16	6	17	5.7%	1.24 [0.53, 2.90]	<del></del>
Ferrer 2003	8	30	16	28	16.1%	0.47 [0.24, 0.92]	<del></del>
Frat 2015	31	110	22	94	23.1%	1.20 [0.75, 1.93]	<del> </del>
Honrubia 2005	10	31	14	33	13.2%	0.76 [0.40, 1.45]	<del></del>
Kramer 1995	1	16	2	15	2.0%	0.47 [0.05, 4.65]	<del></del>
Martin 2000	4	16	7	13	7.5%	0.46 [0.17, 1.25]	<del></del>
Wood 1998	4	16	0	11	0.6%	6.35 [0.38, 107.30]	<del></del>
Wysocki 1995	7	21	10	20	10.0%	0.67 [0.32, 1.41]	<del></del>
Zhan 2012	1	21	5	19	5.1%	0.18 [0.02, 1.41]	<del></del>
Subtotal (95% CI)		285		257	87.5%	0.81 [0.63, 1.05]	•
Total events	76		86				
Heterogeneity: Chi <sup>2</sup> =	12.20, d	f = 9 (1)	P = 0.20		6%		
Test for overall effect:	Z = 1.62	2 (P = 0	0.11)				
1.1.2 CPAP							
Brambilla 2014	2	40	1	41	1.0%	2.05 [0.19, 21.72]	<del></del>
Consentini 2010	0	20	0	27		Not estimable	
Delclaux 2000	9	40	9	41	8.7%	1.02 [0.45, 2.32]	<del></del>
Roessler 2012	1	24	3	25	2.9%	0.35 [0.04, 3.11]	· ·
Subtotal (95% CI)		124		134	12.5%	0.95 [0.46, 1.94]	•
Total events	12		13				
Heterogeneity: Chi <sup>2</sup> =	1.25, df	= 2 (P	= 0.53);	$I^2 = 0\%$	ś		
Test for overall effect:	Z = 0.15	(P = 0	).88)				
Total (95% CI)		409		391	100.0%	0.83 [0.65, 1.05]	•
Total events	88		99				1
Heterogeneity: Chi <sup>2</sup> =		f = 12		2); I <sup>2</sup> =	12%		
Test for overall effect:			,	.,			0.01 0.1 1 10 100
Test for subgroup diff				= 1 (P	= 0.68).	$1^2 = 0\%$	Favours [NIV] Favours [control]
				4-	,		

## Intubation

	NIV	/	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.2.1 NPPV							
Antonelli 1998	3	8	6	7	4.1%	0.44 [0.17, 1.12]	<del></del>
Confalonieri 1999	6	28	14	28	8.9%	0.43 [0.19, 0.95]	
Ferrer 2003	11	30	21	28	13.9%	0.49 [0.29, 0.82]	
Frat 2015	55	110	44	94	30.3%	1.07 [0.80, 1.42]	<b>+</b>
Kramer 1995	5	16	11	15	7.2%	0.43 [0.19, 0.94]	-
Martin 2000	6	16	10	13	7.0%	0.49 [0.24, 0.98]	
Wood 1998	7	16	5	11	3.8%	0.96 [0.41, 2.26]	
Wysocki 1995	13	21	14	20	9.2%	0.88 [0.57, 1.38]	+
Zhan 2012	1	21	4	19	2.7%	0.23 [0.03, 1.85]	<del></del>
Subtotal (95% CI)		266		235	87.1%	0.73 [0.61, 0.88]	<b>•</b>
Total events	107		129				
Heterogeneity: Chi2 =	17.38, d	f = 8	P = 0.03	$I^2 = 5$	4%		
Test for overall effect	Z = 3.32	2 (P = 0)	.0009)				
1.2.2 CPAP							
Brambilla 2014	2	40	1	41	0.6%	2.05 [0.19, 21.72]	<del>-   •</del>
Consentini 2010	0	20	0	27		Not estimable	
Delclaux 2000	15	40	18	41	11.3%	0.85 [0.50, 1.45]	<del></del>
Roessler 2012	0	24	1	25	0.9%	0.35 [0.01, 8.12]	-
Subtotal (95% CI)		124		134	12.9%	0.88 [0.52, 1.46]	•
Total events	17		20				
Heterogeneity: Chi2 =	0.84, df	= 2 (P	= 0.66);	$I^2 = 0\%$	5		
Test for overall effect	Z = 0.5	1 (P = 0)	0.61)				
Total (95% CI)		390		369	100.0%	0.75 [0.63, 0.89]	•
Total events	124		149				
Heterogeneity: Chi <sup>2</sup> =	18.39. d	f = 11	(P = 0.0)	7); I <sup>2</sup> =	40%		
Test for overall effect				., -			0.01 0.1 1 10 100
Test for subgroup dif	ferences:	Chi <sup>2</sup> =	0.43. df	= 1 (P	= 0.51).	$I^2 = 0\%$	Favours [NIV] Favours [control]

