

Effect of Nabiximols Cannabinoid Oromucosal Spray on Spasticity and Muscle Strength in Persons With Multiple Sclerosis Across 3 Randomized Controlled Trials

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SUMMARY

- All 3 trials showed statistically significant improvement in spasticity Numeric Rating Scale (NRS) score with nabiximols vs placebo
- The improvement in spasticity with nabiximols was not accompanied by an increase in muscle weakness, often observed with antispasticity medications, or by a change in preferred walking speed
- There was no meaningful correlation between change in spasticity NRS score and change in Motricity Index (MI), and weak to negligible correlation between change in spasticity NRS score and change in preferred walking speed

INTRODUCTION

- Medications that reduce spasticity may also reduce muscle strength, potentially impairing the ability to walk.
- Using data from 3 randomized controlled trials (RCTs; GWMS0106, GWSP0604, and SAVANT)¹⁻³ of nabiximols vs placebo, the relationship was assessed between measures of spasticity and muscle strength in lower extremities, or walking speed.
- Outcomes assessed:
 - Spasticity:** mean spasticity NRS score
 - Muscle strength:** MI for legs
 - Walking speed:** Timed 10-Meter Walk (T10MW) test
 - The correlation between spasticity and strength or walking speed during the double-blind (DB) phase of each of the 3 trials

Baseline Characteristics (Double-blind Phase)

| | GWMS0106 | | GWSP0604 | | SAVANT | |
|------------------------------------|-------------|-------------|-------------|-------------|---------|------------|
| | Placebo | Nabiximols | Placebo | Nabiximols | Placebo | Nabiximols |
| Mean age, years | 47.8 | 49.7 | 48.1 | 49.1 | 50.1 | 52.0 |
| Mean duration of MS, years | 12.2 | 13.6 | 11.8 | 13.3 | 14.3 | 13.2 |
| Mean duration of spasticity, years | -- | -- | 6.7 | 8.6 | 8.3 | 7.6 |
| Disease severity, mean EDSS score | -- | -- | 5.9 | 6.0 | 5.9 | 5.7 |
| Mean spasticity NRS score | 5.4 | 5.5 | 7.1 | 7.0 | 6.9 | 6.9 |
| Mean leg MI (median) | 51.5 (51.0) | 53.1 (54.0) | 64.4 (67.0) | 63.6 (67.0) | -- | -- |
| Mean T10MW, seconds | -- | -- | 25.3 | 24.5 | 21.1 | 20.8 |

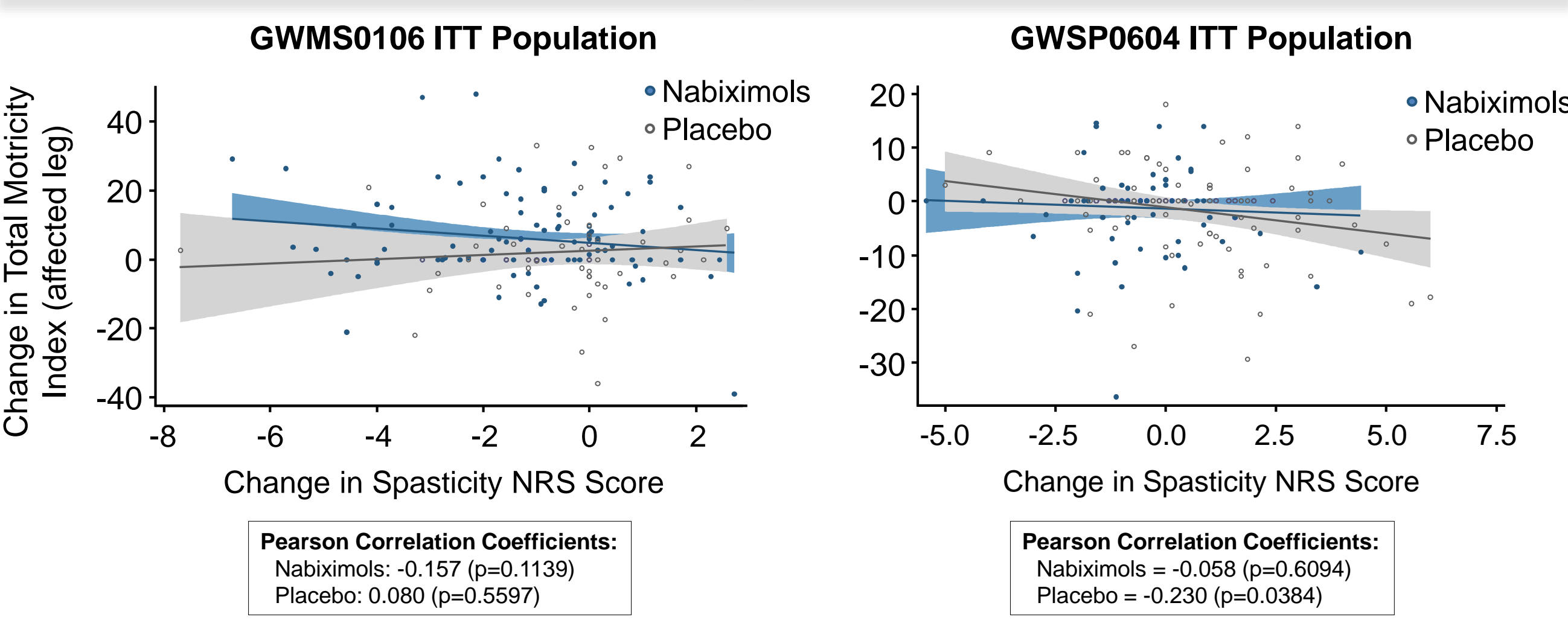
EDSS, Expanded Disability Status Scale; MS, multiple sclerosis.

