**Appendix 8:** Effectiveness of opioids (all types) versus placebo for function outcomes (higher values = more disabled), by type of drug. SD = standard deviation, SMD = standardized mean difference, CI = confidence interval, A = high quality, B = low quality.

itudy ir sub-category	N	Opioid Mean (SD)	N	Placebo Mean (SD)	SMD (random) 95% CI	Weight %	SMD (random) 95% CI	Year	Qualit
1 Controlled-release Codein	ie								
Arkinstall 1995	30	25.00(7.70)	30	35.10(8.20)		2.33	-1.25 [-1.81, -0.70]	1995	A
Peloso 2000	31	456.20(316.20)	35	687.50(415.50)		2.83	-0.61 [-1.11, -0.12]	2000	A
ubtotal (95% CI)	61		65		•	5.16	-0.92 [-1.55, -0.29]		
est for heterogeneity: Chi <sup>a</sup> : est for overall effect: Z = 2									
2 Tramadol									
Babul 2004	124	751.70(320.00)	122	934.60(320.00)	-	7.01	-0.57 [-0.82, -0.31]	2004	A
Fleischmann 2001	63	4.16(2.05)	66	5.04(2.25)	-	4.79	-0.41 [-0.75, -0.06]	2001	A
farati 1998	63	-64.30(30.00)	64	-55.10(32.00)	<del></del> -	4.77	-0.29 [-0.64, 0.06]	1998	A
Ruoff 2003	151	10.70(6.30)	146	11.60(6.30)	-	7.86	-0.14 [-0.37, 0.09]	2003	A
Russell 2000	35	44.60(17.96)	34	47.20(15.72)	<del>-</del>	3.05	-0.15 [-0.62, 0.32]	2000	A
Schinitzer 2000	127	8.80(6.20)	127	10.20(6.20)	-	7.26	-0.23 [-0.47, 0.02]	2000	A
ubtotal (95% CI)	563		559		<b>*</b>	34.73	-0.30 [-0.45, -0.16]		
est for heterogeneity: Chi <sup>2</sup> : est for overall effect: Z = 4.					Ì				
Tramadol + Acetaminophe	en								
Bennett 2003	156	44.00(17.00)	157	50.00(15.00)	-	8.00	-0.37 [-0.60, -0.15]	2003	A
mkey 2004	153	3.90(1.84)	153	4.50(1.86)	-	7.93	-0.32 [-0.55, -0.10]	2004	A
eloso 2004	164	12.80(5.90)	163	13.70(5.70)	<del>-</del>	8.22	-0.15 [-0.37, 0.06]	2004	A
Silverfield 2002	193	3.77(1.76)	109	4.16(1.82)	-	7.61	-0.22 [-0.45, 0.02]	2002	A
ubtotal (95% CI)	666		582		<b>*</b>	31.76	-0.27 [-0.38, -0.15]		
est for heterogeneity: Chi² : est for overall effect: Z = 4.									
4 Controlled-release Oxyco	done								
Gimbel 2003	82	3.80(2.70)	77	4.40(2.60)		5.54	-0.23 [-0.54, 0.09]	2003	A
Watson & Babul 1998	38	0.30(0.80)	38	0.70(1.00)	-	3.24	-0.44 [-0.89, 0.02]	1998	A
Vatson 2003	36	16.80(15.60)	36	25.20(16.70)	-	3.08	-0.51 [-0.98, -0.04]	2003	A
ibtotal (95% CI)	156		151		<b>◆</b>	11.85	-0.34 [-0.57, -0.12]		
est for heterogeneity: Chi² : est for overall effect: Z = 2.									
Long-acting Morphine									
aldwell 2002	73	890.00(328.00)	73	1048.00(313.00)	-	5.17	-0.49 [-0.82, -0.16]	2002	A
faier 2002	23	32.40(12.10)	22	36.80(12.70)	<del></del>	2.11	-0.35 [-0.94, 0.24]	2002	A
foran 1991	7	2.30(0.60)	8	2.30(0.60)	<del>- † -</del>	0.79	0.00 [-1.01, 1.01]	1991	В
Moulin 1996	46	44.60(8.00)	46	45.00(8.00)	+	3.82	-0.05 [-0.46, 0.36]	1996	В
Raja 2002	64	2.30(1.10)	56	2.30(1.00)	<u> </u>	4.61	0.00 [-0.36, 0.36]	2002	A
ibtotal (95% CI)	213		205		•	16.49	-0.21 [-0.44, 0.02]		
est for heterogeneity: Chi² : est for overall effect: Z = 1.		P = 0.28), F = 21.0%							
otal (95% CI)	1659		1562		•	100.00	-0.31 [-0.41, -0.22]		
est for heterogeneity: Chi <sup>2</sup> :		9 (P = 0.05), I <sup>2</sup> = 36.3%			*		,,		

## References

Arkinstall W, Sandler A, Goughnour B, et al. Efficacy of controlled-release codeine in chronic non-malignant pain: a randomized, placebo-controlled clinical trial. *Pain* 1995;62:169-78.

