**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>18Back pain intensity ≥2 on a 0-4 scale (moderate or severe) Currently taking opioidsLow 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: 83Analyzed: 54 for per-protocolanalysis (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 of10mg/5mg q 12hup to 40mg/20mg q12 h B. placeboCrossover design: 4 weeks of each intervention | Due to crossoverdesign, all patients received both A and B. Among the 54 analyzed: women=50%Mean age=50.6Caucasian: 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 age51.3; 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, with70 worst;Quebec Back PainDisability 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; GlobalImpression 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 weekseach on active therapy and placebo | Intention-to-Treat Analysis (n=83):Pain VAS: A. 52.2 mm (SD 23.0; B: 57.8 mm (SD24.2) (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 analysisPer protocol analysis:Pain VAS: A. 48.6 mm (SD 23.1); B: 55.9 mm (SD25.4) (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 (SD15.2), p=0.051;SF-36 General Health: "no difference" Quebec Back Pain Disability: "no difference" | Withdrawals: 9 dropouts during activetreatment; 11 during placebo treatment; Withdrawals due to AEs: 6 on active therapy, 5 on placeboBowel Function Index and use of rescue laxatives: no significant differencesOverall count of AEs: A. 48, B: 40, p=0.068Serious AEs: 2 in each group; all judged not related to study meds.Somnolence: A: 5.4%; B: 0.0%, p=0.04Other AEs (nausea, constipation, fatigue, vomiting, dizziness, abdominal pain): no significant differences | PurduePharma | Good | Main intent oforal naloxone was to reduce constipation side effects; there is very lowsystemic 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 centersSouth 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 randomized196 completed(21% attrition) | A. Extended-release tramadol HCl 75 mg/acetaminophen650 mg fixed- combination tablet (n=125)Max dose=4 tabs/d=300 mg tramadolB. Placebo (n=120) | A vs. BMean age: 59.9 vs.60.4 yearsFemale 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. BPain intensity change ≥30%, full analysis set:57.7% (49/85) vs. 41.1% (37/90); p=0.037Pain intensity change ≥30%, per protocol: 63% (46/73) vs. 44.9% (35/78); p=0.027Pain intensity change ≥50%, full analysis set:31.8% vs. 20.0%; p=0.075Pain intensity change ≥50%, per protocol: 34.3%vs. 21.8%; p=0.088Korean 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 vitalityKorean 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. BAny adverse event: 83.2% (104/125) vs.54.2% (65/120); RR 1.54 (95% CI 1.28 to1.84)Withdrawal due to adverse event: 19.2% (24/125) vs. 5.0% (6/120); RR 3.31 (95% CI 1.40 to 7.83) | JanssenKorea, 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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| **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** |
| Rauck, 2014 | 59 centersUnited States | Males and non-pregnant, non- lactating females age18-75 years, with moderate-to-severe chronic LBP for ≥3 months, average pain score ≥4Exclude: 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 bloodpressure, BMI >45, or depression | 302 randomized183 completed(39% attrition) | A. Extended-release hydrocodone in 10-, 20-, 30-, 40-, and50-mg capsules (n=151) Mean dose=119 mg/dMax dose=200 mg/dB. Placebo (n=151) | A vs. BMean age: 50.4 vs.50.8 yearsFemale sex: 62% vs.49%; p=0.028Race: 82% White,17% Black, 1% other vs. 80% White, 17% Black, 4% otherMean pre-study opioid usage: 76.8 vs. 79.2 mg/day MEDMean pain score before titration (NRS):6.9 vs. 6.9Mean 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. BChange from baseline in mean daily pain intensity score: 0.48 vs. 0.96; p=0.008 | A vs. BWithdrawal due to adverse event: 1.3% (2/151) vs. 3.3% (5/151); RR 0.40 (95% CI0.08 to 2.03) | Zogenix, Inc. | Poor | Dosages,specific AEsEERW design |

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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** |
| SchiphorstPreuper, 2014 | 2 centersThe Netherlands | Age ≥18 years, withchronic LBP lasting>3 months, a VASscore ≥4Exclude: hypertension, mental or physical conditions leading to reduced functioning | 50 randomized43 completed(14% attrition) | A. tramadol 37.5mg/acetaminophen325 mg fixed- combination capsule (n=25)Max dose tramadol=225 mg/d B. Placebo (n=25) | A vs. BMean age: 42 vs. 44 yearsFemale sex: 72% vs.64% Race: NRMean duration of pain:18 vs. 24 months Mean pain score (VAS): 6.1 vs. 4.7 | Chronic | Lifting, carrying, andbending; 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** |
| SchiphorstPreuper, 2014 | 2 weeks | A vs. BLifting (kg), baseline-followup: 18-19 vs. 20-17 kg;change 1 vs. -3 kgCarrying (kg), baseline-followup: 24-20 vs. 24-21 kg; change -4 vs. -3Static bending (s), baseline-followup: 119-143 vs.158-192.5; change 24 vs. 34.5 sDynamic bending (s/rep), baseline-followup: 2.7-2.8 vs. 2.7-3.0; change 0.1 vs. 0.3Roland Morris Disability Questionnaire (0-24), baseline-followup: 13.0-11.5 vs. 13.0-13.0; change -1.5 vs. 0VAS current pain, baseline-followup: 6.1-5.1 vs.4.7-4.5; change -1 vs. -0.2VAS, maximum pain, baseline-followup: 7.3-7.4 vs.7.1-7.7; change 0.1 vs. 0.6VAS, minimum pain, baseline-followup: 4.4-3.8 vs.2.0-2.6; change -0.6 vs. 0.6Pain 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. BWithdrawal due to adverse event: 8% (2/25) vs. 0% (0/25) | Grunenthal BVand StichtingBeatrixoord | Fair |  |

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