Specialist Talk

# Efficient rehabilitation interventions in MS and novel directions

Prof. Peter Feys
Rehabilitation Sciences & Physiotherapy
HASSELT University – Belgium

BIOMED-REVAL
REHABILITATION
RESEARCH CENTER
UHASSELT

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# The challenge of talking on MS rehabilitation

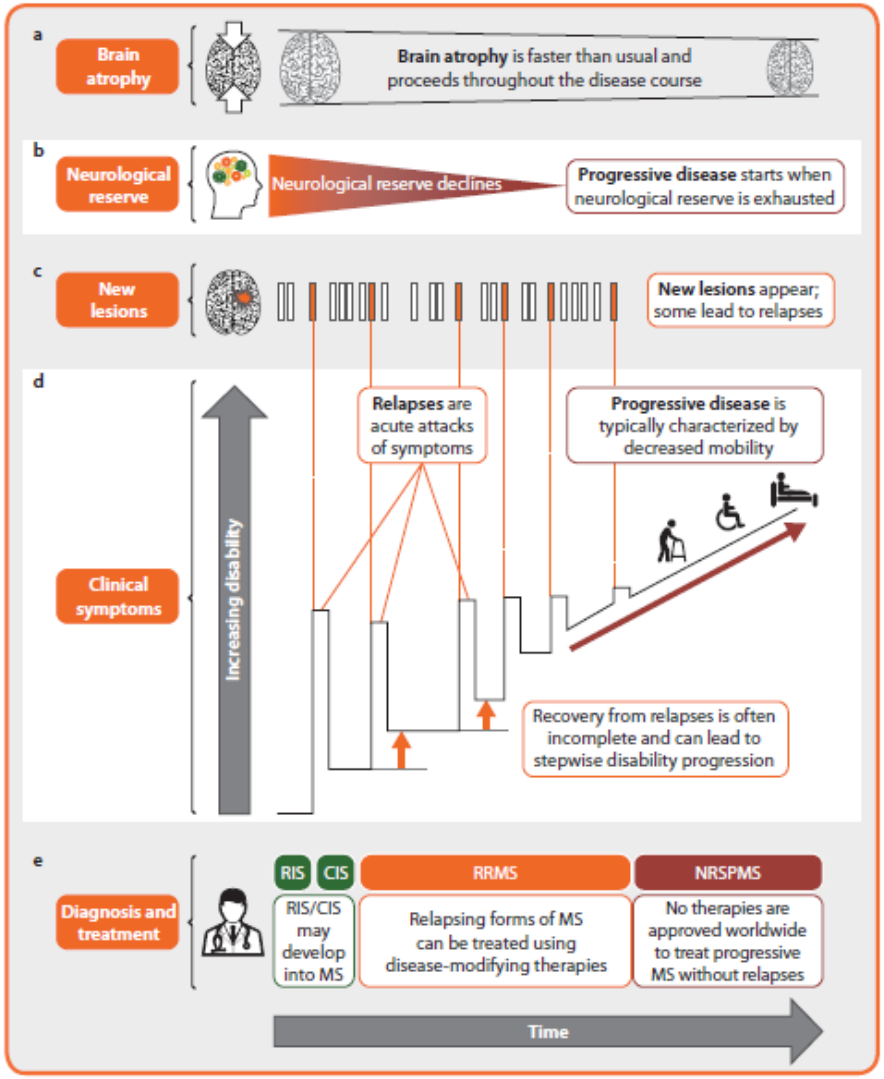
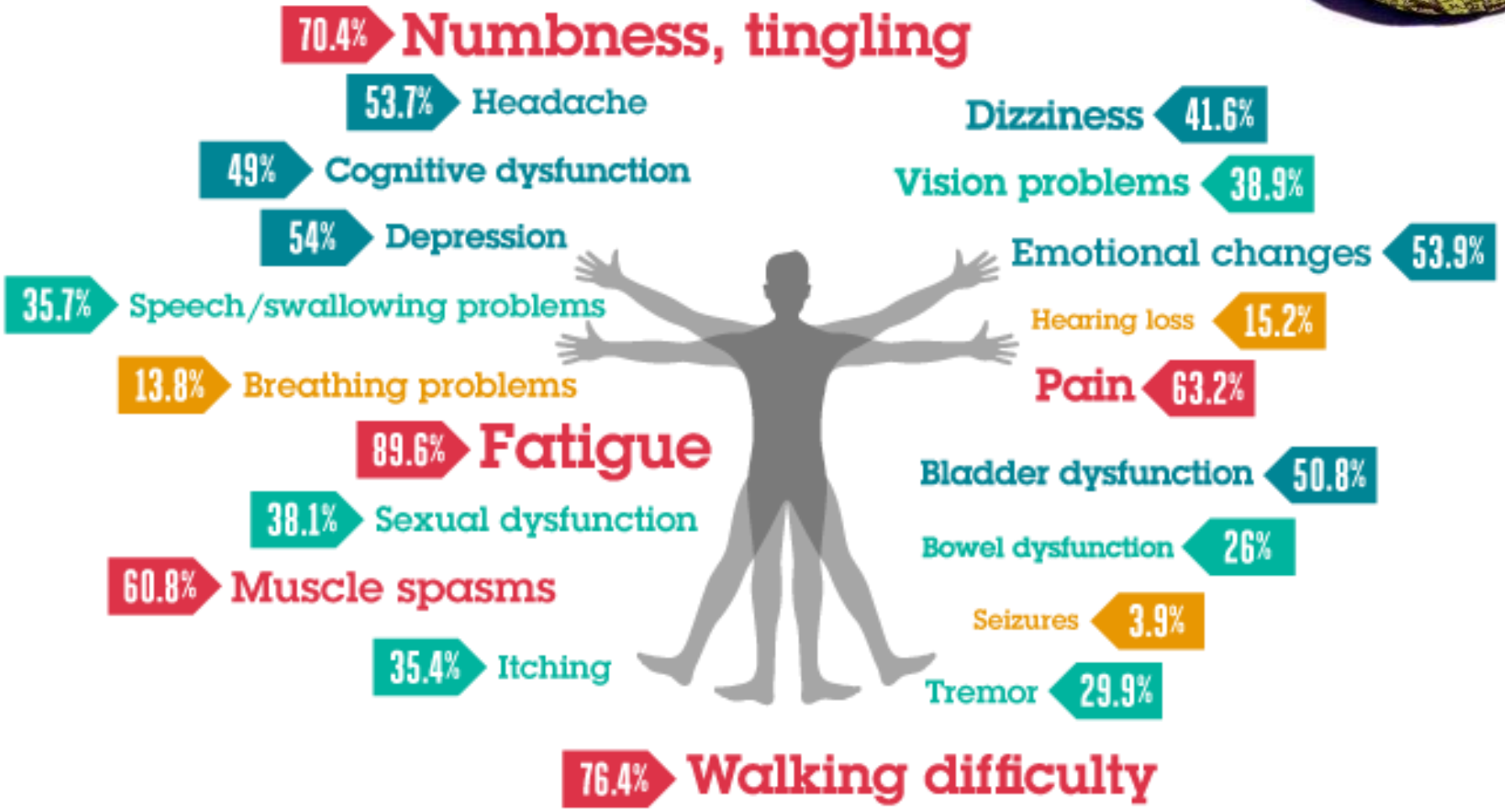


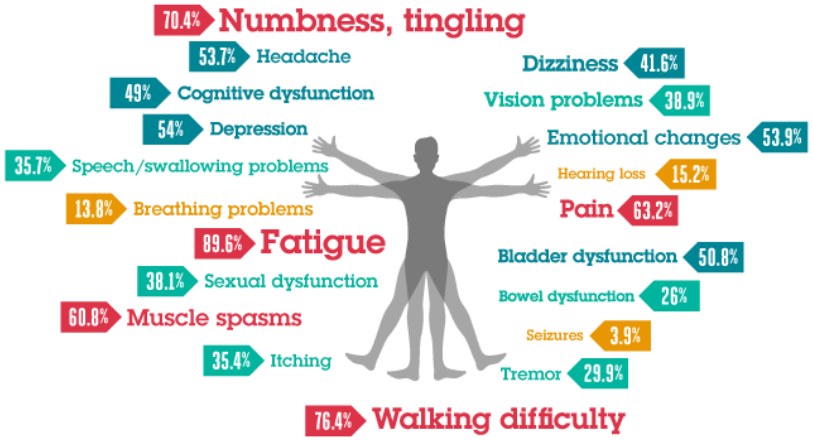

Figure 2. The damage caused by MS typically leads to relapses followed by progressive disease.

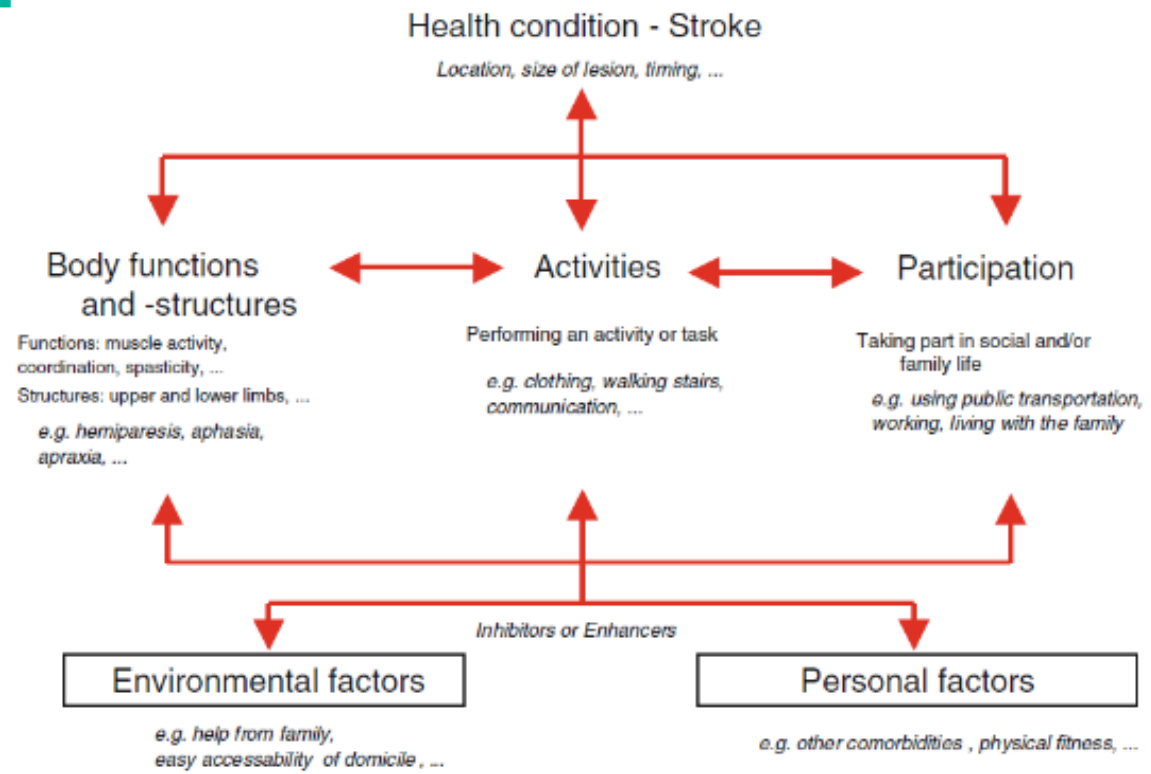
- Chronic disease
- 'Active' versus 'non-active' disease
  - Relapses
  - Progression
- Motor learning potential & Neuroplasticity

