

## Supplement: Evidence Profiles

### ERS Guidelines: High flow nasal cannula in acute respiratory failure

#### Authors

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### **Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure**

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	COT	Relative (95% CI)	Absolute (95% CI)		
Mortality (90 day)											
4 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	CRITICAL
Mortality (ICU, hospital, or 28 day)											
6 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	CRITICAL
Intubation											
11 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	CRITICAL
Escalation to NIV											
6 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	CRITICAL
Hospital length of stay											
5 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	none	683	660	-	MD 0.72 days lower (1.54 lower to 0.1 higher)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	IMPORTANT
ICU length of stay											
2 RCTs	not serious	not serious	not serious	serious <sup>b</sup>	none	494	482	-	MD 1.97 days higher (1.02 higher to 2.93 higher)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	IMPORTANT
Patient comfort											
6 RCTs	not serious	not serious	not serious	not serious	none	303	293	-	SMD 0.54 lower (0.86 lower to 0.23 lower)	<div><div>⊕⊕⊕⊕</div><div>HIGH</div></div>	IMPORTANT
Dyspnea											

### Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

6 RCTs	not serious	not serious	not serious <sup>c</sup>	serious <sup>a</sup>	none	173	189	-	SMD <b>0.32 lower</b> (0.66 lower to 0.03 higher)	⊕⊕⊕○ MODERATE	IMPORTANT
<b>PaO<sub>2</sub>/FiO<sub>2</sub></b>											
4 RCTs	not serious	serious <sup>d</sup>	not serious	serious <sup>a</sup>	none	526	514	-	MD <b>25.01 higher</b> (14.21 lower to 64.24 higher)	⊕⊕○○ LOW	IMPORTANT
<b>PaO<sub>2</sub></b>											
6 RCTs	not serious	not serious	not serious	not serious	none	202	193	-	MD <b>16.72 higher</b> (5.74 higher to 27.71 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>PCO<sub>2</sub></b>											
6 RCTs	not serious	not serious	not serious	not serious	none	202	193	-	MD <b>0.01 higher</b> (1.17 lower to 1.2 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>Respiratory rate</b>											
10 RCTs	not serious	not serious	not serious	not serious	none	713	716	-	MD <b>2.25 lower</b> (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.

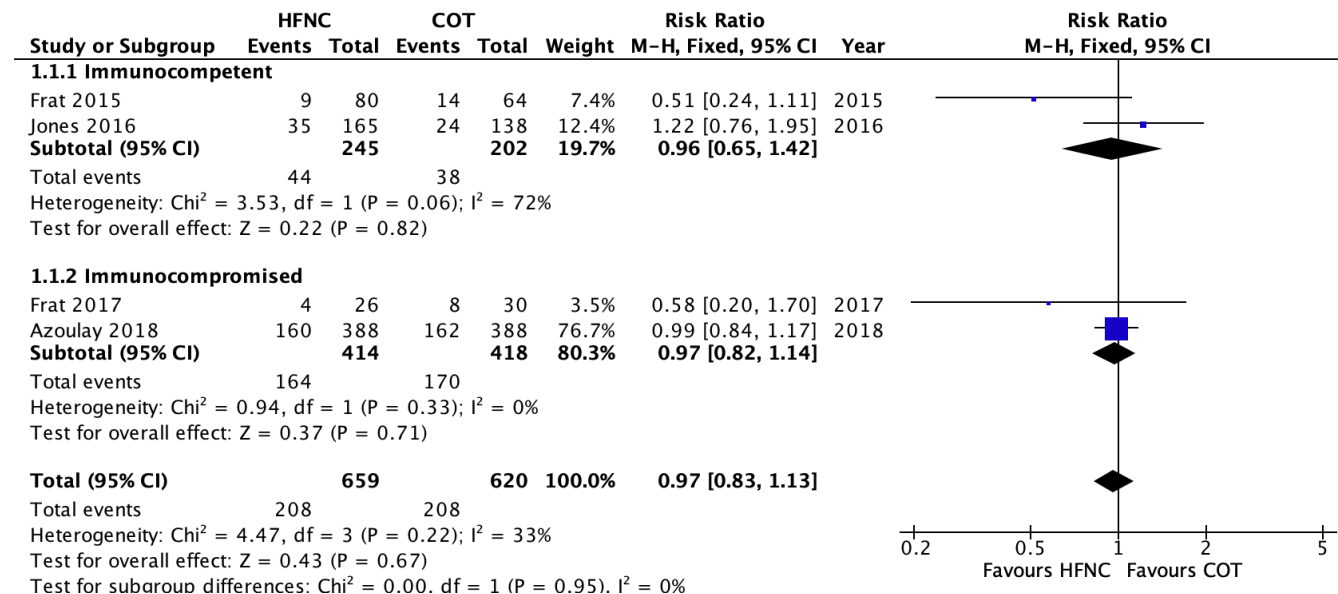
b. Though Azoulay 2018 demonstrates statistically significant increase in ICU length of stay, when estimated means and SD are used, they are not statistically significant when median (IQR) are compared.

c. Most studies used the validated Borg dyspnea scale.

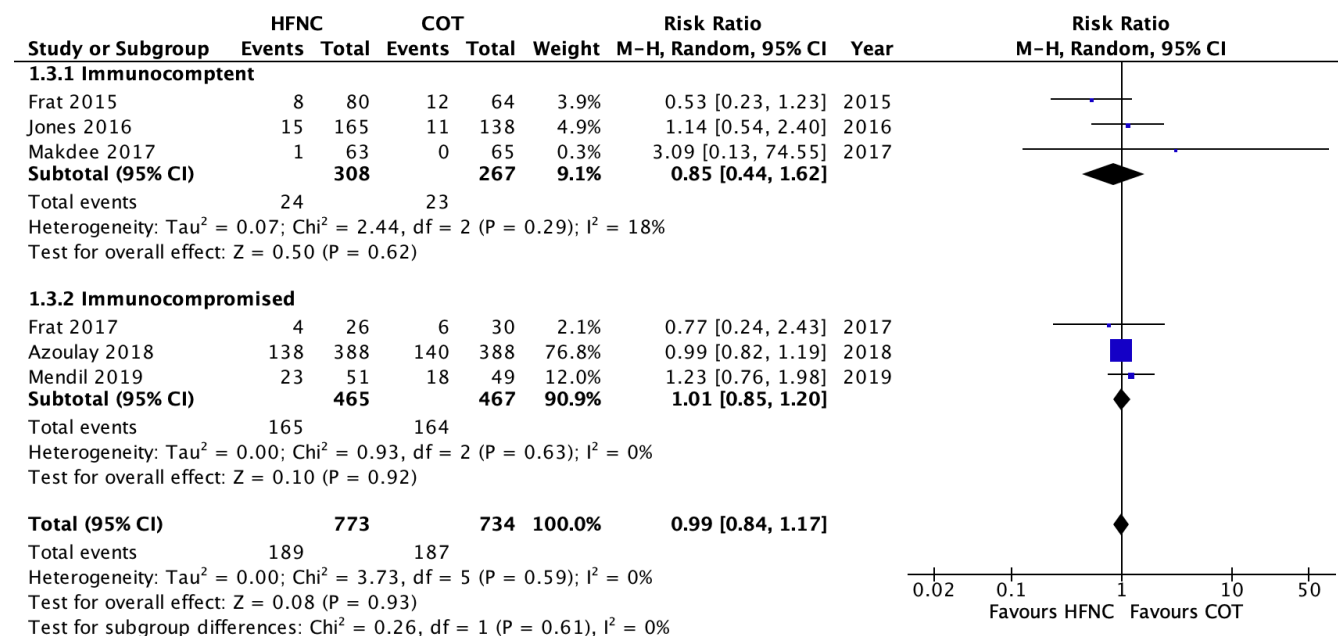
d. Very significant heterogeneity between the Frat 2015 RCT and the other trials (I<sup>2</sup>= 93%) of likely clinical significance.

## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 1. Mortality (90 day)

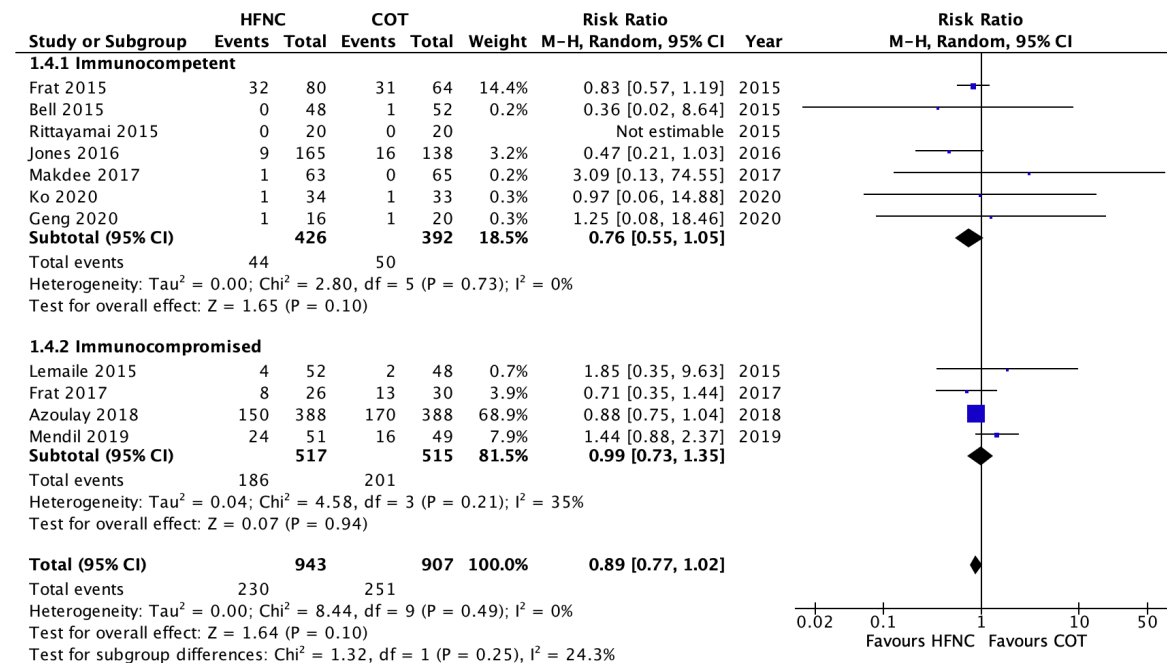


### 2. Mortality (early - ICU, hospital, or 28 day)

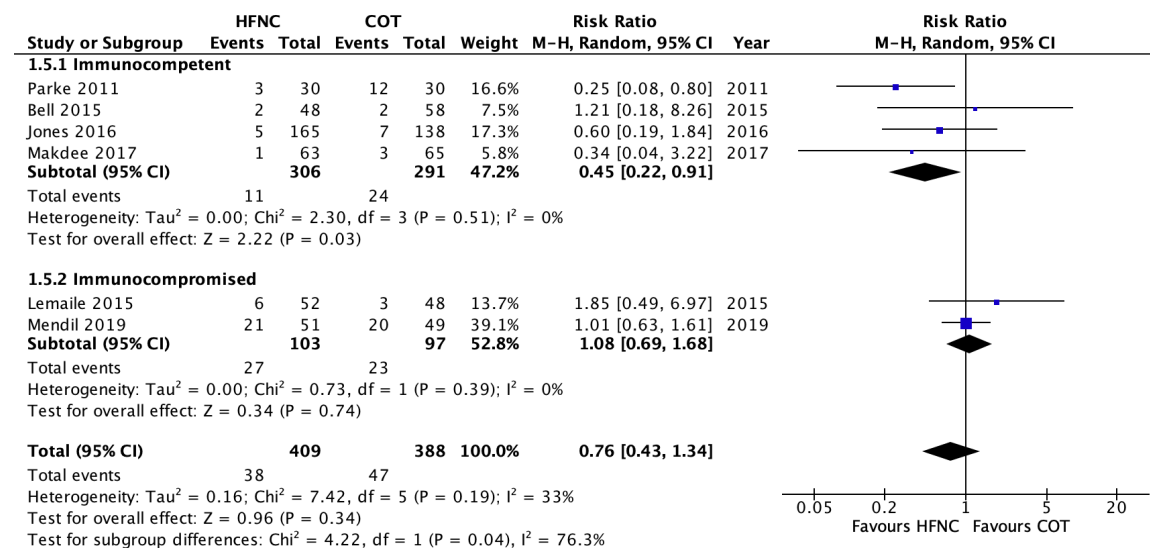


## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 3. Intubation

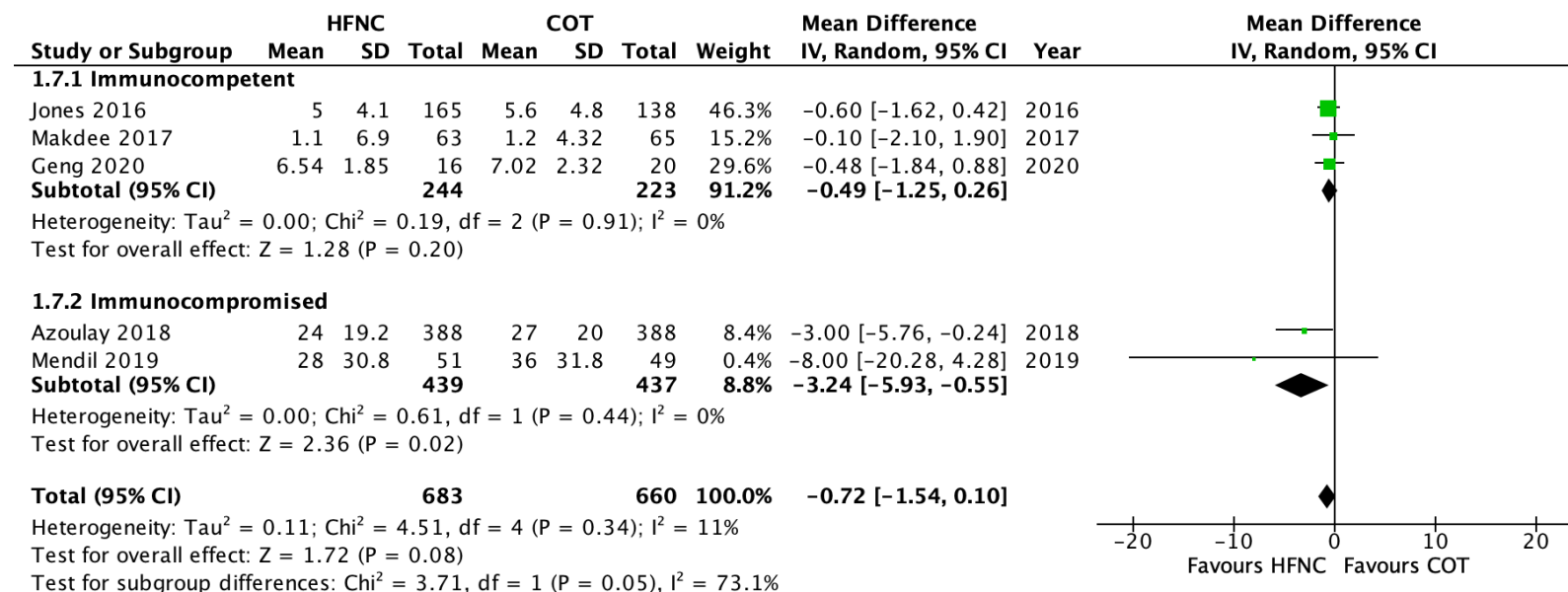


### 4. Escalation to NIV

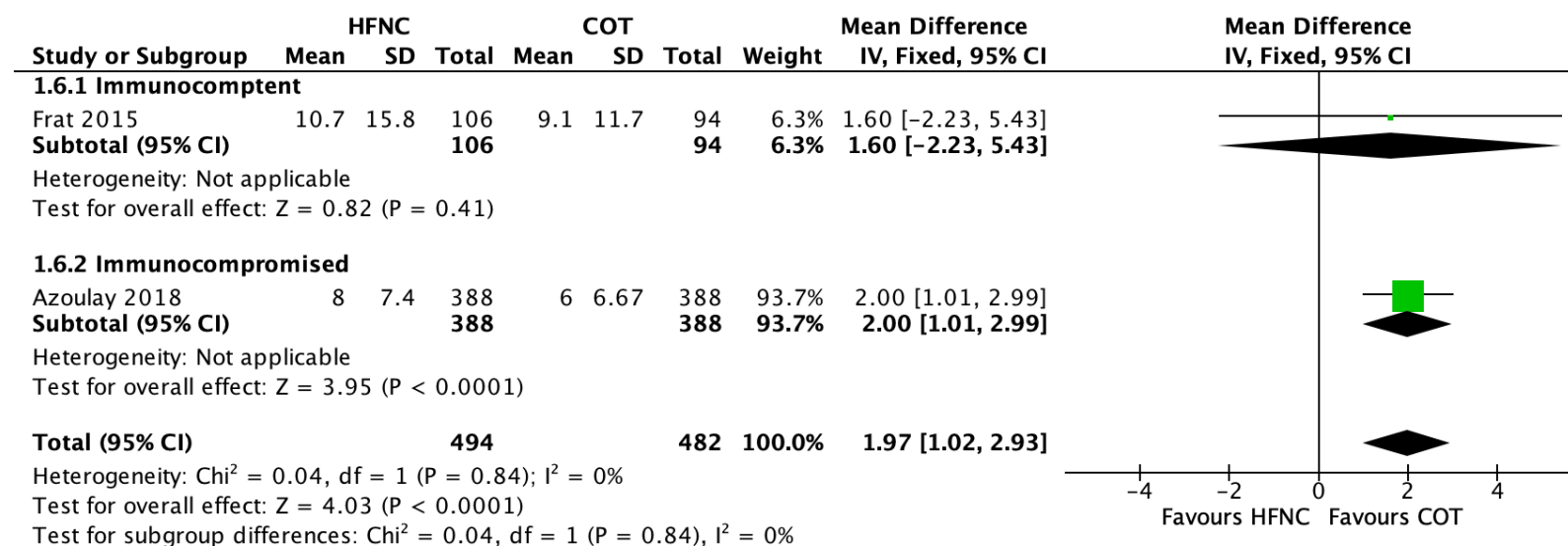


## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 5. Hospital length of stay