		C	Quality assessmen	nt			№ of patients			Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality (assesse	d with: Longest av	railable)										
14 [13, 17, 36, 45- 55]	randomised trials	not serious	not serious	serious 1	serious <sup>2</sup>	none	88/409 (21.5%)	99/391 (25.3%)	RR 0.83 (0.65 to 1.05)	43 fewer per 1000 (from 13 more to 89 fewer)	⊕⊕∭ LOW	CRITICAL
Intubation		•										
13 [13, 17, 36, 45- 51, 53-55]	randomised trials	serious 3	not serious	serious 1	not serious	none	124/390 (31.8%)	149/369 (40.4%)	<b>RR 0.75</b> (0.63 to 0.89)	101 fewer per 1000 (from 44 fewer to 149 fewer)	⊕⊕⊜ LOW	CRITICAL

 $\label{eq:md-mono} \mbox{MD-mean difference, RR-relative risk, NIV-noninvasive ventilation, CI-Confidence interval}$ 

- 1. Most trials used standard medical care comparator, 1 used IMV comparator.
- Wide confidence intervals do not exclude harm.
   Lack of blinding in all studies.

## **Question #6: Should NIV be used in the treatment of acute respiratory failure in postoperative patients?**

### Mortality

#### 1.1.2 Treatment of ARF in postop patients

1.1.2 ITEALINEIL OF ARE	III POS	top pati	ciita					1
Auriant 2001	3	24	9	24	38.3%	0.33 [0.10, 1.08]		†
Squadrone 2005	0	105	3	104	14.9%	0.14 [0.01, 2.71]	<del>-</del>	+-
Subtotal (95% CI)		129		128	53.2%	0.28 [0.09, 0.84]	•	
Total events	3		12					
Heterogeneity: $Chi^2 = 0.2$	9, df	= 1 (P =	$0.59$ ); $I^{2}$	$^{2} = 0\%$				
Test for overall effect: Z =	2.28	(P = 0.0)	2)					
								1

#### Intubation

#### 1.2.2 Treatment of ARF in postop patients

Auriant 2001	5	24	12	24	42.9%	0.42 [0.17, 1.00]	-
Squadrone 2005	1	105	10	104	35.9%	0.10 [0.01, 0.76]	
Subtotal (95% CI)		129		128	78.9%	0.27 [0.12, 0.61]	•
Total events	6		22				
Heterogeneity: $Chi^2 = 1.8$	5, df :	= 1 (P =	0.17); I	<sup>2</sup> = 469	6		

Test for overall effect: Z = 3.13 (P = 0.002)

			Quality assessr	nent				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality (as	sessed with: long	est available)										
2 [56, 57]	randomised trials	not serious 1	not serious	not serious	serious <sup>2</sup>	none	3/129 (2.3%)	12/128 (9.4%)	<b>RR 0.28</b> (0.09 to 0.84)	68 fewer per 1000 (from 15 fewer to 85 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Intubation				•								
2 [56, 57]	randomised trials	serious 3	not serious	not serious	serious 2	none	6/129 (4.7%)	22/128 (17.2%)	<b>RR 0.27</b> (0.12 to 0.61)	125 fewer per 1000 (from 67 fewer to 151 fewer)	⊕⊕© LOW	CRITICAL
Nosocomial	Pneumonia			•								
1 [57]	randomised trials	serious 3	not serious	serious 4	serious 2	none	2/105 (1.9%)	10/104 (9.6%)	<b>RR 0.20</b> (0.04 to 0.88)	77 fewer per 1000 (from 12 fewer to 92 fewer)	⊕∭ VERY LOW	CRITICAL

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

- All studies unblinded but not considered ROB for outcome of mortality.
   Very small number of events leads to high fragility index and lower certainty.
   Lack of blinding may have affected outcome assessment.
   Variability in diagnostic criteria used.

