Eligibility criteria

Inclusion criteria	
MS type	Primary and Secondary Progressive MS (confirmed by attending neurologist)
Age	25-65 years
Cognition	Failure on the SDMT defined by a performance of at least 1.282 SD below published normative data (10th percentile) specific for each center taking part[1,2,3,4,5,6]
Visual acuity	Corrected near vision of at least 20/70 and absence of severe nystagmus.
Disease activity	Exacerbation free for three months.
Language comprehension	To ensure that participants could understand the test instructions, they had to demonstrate at least a low average performance on the Token Test.
Exclusion criteria	
Ambulation	EDSS ≥ 7.0
Neurological History	A history of central nervous system disease other than PMS. Disease exacerbations in the past three months.
Medications	Steroids use within the past three months
Current exercise activity	Regular aerobic training at an estimated intensity of >60% of the maximal Heart Rate reserve, for more than one day per week lasting more than 30min per session for the past 3 months. Assessment of exercise habits based on the Godin Leisure-Time Exercise Questionnaire score > 23.
Medical contraindications	Failure on 2 or more statements on the American College of Sports Medicine and American Heart Association (AHA/ACSM) Health/Fitness Facility pre-participation screening questionnaire, required physician approval
Psychiatric contraindications	History of substance abuse and severe (psychotic) mental illness, including severe depression (≥ 29 on the Beck Depression Inventory.
MRI	Claustrophobia, metal implants, pacemakers.

Cognitive Rehabilitation (CR) protocol:
CR was provided by the computerized RehaCom program. RehaCom is available in over 20 languages including all the languages needed for our trial. The language selection is built into the computer program and accessed via a simple drop down menu. This is a major asset of the RehaCom software as few cognitive rehabilitation programs are available in multiple languages. To address processing speed (PS), the single most common cognitive deficits observed in persons with MS[7] we administered the RehaCom module shown to be effective in targeting this aspect of cognition.[8] In particular, there are five RehaCom training modules, "divided attention 1," "divided attention 2" "attention and concentration," "vigilance 2" and "sustained attention" that are integral to processing speed. For example, in the divided attention 1 module, the person is required to simulate a train conductor, carefully observing the control panel of the train and the countryside. Several distractions, such as animals, railway signals and train speed must be taken into account, with increasing levels of difficulty. In the divided attention 2 module, the person is required to simulate driving a car, carefully observing the control panels and the road. Several distractors, such as billboard signs, speed limit signs, radio noise, and remembering to signal right or left turns must be taken into account, with increasing levels of difficulties. In the attention and concentration module, an individual picture (target) is presented and then compared with a matrix of pictures. The person has to recognize the target picture (coded as symbols, items, animals, or abstract figures) and select it from the matrix. The abilities to differentiate and to concentrate are trained simultaneously. The level of difficulty rises as the number and complexity of pictures to recognize increases. During the vigilance 2 task, the person is trained to sustain his or her attention for a prolonged period by providing response times limited to the various items. The task is to control a conveyor belt and to select the objects that differ from a target sample in one or more details. Finally, in the sustained attention module, is similar to the vigilance task, except the speed of the conveyor belt has increased. Participants began at level 1 on each RehaCom module and advanced through the program as dictated by their performance, under the guidance of the RA. Progression was thus individualized, based on the success on each task. Each session comprised of two out of the five modules randomized each session, each module programmed to last 20 minutes, making the duration of each cognitive session 40 minutes, as has been accomplished successfully in previous RehaCom research in persons with MS.[9,10]

Sham Cognitive Rehabilitation (CR-S) protocol: The CR-S condition consisted of internet training, based closely on the internet control group utilized in previous computer-mediated cognitive rehabilitation studies in the literature.[11] The control condition began with more basic tasks such as learning to use a computer and the internet to search for information, including locating information regarding medications, gardening, getting directions, etc. Participants began at the most appropriate level, completing the 24 sessions that followed to match the frequency of the CR treatment group interventions. The control sessions were designed to equate the two CR groups (active and sham) on social and computer contact. This approach has been demonstrated to be effective in controlling for these factors in previous research.[11]

Exercise protocol: In accordance with the MS literature, the exercise intervention of choice was aerobic and performed by recumbent stepper.[12,13] It consisted of one weekly session of continuous exercise alternating with one weekly session of interval training. This ensured variation as well as a greater volume of high intensity exercise during the interval training, thus allowing more exercise time at intensities approaching the VO_{2peak}. The exercise intervention complied with the basic principle of progressive overload. This meant that there was an inherent progression built into the program involving changes in both exercise time (volume) and intensity.

Type: Aerobic training was performed on an arm-leg recumbent stepper with all centres using the same equipment (NuStep T5XR, https://www.nustep.com/international/products/t5xr/) that allowed individual adjustment of stepper settings as well as providing a valid measure of the applied resistance expressed as wattage or kp.

Frequency: Twice weekly with each session separated by one day of rest.

Supervision: Full supervision of all exercise sessions by the trained RA to match that provided during the cognitive rehabilitation sessions.

Format/duration: (Tables A and B)

One session involved continuous exercise initially commencing at 10 minutes and progressing towards 30min/session, with 5 minutes of warm up and 5 minutes of cool down.

Table A: Continuous exercise schedule

Week	Duration	Target intensity zone (% of HR-reserve*)
1	10 minutes	50-60% of HR-reserve
2	15 minutes	50-60% of HR-reserve
3	20 minutes	50-60% of HR-reserve
4	25 minutes	50-60% of HR-reserve
5	30 minutes	50-60% of HR-reserve
6	30 minutes	50-60% of HR-reserve
7	30 minutes	60-70% of HR-reserve
8	30 minutes	60-70% of HR-reserve
9	30 minutes	65-75% of HR-reserve
10	30 minutes	65-75% of HR-reserve
11	30 minutes	70-80% of HR-reserve
12	30 minutes	70-80% of HR-reserve

* Peak HR was determined by formal cardiopulmonary exercise testing. Resting HR was also determined at baseline.