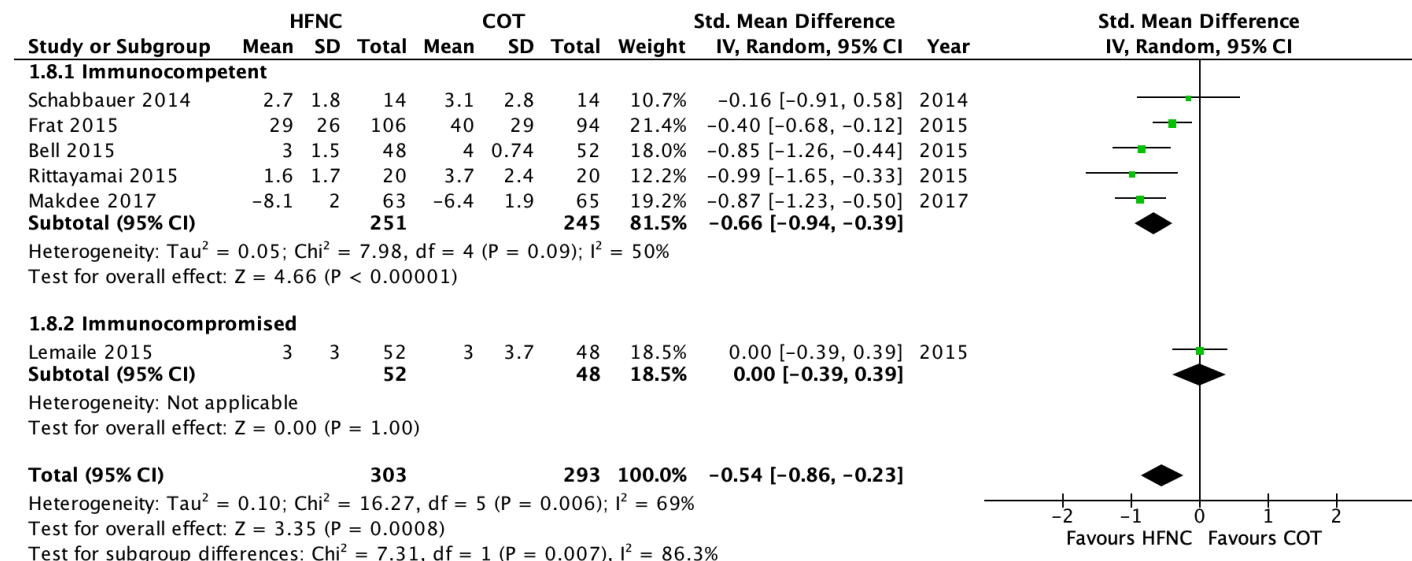


### 6. ICU length of stay

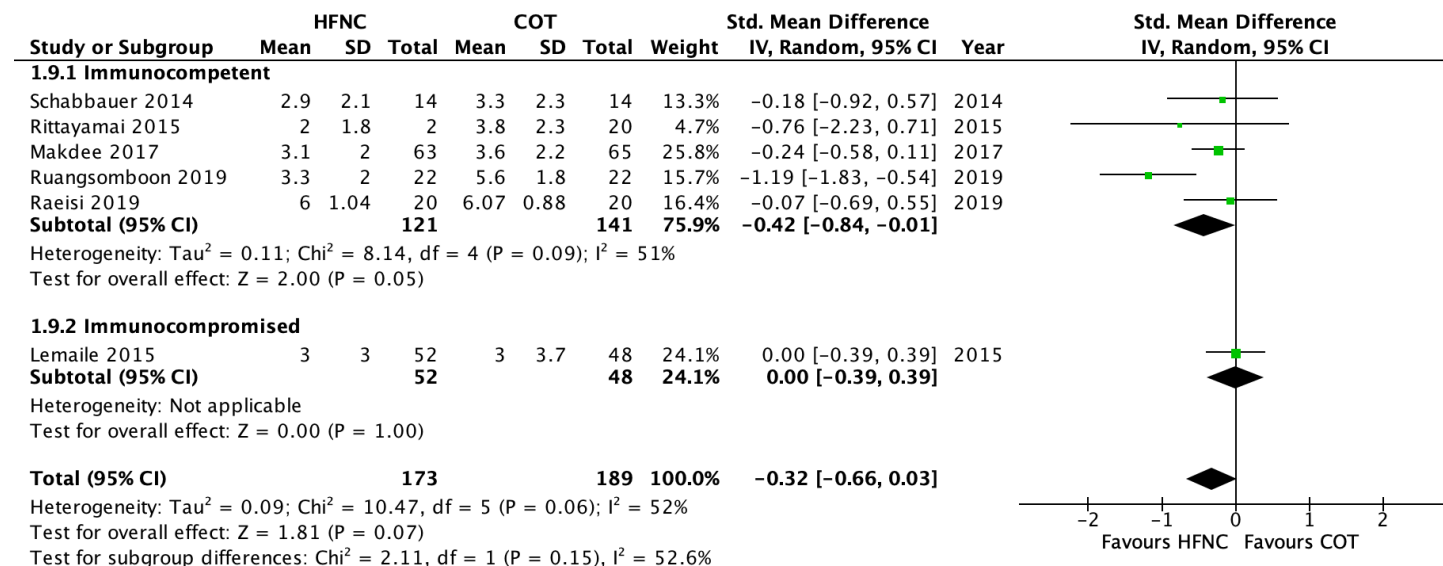


## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 7. Patient comfort (various rating systems)

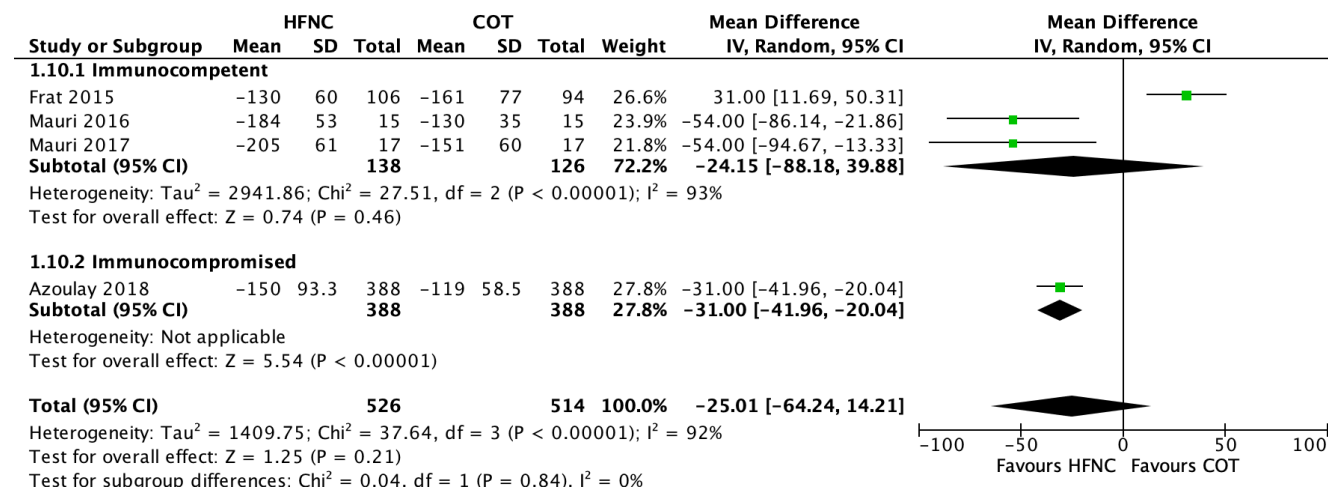


### 8. Dyspnea (various measures, Borg Dyspnea Scale or visual analog scale)

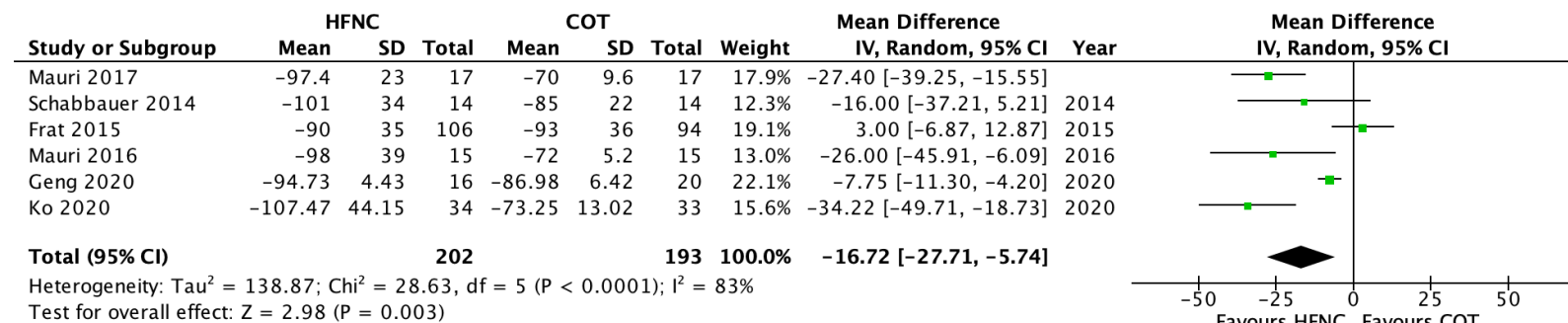


## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 9. PaO<sub>2</sub>:FiO<sub>2</sub>



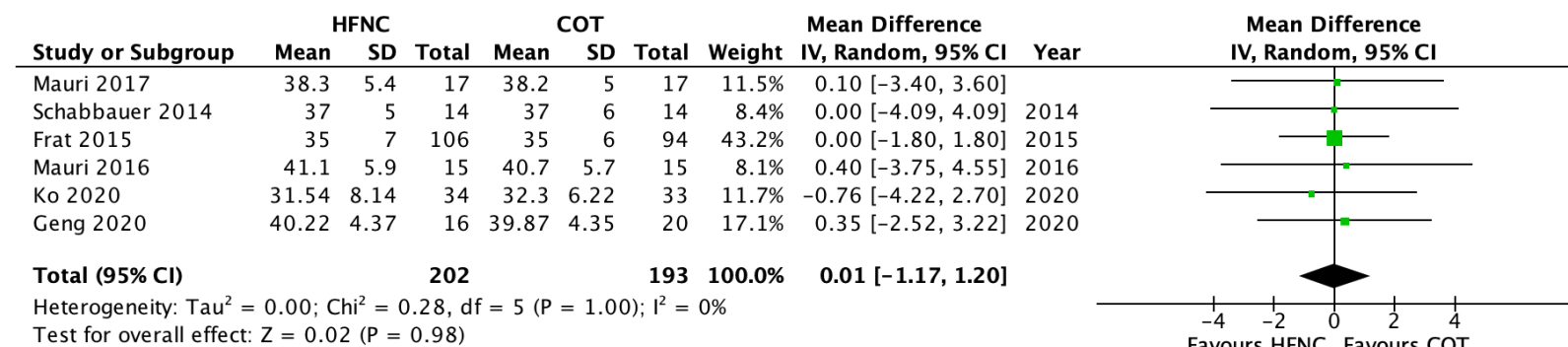
### 10. PaO<sub>2</sub>



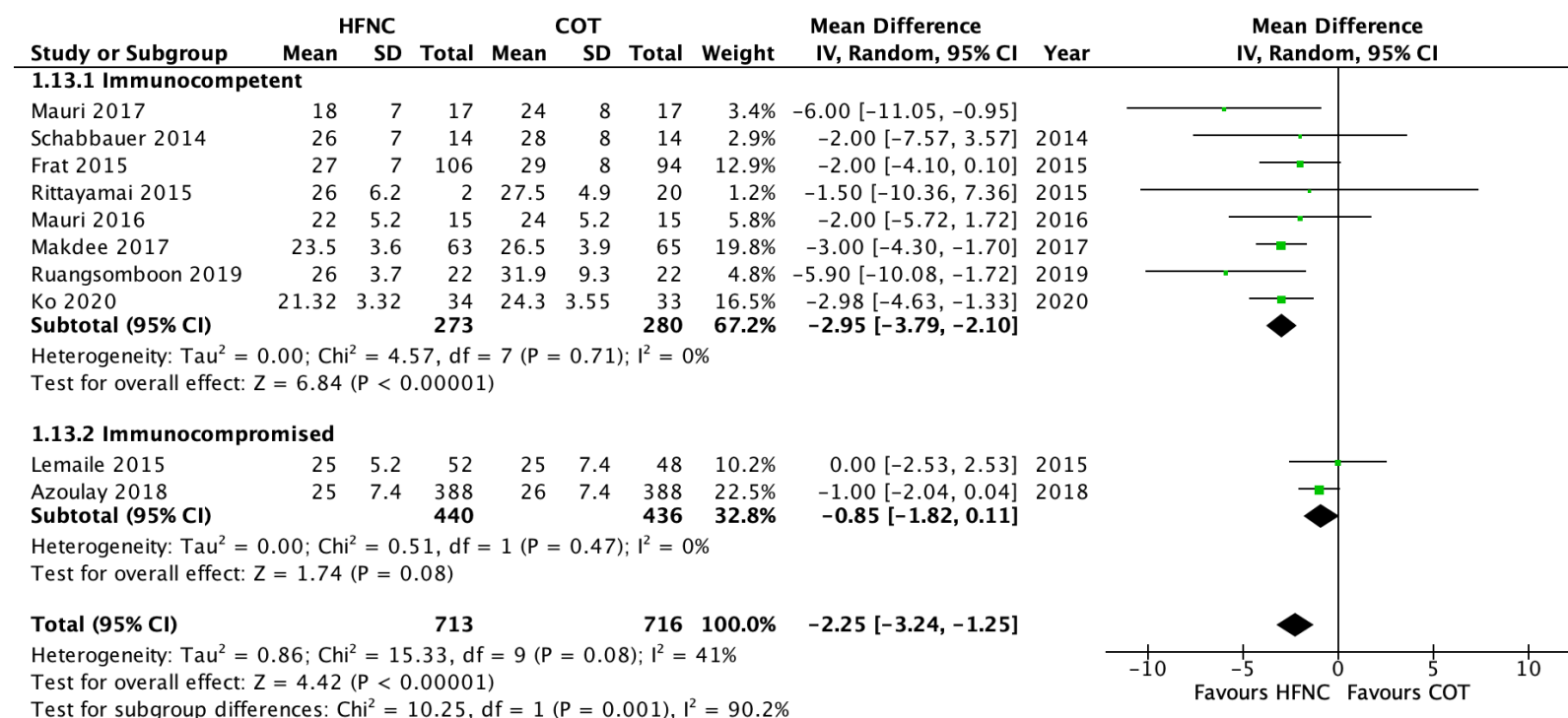


## Recommendation 1: High flow nasal cannula (HFNC) vs conventional oxygen therapy (COT) in hypoxemic respiratory failure

### 11. PCO<sub>2</sub> (most commonly PaCO<sub>2</sub>)



### 12. Respiratory rate



## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	NIV	Relative (95% CI)	Absolute (95% CI)		
Mortality (90 day)											
1 RCT	not serious	not serious	serious <sup>a</sup>	serious <sup>b</sup>	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)	<div><div>⊕⊕○○</div><div>LOW</div></div>	CRITICAL
Mortality (ICU, hospital or 28 day)											
3 RCTs	not serious	serious <sup>c</sup>	serious <sup>a</sup>	serious <sup>d</sup>	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)	<div><div>⊕○○○</div><div>VERY LOW</div></div>	CRITICAL
Intubation											
5 RCTs	not serious	not serious	serious <sup>a</sup>	serious <sup>d</sup>	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)	<div><div>⊕⊕○○</div><div>LOW</div></div>	CRITICAL
Hospital length of stay											
1 RCTs	not serious	not serious	serious <sup>a</sup>	very serious <sup>e</sup>	none	104	100	-	MD 0.8 days higher (0.59 lower to 2.19 higher)	<div><div>⊕○○○</div><div>VERY LOW</div></div>	IMPORTANT
ICU length of stay											
2 RCTs	not serious	not serious	serious <sup>a</sup>	serious <sup>d</sup>	none	154	157	-	MD 0.55 days lower (2 lower to 0.89 higher)	<div><div>⊕⊕○○</div><div>LOW</div></div>	IMPORTANT
Patient comfort											
4 RCTs	not serious	not serious	serious <sup>a</sup>	not serious	none	207	208	-	SMD 0.23 lower (0.55 lower to 0.09 higher )	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	IMPORTANT
Dyspnea											
4 RCTs	not serious	very serious <sup>f</sup>	serious <sup>a</sup>	serious <sup>g</sup>	none	193	194	-	SMD 0.19 higher (0.01 lower to 0.40 higher)	<div><div>⊕○○○</div><div>VERY LOW</div></div>	IMPORTANT

## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

PaO <sub>2</sub> /FiO <sub>2</sub>											
3 RCTs	not serious	not serious	serious <sup>a</sup>	not serious	none	215	219	-	MD 43.26 lower (29.48 lower to 57.04 lower)	⊕⊕⊕○ MODERATE	IMPORTANT
PaO <sub>2</sub>											
4 RCTs	not serious	not serious	serious <sup>a</sup>	not serious	none	229	233	-	MD 19.98 mmHg lower (11.97 lower to 28 lower)	⊕⊕⊕○ MODERATE	IMPORTANT
PCO <sub>2</sub>											
4 RCTs	not serious	serious <sup>c</sup>	serious <sup>a</sup>	not serious	none	209	211	-	MD 0.45 mmHg lower (1.94 lower to 1.05 higher)	⊕⊕○○ LOW	IMPORTANT
Respiratory rate											
5 RCTs	not serious	serious <sup>c</sup>	serious <sup>a</sup>	not serious	none	302	309	-	MD 0.83 breaths per minute higher (1.04 lower to 2.7 higher)	⊕⊕○○ LOW	IMPORTANT

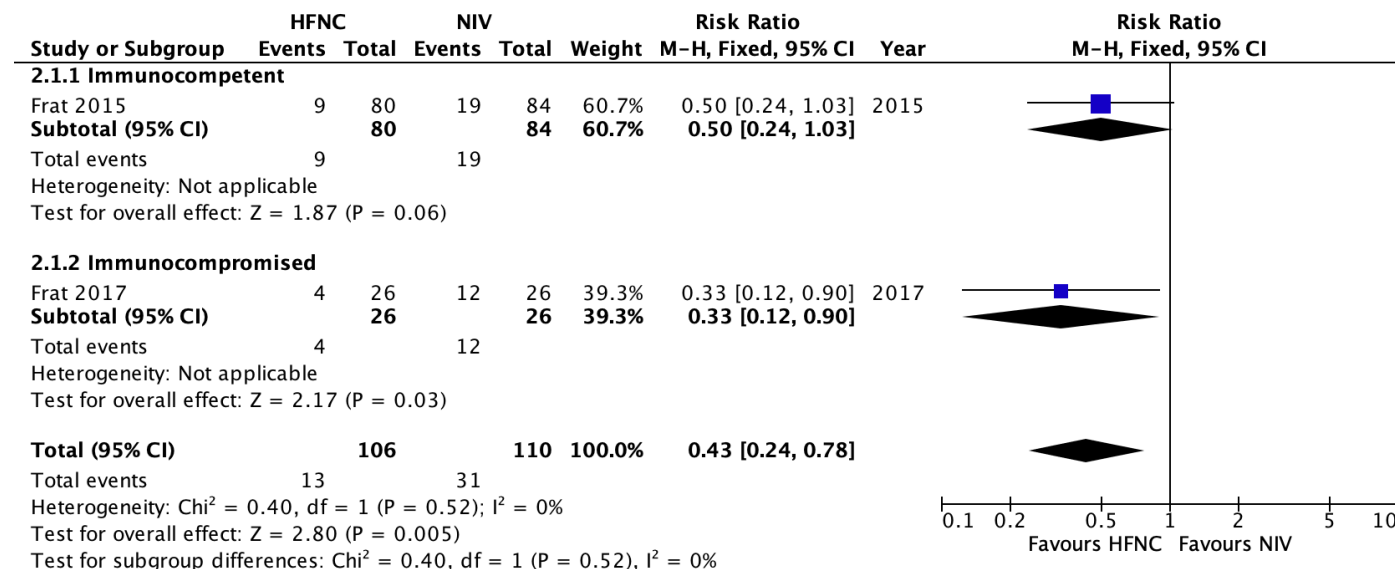
CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

### Explanations

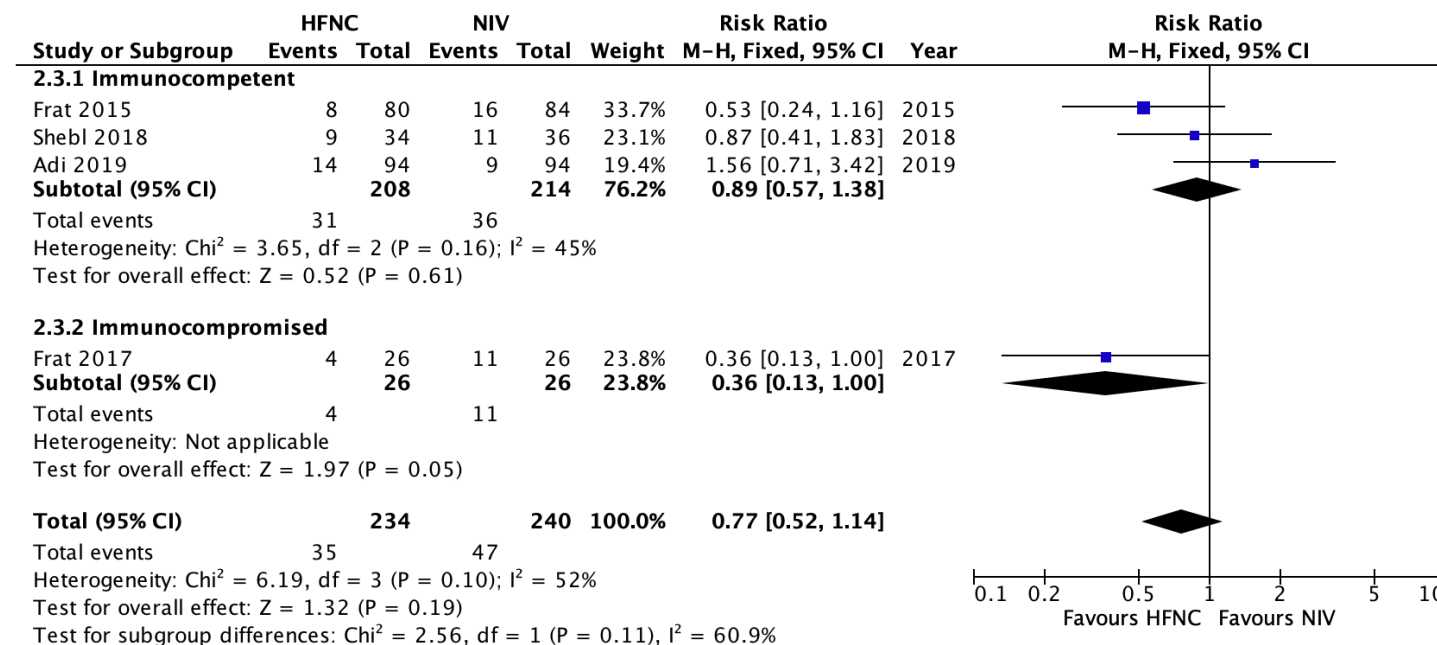
- Concerns were raised about the short duration of NIV in the study with the largest effects (Frat et al); as well NIV interfaces used (face mask vs. helmet) and use of humidification for secretion clearance during NIV varied between studies. As a result, we rated down for indirectness of the comparator.
- 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.
- Substantial heterogeneity ( $I^2 > 40\%$ ) not easily explained by study characteristics.
- Wide 95% confidence intervals which do not exclude clinically meaningful benefit or harm.
- Very wide 95% confidence intervals which do not exclude clinically meaningful benefit or harm.
- Very substantial heterogeneity ( $I^2 > 80\%$ ) with two studies demonstrating opposite effects.
- We chose not to rate down for imprecision as this was accounted for in considering the very significant inconsistency between the included studies.

## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

### 1. Mortality (90 day)

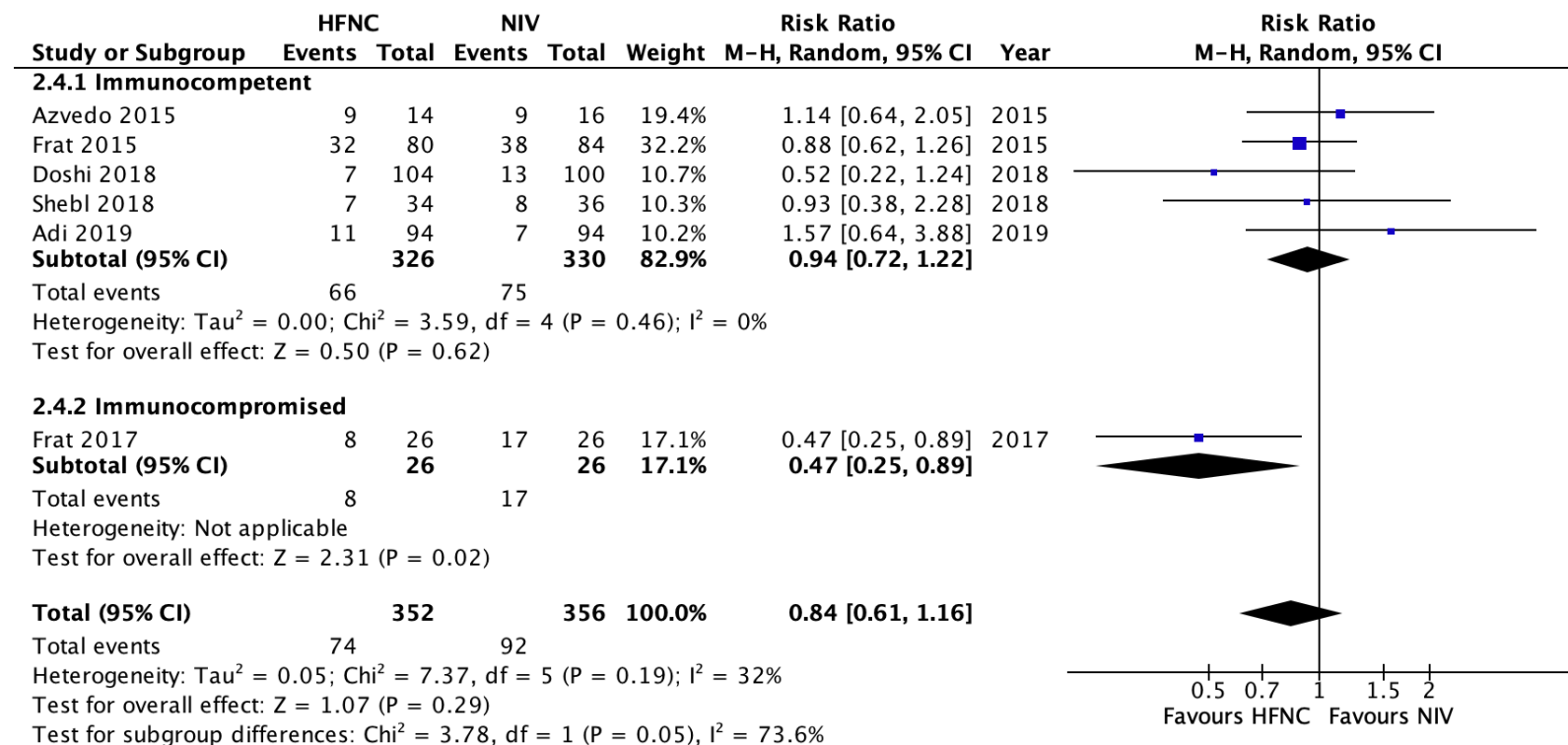


### 2. Mortality (early - ICU, hospital, or 28 day)

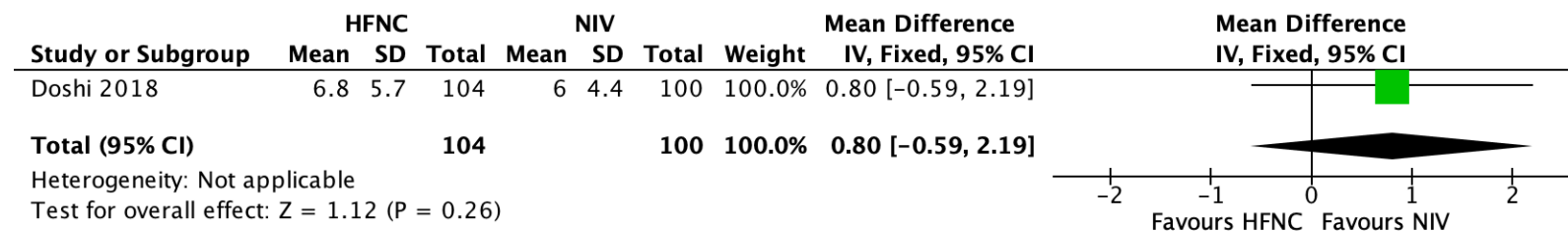


## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

### 3. Intubation

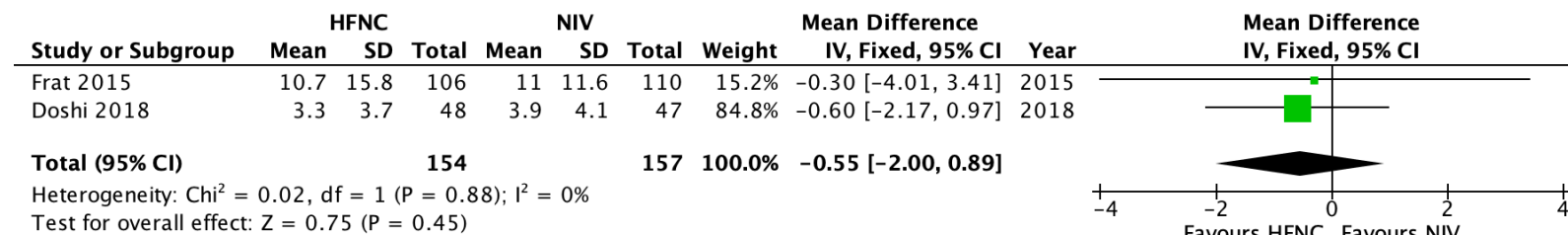


### 4. Hospital length of stay

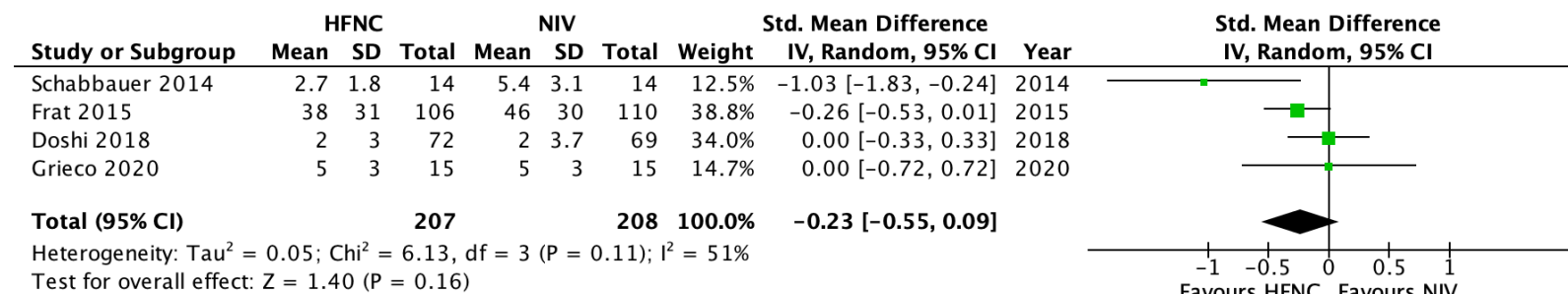


## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

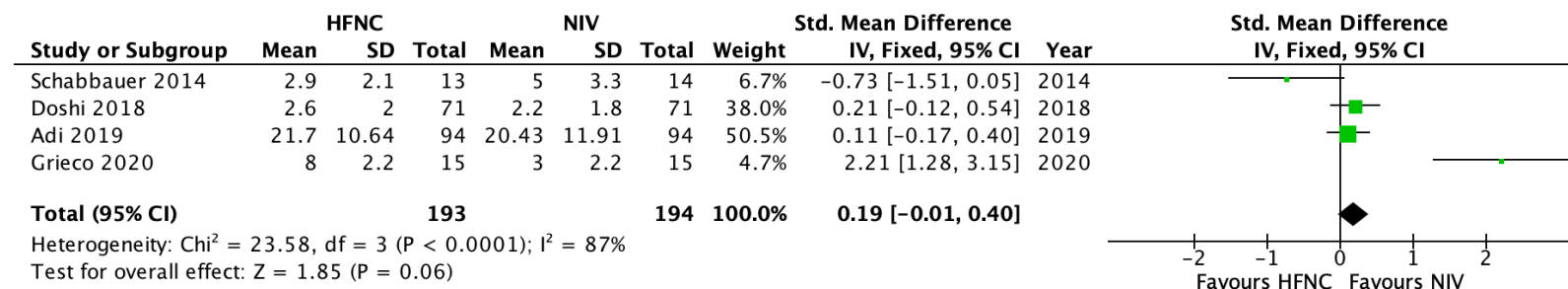
### 5. ICU length of stay



### 6. Patient comfort (various rating systems)

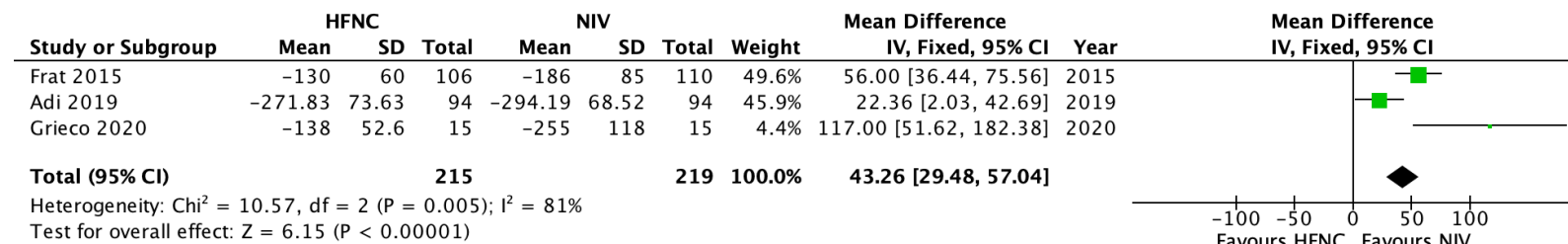


### 7. Dyspnea (various measures, Borg Dyspnea Scale or visual analog scale)

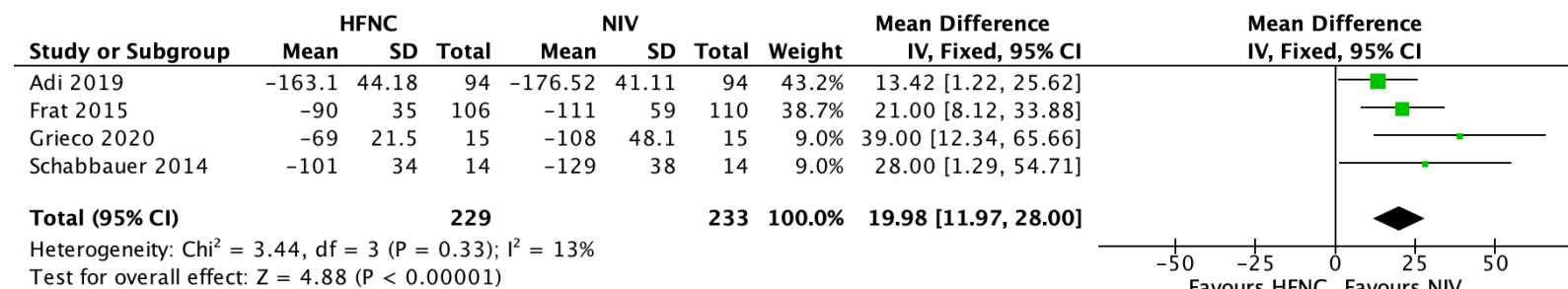


## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

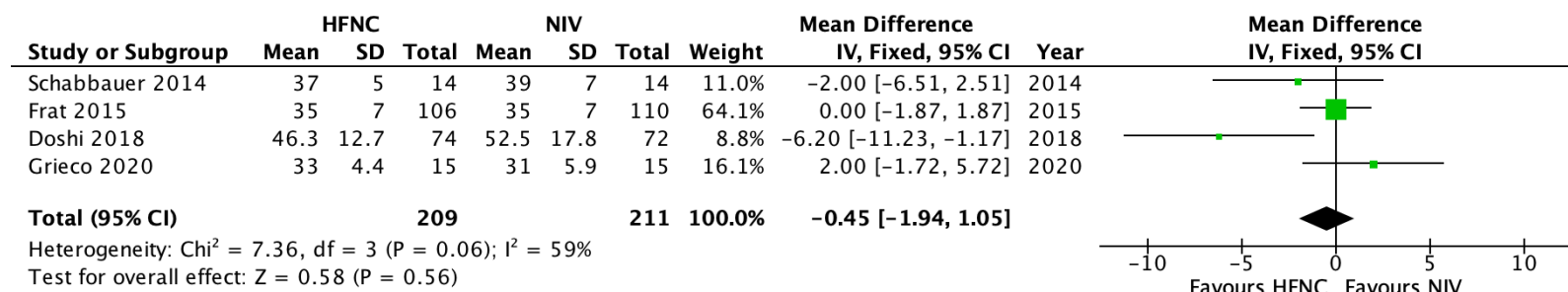
### 8. PaO<sub>2</sub>:FiO<sub>2</sub>



### 9. PaO<sub>2</sub>

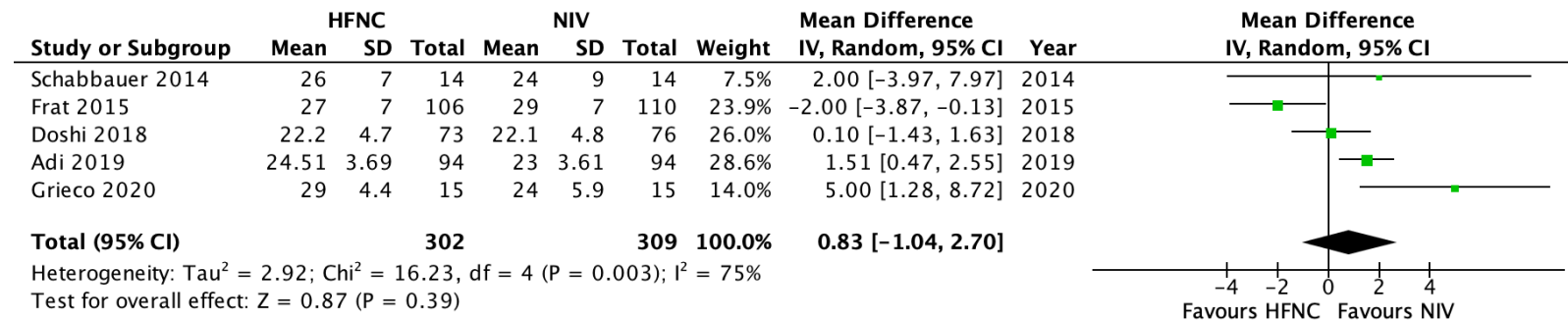


### 10. PCO<sub>2</sub> (most commonly PaCO<sub>2</sub>)



## Recommendation 2: High flow nasal cannula (HFNC) vs non-invasive ventilation (NIV) in hypoxemic respiratory failure

### 11. Respiratory rate





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

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	COT	Relative (95% CI)	Absolute (95% CI)		
Mortality - Post-operative											
7 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕⊕○</div><div>MODERATE</div></div>	CRITICAL
Re-intubation - Post-operative											
8 RCTs	serious <sup>b</sup>	not serious	not serious	serious <sup>a</sup>	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)	<div><div>⊕⊕○○</div><div>LOW</div></div>	CRITICAL
Escalate to NIV - Post-op											
7 RCTs	serious <sup>b</sup>	serious <sup>c</sup>	not serious	serious <sup>a</sup>	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)	<div><div>⊕○○○</div><div>VERY LOW</div></div>	CRITICAL
ICU Length of Stay - 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)	<div><div>⊕⊕⊕⊕</div><div>HIGH</div></div>	CRITICAL
Hospital Length of Stay - 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)	<div><div>⊕⊕⊕⊕</div><div>HIGH</div></div>	IMPORTANT
Comfort - Post-op											
6 RCTs	not serious	very serious <sup>d</sup>	not serious	not serious <sup>e</sup>	none	413	415	-	SMD 0.54 lower (1.12 lower to 0.05 higher)	<div><div>⊕⊕○○</div><div>LOW</div></div>	IMPORTANT
PaO2 - Post-op											
2 RCTs	not serious	not serious	not serious	not serious	none	158	162	-	MD 6.2 lower (8.82 lower to 3.58 lower)	<div><div>⊕⊕⊕⊕</div><div>HIGH</div></div>	IMPORTANT
PCO2 - Post-Op											

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

5 RCTs	not serious	not serious <sup>f</sup>	not serious	not serious	none	284	285	-	MD <b>1.9 lower</b> (4.18 lower to 0.38 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>PaO<sub>2</sub>:FiO<sub>2</sub> - Post-op</b>											
4 RCTs	not serious	not serious <sup>f</sup>	not serious	not serious	none	159	142	-	MD <b>34.89 lower</b> (84.96 lower to 15.19 higher)	⊕⊕⊕○ MODERATE	IMPORTANT
<b>Respiratory Rate - Post-op</b>											
3 RCTs	not serious	serious <sup>e</sup>	not serious	not serious	none	178	167	-	MD <b>0.14 lower</b> (0.83 lower to 0.54 higher)	⊕⊕⊕○ MODERATE	IMPORTANT

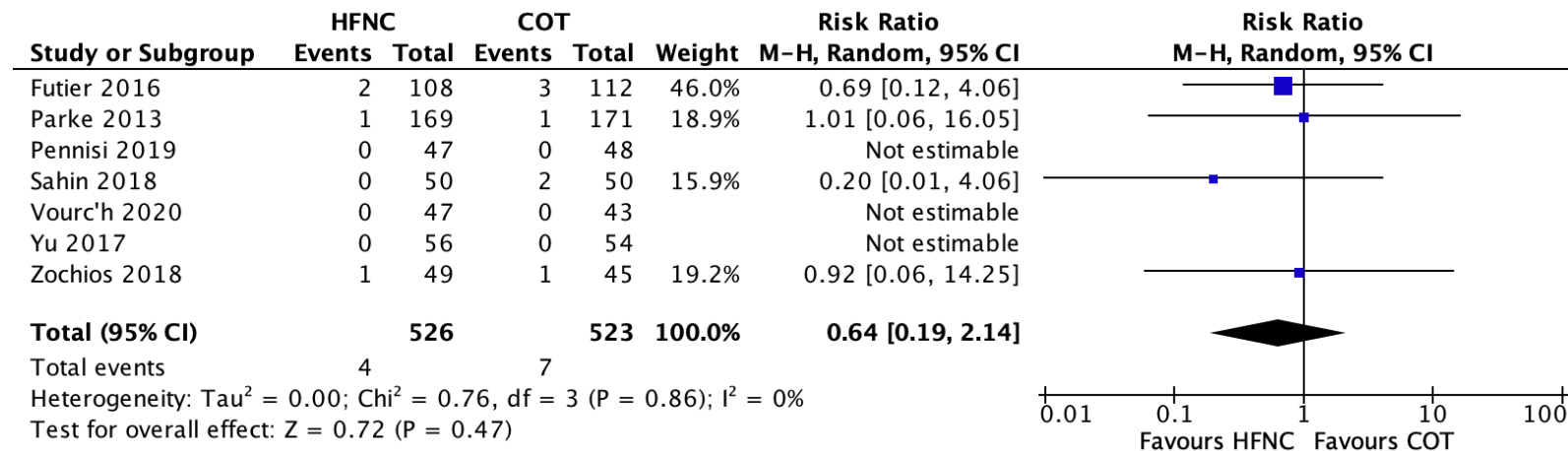
**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

#### **Explanations**

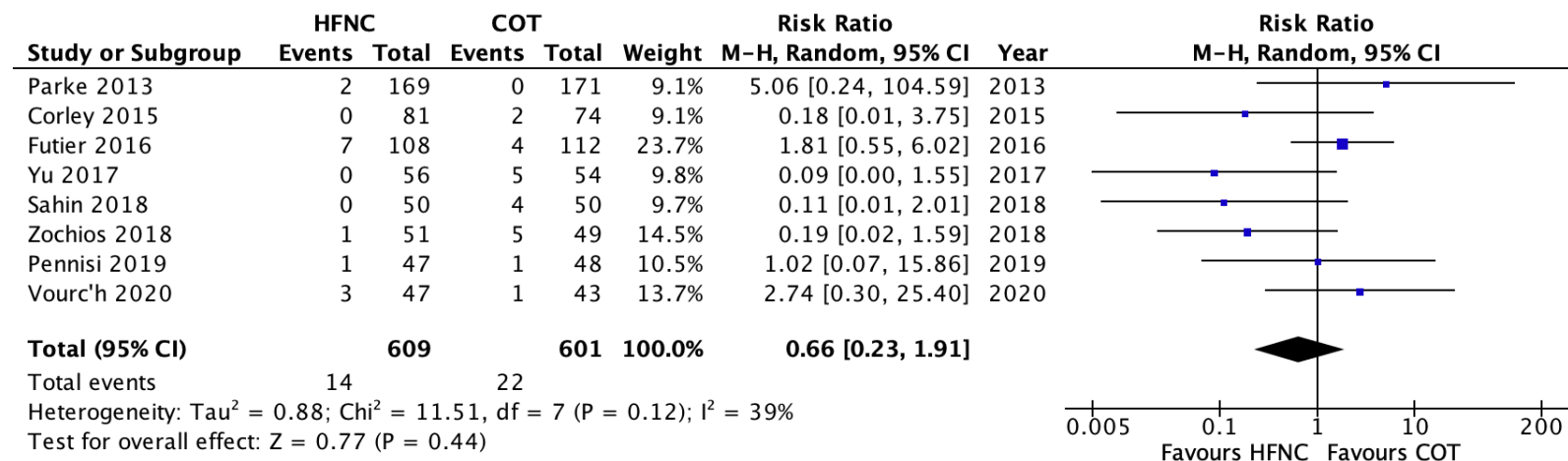
- Wide 95% confidence intervals which do not exclude clinically important benefit or harm.
- Lack of blinding may have resulted in bias from co-intervention as many trials did not have protocols for escalation of respiratory support.
- Significant heterogeneity ( $I^2 > 50\%$ ) with point estimates on both sides of the line of no effect and limited overlap of 95% confidence intervals.
- Very significant heterogeneity ( $I^2 > 90\%$ ) with point estimates on both sides of the line of no effect and limited overlap of 95% confidence intervals.
- We did not rate down for imprecision as this is accounted for in rating down twice for inconsistency.
- Although there is significant heterogeneity ( $I^2 > 90\%$ ) the discrepancies in absolute effect sizes are of questionable significance

