# Supplement 6 Forest plots of adverse events

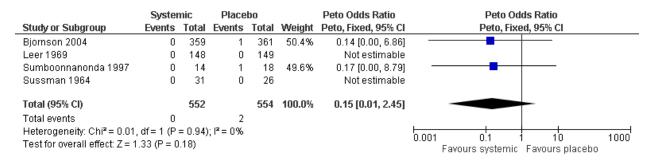
Syst	emic vs. Placebo	
a.	Infection & respiratory system	p. 2-12
b.	Gastro-intestinal tract	p. 13-22
c.	CNS & behaviour effects	p. 23-29
d.	Dermatologic conditions	p. 30-32
e.	Endocrine/ metabolic & musculoskeletal systems	p. 33-35
f.	Cardiovascular system	p. 36-38
g.	General adverse events/ other symptoms	p. 39-40
h.	Immune system & oncology	p. 41
Inha	lled vs. Placebo	
a.	Infection & respiratory system	p. 42-47
b.	Gastro-intestinal tract	p. 48-51
c.	CNS & behaviour effects	p. 52-54
d.	Dermatologic conditions	p. 55-57
e.	Endocrine/ metabolic & musculoskeletal systems	p. 58
f.	Cardiovascular system	p. 59
Dex	amethasone vs. Other steroid	
a.	Gastro-intestinal tract	p. 60-63
b.	CNS & behaviour effects	p. 64-66
c.	Dermatologic conditions	p. 67
d.	Endocrine/ metabolic & musculoskeletal systems	p. 68
e.	Cardiovascular system	p. 69
f.	General adverse events/ other symptoms	p. 70-71

#### SYSTEMIC vs. PLACEBO - Infection & Respiratory

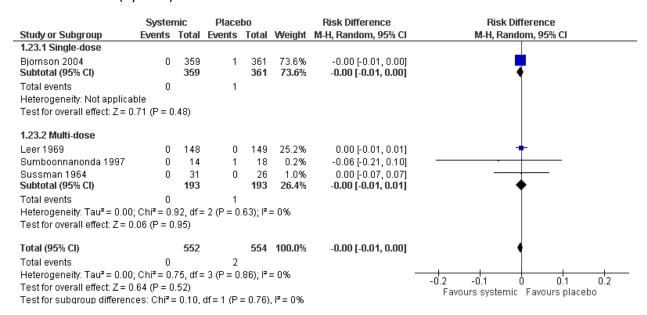
#### Severe infections

	Syster	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	0	359	1	361	73.6%	-0.00 [-0.01, 0.00]	
Leer 1969	0	148	0	149	25.2%	0.00 [-0.01, 0.01]	+
Sumboonnanonda 1997	0	14	1	18	0.2%	-0.06 [-0.21, 0.10]	· ·
Sussman 1964	0	31	0	26	1.0%	0.00 [-0.07, 0.07]	
Total (95% CI)		552		554	100.0%	-0.00 [-0.01, 0.00]	•
Total events	0		2				
Heterogeneity: Tau <sup>2</sup> = 0.00	$I$ ; $Chi^2 = 0$ .	75, df=	3 (P = 0				
Test for overall effect: Z = 0							-0.2 -0.1 0 0.1 0.2 Favours systemic Favours placebo

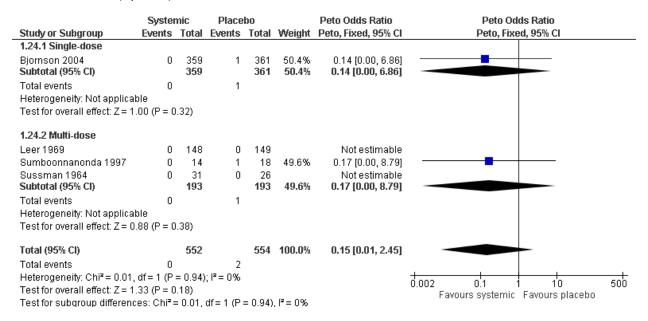
#### Severe infections - Peto



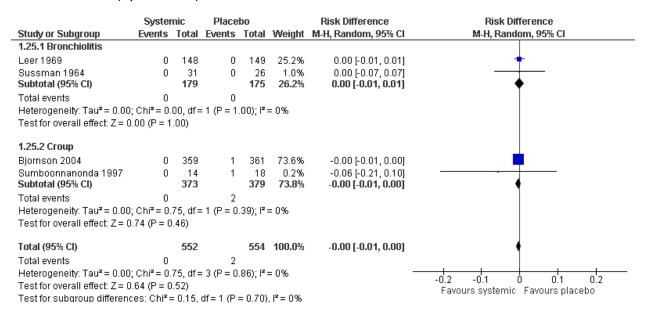
#### Severe infections (by dose)



#### Severe infections (by dose) - Peto



#### Severe infections (by condition)



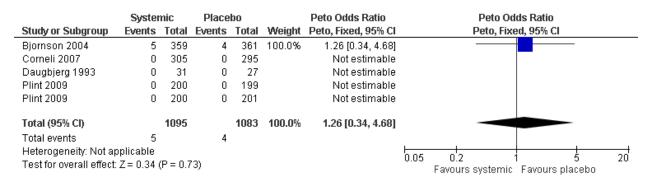
# Severe infections (by condition) – Peto

	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	<b>Events</b>	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.26.1 Bronchiolitis							
Leer 1969	0	148	0	149		Not estimable	
Sussman 1964 Subtotal (95% CI)	0	31 <b>179</b>	0	26 <b>175</b>		Not estimable <b>Not estimable</b>	
Total events	0		0			not ostinable	
Heterogeneity: Not applicat	ole						
Test for overall effect: Not a	pplicable						
1.26.2 Croup							
Bjornson 2004	0	359	1	361	50.4%	0.14 [0.00, 6.86]	
Sumboonnanonda 1997 Subtotal (95% CI)	0	14 373	1	18 <b>379</b>	49.6% <b>100.0</b> %	0.17 [0.00, 8.79] <b>0.15 [0.01, 2.45]</b>	
Total events	0		2				
Heterogeneity: Chi² = 0.01,	df = 1 (P :	= 0.94)	$ I^2 = 0\% $				
Test for overall effect: Z = 1.	33 (P = 0	.18)					
Total (95% CI)		552		554	100.0%	0.15 [0.01, 2.45]	
Total events Heterogeneity: Chi <sup>2</sup> = 0.01, Test for overall effect: Z = 1. Test for subgroup differenc	33 (P = 0	.18)					0.005 0.1 10 200 Favours systemic Favours placebo

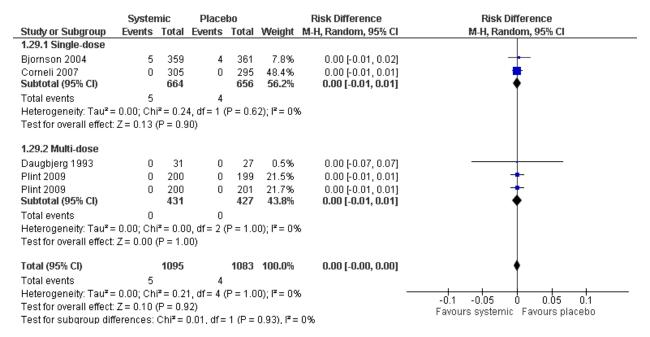
# Systemic infections

	Syster	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	5	359	4	361	7.8%	0.00 [-0.01, 0.02]	+
Corneli 2007	0	305	0	295	48.4%	0.00 [-0.01, 0.01]	•
Daugbjerg 1993	0	31	0	27	0.5%	0.00 [-0.07, 0.07]	<del></del>
Plint 2009	0	200	0	199	21.5%	0.00 [-0.01, 0.01]	+
Plint 2009	0	200	0	201	21.7%	0.00 [-0.01, 0.01]	<b>†</b>
Total (95% CI)		1095		1083	100.0%	0.00 [-0.00, 0.00]	•
Total events	5		4				
Heterogeneity: Tau² =	0.00; Ch	i <b>=</b> 0.2	1, df = 4 (	6 <u> </u>	-0.1 -0.05 0 0.05 0.1		
Test for overall effect:	Z = 0.10	(P = 0.9)		Favours systemic Favours placebo			

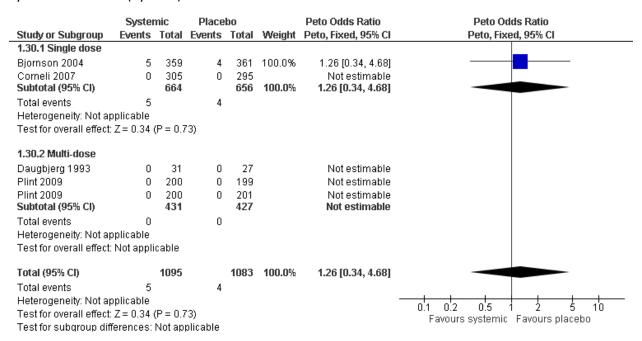
# Systemic infections - Peto



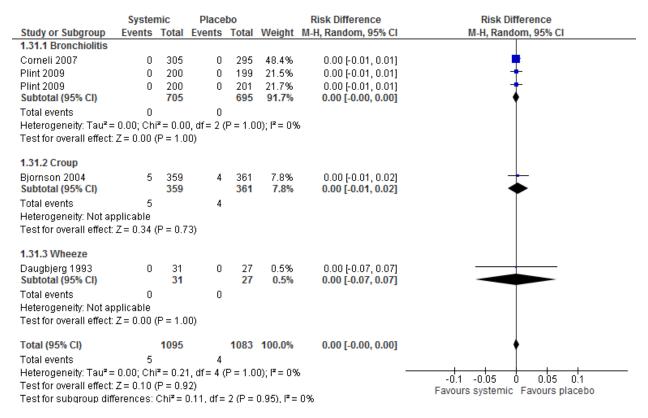
#### Systemic infections (by dose)



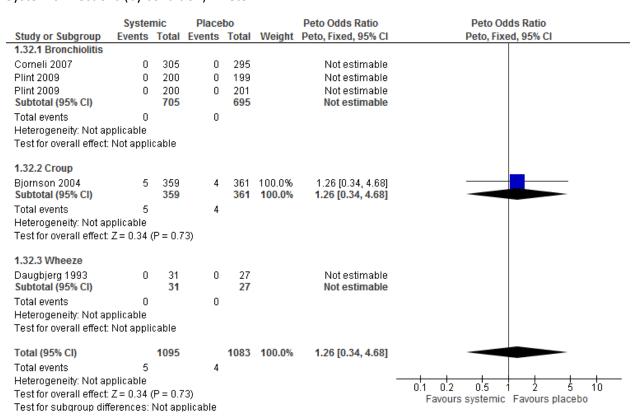
### Systemic infections (by dose) - Peto



#### Systemic infections (by condition)



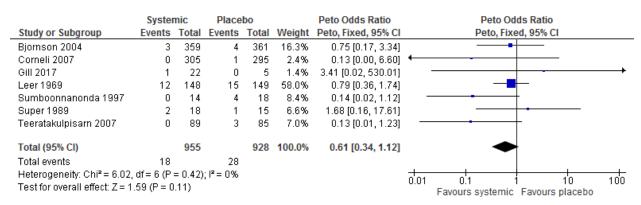
#### Systemic infections (by condition) – Peto



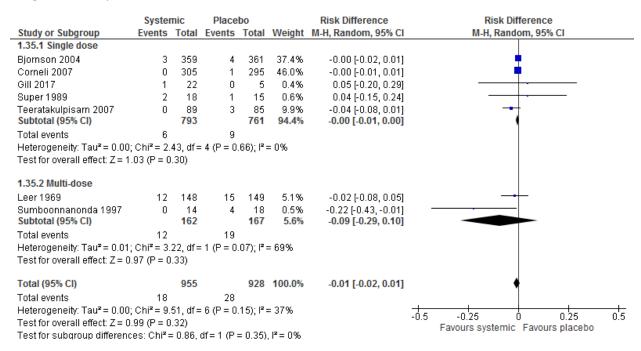
# Lung/trachea

	Syste	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	3	359	4	361	37.4%	-0.00 [-0.02, 0.01]	•
Corneli 2007	0	305	1	295	46.0%	-0.00 [-0.01, 0.01]	•
Gill 2017	1	22	0	5	0.4%	0.05 [-0.20, 0.29]	<del></del>
Leer 1969	12	148	15	149	5.1%	-0.02 [-0.08, 0.05]	<del>-+</del>
Sumboonnanonda 1997	0	14	4	18	0.5%	-0.22 [-0.43, -0.01]	<del></del>
Super 1989	2	18	1	15	0.6%	0.04 [-0.15, 0.24]	<del></del>
Teeratakulpisarn 2007	0	89	3	85	9.9%	-0.04 [-0.08, 0.01]	
Total (95% CI)		955		928	100.0%	-0.01 [-0.02, 0.01]	•
Total events	18		28				
Heterogeneity: Tau² = 0.00	; Chi² = 9.	51, df=	6 (P = 0	.15); l²:	= 37%		-0.5 -0.25 0 0.25 0.5
Test for overall effect: $Z = 0$	1.99 (P = 0)	1.32)					Favours systemic Favours placebo

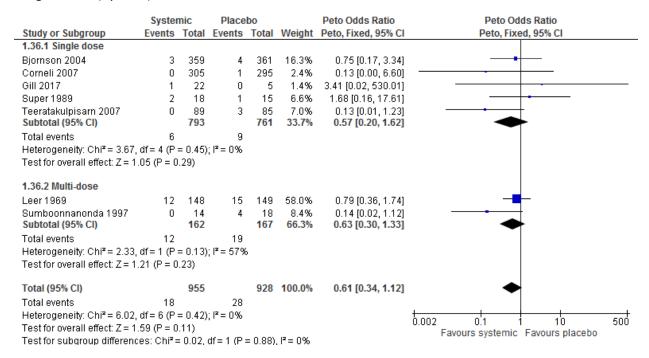
### Lung/trachea - Peto



# Lung/trachea (by dose)



# Lung/trachea (by dose) - Peto



#### Lung/trachea (by condition)

	Syster	nic	Place	bo		Risk Difference	Risk Difference					
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI					
1.37.1 Bronchiolitis												
Corneli 2007	0	305	1	295	46.0%	-0.00 [-0.01, 0.01]	•					
Leer 1969	12	148	15	149	5.1%	-0.02 [-0.08, 0.05]	<del></del>					
Teeratakulpisarn 2007	0	89	3	85	9.9%	-0.04 [-0.08, 0.01]	<del>  </del>					
Subtotal (95% CI)		542		529	61.0%	-0.02 [-0.05, 0.02]	•					
Total events	12		19									
Heterogeneity: Tau² = 0.00; Chi² = 5.18, df = 2 (P = 0.07); l² = 61%												
Test for overall effect: $Z = 0$	.88 (P = 0)	.38)										
1.37.2 Croup												
Bjornson 2004	3	359	4	361	37.4%	-0.00 [-0.02, 0.01]	•					
Gill 2017	1	22	0	5	0.4%	0.05 [-0.20, 0.29]	<del></del>					
Sumboonnanonda 1997	0	14	4	18	0.5%	-0.22 [-0.43, -0.01]						
Super 1989	2	18	1	15	0.6%	0.04 [-0.15, 0.24]	-					
Subtotal (95% CI)		413		399	39.0%	-0.02 [-0.12, 0.07]	<b>—</b>					
Total events	6		9									
Heterogeneity: Tau² = 0.00;	Chi <sup>2</sup> = 5.1	D1, df=	3 (P = 0.	.17); l² :	= 40%							
Test for overall effect: $Z = 0$	.44 (P = 0)	.66)										
Total (95% CI)		955		928	100.0%	-0.01 [-0.02, 0.01]	₹					
Total events	18		28									
Heterogeneity: Tau² = 0.00;			6 (P = 0.	.15); l² :	= 37%		-0.5 -0.25 0 0.25 0.5					
Test for overall effect: Z = 0	•						Favours systemic Favours placebo					
Test for subgroup differenc	es: Chi²=	0.01,	df=1 (P:	= 0.91)	, I² = 0%							