One session involved interval training (5 x 1 min progressing towards 10 x 2min) in line with the schedule in Table 1b.

Table B: Interval Training Schedule

Week	Number of intervals	Duration	Rest	Target intensity zone (% of HR-reserve*)
1	5	1min	1min	80-90% of HR-reserve
2	5	1.5min	1.5min	80-90% of HR-reserve
3	5	2min	2min	80-90% of HR-reserve
4	6	2min	2min	80-90% of HR-reserve
5	7	2min	2min	80-90% of HR-reserve
6	8	2min	2min	80-90% of HR-reserve
7	9	2min	2min	80-90% of HR-reserve
8	10	2min	2min	80-90% of HR-reserve
9	10	2min	2min	90% of HR-reserve
10	10	2min	2min	90% of HR-reserve
11	10	2min	2min	90% of HR-reserve
12	10	2min	2min	90% of HR-reserve

* Peak HR was determined by formal cardiopulmonary exercise testing. Resting HR was also determined at baseline.

Sham exercise protocol: (adapted from Barrett et al.[14])

Generally, this one hour, twice weekly sham exercise intervention did not put any strain on the cardiovascular system, focusing on balance and stretching. Further, it intentionally did not contain any cognitive-motor dual tasking to avoid potentially providing any cognitive training. Also, it did not include complex exercises where patients needed substantial working memory or (sustained) attention. The duration was one hour. Six types of exercises were identified as being appropriate for inclusion: stretches, exercises in crook lying, unilateral exercises in side lying, exercises in prone, exercises in unsupported sitting and exercises in standing.

Type 1: Stretches	**Type 2: Exercises in crook lying**	**Type 3: Exercises in side lying**
Hamstrings Quadriceps Hip flexors Hip abductors Ankle plantar-flexors	Bridging (two legs/single leg) Trunk rotation Pelvic tilt Unilateral hip abduction Bilateral hip abduction Hip and knee flexion/extension	Unilateral hip abduction Unilateral hip lateral rotation Unilateral hip abduction/lateral rotation Unilateral knee flexion/extension
Type 4: Exercises in prone	**Type 5: Exercises in unsupported sitting**	**Type 6: Exercises in standing**
Unilateral hip extension Unilateral/bilateral knee flexion Bilateral isometric gluteal contraction Unilateral/bilateral hip rotation	Anterior/posterior pelvic tilt Trunk rotation Forward trunk flexion Unilateral trunk extension (reach out of base of support) Unilateral knee extension/flexion Unilateral hip abduction Bilateral hip abduction	Squats (two legs/single leg) Step-ups onto low step. Balancing on one leg (single-leg stance) Sideways stepping Backwards stepping Balancing in step-stance Lateral reaching out of base of support

Format/duration: A standardized (minimal) progression of exercises was undertaken over the 12 weeks to reduce the possible cognitive demand that might be required for dealing with exercise variation. To ensure the exercises were at low HR, they were undertaken with rest periods at a 2:1 ratio to avoid a potential aerobic effect of the sham intervention. Further, the number of consecutive repetitions were low. In line with the EX intervention, the sham session initially commenced at 15-30 min. and ultimately progressed towards 60 min/sessions. The program was further designed to avoid improvements of lower limb muscular strength, as this has been associated with faster processing speed.[15,16]

Table C. Summary of sham exercise intervention characteristics.

Week	Duration (in minutes)	Stretching and balance exercises
1	15-20 min	**Type 1, 2 , 3 , 4 , 5 , 6**
2	20-30min	**Type 1, 2 , 3 , 4 , 5 , 6**
3	25-35min	**Type 1, 2 , 3 , 4 , 5 , 6**
4	25-35min	**Type 1, 2 , 3 , 4 , 5 , 6**
5	25-40min	**Type 1, 2 , 3 , 4 , 5 , 6**
6	25-40min	**Type 1, 2 , 3 , 4 , 5 , 6**
7	30-45min	**Type 1, 2 , 3 , 4 , 5 , 6**
8	30-45min	**Type 1, 2 , 3 , 4 , 5 , 6**
9	35-50min	**Type 1, 2 , 3 , 4 , 5 , 6**
10	40-55min	**Type 1, 2 , 3 , 4 , 5 , 6**
11	45-60min	**Type 1, 2 , 3 , 4 , 5 , 6**
12	45-60min	**Type 1, 2 , 3 , 4 , 5 , 6**

CogEx study endpoints.

Outcome	Measurement(s)	Primary/secondary
Cognitive		
SDMT[17]	Information processing speed	*Primary
CVLT[18]	Verbal memory	**Secondary
BVMT-R[19]	Visual memory	**Secondary
Physical		
Accelerometer[20] (derived from ActiGraph wearable device)	Average % of wear time in MVPA	**Secondary
IET[21] (synonymous with CPET)	VO_2 peak (mL/kg/min); Peak Watts, Peak Heart Rate	**Secondary
CMI[22]	DT cost (motor); DT cost (cognitive)	**Secondary
6MWT[23]	Total distance walked in meters in the 6-minute period	**Secondary
Patient reported outcomes (PROs)		
HADS[24]	Anxiety and depression	**Secondary
FAMS[25]	Assessment of Global Function	**Secondary
EQ-5D-5L[26]	Quality of Life (generic)	**Secondary
MSIS-29-V2[27]	Impact of Multiple Sclerosis	**Secondary
MSWS-12[28]	Subjective impact of walking	**Secondary
PDQ-20[29]	Subjective cognitive difficulties	**Secondary
MFIS[30]	Fatigue	**Secondary
⚕ MRI		
Functional (Go/No-Go[31] task and resting state)	Task activation along with reaction times, omission errors, commission errors, and correct responses. RS functional connectivity	**Secondary
Structual	Brain T2-hyperintense and T1-hypointense lesion volume, WMV, GMV, Hipp v, Thal V.	**Secondary

SDMT=Symbol digit modalities test; CVLT=California verbal learning test; Brief visuospatial memory test – revised; MVPA=free-living moderate-to-vigorous physical activity; $V0_2$ peak=peak oxygen uptake; IET=Incremental exercise test; CPET=Cardiopulmonary Exercise Test; HR=heart rate; CMI=Cognitive motor interference; DT=dual task; nr=number; 6MWT=six minute walk test; HADS=Hospital Anxiety and Depression Scale; FAMS= Functional Assessment of Multiple Sclerosis; EQ5D-5=European Quality of Life-5 Dimensions; MSIS-29-V2=Multiple Sclerosis Impact Scale; MSWS-12=Multiple Sclerosis Walking Scale-12; PDQ=Perceived Deficits Questionnaire; MFIS= Modified Fatigue Impact Scale; RS=resting state; WMV=white matter volume; GMV=Gray matter volume; Hipp v=Hippocampus volume; Thal V=Thalamus volume.

