## File e-1: PAIRWISE COMPARISONS

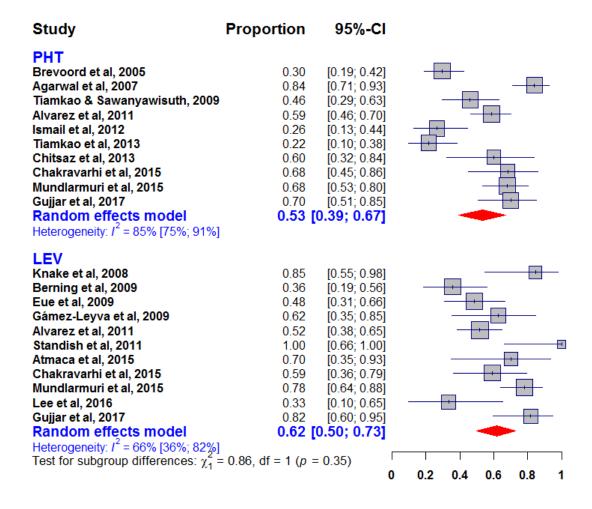
**Phenytoin (PHT) versus phenobarbital (PB).** PB was more effective than PHT [0.8 (95% CI: 0.69-0.88) versus 0.53 (95% CI: 0.39-0.67), p = 0.002254324].

Study	Proportion	95%-CI					
PHT							
Brevoord et al, 2005	0.30	[0.19; 0.42]	_				
Agarwal et al, 2007	0.84	[0.71; 0.93]				-	_
Tiamkao & Sawanyawisuth, 2009	0.46			+	<del>                                     </del>		
Alvarez et al, 2011	0.59	. , .		-		_	
Ismail et al, 2012	0.26	. , .		-			
Tiamkao et al, 2013	0.22	F1		<del></del>			
Chitsaz et al, 2013	0.60				-		
Chakravarhi et al, 2015	0.68			_		1	
Mundlarmuri et al, 2015	0.68						
Gujjar et al, 2017	0.70					1	
Random effects model		[0.39; 0.67]					
Heterogeneity: $I^2 = 85\%$ [75%; 91%]							
PB							
Malamiri et al, 2012	0.77	[0.58; 0.90]					
Su et al, 2016	0.81	[0.65; 0.92]			_	-	
Lee et al, 2016	1.00	[0.69; 1.00]					-1
Random effects model	0.80	[0.69; 0.88]					
Heterogeneity: $I^2 = 0\% [0\%; 87\%]$							_
Test for subgroup differences: $\chi_1^2$	= 9.33, df $= 1$ ( $p$				'	,	
			0 0.2	0.4	0.6	0.8	1

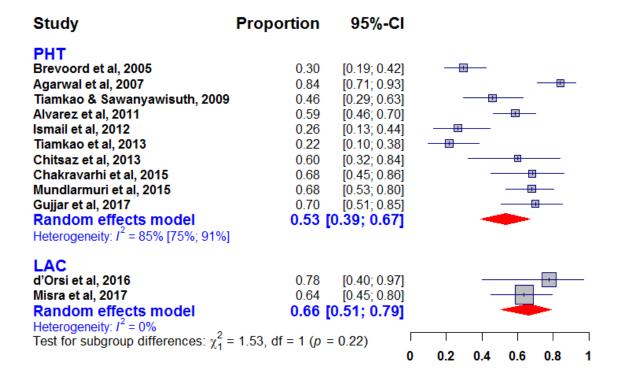
**Phenytoin (PHT) versus valproate (VPA).** VPA was more effective than PHT [0.71 (95% CI: 0.61-0.79) versus 0.53 (95% CI: 0.39-0.67), p = 0.04339366].

Study	Proportion	95%-CI					
PHT							
Brevoord et al, 2005	0.30	[0.19; 0.42]	-				
Agarwal et al, 2007	0.84	[0.71: 0.93]				-	_
Tiamkao & Sawanyawisuth, 2009	0.46	[0.29; 0.63]	-	-	_		
Alvarez et al, 2011	0.59	[0.46; 0.70]				-	
Ismail et al, 2012	0.26	[0.13; 0.44]		-			
Tiamkao et al, 2013	0.22	[0.10; 0.38]	-	_			
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		[0.39; 0.67]		-		_	
Heterogeneity: $I^2 = 85\%$ [75%; 91%]							
MDA							
VPA	4.00	[0.70, 4.00]					-
Yu et al, 2003	1.00 0.88	[0.78; 1.00] [0.76; 0.95]					
Agarwal et al, 2007		. , .					
Olsen et al, 2007	0.73 0.75	[0.56; 0.86]					
Tiamkao & Sawanyawisuth, 2009 Alvarez et al, 2011	0.75	[0.43; 0.95] [0.62; 0.85]					
Chen et al, 2011	0.75	[0.31; 0.69]					
Malamiri et al, 2012	0.90	[0.73; 0.98]					
Tiamkao et al, 2013	0.47	[0.23; 0.72]		,			
Chitsaz et al, 2013	0.47	[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		[0.61; 0.79]			4		
Heterogeneity: $I^2 = 69\%$ [43%; 83%]	0.7 1	[0.01, 0.19]				-	
Test for subgroup differences: $\chi_1^2 = 4$	.08. df = 1 (p = 0)	04) <sup>[</sup>					
	,	0	0.2	0.4	0.6	8.0	1