# Lung/trachea (by condition) – Peto

	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio						
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI						
1.38.1 Bronchiolitis													
Corneli 2007	0	305	1	295	2.4%	0.13 [0.00, 6.60]	-						
Leer 1969	12	148	15	149	58.0%	0.79 [0.36, 1.74]	<del>-</del>						
Teeratakulpisarn 2007	0	89	3	85	7.0%	0.13 [0.01, 1.23]							
Subtotal (95% CI)		542		529	67.3%	0.61 [0.29, 1.28]	•						
Total events	12		19										
Heterogeneity: Chi² = 2.84,	Heterogeneity: Chi² = 2.84, df = 2 (P = 0.24); l² = 30%												
Test for overall effect: $Z = 1$	.31 (P = 0)	.19)											
1.38.2 Croup													
Bjornson 2004	3	359	4	361	16.3%	0.75 [0.17, 3.34]	<del></del>						
Gill 2017	1	22	0	5	1.4%	3.41 [0.02, 530.01]	-						
Sumboonnanonda 1997	0	14	4	18	8.4%	0.14 [0.02, 1.12]							
Super 1989	2	18	1	15	6.6%	1.68 [0.16, 17.61]							
Subtotal (95% CI)		413		399	32.7%	0.61 [0.21, 1.76]	•						
Total events	6		9										
Heterogeneity: Chi² = 3.18,	df = 3 (P	= 0.37)	; I² = 6%										
Test for overall effect: Z = 0	.91 (P = 0)	.36)											
Total (95% CI)		955		928	100.0%	0.61 [0.34, 1.12]	•						
Total events	18		28										
Heterogeneity: Chi² = 6.02,	df=6 (P	= 0.42)	$ I^2 = 0\% $				0.002 0.1 1 10 500						
Test for overall effect: $Z = 1$	•						Favours systemic Favours placebo						
Test for subgroup differenc	es: Chi²=	= 0.00, 1	df=1 (P:	= 1.00)	, I² = 0%		. arears of around braces						

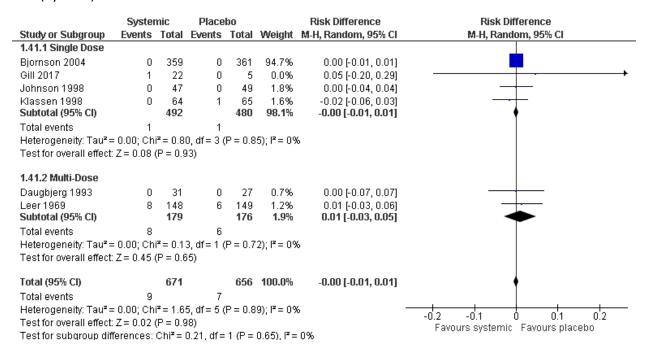
# URT

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	0	359	0	361	94.7%	0.00 [-0.01, 0.01]	
Daugbjerg 1993	0	31	0	27	0.7%	0.00 [-0.07, 0.07]	<del>- + -</del>
Gill 2017	1	22	0	5	0.0%	0.05 [-0.20, 0.29]	<del></del>
Johnson 1998	0	47	0	49	1.8%	0.00 [-0.04, 0.04]	<del></del>
Klassen 1998	0	64	1	65	1.6%	-0.02 [-0.06, 0.03]	<del></del>
Leer 1969	8	148	6	149	1.2%	0.01 [-0.03, 0.06]	
Total (95% CI)		671		656	100.0%	-0.00 [-0.01, 0.01]	<b>•</b>
Total events	9		7				
Heterogeneity: Tau² =	0.00; Ch	i²= 1.6	5, df = 5 (	6	-0.2 -0.1 0 0.1 0.2		
Test for overall effect:	Z = 0.02	(P = 0.9)	38)		Favours systemic Favours placebo		

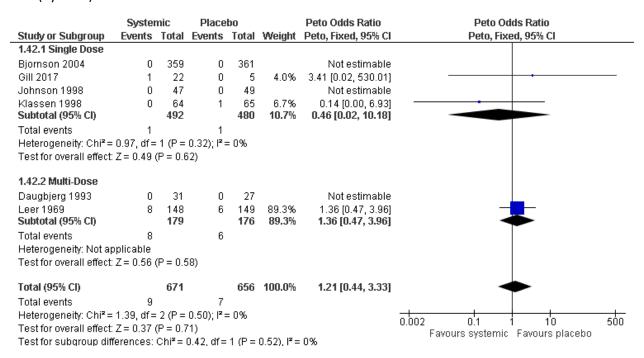
# URT – Peto

	Syster	mic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Bjornson 2004	0	359	0	361		Not estimable	
Daugbjerg 1993	0	31	0	27		Not estimable	
Gill 2017	1	22	0	5	4.0%	3.41 [0.02, 530.01]	<del></del>
Johnson 1998	0	47	0	49		Not estimable	
Klassen 1998	0	64	1	65	6.7%	0.14 [0.00, 6.93]	<u> </u>
Leer 1969	8	148	6	149	89.3%	1.36 [0.47, 3.96]	_
Total (95% CI)		671		656	100.0%	1.21 [0.44, 3.33]	<b>*</b>
Total events	9		7				
Heterogeneity: Chi²=	1.39, df=	2 (P=	0.50); l² =	= 0%			0.001 0.1 1 10 1000
Test for overall effect:	Z = 0.37	(P = 0.7)	'1)				Favours systemic Favours placebo

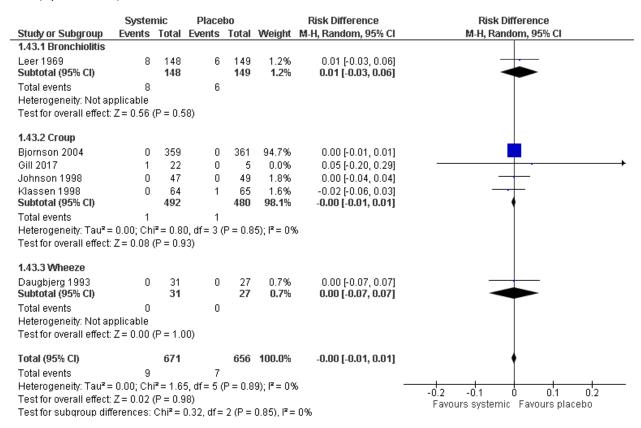
#### URT (by dose)



### URT (by dose) - Peto



#### **URT** (by condition)



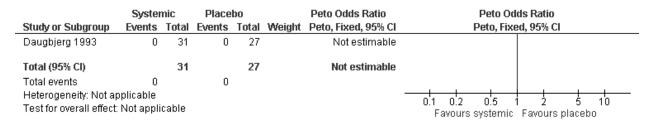
# URT (by condition) - Peto

	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.44.1 Bronchiolitis							<u>L</u>
Leer 1969 Subtotal (95% CI)	8	148 <b>148</b>	6	149 <b>149</b>	89.3% <b>89.3</b> %	1.36 [0.47, 3.96] <b>1.36 [0.47, 3.96]</b>	<del></del>
Total events	8		6				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.56 (	(P = 0.5)	58)				
1.44.2 Croup	_		_				
Bjornson 2004	0	359	0	361		Not estimable	
Gill 2017	1	22	0	5	4.0%	3.41 [0.02, 530.01]	
Johnson 1998	0	47	0	49	0.70	Not estimable	
Klassen 1998 Subtotal (95% CI)	0	64 <b>492</b>	1	65 <b>480</b>	6.7% <b>10.7</b> %	0.14 [0.00, 6.93] <b>0.46 [0.02, 10.18]</b>	
Total events	4	492	4	400	10.778	0.40 [0.02, 10.10]	
Heterogeneity: Chi <sup>2</sup> =	ו - חמק אל	1 /D =	n 22\-i≇-	- 000			
Test for overall effect:	•	,		- 070			
restror overall effect.	2-0.43	(1 – 0.0	,2,				
1.44.3 Wheeze							
Daugbjerg 1993	0	31	0	27		Not estimable	
Subtotal (95% CI)		31		27		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not appli	cable					
Total (OEW CIV		674		CEC	400.00	4 24 (0 44 2 22)	
Total (95% CI)		671	_	000	100.0%	1.21 [0.44, 3.33]	_
Total events	9	2 (D	0.500.13	000			
Heterogeneity: Chi <sup>2</sup> =	•	•		= 0%			0.002 0.1 1 10 500
Test for overall effect:			. ,	4 /D	0.50\ 12	.000	Favours systemic Favours placebo
Test for subgroup diffe	erences:	onr=	∪.4∠, aī =	1 (P=	U.DZ), if =	U%	

# Voice complaints

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Daugbjerg 1993	0	31	0	27	100.0%	0.00 [-0.07, 0.07]	
Total (95% CI)		31		27	100.0%	0.00 [-0.07, 0.07]	
Total events	0		0				
Heterogeneity: Not ap	•	(D. 4.0	101				-0.2 -0.1 0 0.1 0.2
Test for overall effect:	(P = 1.0	JU)				Favours systemic Favours placebo	

# Voice complaints - Peto

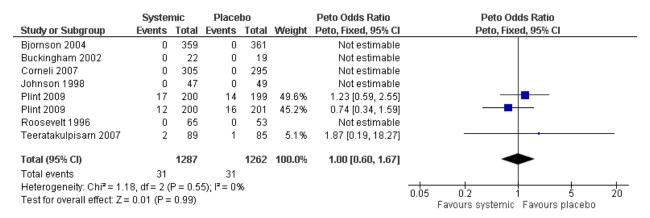


#### SYSTEMIC vs. PLACEBO - GI

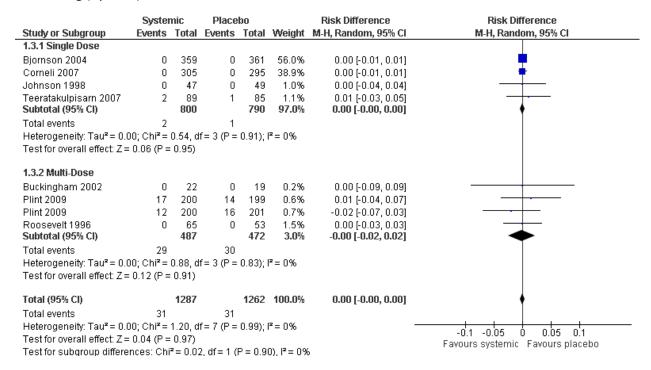
# GI bleeding

	Syster	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	0	359	0	361	56.0%	0.00 [-0.01, 0.01]	•
Buckingham 2002	0	22	0	19	0.2%	0.00 [-0.09, 0.09]	<del></del>
Corneli 2007	0	305	0	295	38.9%	0.00 [-0.01, 0.01]	•
Johnson 1998	0	47	0	49	1.0%	0.00 [-0.04, 0.04]	+
Plint 2009	17	200	14	199	0.6%	0.01 [-0.04, 0.07]	<del></del>
Plint 2009	12	200	16	201	0.7%	-0.02 [-0.07, 0.03]	<del>-+</del>
Roosevelt 1996	0	65	0	53	1.5%	0.00 [-0.03, 0.03]	+
Teeratakulpisarn 2007	2	89	1	85	1.1%	0.01 [-0.03, 0.05]	+
Total (95% CI)		1287		1262	100.0%	0.00 [-0.00, 0.00]	
Total events	31		31				
Heterogeneity: Tau² = 0.0	00; Chi²=	1.20, d	f=7 (P=	0.99);	l² = 0%		-0.5 -0.25 0 0.25 0.5
Test for overall effect: Z =	0.04 (P =	0.97)					-0.5 -0.25 0 0.25 0.5 Favours systemic Favours placebo

# GI bleeding – Peto



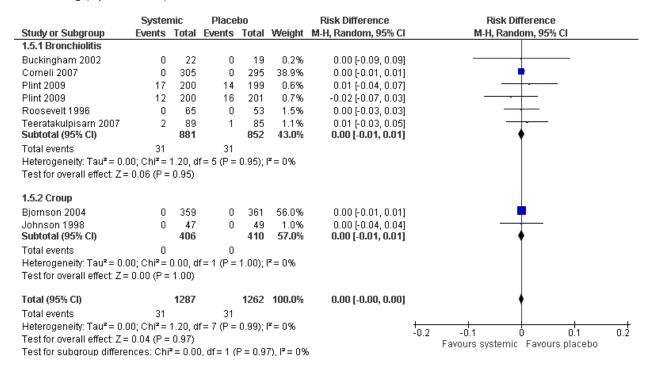
#### GI bleeding (by dose)



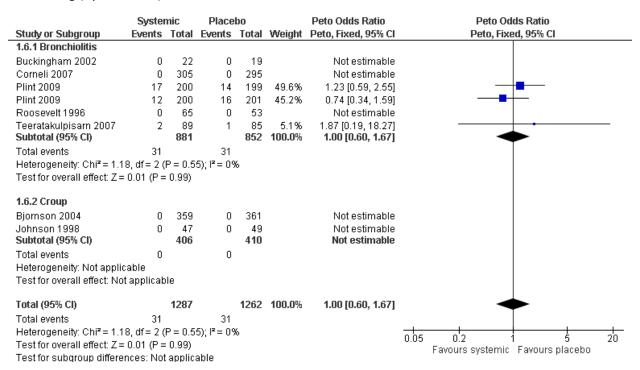
#### GI bleeding (by dose) - Peto

	Syster	nic	Place	hn		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	_				Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.4.1 Single Dose						, ,	Í
Bjornson 2004	0	359	0	361		Not estimable	
Corneli 2007	0	305	0	295		Not estimable	
Johnson 1998	0	47	0	49		Not estimable	
Teeratakulpisarn 2007	2	89	1	85	5.1%	1.87 [0.19, 18.27]	
Subtotal (95% CI)		800		790	5.1%	1.87 [0.19, 18.27]	
Total events	2		1				
Heterogeneity: Not applic	cable						
Test for overall effect: Z=	0.54 (P =	0.59)					
1.4.2 Multi-Dose							
Buckingham 2002	0	22	0	19		Not estimable	
Plint 2009	17	200	14	199	49.6%	1.23 [0.59, 2.55]	
Plint 2009	12	200	16	201	45.2%	0.74 [0.34, 1.59]	_ <del></del>
Roosevelt 1996	0	65	0	53	40.270	Not estimable	
Subtotal (95% CI)	·	487	·	472	94.9%	0.96 [0.57, 1.64]	•
Total events	29		30				Ī
Heterogeneity: Chi <sup>2</sup> = 0.8		P = 0.3	5): $I^2 = 09$	6			
Test for overall effect: Z=			-,,				
Total (95% CI)		1287		1262	100.0%	1.00 [0.60, 1.67]	•
Total events	31		31			,,	Ţ
Heterogeneity: Chi <sup>2</sup> = 1.1		P = 0.5		6			
Test for overall effect: Z=			-,,. 0.	•			0.02 0.1 1 10 50
Test for subgroup differe	•		1. df = 1 (	P = 0.5	8), I <sup>2</sup> = 0%	5	Favours systemic Favours placebo

#### GI bleeding (by condition)



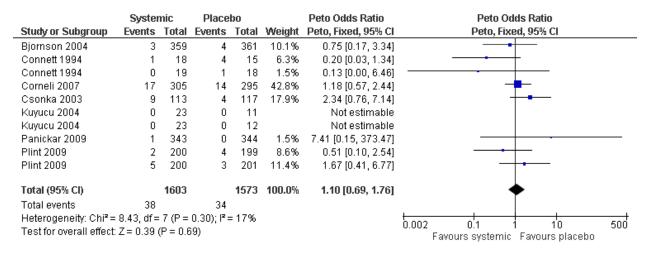
#### GI bleeding (by condition) - Peto



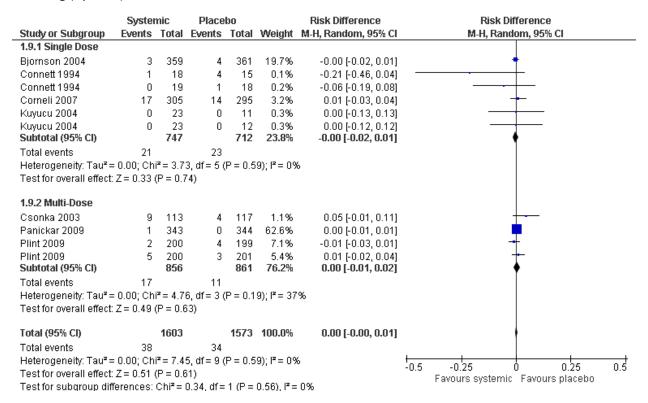
# Vomiting

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	3	359	4	361	19.7%	-0.00 [-0.02, 0.01]	+
Connett 1994	1	18	4	15	0.1%	-0.21 [-0.46, 0.04]	<del></del>
Connett 1994	0	19	1	18	0.2%	-0.06 [-0.19, 0.08]	<del></del>
Corneli 2007	17	305	14	295	3.2%	0.01 [-0.03, 0.04]	<del></del>
Csonka 2003	9	113	4	117	1.1%	0.05 [-0.01, 0.11]	<del> </del>
Kuyucu 2004	0	23	0	11	0.3%	0.00 [-0.13, 0.13]	
Kuyucu 2004	0	23	0	12	0.3%	0.00 [-0.12, 0.12]	<del></del>
Panickar 2009	1	343	0	344	62.6%	0.00 [-0.01, 0.01]	
Plint 2009	2	200	4	199	7.1%	-0.01 [-0.03, 0.01]	+
Plint 2009	5	200	3	201	5.4%	0.01 [-0.02, 0.04]	+
Total (95% CI)		1603		1573	100.0%	0.00 [-0.00, 0.01]	•
Total events	38		34				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	$i^2 = 7.4$	5, df = 9 (	P = 0.5	9); $I^2 = 09$	%	
Test for overall effect:	Z = 0.51	(P = 0.6)	61)				-0.2 -0.1 0 0.1 0.2 Fayours systemic Fayours placebo
							r avoaro oyoternie i avoaro piacebo

