**The Effects of Combining Electrical Stimulation of the Calf and Thigh Muscles in Patients with Knee Osteoarthritis: A Double Blind, Randomised, Sham-Controlled Trial**

**Results summary:**

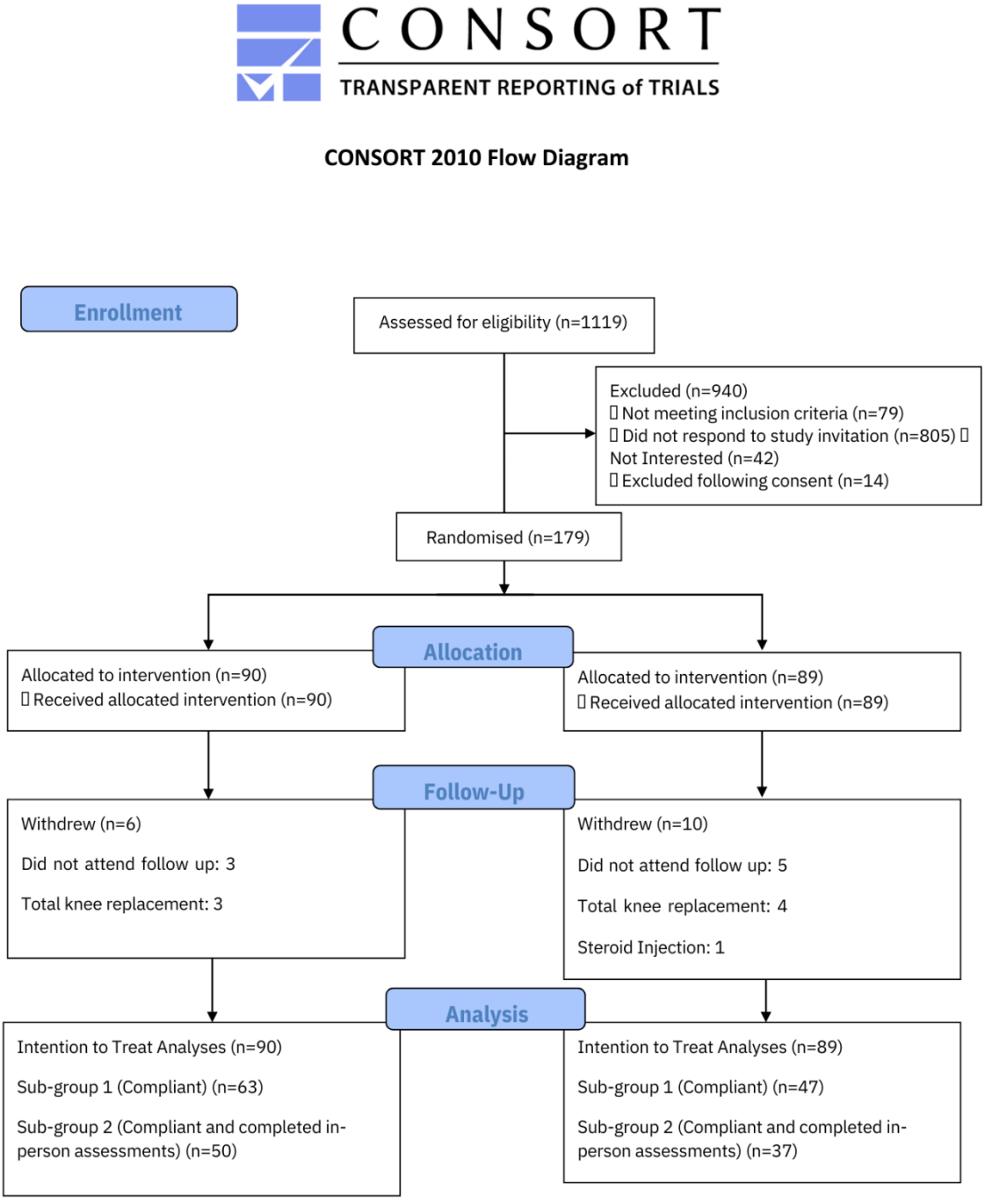


**Figure 1.** CONSORT trial diagram

**Table 1.** Participant demographics

| | Active (N=90) | Sham (N=89) | Total (N=179) |
|---|---|---|---|
| Age (years) | 67.5 (8.5) | 66.2 (8.9) | 66.9 (8.7) |
| BMI (kg/m2) | 30.0 (4.7) | 31.1(4.6) | 30.6 (4.6) |
| Sex (Female) n= (%) | 51 (56.7) | 40 (44.9) | 91 (50.8) |
| Ethnicity n= (%) | | | |
| - White British | 79 (87.8) | 80 (89.9) | 159 (88.8) |
| - Asian/British Asian | 9 (10.0) | 7 (7.9) | 16 (8.9) |
| - Black/Black British Caribbean | 0 | 1 (1.1) | 1 (0.6) |
| - Any other White background | 2 (2.2) | 1 (1.1) | 3 (1.7) |
| Time since OA diagnosis (years) | 7.5 (9.1) | 5.8 (6.7) | 6.6 (8.0) |
| Lives Alone n= (%) | 19 (21.1) | 14 (15.7) | 33 (18.4) |
| Retired n=(%) | 55 (61.1) | 47 (52.8) | 102 (57.0) |