# Complexity in MS



# ICF framework: What's related?



# Psychological disease burden & Inactivity-related comorbidities

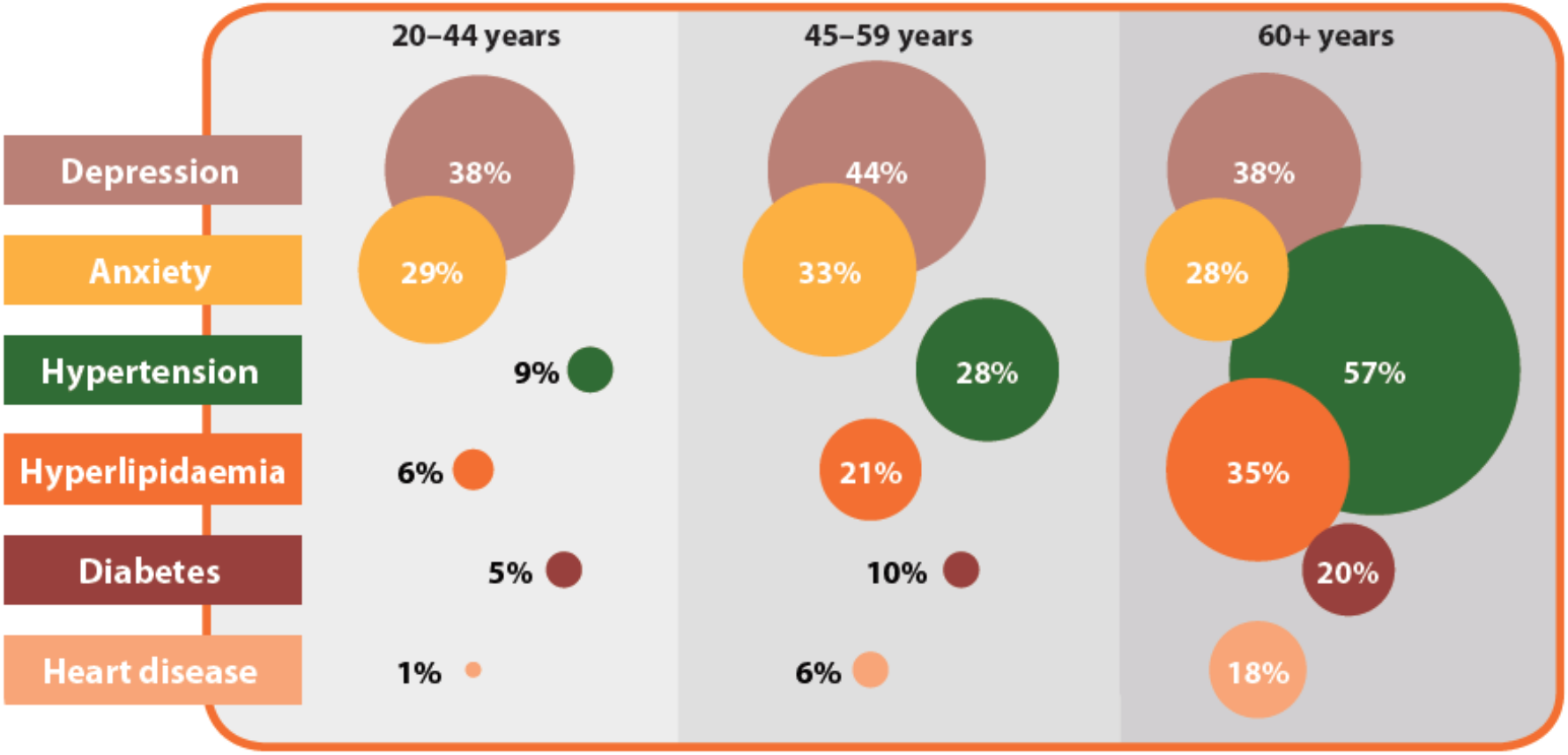


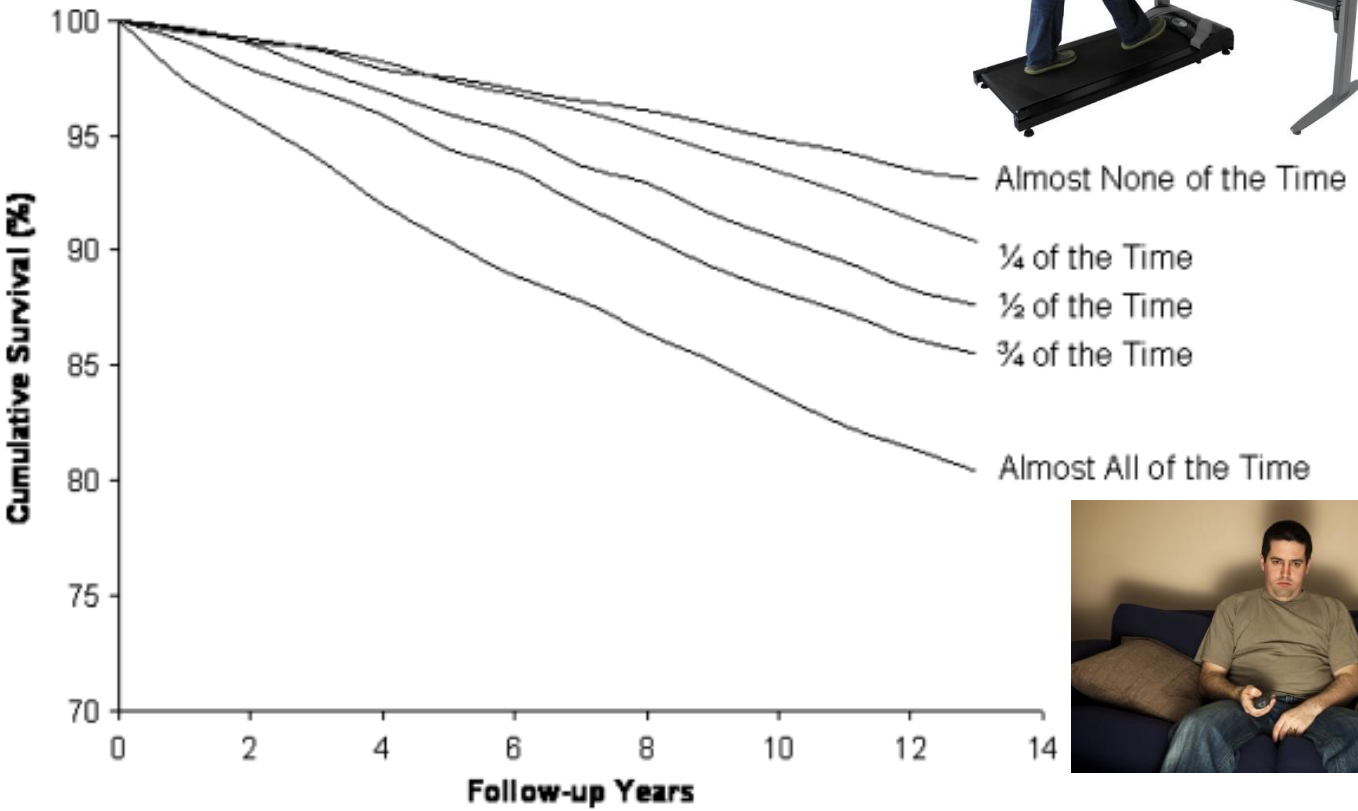

**Figure 1.** Lifetime prevalence of common comorbidities in people with MS, by age group.[1]

# What if one is not moving enough?

**Leisure Time Spent Sitting in Relation to Total Mortality in a Prospective Cohort of US Adults**

**Alpa V. Patel*, Leslie Bernstein, Anusila Deka, Heather Spencer Feigelson, Peter T. Campbell, Susan M. Gapstur, Graham A. Colditz, and Michael J. Thun**

184,190 participants






*Am J Epidemiol* 2010;172:419–429

*Courtesy D. Hanssen (Uhasselt)*

# SUMMARY SLIDE

## Multi-dimensional ASSESSMENT

1. Recommendations
2. ‘Novel’ symptoms

## Efficient Rehabilitation Interventions

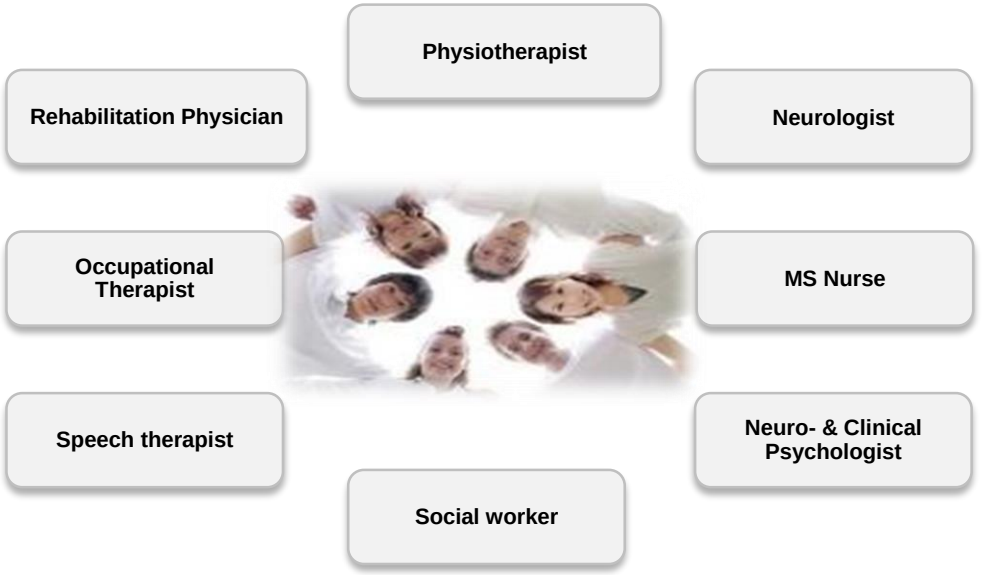
1. Physical Exercise
2. Fatigue management
3. Selecting the right interventions for fatigue & cognition: APPECO

## Novel directions

1. Upper extremity training
2. Technological-supported rehabilitation

# Multi-dimensional assessment recommendations

| Symptom | Instrument(s) |
|---|---|
| Balance, walking capacity and endurance | BBS<br>FES<br>2 or 6MWT<br>T25-FW<br>MSWS-12 |
| Arm functioning | 9-HPT<br>ABILHAND<br>MAM |
| Cognition | BICAMS<br>PASAT |
| Visual | Visual acuity |
| Fatigue | FSS<br>MFIS<br>FMSC |
| Anxiety and depression | HADS<br>STAI<br>Beck's depression |
| Pain | BPI<br>VAS |
| Quality of life | MSIS-29<br>SF-36<br>EQ-5D |




A multi-disciplinary perspective,
to be known by all HCP

Feys, Eelen et al (2016) MSJ: the multi-disciplinary approach

# Measuring balance, walking (endurance)

BBS

FES

T25FW

2/6MWT

Berg Balance scale

▵3 points

Falls Efficacy scale


▵9,6/21 m

MSWS-12 (0-60)

- Standing
- Ability to run
- Need for support
- Moving around the home
- Concentration needed to walk
- Walking speed
- Maintaining balance
- Climbing stairs
- Walking distance
- Effort needed to walk
- Ability to walk
- Gait

▵8-10 points


Feys, Eelen et al (2016) MSJ: the multi-disciplinary approach

# Novel measures: motor fatigability

*Review*

Neurorehabilitation and
Neural Repair
1–19
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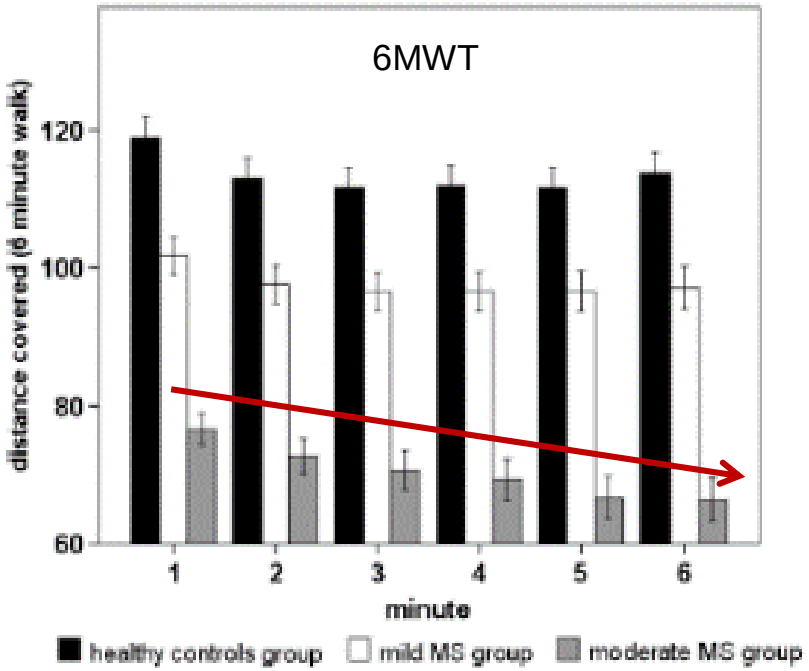
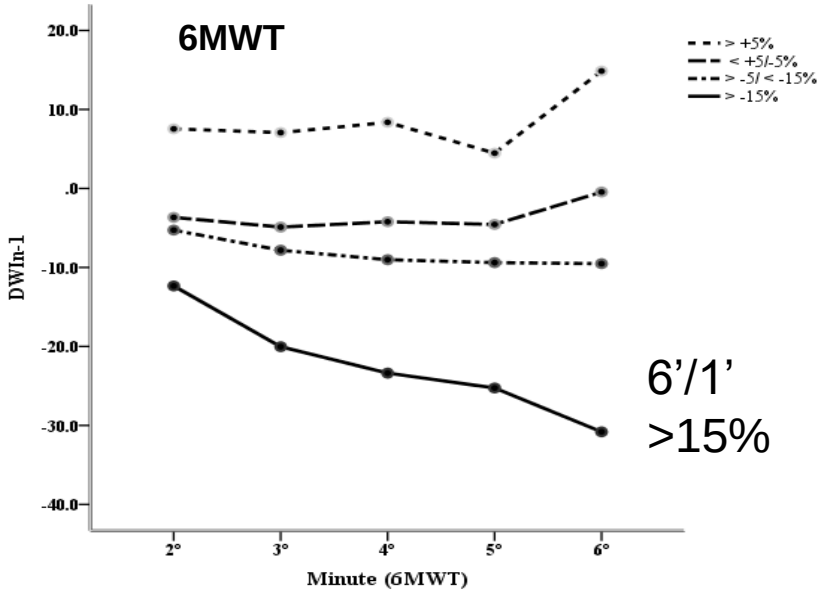
DOI: 10.1177/1545968317690831
journals.sagepub.com/home/nnr
SAGE

**The Assessment of Motor Fatigability in Persons With Multiple Sclerosis: A Systematic Review**

**Deborah Severijns, PhD[1], Inge Zijdewind, PhD[2], Ulrik Dalgas, PhD[3], Ilse Lamers, PhD[1], Caroline Lismont[1], and Peter Feys, PhD[1]**




McLoughlin et al. , 2015




6'/1'
>15%

40% of disabled pwMS slow down ≥ 15% during 6MWT

Severijns et al, 2017, NNR.