* The primary outcome of the study is the change in processing speed at immediate post -12 weeks, assessed with the SDMT.

**All secondary outcomes will be assessed during the in-person interview or baseline assessment, at the post 12-week assessment and at the 6 month follow-up assessment (apart from accelerometer data at 6 month).

⚕ MRI data, not included in this report.

Attendance rates

			Cognitive Sessions Attended		Exercise Sessions Attended	
Treatment Group	Study Status	N	Mean*	Std Dev	Mean*	Std Dev
EX-S + CR-S	Reached End of Study	65	92.2	11.6	91.2	11.6
	Early Termination	10	55.0	40.7	51.2	36.6
EX + CR-S	Reached End of Study	67	92.7	9.4	90.7	12.8
	Early Termination	13	53.5	41.5	50.7	40.3
EX-S + CR	Reached End of Study	73	91.2	14.1	87.6	19.9
	Early Termination	6	59.7	33.9	57.6	32.1
EX + CR	Reached End of Study	67	91.2	9.9	90.3	10.1
	Early Termination	10	44.2	37.3	43.3	37.0

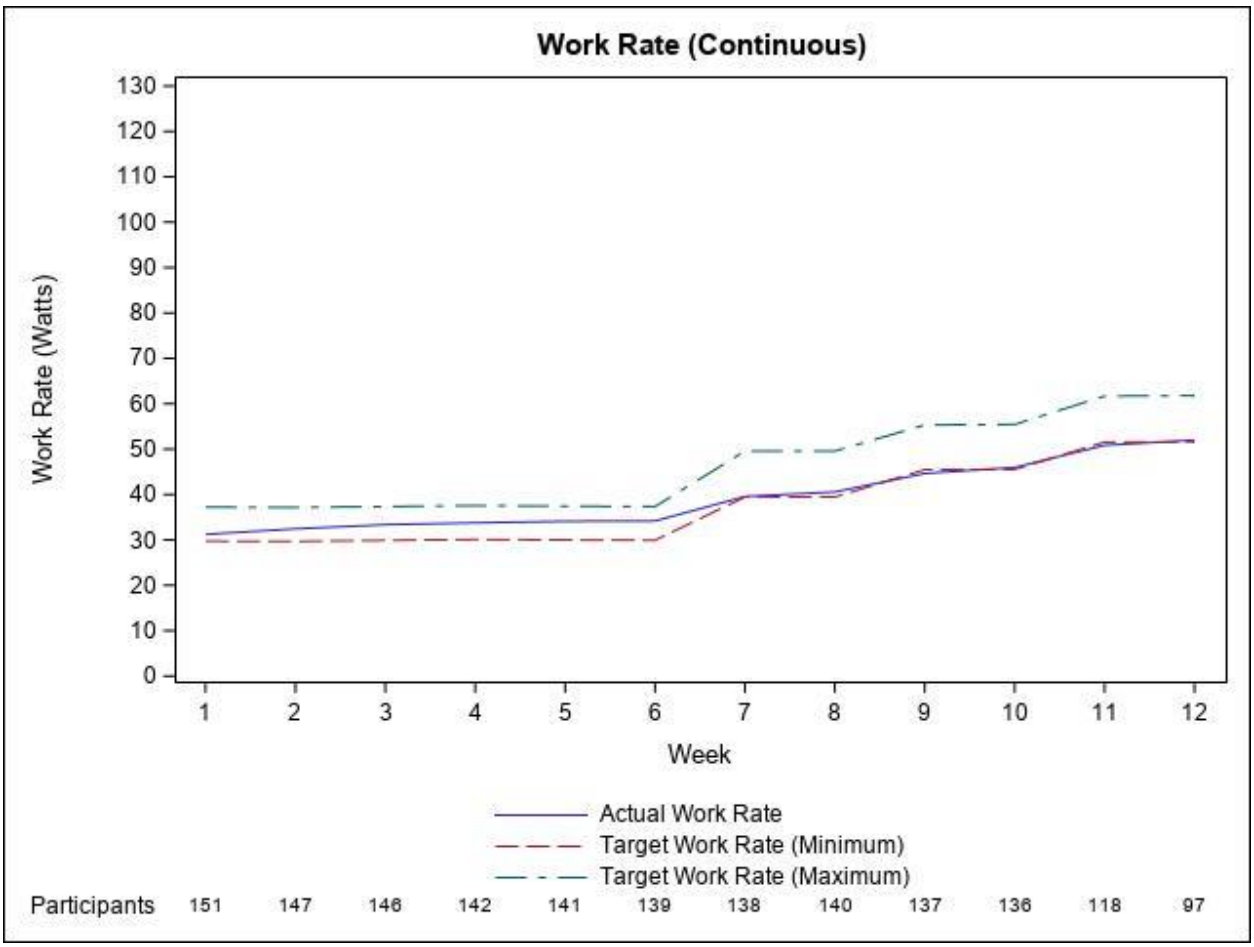
EX=exercise; CR=cognitive rehabilitation; CR-s=sham cognitive rehabilitation; EX-S=sham exercise.