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

### 1. Mortality

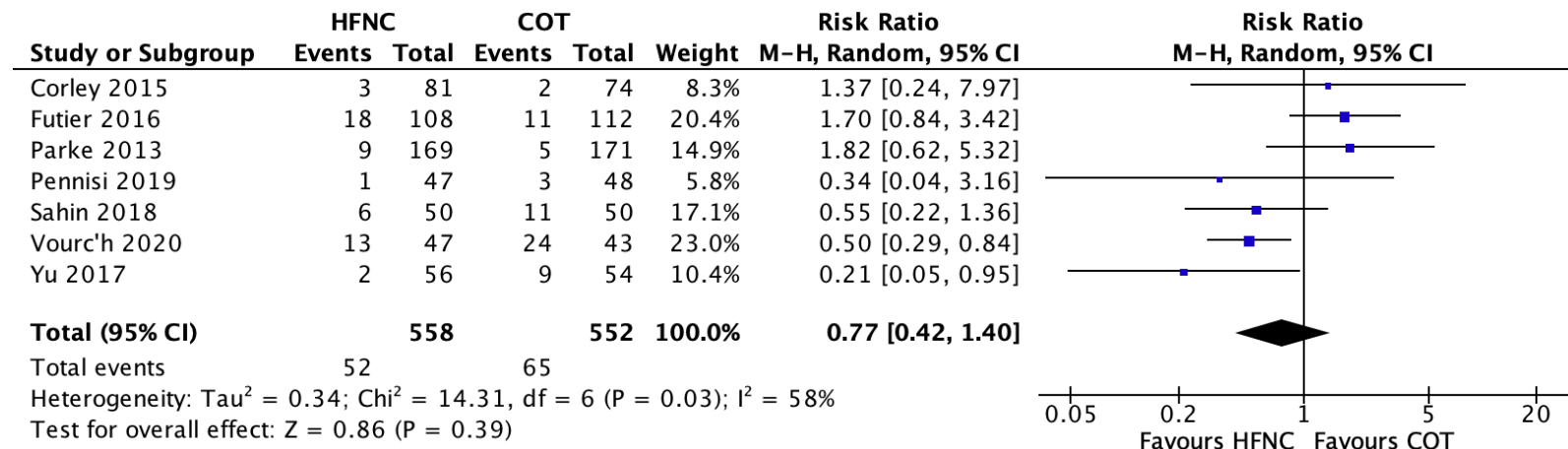


### 2. Re-intubation

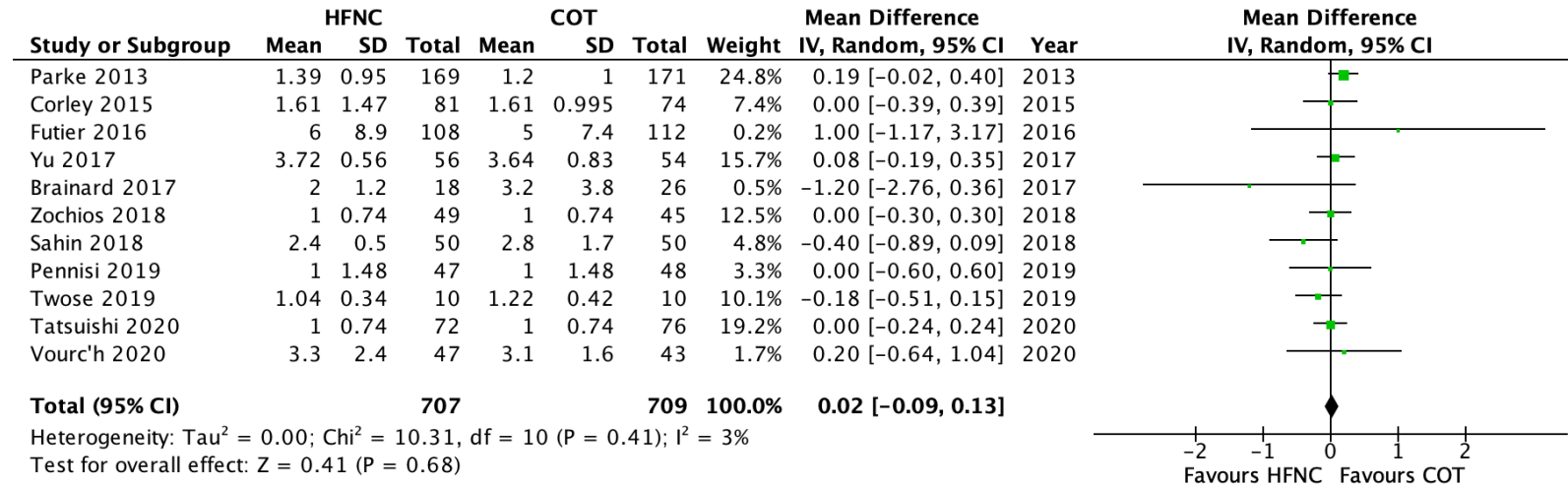


#### Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

### 3. Escalation to NIV

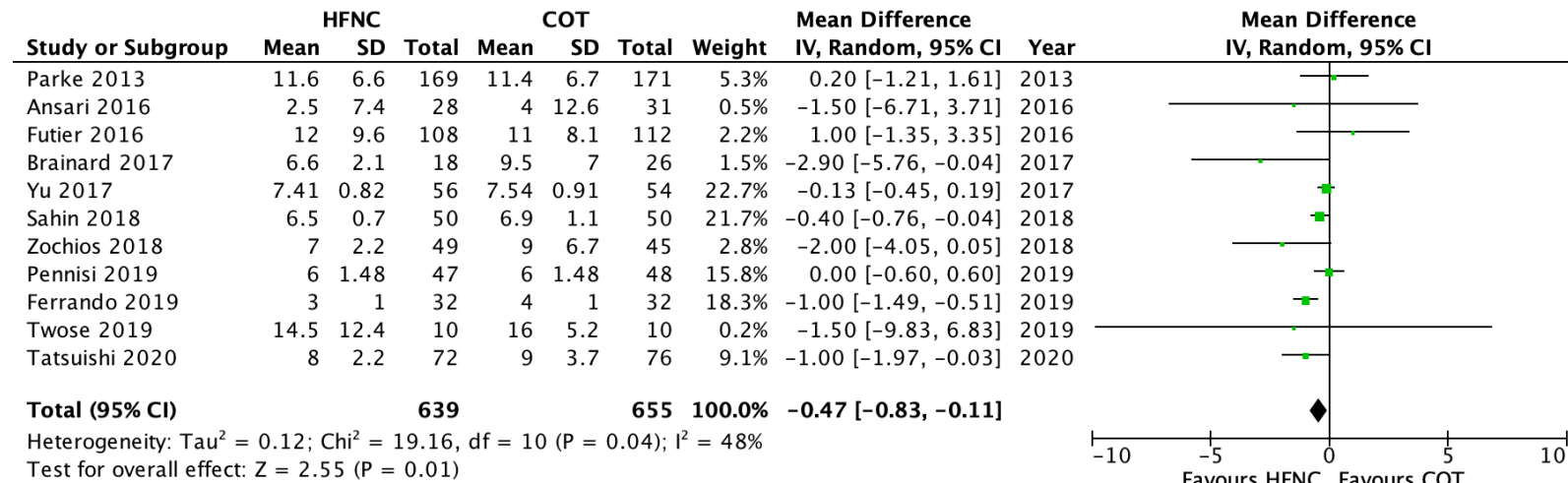


### 4. ICU length of stay

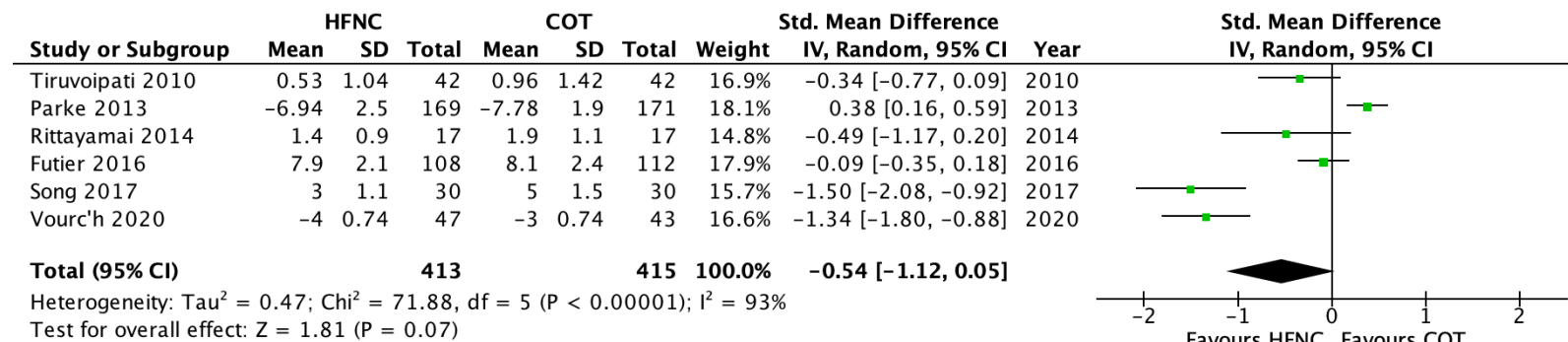


#### Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

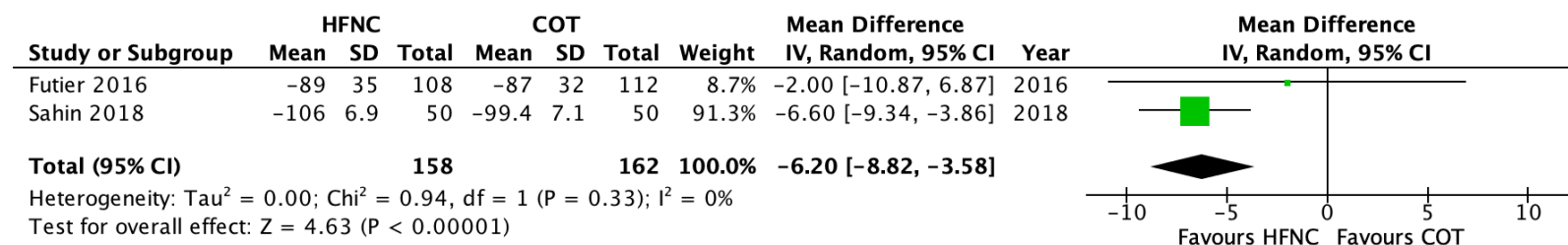
##### 5. Hospital length of stay



##### 6. Comfort

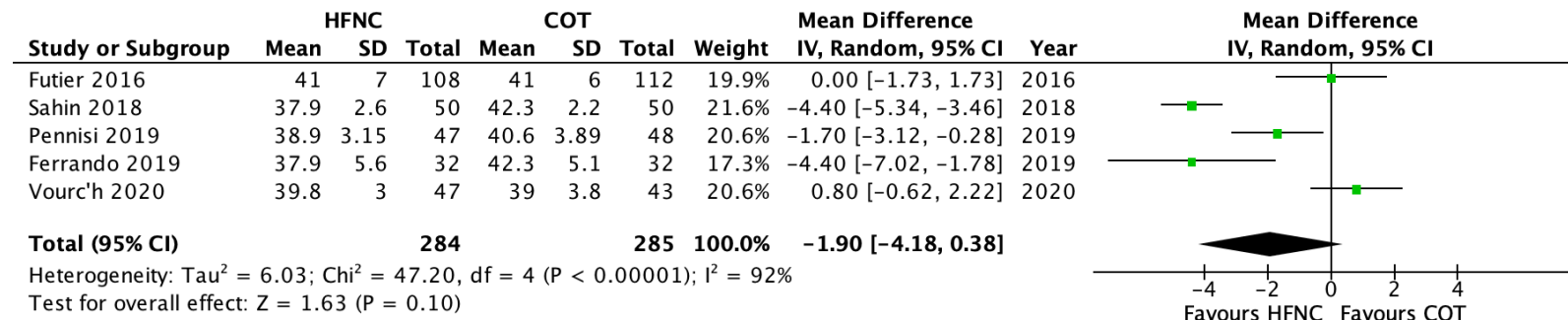


##### 7. PaO2

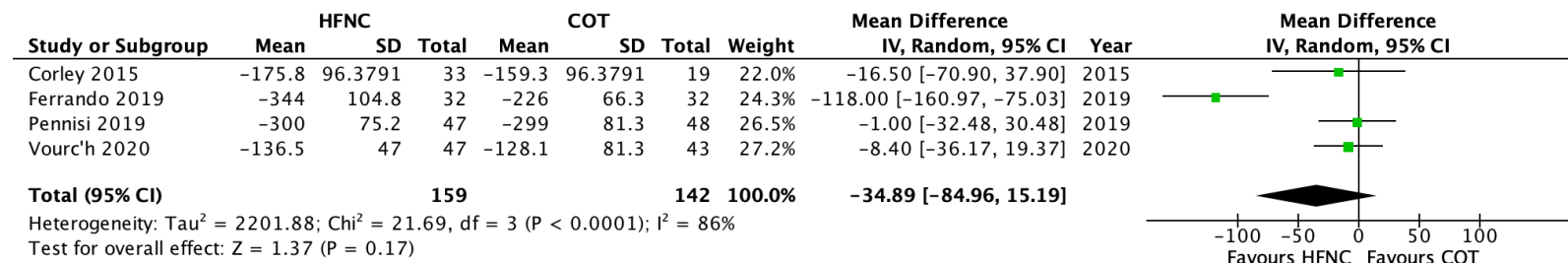


## Recommendation 4: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) in post-operative patients

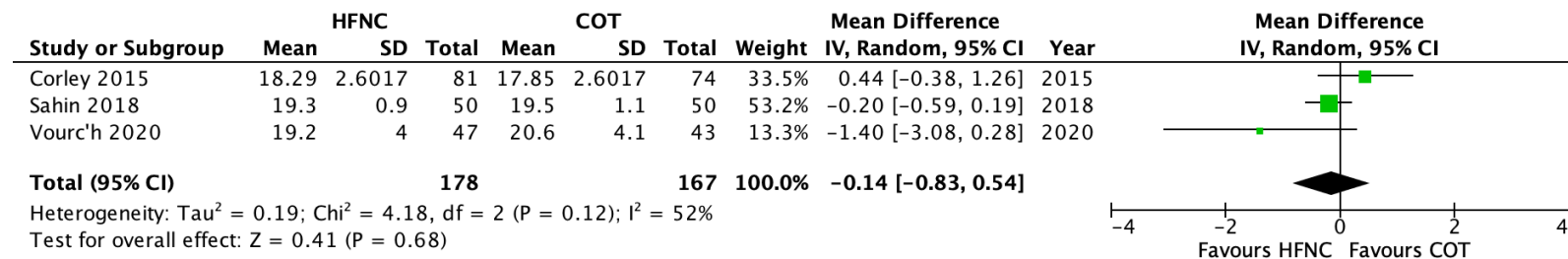
### 8. PCO<sub>2</sub>



### 9. PaO<sub>2</sub>/FiO<sub>2</sub>



### 10. Respiratory rate



### Recommendation 5: High flow nasal cannula (HFNC) vs. Non-invasive ventilation (NIV) in post-operative patients

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	NIV	Relative (95% CI)	Absolute (95% CI)		
Mortality - Post-op											
1 RCT	not serious	not serious	not serious <sup>a</sup>	very serious <sup>b</sup>	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)	⊕⊕○○ LOW	CRITICAL
Re-intubation - Post-op											
1 RCT	not serious <sup>c</sup>	not serious	not serious <sup>a</sup>	serious <sup>d</sup>	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 length of stay - Post-op											
1 RCT	not serious	not serious	not serious <sup>a</sup>	not serious <sup>e</sup>	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 <sup>a</sup>	serious <sup>d</sup>	none	414	416	-	MD 1 lower (2.21 lower to 0.21 higher)	⊕⊕⊕○ MODERATE	IMPORTANT
PCO2 - Post-op											
1 RCT	not serious	not serious	not serious <sup>a</sup>	not serious	none	414	416	-	MD 1.1 mmHg lower (2.02 lower to 0.18 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
PaO2:FIO2 - Post-op											
1 RCT	not serious	not serious	not serious <sup>a</sup>	not serious	none	414	416	-	MD 63 lower (80 lower to 46 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT
Respiratory Rate - Post-op											
1 RCT	not serious	not serious	not serious <sup>a</sup>	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

### **Recommendation 5: High flow nasal cannula (HFNC) vs. Non-invasive ventilation (NIV) in post-operative patients**

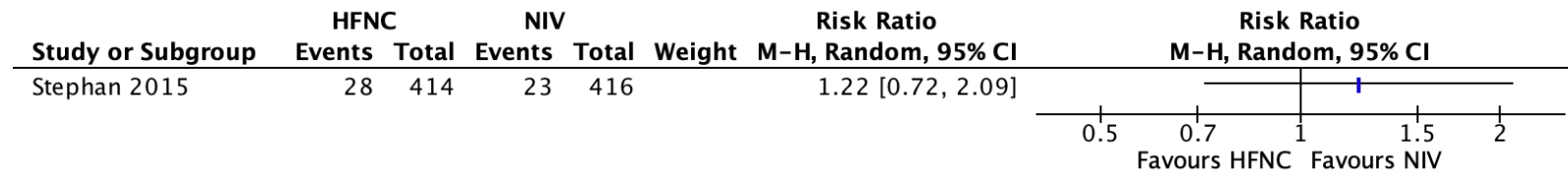
#### **Explanations**

- 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).

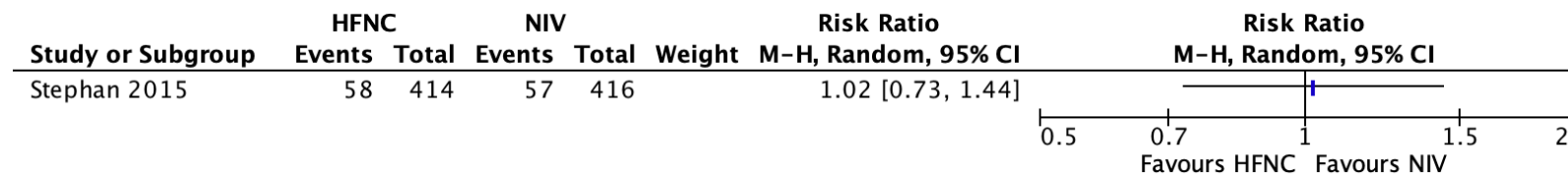


## Recommendation 5: High flow nasal cannula (HFNC) vs. Non-invasive ventilation (NIV) in post-operative patients

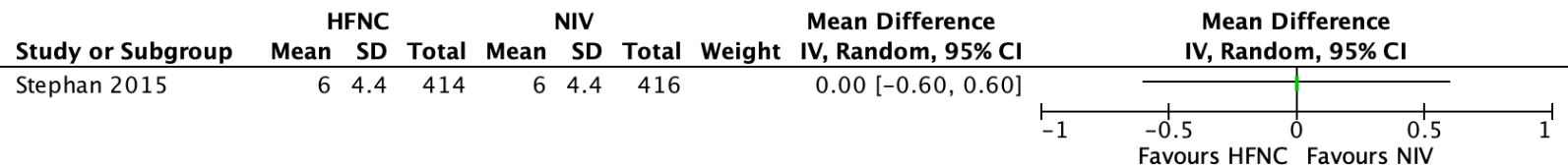
### 1. Mortality



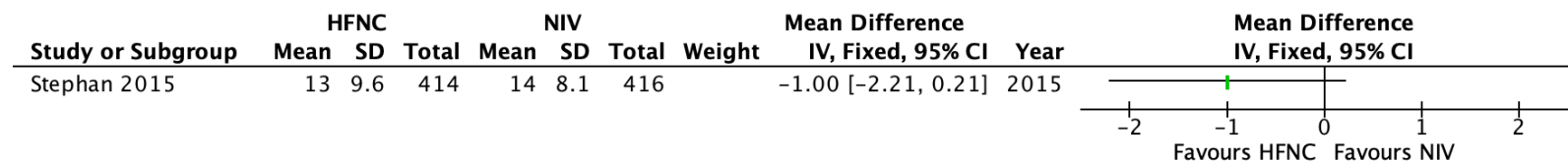
### 2. Re-intubation



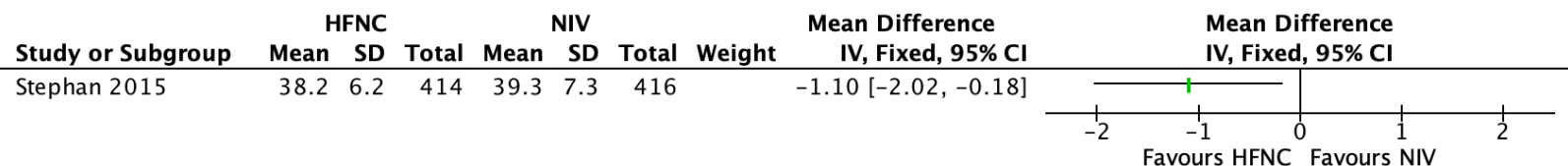
### 3. ICU length of stay



### 4. Hospital length of stay

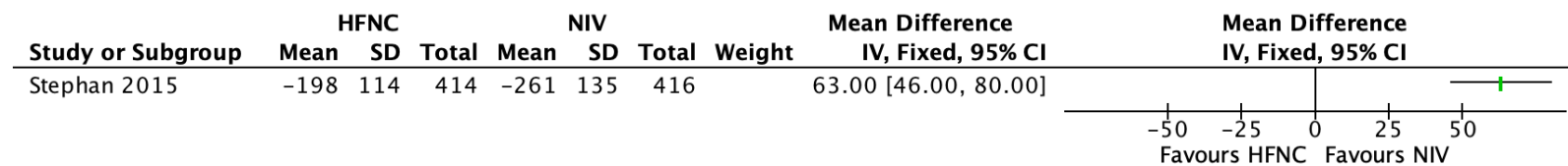


### 5. PCO2

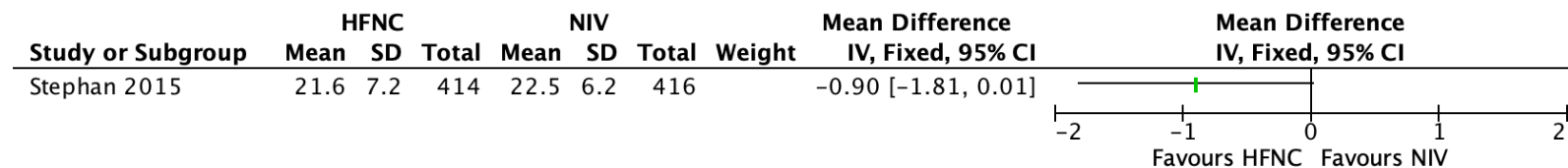


## Recommendation 5: High flow nasal cannula (HFNC) vs. Non-invasive ventilation (NIV) in post-operative patients

### 6. PaO<sub>2</sub>/FiO<sub>2</sub>



### 7. Respiratory rate



**Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients**

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	COT	Relative (95% CI)	Absolute (95% CI)		
Mortality											
9 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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)	⊕⊕⊕○ MODERATE	CRITICAL
Re-intubation											
10 RCTs	serious <sup>b</sup>	not serious	not serious	not serious <sup>c</sup>	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)	⊕⊕⊕○ MODERATE	CRITICAL
Escalate to NIV											
6 RCTs	serious <sup>b</sup>	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)	⊕⊕⊕○ MODERATE	CRITICAL
ICU Length of Stay											
6 RCTs	not serious	not serious	not serious	not serious <sup>c</sup>	none	485	487	-	MD 0.29 higher (0.27 lower to 0.85 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Hospital Length of Stay											
4 RCTs	not serious	serious <sup>d</sup>	not serious	serious <sup>a</sup>	none	424	417	-	MD 1.08 lower (4.83 lower to 2.66 higher)	⊕⊕○○ LOW	IMPORTANT
Comfort											
3 RCTs	not serious	not serious <sup>e</sup>	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											

