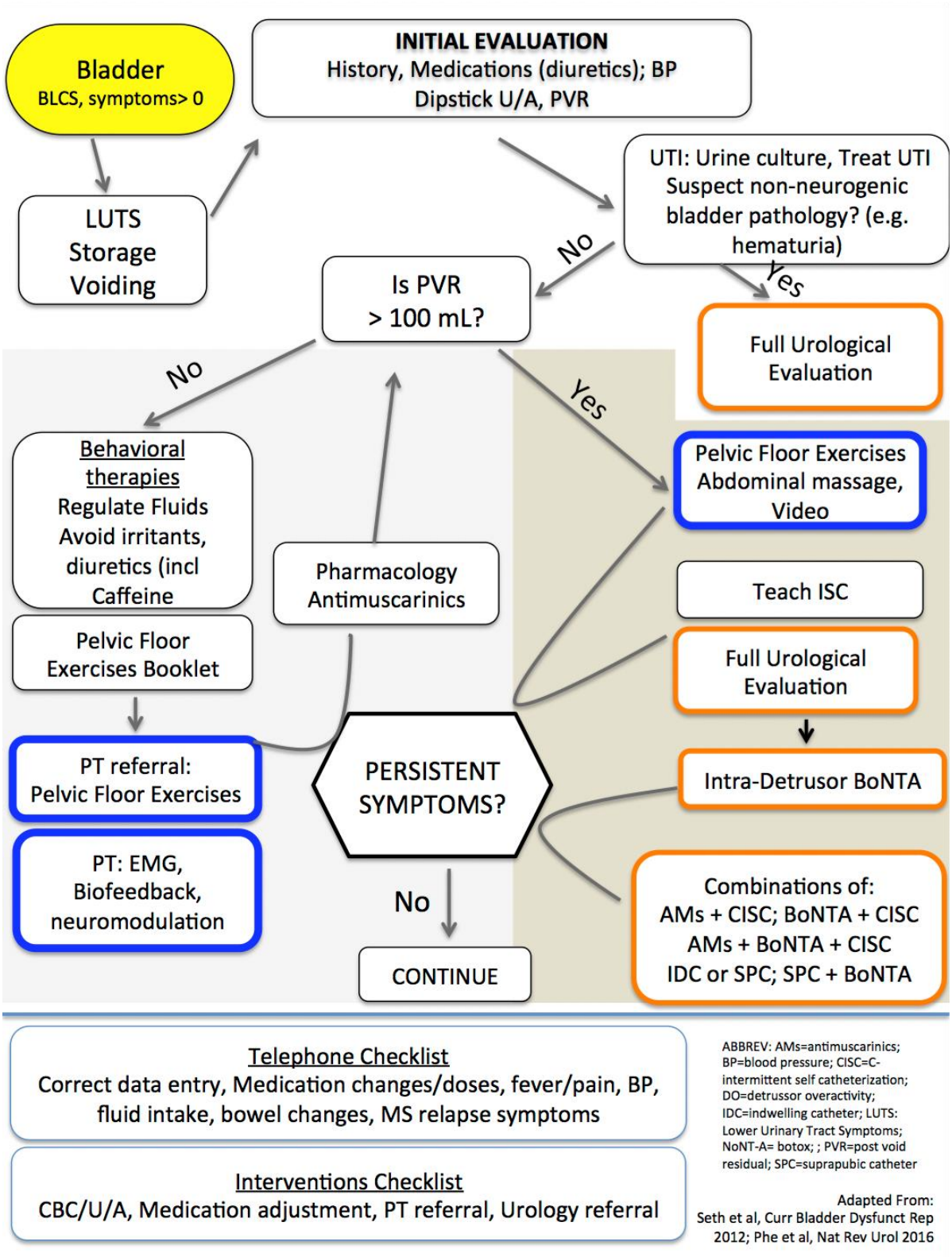
Supplementary - Appendix 2

1. **Major Treatment Modalities for Bladder Dysfunction.**
2. **Major Treatment Modalities for Ambulation.**
3. **Major Treatment Modalities for Mood.**
4. **Literature Supporting Major Treatment Modalities When Considering Making Personalized Recommendations for Each BAM Symptom.**

1. Major Treatment Modalities for Bladder Dysfunction



2. Major Treatment Modalities for Ambulation

AMBULATION EVALUATION

STANDARD MS PT ASSESSMENT
INCL. MOVEMENT PREFERENCES AND GOALS VIA **MAM-CAT**

MAM-CAT: Patients respond to 18 items related to 6 dimensions of movement: flexibility, strength, accuracy, speed, adaptability, and endurance. Patients mark how well they think they move now and how well they would like to be able to move (even if they had to work hard for it). The software calculates the *gaps* between current and preferred movement abilities on each of the 6 dimensions. A gap of 1+ level on any dimension =>trigger a PT assessment and potentially exercise prescription to address that (+/-related) movement dimension (Allen et al, *Qual Life Res* 2015)

