

# Therapietrouw

## Wat te weten en wat te doen

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MIJN PATIËNTEN  
SLIKKEN ALLES



# Onderwerpen

Termen voor aspecten van therapietrouw

Therapietrouw bij MS-ziektemodificerende behandelingen

Gevolgen van therapieontrouw

Factoren die therapietrouw voorspellen of veroorzaken

Methoden om therapietrouw te meten

Interventies die therapietrouw bevorderen

Maatregelen in de praktijk

# Therapietrouw en klinische uitkomsten

Therapietrouw is geen doel op zich

Het is een middel om maximaal effect van behandeling te verkrijgen

Studies van maatregelen om terapietrouw te bevorderen dienen ook voldoende 'power' te hebben om een effect op **klinische uitkomsten** aan te tonen

# Compliance

De mate waarin de patiënt de aanbevelingen van de voorschrijver opvolgt

Zorgverlener vertelt de patiënt wat hij zou moeten doen

Gebaseerd op *eenzijdige besluitvorming*



# Concordantie

Het bereiken van **overeenstemming** tussen patiënt en zorgverlener over de behandeling

*Gedeelde besluitvorming ('shared decision-making')*



## **'Adherence' (adherentie)**

De mate waarin het gedrag van de patiënt overeenkomt met de aanbevelingen van de voorschrijver die met de patiënt zijn afgesproken.

## WHO-definitie 'adherence to long-term therapy'

WHO (World Health Organisation)-definitie uit 2003:

*De mate waarin het gedrag van een persoon - het nemen van medicatie, het volgen van een dieet en/of het uitvoeren van veranderingen in levensstijl, overeenkomt met de afgesproken aanbevelingen van een zorgverlener.<sup>1</sup>*

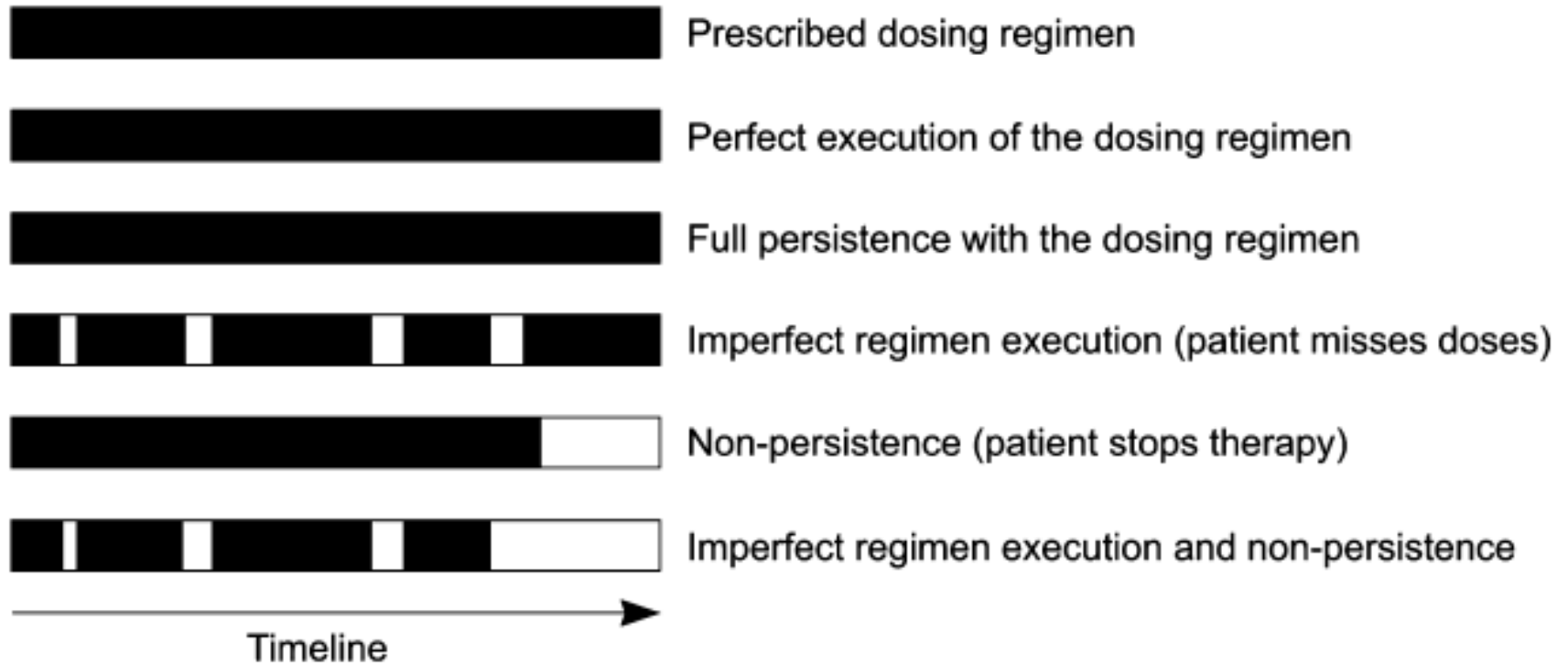


# Persistentie

De mate van **continuïteit** van het gebruik van een geneesmiddel

Met name van belang bij chronische aandoeningen

# Schematische weergave adherentie en persistentie van een doseringsregime



Lowy A, Munk VC, Ong SH, et al. Effects on blood pressure and cardiovascular risk of variations in patients' adherence to prescribed antihypertensive drugs: role of duration of drug action. *Int J Clin Pract.* 2011;65:41-53.