# **Question #7: Should NIV be used in acute respiratory failure in palliative patients?**

# Dyspnea

		NIV Control				Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
Hui 2013	-1.5	1.7	14	-2.1	1.4	16	0.8%	0.60 [-0.52, 1.72]	<u>.</u>	
Nava 2013	-1.2	0.4	99	-0.3	0.3	101	99.2%	-0.90 [-1.00, -0.80]	<b>—</b>	
Total (95% CI)			113			117	100.0%	-0.89 [-0.99, -0.79]		
Heterogeneity: Chi <sup>2</sup> =	6.79, 0	lf = 1	P = 0	.009); I	2 = 8	35%			-100 -50 0 50 10	7
Test for overall effect	Z = 17	.81 (	P < 0.0	00001)					Favours [NIV] Favours [control	-

			Quality assessn	nent				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Dyspnea (follow	Dyspnea (follow up: 1 hour; assessed with: BORG scale, lower means less dyspnea)											
2 [58, 59]	randomised trials	serious 1	not serious <sup>2</sup>	not serious	not serious	none	113	117	-	MD <b>0.89 lower</b> (0.99 lower to 0.79 lower)	⊕⊕⊕○ MODERATE	CRITICAL
Respiratory Rate	e (follow up: 1 hour)											
1 [58]	randomised trials	serious 1	not serious	serious 3	very serious <sup>4</sup>	none	14	16	-	MD 1 higher (2.3 lower to 4.3 higher)	⊕∭ VERY LOW	IMPORTANT
Oxygenation (fo	llow up: 1 hour; asses	ssed with: Chang	je in O2 saturation)									
1 [58]	randomised trials	serious 1	not serious	serious 3	very serious 4	none	14	16	-	MD <b>2 lower</b> (5.77 lower to 1.77 higher)	⊕∭ VERY LOW	IMPORTANT
Morphine Requi	rement (follow up: 2 d	ays; assessed w	rith: milligrams)									
1 [59]	randomised trials	serious 1	not serious	serious <sup>3</sup>	not serious	none	99	101	-	MD <b>32.4 lower</b> (47.41 lower to 17.39 lower)	<del>DD</del> CC LOW	IMPORTANT

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

- Unblinded intervention.
   Results driven mostly by single study therefore insignificant inconsistency.
   Surrogate outcome with unclear clinical implications to patients.
   Wide confidence intervals do not exclude harm. Single study, small number of patients.

# Question #8: Should NIV be used in acute respiratory failure due trauma?

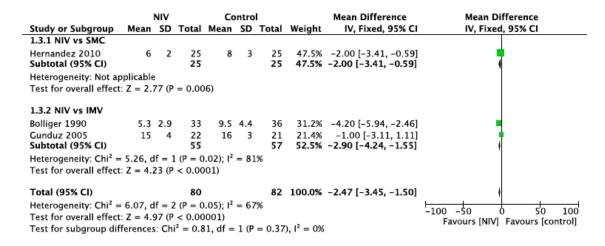
# Mortality

	NIV	,	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 NIV vs SMC							
Ferrer 2003	0	6	3	11	23.0%	0.24 [0.01, 4.08]	
Hernandez 2010	1	25	1	25	8.9%		
Subtotal (95% CI)		31		36	31.9%	0.46 [0.07, 2.94]	
Total events	1		4				
Heterogeneity: Chi <sup>2</sup> =	0.51, df	= 1 (P)	= 0.48);	$I^2 = 0\%$			
Test for overall effect:	Z = 0.83	P = 0	).41)				
1.1.2 NIV vs IMV							
Bolliger 1990	2	33	0	36	4.3%	5.44 [0.27, 109.34]	<del>-   • - • •</del>
Gunduz 2005	2	22	7	21	63.8%	0.27 [0.06, 1.17]	<del></del>
Subtotal (95% CI)		55		57	68.1%	0.60 [0.20, 1.76]	<b>*</b>
Total events	4		7				
Heterogeneity: Chi <sup>2</sup> =	3.20, df	= 1 (P	= 0.07);	$I^2 = 69$	%		
Test for overall effect:	Z = 0.94	P = 0	).35)				
Total (95% CI)		86		93	100.0%	0.55 [0.22, 1.41]	•
Total events	5		11				
Heterogeneity: Chi <sup>2</sup> =	3.64, df	= 3 (P)	= 0.30);	$I^2 = 18$	%		0.01 0.1 1 10 100
Test for overall effect:	Z = 1.24	P = 0	).21)				Favours [NIV] Favours [control]
Test for subgroup diff	erences:	Chi <sup>2</sup> =	0.06, df	= 1 (P	= 0.81),	$I^2 = 0\%$	ravours [iviv] ravours [control]