Address movement dimensions, body parts, tasks of most concern to patient:

Dimension	Assessment	Intervention
flexibility	Goniometric range of motion/ spasticity	Stretching/ positioning
strength	Dynamometry/ manual muscle test	Targeted resistive exercise
accuracy	Coordination tests	Practice with feedback/ motor learning
speed	Timed tasks	Time trials
adaptability	Balance perturbations/ obstacles/ changing environments; sensory tests	Practice correcting errors in progressively challenging environments
endurance	Exertion with longer tasks; vital signs	Aerobic exercise

Recommend as needed: Fampridine trial; Assistive devices; Home safety evaluation; Referrals: vision, other

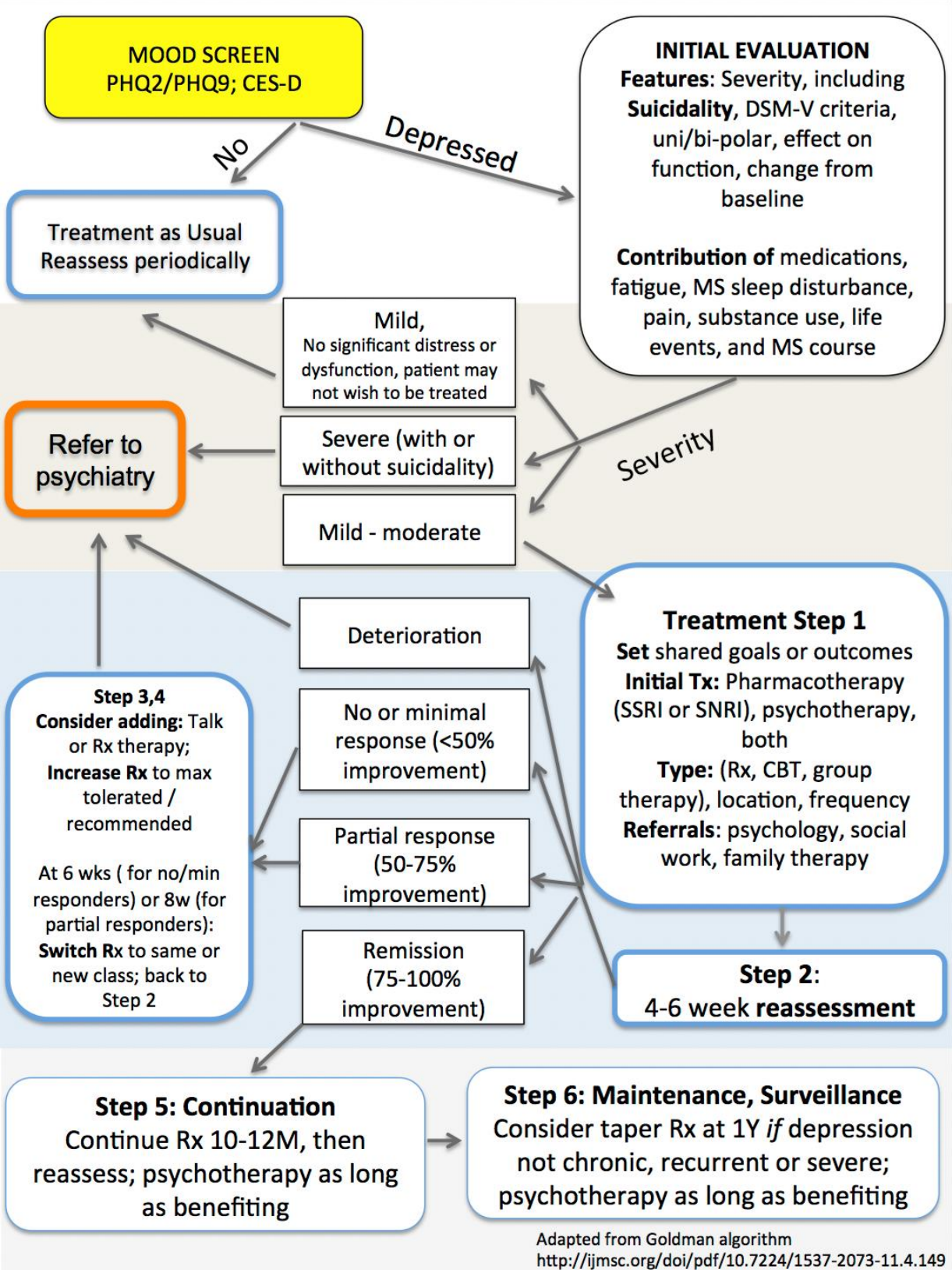
RECOMMENDED EXERCISE LEVEL FOR LEVEL OF DISABILITY

Modified from Heesen et al, *Expert Rev Neurotherapeutics, 2006;6*(3), 347-355.