<u>Phenytoin (PHT) versus levetiracetam (LEV).</u> There were no statistically significant differences in effectiveness between PHT and LEV [0.53 (95% CI: 0.39-0.67) versus 0.62 (95% CI: 0.5-0.73), p = 0.3537387].



**Phenytoin** (PHT) versus lacosamide (LAC). There were no statistically significant differences in effectiveness between PHT and LAC [0.53 (95% CI: 0.39-0.67) versus 0.66 (95% CI: 0.51-0.79), p = 0.2161124].



<u>Phenobarbital (PB) versus valproate (VPA).</u> There were no statistically significant differences in effectiveness between PB and VPA [0.8 (95% CI: 0.69-0.88) versus 0.71 (95% CI: 0.61-0.79), p = 0.1604479].

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]			_		-
Lee et al, 2016	1.00						-1
Random effects model		[0.69; 0.88]					
Heterogeneity: $I^2 = 0\% [0\%; 87\%]$		[,]				_	
7.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0							
VPA							
Yu et al, 2003	1.00	[0.78; 1.00]					
Agarwal et al, 2007	0.88					-	<del>-</del>
Olsen et al, 2007	0.73	[0.56; 0.86]					
Tiamkao & Sawanyawisuth, 2009	0.75	[0.43; 0.95]		_		-	_
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]					-
Tiamkao et al, 2013	0.47	[0.23; 0.72]	_	1		_	
Chitsaz et al, 2013	0.73	[0.45; 0.92]		_			-
Mundlarmuri et al, 2015	0.68	[0.53; 0.80]			-	<del></del>	
Su et al, 2016	0.44	[0.28; 0.62]		1			
Misra et al, 2017	0.70					-	
Random effects model	0.71	[0.61; 0.79]			-		
Heterogeneity: $I^2 = 69\%$ [43%; 83%]		_					
Test for subgroup differences: $\chi_1^2 = 1$		.16)	ı	ı	I	ı	ı
•		0	0.2	0.4	0.6	8.0	1

**Phenobarbital (PB) versus levetiracetam (LEV).** PB was more effective than LEV [0.8 (95% CI: 0.69-0.88) versus 0.62 (95% CI: 0.5-0.73, p = 0.01816672].

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]			_	4++	-
Lee et al, 2016	1.00	[0.69; 1.00]					
Random effects mode	l 0.80	[0.69; 0.88]				-	
Heterogeneity: $I^2 = 0\%$ [ 0%;	87%]	•					
LEV							
Knake et al, 2008	0.85	[0.55; 0.98]				-	_
Berning et al, 2009	0.36	[0.19; 0.56]		-	_		
Eue et al, 2009	0.48	[0.31; 0.66]					
Gámez-Leyva et al, 2009	0.62	[0.35; 0.85]			_		
Alvarez et al, 2011	0.52	[0.38; 0.65]			1		
Standish et al, 2011	1.00	[0.66; 1.00]			_	_	
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]			_	-	
Lee et al, 2016	0.33	[0.10; 0.65]		-			
Gujjar et al, 2017	0.82	[0.60; 0.95]					_
Random effects mode	0.62	[0.50; 0.73]				-	
Heterogeneity: $I^2 = 66\%$ [36%]		4 ( 0.00)					$\neg$
Test for subgroup difference	es: $\chi_1^- = 5.58$ , df =		00	0.4	0.0	0.0	à
		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 [0.8 (95% CI: 0.69-0.88) versus 0.66 (95% CI: 0.51-0.79), p = 0.1035499].

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]			_	1	_
Lee et al, 2016	1.00	[0.69; 1.00]					
Random effects model	0.80	[0.69; 0.88]				-	
Heterogeneity: $I^2 = 0\%$ [ 0%; 8	37%]	-					
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: $I^2 = 0\%$		- · <u>-</u>					
Test for subgroup difference	s: $\chi_1^2 = 2.65$ , df =	1 (p = 0.10)		I		ı	
		0	0.2	0.4	0.6	8.0	1

<u>Valproate (VPA) versus levetiracetam (LEV).</u> There were no statistically significant differences in effectiveness between VPA and LEV [0.71 (95% CI: 0.61-0.79) versus 0.62 (95% CI: 0.5-0.73), p = 0.247034].