### **Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients**

7 RCTs	not serious	not serious	not serious	not serious	none	460	446	-	MD <b>0.15 lower</b> (1.89 lower to 1.58 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>PaO<sub>2</sub>:FiO<sub>2</sub></b>											
4 RCTs	not serious	serious <sup>d</sup>	not serious	serious <sup>a</sup>	none	378	383	-	MD <b>14.13 higher</b> (20.48 lower to 48.75 higher)	⊕⊕○○ LOW	IMPORTANT
<b>Respiratory Rate</b>											
7 RCTs	not serious	not serious <sup>f</sup>	not serious	not serious	none	213	200	-	MD <b>1.98 lower</b> (3.9 lower to 0.06 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT

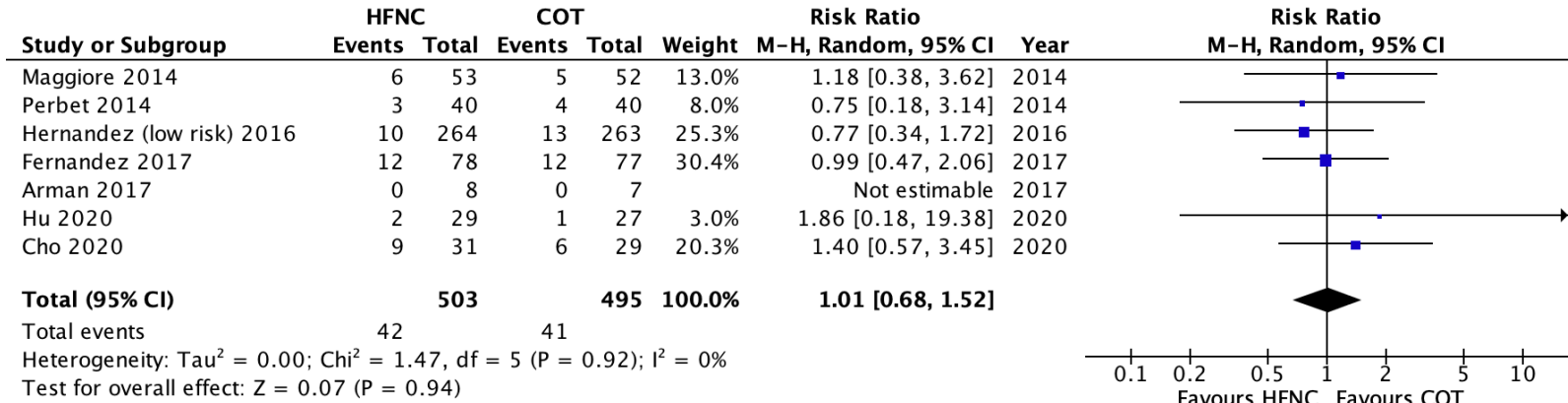
**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

#### **Explanations**

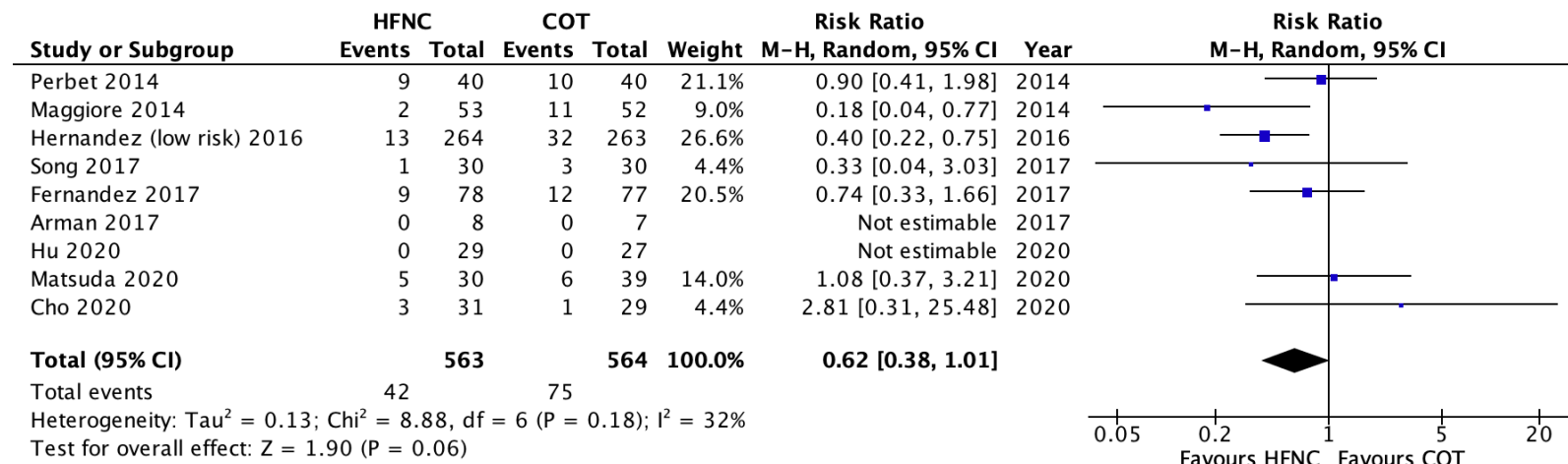
- a. Wide 95% confidence intervals do not exclude clinically significant benefit nor harm.
- b. Lack of blinding may have resulted in bias from co-intervention, though several trials did have specific criteria for escalation of respiratory support.
- c. Though not statistically significant, 95% confidence interval likely excludes a significant differences.
- d. Large values of I<sup>2</sup> (>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.

## Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients

### 1. Mortality

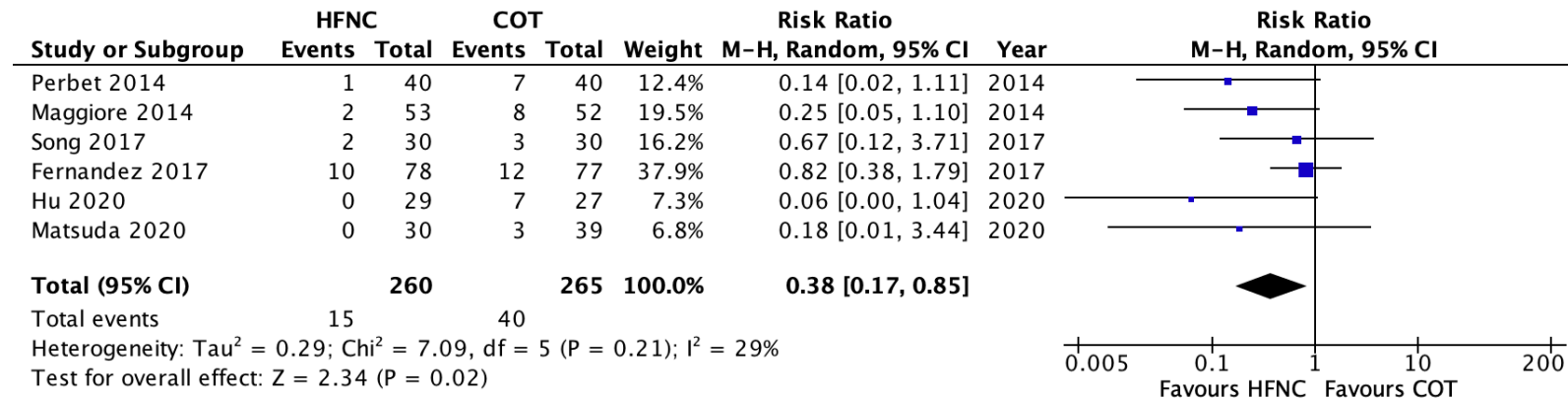


### 2. Re-intubation

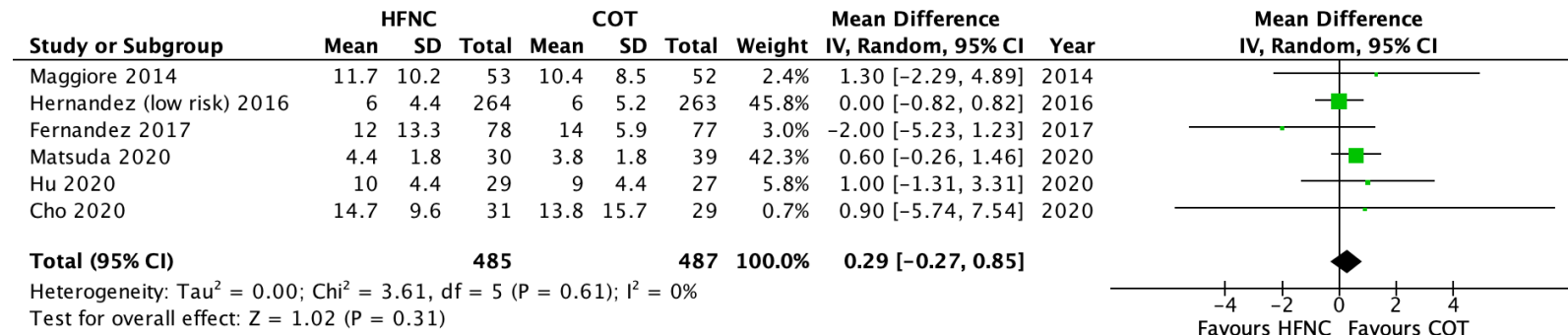


## Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients

### 3. Escalation to NIV

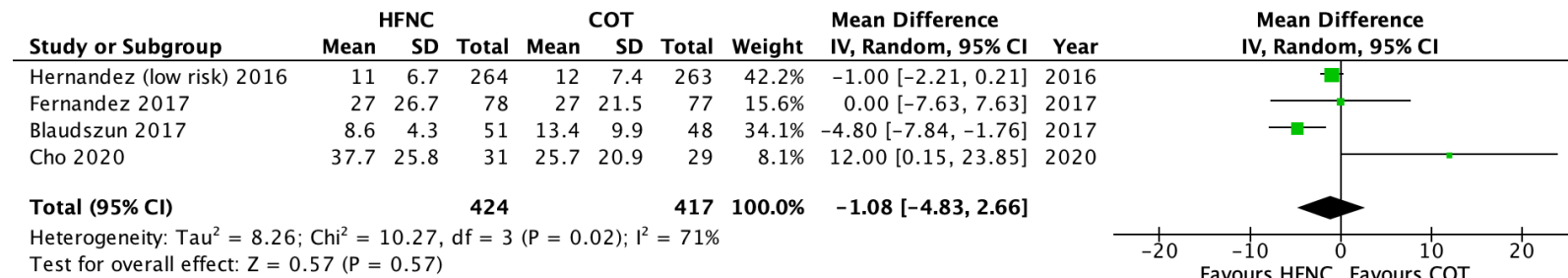


### 4. ICU length of stay

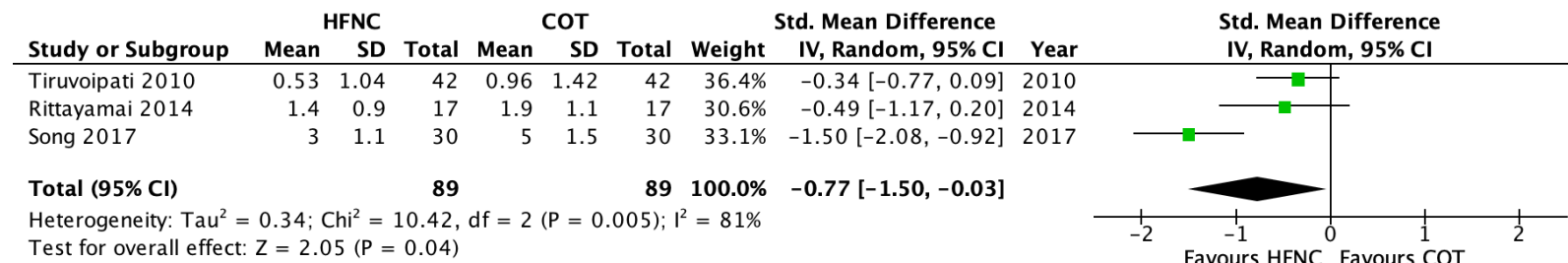


## Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients

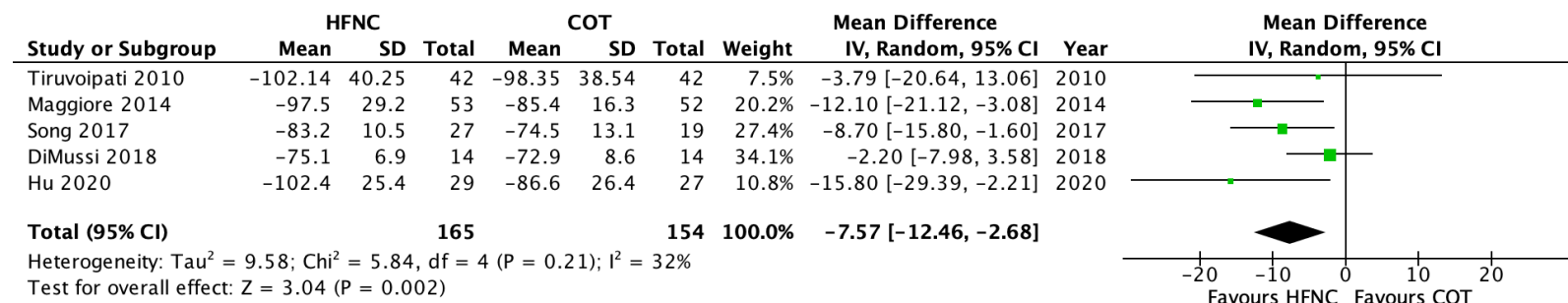
### 5. Hospital length of stay



### 6. Comfort

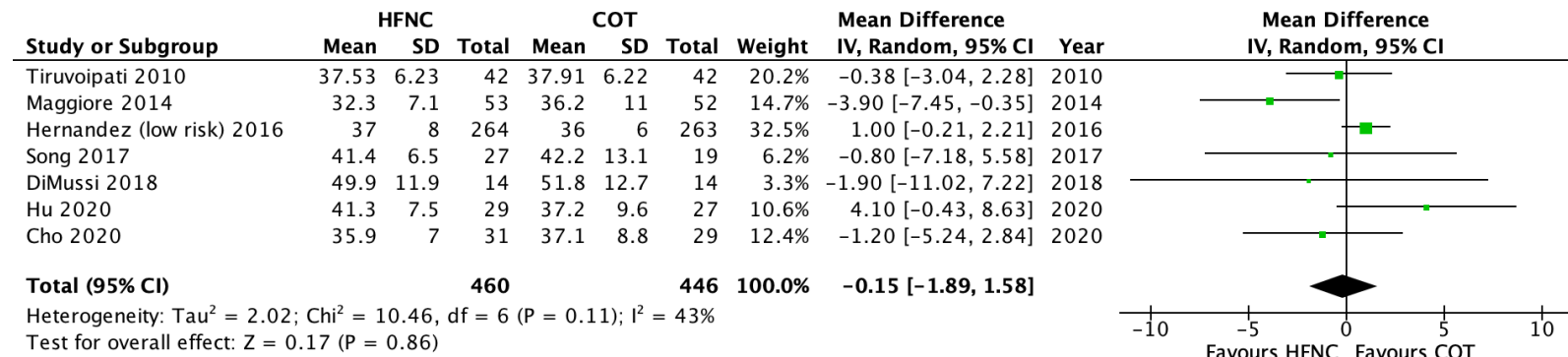


### 7. PaO2

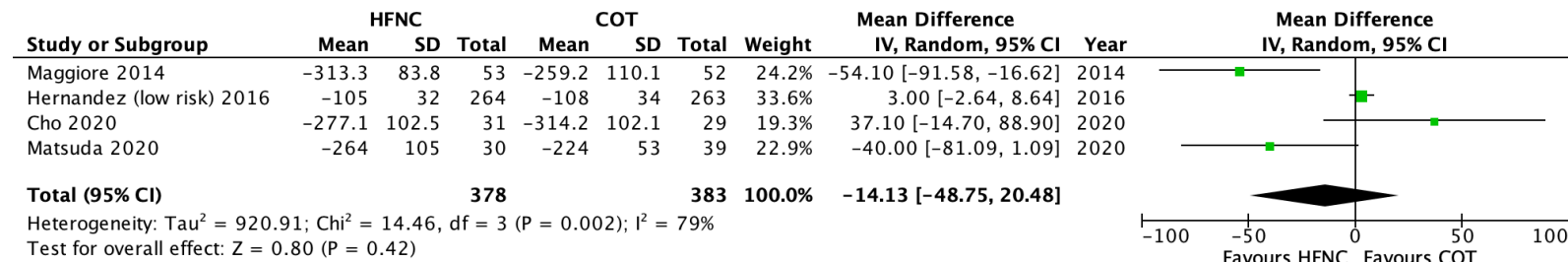


## Recommendation 6: High-flow nasal cannula (HFNC) vs. conventional oxygen therapy (COT) to prevent extubation failure in non-surgical patients