Leone et al, 2015, NNR

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# Measuring balance, walking (endurance) & upper limb function

BBS

FES

T25FW

2/6MWT

Berg Balance scale

↓3 points

↓9,6/21 m

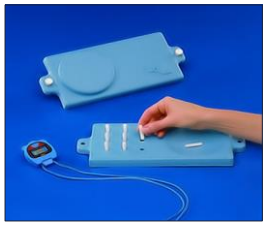
Falls Efficacy scale


MSWS-12

- Standing
- Ability to run
- Need for support
- Moving around the home
- Concentration needed to walk
- Walking speed
- Maintaining balance
- Climbing stairs
- Walking distance
- Effort needed to walk
- Ability to walk
- Gait

↓8-10 points


NHPT



↓20%

MAM

ABILHAND

# Measuring FATIGUE & COGNITIVE IMPAIRMENT

- FSS: Fatigue Severity

- FSMC: Fatigue Scale Motor Cognitive functioning

- **Modified Fatigue Impact Scale (MFIS)**
  38 cut-off for abnormal fatigue.
  Clinical meaningful change: 10 points

  Physical part
  Psychological part
  Psychosocial part


**BICAMS**
Brief International Cognitive Assessment for MS
www.bicams.net/

Symbol Digit Modalities test (SDMT) – *information processing speed*

California Verbal Learning test

Brief Visuospatial Memory test

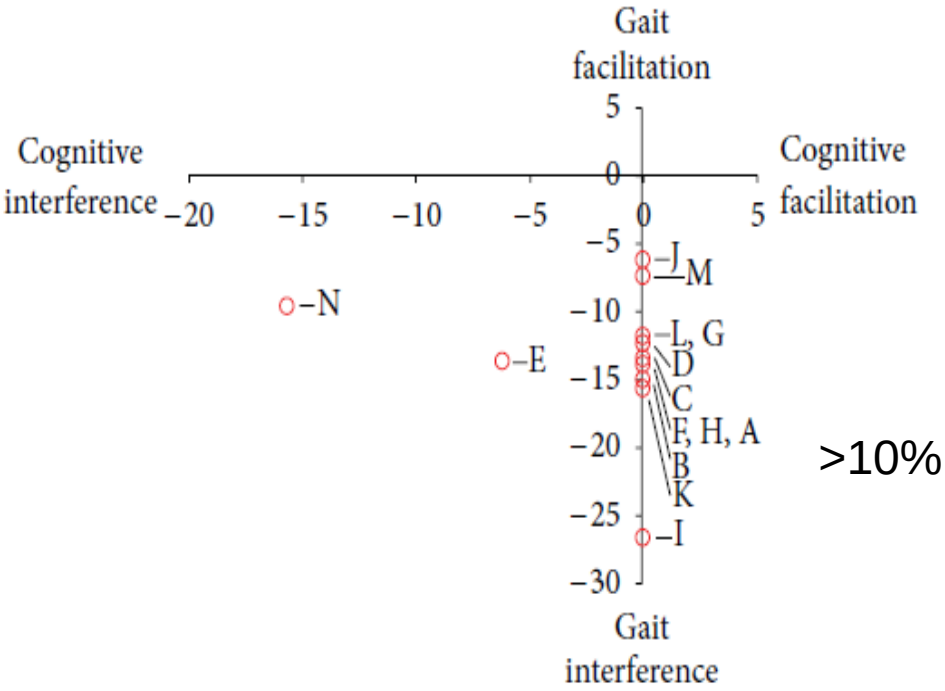
# Novel measure:
# Measuring COGNITIVE-MOTOR INTERFERENCE


MULTIPLE SCLEROSIS JOURNAL | MSJ

*Topical Review*

**Measuring the cost of cognitive-motor du tasking during walking in multiple sclero**

Carmela Leone, Francesco Patti and Peter Feys




>10%

$$DTC = \frac{single\ task - dual\ task}{single\ task} x\ 100$$

Cognitive distractors:
- Substracting by 7 or 3
- Word list generation
- Alternative alfabet
- …

Leone, Feys et al (2014) MSJ
Wadja et al (2014). Learmonth & Motl (2017) APRM

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# Take home Messages

**Assessment**

- A multi-dimensional assessment is required, also in early stage of MS
- There is international agreement on core outcome measures
- Novelties are quantifying symptoms as motor fatigability and cognitive-motor interference

# SUMMARY SLIDE

## Multi-dimensional ASSESSMENT

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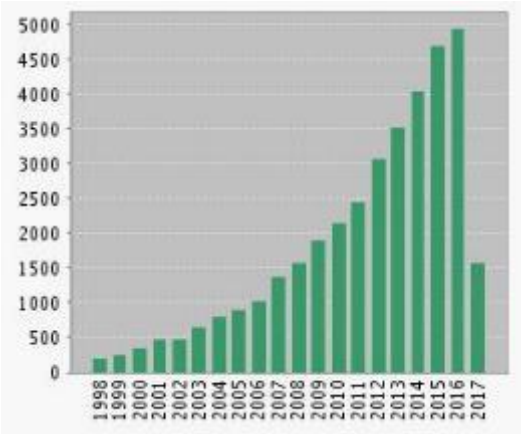
# **Evidence** in MS rehabilitation




Studies addressing
'Rehabilitation' AND 'Multiple Sclerosis'

Khan et al (2016) APRM

ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation
journal homepage: www.archives-pmr.org
Archives of Physical Medicine and Rehabilitation 2016;■:■■■-■■■

REVIEW ARTICLE

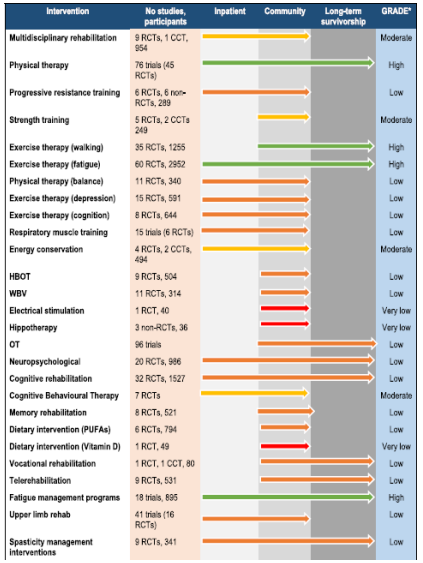
## Rehabilitation in Multiple Sclerosis: A Systematic Review of Systematic Reviews

Fary Khan, MBBS, MD, FAFRM (RACP),[a,b,c] Bhasker Amatya, MD, MPH[a]

*From the [a]Department of Rehabilitation Medicine, Royal Melbourne Hospital, Parkville, Victoria; [b]Department of Medicine, Dentistry and Health Sciences, The University of Melbourne, Parkville, Victoria; and [c]School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia.*

**Systematic reviews included = 39**

- Cochrane reviews: 15
- Other reviews: 24 (1 with 2 reports)

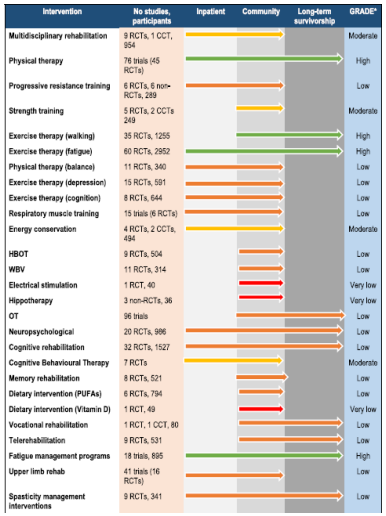


| Intervention | No studies, participants | Inpatient | Community | Long-term survivorship | GRADE* |
|---|---|---|---|---|---|
| Multidisciplinary rehabilitation | 9 RCTs, 1 CCT, 954 | | | | Moderate |
| Physical therapy | 76 trials (45 RCTs) | | | | High |
| Progressive resistance training | 6 RCTs, 6 non-RCTs, 289 | | | | Low |
| Strength training | 5 RCTs, 2 CCTs 249 | | | | Moderate |
| Exercise therapy (walking) | 35 RCTs, 1255 | | | | High |
| Exercise therapy (fatigue) | 60 RCTs, 2952 | | | | High |
| Physical therapy (balance) | 11 RCTs, 340 | | | | Low |
| Exercise therapy (depression) | 15 RCTs, 591 | | | | Low |
| Exercise therapy (cognition) | 8 RCTs, 644 | | | | Low |
| Respiratory muscle training | 15 trials (6 RCTs) | | | | Low |
| Energy conservation | 4 RCTs, 2 CCTs, 494 | | | | Moderate |
| HBOT | 9 RCTs, 504 | | | | Low |
| WBV | 11 RCTs, 314 | | | | Low |
| Electrical stimulation | 1 RCT, 40 | | | | Very low |
| Hippotherapy | 3 non-RCTs, 36 | | | | Very low |
| OT | 96 trials | | | | Low |
| Neuropsychological | 20 RCTs, 986 | | | | Low |
| Cognitive rehabilitation | 32 RCTs, 1527 | | | | Low |
| Cognitive Behavioural Therapy | 7 RCTs | | | | Moderate |
| Memory rehabilitation | 8 RCTs, 521 | | | | Low |
| Dietary intervention (PUFAs) | 6 RCTs, 794 | | | | Low |
| Dietary intervention (Vitamin D) | 1 RCT, 49 | | | | Very low |
| Vocational rehabilitation | 1 RCT, 1 CCT, 80 | | | | Low |
| Telerehabilitation | 9 RCTs, 531 | | | | Low |
| Fatigue management programs | 18 trials, 895 | | | | High |
| Upper limb rehab | 41 trials (16 RCTs) | | | | Low |
| Spasticity management interventions | 9 RCTs, 341 | | | | Low |

# Evidence Summaries

## Highest evidence

- **Exercise therapy (walking & fatigue)**
- **Physical Therapy**
- Fatigue management programs



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## Moderate evidence

- *Upper limb training*
- Spasticity management
- Multi-disciplinary treatment
- Cognitive retraining
- Neuropsychological rehabilitation
- *Energy conservation*
- Vocational rehabiliation

Khan et al (2016) APRM

# Exercise Therapy

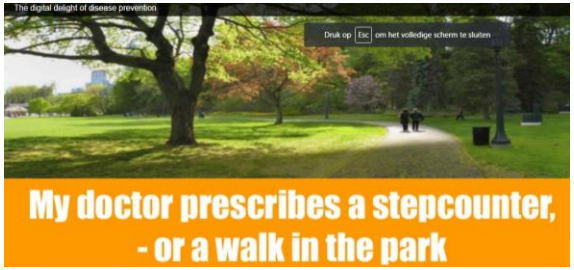
**Personal View**

Lancet Neurology 2017

## Exercise in patients with multiple sclerosis

Robert W Motl, Brian M Sandroff, Gert Kwakkel, Ulrik Dalgas, Anthony Feinstein, Christoph Heesen, Peter Feys, Alan J Thompson