Values expressed as mean (SD) unless displayed as n= (percentage).
Abbreviations: BMI: Body Mass Index; OA: Osteoarthritis.

**Table 2.** WOMAC, OKS, and physical outcomes ITT pre and post intervention

| | NMES | | | | Sham | | | | Between groups | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Adjusted difference** | **P value** |
| WOMAC Pain | 9.8 (3.7) | 8.2 (4.3) | -1.5 (-2.0, -0.9) | **<0.01** | 9.7 (3.3) | 8.8 (3.8) | -0.8 (-1.4, -0.2) | **<0.01** | -0.7 (-1.5, 0.1) | 0.10 |
| WOMAC Stiffness | 4.6 (1.9) | 3.9 (1.9) | -0.6 (-1.0, -0.3) | **<0.01** | 4.4 (1.6) | 4.1 (1.9) | -0.3 (-0.7, 0.0) | 0.07 | -0.3 (-0.8, 0.2) | 0.21 |
| WOMAC Function | 34.8 (14.3) | 29.4 (15.0) | -5.0 (-7.1, -3.0) | **<0.01** | 34.9 (13.0) | 31.0 (13.7) | -3.5 (-5.6, -1.5) | **<0.01** | -1.5 (-4.5, 1.5) | 0.32 |
| WOMAC Total | 49.1 (19.0) | 41.5 (20.5) | -7.2 (-9.9, -4.4) | **<0.01** | 49.0 (17.0) | 43.9 (18.5) | -4.6 (-7.4, -1.8) | **<0.01** | -2.5 (-6.5, 1.4) | 0.21 |
| OKS Total | 24.4 (10.0) | 27.5 (10.7) | 2.8 (1.5, 4.1) | **<0.01** | 24.3 (8.1) | 25.9 (9.5) | 1.5 (0.1, 2.9) | **<0.05** | 1.3 (-0.6, 3.3) | 0.18 |
| OKS Pain Domain | 47.8 (20.6) | 53.5 (23.0) | 5.4 (2.3, 8.5) | **<0.01** | 46.3 (17.4) | 50.8 (20.8) | 4.2 (0.9, 7.5) | **<0.05** | 1.2 (-3.4, 5.7) | 0.61 |
| OKS Function | 55.4 (23.0) | 60.8 (23.6) | 4.8 (1.7, 8.0) | **<0.01** | 55.5 (18.4) | 58.6 (20.7) | 2.4 (-0.9, 5.6) | 0.15 | 2.5 (-2.1, 7.0) | 0.29 |
| KE Strength (N) | 81.1 (50.7) | 103.1 (54.2) | 19.9 (13.6, 26.3) | **<0.01** | 88.8 (43.6) | 110.1 (47.9) | 15.6 (8.3, 22.8) | **<0.01** | 4.4 (-6.2, 15.0) | 0.41 |
| KE Strength/BW (N/kg) | 1.0 (0.6) | 1.2 (0.6) | 0.2 (0.2, 0.3) | **<0.01** | 1.0 (0.4) | 1.2 (0.5) | 0.2 (0.1, 0.3) | **<0.01** | 0.1 (0.0, 0.2) | 0.21 |
| Knee Swelling (mm) | 40.0 (4.3) | 40.0 (4.1) | -0.2 (2.6)* | 0.39 | 40.3 (3.6) | 39.7 (4.5) | -0.9 (3.2)* | 0.14 | 0.0 (-0.1, 0.3)* | 0.73 |
| Ankle swelling (mm) | 27.2 (2.9) | 26.6 (2.6) | -0.6 (2.2)* | 0.15 | 27.5 (3.2) | 27.4 (3.5) | 0.1 (2.8)* | 0.93 | 0.0 (-0.5, 0.1)* | 0.45 |
| ISWT (metres) | 311.7 (165.5) | 308.8 (178.2) | 8.4 (-11.8, 28.7) | 0.41 | 332.5 (187.3) | 334.4 (206.0) | 4.1 (-15.3, 23.5) | 0.68 | 4.4 (-25.4, 34.1) | 0.77 |
| ESWT (minutes) | 5.7 (5.3) | 7.2 (6.2) | 1.7 (0.5, 2.8) | **<0.01** | 6.1 (5.3) | 7.9 (7.4) | 2.1 (0.9, 3.3) | **<0.01** | -0.4 (-2.1, 1.2) | 0.62 |
| SPPB | 9.0 (2.5) | 9.1 (2.2) | 0.1 (-0.3, 0.4) | 0.61 | 9.5 (2.1) | 9.1 (2.5) | -0.2 (-0.6, 0.1) | 0.17 | 0.3 (-0.2, 0.8) | 0.19 |