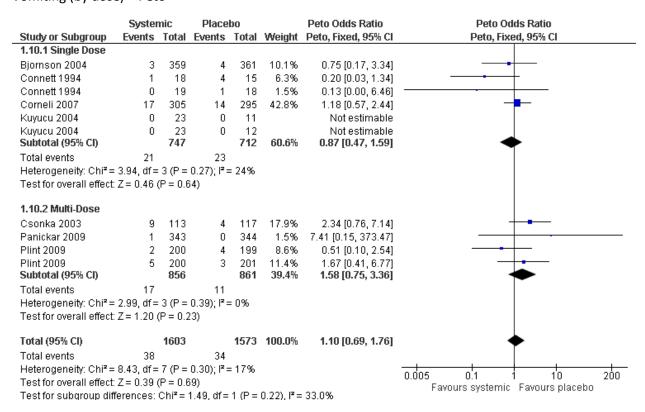
# Vomiting - Peto



#### Vomiting (by dose)



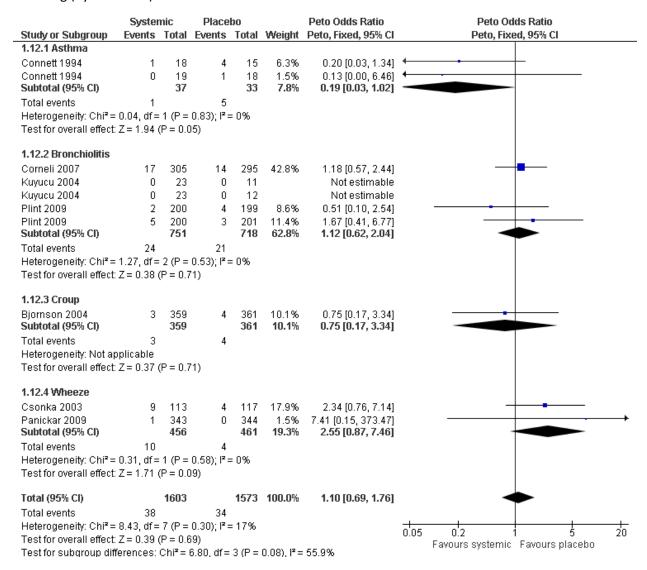
#### Vomiting (by dose) - Peto



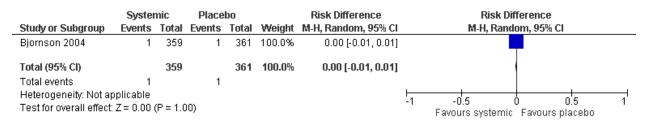
# Vomiting (by condition)

	Syster		Place			Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
1.11.1 Asthma							
Connett 1994	1	18	4	15	0.1%	-0.21 [-0.46, 0.04]	-
Connett 1994	0	19	1	18	0.2%	-0.06 [-0.19, 0.08]	
Subtotal (95% CI)		37		33	0.3%	-0.11 [-0.27, 0.06]	
Total events	1		5				
Heterogeneity: Tau² =				P = 0.2	(2); <b>I²</b> = 33	1%	
Test for overall effect:	Z = 1.28	(P = 0.2)	20)				
1.11.2 Bronchiolitis							
Corneli 2007	17	305	14	295	3.2%	0.01 [-0.03, 0.04]	+
Kuyucu 2004	0	23	0	11	0.3%	0.00 [-0.13, 0.13]	
Kuyucu 2004	0	23	0	12	0.3%	0.00 [-0.12, 0.12]	
Plint 2009	2	200	4	199	7.1%	-0.01 [-0.03, 0.01]	-
Plint 2009	5	200	3	201	5.4%	0.01 [-0.02, 0.04]	+
Subtotal (95% CI)		751		718	16.3%	0.00 [-0.02, 0.02]	<b>♦</b>
Total events	24		21				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i² = 1.5	4, df = 4 (	P = 0.8	2); <b>I²</b> = 09	6	
Test for overall effect:	Z = 0.07	(P = 0.9)	34)				
1.11.3 Croup							
Biornson 2004	3	359	4	361	19.7%	-0.00 [-0.02, 0.01]	<b>+</b>
Subtotal (95% CI)	·	359	7	361	19.7%	-0.00 [-0.02, 0.01]	•
Total events	3		4				
Heterogeneity: Not ap	-						
Test for overall effect:	•	(P = 0.7)	<sup>7</sup> 1)				
1.11.4 Wheeze							
		440		447	4.400	0.051.0.04.0.441	
Csonka 2003	9	113	4	117	1.1%	0.05 [-0.01, 0.11]	
Panickar 2009 Subtotal (95% CI)	1	343 <b>456</b>	0	344 461	62.6% <b>63.8</b> %	0.00 [-0.01, 0.01] <b>0.02 [-0.06, 0.11]</b>	
Total events	10	430	4	401	03.070	0.02 [-0.00, 0.11]	
Heterogeneity: Tau²=		z_ 7 0		n = 0.0	05313=0	170	
Test for overall effect:				r – 0.0	00),1 = 0	17 70	
TOSTION OVERAIL CITECT.	2-0.50	, - 0.0	′'/				
Total (95% CI)		1603		1573	100.0%	0.00 [-0.00, 0.01]	
Total events	38		34			- · · · ·	
Heterogeneity: Tau <sup>2</sup> =		$i^2 = 7.4$		P = 0.5	9); <b>I</b> ²= 09	6	-0.5 -0.25 0 0.25 0.5
Test for overall effect:							
Test for subgroup diffe	erences:	Chi²=	1.99, df=	3 (P =	0.58), l <sup>z</sup> =	: 0%	Favours systemic Favours placebo

#### Vomiting (by condition) - Peto



#### Abdominal pain



#### Abdominal pain - Peto

	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Bjornson 2004	1	359	1	361	100.0%	1.01 [0.06, 16.11]	
Total (95% CI)		359		361	100.0%	1.01 [0.06, 16.11]	
Total events	1		1				
Heterogeneity: Not ap Test for overall effect:	•	(P = 1.0	00)				0.01 0.1 1 10 100 Favours systemic Favours placebo

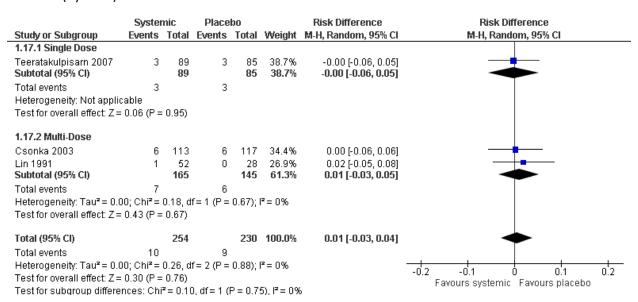
#### Diarrhea

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Csonka 2003	6	113	6	117	34.4%	0.00 [-0.06, 0.06]	<del></del>
Lin 1991	1	52	0	28	26.9%	0.02 [-0.05, 0.08]	<del>-   • -</del>
Teeratakulpisarn 2007	3	89	3	85	38.7%	-0.00 [-0.06, 0.05]	<del>-</del>
Total (95% CI)		254		230	100.0%	0.01 [-0.03, 0.04]	<b>*</b>
Total events	10		9				
Heterogeneity: Tau² = 0.0	00; Chi²=	0.26, d	f= 2 (P=	0.88);	l² = 0%		-0.2 -0.1 0 0.1 0.2
Test for overall effect: Z=	0.30 (P =	0.76)					Favours systemic Favours placebo

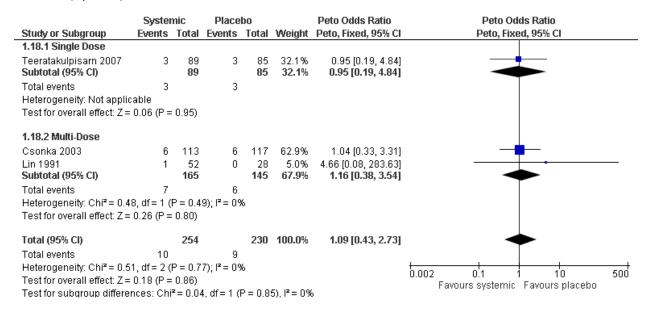
#### Diarrhea - Peto

	Syster	mic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% Cl	Peto, Fixed, 95% CI
Csonka 2003	6	113	6	117	62.9%	1.04 [0.33, 3.31]	<del></del>
Lin 1991	1	52	0	28	5.0%	4.66 [0.08, 283.63]	<del></del>
Teeratakulpisarn 2007	3	89	3	85	32.1%	0.95 [0.19, 4.84]	<del></del>
Total (95% CI)		254		230	100.0%	1.09 [0.43, 2.73]	<b>*</b>
Total events	10		9				
Heterogeneity: Chi² = 0.5 Test for overall effect: Z =			7); I² = 09	6			0.005 0.1 1 10 200 Favours systemic Favours placebo

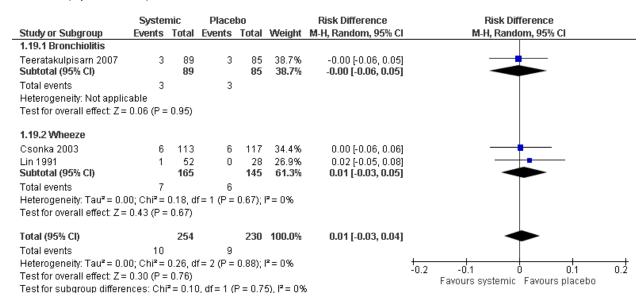
#### Diarrhea (by dose)



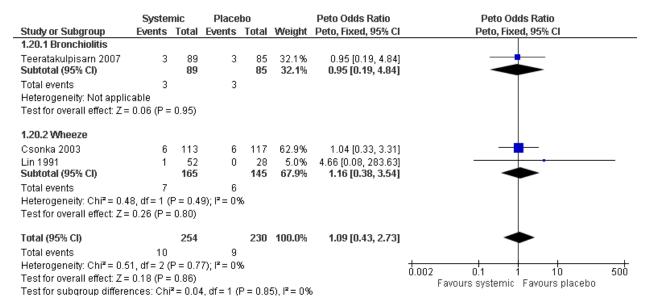
#### Diarrhea (by dose) - Peto



#### Diarrhea (by condition)



# Diarrhea (by condition) - Peto

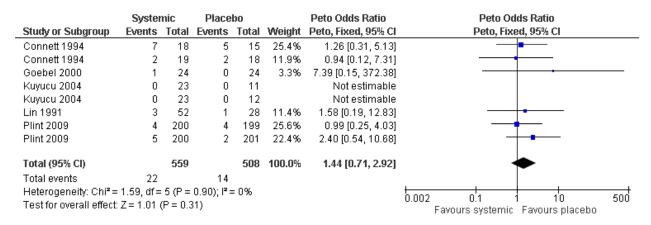


#### SYSTEMIC vs. PLACEBO - CNS & Behaviour

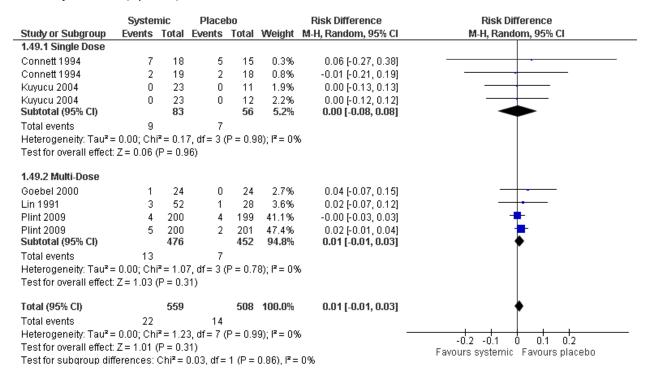
# Tremor/jitteriness

	Syster	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Connett 1994	7	18	5	15	0.3%	0.06 [-0.27, 0.38]	
Connett 1994	2	19	2	18	0.8%	-0.01 [-0.21, 0.19]	
Goebel 2000	1	24	0	24	2.7%	0.04 [-0.07, 0.15]	<del> </del>
Kuyucu 2004	0	23	0	11	1.9%	0.00 [-0.13, 0.13]	
Kuyucu 2004	0	23	0	12	2.2%	0.00 [-0.12, 0.12]	<del></del>
Lin 1991	3	52	1	28	3.6%	0.02 [-0.07, 0.12]	<del></del>
Plint 2009	4	200	4	199	41.1%	-0.00 [-0.03, 0.03]	<b>+</b>
Plint 2009	5	200	2	201	47.4%	0.02 [-0.01, 0.04]	<u></u>
Total (95% CI)		559		508	100.0%	0.01 [-0.01, 0.03]	<b>•</b>
Total events	22		14				
Heterogeneity: Tau² =	= 0.00; Ch	i²= 1.2	3, df = 7 (	P = 0.9	9); I² = 09	6	-0.5 -0.25 0 0.25 0.5
Test for overall effect:	Z=1.01	(P = 0.3)	31)				Favours systemic Favours placebo

# Tremor/jitteriness - Peto



# Tremor/jitteriness (by dose)



# Tremor/jitteriness (by dose) - Peto

Study or Subgroup				bo		Peto Odds Ratio	Peto Odds Ratio
	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.50.1 Single Dose							
Connett 1994	7	18	5	15	25.4%	1.26 [0.31, 5.13]	<del></del>
Connett 1994	2	19	2	18	11.9%	0.94 [0.12, 7.31]	<del></del>
Kuyucu 2004	0	23	0	11		Not estimable	
Kuyucu 2004	0	23	0	12		Not estimable	
Subtotal (95% CI)		83		56	37.3%	1.15 [0.36, 3.66]	-
Total events	9		7				
Heterogeneity: Chi² =	0.05, df=	1 (P =	0.82); l² =	= 0%			
Test for overall effect	Z = 0.24	(P = 0.8)	31)				
1.50.2 Multi-Dose							
Goebel 2000	1	24	0	24	3.3%	7.39 [0.15, 372.38]	-
Lin 1991	3	52	1	28	11.4%	1.58 [0.19, 12.83]	<del></del>
Plint 2009	4	200	4	199	25.6%	0.99 [0.25, 4.03]	<del></del> -
Plint 2009	5	200	2	201	22.4%	2.40 [0.54, 10.68]	<del> </del>
Subtotal (95% CI)		476		452	62.7%	1.65 [0.67, 4.02]	-
Total events	13		7				
Heterogeneity: Chi <sup>2</sup> =	: 1.31, df=	3 (P =	0.73); l² :	= 0%			
Test for overall effect	Z = 1.09	(P = 0.2)	27)				
							_
Total (95% CI)		559		508	100.0%	1.44 [0.71, 2.92]	<b>◆</b>
Total events	22		14				
Heterogeneity: Chi <sup>z</sup> =	: 1.59, df=	5 (P =	$0.90$ ); $I^2$ :	= 0%			0.005 0.1 1 10 200
Test for overall effect	Z = 1.01	(P = 0.3)	31)				
Test for subgroup di	ferences:	Chi <sup>z</sup> =	0.23, df=	1 (P=	0.63), I <sup>z</sup> =	: 0%	Taroaro oyotonno Taroaro piacoso
Connett 1994 Kuyucu 2004 Kuyucu 2004 Subtotal (95% CI) Total events Heterogeneity: Chi²= Test for overall effect  1.50.2 Multi-Dose Goebel 2000 Lin 1991 Plint 2009 Plint 2009 Subtotal (95% CI) Total events Heterogeneity: Chi²= Test for overall effect  Total (95% CI) Total events Heterogeneity: Chi²= Test for overall effect	2 0 0 9 0.05, df= Z= 0.24 1 3 4 5 1.31, df= : Z= 1.09 22 :1.59, df= : Z= 1.01	19 23 23 83 83 11 (P = 0.8 24 52 200 200 476 15 (P = 0.2 559 15 (P = 0.3 15 (P	2 0 0 7 0.82);  == 31) 0 1 4 2 7 0.73);  == 27) 14 0.90);  == 31)	18 11 12 56 = 0% 24 28 199 201 452 = 0% 508 = 0%	37.3% 37.3% 3.3% 11.4% 25.6% 22.4% 62.7%	0.94 [0.12, 7.31] Not estimable Not estimable 1.15 [0.36, 3.66]  7.39 [0.15, 372.38] 1.58 [0.19, 12.83] 0.99 [0.25, 4.03] 2.40 [0.54, 10.68] 1.65 [0.67, 4.02]	0.005 0.1 10 200 Favours systemic Favours placebo