Average Duration of Cognitive sessions

Treatment Group	Study Status	N	Mean*	Std Dev
EX-S + CR-S	Reached End of Intervention	65	41.4	3.0
	Early Termination	10	43.3	4.1
EX + CR-S	Reached End of Intervention	67	41.9	3.1
	Early Termination	13	40.3	1.6
EX-S + CR	Reached End of Intervention	73	42.0	2.9
	Early Termination	6	41.2	4.6
EX + CR	Reached End of Intervention	67	41.8	3.7
	Early Termination	10	41.7	2.5

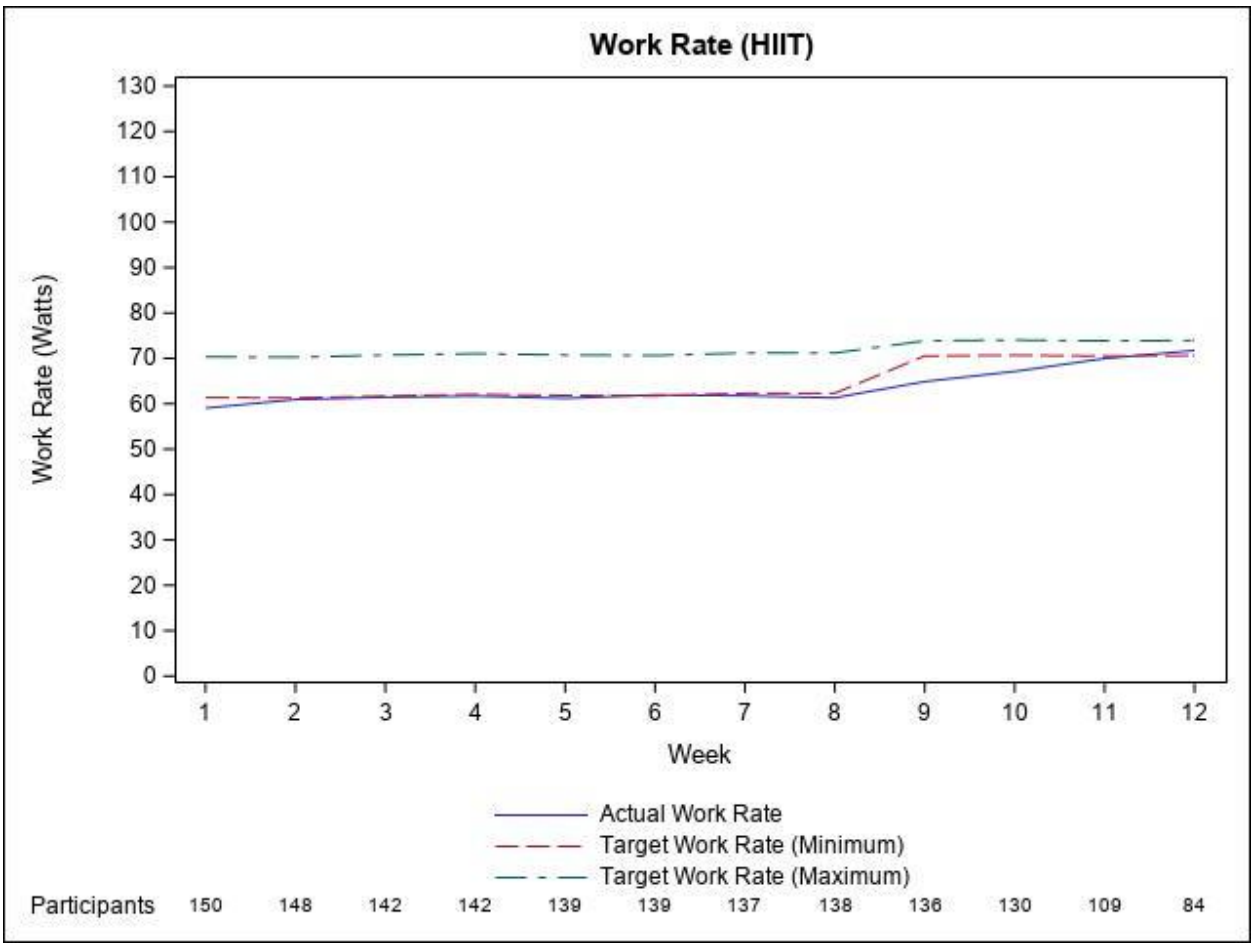
EX=exercise; CR=cognitive rehabilitation; CR-s=sham cognitive rehabilitation; EX-S=sham exercise.

