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| **Appendix Table E7. Trials of Different Methods for Initiating and Titrating Opioids** | | | | | | |
| **Author Year** | **Study design Duration** | **Setting Country** | **Eligibility Criteria** | **Interventions** | **Sample Characteristics** | **Screened Eligible Enrolled Analyzed**  **Loss to Followup** |
| Jamison, 1998 | RCT  16 weeks | Single center Pain clinic United States | Chronic back pain >6 months duration, age 25 to 65 years, average pain intensify >40 on scale of 0 to 100, unsuccessful response to traditional pain treatment  Exclude: Cancer, acute osteomyelitis or acute bone disease, spinal stenosis and neurogenic claudication, non- ambulatory, significant psychiatric history, pregnancy, treatment for drug or alcohol abuse, clinically unstable systemic illness, acute herniated disc within 3 months | 1. Long acting morphine + short-acting oxycodone (titrated doses) + Naproxen 2. Short-acting oxycodone (set dose) + Naproxen 3. Naproxen   A vs. B vs. C  Mean dose 41.1 mg vs. NR (max 20 mg oxycodone/day) vs. NR  In all groups, max 1000 mg/day of naproxen 16 weeks | Mean age (years): 43 Female sex: 57% Race: NR  Indication: 39% failed back syndrome, 25% myofascial pain syndrome, 19% degenerative spine disease, 14% radiculopathy, 3% discogenic back pain  Prior opioid use: NR  Mean pain duration: 79 months | Screened: 48 Eligible: NR Enrolled: 36  Analyzed: 36 |
| Salzman, 1999 | RCT  10 days | Multicenter Rheumatolog y clinics and others  United States | 18 years or older, chronic stable moderate to severe back pain despite analgesic therapy with or without opioids Exclude: Contraindication to opioid history of substance abuse, unable to discontinue nonstudy narcotic, or current oxycodone dose >80 mg/day  Titration to 80 mg without achieving pain control | A: Sustained-release Oxycodone (titrated)  B: Immediate-release Oxycodone (titrated)  Titration comparison Mean dose A: 104 mg/day Mean dose B: 113 mg/day 10 days | Mean age (years): 56 Female sex: 54%  Race: 87% White, 13% Hispanic Indication: Intervertebral disc disease, nerve root entrapment, spondylolisthesis, osteoarthritis, and other non-malignant conditions  84% (48/57)  Pain duration: NR | Screened: NR Eligible: NR Enrolled: 57  Analyzed: 57 |
| Note: The references are located in Appendix C.  NR=not reported; RCT=randomized control trial; SF=short form | | | | | | |

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| **Author Year** | **Outcomes Assessed** | **Results** | **Adverse Events and Withdrawals Due To Adverse Events** | **Sponsor** | **Quality** |
| Jamison, 1998 | Pain Intensity: timing not specified, Comprehensive Pain Evaluation Questionnaire Functional status: baseline and at end of treatment (SF-36) Symptom checklist: baseline and at end of treatment (Symptom Checklist-90)  Weekly activity record at baseline and once a month  Medication diary weekly Overall helpfulness during titration and at end of study (categorical scale, 0= no help, 10=extremely helpful) | A vs. B vs. C  Average pain (means, 0-100 VAS): 54.9 vs. 59.8 vs. 65.5  Current pain (means, 0-100 VAS): 51.3 vs. 55.3 vs. 62.7  Highest pain (means, 0-100 VAS): 71.4 vs. 75.5 vs. 78.9  Anxiety (means): 11.2 vs. 15.0 vs.  31.6  Depression (means): 10.8 vs. 16.4  vs. 26.9  Irritability (means): 17.7 vs. 20.5 vs.  33.7  Level of activity (means, 0-100 scale): 49.3 vs. 49.3 vs. 51.5 Hours of sleep (means): 5.9 vs. 5.9 vs. 6.1 | A vs. B  Somnolence: 27% (8/30) vs. 37% (10/27)  Nausea: 50% (15/30) vs. 33% (9/27)  Vomiting: 20% (6/30) vs. 4% (1/27)  Postural hypotension: 0% vs. 0%  Constipation: 30% (9/30) vs. 37% (10/27)  Pruritus: 30% (9/30) vs. 26% (7/27)  Confusion: 3% (1/30) vs. 0%  Dry mouth: 0% vs. 11% (3/27)  Dizziness: 30% (9/30) vs. 22% (6/27)  Nervousness: 0% vs. 7% (2/27)  Asthenia: 7% (2/30) vs. 11% (3/27)  Headache: 13% (4/30) vs. 26% (7/27)  Withdrawal due to adverse events: 20% (6/30) vs. 7% (2/27) | Roxane Laboratories (maker of long-acting morphine and short-acting oxycodone). Not clear if authors employed by Roxane | Fair |
| Salzman, 1999 | Pain Intensity: daily diary, categorical scale (0-3, none- severe)  Study Medication Use: daily diary, amount used  Rescue Drug Use: daily diary, amount used  Achievement of Stable Pain Control: Stable pain control considered achieved if pain intensity rated as 1.5 or less for 48 hours with no more than 2 doses of rescue medication  Time to Stable Pain Control: Days | A vs. B  Mean decrease in pain intensity (0 to 3 scale): 1.1 vs. 1.3 (NS)  Proportion achieving stable analgesia: 87% (26/30) vs. 96% (26/27) (p = 0.36)  Time to stable pain control: 2.7 vs. 3.0 days (p = 0.90).  Mean number of dose adjustments:  1.1 vs. 1.7 adjustments (p = 0.58) | A vs. B vs. C  Withdrawal due to adverse events: 54% (29/54) vs. 34% (20/59) vs. 130% (6/54) (p=0.008 for A or C vs. B) Withdrawal due to nausea and/or vomiting: 46% (25/54) vs. 22% (13/59) vs. 22% (12/54)  Any adverse event: 76% vs. 70% vs. 61%  Dizziness: 7% vs. 7% vs. 7%  Headache: 18% vs. 15% vs. 13%  Dry mouth: 0% vs. 2% vs. 6%  Constipation: 7% vs. 3% vs. 11%  Diarrhea: 7% vs. 5% vs. 2%  Vomiting: 18% vs. 12% vs. 7%  Nausea: 54% vs. 42% vs. 33%  Somnolence: 9% vs. 7% vs. 0%  Pruritus: 4% vs. 2% vs. 7% | Purdue Pharma sponsored study  2 authors employees of Purdue  Role not otherwise reported. | Fair |