Babul N, Noveck R, Chipman H, Roth SH, Gana T, Albert K. Efficacy and safety of extended-release, once-daily tramadol in chronic pain: a randomized 12-week clinical trial in osteoarthritis of the knee. *J Pain Symptom Manage* 2004;28:59-71.

Bennett RM, Kamin M, Karim R, Rosenthal N. Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. *Am J Med* 2003;114:537-45.

Caldwell JR, Rapoport RJ, Davis JC, et al. Efficacy and safety of a once-daily morphine formulation in chronic, moderate-to-severe osteoarthritis pain: results from a randomized, placebo-controlled, double-blind trial and an open-label extension trial. *J Pain Symptom Manage* 2002;23:278-91.

Emkey R, Rosenthal N, Wu S-C, et al. Efficacy and safety of tramadol/acetaminophen tablets (Ultracet) as add-on therapy for osteo-arthritis pain in subjects receiving a COX-2 nonsteroidal antiinflammatory drug: a multicenter, randomized, double-blind, placebo-controlled trial. *J Rheumatol* 2004;31:150-6.

Fleischmann RM, Caldwell JR, Roth SH, et al. Tramadol for the treatment of joint pain associated with osteoarthritis: a randomized, double-blinded, placebo-controlled trial. *Curr Ther Res* 2001;62:113-28.

Gimbel JS, Richards P, Portenoy RK. Controlled-release oxycodone for pain in diabetic neuropathy: a randomized controlled trial. *Neurology* 2003;60:927-34.

Harati Y, Gooch C, Swenson M, et al. Double-blind randomized trial of tramadol for the treatment of the pain of diabetic neuropathy. *Neurology* 1998;50:1842-6.

Maier C, Hildebrandt J, Klinger R, et al.; MONTAS Study Group. Morphine responsiveness, efficacy and tolerability in patients with chronic non-tumor associated pain — results of a double-blind placebo-controlled trial (MONTAS). *Pain* 2002;97:223-33.

Moran C. MST continus tablets and pain control in severe rheumatoid arthritis. Br J Clin Res 1991;2:1-12.

Moulin DE, Iezzi A, Amireh R, et al. Randomised trial of oral morphine for chronic non-cancer pain. Lancet 1996;347:143-7.

Peloso PM, Bellamy N, Bensen W, et al. Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee. *J Rheumatol* 2000;27:764-71.

Peloso PM, Fortin L, Beaulieu A, et al. Analgesic efficacy and safety of tramadol/acetaminophen combination tablets (Ultracet) in treatment of chronic low back pain: a multicenter, outpatient, randomized, double blind, placebo controlled trial. *J Rheumatol* 2004;31:2454-63.

Raja SN, Haythornthwaite JA, Pappagallo M, et al. Opioids versus antidepressants in postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology* 2002;59:1015-21.

Ruoff GE, Rosenthal N, Jordan D, et al. Tramadol/acetaminophen combination tablets for the treatment of chronic lower back pain: a multicenter, randomized, double-blind, placebo-controlled outpatient study. *Clin Ther* 2003;25:1123-41.

Russell J, Kamin M, Bennett RM, et al. Efficacy of tramadol in treatment of pain in fibromyalgia. J Clin Rheumatol 2000;6:250-7.

Schnitzer TJ, Gray WL, Paster RZ, et al. Efficacy of tramadol in treatment of chronic low back pain. J Rheumatol 2000;27:772-8.

Silverfield JC, Kamin M, Wu SC, et al. Study Group. Tramadol/acetaminophen combination tablets for the treatment of osteoarthritis flare pain: a multicenter, outpatient, randomized, double-blind, placebo-controlled, parallel-group, add-on study. *Clin Ther* 2002;24: 282-97.

Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomized trial in postherpetic neuralgia. *Neurology* 1998;50:1837-41. Watson CP, Moulin D, Watt-Watson J, et al. Controlled-release oxycodone relieves neuropathic pain: a randomized controlled trial in painful diabetic neuropathy. *Pain* 2003;105:71-8.