Work rate for continuous exercise, recorded over 12 weeks



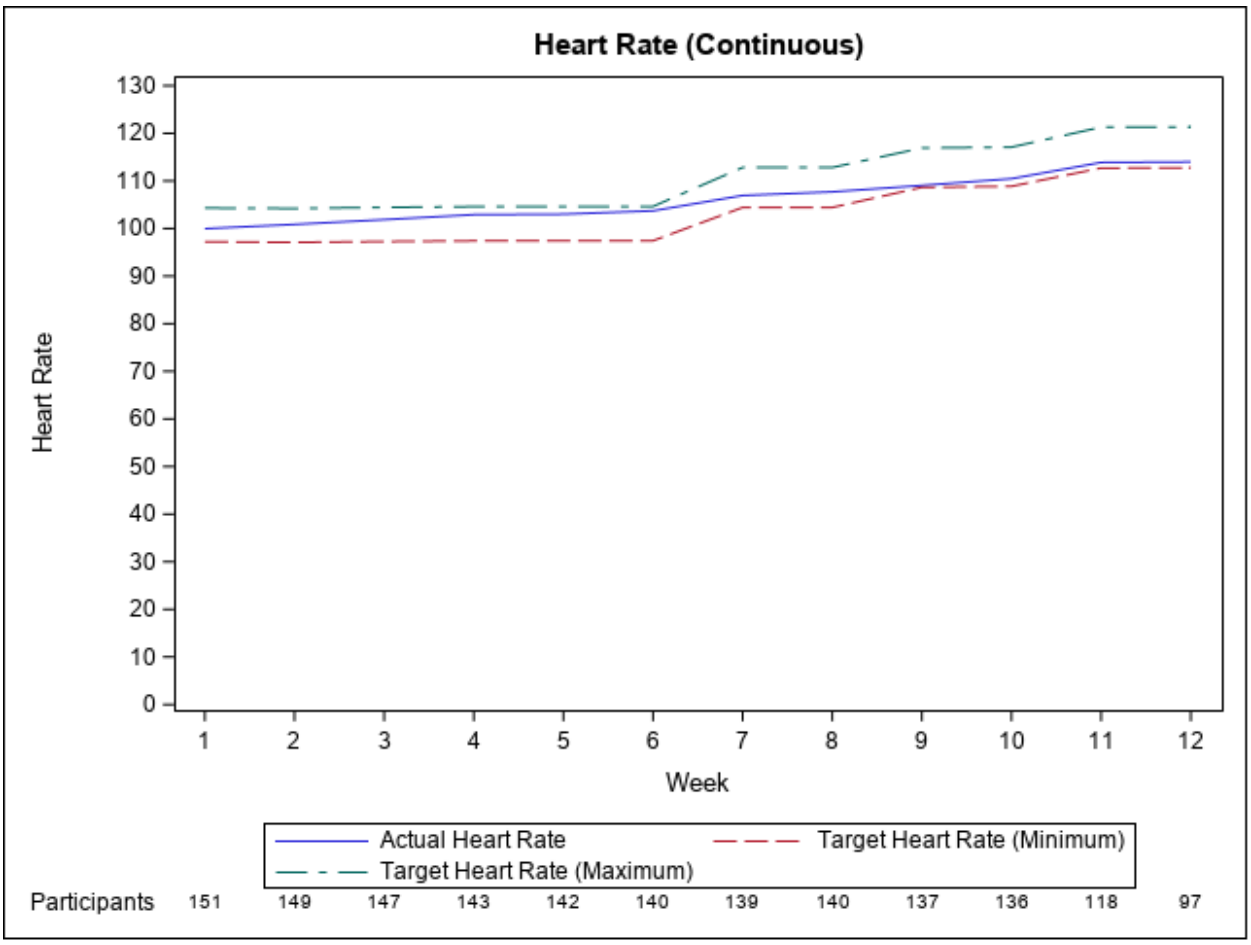
The figure depicts the work rate target zone (red line: lower limit target work rate; green line: upper limit target work rate) and the actual work rate (blue line) during continuous exercise for the pooled exercise groups.

Work rate for high intensity interval training (HIIT) exercise, recorded over 12 weeks

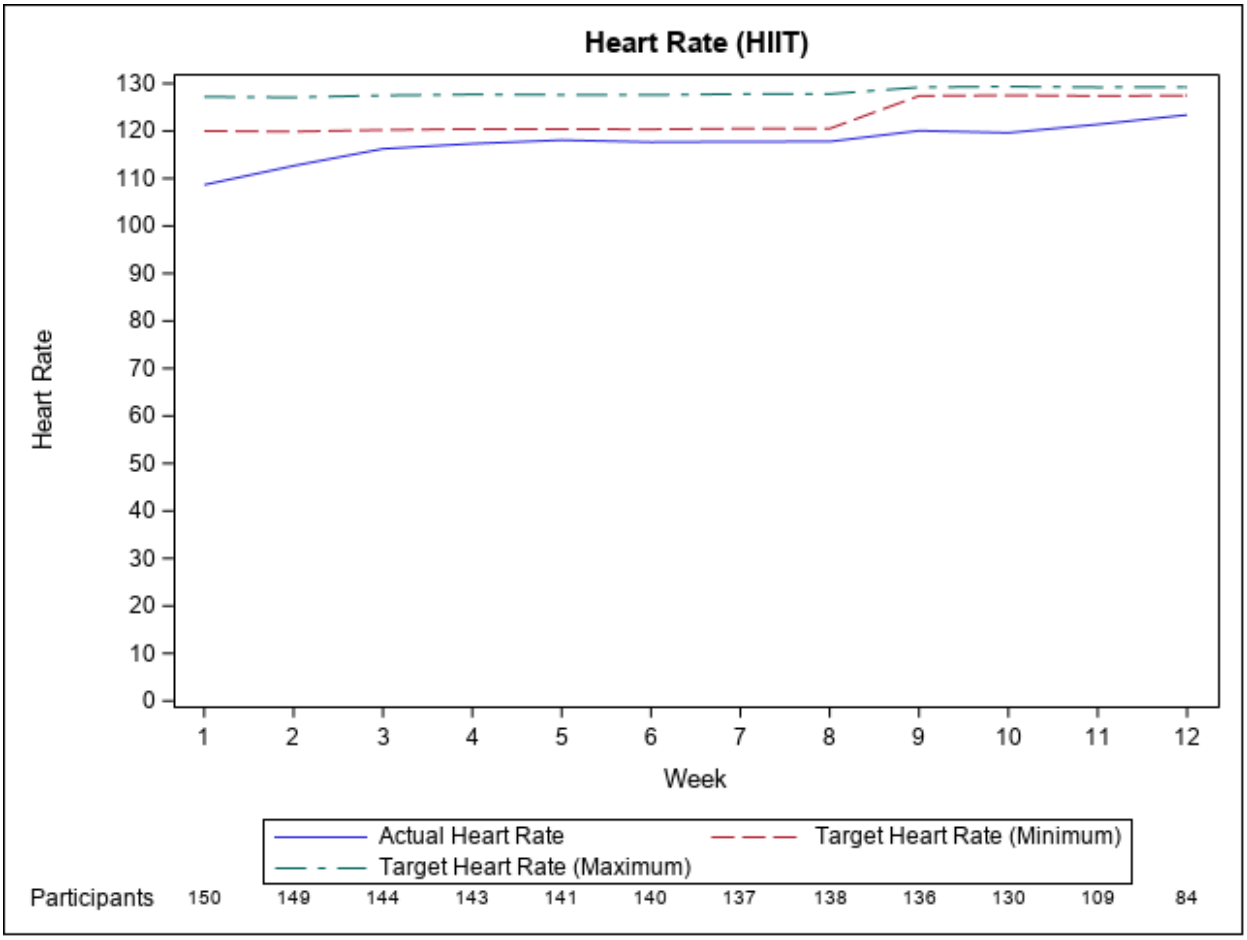


The figure depicts the work rate target zone (red line: lower limit target work rate; green line: upper limit target work rate) and the actual work rate (blue line) during HIIT exercise for the pooled exercise groups.

