**Supplementary Table 1**: Study characteristics

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| **Author (Year)** | **Study Location** | **Aim** | **Sample** | **Average Time since diagnosis (Years)** | **Intervention and Control** | **Setting** | **Therapy Provider** | **Outcomes measured** | | **Results** |
| Nazari, et al (2015)(28) | Isfahan,Iran | To compare the effects of reflexology and relaxation on fatigue in women with MS | **Reflexology** n=25 Age=34.4 (SD 6.6)  **Relaxation** n=25 Age=33.9 (SD 5.6)  **Control** n=25 Age=34.4 (SD 7.7)  **100% Females**  EDDS=Not stated | **Reflexology**:6.66 (5.47)  **Relaxation**:5.18 (4.69)  **Control**:4.78 (3.36) | **Relaxation group**: Combination of Jacobson and Benson technique **Reflexology group**: Massaging plantar reflexology points, solar plexus and special reflex therapy  **Control:** Routine treatment and | 40 minute sessions at Kashani MS clinic, held twice a week for 4 weeks, in a bright, silent warm room. | Delivered by a physician | **Fatigue:** Fatigue Severity Scale (FSS).  Questionnaires completed before, immediately after and 2 months post intervention. | | Statistically significant difference in mean fatigue severity scores between groups immediately after and 2 months after the intervention (P<0.001). |
| Nazari, et al (2016)(29) | Isfahan,Iran | To determine and compare the effects of reflexology and relaxation on pain in women suffering from MS | **Reflexology** n=25 Age=34.4 (SD6.6)  **Relaxation** n=25 Age=33.9 (SD 5.6)  **Control** n=25 Age=34.4 (SD 6.6)  **100% Female**  EDDS=Not stated | **Reflexology:**4.78 (3.36)  **Relaxation:**5.18 (4.69)  **Control:**6.66 (5.47) | **Relaxation group**: Combination of Jacobson's and Benson's relaxation technique via audio tapes. Participants divided into 5 groups of 5. **Reflexology group**: Generic reflexology and precision reflexology. **Control:** Routine care and medical treatments as directed by a doctor. | 40 minute sessions at Kashani MS clinic, held twice a week for four weeks, in a bright, silent warm room. | Delivered by researcher trained by a physician qualified in reflexology. | **Pain**: Numeric Rating Scale (NRS).  Questionnaire completed before, immediately after and 2 months post intervention. | | Significantly higher reduction in pain scores with the reflexology intervention group compared to the other groups (P<0.001). |
| I Siev-Ner, et al (2003)(36 | Tel-Hashomer, Israel | To compare the effect of reflexology treatment versus non-specific massage on MS patients with spasticity, sensory and urinary symptoms | **Reflexology** n=27 Age=46.2 (SD 9.3) Females=17  **Control**  n=26 Age= 49.2 (SD 11) Females=17  EDDS=Not stated | **Reflexology:**11.9 (9.2)  **Control:**13.4 (9.1) | **Intervention:** Reflexology treatment applying manual pressure on specific points of foot soles and massage of the calf area. **Control:** Sham treatment of nonspecific massage of the calf conducted by the same therapists in both groups. | 45 minute sessions, once a week for 11 weeks. At Sheba Medical Centre (Clinic of Complementary Medicine). | Delivered by reflexologists | 11. Spasticity: Assessed by Ashworth scale  Assessments performed before, start, 6 weeks, end and 3 months after. | | Statistically significant improvements observed in reflexology group for outcome: spasticity (P=0.03) |
| Sajadi, et al (2020-B.(30) | Arak,Iran | To investigate the effect of foot reflexology on constipation and QoL in patients with MS | **Reflexology** n=33 Age=34.5 (SD 8.4) Females=31  **Control**  n=30 Age=32.1 (SD 7.7) Females=28  EDDS=Not stated | Not stated | **Intervention:** Foot reflexology using the Rwo Shur method.  **Control**: Foot surface massage without pressure.  Patients received standard MS therapeutic protocols. | Sessions took place in separate room lasting 30-40 minutes, twice a week for 6 weeks. Conducted in MS Society of Arak | Author trained and certified at the MS society of Arak. | 1. **QoL:**SF36 QOL questionnaire.  2. Fatigue: Subscale of SF36 QOL questionnaire.  3. Pain: SF36 QOL questionnaire.  4. Emotional well-being: SF36 QOL questionnaire.  Outcomes measured before and after intervention | | QoL improved in intervention group, however not statistically significant. |