Level of Disability	EDSS	Training Program
None: No fatigue or thermosensitivity	0	Full exertion, aerobic and resistance exercise, no extreme sports
Minimal: Limited fatigue and heat sensitivity; minor balance/ gait problems	1-2	Monitored exercise program, including strengthening and endurance using a variety of exercise types; precooling if heat sensitive; avoidance of overtraining
Moderate: Limited gait; may have spasticity, weakness, ataxia, balance problems	3-5	Deficit-driven exercise protocols, including strengthening and endurance training using methods tolerated, walking, cycle ergometry, precooling if needed
Severe: Cannot participate in all daily activities; short-distance, aided walking only	6-7	Movement preservation, stretching, targeted strengthening needed for task-specific training
Wheelchair used exclusively	8	Exercise to maintain motion, task-specific training
Bedridden	9	Primarily passive movements to maintain motion, breathing exercises

Telephone Checklist: Technical difficulties (FitBit battery, bracelet; password; wifi); Travel, Falls, pain, nocturia, vision, medication changes, light-headedness, MS relapse symptoms, fever/pain, fluid intake, changes in weather or environment

3. Major Treatment Modalities for Mood



4. Literature Supporting Major Treatment Modalities When Considering Making Personalized Recommendations for Each BAM Symptom.

Bladder:

Measurement and Treatment. Scales relate both to bladder function and quality of life (QOL).[1] Interventions in MS ranging from behavioral strategies,[2] physical therapy (PT),[3,4,5] nerve stimulation[6] and pharmacology have demonstrated efficacy in targeting bladder dysfunction;[7-9] including first-line stepwise management models (e.g. PT modalities for urinary incontinence [UI]:[10] electromyography (EMG) biofeedback, electrical stimulation and pelvic floor muscle training).[5,7,11] Improving UI can, in turn, reduce fatigue and depression, amplifying an effect on QOL.

Behavioral considerations. Motivation and adherence[12] have a strong association with improvements in bladder function.[2,8] Trials typically last 3-6 months and lack follow-up monitoring to measure sustained effects of therapies; however, one study of combination therapy for 9 weeks reported maintenance of reduced leakage episodes and adherence persisting until the end of the 24-week observation.[8]

Ambulation:

Measurement and Treatment. Remote monitoring of step count readily measures ambulation and has demonstrated associations with disability and QOL. ***An 800 average daily step count*** change has been suggested as clinically important.[13] Daily step count captures potentially actionable variability amongst persons within a specific EDSS category.[14] A range of interventions (e.g. endurance or resistance training, adapted yoga) have demonstrated efficacy in targeting individual contributors to ambulation (e.g. endurance, speed, strength, fall risk, balance), as assessed using traditional measures.[15-30] Systematic reviews suggest that exercise does improve walking speed and endurance.[15] Yet, exercise recommendations remain quite general,[31] reflecting the need for individualized goals and interventions. Walking speed and endurance can also improve with 4-aminopyridine pills.[32,33]

Behavioral considerations. Typical rehabilitation trials last only 8 weeks, with benefits that may only persist a few weeks beyond this.[34] Even pragmatic trials recognizing the need for sustained behavior change typically last only 12 weeks.[35] For this reason, recent approaches have included rehabilitation through telemedicine (with heterogeneous results[36,37]) and promotion of at-home activity.[38] Despite the importance of ambulation for general health and QOL, the *relatively low uptake of exercise by persons with MS* reflects in part unmet needs for education, on (i) the benefits and optimal frequency of exercise while avoiding falls/overexertion, (ii) materials on home and community exercise and (iii) tools for initiating and maintaining exercise behavior.[39] Physical therapists are increasingly called to partner with MS patients to address individual barriers to participation in community-based physical activity;[40] i.e., *to coach them.*

Mood:

Measurement and Treatment. A number of scales have been validated for assessment and monitoring of treatment of depression, and both psychological and pharmacological interventions have demonstrated effectiveness in controlled clinical trials of patients with MS.[41]

Behavioral considerations. Patients with MS and low socioeconomic status may disproportionately experience difficulty coping with their MS due to ***difficulty navigating their clinical care***.[42] In addition, affordable psychotherapy and access to psychiatrists is challenging for people with non-specialty mental health needs, in MS[43] and more broadly.[44]

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