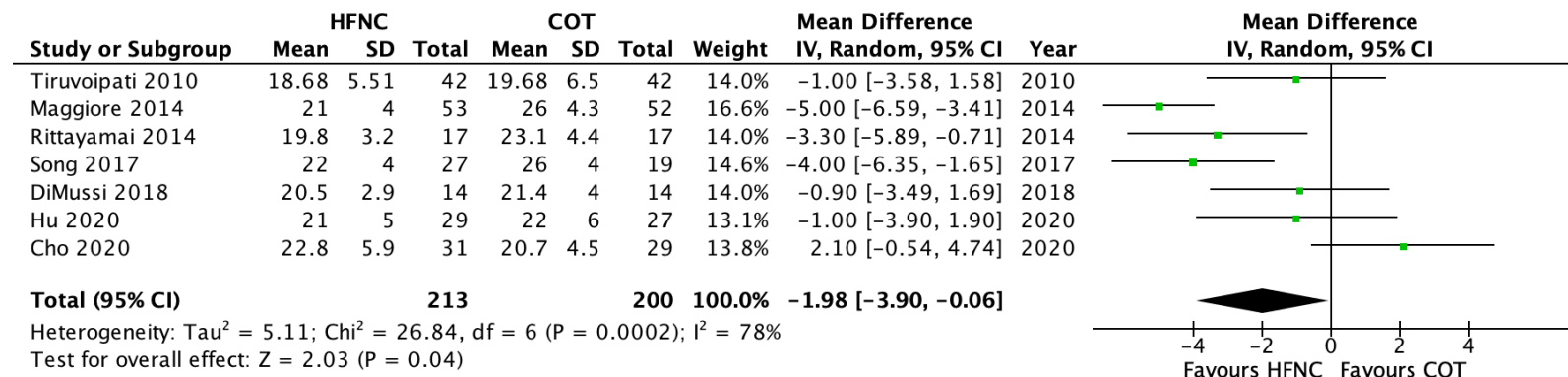
### 8. PCO<sub>2</sub>



### 9. PaO<sub>2</sub>/FiO<sub>2</sub>



### 10. Respiratory rate





### Recommendation 7: High flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) to prevent extubation failure in non-surgical patients

Certainty assessment						№ of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	HFNC	NIV	Relative (95% CI)	Absolute (95% CI)		
Mortality - General ICU											
5 RCTs	not serious	not serious	not serious	serious <sup>a</sup>	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-intubation - General ICU											
5 RCTs	not serious <sup>b</sup>	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 length of stay - General ICU											
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 stay - General ICU											
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 ICU											
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 - General ICU											
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:FIO2 - General ICU											
3 RCTs	not serious	not serious	not serious	not serious <sup>c</sup>	none	356	376	-	MD 3.86 higher (0.39 higher to 7.34 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Respiratory Rate - General ICU											
2 RCTs	not serious	not serious <sup>d</sup>	not serious	not serious <sup>c</sup>	none	66	62	-	MD 0.59 respirations per minute lower (2.48 lower to 1.29 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

### **Recommendation 7: High flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) to prevent extubation failure in non-surgical patients**

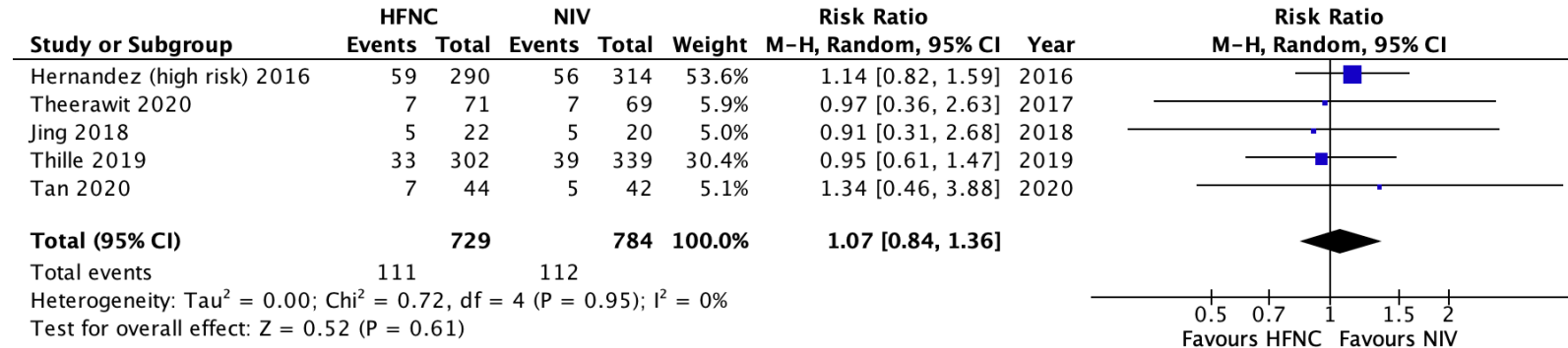
**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

#### **Explanations**

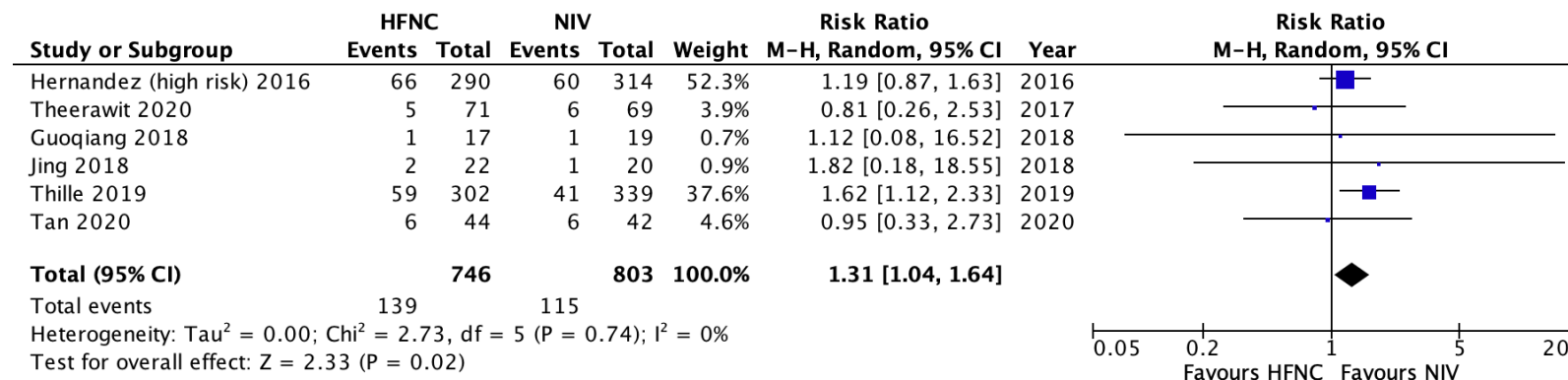
- a. Wide 95% confidence intervals do not exclude the possibility of meaningful benefit nor harm.
- b. Lack of blinding may have resulted in bias from co-intervention, though most trials did have specific criteria for escalation of respiratory support, including intubation.
- c. Though not statistically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

## Recommendation 7: High flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) to prevent extubation failure in non-surgical patients

### 1. Mortality

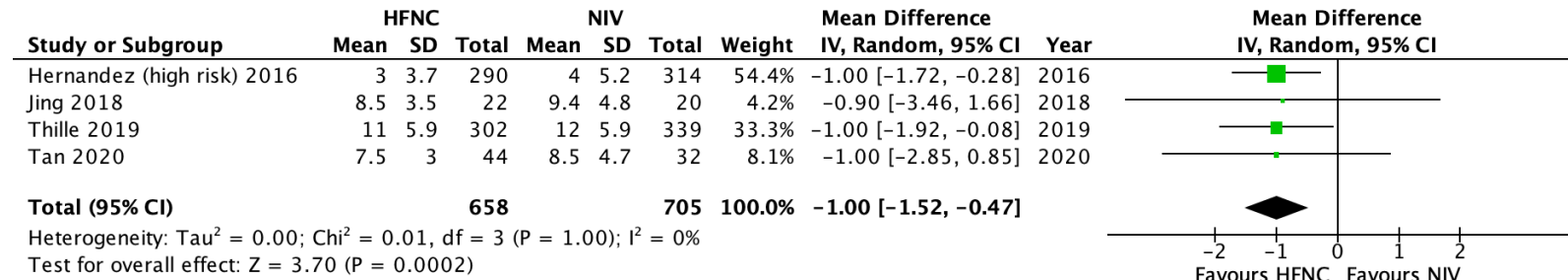


### 2. Re-intubation

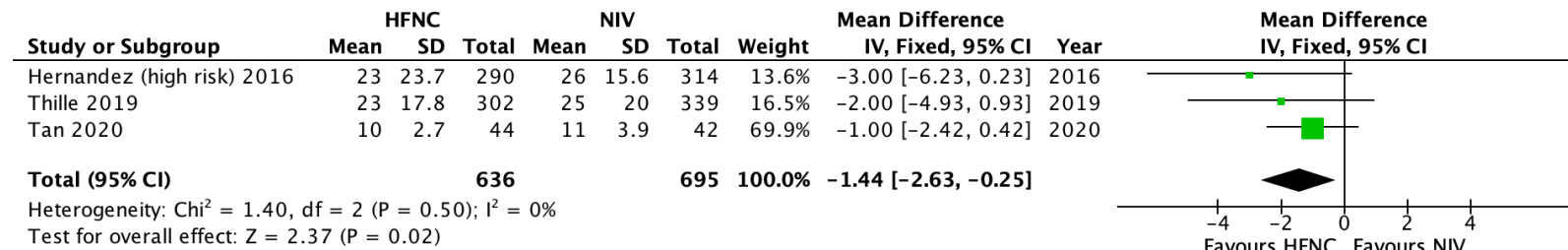


## Recommendation 7: High flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) to prevent extubation failure in non-surgical patients

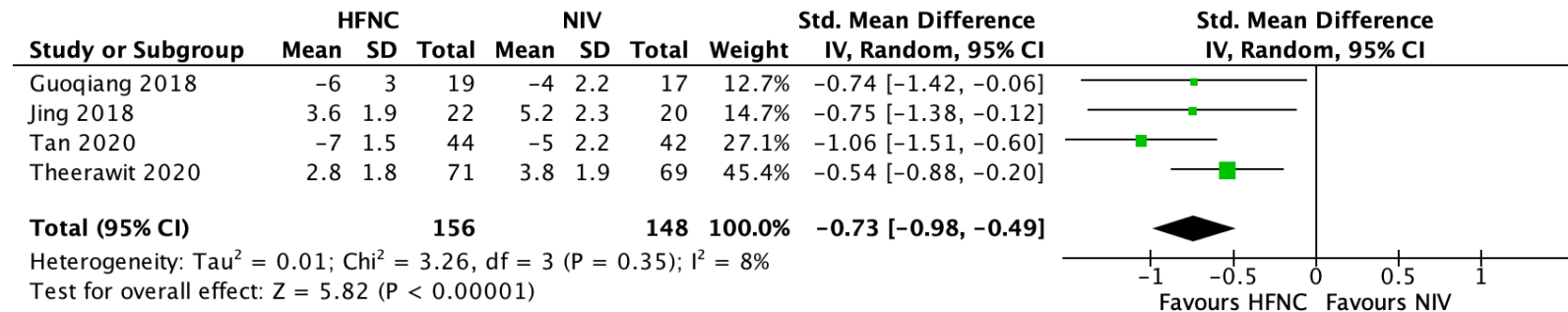
### 3. ICU length of stay



### 4. Hospital length of stay

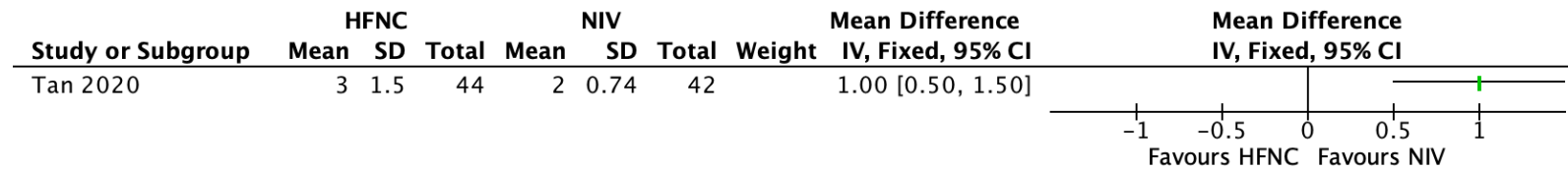


### 5. Comfort

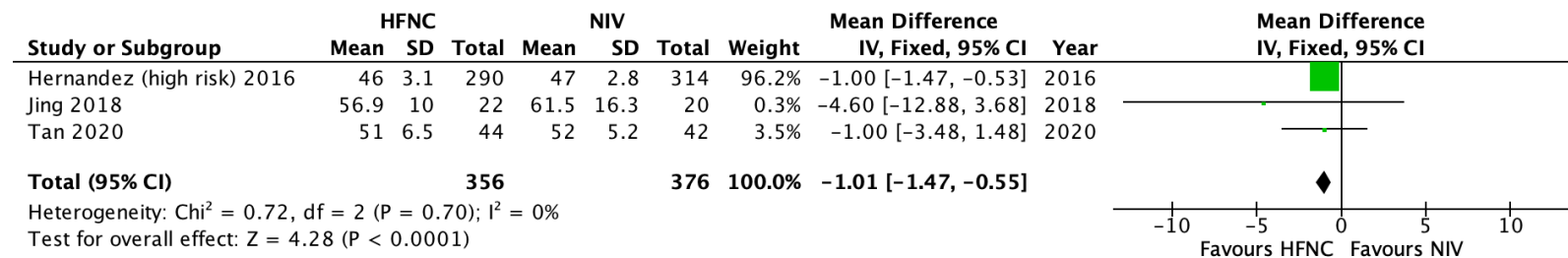


## Recommendation 7: High flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) to prevent extubation failure in non-surgical patients

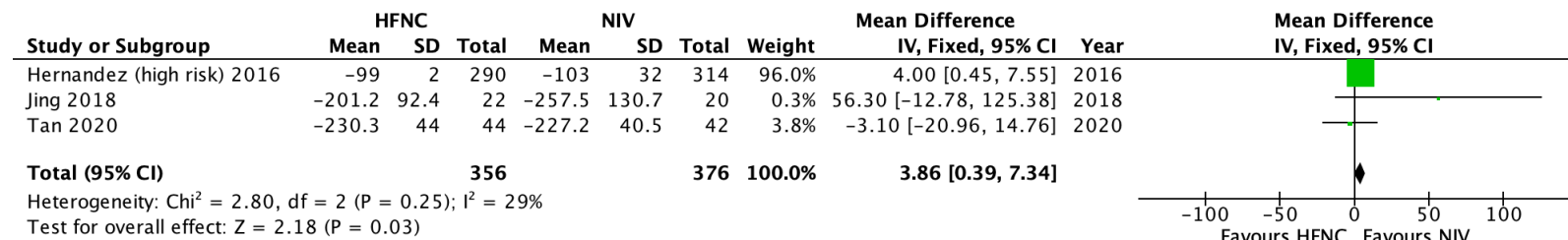
### 6. Dyspnea



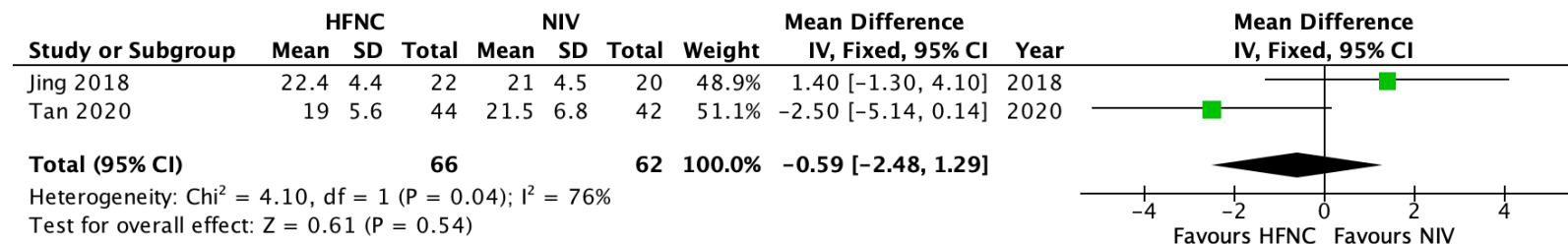
### 8. PCO<sub>2</sub>









### 9. PaO<sub>2</sub>/FiO<sub>2</sub>



### 9. Respiratory rate



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

Certainty assessment						Ne of patients		Effect		Certainty	Importance
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HFNC	NIV	Relative (95% CI)	Absolute (95% CI)		
Mortality - RCTs											
4 RCTs	not serious	not serious	not serious <sup>a</sup>	very serious <sup>b</sup>	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)	 LOW	CRITICAL
Intubation - RCTs											
4 RCTs	not serious	not serious	not serious <sup>a</sup>	very serious <sup>b</sup>	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)	 LOW	CRITICAL
ICU length of stay - RCTs											
3 RCTs	not serious	not serious	not serious	serious <sup>c</sup>	none	118	117	-	MD 0.1 higher (0.73 lower to 0.94 higher)	 MODERATE	IMPORTANT
Hospital length of stay - RCTs											
4 RCTs	not serious	not serious	not serious	serious <sup>c</sup>	none	178	174	-	MD 0.82 days lower (1.83 lower to 0.2 higher)	 MODERATE	IMPORTANT
Comfort (lower is better) (Scale from: 0 to 10)											
2 RCTs	not serious <sup>d</sup>	serious <sup>e</sup>	not serious	serious <sup>f</sup>	none	49	52	-	SMD 0.57 SD lower (0.98 lower to 0.16 lower)	 LOW	IMPORTANT
Dyspnea											
3 RCTs	not serious <sup>d</sup>	not serious	not serious	serious <sup>c</sup>	none	77	76	-	MD 0.31 lower (0.94 lower to 0.33 higher)	 MODERATE	IMPORTANT
PaO2/FiO2 - RCTs (follow 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 <sup>a</sup>	not serious	none	44	44	-	MD <b>0.52 lower</b> (3.59 lower to 2.56 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>PO2 - RCTs</b>											
3 RCTs	not serious	not serious	not serious	not serious	none	151	109	-	MD <b>0.32 higher</b> (3.83 lower to 4.47 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
<b>PCO2 - RCTs</b>											
6 RCTs	not serious	serious <sup>e</sup>	not serious	serious <sup>c</sup>	none	230	227	-	MD <b>0.79 mmHg lower</b> (5.19 lower to 3.61 higher)	⊕⊕○○ LOW	IMPORTANT
<b>Respiratory rate - RCTs</b>											
5 RCTs	not serious	not serious	not serious	not serious	none	148	144	-	MD <b>0.40 lower</b> (1.60 lower to 0.8 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

