APPENDICES

APPENDIX 1: SIGN 50 levels of evidence (2012)

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

Levels of evidence

1^{++} High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

1^{+} Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2^{++} High quality systematic reviews of case control or cohort or studies
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2^{+} Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2^{-} Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3 Non-analytic studies, e.g. case reports, case series

4 Expert opinion

Grades of recommendations

[A] At least one meta-analysis, systematic review, or RCT rated as $1^{++,}$ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results

[B] A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1^{++} or 1^{+}

[C] A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}

[D] Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+} 25

Appendix 2: SIGN 50 COMPLETED RCT CHECKLIST (VARIOUS APPRAISED STUDIES; TABLE 2.1 TO 2.6)

Table 2.1

Completed Appraisal Checklist		
Study Identification: Forough F, Moosa S, Habib S, Payam S, Mahnaz S (2017) Pelvic floor muscle training instruction to control urinary incontinence and its resulting, anxiety and depression in patients with multiple sclerosis. Jundishapur J Chronic Dis Care. 2017		
Guideline Topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered**
1.3	An adequate concealment method is used	**Adequately covered**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Single-arm clinical trial**
1.5	The treatment and control groups are similar at the start of the trial	**NA**
1.6	The only difference between groups is the treatment under investigation	**NA**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**Well covered**

1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**NA**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**Not applicable**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	++
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**yes**
2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**Yes- studies physical therapy intervention and its impact and shows better response.**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**50 MS**
3.2	What are the main characteristics of the patient population?	**MS with UI**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**PFMT**
3.4	What comparison are made in the study	**NA**
3.5	How long are patients followed up in the study?	**Three months**
3.6	What outcome measure(s) are used in the study?	**Incontinence Questionnaires-Urinary incontinence short form (ICIQ-UI-SF) , and 21-Item depression, anxiety and stress scale (DASS-21)**
3.7	What size of the effect is identified in the study?	**The significant improvement in incontinence and decrease in stress, depression and anxiety.**
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Yes, Physical therapy interventions give good outcome in the MS population with UI.**

Table 2.2

Completed Appraisal Checklist		
Study Identification: Lucio AC, Perissionto MC, Natalin RA, Prudente A, Damasceno BP, et al. (2011) Comparative study of pelvic floor muscle training in women with MS: its impact on lower urinary tract symptoms and quality of life. Clinics 2011.		
Guideline topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered**
1.3	An adequate concealment method is used	**Well covered**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Yes**
1.5	The treatment and control groups are similar at the start of the trial	**The treatment group received PFMT & vaginal perineometer with instruction from therapist. Control group only perineometer inside the vagina instructed to do it twice /week for 30 min.**
1.6	The only difference between groups is the treatment under investigation	**Well covered**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**Treatment group 18 women, sham group 17 women**
1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**Well covered**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**Not applicable**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	++
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	**NA**
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**Yes**
2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**Yes –studies MS population with urinary incontinence**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**35 women 18 treatment group, and 17 control group**
3.2	What are the main characteristics of the patient population?	**MS patients with UI.**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**Pelvic floor muscle training exercises, perineometer.**
3.4	What comparison are made in the study	**Pelvic floor muscle exercise perineometer v perineometer with no exercise.**
3.5	How long are patients followed up in the study?	**Up to 3 months**
3.6	What outcome measure(s) are used in the study?	**Incontinence Questionnaires-Urinary incontinence short form (ICIQ-UI-SF), overactive bladder questionnaires, and QOL**

3.7	What size of the effect is identified in the study?	**Significant reduction in urinary incontinence and improvement of QOL in MS population.**
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Yes, there is significant improvement in urinary continence and QOL in the MS population than without physical therapy intervention**

Table 2.3

Completed Appraisal Checklist		
Study Identification: McClurg D, Ashe RG, Lowe-Strong AS (2009) Electrical Stimulation is a useful adjunct in the management of urinary incontinence in people with multiple sclerosis. Australian Journal of physiotherapy.		
Guideline topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered**
1.3	An adequate concealment method is used	**Well covered**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Adequately addressed**
1.5	The treatment and control groups are similar at the start of the trial	**Yes, Well covered**
1.6	The only difference between groups is the treatment under investigation	**The electrical stimulation**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**none**
1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**Adequately covered**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**Not applicable**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	++
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**Yes**
2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**YES –showed improvement in both UI (QOL**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**74 Participants**
3.2	What are the main characteristics of the patient population?	**MS with UI**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**PFMT & Electrical stimulation**
3.4	What comparison are made in the study	**Pelvic floor muscle exercise (PFMT) &ENMS v Non- intervention**
3.5	How long are patients followed up in the study?	**24 Weeks**
3.6	What outcome measure(s) are used in the study?	**Episode of leakage & weight of pads,**
3.7	What size of the effect is identified in the study?	**At 9 weeks 0.8 less incontinence, episodes (95% CI 0.1 TO 1.4 AND 89%lighter pads (95%ci 8 to 1.71) than the control group.at 24 weeks pad weights were the only objective outcome that remained statistically significant.**
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Yes-there is significant improvement in continence and QOL in MS population with UI.**

Table 2.4

Completed Appraisal Checklist		
Study Identification: Khan F, Pallant JF, Pallant JI, Brand C, Kilpatrick TJ (2010) A randomized controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis. J Neural Neurosurg Psychiatry.		
Guideline topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered**
1.3	An adequate concealment method is used	**Well covered**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Yes**