# Tremor/jitteriness (by condition)

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.51.1 Asthma							
Connett 1994	7	18	5	15	0.3%	0.06 [-0.27, 0.38]	<del></del>
Connett 1994	2	19	2	18	0.8%	-0.01 [-0.21, 0.19]	
Subtotal (95% CI)		37		33	1.1%	0.01 [-0.16, 0.18]	
Total events	9		7				
Heterogeneity: Tau² =	0.00; Ch	$i^2 = 0.1$	2, df = 1 (	P = 0.7	3); $I^2 = 09$	6	
Test for overall effect:	Z = 0.12	(P = 0.9)	30)				
1.51.2 Bronchiolitis							
Goebel 2000	1	24	0	24	2.7%	0.04 [-0.07, 0.15]	
Kuyucu 2004	Ö	23	Ö	11	1.9%	0.00 [-0.13, 0.13]	
Kuyucu 2004	0	23	0	12	2.2%	0.00 [-0.12, 0.12]	
Plint 2009	4	200	4	199	41.1%	-0.00 [-0.03, 0.03]	<b>+</b>
Plint 2009	5	200	2	201	47.4%	0.02 [-0.01, 0.04]	•
Subtotal (95% CI)		470		447	95.4%	0.01 [-0.01, 0.03]	<b>*</b>
Total events	10		6				
Heterogeneity: Tau <sup>z</sup> =	0.00; Ch	i² = 1.0	3, df = 4 (	P = 0.9	1); $I^2 = 09$	%	
Test for overall effect:	Z= 0.93	(P = 0.3)	35)				
1.51.3 Wheeze							
Lin 1991	3	52	1	28	3.6%	0.02 [-0.07, 0.12]	
Subtotal (95% CI)		52		28	3.6%	0.02 [-0.07, 0.12]	-
Total events	3		1				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z= 0.46	(P = 0.6)	64)				
Total (95% CI)		559		508	100.0%	0.01 [-0.01, 0.03]	<b>*</b>
Total events	22		14				
Heterogeneity: Tau² =	0.00; Ch	i²=1.2	3, df = 7 (	P = 0.9	9); <b>I²</b> = 09	6	-0.2 -0.1 0 0.1 0.2
Test for overall effect:	Z = 1.01	(P = 0.3)	31)				Favours systemic Favours placebo
Test for subgroup diff	erences:	Chi <sup>2</sup> =	0.08, df=	2(P =	$0.96$ ), $I^2 =$	: 0%	r around dysterning it around placebo

# Tremor/jitteriness (by condition) – Peto

	Syster		Place			Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% Cl
1.52.1 Asthma							
Connett 1994	7	18	5	15	25.4%	1.26 [0.31, 5.13]	<del>-</del>
Connett 1994	2	19	2	18	11.9%	0.94 [0.12, 7.31]	
Subtotal (95% CI)		37		33	37.3%	1.15 [0.36, 3.66]	<b>—</b>
Total events	9		7				
Heterogeneity: Chi²=		,		= 0%			
Test for overall effect:	Z = 0.24	P = 0.8	81)				
1.52.2 Bronchiolitis							
Goebel 2000	1	24	0	24	3.3%	7.39 [0.15, 372.38]	-
Kuyucu 2004	0	23	0	11		Not estimable	
Kuyucu 2004	0	23	0	12		Not estimable	
Plint 2009	4	200	4	199	25.6%	0.99 [0.25, 4.03]	<del></del>
Plint 2009	5	200	2	201	22.4%	2.40 [0.54, 10.68]	<del> </del>
Subtotal (95% CI)		470		447	51.3%	1.66 [0.62, 4.46]	<b>◆</b>
Total events	10		6				
Heterogeneity: Chi²=	1.31, df=	2 (P=	0.52); l² =	= 0%			
Test for overall effect:	Z = 1.01	(P = 0.3)	31)				
1.52.3 Wheeze							
Lin 1991	3	52	1	28	11.4%	1.58 [0.19, 12.83]	
Subtotal (95% CI)		52		28	11.4%	1.58 [0.19, 12.83]	
Total events	3		1				
Heterogeneity: Not ap							
Test for overall effect:	Z = 0.43	P = 0.8	i7)				
Total (95% CI)		559		508	100.0%	1.44 [0.71, 2.92]	<b>*</b>
Total events	22		14				
Heterogeneity: Chi <sup>z</sup> =	1.59, df=	5 (P=	0.90); l <sup>z</sup> :	= 0%			0.002 0.1 1 10 500
Test for overall effect:	Z = 1.01 (	P = 0.3	31)				Favours systemic Favours placebo
Test for subgroup diffe	erences:	Chi²=	0.23, df=	2 (P =	0.89), I <b>z</b> =	0%	r around dysternic in around praceut

# Behaviour change

	Syster	mic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	1	359	1	361	70.0%	0.00 [-0.01, 0.01]	
Csonka 2003	3	113	2	117	11.0%	0.01 [-0.03, 0.05]	<del></del>
Klassen 1998	0	64	0	65	16.5%	0.00 [-0.03, 0.03]	<del>-</del>
Lin 1991	3	52	0	28	2.6%	0.06 [-0.02, 0.14]	
Total (95% CI)		588		571	100.0%	0.00 [-0.01, 0.02]	•
Total events	7		3				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 3.7	2, df = 3 (	P = 0.2	$(9); I^2 = 19$	% -	14 005 0 005 04
Test for overall effect	Z= 0.37	(P = 0.7)	'1)				-0.1 -0.05 0 0.05 0.1 Favours systemic Favours placebo

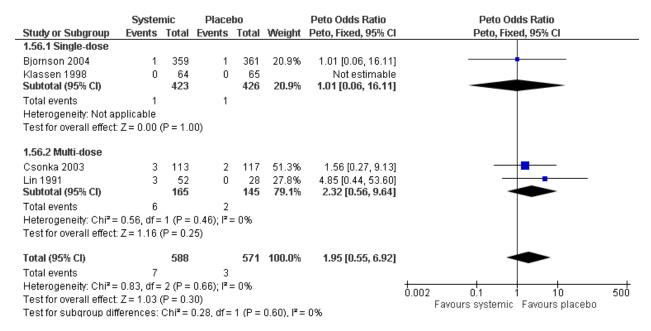
# Behaviour change – Peto

	Syster	mic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Bjornson 2004	1	359	1	361	20.9%	1.01 [0.06, 16.11]	
Csonka 2003	3	113	2	117	51.3%	1.56 [0.27, 9.13]	<del>-  </del>
Klassen 1998	0	64	0	65		Not estimable	
Lin 1991	3	52	0	28	27.8%	4.85 [0.44, 53.60]	-
Total (95% CI)		588		571	100.0%	1.95 [0.55, 6.92]	-
Total events	7		3				
Heterogeneity: Chi²=	0.83, df =	2 (P =	0.66); l² =	= 0%			0.000 04 4 40 500
Test for overall effect:	Z=1.03	(P = 0.3)	30)				0.002 0.1 1 10 500 Favours systemic Favours placebo

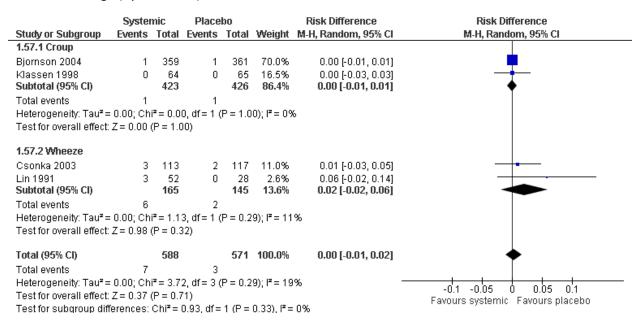
# Behaviour change (by dose)

	Syster	nic	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.55.1 Single-dose							
Bjornson 2004	1	359	1	361	70.0%	0.00 [-0.01, 0.01]	
Klassen 1998	0	64	0	65	16.5%	0.00 [-0.03, 0.03]	<del>-  </del>
Subtotal (95% CI)		423		426	86.4%	0.00 [-0.01, 0.01]	<b>•</b>
Total events	1		1				
Heterogeneity: Tau² =	0.00; Ch	$i^2 = 0.01$	0, df = 1 (	P = 1.0	$0); I^2 = 09$	6	
Test for overall effect:	Z = 0.00	(P = 1.0)	00)				
1.55.2 Multi-dose							
Csonka 2003	3	113	2	117	11.0%	0.01 [-0.03, 0.05]	<del></del>
Lin 1991	3	52	0	28	2.6%	0.06 [-0.02, 0.14]	<del>                                     </del>
Subtotal (95% CI)		165		145	13.6%	0.02 [-0.02, 0.06]	<b>—</b>
Total events	6		2				
Heterogeneity: Tau² =	0.00; Ch	i² = 1.13	3, df = 1 (	P = 0.2	9); I² = 11	%	
Test for overall effect:	Z = 0.98	(P = 0.3)	32)				
Total (DEII) CIV		588		E74	100.0%	0.00 [-0.01, 0.02]	_
Total (95% CI)	_	300	_	371	100.078	0.00 [-0.01, 0.02]	Y
Total events	7		3				
Heterogeneity: Tau <sup>2</sup> =				P = 0.2	9);	96 –	-0.1 -0.05 0 0.05 0.1
Test for overall effect:		•	,				Favours systemic Favours placebo
Test for subgroup diff	erences:	Chi²=1	0.93, df=	1 (P =	$0.33$ ), $I^2 =$	: 0%	,

#### Behaviour change (by dose) - Peto



#### Behaviour change (by condition)



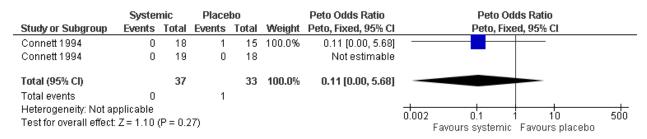
# Behaviour change (by condition) – Peto

	Syster	mic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.58.1 Croup							
Bjornson 2004	1	359	1	361	20.9%	1.01 [0.06, 16.11]	
Klassen 1998	0	64	0	65		Not estimable	
Subtotal (95% CI)		423		426	20.9%	1.01 [0.06, 16.11]	
Total events	1		1				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.00	(P = 1.0)	00)				
1.58.2 Wheeze							
Csonka 2003	3	113	2	117	51.3%	1.56 [0.27, 9.13]	<del>-  </del>
Lin 1991	3	52	0	28	27.8%	4.85 [0.44, 53.60]	<del>-</del>
Subtotal (95% CI)		165		145	79.1%	2.32 [0.56, 9.64]	
Total events	6		2				
Heterogeneity: Chi²=	0.56, df =	1 (P=	0.46); l² =	= 0%			
Test for overall effect:	Z = 1.16	(P = 0.2)	25)				
Total (95% CI)		588		571	100.0%	1.95 [0.55, 6.92]	-
Total events	7		3				
Heterogeneity: Chi <sup>2</sup> =	0.83, df =	2 (P =	0.66);	= 0%			0.005 0.1 1 10 200
Test for overall effect:	Z = 1.03	(P = 0.3)	30)				0.005 0.1 1 10 200 Favours systemic Favours placebo
Test for subgroup diff	erences:	Chi <sup>z</sup> =	0.28, df=	1 (P=	$0.60$ ), $I^2 =$	: 0%	i avoui a ayateiiiic - Favoui a piacebo

#### Headache

	Systemic Placebo			Risk Difference	Risk Difference		
Study or Subgroup	Events Total Events Total			Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Connett 1994	0	18	1	15	27.8%	-0.07 [-0.23, 0.09]	-
Connett 1994	0	19	0	18	72.2%	0.00 [-0.10, 0.10]	<del></del>
Total (95% CI)		37		33	100.0%	-0.02 [-0.10, 0.07]	
Total events	0		1				
Heterogeneity: Tau² = Test for overall effect:				P = 0.4	5); I² = 09	6	-0.2 -0.1 0 0.1 0.2 Favours systemic Favours placebo

#### Headache – Peto

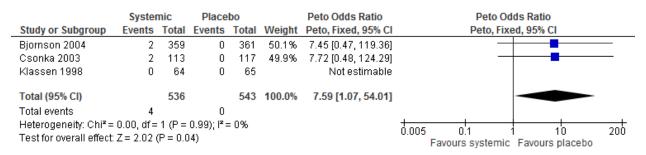


#### SYSTEMIC vs. PLACEBO – Dermatologic

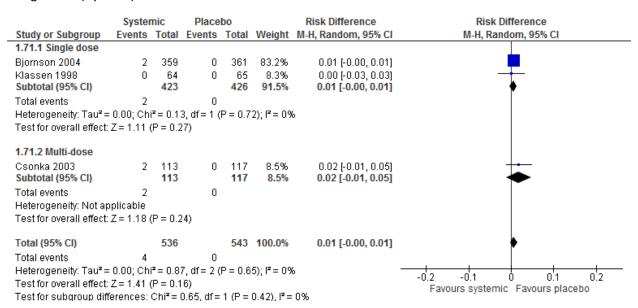
#### Integument

	Systemic Placebo		Systemic Placebo Risk Difference		Risk Difference	Risk Difference		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Bjornson 2004	2	359	0	361	83.2%	0.01 [-0.00, 0.01]		
Csonka 2003	2	113	0	117	8.5%	0.02 [-0.01, 0.05]	+-	
Klassen 1998	0	64	0	65	8.3%	0.00 [-0.03, 0.03]	+	
Total (95% CI)		536		543	100.0%	0.01 [-0.00, 0.01]	•	
Total events	4		0					
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Ch	$i^2 = 0.8^\circ$	7, df = 2 (	P = 0.6	5); I² = 09	6	-0.2 -0.1 0 0.1 0.2	
Test for overall effect	Z = 1.41	(P = 0.1)	6)				Favours systemic Favours placebo	

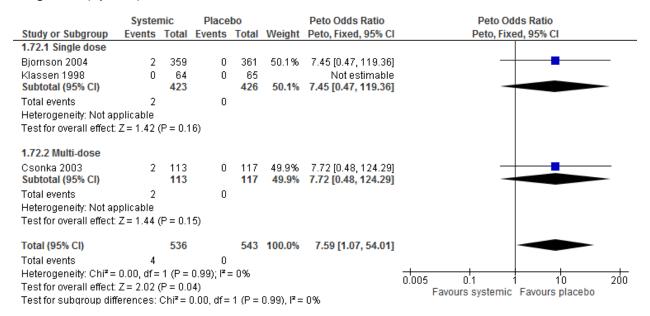
#### Integument - Peto



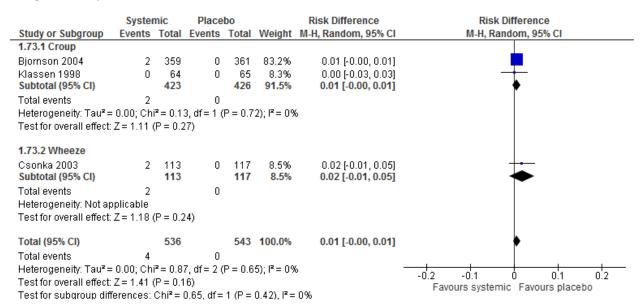
#### Integument (by dose)