Values for baseline and week 8 displayed as mean (SD). Adjusted difference: least squares mean from ANCOVA with a factor for treatment group and baseline as a covariate. Values for adjusted change displayed as mean change (95% CI). *Non-adjusted change displayed as mean (SD) for within group and mean (95% CI) for between group differences. Abbreviations: **ITT**: Intention to Treat; **WOMAC**: Western Ontario and McMaster Universities Arthritis Index; **OKS**: Oxford Knee Score; **KE**: Knee Extensor; **BW**: Body weight; **N**: Newtons; **N/kg**: Newtons per Kilogram; **mm**: Millimetres.

**Table 3.** Health related quality of life outcomes ITT pre and post intervention

| | NMES | | | | Sham | | | | Between groups | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Adjusted difference** | **P value** |
| EQ-5D-5L Index | 0.7 (0.2) | 0.7 (0.2) | 0.0 (0.0, 0.1) | **<0.05** | 0.6 (0.3) | 0.7 (0.2) | 0.0 (0.0, 0.1) | **<0.01** | 0.0 (-0.1, 0.0) | 0.57 |
| EQ-5D-5L VAS | 72.8 (17.8) | 71.1 (19.2) | -2.0 (-5.0, 1.1) | 0.20 | 68.3 (19.5) | 68.1 (19.7) | 1.3 (-4.4,1.8) | 0.41 | -0.7 (-5.0, 3.6) | 0.75 |
| SF-36 Physical Functioning | 40.0 (24.9) | 46.6 (25.9) | 6.2 (2.6, 9.9) | **<0.01** | 40.3 (23.3) | 45.6 (27.6) | 4.5 (0.5, 8.5) | **<0.05** | 1.7 (-3.6, 7.1) | 0.52 |
| SF-36 Role Limitations (Physical) | 29.8 (35.5) | 44.0 (38.8) | 13.2 (5.9, 20.4) | **<0.01** | 32.7 (39.5) | 41.8 (42.7) | 10.2 (3.0, 17.5) | **<0.01** | 2.9 (-7.3, 13.2) | 0.57 |
| SF-36 Role Limitations (Emotional) | 68.2 (41.0) | 74.3 (37.7) | 7.1 (-0.1, 14.2) | 0.05 | 62.3 (41.0) | 64.5 (40.5) | -0.3 (-7.4, 6.8) | 0.93 | 7.4 (-2.7, 17.5) | 0.15 |
| SF-36 Energy | 49.9 (21.8) | 53.7 (20.5) | 2.9 (0.0, 5.8) | **<0.05** | 50.6 (20.2) | 50.3 (19.5) | -0.1 (-3.1, 3.0) | 0.96 | 3.0 (-1.2, 7.1) | 0.17 |
| SF-36 Emotional Well-being | 73.4 (17.8) | 75.2 (19.8) | 1.8 (-1.2, 4.8) | 0.24 | 70.4 (18.4) | 71.3 (16.8) | 0.3 (-2.8, 3.5) | 0.83 | 1.5 (-2.9, 5.8) | 0.51 |
| SF-36 Social Functioning | 62.6 (28.7) | 71.0 (27.8) | 6.9 (2.8, 11.0) | **<0.01** | 63.9 (24.5) | 68.2 (25.6) | 3.6 (-0.5, 7.8) | 0.08 | 3.2 (-2.5, 8.9) | 0.27 |
| SF-36 Bodily Pain | 45.7 (22.5) | 49.7 (24.6) | 3.5 (-0.3, 7.3) | 0.07 | 44.9 (19.3) | 47.0 (20.6) | 2.3 (-1.6, 6.2) | 0.25 | 1.2 (-4.2, 6.6) | 0.66 |
| SF-36 General Health | 56.0 (20.7) | 58.5 (19.3) | 2.3 (-0.4, 5.0) | 0.09 | 55.1 (20.2) | 55.0 (19.9) | -0.4 (-3.2, 2.5) | 0.79 | 2.7 (-1.1, 6.6) | 0.17 |

Values for baseline and week 8 displayed as mean (SD). Adjusted difference: least squares mean from ANCOVA with a factor for treatment group and baseline as a covariate. Values for adjusted change displayed as mean change (95% CI). Abbreviations: **ITT**: Intention to Treat; **EQ-5D-5L**: EuroQol 5-Dimension 5-Level; **VAS**: Visual Analogue Scale; **SF-36**: Short Form Health Survey is a 36-item.