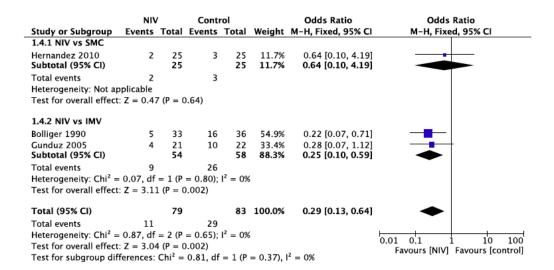
#### Intubation

	NIV		Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Ferrer 2003	1	6	5	11	25.1%	0.24 [0.02, 2.79]	
Hernandez 2010	3	25	10	25	74.9%	0.20 [0.05, 0.87]	
Total (95% CI)		31		36	100.0%	0.21 [0.06, 0.74]	•
Total events	4		15				
Heterogeneity: Chi <sup>2</sup> = Test for overall effect				I <sup>2</sup> = 0%	5		0.01 0.1 1 10 100 Favours [NIV] Favours [control]

#### ICU Length of Stay



#### Nosocomial Pneumonia



			Quality assessr	ment				№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality	Mortality											
4 [50, 60- 62]	randomised trials	not serious 1	not serious	not serious	serious <sup>2</sup>	none	5/86 (5.8%)	11/93 (11.8%)	<b>RR 0.55</b> (0.22 to 1.41)	53 fewer per 1000 (from 48 more to 92 fewer)	MODERATE	CRITICAL
Intubation												
2 [50, 62]	randomised trials	serious 3	not serious	not serious	not serious	none	4/31 (12.9%)	15/36 (41.7%)	OR 0.21 (0.06 to 0.74)	329 fewer per 1000 (from 108 fewer to 392 fewer)	MODERATE	CRITICAL
ICU Length of	of Stay (assessed w	vith: days)	<u>,                                      </u>									
4 [50, 60- 62]	randomised trials	serious 3	not serious	not serious	not serious	none	80	82	not estimable	MD <b>2.47 lower</b> (3.45 lower to 1.5 lower)	⊕⊕⊕⊜ MODERATE	IMPORTANT
Nosocomial Pneumonia												
3 [60-62]	randomised trials	serious 3	not serious	serious 4	not serious	none	11/79 (13.9%)	29/83 (34.9%)	OR 0.29 (0.13 to 0.64)	248 fewer per 1000 (from 126 fewer to 304 fewer)	LOW	CRITICAL

 $\label{eq:md-mono} \mbox{MD-mean difference, RR-relative risk, NIV-noninvasive ventilation, CI-Confidence interval}$ 

- Wide confidence intervals.
- Intervention was unblinded in included studies.
   Variability in diagnosing nosocomial pneumonia.

<sup>1.</sup> Intervention was not blinded however not as important for outcome of mortality. Also Hernandez et al was stopped early for benefit however not lowered for ROB.