#### Integument (by dose) - Peto



#### Integument (by condition)



# Integument (by condition) – Peto

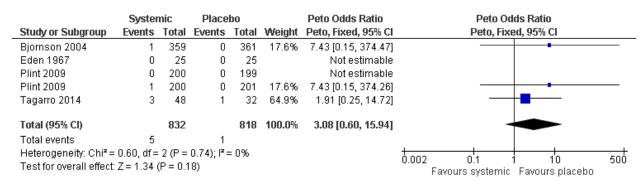
	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.74.1 Croup							
Bjornson 2004	2	359	0	361	50.1%	7.45 [0.47, 119.36]	<del>                                     </del>
Klassen 1998	0	64	0	65		Not estimable	
Subtotal (95% CI)		423		426	50.1%	7.45 [0.47, 119.36]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.42 (	(P = 0.1)	6)				
1.74.2 Wheeze							
Csonka 2003	2	113	0	117	49.9%	7.72 [0.48, 124.29]	
Subtotal (95% CI)		113		117	49.9%	7.72 [0.48, 124.29]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.44 (	(P = 0.1)	5)				
Total (95% CI)		536		543	100.0%	7.59 [1.07, 54.01]	
Total events	4		0				
Heterogeneity: Chi²=	0.00, df=	1 (P =	0.99); [*=	= 0%			0.005 0.1 1 10 200
Test for overall effect:	Z = 2.02 (	(P = 0.0)	14)				Favours systemic Favours placebo
Test for subgroup diff	erences:	Chi <sup>z</sup> =1	0.00, df=	1 (P=	0.99), l <sup>z</sup> =	0%	

#### SYSTEMIC vs. PLACEBO - Endocrine/Metabolic & Musculoskeletal

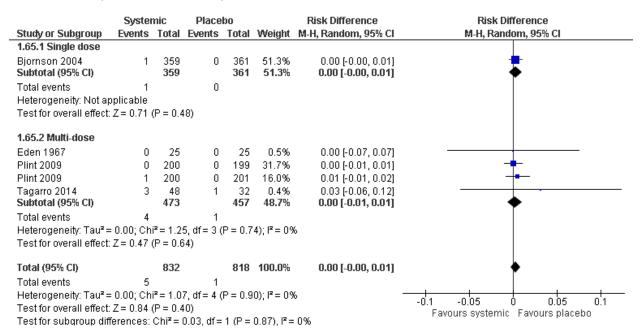
#### Fluid & electrolyte abnormalities

	Systemic Placebo			Risk Difference	Risk Difference		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bjornson 2004	1	359	0	361	51.3%	0.00 [-0.00, 0.01]	•
Eden 1967	0	25	0	25	0.5%	0.00 [-0.07, 0.07]	
Plint 2009	0	200	0	199	31.7%	0.00 [-0.01, 0.01]	+
Plint 2009	1	200	0	201	16.0%	0.01 [-0.01, 0.02]	+
Tagarro 2014	3	48	1	32	0.4%	0.03 [-0.06, 0.12]	
Total (95% CI)		832		818	100.0%	0.00 [-0.00, 0.01]	•
Total events	5		1				
Heterogeneity: Tau² =	: 0.00; Ch	i² = 1.0	7, df = 4 (	P = 0.9	0); I² = 0%	6	-0.2 -0.1 0 0.1 0.2
Test for overall effect:	Z = 0.84	(P = 0.4)	10)				Favours systemic Favours placebo

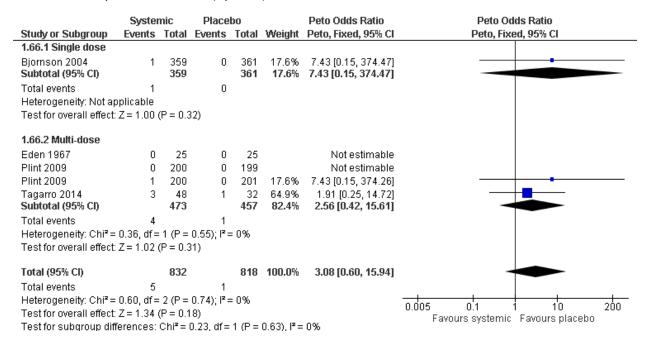
#### Fluid & electrolyte abnormalities - Peto



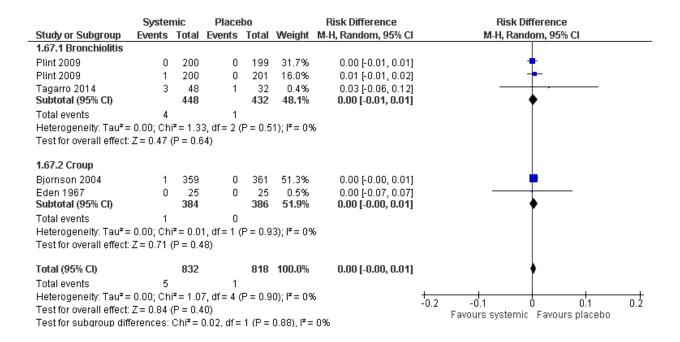
#### Fluid & electrolyte abnormalities (by dose)



Fluid & electrolyte abnormalities (by dose) - Peto



Fluid & electrolyte abnormalities (by condition)



Fluid & electrolyte abnormalities (by condition) - Peto

	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI		
1.68.1 Bronchiolitis									
Plint 2009	0	200	0	199		Not estimable			
Plint 2009	1	200	0	201	17.6%	7.43 [0.15, 374.26]	-		
Tagarro 2014	3	48	1	32	64.9%	1.91 [0.25, 14.72]			
Subtotal (95% CI)		448		432	82.4%	2.56 [0.42, 15.61]			
Total events	4		1						
Heterogeneity: Chi²=	0.36, df=	1 (P=	0.55); l² =	= 0%					
Test for overall effect:	Z = 1.02 (	(P = 0.3)	31)						
4.00.0.0									
1.68.2 Croup									
Bjornson 2004	1	359	0	361	17.6%		-		
Eden 1967	0	25	0	25	47 000	Not estimable			
Subtotal (95% CI)		384		386	17.6%	7.43 [0.15, 374.47]			
Total events	1		0						
Heterogeneity: Not ap									
Test for overall effect:	Z = 1.00	(P = 0.3)	32)						
Total (95% CI)		832		040	100.0%	3.08 [0.60, 15.94]			
	_	OJZ		010	100.078	3.00 [0.00, 13.94]			
Total events	5	0.75	7	001					
Heterogeneity: Chi <sup>2</sup> =		•		= 0%			0.002 0.1 1 10 500		
Test for overall effect:		•					Favours systemic Favours placebo		
Test for subgroup diffi	erences:	Chi²=1	0.23, df=	1 (P=	$0.63$ ), $I^2 =$	: 0%	•		

#### SYSTEMIC vs. PLACEBO - Cardiovascular

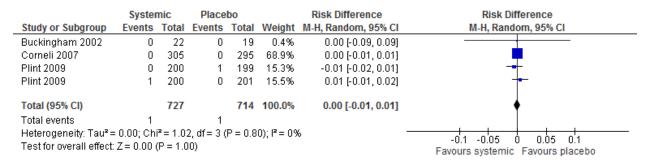
#### Arrhythmia

	Systemic Placebo			Risk Difference	Risk Difference		
Study or Subgroup	Events	vents Total Events Total Weight M-H, Random, 95% CI M-H, Random, 95% CI				M-H, Random, 95% CI	
Daugbjerg 1993	0	31	0	27	100.0%	0.00 [-0.07, 0.07]	
Total (95% CI)		31		27	100.0%	0.00 [-0.07, 0.07]	
Total events	0		0				
Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)							-0.2 -0.1 0 0.1 0.2 Favours systemic Favours placebo

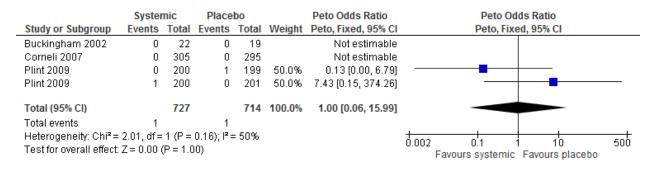
#### Arrhythmia - Peto

	Systemic Placebo		Peto Odds Ratio			Peto Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixe	ed, 95% CI	
Daugbjerg 1993	0	31	0	27		Not estimable				
Total (95% CI)		31		27		Not estimable				
Total events	0		0							
Heterogeneity: Not applicable							0.05	n 2	<u> </u>	20
Test for overall effect: Not applicable							0.00	Favours systemic	Favours placebo	20

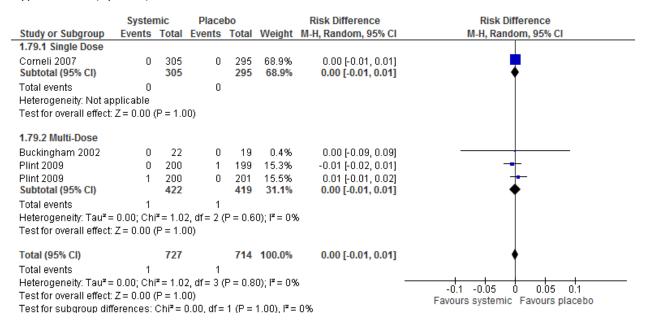
# Hypertension



# Hypertension - Peto



### Hypertension (by dose)



### Hypertension (by dose) - Peto

	Systemic Placebo			Peto Odds Ratio	Peto Odds Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI			
1.81.1 Single Dose										
Corneli 2007 Subtotal (95% CI)	0	305 <b>305</b>	0	295 <b>295</b>		Not estimable Not estimable				
Total events	0		0							
Heterogeneity: Not a	pplicable									
Test for overall effect	: Not appli	cable								
4 04 2 Multi Dogo										
1.81.2 Multi-Dose										
Buckingham 2002	0	22	0	19		Not estimable	_			
Plint 2009	0	200	1	199	50.0%	0.13 [0.00, 6.79]				
Plint 2009	1	200	0	201	50.0%	7.43 [0.15, 374.26]	<del></del>			
Subtotal (95% CI)		422		419	100.0%	1.00 [0.06, 15.99]				
Total events	1		1							
Heterogeneity: Chi <sup>2</sup> =	= 2.01. df=	1 (P =	0.16); l <sup>2</sup> =	= 50%						
Test for overall effect		•								
			,							
Total (95% CI)		727		714	100.0%	1.00 [0.06, 15.99]				
Total events	1		1							
Heterogeneity: Chi <sup>2</sup> =	= 2.01, df=	1 (P=	0.16);	= 50%			0.002 0.1 1 10 500			
Test for overall effect	: Z = 0.00 i	(P = 1.0)	00)							
Test for subgroup dit		•	•				Favours systemic Favours placebo			
. ccc. babaloap an	rest for subgroup differences. Not applicable									

### Congestive heart failure



# Congestive heart failure - Peto

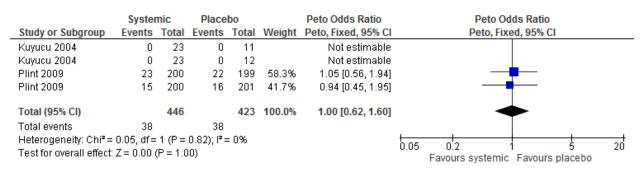
	Syster	nic	Place	bo		Peto Odds Ratio		Peto Od	ds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixe	ed, 95% CI	
Eden 1967	0	25	0	25		Not estimable				
Total (95% CI)		25		25		Not estimable				
Total events	0		0							
Heterogeneity: Not applicable Test for overall effect: Not applicable							0.05	0.2 Favours systemic	5 Favours placebo	20

#### SYSTEMIC vs. PLACEBO - General

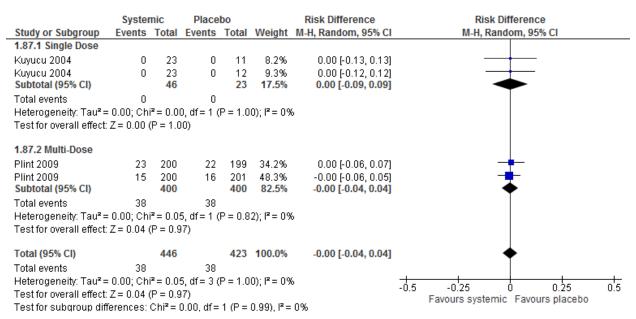
### General complaints

	Syster	mic	Place	bo		Risk Difference		Risk Difference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI	
Kuyucu 2004	0	23	0	11	8.2%	0.00 [-0.13, 0.13]			
Kuyucu 2004	0	23	0	12	9.3%	0.00 [-0.12, 0.12]			
Plint 2009	23	200	22	199	34.2%	0.00 [-0.06, 0.07]		<del></del>	
Plint 2009	15	200	16	201	48.3%	-0.00 [-0.06, 0.05]		+	
Total (95% CI)		446		423	100.0%	-0.00 [-0.04, 0.04]		<b>+</b>	
Total events	38		38						
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	$i^2 = 0.0$	5, df = 3 (	P = 1.0	$0); I^2 = 09$	6	+-	125	<del></del>
Test for overall effect:	Z = 0.04	(P = 0.9)	17)	-0.5	-0.25 0 0.25 Favours systemic Favours placebo	0.5			

## General complaints - Peto



## General complaints (by dose)



## General complaints (by dose) – Peto

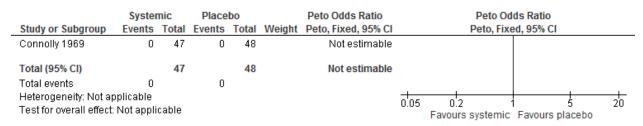
	Syster	nic	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
1.89.1 Single Dose							
Kuyucu 2004	0	23	0	11		Not estimable	
Kuyucu 2004	0	23	0	12		Not estimable	
Subtotal (95% CI)		46		23		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not appli	cable					
1.89.2 Multi-Dose							$\perp$
Plint 2009	23	200	22	199	58.3%	1.05 [0.56, 1.94]	— <del>-</del>
Plint 2009	15	200	16	201	41.7%	0.94 [0.45, 1.95]	<del></del>
Subtotal (95% CI)		400		400	100.0%	1.00 [0.62, 1.60]	•
Total events	38		38				
Heterogeneity: Chi²=	0.05, df =	1 (P=	0.82); l² =	= 0%			
Test for overall effect:	Z = 0.00 (	(P = 1.0)	10)				
							1
Total (95% CI)		446		423	100.0%	1.00 [0.62, 1.60]	•
Total events	38		38				
Heterogeneity: Chi²=	0.05, df =	1 (P=	0.1 0.2 0.5 1 2 5 10				
Test for overall effect:	Z = 0.00 (	(P = 1.0)	10)				Favours systemic Favours placebo
Test for subgroup diff	erences:	Not ap	olicable				

## **SYSTEMIC vs. PLACEBO – Immune System**

## Immunosuppression

	Systemic Placebo			bo		Risk Difference	Risk Difference			
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI			
Connolly 1969	0	47	0	48	100.0%	0.00 [-0.04, 0.04]	-			
Total (95% CI)		47		48	100.0%	0.00 [-0.04, 0.04]	<b>*</b>			
Total events	0		0							
Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)							-0.2 -0.1 0 0.1 0.2 Favours systemic Favours placebo			

## Immunosuppression – Peto



## INHALED vs. PLACEBO - Infection & Respiratory

## Severe infections

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Ducharme 2009	2	62	4	67	100.0%	-0.03 [-0.10, 0.04]	<del></del>
Total (95% CI)		62		67	100.0%	-0.03 [-0.10, 0.04]	
Total events	2		4				
Heterogeneity: Not applicable Test for overall effect: Z = 0.75 (P = 0.45)							-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

### Severe infections - Peto

	Inhal	ed	Place	bo		Peto Odds Ratio		Peto Od	ds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixe	ed, 95% CI	
Ducharme 2009	2	62	4	67	100.0%	0.54 [0.11, 2.77]				
Total (95% CI)		62		67	100.0%	0.54 [0.11, 2.77]				
Total events	2		4							
Heterogeneity: Not ap Test for overall effect:	16)				0.01	0.1 Favours inhaled	1 10 Favours placebo	100		

