**Table E6. Data abstraction of randomized controlled trials of opioids**

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| **Author, Year** | **Country**  **Number of Centers and Setting** | **Inclusion Criteria** | **Number**  **Randomized, Analyzed Attrition** | **Intervention** | **Study Participants** | **Duration of Pain (acute, subacute, chronic)** | **Outcome Measures** |
| Cloutier, 2013 | Canada; 10 centers; setting unclear | Age>18  Back pain intensity ≥2 on a 0-4 scale (moderate or severe) Currently taking opioids  Low back pain ≥3 mos.  Must undergo 2-7 day washout of pre- study opioids Exclusions: psychological dependence on opioids or alcohol; major psychiatric disorder; litigation | Randomized: 83  Analyzed: 54 for per-protocol  analysis (completed at least 2 weeks each of active therapy and placebo)  Attrition: 29 (35%) The intention-to- treat analysis included all 83, who had at least one dose of medication and at least one post-randomization data point. | A. Oxycodone/  Naloxone, both controlled release, titrated dose of  10mg/5mg q 12h  up to 40mg/20mg q  12 h B. placebo  Crossover design: 4 weeks of each intervention | Due to crossover  design, all patients received both A and B. Among the 54 analyzed: women=50%  Mean age=50.6  Caucasian: 94.4% Baseline score on Pain and Disability Index was 42 on a 0-  70 scale (70 worst) Among the full 83 enrolled, 39 men, 44 women; mean age  51.3; 91.6% Caucasian | Subacute or chronic | Pain ordinal scale, 0-4  (0=none,  4=excruciating); Pain VAS - 100mm; Pain & Sleep Questionnaire: each item on a 0-100 VAS; Pain Disability Index: overall score 0-70, with  70 worst;  Quebec Back Pain  Disability Questionnaire:  20 items on 0-5 ordinal scale;  Bowel Function Index: 3 items on numerical analog scale, 0-100; General Health status scale from SF-36; Effectiveness of Treatment on 4-point scale; Global  Impression of change on 7-point scale |

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| **Author, Year** | **Duration of Followup** | **Results** | **Adverse Events Including Withdrawals** | **Funding**  **Source** | **Quality**  **Rating** | **Comments** |
| Cloutier, 2013 | 4 weeks  each on active therapy and placebo | Intention-to-Treat Analysis (n=83):  Pain VAS: A. 52.2 mm (SD 23.0; B: 57.8 mm (SD  24.2) (p=0.053)  Ordinal pain score: A: 2.3 (SD 0.8); B: 2.5 (SD 0.9), (p=0.086)  No other results for ITT analysis  Per protocol analysis:  Pain VAS: A. 48.6 mm (SD 23.1); B: 55.9 mm (SD  25.4) (p=0.03)  Ordinal pain score: A: 2.1 (SD 0.8); B: 2.4 (SD 0.9), (p=0.042)  Pain Disability Index: A: 34.3 (SD 15.6); B:37.5 (SD  15.2), p=0.051;  SF-36 General Health: "no difference" Quebec Back Pain Disability: "no difference" | Withdrawals: 9 dropouts during active  treatment; 11 during placebo treatment; Withdrawals due to AEs: 6 on active therapy, 5 on placebo  Bowel Function Index and use of rescue laxatives: no significant differences  Overall count of AEs: A. 48, B: 40, p=0.068  Serious AEs: 2 in each group; all judged not related to study meds.  Somnolence: A: 5.4%; B: 0.0%, p=0.04  Other AEs (nausea, constipation, fatigue, vomiting, dizziness, abdominal pain): no significant differences | Purdue  Pharma | Good | Main intent of  oral naloxone was to reduce constipation side effects; there is very low  systemic bioavailability due to first-pass metabolism by liver. |

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| **Author, Year** | **Country**  **Number of Centers and Setting** | **Inclusion Criteria** | **Number**  **Randomized, Analyzed Attrition** | **Intervention** | **Study Participants** | **Duration of Pain (acute, subacute, chronic)** | **Outcome Measures** |
| Hyup Lee, 2013 | 15 centers  South Korea | Age 25-75 years,  able to walk, with moderate to severe LBP with average intensity ≥4 and duration ≥3 months requiring analgesics Exclude: recent back surgery or steroid injection, more severe pain in an area other than the back, or comorbid conditions that may interfere with assessment | 248 randomized  196 completed  (21% attrition) | A. Extended-  release tramadol HCl 75 mg/acetaminophen  650 mg fixed- combination tablet (n=125)  Max dose=4 tabs/d=300 mg tramadol  B. Placebo (n=120) | A vs. B  Mean age: 59.9 vs.  60.4 years  Female sex: 75% vs.  74% Race: NR | Subacute or chronic | 10-cm VAS, SF-36, ODI |