# Question #9: Should NIV be used in acute respiratory failure due to pandemic viral illness

# Mortality

	NIV Co			ol lo		Risk Ratio	Risk Ratio
Study or Subgroup	<b>Events</b>	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 SARS							
Zhao 2003 Subtotal (95% CI)	2	100 <b>100</b>	9	90 <b>90</b>	14.7% <b>14.7%</b>	0.20 [0.04, 0.90] <b>0.20 [0.04, 0.90]</b>	
Total events Heterogeneity: Not applicable	2		9				
Test for overall effect: $Z = 2.1$	0 (P = 0.	04)					
1.1.2 H1N1							
Belenguer-Muncharaz 2011	0	5	0	5		Not estimable	_
Masclans 2012 Subtotal (95% CI)	31	177 <b>182</b>	76	312 <b>317</b>	85.3% <b>85.3%</b>	0.72 [0.49, 1.05] <b>0.72 [0.49, 1.05]</b>	
Total events Heterogeneity: Not applicable	31		76				
Test for overall effect: Z = 1.7	3 (P = 0.	08)					
Total (95% CI)		282		407	100.0%	0.64 [0.45, 0.92]	<b>•</b>
Total events  Heterogeneity: Chi <sup>2</sup> = 2.65, di  Test for overall effect: Z = 2.4  Test for subgroup differences	1 (P = 0.	02)			I <sup>2</sup> = 61.7	7%	0.01 0.1 1 10 100 Favours [NIV] Favours [control]

			Quality as:	sessment			Nº of p	atients	Effec	t		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality												
3 [63-65]	observational studies	not serious	serious 1	not serious	serious <sup>2</sup>	none	33/282 (11.7%) 85/407 (20.9		RR 0.64 (0.45 to 0.92) 75 fewer per 1,000 (from 17 fewer to 115 fewer)		VERY LOW	CRITICAL

CI: Confidence interval; RR: Risk ratio, NIV – noninvasive ventilation, CI – Confidence interval

- 1. High Isquared (over 60%)
  2. Low number of events

# **Question #10a: Should NIV be used in the prevention of respiratory failure post extubation?**

# Mortality

	NIV	1	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.2.1 Unselected Pat	ients						
Su 2012 <b>Subtotal (95% CI)</b>	3	202 <b>202</b>	2	204 <b>204</b>		1.51 [0.26, 8.97] 1.51 [0.26, 8.97]	
Total events	3		2				
Heterogeneity: Not ap	plicable		_				
Test for overall effect		6 (P = 0)	).65)				
1.2.2 At Risk Patient	s						
Ferrer 2006	2	79	12	83	21.6%	0.18 [0.04, 0.76]	
Ferrer 2009	3	54	4	52	22.1%	0.72 [0.17, 3.07]	
Nava 2005	3	48	9	49	29.9%	0.34 [0.10, 1.18]	<del></del>
Ornico 2013 Subtotal (95% CI)	1	20 <b>201</b>	7	18 <b>202</b>		0.13 [0.02, 0.95] 0.31 [0.15, 0.64]	
Total events	9	201	32	202	03.570	0.51 [0.15, 0.04]	•
Heterogeneity: Chi <sup>2</sup> =	-	= 3 (P	-	$I^2 = 0\%$	(		
Test for overall effect				- 0/	,		
Total (95% CI)		403		406	100.0%	0.39 [0.20, 0.76]	•
Total events	12		34				
Heterogeneity: Chi <sup>2</sup> =	5.31, df	= 4 (P	= 0.26);	$I^2 = 25$	%		
Test for overall effect	Z = 2.7	12 - 62 20/	0.01 0.1 1 10 100 Favours [NIV] Favours [control]				
Test for subgroup dif	rerences:	Cm- =	2.65, ar	= 1 (P	= 0.10),	1 = 02.3%	