| Sajadi, et al (2020)-A(31) | Arak,Iran | To indicate the role of reflexology as a complementary therapy on the improvement of fatigue, sleep quality and anxiety in patients with MS | **Reflexology** n=33 Females=31  **Control**  n=30 Females=28  Age Range=20-49  EDDS=Not stated | Not Stated | **Intervention**: Rwo Shur method of reflexology.  **Control**: Non-specialised foot massage. | 8 sessions, twice a week for 4 weeks in a private room. | Delivered by a qualified reflexologist. | **1.** **Fatigue**: Fatigue Impact Scale  **2.** **Anxiety**: State-Trait Anxiety Inventory. Measured using four part questionnaire at baseline and at week 4. | | Reflexology showed improvements in physical fatigue (P=0.042), anxiety (P=0.034). Lower fatigue scores were observed with reflexology, however not statistically significant (P=0.134). |
| Hughes, et al (2009)(35) | Northern Ireland | To determine the effectiveness of reflexology on the modification of pain in people with MS | **Precision reflexology** n=35 Age= 50 (SD11.1) Females=30  EDSS=5.8 (SD 1.0)  **Sham reflexology** n=36 Age=53 (SD 11) Females=29  EDSS=6.2 (SD 0.8) | **Precision reflexology**:12.9(8.9) **Sham reflexology**:12.2(8.4) | **Precision reflexology:** Reflexology based on Eunice Ingham's method  **Sham reflexology group:** Standardised foot massage using same predefined sequences. | 45 minute sessions every week for 10 weeks in partcipants own home or at local venue. | Delivered by a reflexologist. | **Primary outcome: Pain**: Visual analogue scale (VAS). **Secondary outcomes:**, , Spasticity, , Fatigue using Fatigue Severity Scale, Measurements were taken at baseline, week 10,16 and 22. | | Significant reductions observed in the majority of the outcomes for both intervention and control groups. |
| Ebrahimi, et al (2020)(32) | Yazd,Iran | To explore the impact of foot reflexology on fatigue,  stress, and serum cortisol levels in women with MS | **Intervention** n=30 Age=32.7 (SD 5.6)  EDSS=25.3 (SD 0.3)  **Control**  n=30 Age=32.3 (SD 5.4)  100% Females  EDSS=2.4 (SD 0.4) | **Intervention**:7.1 (4.57)  **Control:**5.79 (2.43) | **Intervention**: Foot reflexology  **Control**: Simple foot massage  , | Three times a week for 4 weeks at participants home. | Care giver trained to give reflexology | **1.** **Fatigue:** Fatigue Severity Scale (FSS) | | Statistically significant reduction in fatigue observed in the intervention group. |
| Miller, et al (2013)(34) | Scotland | To investigate the feasibility of delivering reflexology to people more severely affected by MS and to evaluate the effects of the treatment on QoL and a range of symptoms | **Intervention** n=10 Age=53.6 (SD 10.3) Females=6  EDSS=7.2 (SD 0.5)  **Control**  n=10 Age=58.1 (SD 9.6) Females=3  EDSS= 7.4 (SD 0.5) | **Reflexology:**17.8 (5.8)  **Sham:**21.7 (12.1) | **Reflexology group**: Standardised sequence of pressure massage adapting to patients needs.  **Sham reflexology group**: Lower leg and foot massage using no pressure.  . | 1 hour, weekly sessions for 8 weeks at a rehabilitation unit | Delivered by a reflexologist | **1**. **QoL**: MS Impact Scale (MSIS29) **2.** Visual analogue scale assessing muscle stiffness, muscle spasm, body pain, **3**.**Mood:**The Hospital Anxiety and Depression Scale. Measurements were taken at baseline, 8 weeks (end of intervention) and 8 weeks after intervention (week 16) | | No statistically significant differences in MSIS29 in reflexology group. Both groups showed non-significant improvements in most of the outcomes post intervention, however most scores returned to baseline after 16 weeks. |
| Seddighi-khavidak, et al (2020)(33) | Tehran,Iran | To evaluate the effect of using lavender oil as an olfactory stimulus with vestibular rehabilitation (VR) on balance, fear of falling down, and ADL of people with MS. | **Intervention** n=15 Age=45.8 (SD 5.7) Females=10  **Control** n=15 Age=44.6 (SD 7.8) Females=10  EDDS=Not stated | **Intervention:**14.1 (3.8)  **Control:**16.2 (6.3) | **Intervention group**: VR exercises with participants wearing a mask with lavender oil essence.  **Control:** VR exercises with no mask and essence.  Both groups received standard therapy based on a VR exercise protocol. | One on one, 45 minute sessions on even days for 10 sessions at Iran MS Society Centre | Delivered by a physiotherapist | **.1.** **ADL**: MS Impact Scale (MSIS29)  Measurements were taken at baseline and after the last session. | Significant improvements in outcome measures in the intervention group compared to control. | | |