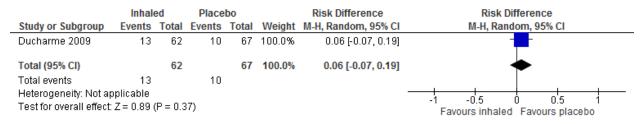
## Systemic infections

	Inhale	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Daugbjerg 1993	0	29	0	27	84.6%	0.00 [-0.07, 0.07]	<del>-</del>
Ducharme 2009	18	62	20	67	15.4%	-0.01 [-0.17, 0.15]	-
Total (95% CI)		91		94	100.0%	-0.00 [-0.06, 0.06]	•
Total events	18		20				
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 0.0$	3, df = 1 (	%	-0.2 -0.1 0 0.1 0.2		
Test for overall effect:	Z = 0.04	(P = 0.9)	17)		Favours inhaled Favours placebo		

## Systemic infections – Peto

	Inhale	ed	Place	bo		Peto Odds Ratio		Peto Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixed, 95% CI	
Daugbjerg 1993	0	29	0	27		Not estimable			
Ducharme 2009	18	62	20	67	100.0%	0.96 [0.45, 2.05]		-	
Total (95% CI)		91		94	100.0%	0.96 [0.45, 2.05]		•	
Total events	18		20						
Heterogeneity: Not ap Test for overall effect:	•	(P = 0.9	32)				0.01	0.1 1 10 Favours inhaled Favours placebo	100

## Lung/trachea



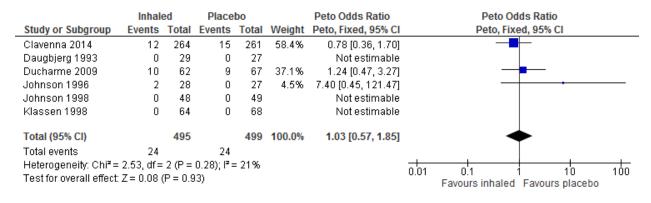
## Lung/trachea – Peto

	Inhal	ed	Place	bo		Peto Odds Ratio		Peto Od	ds Ratio		
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixe	ed, 95% CI		
Ducharme 2009	13	62	10	67	100.0%	1.51 [0.61, 3.70]		_			
Total (95% CI)		62		67	100.0%	1.51 [0.61, 3.70]		-	•		
Total events	13		10								
Heterogeneity: Not ap Test for overall effect:		(P = 0.3	37)				0.01	0.1 Favours inhaled		0 acebo	100

### URT

	Inhale	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Clavenna 2014	12	264	15	261	24.3%	-0.01 [-0.05, 0.03]	<del></del>
Daugbjerg 1993	0	29	0	27	7.7%	0.00 [-0.07, 0.07]	<del></del>
Ducharme 2009	10	62	9	67	2.3%	0.03 [-0.10, 0.15]	<del></del>
Johnson 1996	2	28	0	27	2.7%	0.07 [-0.04, 0.18]	<del></del>
Johnson 1998	0	48	0	49	22.3%	0.00 [-0.04, 0.04]	<del>-</del>
Klassen 1998	0	64	0	68	40.7%	0.00 [-0.03, 0.03]	+
Total (95% CI)		495		499	100.0%	-0.00 [-0.02, 0.02]	<b>+</b>
Total events	24		24				
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 2.13$	2, df = 5 (	P = 0.8	3); $I^2 = 0.9$	6	-0.2 -0.1 0 0.1 0.2
Test for overall effect:	Z = 0.04 (	(P = 0.9)	7)			Favours inhaled Favours placebo	

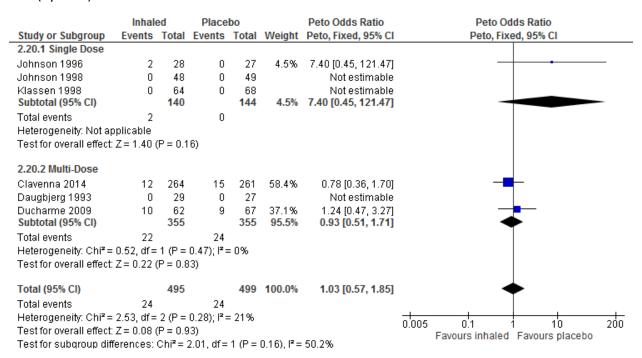
### URT - Peto



### URT (by dose)

	Inhale	ed	Place	bo		Risk Difference	Risk Difference			
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI			
2.19.1 Single Dose										
Johnson 1996	2	28	0	27	2.7%	0.07 [-0.04, 0.18]	-			
Johnson 1998	0	48	0	49	22.3%	0.00 [-0.04, 0.04]	<del></del>			
Klassen 1998	0	64	0	68	40.7%	0.00 [-0.03, 0.03]	<del></del>			
Subtotal (95% CI)		140		144	65.7%	0.00 [-0.02, 0.03]	•			
Total events	2		0							
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 2.33$	3, df = 2 (	P = 0.3	1); $I^2 = 14$	%				
Test for overall effect: 2	Z = 0.28 (	(P = 0.7)	'8)							
2.19.2 Multi-Dose										
Clavenna 2014	12	264	15	261	24.3%	-0.01 [-0.05, 0.03]	<del></del>			
Daugbjerg 1993	0	29	0	27	7.7%	0.00 [-0.07, 0.07]				
Ducharme 2009	10	62	9	67	2.3%	0.03 [-0.10, 0.15]				
Subtotal (95% CI)		355		355	34.3%	-0.01 [-0.04, 0.03]	•			
Total events	22		24							
Heterogeneity: Tau <sup>z</sup> =	0.00; Chi	$i^2 = 0.43$	3, df = 2 (	P = 0.8	1); $I^2 = 0.9$	6				
Test for overall effect:	Z = 0.41 (	(P = 0.6)	8)							
Total (95% CI)		495		499	100.0%	-0.00 [-0.02, 0.02]	<b>+</b>			
Total events	24		24							
Heterogeneity: Tau <sup>2</sup> =	Heterogeneity: Tau² = 0.00; Chi² = 2.12, df = 5 (P = 0.83); I² = 0%									
Test for overall effect: 2							-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo			
Test for subgroup differences: Chi <sup>2</sup> = 0.25, df = 1 (P = 0.62), i <sup>2</sup> = 0%										

## URT (by dose) - Peto



## URT (by condition)

	Inhale	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	<b>Events</b>	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.21.1 Croup							
Johnson 1996	2	28	0	27	2.7%	0.07 [-0.04, 0.18]	<del>                                     </del>
Johnson 1998	0	48	0	49	22.3%	0.00 [-0.04, 0.04]	<del>-</del>
Klassen 1998	0	64	0	68	40.7%	0.00 [-0.03, 0.03]	<del>-  </del> -
Subtotal (95% CI)		140		144	65.7%	0.00 [-0.02, 0.03]	•
Total events	2		0				
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 2.33$	3, df = 2 (	P = 0.3	1); $I^2 = 14$	%	
Test for overall effect:	Z = 0.28 (	(P = 0.7)	'8)				
2.21.2 Wheeze							
Clavenna 2014	12	264	15	261	24.3%	-0.01 [-0.05, 0.03]	<del></del>
Daugbjerg 1993	0	29	0	27	7.7%	0.00 [-0.07, 0.07]	<del>- +</del> -
Ducharme 2009	10	62	9	67	2.3%	0.03 [-0.10, 0.15]	
Subtotal (95% CI)		355		355	34.3%	-0.01 [-0.04, 0.03]	•
Total events	22		24				
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 0.43$	3, df = 2 (	P = 0.8	1); $I^2 = 09$	6	
Test for overall effect:	Z = 0.41 (	(P = 0.6)	8)				
							1
Total (95% CI)		495		499	100.0%	-0.00 [-0.02, 0.02]	•
Total events	24		24				
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 2.13$	2, df = 5 (	P = 0.8	3); $I^2 = 09$	6	-0.2 -0.1 0 0.1 0.2
Test for overall effect:	Z = 0.04 (	(P = 0.9)	97)				Favours inhaled Favours placebo
Test for subgroup diff	erences:	Chi² = I	0.25, df=	1 (P=	0.62), I <sup>z</sup> =	: 0%	. a.caro filitalea il avodro piacebo

## URT (by condition) – Peto

	Inhal	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
2.22.1 Croup							
Johnson 1996	2	28	0	27	4.5%	7.40 [0.45, 121.47]	-
Johnson 1998	0	48	0	49		Not estimable	
Klassen 1998	0	64	0	68		Not estimable	
Subtotal (95% CI)		140		144	4.5%	7.40 [0.45, 121.47]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.40	(P = 0.1)	6)				
2.22.2 Wheeze							
Clavenna 2014	12	264	15	261	58.4%	0.78 [0.36, 1.70]	<del></del>
Daugbjerg 1993	0	29	0	27		Not estimable	
Ducharme 2009	10	62	9	67	37.1%	1.24 [0.47, 3.27]	<del></del>
Subtotal (95% CI)		355		355	95.5%	0.93 [0.51, 1.71]	•
Total events	22		24				
Heterogeneity: Chi²=	0.52, df =	1 (P=	0.47); l² =	= 0%			
Test for overall effect:	Z = 0.22	(P = 0.8)	33)				
Total (95% CI)		495		400	100.0%	1.03 [0.57, 1.85]	
	24	433	24	433	100.070	1.03 [0.37, 1.03]	
Total events Heterogeneity: Chi²=		270-	24 0.20\:18-	- 210/			
Test for overall effect:		,		- 2170			0.05 0.2 1 5 20
Test for subgroup diff		•		1 /P -	0.16\ [2-	50.2%	Favours inhaled Favours placebo
restion sundingly and	erences.	Om =	2.01, ul =	1 (1-	0.10), 1"=	30.270	

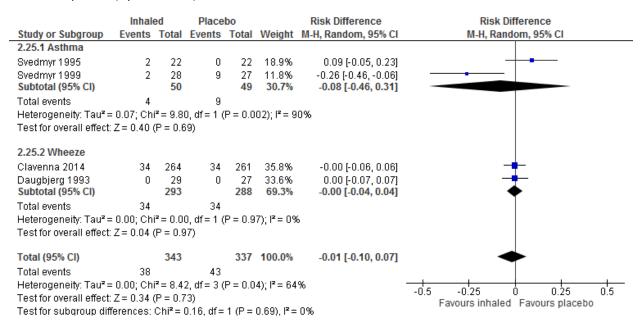
### Voice complaints

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Clavenna 2014	34	264	34	261	35.8%	-0.00 [-0.06, 0.06]	-
Daugbjerg 1993	0	29	0	27	33.6%	0.00 [-0.07, 0.07]	<del>-</del>
Svedmyr 1995	2	22	0	22	18.9%	0.09 [-0.05, 0.23]	<del>  •</del>
Svedmyr 1999	2	28	9	27	11.8%	-0.26 [-0.46, -0.06]	
Total (95% CI)		343		337	100.0%	-0.01 [-0.10, 0.07]	•
Total events	38		43				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 8.4	2, df = 3 (	P = 0.0	4); $I^2 = 64$	%	-0.5 -0.25 0 0.25 0.5
Test for overall effect:	Z= 0.34	(P = 0.7)	'3)				-0.5 -0.25 0 0.25 0.5 Favours inhaled Favours placebo

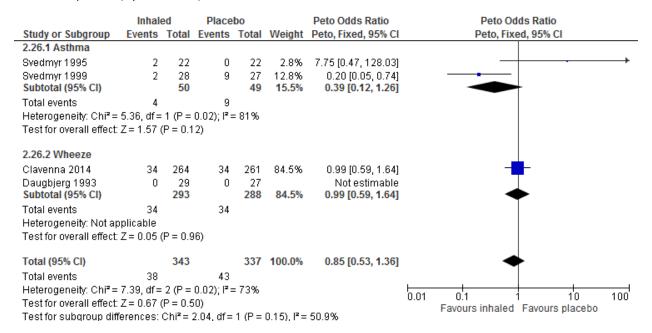
### Voice complaints - Peto

	Inhal	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Clavenna 2014	34	264	34	261	84.5%	0.99 [0.59, 1.64]	-
Daugbjerg 1993	0	29	0	27		Not estimable	
Svedmyr 1995	2	22	0	22	2.8%	7.75 [0.47, 128.03]	<del></del>
Svedmyr 1999	2	28	9	27	12.8%	0.20 [0.05, 0.74]	
Total (95% CI)		343		337	100.0%	0.85 [0.53, 1.36]	•
Total events	38		43				
Heterogeneity: Chi <sup>2</sup> =	7.39, df=	2 (P =	0.02); l² =	= 73%			
Test for overall effect:	Z = 0.67	(P = 0.5)	50)				0.01 0.1 1 10 100 Favours inhaled Favours placebo

## Voice complaints (by condition)



## Voice complaints (by condition) - Peto



### **INHALED vs. PLACEBO - GI**

## GI bleeding

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Johnson 1998	0	48	0	49	100.0%	0.00 [-0.04, 0.04]	-
Total (95% CI)		48		49	100.0%	0.00 [-0.04, 0.04]	<b>*</b>
Total events	0		0				
Heterogeneity: Not a Test for overall effect		(P = 1.0	10)				-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

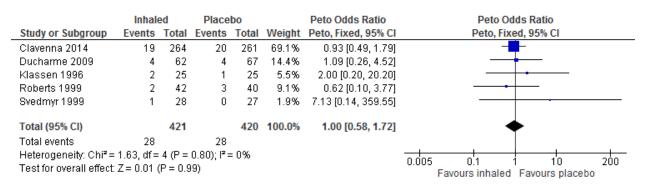
## GI bleeding - Peto

	Inhale	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Johnson 1998	0	48	0	49		Not estimable	
Total (95% CI)		48		49		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable Test for overall effect: Not applicable							0.1 0.2 0.5 1 2 5 10
1 0 0 t 10 t 0 7 C f all Cilcot.	140r appil	Cabic					Favours inhaled Favours placebo

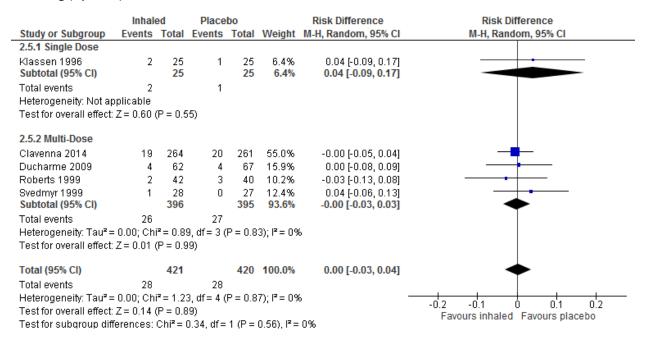
## Vomiting

	Inhale	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Clavenna 2014	19	264	20	261	55.0%	-0.00 [-0.05, 0.04]	<del></del>
Ducharme 2009	4	62	4	67	15.9%	0.00 [-0.08, 0.09]	<del></del>
Klassen 1996	2	25	1	25	6.4%	0.04 [-0.09, 0.17]	<del></del>
Roberts 1999	2	42	3	40	10.2%	-0.03 [-0.13, 0.08]	<del></del>
Svedmyr 1999	1	28	0	27	12.4%	0.04 [-0.06, 0.13]	<del></del>
Total (95% CI)		421		420	100.0%	0.00 [-0.03, 0.04]	<b>*</b>
Total events	28		28				
Heterogeneity: Tau² =	0.00; Chi	i² = 1.23	6 -	-0.2 -0.1 0 0.1 0.2			
Test for overall effect:	Z = 0.14	(P = 0.8)	9)				-0.2 -0.1 0 0.1 0.2  Favours inhaled Favours placebo

