ONLY PROSPECTIVE STUDIES PAIRWISE COMPARISONS

<u>Phenytoin (PHT) versus phenobarbital (PB).</u> There were no statistically significant differences in effectiveness between PHT and PB [0.68 (95% CI: 0.6-0.76) versus 0.79 (95% CI: 0.68-0.87), p = 0.125283].

Study	Proportion	95%-CI					
PHT							
Agarwal et al, 2007	0.84	[0.71; 0.93]				+	_
Alvarez et al, 2011	0.59	[0.46; 0.70]		_		-	
Chitsaz et al, 2013	0.60	[0.32; 0.84]			-		
Chakravarhi et al, 2015	0.68	[0.45; 0.86]		_	1		
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-	 	
Gujjar et al, 2017	0.70	[0.51; 0.85]				1	
Random effects model		[0.60; 0.76]			-		
Heterogeneity: $I^2 = 43\%$ [0%;	77%]						
PB							
Malamiri et al, 2012	0.77	[0.58; 0.90]				-	
Su et al, 2016	0.81	[0.65; 0.92]			_		-
Random effects model	0.79	[0.68; 0.87]			•		
Heterogeneity: $I^2 = 0\%$		· · · _					
Test for subgroup difference	s: $\chi_1^2 = 2.35$, df =	: 1 (p = 0.13)	I	I	1	I	1
		0	0.2	0.4	0.6	8.0	1

<u>Phenytoin (PHT) versus valproate (VPA).</u> There were no statistically significant differences in effectiveness between PHT and VPA [0.68 (95% CI: 0.6-0.76) versus 0.71 (95% CI: 0.6-0.8), p = 0.708281].

Study	Proportion	95%-CI					
PHT							
Agarwal et al, 2007	0.84	[0.71; 0.93]				-	\vdash
Alvarez et al, 2011	0.59	[0.46; 0.70]		_	-		
Chitsaz et al, 2013	0.60	[0.32; 0.84]			-		
Chakravarhi et al, 2015	0.68	[0.45; 0.86]		_	-		
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Gujjar et al, 2017	0.70	[0.51; 0.85]			-	-	
Random effects mode	I 0.68	[0.60; 0.76]			4		
Heterogeneity: $I^2 = 43\%$ [0%	; 77%]						
VPA							
Agarwal et al, 2007	0.88	[0.76; 0.95]				_	-
Olsen et al, 2007	0.73	[0.56; 0.86]				_	_
Alvarez et al, 2011	0.75	[0.62; 0.85]				-	
Chen et al, 2011	0.50	[0.31; 0.69]			-	_	
Malamiri et al, 2012	0.90	[0.73; 0.98]					+
Chitsaz et al, 2013	0.73	[0.45; 0.92]		_		1	_
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Su et al, 2016	0.44	[0.28; 0.62]		1			
Misra et al, 2017	0.70	[0.51; 0.84]				+	
Random effects mode	I 0.71	[0.60; 0.80]			-		
Heterogeneity: $I^2 = 72\%$ [44%]	k; 86%]	- · ·					
Test for subgroup difference		$= 1 (p = 0.71)^{-1}$					\neg
	~1	. 0	0.2	0.4	0.6	8.0	1

Phenytoin (PHT) versus levetiracetam (LEV). There were no statistically significant differences in effectiveness between PHT and VPA [0.68 (95% CI: 0.6-0.76) versus 0.64 (95% CI: 0.51-0.76), p = 0.5838824].

Study	Proportion	95%-CI					
PHT							
Agarwal et al, 2007	0.84	[0.71; 0.93]				-	_
Alvarez et al, 2011	0.59	[0.46; 0.70]		_			
Chitsaz et al, 2013	0.60	[0.32; 0.84]			-		
Chakravarhi et al, 2015	0.68	[0.45; 0.86]		_		_	
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Gujjar et al, 2017	0.70	[0.51; 0.85]				•	
Random effects model	0.68	[0.60; 0.76]			-		
Heterogeneity: $I^2 = 43\%$ [0%;	77%]						
LEV							
Eue et al, 2009	0.48	[0.31; 0.66]					
Alvarez et al, 2011	0.52	[0.38; 0.65]		-	+		
Atmaca et al, 2015	0.70	[0.35; 0.93]				1	_
Chakravarhi et al, 2015	0.59	[0.36; 0.79]			-		
Mundlarmuri et al, 2015	0.78	[0.64; 0.88]			_	-	
Gujjar et al, 2017	0.82	[0.60; 0.95]				-	_
Random effects model	0.64	[0.51; 0.76]				-	
Heterogeneity: $I^2 = 64\%$ [13%]	; 85%]						
Test for subgroup difference	s: $\chi_1^2 = 0.30$, df =	= 1 (p = 0.59)	I	I		I	ı
		0	0.2	0.4	0.6	8.0	1

Phenytoin (PHT) versus lacosamide (LAC). There were no statistically significant differences in effectiveness between PHT and VPA [0.68 (95% CI: 0.6-0.76) versus 0.66 (95% CI: 0.51-0.79), p = 0.8064959].