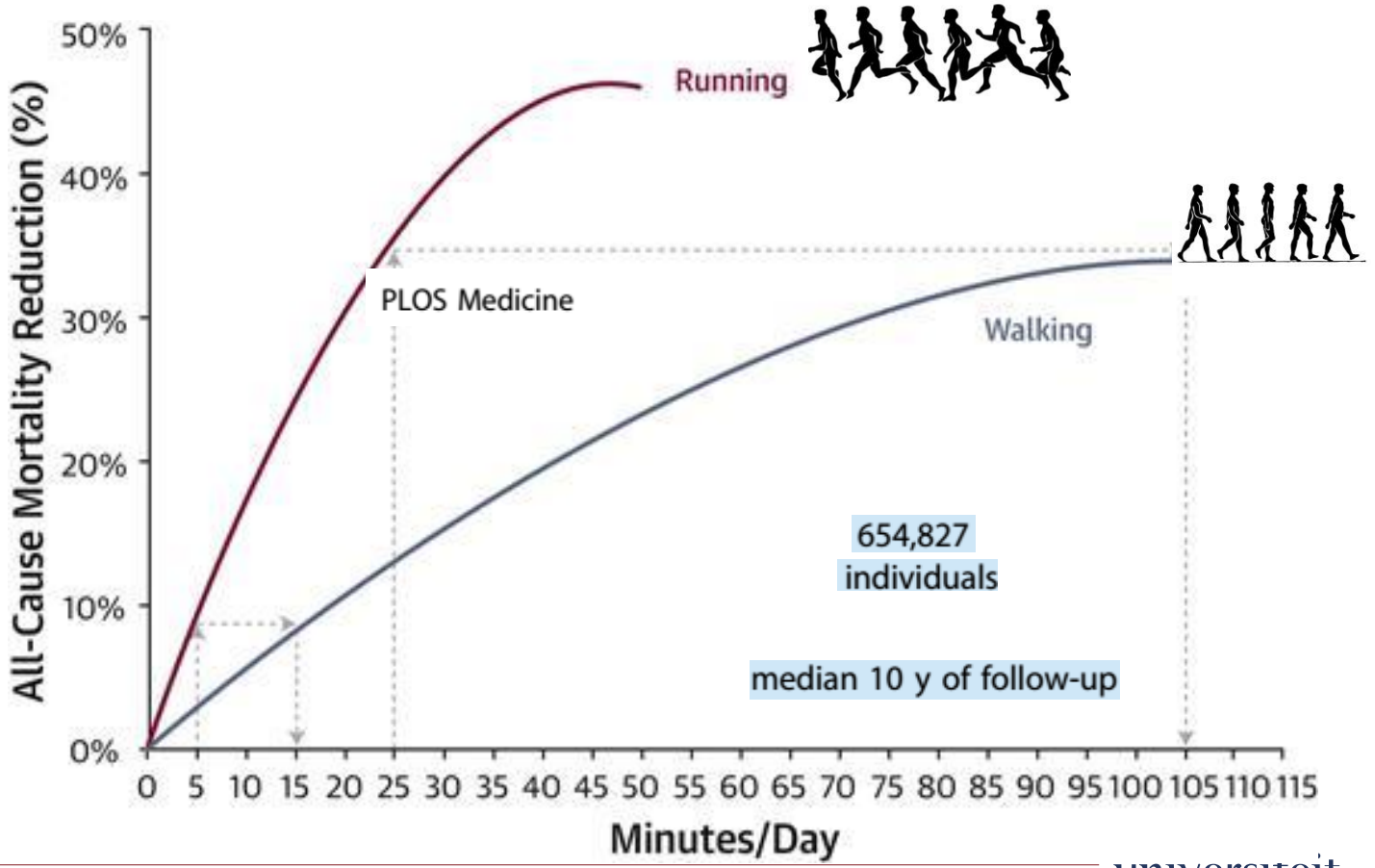




# Impact of exercise in healthy subjects

## Leisure Time Physical Activity of Moderate to Vigorous Intensity and Mortality: A Large Pooled Cohort Analysis

Steven C. Moore[1]*, Alpa V. Patel[2], Charles E. Matthews[1], Amy Berrington de Gonzalez[1], Yikyung Park[1], Hormuzd A. Katki[1], Martha S. Linet[1], Elisabete Weiderpass[3,4,5,6], Kala Visvanathan[7], Kathy J. Helzlsouer[7], Michael Thun[2], Susan M. Gapstur[2], Patricia Hartge[1], I-Min Lee[8]

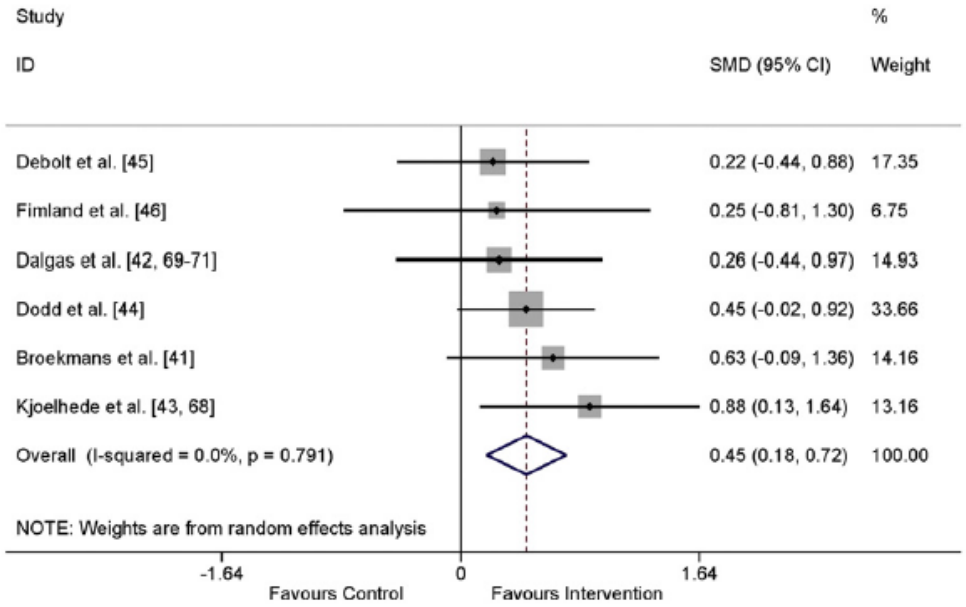


# Resistance training improves **muscle strength**

Improved muscle strenght

Changes in  muscle fiber diameter & type

Changes in BNDF




*Jorgerson, Daglas et al.(2017) J Neurol Sci*
*Wens et al (2018) Eu J Neurol*

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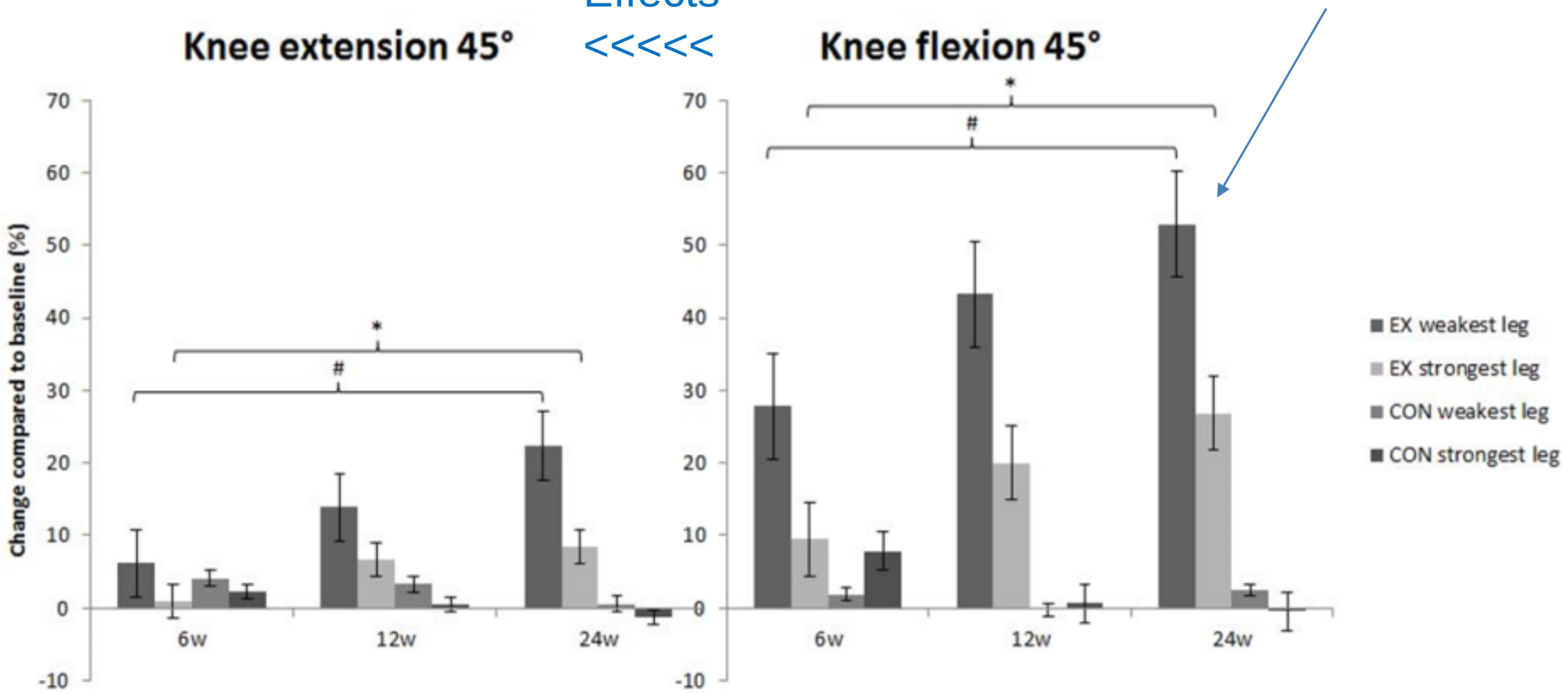
# Effect of resistance training on knee muscle strength

Training effects proportional with training duration

Largest effects in most affected leg

Effects <<<<<




Percentage change of knee 45° muscle strength of exercised (EX) and sedentary (CON) MS patients after 6, 12 en 24 weeks of combined exercise or sendentarims, compared to baseline.

Wens et al (2014) PLOS ONE

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# Skilled supervision needed to avoid ‘maladaptive learning’ & harm

Compensations

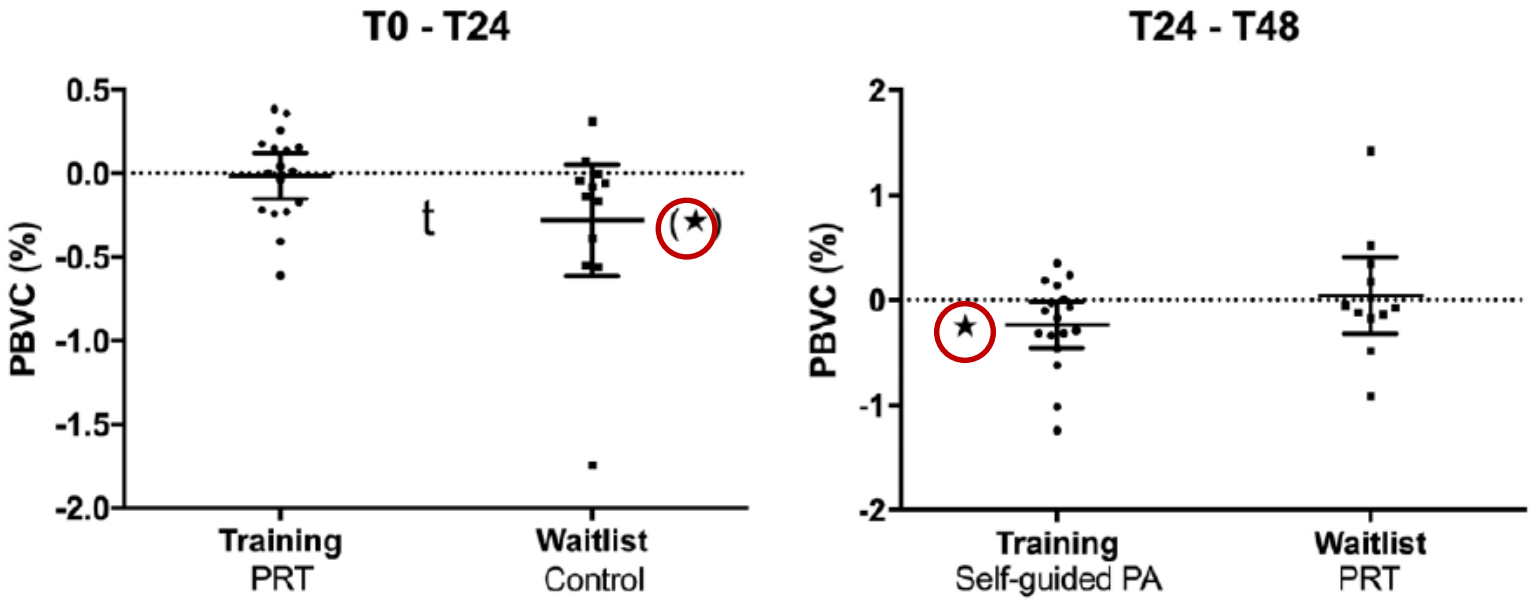
Normal execution is possible

# **Neurobiology** & exercise: **Resistance training**

**Neuroprotective effect of exercise therapy**

Brain volume decrease in waiting list control group

24 weeks Resistance training
***or***
24 weeks
'waiting list control'/
Self-guided physical activity