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| **Author, Year** | **Duration of Followup** | **Results** | **Adverse Events Including Withdrawals** | **Funding**  **Source** | **Quality**  **Rating** | **Comments** |
| Hyup Lee, 2013 | 29 days | A vs. B  Pain intensity change ≥30%, full analysis set:  57.7% (49/85) vs. 41.1% (37/90); p=0.037  Pain intensity change ≥30%, per protocol: 63% (46/73) vs. 44.9% (35/78); p=0.027  Pain intensity change ≥50%, full analysis set:  31.8% vs. 20.0%; p=0.075  Pain intensity change ≥50%, per protocol: 34.3%  vs. 21.8%; p=0.088  Korean SF-36: patients in the intervention group had significant improvements in role-physical, general health, and reported health transition domains, and a tendency (p=0.052) toward improvement in vitality  Korean ODI: patients in the intervention group had significant functional improvement in the personal care section (p=0.045) and a tendency (p=0.053) toward improvement in total ODI scores | A vs. B  Any adverse event: 83.2% (104/125) vs.  54.2% (65/120); RR 1.54 (95% CI 1.28 to  1.84)  Withdrawal due to adverse event: 19.2% (24/125) vs. 5.0% (6/120); RR 3.31 (95% CI 1.40 to 7.83) | Janssen  Korea, Ltd. | Good | Also available:  patient-reported efficacy, investigator- reported pain improvement, all subscores of SF-  36 (Table 2) and ODI (Table 3), specific AEs |

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| Rauck, 2014 | 59 centers  United States | Males and non-  pregnant, non- lactating females age  18-75 years, with moderate-to-severe chronic LBP for ≥3 months, average pain score ≥4  Exclude: history of opioid or alcohol or illicit drug abuse in previous 5 years, history of intolerance to hydrocodone or acetaminophen N- acetyl-para- aminophenol, comorbid conditions that could interfere with pain assessment, uncontrolled blood  pressure, BMI >45, or depression | 302 randomized  183 completed  (39% attrition) | A. Extended-  release hydrocodone in 10-  , 20-, 30-, 40-, and  50-mg capsules (n=151) Mean dose=119 mg/d  Max dose=200 mg/d  B. Placebo (n=151) | A vs. B  Mean age: 50.4 vs.  50.8 years  Female sex: 62% vs.  49%; p=0.028  Race: 82% White,  17% Black, 1% other vs. 80% White, 17% Black, 4% other  Mean pre-study opioid usage: 76.8 vs. 79.2 mg/day MED  Mean pain score before titration (NRS):  6.9 vs. 6.9  Mean pain score after titration (NRS): 3.1 vs.  3.1 | Chronic | 10-point NRS |

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| **Author, Year** | **Duration of Followup** | **Results** | **Adverse Events Including Withdrawals** | **Funding**  **Source** | **Quality**  **Rating** | **Comments** |
| Rauck, 2014 | 12 weeks | A vs. B  Change from baseline in mean daily pain intensity score: 0.48 vs. 0.96; p=0.008 | A vs. B  Withdrawal due to adverse event: 1.3% (2/151) vs. 3.3% (5/151); RR 0.40 (95% CI  0.08 to 2.03) | Zogenix, Inc. | Poor | Dosages,  specific AEs  EERW design |

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| Schiphorst  Preuper, 2014 | 2 centers  The Netherlands | Age ≥18 years, with  chronic LBP lasting  >3 months, a VAS  score ≥4  Exclude: hypertension, mental or physical conditions leading to reduced functioning | 50 randomized  43 completed  (14% attrition) | A. tramadol 37.5  mg/acetaminophen  325 mg fixed- combination capsule (n=25)  Max dose tramadol=225 mg/d B. Placebo (n=25) | A vs. B  Mean age: 42 vs. 44 years  Female sex: 72% vs.  64% Race: NR  Mean duration of pain:  18 vs. 24 months Mean pain score (VAS): 6.1 vs. 4.7 | Chronic | Lifting, carrying, and  bending; 10-cm VAS; RDQ; global pain assessment |

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| **Author, Year** | **Duration of Followup** | **Results** | **Adverse Events Including Withdrawals** | **Funding**  **Source** | **Quality**  **Rating** | **Comments** |
| Schiphorst  Preuper, 2014 | 2 weeks | A vs. B  Lifting (kg), baseline-followup: 18-19 vs. 20-17 kg;  change 1 vs. -3 kg  Carrying (kg), baseline-followup: 24-20 vs. 24-21 kg; change -4 vs. -3  Static bending (s), baseline-followup: 119-143 vs.  158-192.5; change 24 vs. 34.5 s  Dynamic bending (s/rep), baseline-followup: 2.7-  2.8 vs. 2.7-3.0; change 0.1 vs. 0.3  Roland Morris Disability Questionnaire (0-24), baseline-followup: 13.0-11.5 vs. 13.0-13.0; change -  1.5 vs. 0  VAS current pain, baseline-followup: 6.1-5.1 vs.  4.7-4.5; change -1 vs. -0.2  VAS, maximum pain, baseline-followup: 7.3-7.4 vs.  7.1-7.7; change 0.1 vs. 0.6  VAS, minimum pain, baseline-followup: 4.4-3.8 vs.  2.0-2.6; change -0.6 vs. 0.6  Pain relief: 42% (10/24) vs. 4% (1/25); RR 10.42 (95% CI 1.44 to 75.29)  Same pain or worsened: 58% (14/24) vs. 96% (24/25); RR 0.61 (95% CI 0.43 to 0.86) | A vs. B  Withdrawal due to adverse event: 8% (2/25) vs. 0% (0/25) | Grunenthal BV  and Stichting  Beatrixoord | Fair |  |

**Please see Appendix C. Included Studies for full study references.**