Study	Proportion	95%-CI					
PHT							
Agarwal et al, 2007	0.84	[0.71; 0.93]					_
Alvarez et al, 2011	0.59	[0.46; 0.70]		_	1	-	
Chitsaz et al, 2013	0.60	[0.32; 0.84]					
Chakravarhi et al, 2015	0.68	[0.45; 0.86]		_	1		
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Gujjar et al, 2017	0.70	[0.51; 0.85]				+	
Random effects model		[0.60; 0.76]			-		
Heterogeneity: $I^2 = 43\%$ [0%;	77%]	_					
LAC							
d'Orsi et al, 2016	0.78	[0.40; 0.97]				1	
Misra et al, 2017	0.64	[0.45; 0.80]		_	-		
Random effects model	0.66	[0.51; 0.79]					
Heterogeneity: I ² = 0%	0	· •					
Test for subgroup difference	s: $\chi_1^2 = 0.06$, df =	1 (p = 0.80)			T	I	
		0	0.2	0.4	0.6	8.0	1

<u>Phenobarbital (PB) versus valproate (VPA).</u> There were no statistically significant differences in effectiveness between PB and VPA [0.79 (95% CI: 0.68-0.87) versus 0.71 (95% CI: 0.6-0.8), p = 0.2597667].

Study	Proportion	95%-CI					
PB							
Malamiri et al, 2012	0.77	[0.58; 0.90]				-	
Su et al, 2016	0.81	[0.65; 0.92]			_	7.	-
Random effects model	0.79	[0.68; 0.87]			-		
Heterogeneity: $I^2 = 0\%$		•					
VPA							
Agarwal et al, 2007	0.88	[0.76; 0.95]				-	_
Olsen et al, 2007	0.73	[0.56; 0.86]				1	
Alvarez et al, 2011	0.75	[0.62; 0.85]				1	
Chen et al, 2011	0.50	[0.31; 0.69]			+		
Malamiri et al, 2012	0.90	[0.73; 0.98]				-	-
Chitsaz et al, 2013	0.73	[0.45; 0.92]		_			-
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			1		
Su et al, 2016	0.44	[0.28; 0.62]	-	1			
Misra et al, 2017	0.70	[0.51; 0.84]					
Random effects model		[0.60; 0.80]			-		
Heterogeneity: $I^2 = 72\%$ [44%]							_
Test for subgroup difference	es: χ ₁ = 1.27, df =		' -	١.	_ '_	'-	
		0	0.2	0.4	0.6	8.0	1

<u>Phenobarbital (PB) versus levetiracetam (LEV).</u> There were no statistically significant differences in effectiveness between PB and VPA [0.79 (95% CI: 0.68-0.87) versus 0.64 (95% CI: 0.51-0.76), p = 0.07098913].

Study	Proportion	95%-CI					
PB Malamiri et al, 2012	0.77	[0.58; 0.90]					
Su et al, 2016	0.81	[0.65; 0.92]			_		_
Random effects model		[0.68; 0.87]				-	
Heterogeneity: $I^2 = 0\%$		(o.oo, o.o.)					
LEV							
Eue et al, 2009	0.48	[0.31; 0.66]		-			
Alvarez et al, 2011	0.52	[0.38; 0.65]			+		
Atmaca et al, 2015	0.70	[0.35; 0.93]				-	_
Chakravarhi et al, 2015	0.59	[0.36; 0.79]			1		
Mundlarmuri et al, 2015	0.78	[0.64; 0.88]			_	1	
Gujjar et al, 2017	0.82	[0.60; 0.95]			_	1	_
Random effects model		[0.51; 0.76]			-	-	
Heterogeneity: $I^2 = 64\%$ [13%]	; 85%]	_					
Test for subgroup difference	es: χ ₁ = 3.26, df =		· ·			· ·	
		0	0.2	0.4	0.6	8.0	1

<u>Phenobarbital (PB) versus lacosamide (LAC).</u> There were no statistically significant differences in effectiveness between PB and VPA [0.79 (95% CI: 0.68-0.87) versus 0.66 (95% CI: 0.51-0.79), p = 0.1463393].

Study	Proportion	95%-CI					
PB Malamiri et al, 2012 Su et al, 2016 Random effects model Heterogeneity: $I^2 = 0\%$	0.77 0.81 0.79	[0.58; 0.90] [0.65; 0.92] [0.68; 0.87]				•	-
LAC d'Orsi et al, 2016 Misra et al, 2017 Random effects model Heterogeneity: $I^2 = 0\%$	0.78 0.64 0.66	[0.40; 0.97] [0.45; 0.80] [0.51; 0.79]			_	1	
Test for subgroup difference	s: $\chi_1^2 = 2.11$, df	= 1 (p = 0.15)	0.2	0.4	0.6	0.8	1

<u>Valproate (VPA) versus levetiracetam (LEV).</u> There were no statistically significant differences in effectiveness between VPA and LEV [0.71 (95% CI: 0.6-0.8) versus 0.64 (95% CI: 0.51-0.76), p = 0.4095867].