### Re-Intubation

	NIV	/	Cont	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
1.1.1 Unselected Pat	ients						
Jiang 1999	13	47	7	46	9.4%	1.82 [0.80, 4.14]	<del>  • </del>
Su 2012	21	202	16	204	21.2%	1.33 [0.71, 2.47]	<del> </del>
Subtotal (95% CI)		249		250	30.7%	1.48 [0.90, 2.42]	•
Total events	34		23				
Heterogeneity: Chi2 =	0.36, df	= 1 (P	= 0.55);	$I^2 = 0\%$	5		
Test for overall effect							
1.1.2 At Risk Patient	s						
Ferrer 2006	9	79	18	83	23.4%	0.53 [0.25, 1.10]	<del></del>
Ferrer 2009	6	54	10	52	13.6%	0.58 [0.23, 1.48]	<del></del>
Kihlnani 2011	3	20	5	20	6.7%	0.60 [0.17, 2.18]	<del></del>
Nava 2005	4	48	12	49	15.8%	0.34 [0.12, 0.98]	
Ornico 2013	1	20	7	18	9.8%	0.13 [0.02, 0.95]	-
Subtotal (95% CI)		221		222	69.3%	0.44 [0.28, 0.70]	<b>◆</b>
Total events	23		52				
Heterogeneity: Chi2 =	2.43, df	= 4 (P)	= 0.66);	$I^2 = 0\%$	5		
Test for overall effect	z = 3.50	O(P = 0)	0.0005)				
Total (95% CI)		470		472	100.0%	0.76 [0.55, 1.05]	•
Total events	57		75				
Heterogeneity: Chi2 =	: 14.06, d	f = 6 (	P = 0.03	); $I^2 = 5$	7%		0.01 0.1 1 10 100
Test for overall effect	: Z = 1.67	7 (P = 0)	0.09)				0.01 0.1 1 10 100 Favours [NIV] Favours [control]
Test for subgroup dif	ferences:	Chi2 =	12.29, 0	df = 1 (	P = 0.000	$(5), I^2 = 91.9\%$	ravours [iviv] ravours [control]

			Quality assessm	ent			Nº	of patients		Effect				
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen	Relative (95% CI)	Absolute (95% CI)	Quality	Importance		
Mortality (asse	Mortality (assessed with: hospital mortality)													
5 [66-70]	randomised trials	not serious	not serious	not serious	serious 1	none	11/383 (2.9%)	27/388 (7.0%)	RR 0.41 (0.21 to 0.82)	41 fewer per 1000 (from 13 fewer to 55 fewer)	⊕⊕⊕○ MODERATE	CRITICAL		
Re-intubation														
7 [66-72]	randomised trials	serious <sup>2</sup>	not serious	not serious	serious 3	none	79/538 (14.7%)	101/542 (18.6%)	<b>RR 0.75</b> (0.49 to 1.15)	47 fewer per 1000 (from 28 more to 95 fewer)	⊕⊕© LOW	CRITICAL		

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

- Small number of events leading to high fragility index.
   Unblinded intervention in all studies.
- 3. Wide confidence intervals do not exclude harm.

### **Question #10b: Should NIV be used in the treatment of respiratory failure post extubation?**

Mortality & Re-intubation

	NIV gro	oup	SMT gr	oup		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI
1.1.1 reintubation								
Keenan 2002	28	39	29	42	34.7%	1.04 [0.78, 1.38]	2002	<u>*</u>
Esteban 2004	55	114	51	107	65.3%	1.01 [0.77, 1.33]	2004	<b>.</b>
Subtotal (95% CI)		153		149	100.0%	1.02 [0.83, 1.25]		<b>†</b>
Total events	83		80					
Heterogeneity: Chi <sup>2</sup> =	0.02, df =	1 (P = 0	0.89); I <sup>2</sup> =	0%				
Test for overall effect:	Z = 0.21 (	P = 0.8	4)					
1.1.2 ICU mortality								
Keenan 2002	6	39	10	42	38.4%	0.65 [0.26, 1.61]	2002	<del></del>
Esteban 2004	28	114	15	107	61.6%	1.75 [0.99, 3.09]	2004	<del>_</del>
Subtotal (95% CI)		153		149	100.0%	1.33 [0.83, 2.13]		•
Total events	34		25					
Heterogeneity: Chi <sup>2</sup> =	3.30, df =	1 (P = (	0.07); I <sup>2</sup> =	70%				
Test for overall effect:	Z = 1.18 (	P = 0.2	4)					
								0.01 0.1 1 10 100
								0.01
								ravours into ravours SIVII

Reference: Changyang Lin, Dr, Huapeng Yu, MD, Huizhen Fan, Dr, Zhongli Li, Dr. The efficacy of noninvasive ventilation in managing postextubation respiratory failure: A meta-analysis. Heart & Lung 43 (2014) 99e104.