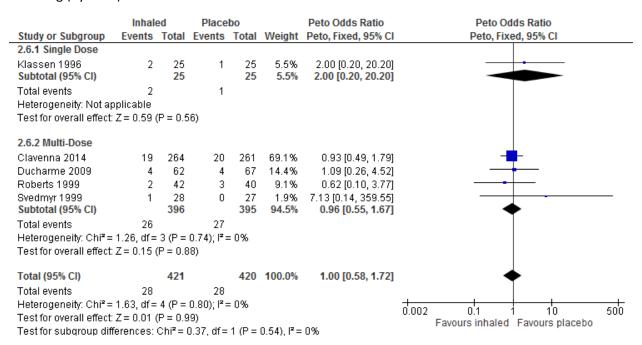
## Vomiting - Peto



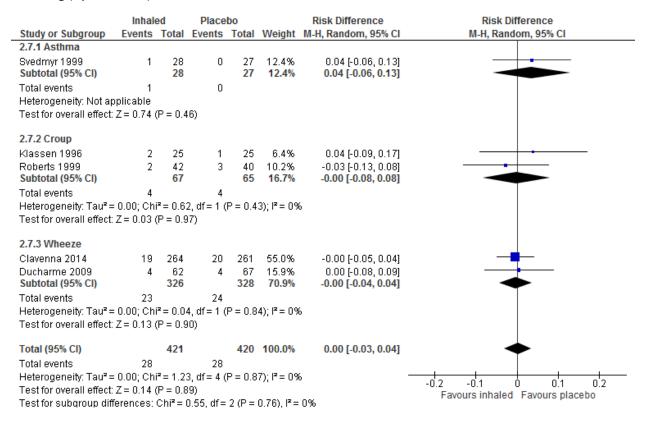
### Vomiting (by dose)



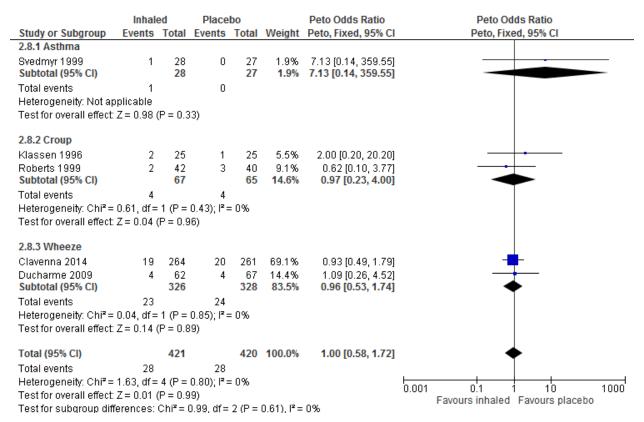
### Vomiting (by dose) - Peto



### Vomiting (by condition)



## Vomiting (by condition) - Peto



#### Diarrhea

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Clavenna 2014	27	264	35	261	72.7%	-0.03 [-0.09, 0.02]	<del></del>
Ducharme 2009	14	62	11	67	27.3%	0.06 [-0.08, 0.20]	-
Total (95% CI)		326		328	100.0%	-0.01 [-0.09, 0.08]	
Total events	41		46				
Heterogeneity: Tau² = Test for overall effect:				P = 0.2	1); l² = 37	%	-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

### Diarrhea - Peto

	Inhale	ed	Place	bo		Peto Odds Ratio		Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fixed, 95% CI
Clavenna 2014	27	264	35	261	73.0%	0.74 [0.43, 1.25]		
Ducharme 2009	14	62	11	67	27.0%	1.48 [0.62, 3.53]		<del></del>
Total (95% CI)		326		328	100.0%	0.89 [0.57, 1.40]		•
Total events	41		46					
Heterogeneity: Chi² = Test for overall effect:				= 44%			0.01	0.1 1 10 100 Favours inhaled Favours placebo

#### INHALED vs. PLACEBO - CNS & Behaviour

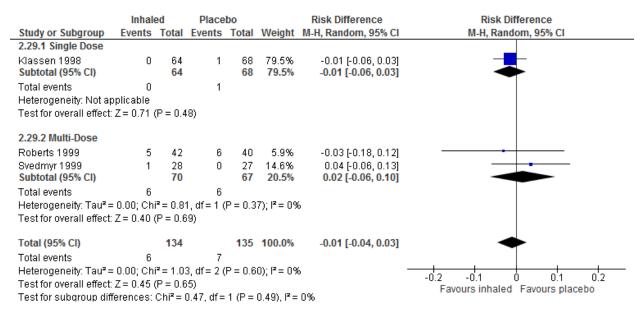
### Behaviour change

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Klassen 1998	0	64	1	68	79.5%	-0.01 [-0.06, 0.03]	<b>—</b>
Roberts 1999	5	42	6	40	5.9%	-0.03 [-0.18, 0.12]	-
Svedmyr 1999	1	28	0	27	14.6%	0.04 [-0.06, 0.13]	-
Total (95% CI)		134		135	100.0%	-0.01 [-0.04, 0.03]	•
Total events	6		7				
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Ch	$i^2 = 1.03$	3, df = 2 (	P = 0.6	$0); I^2 = 09$	6	-02 -01 0 01 02
Test for overall effect:	Z = 0.45	(P = 0.6)	i5)				-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

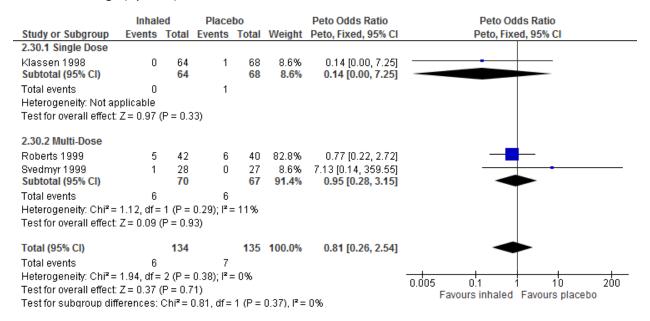
## Behaviour change – Peto

	Inhal	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Klassen 1998	0	64	1	68	8.6%	0.14 [0.00, 7.25]	<u> </u>
Roberts 1999	5	42	6	40	82.8%	0.77 [0.22, 2.72]	<del></del>
Svedmyr 1999	1	28	0	27	8.6%	7.13 [0.14, 359.55]	-
Total (95% CI)		134		135	100.0%	0.81 [0.26, 2.54]	•
Total events	6		7				
Heterogeneity: Chi²=	1.94, df=	2 (P =	0.38); l² =	= 0%			0.005 0.1 1 10 200
Test for overall effect:	Z = 0.37	(P = 0.7)	'1)				Favours inhaled Favours placebo

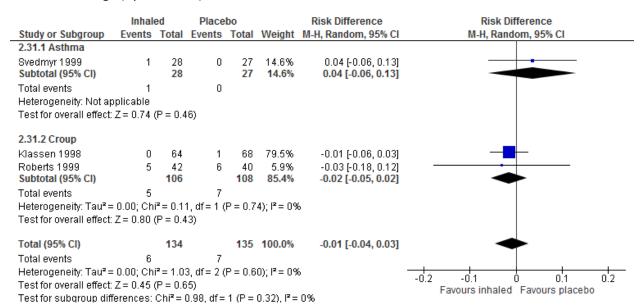
## Behaviour change (by dose)



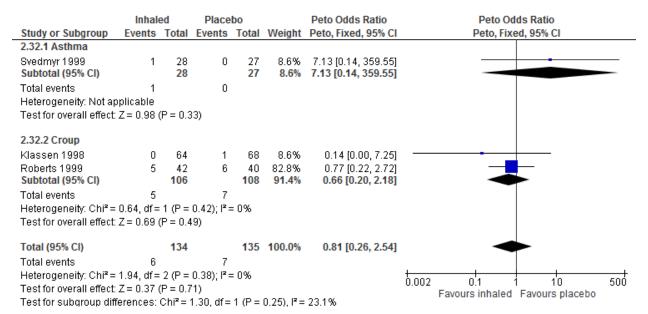
### Behaviour change (by dose) - Peto



### Behaviour change (by condition)



## Behaviour change (by condition) - Peto



## **INHALED vs. PLACEBO – Dermatologic**

### Burn

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Klassen 1994	0	27	1	27	100.0%	-0.04 [-0.13, 0.06]	
Total (95% CI)		27		27	100.0%	-0.04 [-0.13, 0.06]	
Total events	0		1				
Heterogeneity: Not ap Test for overall effect:	•	(P = 0.4	15)				-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

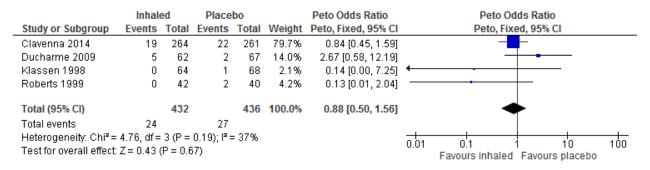
### Burn - Peto

	Inhal	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Klassen 1994	0	27	1	27	100.0%	0.14 [0.00, 6.82]	
Total (95% CI)		27		27	100.0%	0.14 [0.00, 6.82]	
Total events	0		1				
Heterogeneity: Not ap Test for overall effect:	•	(P = 0.3	32)				0.002 0.1 1 10 500 Favours inhaled Favours placebo

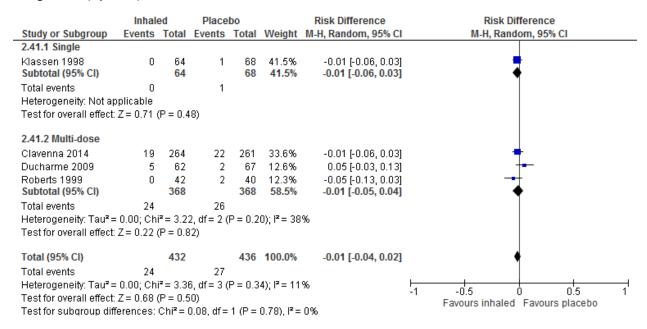
## Integument

	Inhal	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Clavenna 2014	19	264	22	261	33.6%	-0.01 [-0.06, 0.03]	<del></del>
Ducharme 2009	5	62	2	67	12.6%	0.05 [-0.03, 0.13]	<del>  •</del>
Klassen 1998	0	64	1	68	41.5%	-0.01 [-0.06, 0.03]	<del></del>
Roberts 1999	0	42	2	40	12.3%	-0.05 [-0.13, 0.03]	
Total (95% CI)		432		436	100.0%	-0.01 [-0.04, 0.02]	•
Total events	24		27				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	$i^2 = 3.31$	6, df = 3 (	P = 0.3	4); $I^2 = 11$	%	
Test for overall effect:	Z = 0.68	(P = 0.5)	(0)				-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

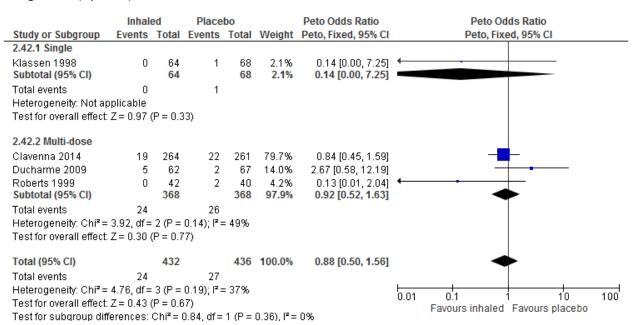
### Integument – Peto



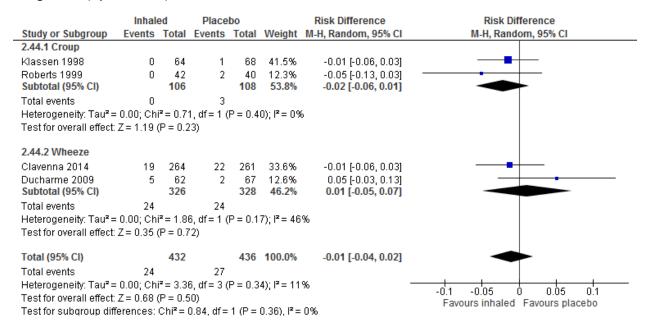
### Integument (by dose)



### Integument (by dose) - Peto



### Integument (by condition)



## Integument (by condition) - Peto

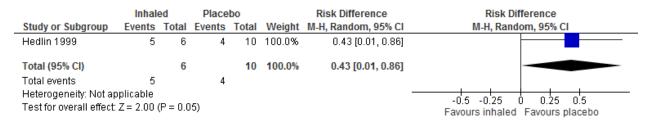
	Inhale	ed	Place	bo		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
2.46.1 Croup							
Klassen 1998	0	64	1	68	2.1%	0.14 [0.00, 7.25]	· -
Roberts 1999	0	42	2	40	4.2%	0.13 [0.01, 2.04]	
Subtotal (95% CI)		106		108	6.3%	0.13 [0.01, 1.27]	
Total events	0		3				
Heterogeneity: Chi²=	0.00, df =	1 (P =	0.96); l <sup>a</sup> =	= 0%			
Test for overall effect:	Z = 1.75 (	P = 0.0	18)				
2.46.2 Wheeze							
Clavenna 2014	19	264	22	261	79.7%	0.84 [0.45, 1.59]	- <del></del> -
Ducharme 2009	5	62	2	67	14.0%	2.67 [0.58, 12.19]	<del>  •                                   </del>
Subtotal (95% CI)		326		328	93.7%	1.00 [0.56, 1.80]	•
Total events	24		24				
Heterogeneity: Chi <sup>2</sup> =	1.88, df=	1 (P=	0.17);	47%			
Test for overall effect:	Z = 0.01 (	P = 1.0	10)				
Total (95% CI)		432		436	100.0%	0.88 [0.50, 1.56]	•
Total events	24		27				
Heterogeneity: Chi²=	4.76, df=	3 (P =	0.19); l² =	37%			0.005 0.1 1 10 200
Test for overall effect:	Z = 0.43 (	P = 0.8	7)				Favours inhaled Favours placebo
Test for subgroup diff	erences:	Chi <sup>z</sup> = :	2.88, df=	1 (P =	0.09), I²=	65.2%	1 divalo lililatos 1 divolio pidecoo

## INHALED vs. PLACEBO - Endocrine/Metabolic & Musculoskeletal

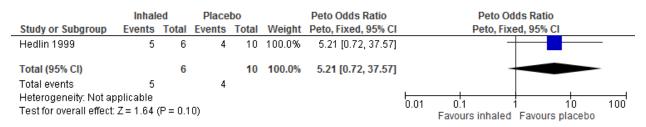
## Growth – change from baseline, cm

	In	Inhaled Placebo						Mean Difference	Mean Difference			
Study or Subgroup	Mean	Mean SD Total Mean SD Total		Weight	IV, Random, 95% CI	IV, Random, 95% CI						
Bacharier 2008	7.8	1.75	96	7.5	1.9	47	68.3%	0.30 [-0.35, 0.95]	-			
Ducharme 2009	6.23	2.62	58	6.56	2.9	62	31.7%	-0.33 [-1.32, 0.66]	-			
Total (95% CI)			154			109	100.0%	0.10 [-0.47, 0.67]	<b>*</b>			
	eity: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 1.09, df = 1 (P = 0.30); I <sup>2</sup> = 9% erall effect: Z = 0.34 (P = 0.73)								-4 -2 0 2 4 Favours inhaled Favours placebo			

## Adrenal suppression



### Adrenal suppression - Peto

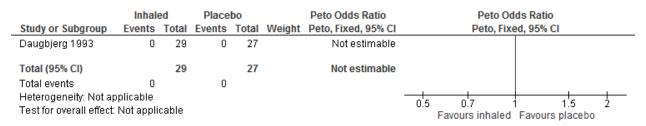


### INHALED vs. PLACEBO - Cardiovascular

## Arrhythmia

	Inhale	ed	Place	bo		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Daugbjerg 1993	0	29	0	27	100.0%	0.00 [-0.07, 0.07]	_
Total (95% CI)		29		27	100.0%	0.00 [-0.07, 0.07]	
Total events	0		0				
Heterogeneity: Not ap Test for overall effect:		(P = 1.0	00)				-0.2 -0.1 0 0.1 0.2 Favours inhaled Favours placebo