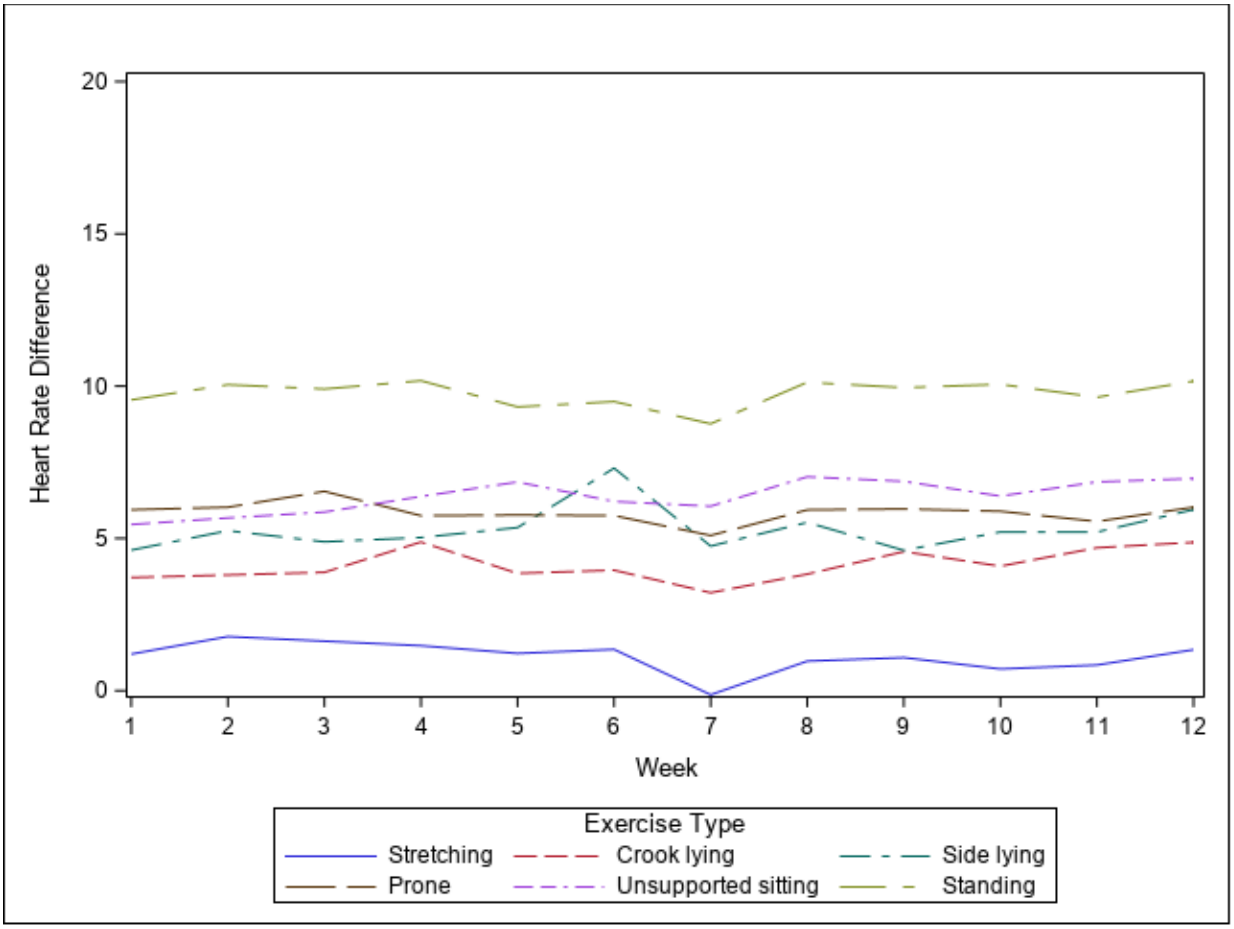
Heart Rate for continuous exercise, recorded over 12 weeks



Heart Rate for high intensity interval training



Exercise sham average heart rate (HR) differences (peak HR – resting HR), recorded over 12 weeks



Adverse events			
Group	**Description**	**Relationship to intervention**	**Outcome**
EX-S + CR-S	Fell during sham exercise. Not hurt.	Probably related	Resolved.
EX + CR-S	Transient, mild back pain that worsened after exercise session.	Probably related	Condition worsening
EX + CR-S	Transient left knee pain.	Probably related	Resolved
EX + CR	Fatigue and a flare in fibromyalgia following baseline IET.	Probably related	Recovered with minor ongoing pain
EX-S + CR	Transiet headache after RehaCom session brough on my image disortion on the computer screen.	Probably related	Resolved
EX-S + CR	Painful, swollen and hot knee.	Possibly related	Ongoing/Continuing treatment
EX + CR-S	Trip and fall with no injury sustained.	Possibly related	Resolved
EX + CR-S	Low back pain	Possibly related	Unknown
EX + CR	Transient thight pain during the continuous exercise session.	Possibly related	Resolved
EX + CR-S	Dizziness, loss of balance and a fall after completing an exercise session. Unhurt.	Possibly related	Resolved
EX + CR-S	Transient pain in both legs during an exercise session.	Probably related	Resolved
EX-S + CR-S=Exercise-sham plus Cognitive rehabitation-sham; EX + CR-S=Exercise plus cognitive rehabilitation-sham; EX + CR=Exercise plus cogitive rehabiliation; EX-S + CR=Exercise-sham plus cognitive rehabiliation.			