Kjolhede, Dalgas et al (2017) MSJ

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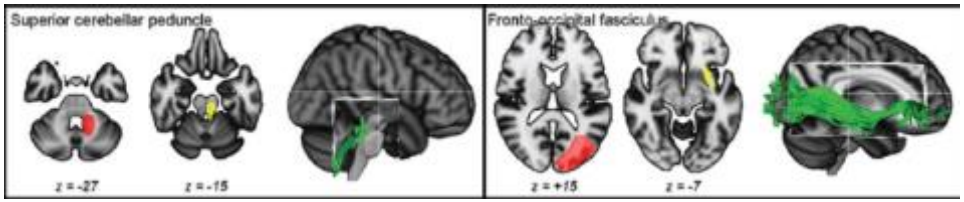
# **Neurobiology** & exercise:
# Improved Neural tract structural integrity

**Multiple Sclerosis:** Changes in Microarchitecture of White Matter Tracts after Training with a Video Game Balance Board[1]

## BALANCE TRAINING

Cross-over design in 27 pwMS
(24 RRMS). 12 weeks of training.

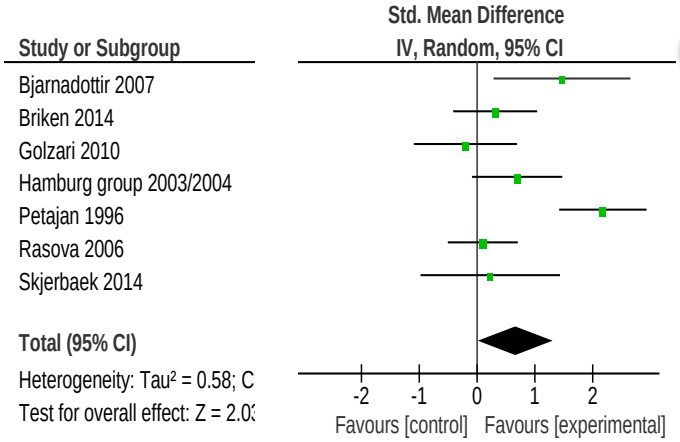


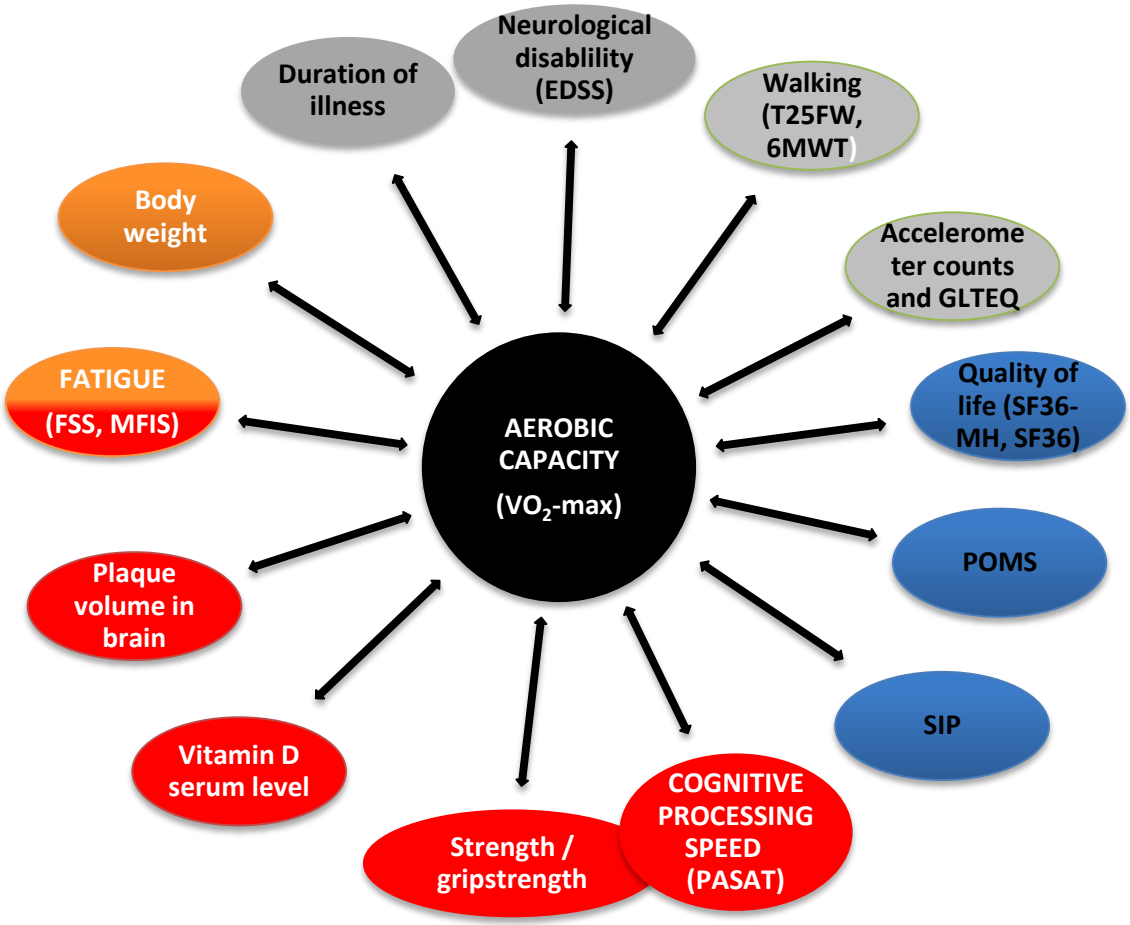

*Changes in microstructure*
*of the superior cerebellar peduncles (DTI)*

*Prosperini et al (2014) Radiology*

# Exercise improves **physical fitness**

**Treadmill walking & Cycling**
**Improvements >> 10%**




*Langeskov-Christensen, Daglas et al.(2015) Sport Med*

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# Exercise improves **physical fitness**

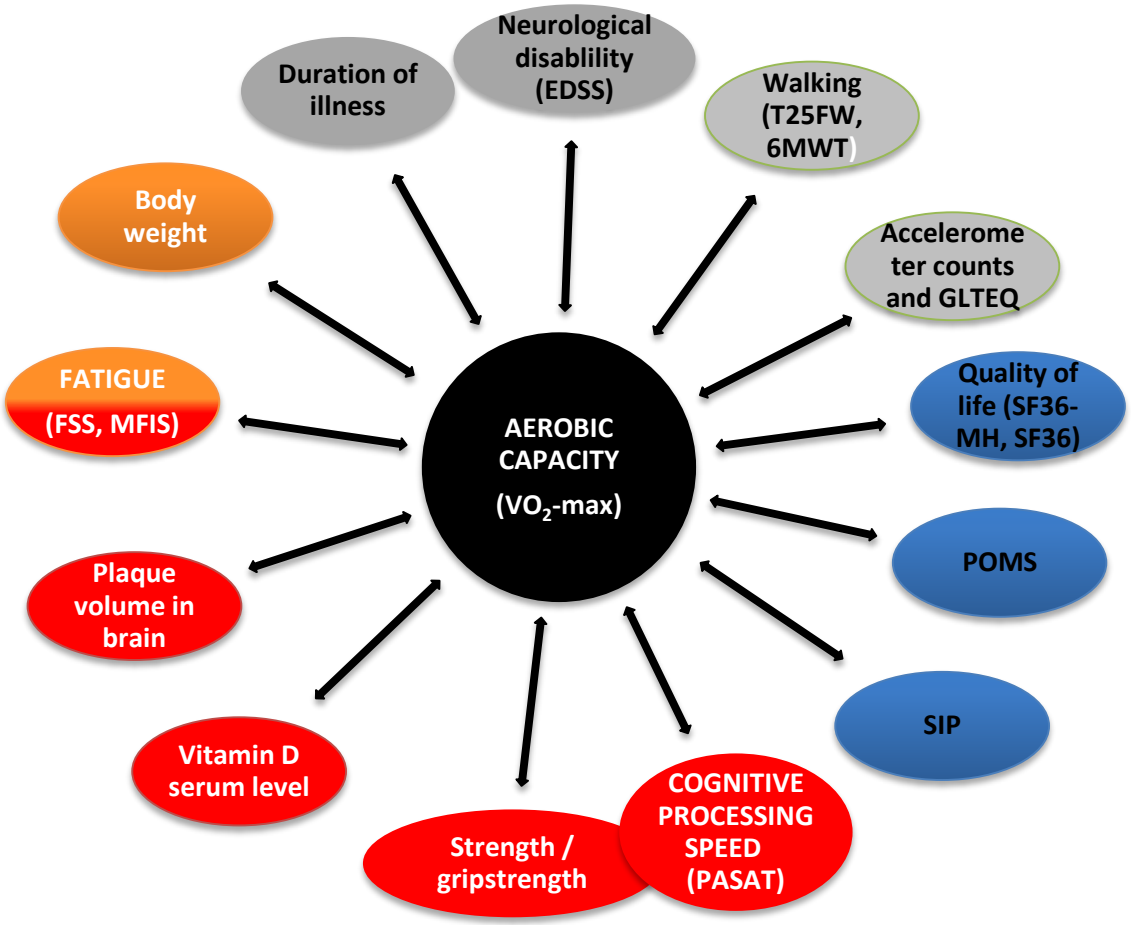
Exercise therapy for fatigue in multiple sclerosis (Review)

THE COCHRANE COLLABORATION®

**Endurance training reduces FATIGUE**

Largest effect size (0,4-0,56)

**Treadmill walking & Cycling**
**Improvements >> 10%**




*Langeskov-Christensen, Daglas et al.(2015) Sport Med*

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# Exercise therapy in advanced MS stadium

Short Report

MULTIPLE SCLEROSIS JOURNAL | MSJ

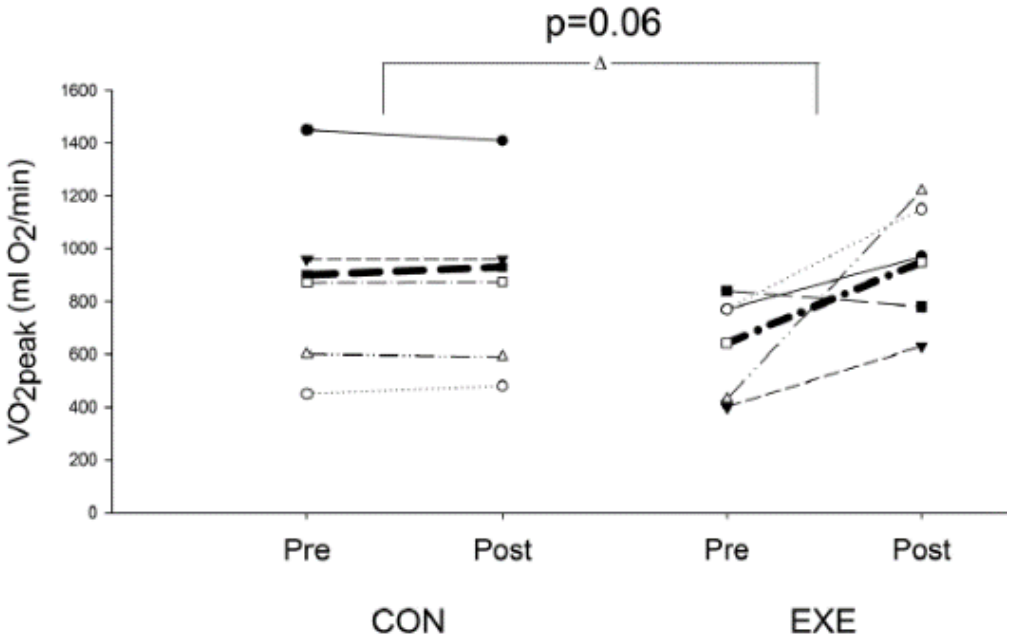
**Endurance training is feasible in severely disabled patients with progressive multiple sclerosis**

