S5 Table. Interrupted time series, disease modifying MS agents, comparison of groups.

|                        | Slope (x 10 <sup>-3</sup> ) (95% CI) |                  | р      | Intercept (95% CI) |                | р     |
|------------------------|--------------------------------------|------------------|--------|--------------------|----------------|-------|
| LDN x 1 vs. LDN x 2-3  | 34.2                                 | (14.3 to 54.0)   | 0.001  | -5.1               | (-13.5 to 3.3) | 0.234 |
| LDN x 1 vs. LDN x 4+   | -9.0                                 | (-22.7 to 4.6)   | 0.199  | -3.3               | (-9.0 to 2.5)  | 0.271 |
| LDN x 2-3 vs. LDN x 4+ | -43.2                                | (-59.9 to -26.5) | <0.001 | 1.9                | (-5.2 to 9.0)  | 0.604 |

Difference in difference of slope (coefficient) and intercept two years before and two years after first low dose naltrexone (LDN) dispense. Sum of DDD/patient in 30 days intervals in three groups with different LDN exposure.