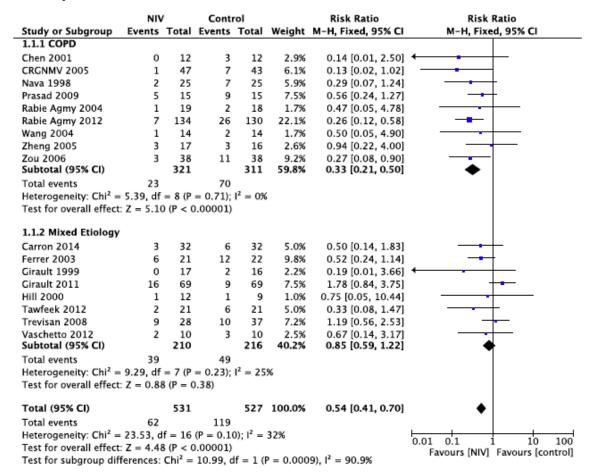
			Quality assess	ment				№ of patients		Effect		Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	supplemental oxygen +/- invasive mechanical ventilation	Relative (95% CI)	Absolute (95% CI)	Quality	
ICU Mortality	ICU Mortality											
2 [73, 74]	randomised trials	not serious	serious <sup>1</sup>	not serious	serious <sup>2</sup>	none	34/153 (22.2%)	25/149 (16.8%)	RR 1.33 (0.83 to 2.13)	<b>55 more per 1,000</b> (from 29 fewer to 190 more)	⊕⊕◯◯ LOW	CRITICAL
Re-intubation	n											
2 [73, 74]	randomised trials	serious <sup>3</sup>	not serious	not serious	serious <sup>2</sup>	none	83/153 (54.2%)	80/149 (53.7%)	RR 1.02 (0.83 to 1.25)	<b>11 more per 1,000</b> (from 91 fewer to 134 more)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; RR: Risk ratio, NIV – noninvasive ventilation, CI – Confidence interval

- High Isquared value and non-overlapping confidence intervals.
   Wide confidence intervals do not exclude harm or benefit.
   Unblinded intervention.

#### Question #11: Should NIV be used in to facilitate weaning patients from invasive mechanical ventilation?

#### Mortality



# Weaning Failure

	NIV	,	Cont	rol		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
1.2.1 COPD									
Nava 1998	3	25	8	25	6.7%	0.38 [0.11, 1.25]	<del></del>		
Rabie Agmy 2004	4	19	6	18	5.1%	0.63 [0.21, 1.88]	<del></del>		
Rabie Agmy 2012	28	134	52	130	43.9%	0.52 [0.35, 0.77]	<del></del>		
Subtotal (95% CI)		178		173	55.7%	0.51 [0.36, 0.73]	<b>◆</b>		
Total events	35		66						
Heterogeneity: Chi <sup>2</sup> =				$I^2 = 0\%$					
Test for overall effect:	Z = 3.70	P = 0	0.0002)						
1.2.2 Mixed Etiology									
Carron 2014	5	32	11	32	9.2%	0.45 [0.18, 1.16]	<del></del>		
Girault 1999	4	17	4	16	3.4%	0.94 [0.28, 3.14]	<del></del>		
Girault 2011	23	69	22	69	18.3%	1.05 [0.65, 1.69]	+		
Hill 2000	4	12	1	9	1.0%	3.00 [0.40, 22.47]	<del></del>		
Tawfeek 2012	3	21	10	21	8.3%	0.30 [0.10, 0.94]			
Vaschetto 2012	1	10	5	10	4.2%		<del></del>		
Subtotal (95% CI)		161		157	44.3%	0.74 [0.52, 1.05]	◆		
Total events	40		53						
Heterogeneity: Chi <sup>2</sup> =	9.17, df	= 5 (P	= 0.10);	$I^2 = 45$	%				
Test for overall effect:	Z = 1.68	B (P = 0	0.09)						
Total (95% CI)		339		330	100.0%	0.61 [0.48, 0.79]	<b>•</b>		
Total events	75		119						
Heterogeneity: Chi2 =	12.07, d	f = 8 (1)	P = 0.15	$     ^2 = 3$	4%		0.01 0.1 1 10 100		
Test for overall effect:	Z = 3.85	5 (P = 0	0.0001)				Favours [NIV] Favours [control]		
Test for subgroup diff-	erences:	Chi2 =	2.00, df	= 1 (P	= 0.16), 1	$l^2 = 50.0\%$	ravours [iviv] ravours [control]		