Changes in Spasticity, Muscle Strength, and Mobility (DB Phase)

| Trial | Placebo | Nabiximols | Treatment difference* | p value |
|--|---------|------------|-----------------------|---------|
| Change in Mean Spasticity NRS Score | | | | |
| GWMS0106 | -0.63 | -1.18 | -0.52 | 0.048 |
| GWSP0604 | 0.64 | -0.19 | -0.83 | 0.0002 |
| SAVANT | -1.6 | -3.5 | -1.9 | <0.0001 |
| Change in Adjusted Mean MI for Legs | | | | |
| GWMS0106 | 1.85 | 5.71 | 3.86 | 0.054 |
| GWSP0604 | -4.21 | -3.24 | 0.97 | 0.439 |
| Change in Mean T10MW (seconds) | | | | |
| GWSP0604 | 3.22 | -0.13 | -3.34 | 0.069 |
| SAVANT | -1.08 | -2.79 | -1.71 | 0.11 |

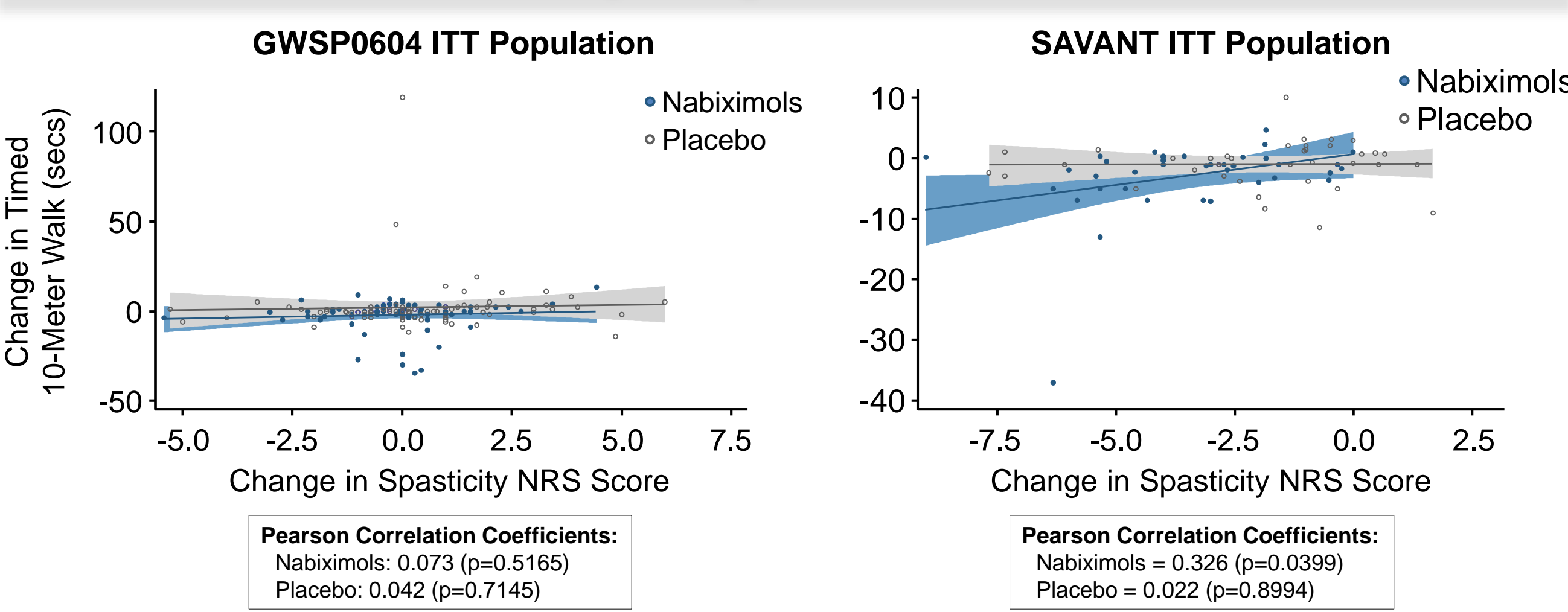
*Treatment difference favors nabiximols when it is negative for NRS and T10MW, and when it is positive for MI; all treatment differences favored nabiximols. MI was not assessed in SAVANT. T10MW was not assessed in GWMS0106.