## Peristentie en Adherentie (s.s.)

Het niet correct uitvoeren van een doseerschema (*non-adherentie*) gedurende de voorgeschreven periode

zal een ander effect hebben dan het voortijdig

beëindigen (*non-persistentie*) maar wel juist uitvoeren van het doseerschema

**In de (Engelstalige) literatuur wordt dit onderscheid in zeer beperkte mate gemaakt**

## Wanneer is sprake van therapieontrouw?

**Non-persistentie:** eerder stoppen dan overeengekomen

**Non-adherentie d.w.z. gemiste doseringen:**

minder dan **80%-90%** van doseringen

## **‘Concordante non-persistentie’**

Voortijdig stoppen na overleg met voorschrijver

Meestal wegens:

- onvoldoende effect
- blijvende hinderlijke bijwerkingen
- ernstige bijwerkingen

**Geen therapieontrouw**

## 'Intelligente' therapieontrouw

Doses overslaan en/of tijdelijk stoppen

Op geleide van

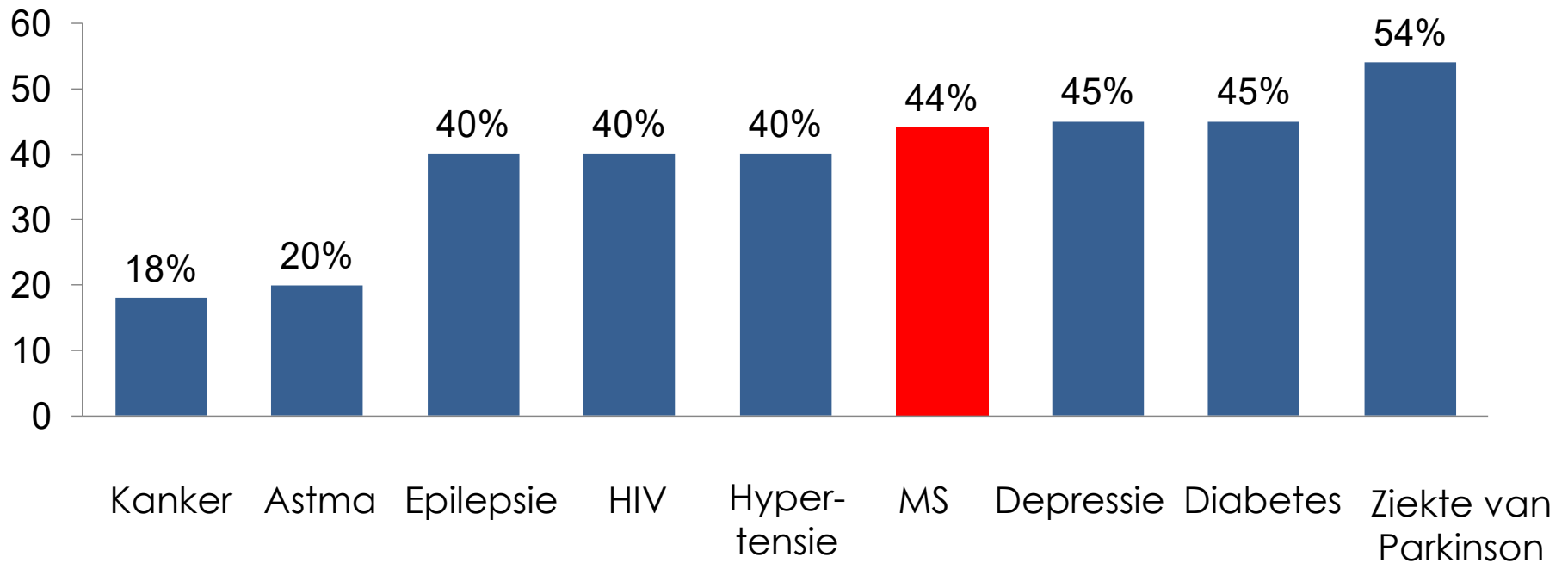
- klachten
- zelfmonitoren (bijv. bloeddruk)
- bijwerkingen