Multiple Sclerosis Journal
0(0) 1–4

DOI: 10.1177/1352458513505351
msj.sagepub.com
SAGE

AG Skjerbæk[1], M Næsby[1], K Lützen[1], AB Møller[2,6], E Jensen[1], I Lamers[5], E Stenager[3,4] and U Dalgas[2]

- 11 pwMS
- EDSS 6,5-8,5
  - CON (n=5)
  - EXE (n= 6)
- 10 sessions ergometry during 4 weeks




*Sjerbaek, Dalgas et al (2013) MSJ*

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# Take home Messages

**Assessment**

- A multi-dimensional assessment is required, also in early stage of MS
- Novelties are quantifying symptoms as motor fatigability and cognitive-motor interference

**Rehabilitation**

- A strong body of evidence for exercise therapy
- Exercise may be neuro-protective and neuro-restorative
- Exercise is effective across the disability spectrum

# PATIENT ACTIVATION & BEHAVIOUR CHANGE


Quellenhof Centre, Bad Wildbad, Germany, 12/2011

- Adherence
- Self-Efficacy
- Behavioral change

**Lifestyle physical activity in persons with multiple sclerosis: the new kid on the MS block**

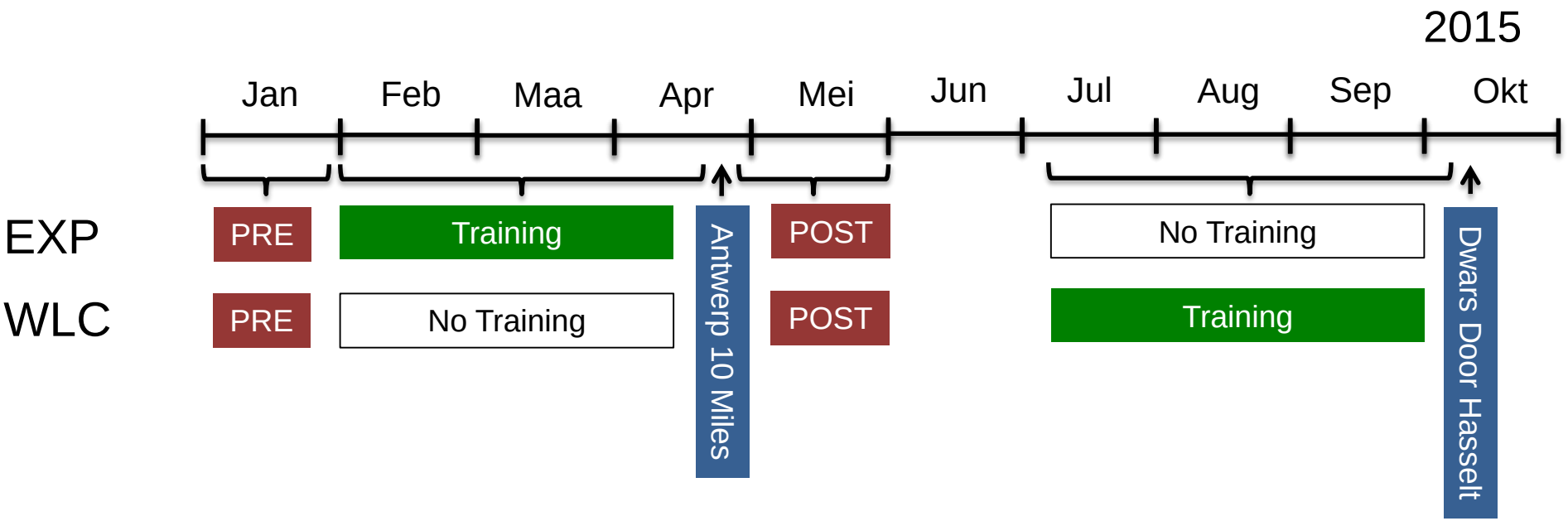
Robert W Motl





# Neurobiology & exercise: **Endurance training**

## MS 'start-to-run' 5 kilometer



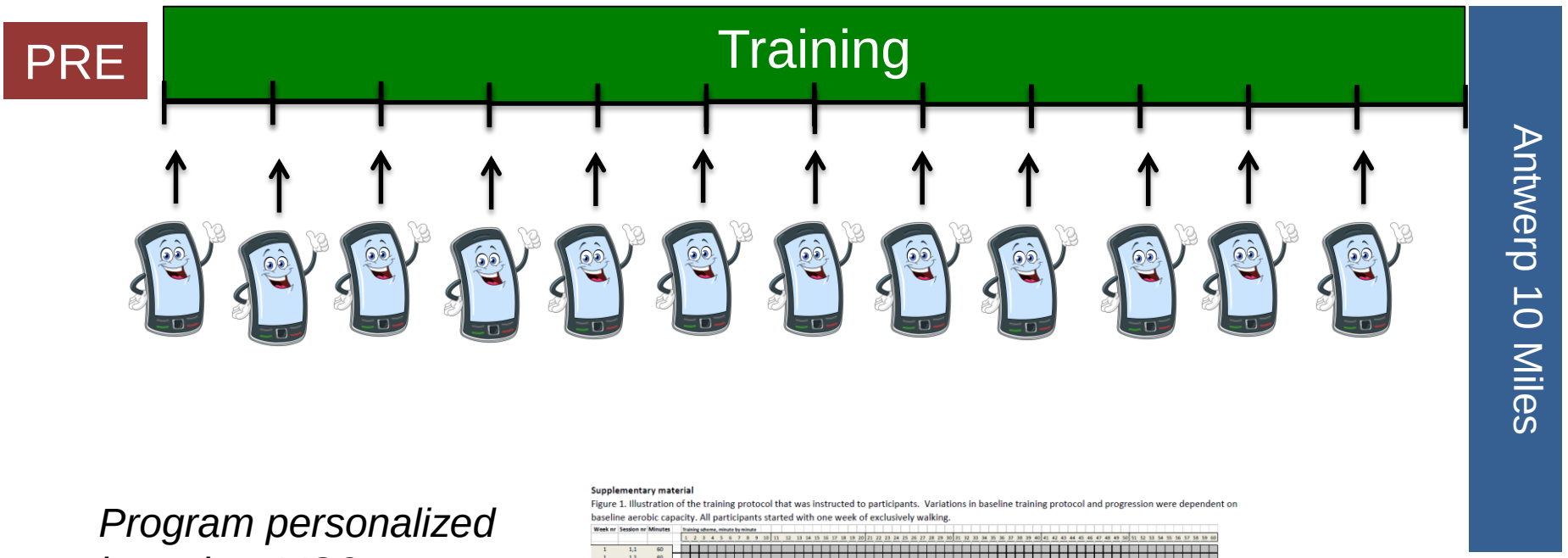

Start-to-run 5km training program in one's own community
3x/week during 12 weeks

Training was remotely supervised by means of accelerometry.

Tests Training Event

Feys, Van Asch et al (2017) MSJ
www.movetosport.be

# MS 'start-to-run' 5 kilometer




*Program personalized based on VO2max. Instructions weekly.*

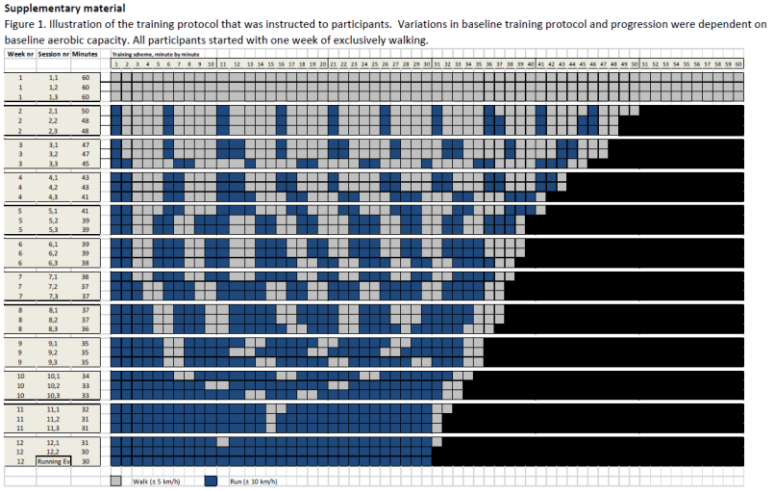

Supplementary material

Figure 1. Illustration of the training protocol that was instructed to participants. Variations in baseline training protocol and progression were dependent on baseline aerobic capacity. All participants started with one week of exclusively walking.

26/4

Feys, Van Asch et al (2017) MSJ

www.movetosport.be

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# MS 'start-to-run' 5 kilometer

PRE

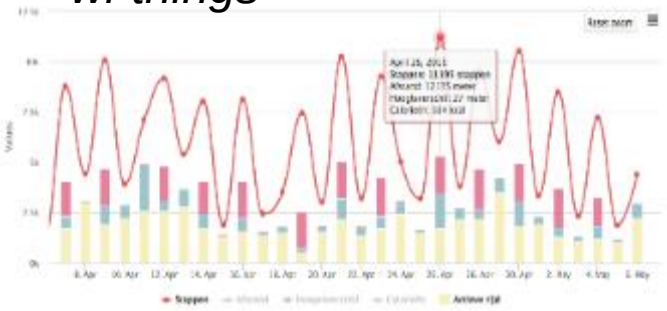
Training

Antwerp 10 Miles

26/4

Group training

*wi-things*




Feys, Van Asch et al (2017) MSJ

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# MS 'start-to-run' 5 kilometer: RESULTS

15% drop-out due to time constraints, and mild injuries

94% adherence to the training sessions

Positive effects in favour of EXP group

- Physical fitness
- 5x Sit-to-stand
- MSWS-12 walking ability
- FSMC fatigue scale for motor & cognitive function
- MSIS-29 quality of life

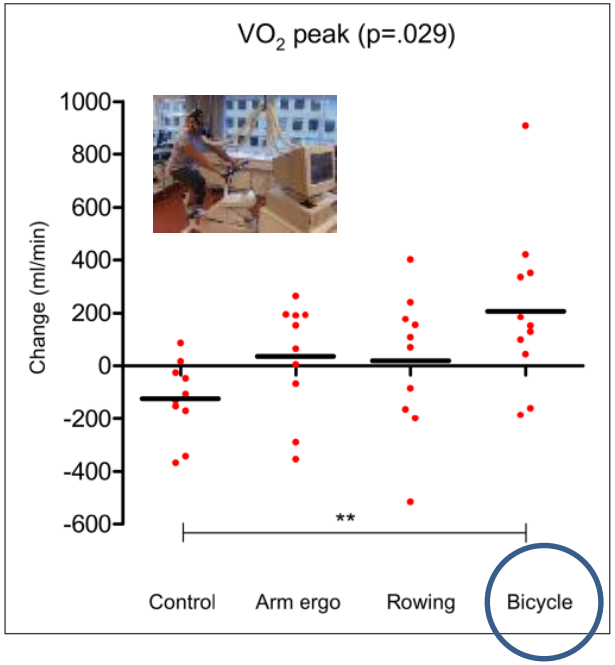
- Cognition: spatial recall test (visuospatial memory)

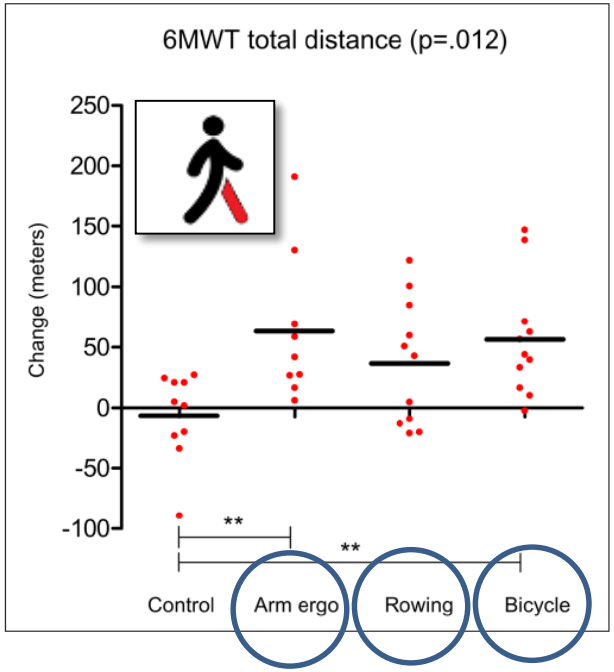
- Neurobiology: Pallidum (basal ganglia)
  brain nucleus involved in subtle regulation of voluntary movements that occur on the subconscious level