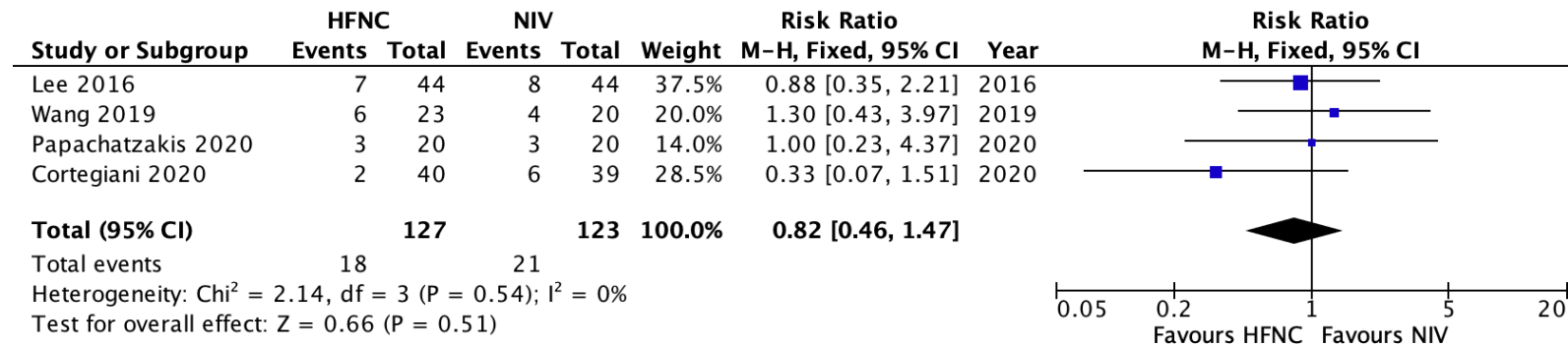
**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

#### **Explanations**

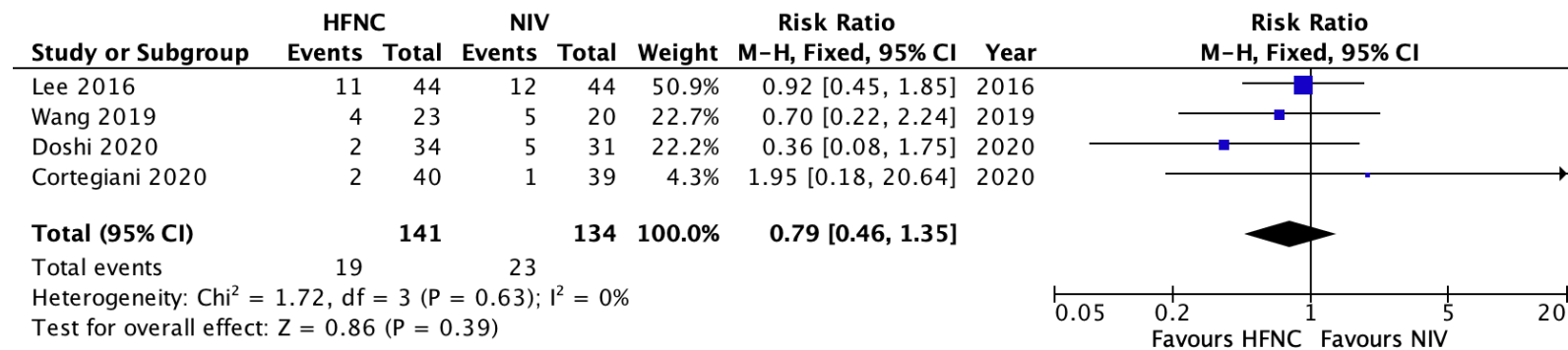
- a. NIV settings in comparison group appear to have been reasonable and titrated to patient need in most studies.
- b. Very wide 95% confidence intervals resulting in very serious imprecision.
- c. Wide 95% confidence intervals which do not rule out significant benefit nor harm.
- d. High statistical 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 hypercapnic respiratory failure

### 1. Mortality



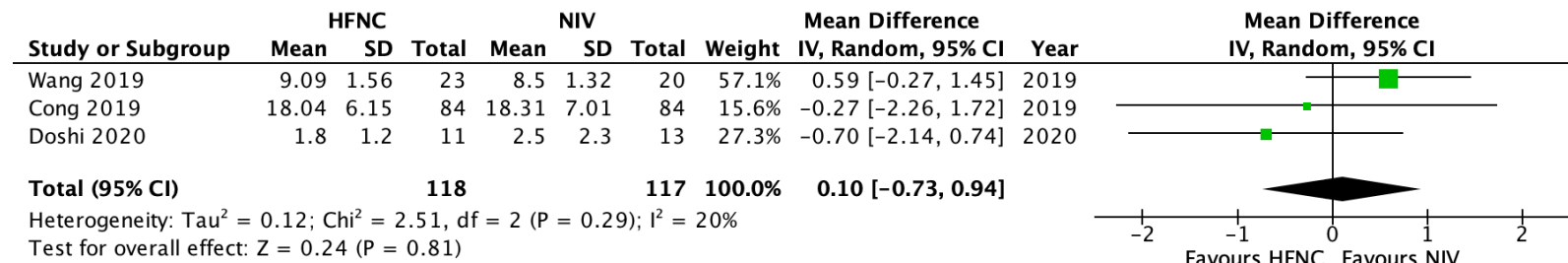
### 2. Intubation



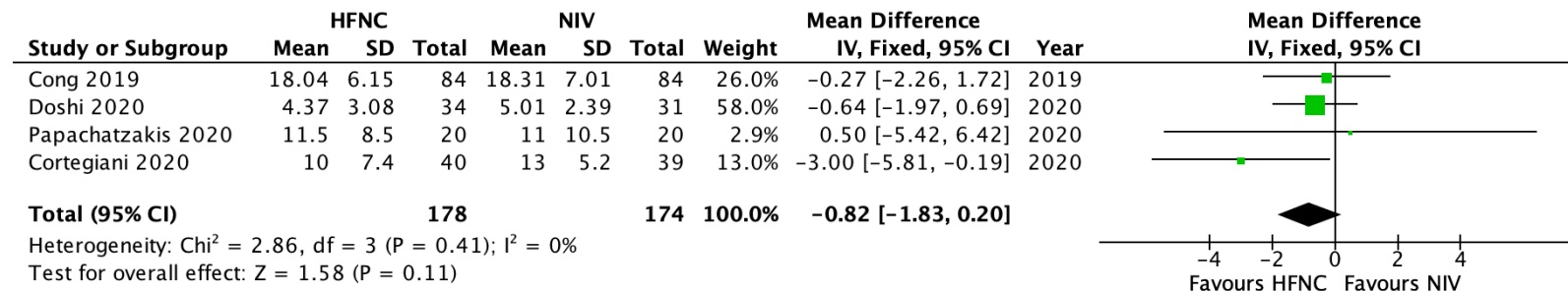


## Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

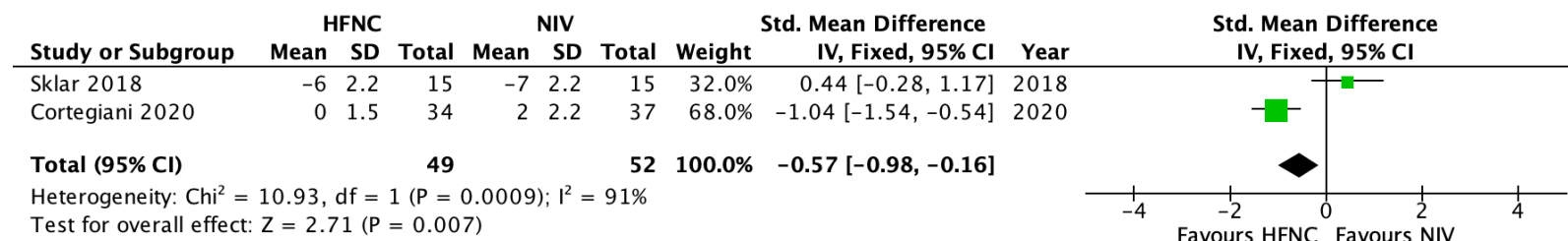
### 3. ICU length of stay



### 4. Hospital length of stay

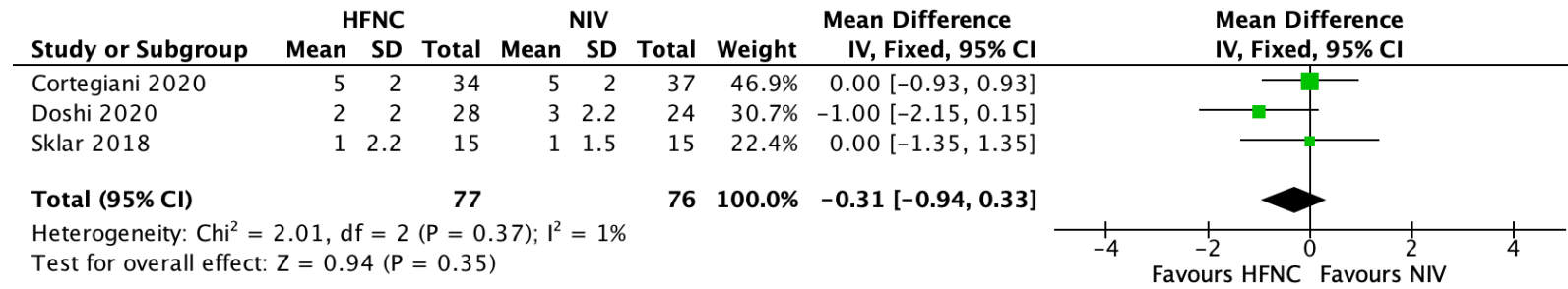


### 5. Comfort

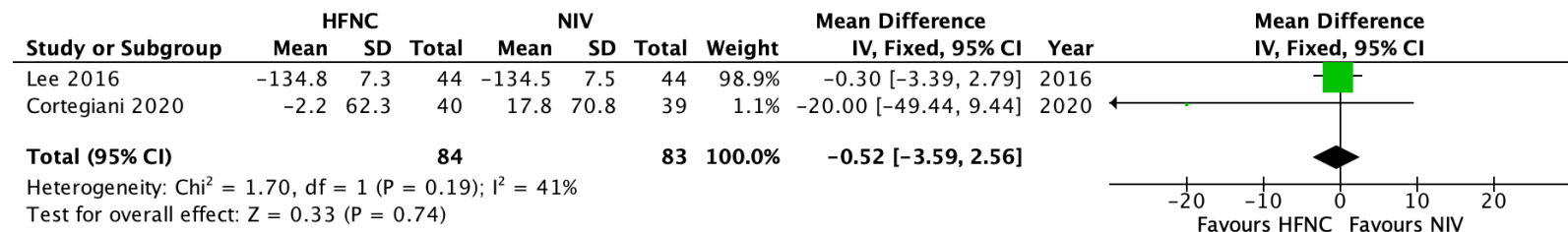


## Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

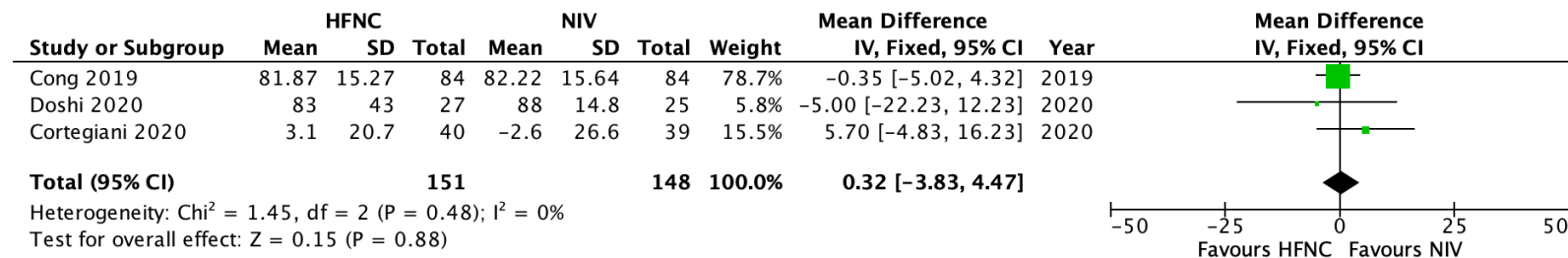
### 6. Dyspnea



### 7. PaO<sub>2</sub>/FiO<sub>2</sub>

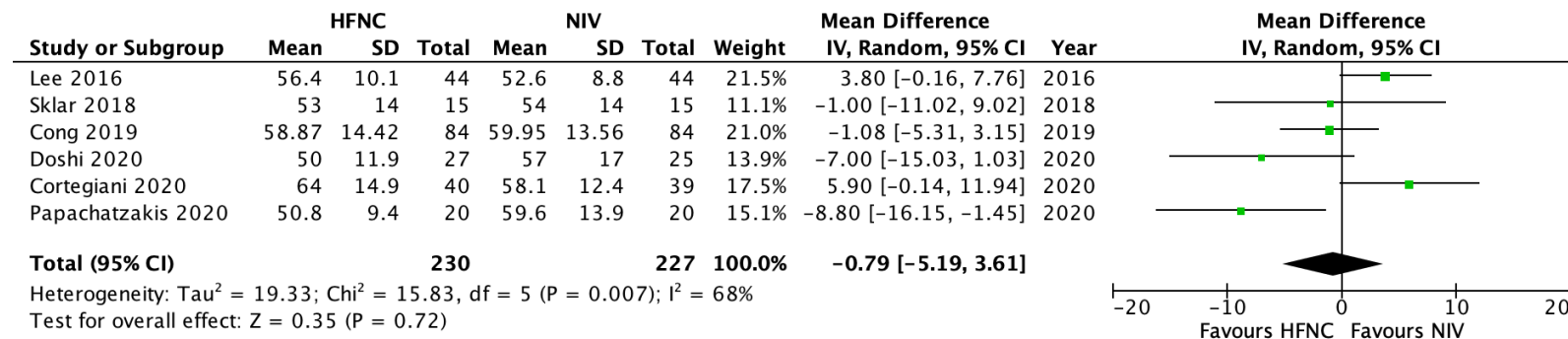


### 8. PO<sub>2</sub>

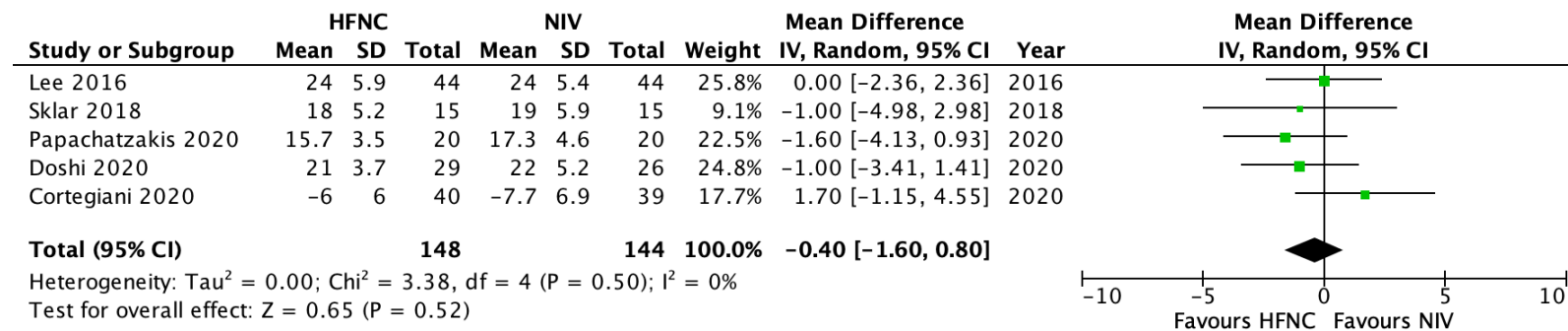


## Recommendation 8: High-flow nasal cannula (HFNC) vs. non-invasive ventilation (NIV) in hypercapnic respiratory failure

### 9. PCO<sub>2</sub>



### 10. Respiratory rate



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