### Ventilator Associated Pneumonia

	NIV	/	Cont	rol		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
1.3.1 COPD									
Chen 2001	0	12	7	12	5.4%	0.07 [0.00, 1.05]	<del>-</del>		
CRGNMV 2005	3	47	12	43	9.1%	0.23 [0.07, 0.76]			
Nava 1998	0	25	7	25	5.4%	0.07 [0.00, 1.11]	<del></del>		
Prasad 2009	1	15	5	15	3.6%	0.20 [0.03, 1.51]	<del></del>		
Rabie Agmy 2004	0	19	4	18	3.3%	0.11 [0.01, 1.83]	<del></del>		
Rabie Agmy 2012	3	134	30	130	22.0%	0.10 [0.03, 0.31]	<del></del>		
Wang 2004	1	14	8	14	5.8%	0.13 [0.02, 0.87]	<del></del>		
Zheng 2005	1	17	4	16	3.0%	0.24 [0.03, 1.89]	<del></del>		
Zou 2006	7	38	15	38	10.8%	0.47 [0.21, 1.01]			
Subtotal (95% CI)		321		311	68.4%	0.18 [0.11, 0.30]	•		
Total events	16		92						
Heterogeneity: Chi <sup>2</sup> =	8.25, df	= 8 (P	= 0.41);	$I^2 = 3\%$	5				
Test for overall effect:	Z = 6.93	2 (P < 0	0.00001)						
1.3.2 Mixed Etiology									
Carron 2014	1	32	10	32	7.2%	0.10 [0.01, 0.74]			
Girault 1999	î	17	1	16	0.7%	0.94 [0.06, 13.82]			
Girault 2011	9	69	10		7.2%	0.90 [0.39, 2.08]			
Tawfeek 2012	1	21	8	21	5.8%	0.13 [0.02, 0.91]			
Trevisan 2008	1	28	17	37	10.6%	0.08 [0.01, 0.55]			
Subtotal (95% CI)	-	167		175	31.6%	0.30 [0.16, 0.55]	•		
Total events	13		46						
Heterogeneity: Chi <sup>2</sup> =	11.06, d	f = 4 (	P = 0.03	): $I^2 = 6$	4%				
Test for overall effect:									
Total (95% CI)		488		486	100.0%	0.22 [0.15, 0.32]	•		
Total events	29		138			0.22 (0.25) 0.52,	•		
Heterogeneity: Chi <sup>2</sup> =		f = 13			40%				
Test for overall effect:					70/0		0.01 0.1 1 10 100		
Test for subgroup diff					= 0.20\	$1^2 = 37.9\%$	Favours [NIV] Favours [control]		
. est for subgroup uni	c. enecs.	-	2.02, ui	- x (r	- 0.20/,	- 371374			

		Quali	ty assessment				Nº of p	patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NIV	routine practice	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Mortality	vlortality											
17 [75-91]	randomised trials	not serious 1	not serious	serious <sup>2</sup>	not serious	none	62/531 (11.7%)	119/527 (22.6%)	<b>RR 0.54</b> (0.41 to 0.70)	104 fewer per 1000 (from 68 fewer to 133 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Weaning Failure		•										
9 [76, 79-82, 84-86, 88]	randomised trials	serious <sup>3</sup>	not serious	serious <sup>4</sup>	not serious	none	75/339 (22.1%)	119/330 (36.1%)	RR 0.61 (0.48 to 0.79)	141 fewer per 1000 (from 76 fewer to 188 fewer)	⊕⊕◯◯ LOW	CRITICAL
Ventilator Associated Pneu	/entilator Associated Pneumonia											
14 [75-77, 79, 80, 82-87, 89-91]	randomised trials	serious <sup>3</sup>	not serious	serious <sup>5</sup>	not serious	none	29/488 (5.9%)	138/486 (28.4%)	<b>RR 0.22</b> (0.15 to 0.32)	221 fewer per 1000 (from 193 fewer to 241 fewer)	⊕⊕◯◯ LOW	CRITICAL

MD – mean difference, RR – relative risk, NIV – noninvasive ventilation, CI – Confidence interval

- Despite a lack of blinding this was not judged to be as important for objective outcome of mortality.
   Protocols for initiation of NIV varied including when to extubate.
   Lack of blinding of the intervention affected overall ROB.
   Weaning failure was heterogeniously defined across studies. Protocols for initiation of NIV also varied.
   Different definitions of VAP employed. Also varying NIV protocols.

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