1.5	The treatment and control groups are similar at the start of the trial	**Treatment group received personalized, multidisciplinary rehabilitation program 2-3/week for 6 weeks. continue with maintenance program for twelve months. Control group maintenance program only**
1.6	The only difference between groups is the treatment under investigation	**Well covered**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**Treatment group 34, control group 24**
1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**Well covered**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**NA**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	**++**
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**YES**
2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**Yes –compares personalized, multidisciplinary rehabilitation program 2-3/week for 6 weeks. continue with maintenance program for twelve months. Versus control group maintenance program only, and the intervention group has significantly better results**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**58 patients: 34 treatment group and 24 control group**
3.2	What are the main characteristics of the patient population?	**MS with UI**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**Physical therapy intervention for MS population.**
3.4	What comparison are made in the study	**rehabilitation program 2-3/week for 6 weeks, continue with maintenance program for twelve months v maintenance program only**
3.5	How long are patients followed up in the study?	**12 MONTHS**
3.6	What outcome measure(s) are used in the study?	**IIQ-7, UDI-6, and QOL.**
3.7	What size of the effect is identified in the study?	The treatment group compared with the control group showed improvement: 78% versus 27% for UDI6 and 59% versus 17% improved for IIQ7. More patients in the control group deteriorated over the study period on the UDI6 (30% vs 0%; p<0.001) and IIQ7 (39 vs 0%; p=0.001).
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Yes**

Table 2. 5

Completed Appraisal Checklist		
Study Identification: McClurg D, Ashe RG, Mashall K, Lowe-Strong AS (2006) Comparison of pelvic floor muscle training, electromyography biofeedback, and neuromuscular electrical stimulation for bladder dysfunction in people with multiple sclerosis: a randomized pilot study. Neurourol Urodyn. 2006		
Guideline topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered.**
1.3	An adequate concealment method is used	**Well covered**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Yes**
1.5	The treatment and control groups are similar at the start of the trial	**Three groups** **1-Pelvic Floor Training and Advice (PFTA),** **2-PFTA, and EMG Biofeedback,** **3-PFTA, EMG Biofeedback and Neuromuscular electrical stimulation** **(NMES)**
1.6	The only difference between groups is the treatment under investigation	**Well covered**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**

1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**30 patients**
1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**Well covered**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**Not applicable**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	+ +
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**Yes**
2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**Yes**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**30, 10 in each group**
3.2	What are the main characteristics of the patient population?	**MS with UI**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**Impact of physical therapy with different modalities on the MS patients**
3.4	What comparison are made in the study	**Pelvic Floor Training and Advice (PFTA),** **V. PFTA, and EMG Biofeedback, V. PFTA, EMG Biofeedback and Neuromuscular electrical stimulation (NMES)**
3.5	How long are patients followed up in the study?	**9 WEEKS**
3.6	What outcome measure(s) are used in the study?	**24-hour pad test, digital assessment of pelvic floor, EMG, QOL questionnaire (QII and UDI)**
3.7	What size of the effect is identified in the study?	**Group 3 demonstrated superior benefit as measured by the number of leaks and pad test than Group 2, with Group 1 showing less improvement when compared to week 0; this was statistically significant between Groups 1 and 3 for number of leaks (P = 0.014) and pad tests (P = 0.001), and Groups 1 and 2 for pad tests (P = 0.001). A similar pattern was evident for all other outcome measures.**
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Yes.**

Table 2.6

Completed Appraisal Checklist		
Study Identification: Deseze M, Raibaut P, Gallien P (2011) Transcutaneous posterior tibial nerve stimulation for treatment of the overactive bladder syndrome in multiple sclerosis: result of a multicenter prospective study. Neurourol Urodyn. 2011		
Guideline Topic: Physical therapy intervention in treatment of urinary incontinence in MS patients		
Checklist completed by: NAJWA ALFARRA		
Section 1: Internal validity		
In a well conducted RCT study		In this study this criterion is:
1.1	The study addresses an appropriate and clearly focused question	**Well covered**
1.2	The assignment of subjects to treatment groups is randomized	**Well covered**
1.3	An adequate concealment method is used	**Adequately addressed**
1.4	Subjects and investigators are kept 'blind' about treatment allocation	**Well covered**
1.5	The treatment and control groups are similar at the start of the trial	**Well covered**
1.6	The only difference between groups is the treatment under investigation	**YES**
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	**Well covered**
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**None**
1.9	All the subjects analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	**Well covered**
1.10	Where the study is carried out at more than one site, results are comparable for all sites	**Not applicable**
Section 2: Overall assessment of the study		
2.1	How well was the study done to minimize bias? Code ++,+,or -	++
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, is you certain that the overall effect is due to the study intervention?	**YES-**

2.4	Are the results of the study directly applicable to the patient group targeted by this guideline?	**YES -**
Section 3: Description of the study		
3.1	How many patients are included in the study (No. in each arm at the beginning)	**70 Patients, 35 treatment group, 35 control group**
3.2	What are the main characteristics of the patient population?	**MS with UI**
3.3	What intervention (treatment, procedure) is being investigated in the study?	**Supervised for treatment group**
3.4	What comparison are made in the study	**TPTNS with supervision V. non supervision**
3.5	How long are patients followed up in the study?	**3 months**
3.6	What outcome measure(s) are used in the study?	**QOL Questionnaires**
3.7	What size of the effect is identified in the study?	**Clinical improvement of OAB was shown in 82.6% and 83.3% of the patients on D30 and D90, respectively, with significant improvement of primary and secondary outcomes compared to baseline.**
3.8	How was this study funded/	**Not stated**
3.9	Does this study help to answer the key question?	**Evidence derived shows that MS patients have better urinary incontinence prognosis compared to non-intervention group**