

S4 Table. Odds of starting (use only after LDN), discontinuing (use only before LDN), or continuing (use before and after LDN) the examined drugs, by LDN exposure.

| | | Odds of starting drug after LDN | | | Odds of discontinuing drug after LDN | | | Odds of continuing drug after LDN | | |
|--|-----------------------|--|-----------------|----------|---|-----------------|----------|--|----------------|----------|
| | | OR | 95% CI | P | OR | 95% CI | P | OR | 95% CI | P |
| Any examined drug | LDN x 2-3 vs LDN x 1 | NA | NA | 0.017 | 0.34 | (0.04 to 3.12) | 0.319 | 0.58 | (0.17 to 1.96) | 0.371 |
| | LDN x 4+ vs LDN x 1 | NA | NA | 0.085 | 1.64 | (0.51 to 5.30) | 0.401 | 0.38 | (0.14 to 1.04) | 0.051 |
| | LDN x 4+ vs LDN x 2-3 | 0.51 | (0.13 to 1.94) | 0.314 | 4.82 | (0.61 to 37.99) | 0.101 | 0.66 | (0.25 to 1.70) | 0.386 |
| DMARDs | LDN x 2-3 vs LDN x 1 | 1.27 | (0.47 to 3.47) | 0.636 | 0.54 | (0.16 to 1.78) | 0.301 | 0.86 | (0.47 to 1.56) | 0.612 |
| | LDN x 4+ vs LDN x 1 | 0.50 | (0.19 to 1.33) | 0.156 | 1.19 | (0.53 to 2.64) | 0.674 | 0.52 | (0.32 to 0.85) | 0.009 |
| | LDN x 4+ vs LDN x 2-3 | 0.39 | (0.14 to 1.08) | 0.062 | 2.22 | (0.73 to 6.73) | 0.150 | 0.61 | (0.36 to 1.05) | 0.074 |
| NSAIDs | LDN x 2-3 vs LDN x 1 | 1.18 | (0.35 to 4.01) | 0.793 | 0.96 | (0.42 to 2.20) | 0.916 | 1.07 | (0.59 to 1.95) | 0.820 |
| | LDN x 4+ vs LDN x 1 | 1.50 | (0.56 to 3.99) | 0.414 | 0.77 | (0.39 to 1.55) | 0.470 | 1.03 | (0.63 to 1.67) | 0.907 |
| | LDN x 4+ vs LDN x 2-3 | 1.27 | (0.45 to 3.64) | 0.652 | 0.81 | (0.37 to 1.77) | 0.596 | 0.96 | (0.56 to 1.65) | 0.884 |
| Analgesics | LDN x 2-3 vs LDN x 1 | 2.84 | (1.00 to 8.05) | 0.043 | 2.39 | (0.75 to 7.61) | 0.131 | 0.70 | (0.38 to 1.32) | 0.271 |
| | LDN x 4+ vs LDN x 1 | 1.07 | (0.39 to 2.99) | 0.891 | 2.36 | (0.85 to 6.52) | 0.089 | 0.48 | (0.29 to 0.80) | 0.004 |
| | LDN x 4+ vs LDN x 2-3 | 0.38 | (0.16 to 0.92) | 0.027 | 0.99 | (0.41 to 2.37) | 0.979 | 0.68 | (0.39 to 1.18) | 0.171 |
| TNF-α antagonists | LDN x 2-3 vs LDN x 1 | 2.15 | (0.35 to 13.17) | 0.399 | 0.27 | (0.03 to 2.36) | 0.206 | 1.13 | (0.43 to 3.03) | 0.801 |
| | LDN x 4+ vs LDN x 1 | 0.00 | NA | 0.063 | 0.57 | (0.16 to 2.02) | 0.380 | 0.99 | (0.44 to 2.25) | 0.982 |
| | LDN x 4+ vs LDN x 2-3 | 0.00 | NA | 0.007 | 2.11 | (0.24 to 18.41) | 0.488 | 0.87 | (0.36 to 2.12) | 0.765 |
| Systemic corticosteroids | LDN x 2-3 vs LDN x 1 | 1.06 | (0.42 to 2.65) | 0.906 | 1.06 | (0.42 to 2.65) | 0.906 | 0.42 | (0.22 to 0.83) | 0.012 |
| | LDN x 4+ vs LDN x 1 | 0.55 | (0.24 to 1.28) | 0.163 | 0.97 | (0.45 to 2.07) | 0.935 | 0.48 | (0.28 to 0.80) | 0.005 |
| | LDN x 4+ vs LDN x 2-3 | 0.52 | (0.21 to 1.30) | 0.158 | 0.92 | (0.40 to 2.12) | 0.839 | 1.12 | (0.58 to 2.15) | 0.728 |
| Other DMARDs | LDN x 2-3 vs LDN x 1 | 1.22 | (0.39 to 3.78) | 0.733 | 0.54 | (0.16 to 1.78) | 0.301 | 1.14 | (0.6 to 2.15) | 0.685 |
| | LDN x 4+ vs LDN x 1 | 0.00 | NA | <0.001 | 0.68 | (0.28 to 1.63) | 0.383 | 0.76 | (0.45 to 1.3) | 0.315 |
| | LDN x 4+ vs LDN x 2-3 | 0.00 | NA | <0.001 | 1.27 | (0.40 to 4.07) | 0.689 | 0.67 | (0.37 to 1.20) | 0.174 |
| Opioids | LDN x 2-3 vs LDN x 1 | 1.27 | (0.47 to 3.47) | 0.636 | 2.08 | (0.79 to 5.46) | 0.129 | 0.90 | (0.50 to 1.65) | 0.741 |
| | LDN x 4+ vs LDN x 1 | 1.11 | (0.48 to 2.59) | 0.805 | 3.14 | (1.40 to 7.03) | 0.004 | 0.37 | (0.22 to 0.62) | <0.001 |
| | LDN x 4+ vs LDN x 2-3 | 0.87 | (0.36 to 2.12) | 0.765 | 1.51 | (0.72 to 3.14) | 0.273 | 0.41 | (0.23 to 0.72) | 0.002 |
| Other analgesics | LDN x 2-3 vs LDN x 1 | 2.67 | (1.00 to 7.14) | 0.045 | 2.43 | (0.56 to 10.49) | 0.221 | 0.59 | (0.33 to 1.08) | 0.087 |
| | LDN x 4+ vs LDN x 1 | 0.91 | (0.34 to 2.43) | 0.852 | 2.87 | (0.80 to 10.22) | 0.091 | 0.59 | (0.36 to 0.96) | 0.031 |
| | LDN x 4+ vs LDN x 2-3 | 0.34 | (0.14 to 0.81) | 0.012 | 1.18 | (0.41 to 3.40) | 0.758 | 0.99 | (0.57 to 1.71) | 0.974 |

LDN, low dose naltrexone. OR: Odds Ratio. DMARD, disease modifying antirheumatic drug. NSAID, non-steroid anti-inflammatory drug. Three groups based on number of LDN dispenses: LDN x1 (N = 105) collected LDN once, LDN x2-3 (N = 75) two or three times and LDN x4+ (N = 180) four or more times. Other DMARDs include methotrexate, antimalarials, aminosalicylates and leflunomide. DMARDs is the sum of TNF- α antagonists, systemic corticosteroids and other DMARDs. Other analgesics include paracetamol/acetaminophen and other non-opioid analgesics. NA, not possible to calculate per definition.