## Arrhythmia – Peto

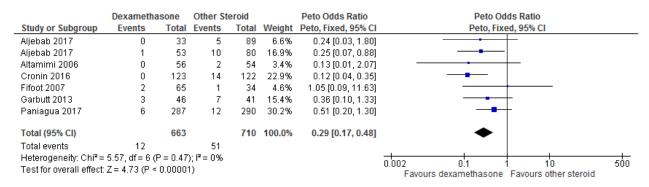


#### **DEXAMETHASONE vs. OTHER STEROID - GI**

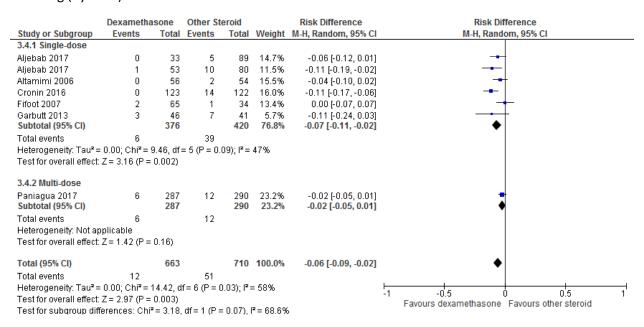
### Vomiting

	Dexamethasone Other Steroid			Risk Difference	Risk Difference		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Aljebab 2017	0	33	5	89	14.7%	-0.06 [-0.12, 0.01]	
Aljebab 2017	1	53	10	80	11.5%	-0.11 [-0.19, -0.02]	
Altamimi 2006	0	56	2	54	15.5%	-0.04 [-0.10, 0.02]	<del></del>
Cronin 2016	0	123	14	122	16.0%	-0.11 [-0.17, -0.06]	
Fifoot 2007	2	65	1	34	13.4%	0.00 [-0.07, 0.07]	+
Garbutt 2013	3	46	7	41	5.7%	-0.11 [-0.24, 0.03]	<del></del>
Paniagua 2017	6	287	12	290	23.2%	-0.02 [-0.05, 0.01]	<del>-</del>
Total (95% CI)		663		710	100.0%	-0.06 [-0.09, -0.02]	<b>◆</b>
Total events	12		51				
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>2</sup> =	14.42, d	f = 6 (P = 0	0.03); l <sup>a</sup> :	= 58%		- 15 025 05 05
Test for overall effect	Z = 2.97 (P =	0.003)					-0.5 -0.25 0 0.25 0.5 Favours dexamethasone Favours other steroid

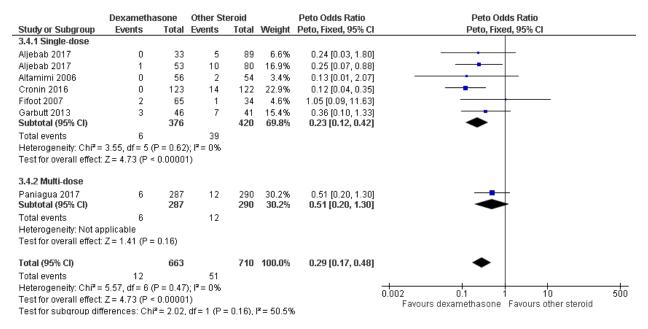
### Vomiting - Peto



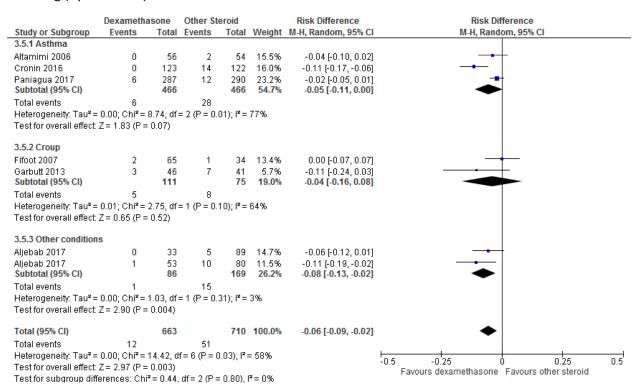
### Vomiting (by dose)



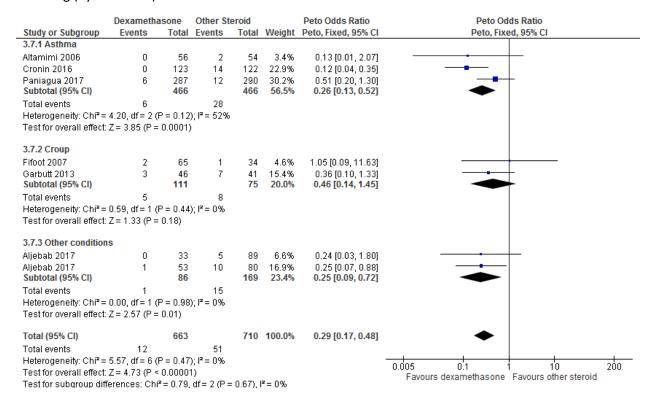
### Vomiting (by dose) - Peto



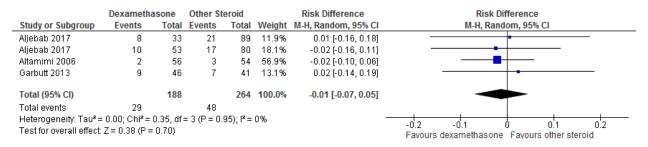
## Vomiting (by condition)



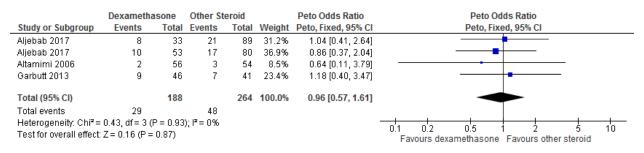
### Vomiting (by condition) - Peto



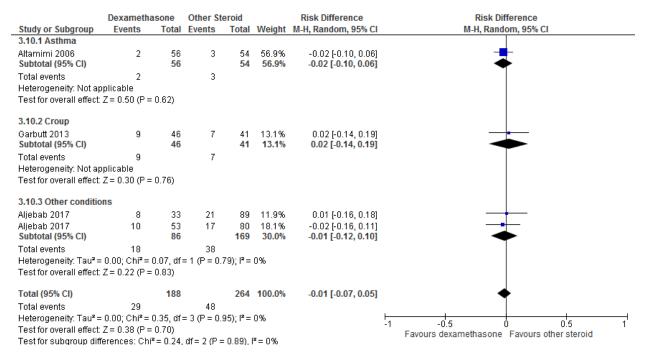
#### Abdominal pain



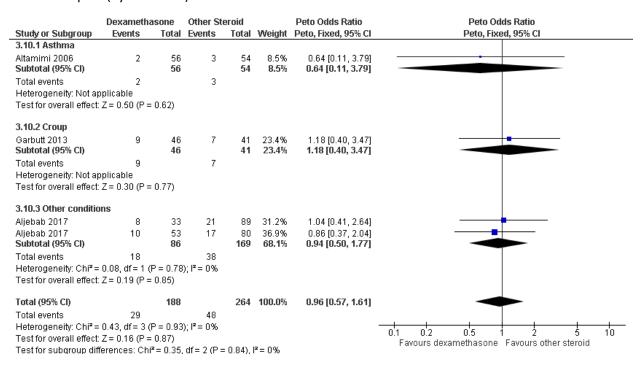
### Abdominal pain - Peto



### Abdominal pain (by condition)



### Abdominal pain (by condition) - Peto



### **DEXAMETHASONE vs. OTHER STEROID - CNS & Behaviour**

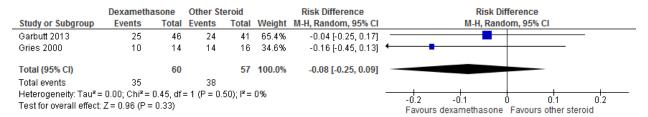
## Tremor/jitteriness

	Dexametha	xamethasone Other Steroid				Risk Difference	Risk Difference
Study or Subgroup	Events	Total Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Garbutt 2013	1	46	0	41	100.0%	0.02 [-0.04, 0.08]	
Total (95% CI)		46		41	100.0%	0.02 [-0.04, 0.08]	
Total events	1		0				
Heterogeneity: Not a Test for overall effect		0.48)					-0.1 -0.05 0 0.05 0.1 Favours dexamethasone Favours other steroid

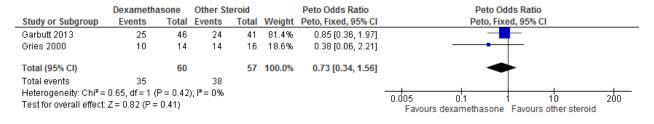
## Tremor/jitteriness - Peto

	Dexametha	asone	Other St	eroid		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Garbutt 2013	1	46	0	41	100.0%	6.63 [0.13, 336.21]	
Total (95% CI)		46		41	100.0%	6.63 [0.13, 336.21]	
Total events	1		0				
Heterogeneity: Not ap Test for overall effect:		0.35)					0.002 0.1 10 500 Favours dexamethasone Favours other steroid

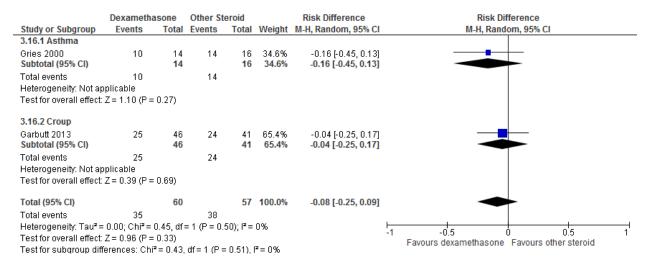
## Behaviour change



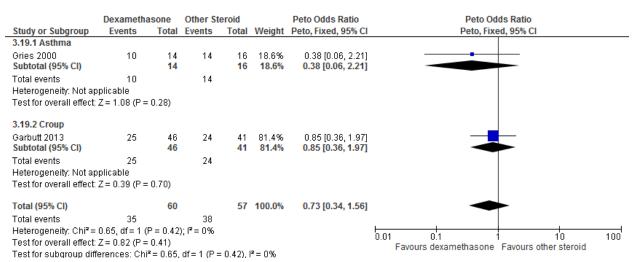
### Behaviour change – Peto



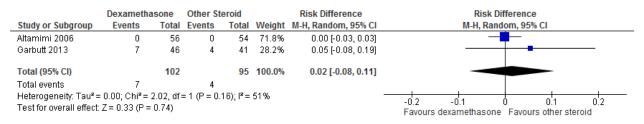
### Behaviour change (by condition)



### Behaviour change (by condition) - Peto



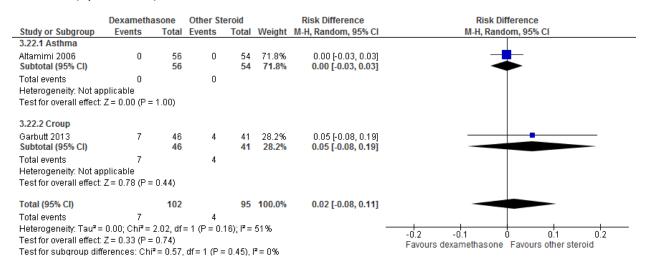
### Headache



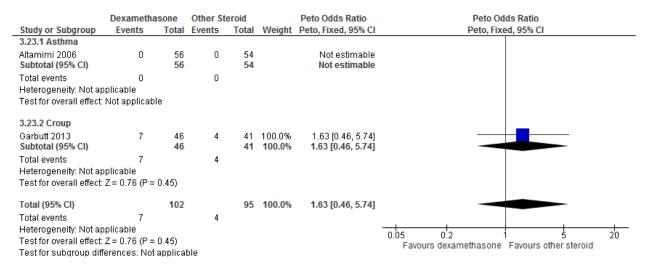
#### Headache - Peto

	Dexametha	sone	Other Steroid		Peto Odds Ratio		Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Altamimi 2006	0	56	0	54		Not estimable	
Garbutt 2013	7	46	4	41	100.0%	1.63 [0.46, 5.74]	<del>-  </del>
Total (95% CI)		102		95	100.0%	1.63 [0.46, 5.74]	
Total events	7		4				
Heterogeneity: Not ap Test for overall effect:	•	0.45)					0.05 0.2 1 5 20 Favours dexamethasone Favours other steroid

### Headache (by condition)



### Headache (by condition) - Peto

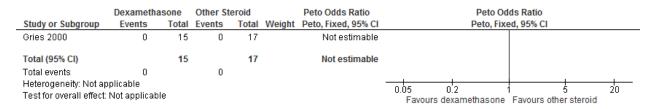


## **DEXAMETHASONE vs. OTHER STEROID – Dermatologic**

## **Phlebitis**

	Dexamethasone Other Steroid			eroid		Risk Difference	Risk Difference				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI				
Gries 2000	0	15	0	17	100.0%	0.00 [-0.11, 0.11]					
Total (95% CI)		15		17	100.0%	0.00 [-0.11, 0.11]					
Total events	0		0								
Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)							-0.2 -0.1 0 0.1 0.2 Favours dexamethasone Favours other steroid				

### Phlebitis – Peto

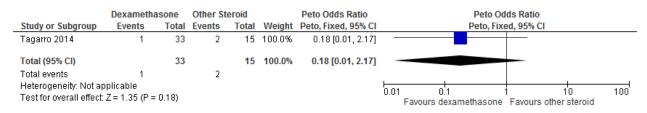


## **DEXAMETHASONE vs. OTHER STEROID – Endocrine/Metabolic & Musculoskeletal**

## Fluid & electrolyte abnormalities

	Dexametha	asone	Other St	eroid		Risk Difference	Risk Difference				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI				
Tagarro 2014	1	33	2	15	100.0%	-0.10 [-0.28, 0.08]					
Total (95% CI)		33		15	100.0%	-0.10 [-0.28, 0.08]					
Total events	1		2								
Heterogeneity: Not ap Test for overall effect		0.27)					-0.2 -0.1 0 0.1 0.2 Favours dexamethasone Favours other steroid				

## Fluid & electrolyte abnormalities – Peto



### **DEXAMETHASONE vs. OTHER STEROID – Cardiovascular**

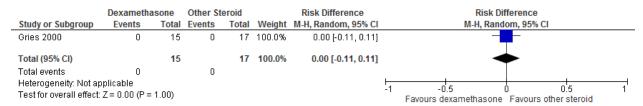
## Arrhythmia

	Dexamethasone Other Steroid					Risk Difference		Risk Difference			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Ran	dom, 95	5% CI	
Altamimi 2006	0	56	0	54	100.0%	0.00 [-0.03, 0.03]					
Total (95% CI)		56		54	100.0%	0.00 [-0.03, 0.03]			•		
Total events	0		0								
Heterogeneity: Not ap Test for overall effect	•	1.00)					-1	-0.5 Favours dexamethasone	0 Favor	0.5 urs other steroid	1

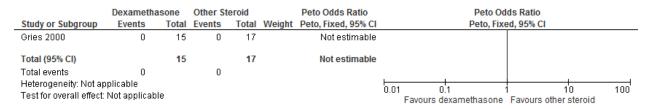
## Arrhythmia - Peto

	Dexamethasone		Other Steroid			Peto Odds Ratio	Peto Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI		Peto, Fix	ed, 95% CI	
Altamimi 2006	0	56	0	54		Not estimable				
Total (95% CI)		56		54		Not estimable				
Total events	0		0							
Heterogeneity: Not ap Test for overall effect:					0.01 F	0.1 avours dexamethasone	1 10 Favours other steroid	100		

## Hypertension



## Hypertension - Peto

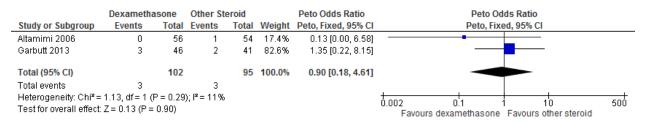


#### **DEXAMETHASONE vs. OTHER STEROID – General**

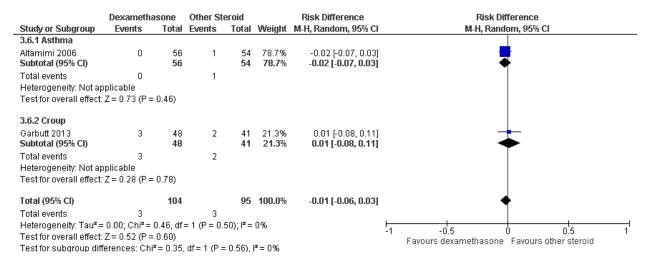
### General complaints

	Dexamethasone		Other Steroid		Risk Difference		Risk Difference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Altamimi 2006	0	56	1	54	79.5%	-0.02 [-0.07, 0.03]	<del></del>	
Garbutt 2013	3	46	2	41	20.5%	0.02 [-0.08, 0.11]		
Total (95% CI)		102		95	100.0%	-0.01 [-0.06, 0.03]		
Total events	3		3					
Heterogeneity: Tau² = Test for overall effect:			= 1 (P = 0.	-0.1 -0.05 0 0.05 0.1 Favours dexamethasone Favours other steroid				

## General complaints - Peto



### General complaints (by condition)



## General complaints (by condition) - Peto