**Table 4.** Anxiety, depression, and sleep outcomes ITT pre and post intervention

| | NMES | | | | Sham | | | | Between groups | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Baseline** | **Week 8** | **Adjusted change** | **P value** | **Adjusted difference** | **P value** |
| HADS A | 6.1 (4.5) | 5.4 (3.9) | -0.8 ( -1.4, -0.3) | **<0.01** | 7.6 (3.8) | 6.8 (3.6) | -0.6 ( -1.2, 0.1) | 0.08 | -0.3 (-1.1,0.6) | 0.53 |
| HADS D | 5.4 (3.6) | 4.5 (3.4) | -1.0 ( -1.5, -0.5) | **<0.01** | 5.4 (3.5) | 5.0 (3.3) | -0.6 ( -1.1, -0.0) | **<0.05** | -0.4 (-1.2,0.3) | 0.26 |
| MOS Sleep Disturbance | 35.2 (21.9) | 30.5 (24.0) | -4.3 ( -7.5, -1.0) | **<0.05** | 35.2 (19.9) | 32.8 (22.6) | -2.7 ( -6.0, 0.6) | 0.11 | -1.6 (-6.2, 3.1) | 0.51 |
| MOS Snoring | 33.9 (30.1) | 31.6 (28.0) | -3.0 ( -6.7, 0.6) | 0.11 | 39.1 (34.4) | 38.2 (35.1) | 1.0 (-2.8, 4.7) | 0.61 | -4.0 (-9.2, 1.2) | 0.13 |
| MOS Awaken Short of Breath/Headache | 10.2 (19.9) | 10.8 (20.6) | 1.0 ( -3.2, 5.3) | 0.63 | 10.3 (18.4) | 12.4 (25.1) | 3.8 ( -0.5, 8.1) | 0.08 | -2.8 (-8.8, 3.3) | 0.37 |
| MOS Sleep Adequacy | 52.1 (25.4) | 54.0 (24.4) | 2.3 ( -2.4, 7.1) | 0.34 | 50.1 (25.7) | 51.6 (24.8) | 0.4 ( -4.6, 5.5) | 0.87 | 1.9 (-5.1, 8.8) | 0.59 |
| MOS Sleep Somnolence | 31.3 (19.9) | 25.0 (17.5) | -5.0 ( -7.9, -2.1) | **<0.01** | 25.9 (20.5) | 27.5 (23.0) | 2.1 ( -0.9, 5.2) | 0.16 | -7.1 (-11.3, -3.0) | **<0.01** |
| MOS Quantity of Sleep/Optimal Sleep | 6.5 (1.3) | 6.6 (1.4) | 0.1 ( -0.1, 0.3) | 0.42 | 6.7 (1.1) | 6.7 (1.2) | 0.1 ( -0.1, 0.3) | 0.47 | 0.0 (-0.3, 0.3) | 0.96 |
| MOS Sleep Problems Index I | 34.3 (18.0) | 30.6 (17.0) | -3.3 ( -6.0, -0.6) | **<0.05** | 33.5 (15.5) | 33.4 (18.4) | -0.3 ( -3.1, 2.5) | 0.82 | -3.0 (-6.8, 0.8) | 0.12 |
| MOS Sleep Problems Index II | 34.6 (17.3) | 30.5 (17.2) | -3.5 ( -6.2, -0.9) | **<0.01** | 33.7 (15.2) | 32.5 (18.5) | -1.5 ( -4.3, 1.2) | 0.28 | -2.0 (-5.8, 1.8) | 0.30 |

Values for baseline and week 8 displayed as mean (SD). Adjusted difference: least squares mean from ANCOVA with a factor for treatment group and baseline as a covariate. Values for adjusted change displayed as mean change (95% CI). Abbreviations: **ITT**: Intention to Treat; **HADS**: Hospital Anxiety (A) and Depression (D) Scale; **MOS**: Medical Outcomes Study Sleep Scale.

**Table 5. Summary of adverse events**

| Study Number | Type | Description | Relationship to Procedure |
|---|---|---|---|
| **30** | AE | Participant reported superficial non referring chest pain and therefore exercise testing was not performed. | No relationship (sham) |
| **32** | AE | Withdrawn as under investigations for abdominal pain (prior to randomisation) | No relationship (withdrawn prior to randomisation) |
| **45** | AE | Fractured left foot (prior to randomisation) | No relationship (withdrawn prior to randomisation) |
| **95** | SAE | Participant experienced symptoms of fatigue; medical investigation revealed problem with previous mitral valve replacement. Hospitalised to perform mitral valve surgery. | No relationship (sham) |