Study	Proportion	95%-CI					
VPA							
Agarwal et al, 2007	0.88	[0.76; 0.95]				-	
Olsen et al, 2007	0.73	[0.56; 0.86]				-	
Alvarez et al, 2011	0.75	[0.62; 0.85]			_	1	
Chen et al, 2011	0.50	[0.31; 0.69]					
Malamiri et al, 2012	0.90	[0.73; 0.98]					1
Chitsaz et al, 2013	0.73	[0.45; 0.92]		_		-	_
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Su et al, 2016	0.44	[0.28; 0.62]	_	-			
Misra et al, 2017	0.70	[0.51; 0.84]				•	
Random effects model		[0.60; 0.80]			-		
Heterogeneity: $I^2 = 72\%$ [44%]	; 86%]						
LEV							
Eue et al, 2009	0.48	[0.31; 0.66]		-			
Alvarez et al, 2011	0.52	[0.38; 0.65]		4	•		
Atmaca et al, 2015	0.70	[0.35; 0.93]				+	_
Chakravarhi et al, 2015	0.59	[0.36; 0.79]			-		
Mundlarmuri et al, 2015	0.78	[0.64; 0.88]				-	
Gujjar et al, 2017 [°]	0.82	[0.60; 0.95]				-	_
Random effects model	0.64	[0.51; 0.76]				_	
Heterogeneity: $I^2 = 64\%$ [13%	; 85%]	• • •					
Test for subgroup difference		$= 1 (p = 0.41)^{-1}$					
- •	7.1	0	0.2	0.4	0.6	0.8	1

<u>Valproate (VPA) versus lacosamide (LAC).</u> There were no statistically significant differences in effectiveness between VPA and LEV [0.71 (95% CI: 0.6-0.8) versus 0.66 (95% CI: 0.51-0.79), p = 0.6033318].

Study	Proportion	95%-CI					
VPA							
Agarwal et al, 2007	0.88	[0.76; 0.95]				-	-
Olsen et al, 2007	0.73	[0.56; 0.86]					
Alvarez et al, 2011	0.75	[0.62; 0.85]			_	1	
Chen et al, 2011	0.50	[0.31; 0.69]	_	-	-		
Malamiri et al, 2012	0.90	[0.73; 0.98]					-
Chitsaz et al, 2013	0.73	[0.45; 0.92]		_			_
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-		
Su et al, 2016	0.44	[0.28; 0.62]	_	1			
Misra et al, 2017	0.70	[0.51; 0.84]				-	
Random effects mode	I 0.71	[0.60; 0.80]			-		
Heterogeneity: $I^2 = 72\%$ [44%]	6; 86%]	• •					
LAC							
d'Orsi et al, 2016	0.78	[0.40; 0.97]				1	
Misra et al, 2017	0.64	[0.45; 0.80]		_	-		
Random effects mode		[0.51; 0.79]			-		
Heterogeneity: $I^2 = 0\%$		• '					
Test for subgroup difference	es: $\chi_4^2 = 0.27$, df =	= 1 (p = 0.60)				ı	
3-	<i>N</i> 1 , 2.	0	0.2	0.4	0.6	8.0	1

<u>Levetiracetam (LEV) versus lacosamide (LAC).</u> There were no statistically significant differences in effectiveness between LEV and LAC [0.64 (95% CI: 0.51-0.76) versus 0.66 (95% CI: 0.51-0.79), p = 0.8414806].

Study	Proportion	95%-CI					
LEV							
Eue et al, 2009	0.48	[0.31; 0.66]		-			
Alvarez et al, 2011	0.52	[0.38; 0.65]			+		
Atmaca et al, 2015	0.70	[0.35; 0.93]					_
Chakravarhi et al, 2015	0.59	[0.36; 0.79]			1		
Mundlarmuri et al, 2015	0.78	[0.64; 0.88]			_	1	
Gujjar et al, 2017	0.82	[0.60; 0.95]				1	_
Random effects model		[0.51; 0.76]			-	-	
Heterogeneity: $I^2 = 64\%$ [13%]	; 85%]						
LAC							
d'Orsi et al, 2016	0.78	[0.40; 0.97]				1	
Misra et al, 2017	0.64	[0.45; 0.80]		_	-		
Random effects model	0.66	[0.51; 0.79]			-		
Heterogeneity: $I^2 = 0\%$		•					
Test for subgroup difference	es: $\chi_1^2 = 0.04$, df =	1 $(p = 0.84)$					
		. 0	0.2	0.4	0.6	8.0	1