*Feys, Moumdjian, Eijnde, Wens, Van Wijmeersch, Popescu, Van Halewyck, Van Asch et al (2017) MSJ*

# Multi-dimensional effects of exercise in persons with PROGRESSIVE TYPE OF MS

*42 pwMS. EDSS 4-6. 8-10 weeks training (10% drop-out)*



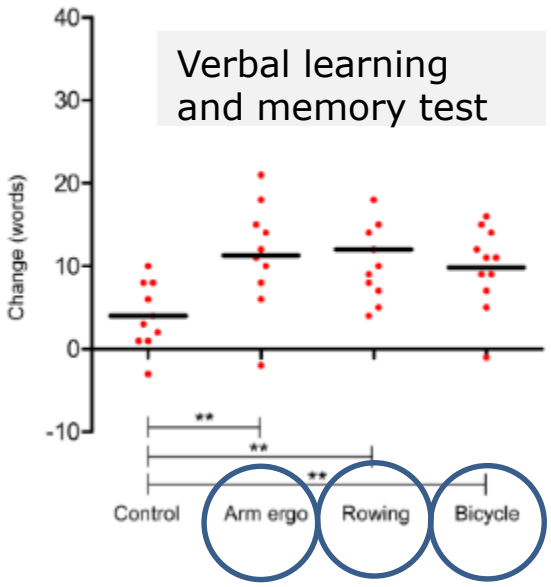



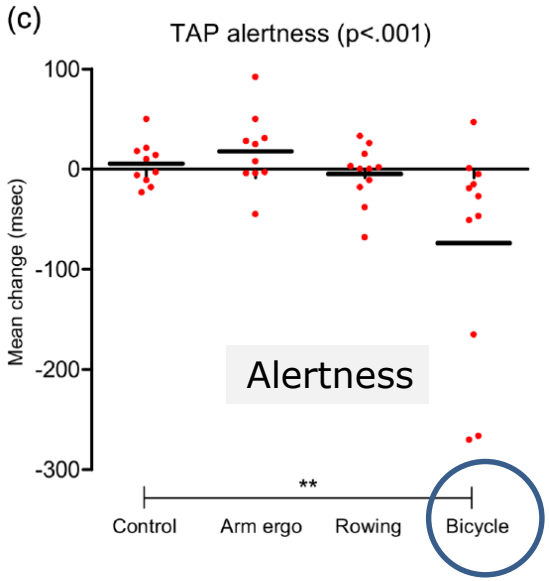

Cycling has best results
on both aerobic fitness & walking distance.

# Effects of exercise on COGNITION in persons with PROGRESSIVE TYPE OF MS

*42 pwMS. EDSS 4-6.*

*8-10 weeks training (10% drop-out)*




Cycling has best results
on both learning & memory, and Alertness

*Briken, Heesen et al (2014) MSJ*

# Take home Messages

**Assessment**

- A multi-dimensional assessment is required, also in early stage of MS
- Novelties are quantifying symptoms as motor fatigability and cognitive-motor interference

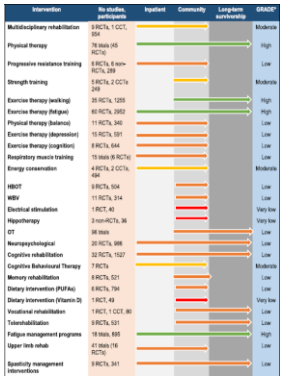
**Rehabilitation**

- A strong body of evidence for exercise therapy with multi-dimensional effects including on fatigue & cognition
- Exercise may be neuro-protective and neuro-restorative
- Exercise is effective across the disability spectrum

# Evidence Summaries

## Highest evidence

- Physical Therapy
- Exercise therapy (walking & fatigue)
- **Fatigue management programs**




## Moderate evidence

- Upper limb training
- Spasticity management
- Multi-disciplinary treatment
- Cognitive retraining
- Neuropsychological rehabilitation
- Energy conservation
- Vocational rehabiliation

Khan et al (2016) APRM

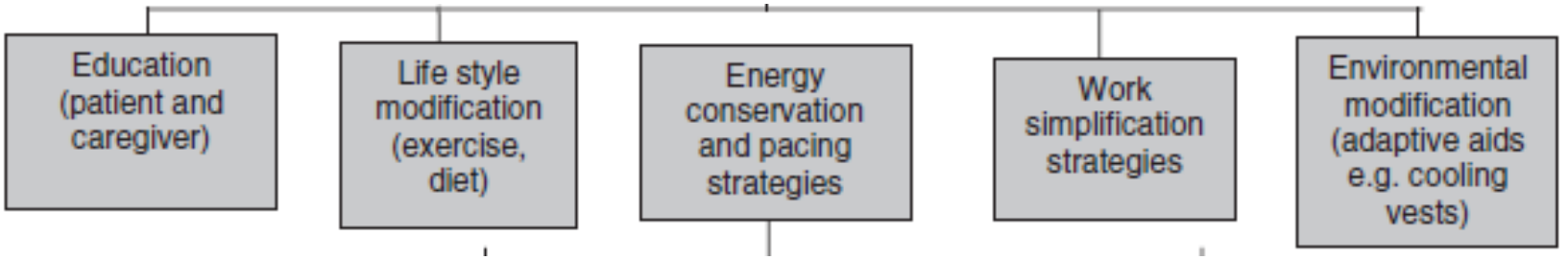
# Multi-disciplinary approaches for fatigue

## One size does not fit all!

- Aerobic exercise
- Cognitive behavioural therapy
- Energy conservation programs

- Self-management programs

- Environmental modifications

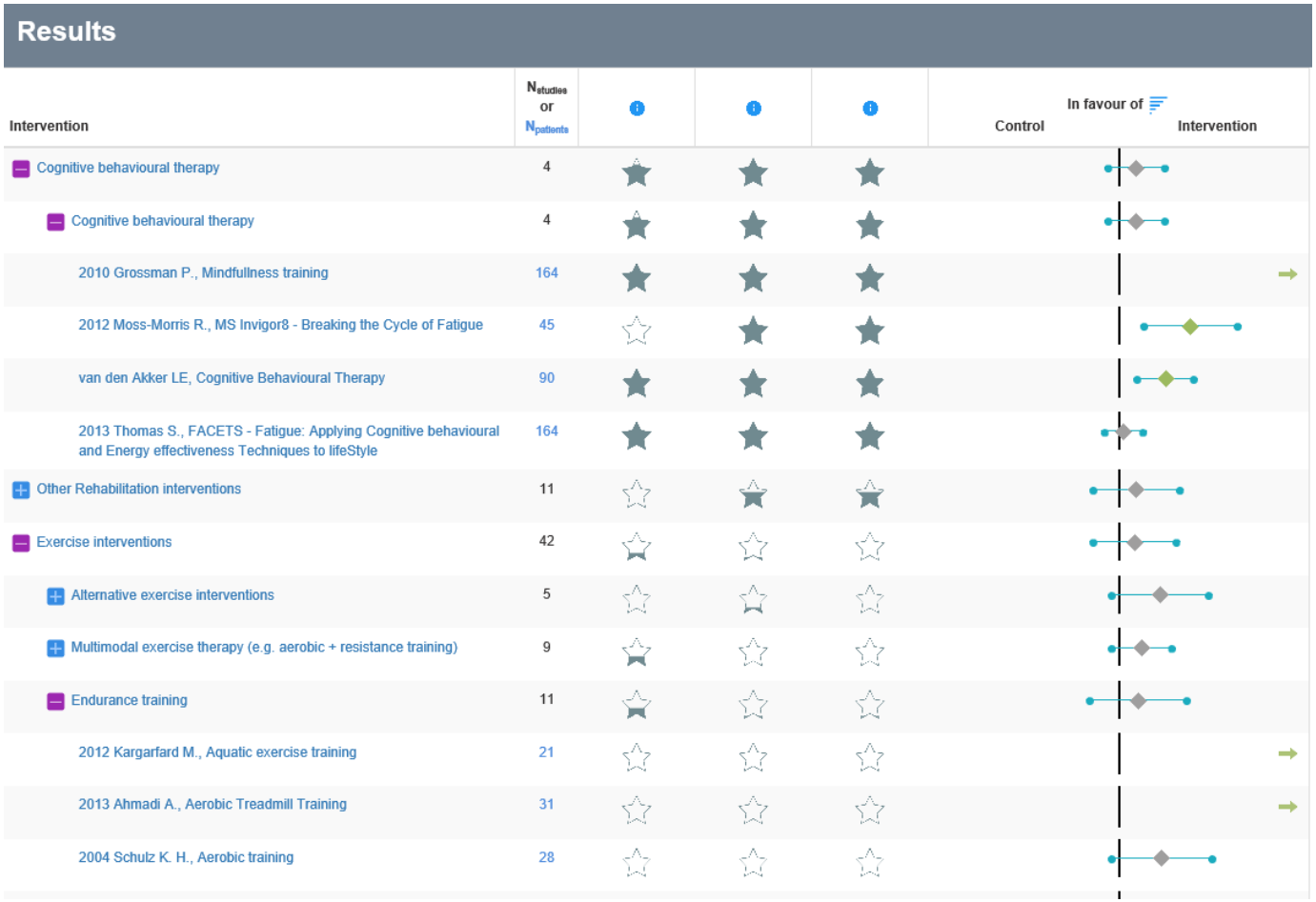



*Khan et al (2014) Frontiers in Neurology*
*Finlayson, Khan, Kos, ..*

# How to find a best evidence-based intervention?

Established by European MS rehabilitation network (www.eurims.org)

**Targeting FATIGUE & COGNITIVE FUNCTION**




www.appeco.net

Applying Evidence with Confidence in clinical practice

# SUMMARY SLIDE

## Multi-dimensional ASSESSMENT

1. Recommendations
2. 'Novel' symptoms

## Efficient Rehabilitation Interventions

1. Physical Exercise
2. Fatigue management
3. Selecting the right interventions for fatigue & cognition: APPECO

## Novel directions

1. Upper extremity training
2. Technological-supported rehabilitation

# An increasing research interest in upper limb rehabilitation in MS.

May 2011. BMC

Spooren *et al. BMC Neurology* 2012, **12**:49
http://

BMC Neurology

**RESEARCH ARTICLE** **Open Access**

## Motor training programs of arm and hand in patients with MS according to different levels of the ICF: a systematic review

Annemie IF Spooren[1,2,3,4*], Annick AA Timmermans[2,3†] and Henk AM Seelen[2,3†]