Study	Proportion	95%-CI	
VPA			
Yu et al, 2003	1.00	[0.78; 1.00]	
Agarwal et al, 2007	0.88	[0.76; 0.95]	
Olsen et al, 2007	0.73	[0.56; 0.86]	
Tiamkao & Sawanyawisuth, 2009	0.75	[0.43; 0.95]	
Alvarez et al, 2011	0.75		
Chen et al, 2011	0.50	[]	
Malamiri et al, 2012	0.90	L	_
Tiamkao et al, 2013	0.47	[]	
Chitsaz et al, 2013	0.73	. , ,	
Mundlarmuri et al, 2015	0.68	[]	
Su et al, 2016	0.44		
Misra et al, 2017	0.70		
Random effects model		[0.61; 0.79]	
Heterogeneity: $I^2 = 69\%$ [43%; 83%]			
LEV			
Knake et al, 2008	0.85	[0.55; 0.98]	-
Berning et al, 2009	0.36	[0.19; 0.56]	
Eue et al, 2009	0.48	[0.31; 0.66]	
Gámez-Leyva et al, 2009	0.62	[0.35; 0.85]	
Alvarez et al, 2011	0.52		
Standish et al, 2011	1.00	[0.66; 1.00]	
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		
Lee et al, 2016	0.33		
Gujjar et al, 2017	0.82	[0.60; 0.95]	-
Random effects model	0.62	[0.50; 0.73]	
Heterogeneity: $I^2 = 66\%$ [36%; 82%] Test for subgroup differences: $\chi_1^2 = 1$			
Test for subgroup differences: $\chi_1^2 = 1$	.34, df = 1 ( $p = 0$ .		
		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 LAC [0.71 (95% CI: 0.61-0.79) versus 0.66 (95% CI: 0.51-0.79), p = 0.6170751].

Study	Proportion	95%-CI					
VPA							
Yu et al, 2003	1.00	[0.78; 1.00]					
Agarwal et al, 2007	0.88	[0.76; 0.95]					<b>—</b>
Olsen et al, 2007	0.73	[0.56; 0.86]				-	
Tiamkao & Sawanyawisuth, 2009	0.75	[0.43; 0.95]		_		-	_
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]					-
Tiamkao et al, 2013	0.47	[0.23; 0.72]	_			_	
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 model		0.61; 0.79]			-		
Heterogeneity: $I^2 = 69\%$ [43%; 83%]							
1.40							
LAC	0.70	[0.40:0.07]					
d'Orsi et al, 2016	0.78	[0.40; 0.97]					
Misra et al, 2017	0.64	[0.45; 0.80]					
Random effects model Heterogeneity: $I^2 = 0\%$	0.00 [	0.51; 0.79]					
Test for subgroup differences: $\chi_1^2 = 0$	125 df = 1 (n = 0.6	2) L					$\neg$
restror subgroup differences. χ <sub>1</sub> – t	7.23, ui – 1 (p – 0.0	0	0.2	0.4	0.6	0.8	1
		·	0.2	v. <del>-</del>	0.0	0.0	

<u>Levetiracetam (LEV) versus lacosamide (LAC).</u> There were no statistically significant differences in effectiveness between LEV and LAC [0.62 (95% CI: 0.5-0.73) versus 0.66 (95% CI: 0.51-0.79), p = 0.6467674].

Study	Proportion	95%-CI	
LEV			
Knake et al, 2008	0.85	[0.55; 0.98]	
Berning et al, 2009	0.36	[0.19; 0.56]	
Eue et al, 2009	0.48	[0.31; 0.66]	<del></del>
Gámez-Leyva et al, 2009	0.62	[0.35; 0.85]	
Alvarez et al, 2011	0.52	[0.38; 0.65]	<del></del>
Standish et al, 2011	1.00	[0.66; 1.00]	
Atmaca et al, 2015	0.70	[0.35; 0.93]	
Chakravarhi et al, 2015	0.59	[0.36; 0.79]	<del></del>
Mundlarmuri et al, 2015	0.78	[0.64; 0.88]	<del></del>
Lee et al, 2016	0.33	[0.10; 0.65]	<del></del>
Gujjar et al, 2017	0.82	[0.60; 0.95]	
Random effects mode		[0.50; 0.73]	
Heterogeneity: $I^2 = 66\%$ [36%]	6; 82%]		
LAC			
d'Orsi et al, 2016	0.78	[0.40; 0.97]	
Misra et al, 2017	0.64	[0.45; 0.80]	
Random effects mode	I 0.66 I	0.51; 0.79]	
Heterogeneity: $I^2 = 0\%$		•	
Test for subgroup difference	es: $\chi_1^2 = 0.21$ , df =	1 $(p = 0.65)$	
· .	~1	ຶ 0	0.2 0.4 0.6 0.8 1