Serious adverse events			
EX-S + CR	Surgery for knee prosthesis	Unrelated	Hospitalization/Surgery
EX-S + CR	Exacerbation in symptoms possibly caused by humid and hot weather.	Unrelated	Hospitalization.
EX-S + CR-S	Urinary tract infecrtion	Unrelated	Hospitalization/antibiotic medication
EX-S + CR	Fall at home home causing lumber spine fractures.	Unrelated	Hospitalization/ Behavioral/lifestyle
EX + CR	Syncope with loss of consciousness. Further frequent panic attacks	Unrelated	Hospitalization/Medication change
EX-S + CR	Surgery for knee prosthesis	Unrelated	Hospitalization/Surgery
EX-S + CR-S=Exercise-sham plus Cognitive rehabitation-sham; EX + CR-S=Exercise plus cognitive rehabilitation-sham; EX + CR=Exercise plus cogitive rehabiliation; EX-S + CR=Exercise-sham plus cognitive rehabiliation.			

References

1. Benedict, R. H., Amato, M. P., Boringa, J., Brochet, B., Foley, F., Fredrikson, S., … Langdon, D. (2012). Brief International Cognitive Assessment for MS (BICAMS): international standards for validation. *BMC Neurology*, *12*(1), 55. http://doi.org/10.1186/1471-2377-12-55

2. Boringa, J. B., Lazeron, R. H., Reuling, I. E., Adèr, H. J., Pfennings, L. E., Lindeboom, J., … Polman, C. H. (2001). The Brief Repeatable Battery of Neuropsychological Tests: normative values allow application in multiple sclerosis clinical practice. *Multiple Sclerosis Journal*, *7*(4), 263–267. http://doi.org/10.1177/135245850100700409

3. Costers, L., Gielen, J., Eelen, P. L., Schependom, J. Van, Laton, J., Remoortel, A. Van, … Nagels, G. (2017). Does including the full CVLT-II and BVMT-R improve BICAMS? Evidence from a Belgian (Dutch) validation study. *Multiple Sclerosis and Related Disorders*, *18*, 33–40. http://doi.org/10.1016/J.MSARD.2017.08.018

4. Goretti, B., Niccolai, C., Hakiki, B., Sturchio, A., Falautano, M., Minacapelli, E., … Amato, M. P. (2014). The brief international cognitive assessment for multiple sclerosis (BICAMS): normative values with gender, age and education corrections in the Italian population. *BMC Neurology*, *14*(1), 171. http://doi.org/10.1186/s12883-014-0171-6

5. Parmenter, B., Testa, S. M., Schretlen, D., Weinstock-Guttman, B., & Benedict, R. H. B. (2010). The utility of regression-based norms in interpreting the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). *Journal of the International Neuropsychological Society*, *16*(01), 6. http://doi.org/10.1017/S1355617709990750

6. Walker, L. A. S., Osman, L., Berard, J. A., Rees, L. M., Freedman, M. S., MacLean, H., & Cousineau, D. (2016). Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS): Canadian contribution to the international validation project. *Journal of the Neurological Sciences*, *362*, 147–152. http://doi.org/10.1016/J.JNS.2016.01.040

7. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis [Internet]. Vol. 7, The Lancet Neurology. 2008 [cited 2020 Nov 17]. p. 1139–51. Available from: www.thelancet.com/neurology

8. Parisi L, Rocca M a, Mattioli F, Copetti M, Capra R, Valsasina P, et al. Changes of brain resting state functional connectivity predict the persistence of cognitive rehabilitation effects in patients with multiple sclerosis. Mult Scler [Internet]. 2014;20(6):686–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24072724

9. Cerasa A, Gioia MC, Valentino P, Nisticò R, Chiriaco C, Pirritano D, et al. Computer-Assisted Cognitive Rehabilitation of Attention Deficits for Multiple Sclerosis A Randomized Trial With fMRI Correlates. Neurorehabil Neural Repair. 2013;27(4):284–95.

10. Mattioli F, Stampatori C, Zanotti D, Parrinello G, Capra R. Efficacy and specificity of intensive cognitive rehabilitation of attention and executive functions in multiple sclerosis. J Neurol Sci. 2010;288(1–2):101–5. Mattioli F, Stampatori C, Scarpazza C, Parrinello G, Capra R. Persistence of the effects of attention and executive functions intensive rehabilitation in relapsing remitting multiple sclerosis. Mult Scler Relat Disord. 2012;1(4):168–73.

11. Ball K, Berch DB, Helmers KF, Jobe JB, Leveck MD, Marsiske M, et al. Effects of cognitive training interventions with older adults: a randomized controlled trial. Jama. 2002;288(18):2271–81.

12. Briken S, Gold SM, Patra S, Vettorazzi E, Harbs D, Tallner A, et al. Effects of exercise on fitness and cognition in progressive MS: a randomized, controlled pilot trial. Mult Scler J [Internet]. 2013;20(3):382–90. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24158978

13. Dalgas U, Stenager E, Ingemann-Hansen T. Multiple sclerosis and physical exercise: recommendations for the application of resistance-, endurance- and combined training. Mult Scler. 2008;14(1):35–53.

14. Barrett CL, Mann GE, Taylor PN, Strike P. A randomized trial to investigate the effects of functional electrical stimulation and therapeutic exercise on walking performance for people with multiple sclerosis. Mult Scler. 2009;15(4):493–504.

15. Sandroff BM, Motl RW. Fitness and cognitive processing speed in persons with multiple sclerosis: a cross-sectional investigation. J Clin Exp Neuropsychol. 2012;34(10):1041–52.

16. Sandroff BM, Pilutti LA, Benedict RHB, Motl RW. Association Between Physical Fitness and Cognitive Function in Multiple Sclerosis Does Disability Status Matter? Neurorehabil Neural Repair. 2015;29(3):214–23.

17. Smith A. Symbol Digit Modalities Test: Manual. Los Angeles, CA: Western Psychological Services, 1982.

18. Delis D, Kramer J, Kaplan E, et al. California Verbal Learning Test manual: Second edition, adult version. San Antonio, TX: Psychological Corporation, 2000.

19. Benedict R. Brief Visuospatial Memory Test – Revised: Professional manual. Odessa, FL: Psychological Assessment Resources, 1997.