Pearson Correlation Between Spasticity NRS and MI



Total possible score for MI is 100. ITT, intent-to-treat.

Pearson Correlation Between Spasticity NRS and T10MW



Mean T10MW speed at baseline was 25 seconds for GWSP0604 and 21 seconds for SAVANT

Correlations Between Changes in Spasticity NRS and Changes in Other Outcomes

| Outcome | Trial* | Statistic | Nabiximols | Placebo |
|---------------------|----------|----------------------|---------------------------|---------------------------|
| Change in MI (legs) | GWMS0106 | n | 102 | 55 |
| | | Correlation (95% CI) | -0.157 (-0.341 to +0.039) | 0.080 (-0.189 to +0.338) |
| | | p value | 0.1139 | 0.5597 |
| Change in T10MW | GWSP0604 | n | 79 | 81 |
| | | Correlation (95% CI) | -0.058 (-0.276 to +0.138) | -0.230 (-0.427 to -0.012) |
| | | p value | 0.6094 | 0.0384 |
| Change in T10MW | GWSP0604 | n | 82 | 80 |
| | | Correlation (95% CI) | 0.073 (-0.146 to +0.285) | 0.042 (-0.179 to +0.259) |
| | | p value | 0.5165 | 0.7145 |
| Change in T10MW | SAVANT | n | 40 | 37 |
| | | Correlation (95% CI) | 0.326 (+0.016 to +0.579) | 0.022 (-0.304 to +0.344) |
| | | p value | 0.0399 | 0.8994 |

*Correlations only apply to data from the double-blind phase of trials. CI, confidence interval.

- Data suggest there is no meaningful correlation between change in spasticity NRS score and change in lower extremity muscle strength, and weak to negligible correlation between change in spasticity NRS score and change in preferred walking speed.

METHODS

| | GWMS0106 | GWSP0604 | | SAVANT | |
|----------------|-----------------------|----------------|-------------------------------|----------------------|--------------------------|
| | | Phase A | Phase B | Phase A | Phase B |
| PwMS, n | 184 | 572 | 241 | 191 | 106 |
| Trial design | Placebo-controlled | Single-blind | Placebo-controlled | Single-blind | Placebo-controlled |
| Follow-up time | 6 weeks | 4 weeks | 12 weeks | 4 weeks (+ wash-out) | 12 weeks |
| Outcomes | Spasticity NRS and MI | Spasticity NRS | Spasticity NRS, MI, and T10MW | Spasticity NRS | Spasticity NRS and T10MW |

- All 3 trials enrolled persons with multiple sclerosis (PwMS) and spasticity inadequately managed by current medications.
- GWSP0604 and SAVANT used an enriched trial design: PwMS were treated with single-blind standard of care (SOC) + nabiximols in Phase A, and those reporting at least a 20% improvement in spasticity NRS score were randomized in Phase B to either SOC + nabiximols or SOC + placebo.

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