September 2016. NNR

*Review*

## Upper Limb Rehabilitation in People With Multiple Sclerosis: A Systematic Review

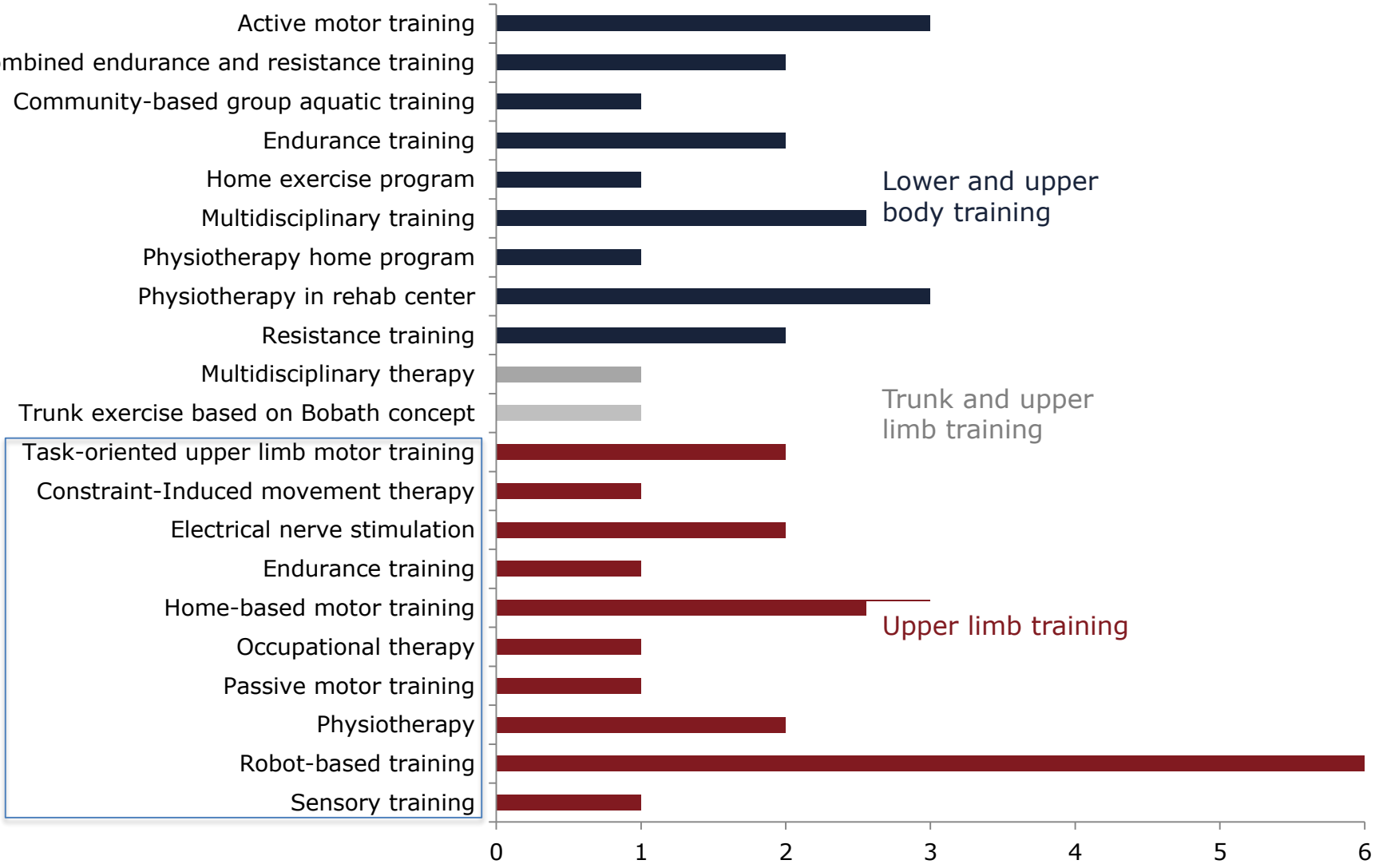
Neurorehabilitation and Neural Repair
1–21

DOI: 10.1177/1545968315624785
nnr.sagepub.com
SAGE

**Ilse Lamers, PhD[1], Anneleen Maris, PhD[1], Deborah Severijns, MSc[1], Wouter Dielkens, MSc[1], Sander Geurts, MSc[1], Bart Van Wijmeersch, PhD[1,2], and Peter Feys, PhD[1]**

# Content of therapy

- 30 studies, of which 11 (small) RCT
- Promising effects at the level of training (body function or activity level)




Lamers et al (2016) NNR

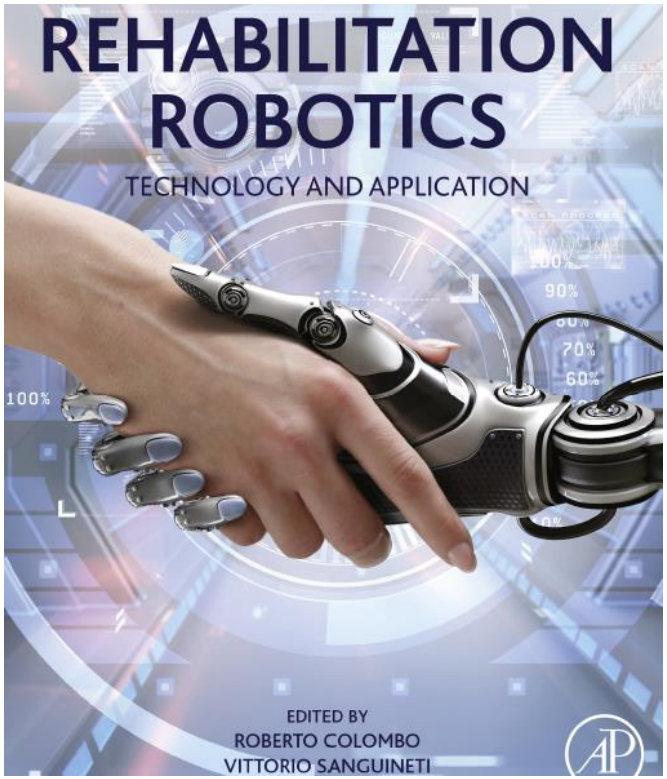
MULTIPLE SCLEROSIS JOURNAL | MSJ

Editorial 2016. MSJ

*Editorial*

# Potential of robot-assisted therapy for disabled persons with MS

Peter Feys




Book published in 2018

CHAPTER 18

# Robot-assisted rehabilitation in multiple sclerosis: Overview of approaches, clinical outcomes, and perspectives

**Ilse Lamers**[*,†], **Peter Feys**[*], **Eva Swinnen**[‡]

*Hasselt University, Hasselt, Belgium[*] Rehabilitation and MS center, Overpelt, Belgium[†] Vrije Universiteit Brussel, Brussel, Belgium[‡]*

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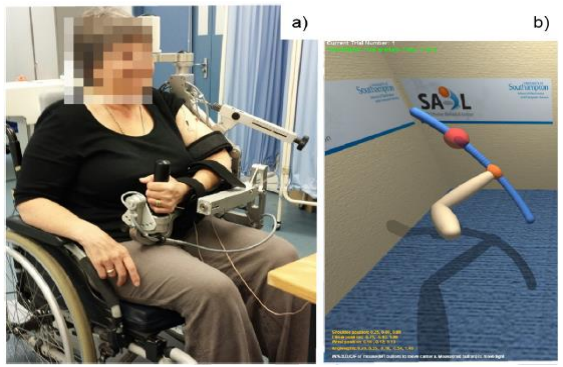
# ROBOT-ASSISTED UPPER LIMB REHABILITATION

Brachio di Ferro – 2DOF

Haptic Master– 3DOF & I-TRAVLE

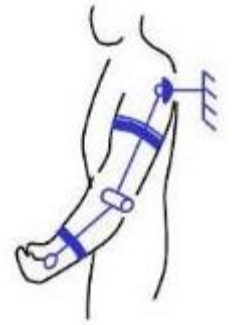
**END-EFFECTOR**

Armeo Spring – multiple joints




Armeo Spring– 3DOF & SAIL

**EXOSKELETON**



Unilateral and mainly proximal (shoulder-elbow) training systems

*Different underlying training principles in software programs*

# Robot-assisted Upper Limb Training

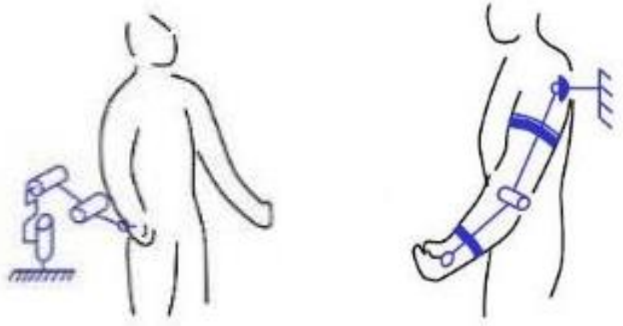




**Table 1** Overview of studies investigating robot-assisted upper limb training

| Publication | N | Training | EDSS | Name of the device | Type of device | Significant treatment effects |
|---|---|---|---|---|---|---|
| Carpinella et al. [13] | 7 pwMS 9 HC | 8×1 h over 2 weeks | 5.7 | Braccio di Ferro | End-effector 2DOF with haptic forces | Manual dexterity |
| Gijbels et al. [14] | 9 pwMS | 24×30′ over 8weeks | 7.9 | Armeo Spring | Exoskeleton with antigravity support | Manual dexterity, proximal and distal upper limb capacity |
| Carpinella et al. [15] RCT | 22 pwMS (11/11) | 8×1 h over 2 weeks | 6.4–6.9 | Braccio di Ferro | End-effector 2DOF with haptic forces | Tremor, manual dexterity, proximal and distal upper limb capacity |
| Feys et al. [16] RCT | 17 pwMS (8/9) | 24×30′ over 8 weeks | 7.3–8 | HapticMaster/I-TRAVLE | End-effector 3DOF with haptic environment | More efficient movement execution measured with the system, no clinical effects |
| Sampson et al. [17] | 5 pwMS | 18×1 h over 10 weeks | NR | Armeo Spring/ SAIL System | FES with Exoskeleton 3DOF with antigravity support | Accuracy of tracking performance, amount of FES needed to perform the movements, range of motion, and motor control in the proximal upper limb |
| Maris et al. [18] | 13 pwMS 14 stoke | 18×1 h over 8 weeks | 6.5 | HapticMaster/I-TRAVLE | End-effector 3DOF with haptic environment | Active shoulder range of motion, handgrip strength, perceived upper limb strength, proximal and distal upper limb capacity, speed and movement duration measured with the system |

*RCT, randomized controlled trial; pwMS, persons with multiple sclerosis; HC, healthy controls; EDSS, expanded disability status scale; DOF, degrees of freedom; FES, functional electric stimulation.*

- Small sampled studies
- Pilot trials show beneficial effects of robot-assisted upper limb rehabilitation: movement efficiency, clinical effects on body function & activity level
- 2 RCT's
  - **No superiority** of the robot training compared to conventional therapy however, **effects may last longer**
  - Increased clinical effects if object manipulation is included

# Robot-Assisted Gait Training (RAGT)


Lokomat - Hocoma

Gait Trainer

## Powered Exoskeleton

# Robot-assisted Gait Training

RAGT is
- Mostly clinically effective
- **Mostly as effective as CWT** (conventional walking training) for improving walking and QoL* (and other)
- Is well accepted by persons with MS

**Table 2** Overview of studies investigating robot-assisted gait training (RAGT)

| Publication | N | Training (RAGT) | EDSS (RAGT) | Robotic device | Type | Significant treatment effects |
|---|---|---|---|---|---|---|
| Lo et al. [26] NNR—pilot RCT BWSTT and RAGT | 13 (crossover design) | 2×40′/week for 3 weeks, 6 sessions | 4.9 | LOKOMAT | Exoskeleton | Walking speed (timed 25 ft walk), walking capacity (6-min walk distance), percentage of double support time, severity of MS (EDSS) |
| Pompa et al. [30] MSJ | 13 (crossover design) | idem Lo et al. [26] | idem Lo et al. [26] | idem Lo et al. [26] | idem Lo et al. [26] | Quality of life |
| Beer et al. [31] MS—RCT RAGT versus CWT | 35 (19 RAGT) | 5×30′ walking time/week for 3 weeks, 15 sessions | 6.5 | Lokomat | Exoskeleton | Walking speed, distance and knee extensor strength |
| Vaney et al. [32] NNR—RCT RAGT versus CWT | 49 (26 RAGT) | 3×30′/week for 3 weeks, 9 sessions | 5.9 | Lokomat | Exoskeleton | |
| Schwartz et al. [33] MSJ RCT RAGT versus CWT | 32 (15 RAGT) | 2–3×30′ walking time/week for 4 weeks, 12 sessions | 6.3 | Lokomat | Exoskeleton | Functional mobility, functional independence measure, overall disability |
| Ruiz et al. [34] JNPT | 7 (immediate/delayed treatment group) | 2×20′/w for 2 months, 16 sessions | 5 | Lokomat | Exoskeleton | Walking distance, functional balance |

*Continued*



**Superiority of RAGT compared to CWT** in those studies with higher EDSS (≥6)
- QoL – physical domain
- Walking distance (but not always walking speed)
- Number of pwMS reaching clinical meaningful change in walking (2MWT, FAC) chance to change from ‘dependent’ to ‘independent’ walking (20meter walking)

# Take home Messages

**Assessment**

- A multi-dimensional assessment is required, also in early stage of MS
- Novelties are quantifying symptoms as motor fatigability and cognitive-motor interference

**Rehabilitation**

- A strong body of evidence for exercise therapy with multi-dimensional effects including on fatigue & cognition
- Exercise may be neuro-protective and neuro-restorative
- Exercise is effective across the disability spectrum
- There are different types of effective fatigue rehabilitation programs
- Novelties are upper limb training & the technological-supported programs

# Acknowledgments

The Flemish MS CENTERS Brasschaat, Melsbroek, Overpelt
The MS centers CHU Liege-Esneux & CNRF Fraiture
The European Rehabilitation in MS Netwerk RIMS

v.l.n.r.: prof. dr. P. Feys, dr. I. Lamers, dr. I. Baert, L. Moumdijan, J. Raats, F. Van Geel and R. Veldkamp.

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KNOWLEDGE IN ACTION