20. Sasaki, J. E., John, D., & Freedson, P. S. (2011). Validation and comparison of ActiGraph activity monitors. Journal of Science and Medicine in Sport, 14(5), 411–416. https://doi.org/10.1016/j.jsams.2011.04.003

21. Nagasawa, Y., Nakamura, K., Yokokawa, Y., & Ohira, M. (2019). Validity and reproducibility of an incremental sit-to-stand exercise test in healthy middle-aged individuals. Journal of Physical Therapy Science, 31(5), 414–417. https://doi.org/10.1589/jpts.31.414

22. Veldkamp, R., Romberg, A., Hämäläinen, P., Giffroy, X., Moumdjian, L., Leone, C., Feys, P., & Baert, I. (2019). Test-retest reliability of cognitive-motor interference assessments in walking with various task complexities in persons with multiple sclerosis. Neurorehabilitation and Neural Repair, 33(8), 623–634. https://doi.org/10.1177/1545968319856897

23. Sandroff, B. M., Pilutti, L. A., & Motl, R. W. (2015). Does the six-minute walk test measure walking performance or physical fitness in persons with multiple sclerosis? NeuroRehabilitation, 37(1), 149–155. https://doi.org/10.3233/nre-151247

24. Zigmond A, Snaith R. The Hospital Anxiety and Depression Scale. Acta Psychiat Scand 1983; 67: 361–370. Crossref. PubMed. ISI.

20. Cella, D. F., Dineen, K., Arnason, B., Reder, A., Webster, K. A., Karabatsos, G., Chang, C., Lloyd, S., Mo, F., Stewart, J., & Stefoski, D. (1996). Validation of the functional assessment of multiple sclerosis quality of Life Instrument. Neurology, 47(1), 129–139. https://doi.org/10.1212/wnl.47.1.129

25. Kuspinar, A., & Mayo, N. E. (2014). A review of the psychometric properties of generic utility measures in multiple sclerosis. PharmacoEconomics, 32(8), 759–773. https://doi.org/10.1007/s40273-014-0167-5

26. Bacci, E., Wyrwich, K., Phillips, G., Vollmer, T., & Guo, S. (2016). Analysis of the psychometric properties of the multiple sclerosis impact scale-29 (MSIS-29) in relapsing–remitting multiple sclerosis using classical and modern test theory. Multiple Sclerosis Journal - Experimental, Translational and Clinical, 2, 205521731667323. https://doi.org/10.1177/2055217316673235

27. Hobart, J. C., Riazi, A., Lamping, D. L., Fitzpatrick, R., & Thompson, A. J. (2003). Measuring the impact of MS on walking ability: The 12-item MS walking scale (MSWS-12). Neurology, 60(1), 31–36. https://doi.org/10.1212/wnl.60.1.31

28. Strober, L. B., Binder, A., Nikelshpur, O. M., Chiaravalloti, N., & DeLuca, J. (2016). The perceived deficits questionnaire. International Journal of MS Care, 18(4), 183–190. https://doi.org/10.7224/1537-2073.2015-028

29. Larson, R. D. (2013). Psychometric properties of the Modified Fatigue Impact Scale. International Journal of MS Care, 15(1), 15–20. https://doi.org/10.7224/1537-2073.2012-019

30. Murphy, F. C., Sahakian, B. J., Rubinsztein, J. S., Michael, A., Rogers, R. D., Robbins, T. W., et al. (1999). Emotional bias and inhibitory control processes in mania and depression. Psychol. Med. 29, 1307–1321. doi: 10.1017/S0033291799001233

31. Veldkamp, R., D'hooge, M., Sandroff, B. M., DeLuca, J., Kos, D., Salter, A., Feinstein, A., Amato, M. P., Brichetto, G., Chataway, J., Farrell, R., Chiaravalloti, N. D., Dalgas, U., Filippi, M., Freeman, J., Motl, R. W., Meza, C., Inglese, M., Rocca, M. A., … on behalf of the CogEx Research Team , . (2023). Profiling cognitive–motor interference in a large sample of persons with progressive multiple sclerosis and impaired processing speed: Results from the COGEX study. Journal of Neurology, 270(6), 3120–3128. https://doi.org/10.1007/s00415-023-11636-y

CogEx research team

First, and middle name	Surname
Alex	Pietrusz
Andrea	Tacchino
Angela	Smith
Anne Sophie	Michelsen
Ashlie	Kristin
Blake	Bichler
Brendon	Truax
Carmen	Vizzino
Catherine Danielle	Jones
Catherine	Holme
Catherine	Smith
Charly	Keytsman
Chiara	Pollio
Chris	Cole
Claudia	Niccolai
Claudio	Cordani
Eleonora	Colombo
Elisa	Pelosin
Ellen	Vanzeir
Fedrica	Vannetti
Filippo	Gerli
Francesco	Maranta
Gianna	Riccitelli
Guido	Pasquini
Holly	Wilkinson
Irene	Mosca
James	Braisher
Jessica	Baird
Jessica	Podda
Jimmy	Morecraft
Joke	Lenaerts
Juliana	Puopolo
Kimberley	Algie

Laura	Kenton
Laura	Toll
Laurits T.	Madsen
Leen	Knevels
Louie	Lee
Ludovico	Pedullà
Maria	Cellerino
Marie	Braisher
Marie-Louise Kjeldgaard	Jørgensen
Matteo	Pardini
Mauro	Sibilia
Max	Nabarro
Mette Dahl	Diedmann
Michael	DiBenedetto
Michele	Curran
Michelle	Koch
Mieke	D'Hooge
Nancy	Moore
Natasja De	Weerdt
Paolo	Preziosa
Patrizia	Pajak
Petra	Silic
Rebecca Bex	Walters
Rebecca	Finegan
Renee	Veldkamp
Roberto	Hernandez
Rudi	Donnee
Sabrina	Casagrande
Samantha	Lancia
Sara Della	Bella
Séline	Vandecasteele
Veerle	Vandael