Permanent lagere dosis bij blijvende bijwerkingen

NB: Trouw gebruik van NSAID's kan bij ouderen maagbloedingen geven

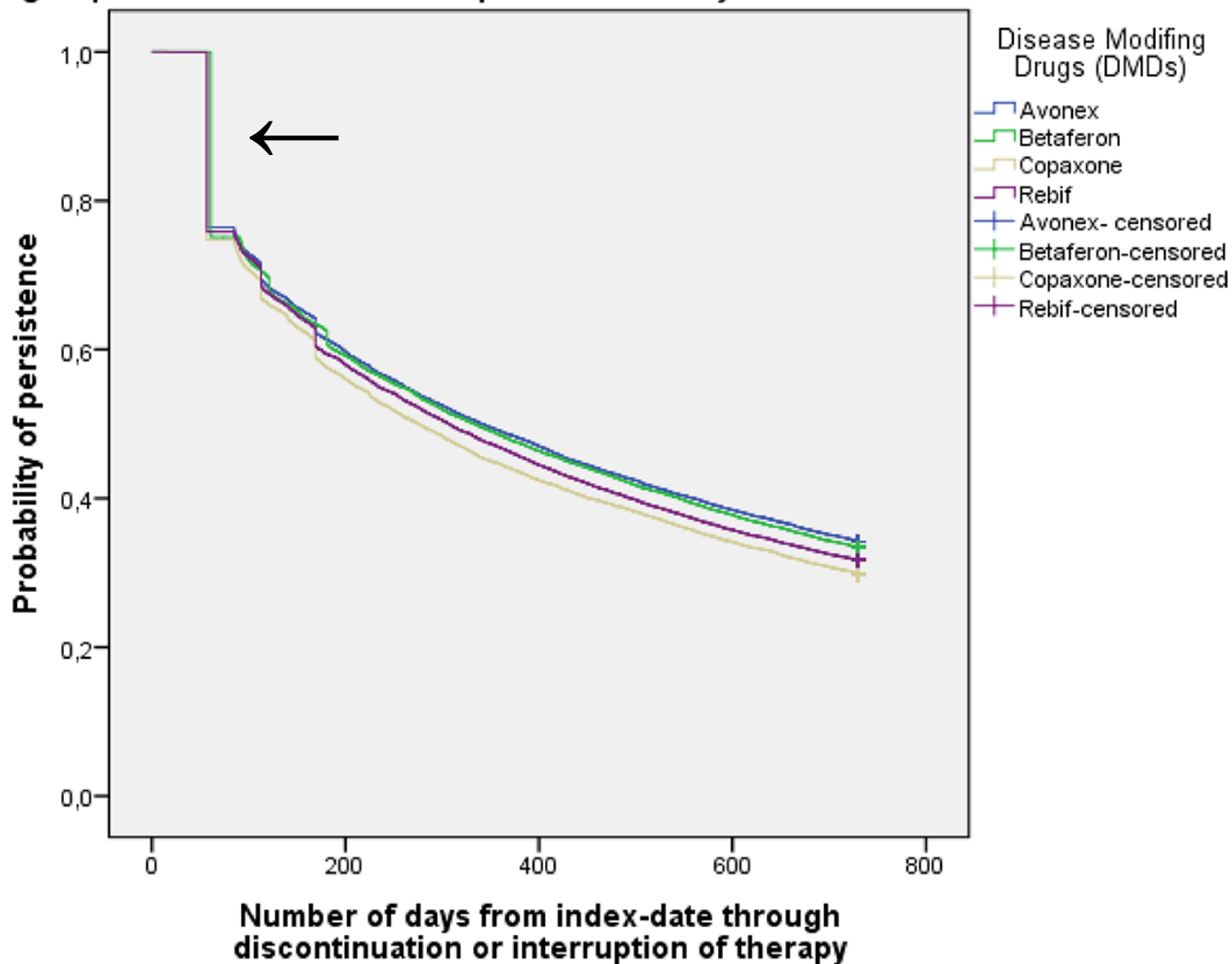
# Adherentie bij chronische aandoeningen

Weergave % van de patiënten met een chronische aandoening dat **therapieontrouw** is, ongeacht de toedieningsvorm van de medicatie



Adherence to Long-term Therapies: Evidence for Action, WHO 2003, ISBN 92 4 154599 2. Cuzick J & Edwards R. Lancet. 1999;353:930. 3. Berg JS et al. Ann Pharmacother. 1993;27(9 suppl):S1-24. 4. Hadjimihael O & Vollmer TL. Neurology. 1999;52:A549. 5. Treadaway K et al. American Academy of Neurology 58<sup>th</sup> Annual Meeting 2006; San Diego, CA, USA. 6. Leopold NA et al. Mov Disord. 2004;19:513-7.

**Kaplan-Meier persistence curves of the four DMD groups within the observation period of 730 days**



Hansen K, Schüssel K, Kieble M, et al. Adherence to Disease Modifying Drugs among Patients with Multiple Sclerosis in Germany: A Retrospective Cohort Study. PLoS One. 2015;10:e0133279.



# Adherence to Disease Modifying Drugs among Patients with Multiple Sclerosis in Germany: A Retrospective Cohort Study



**Retrospective cohort** study using pharmacy claims data from **Deutsche Arzneiprüfungsinstitut e.V. (DAPI)**

**2001-2009**

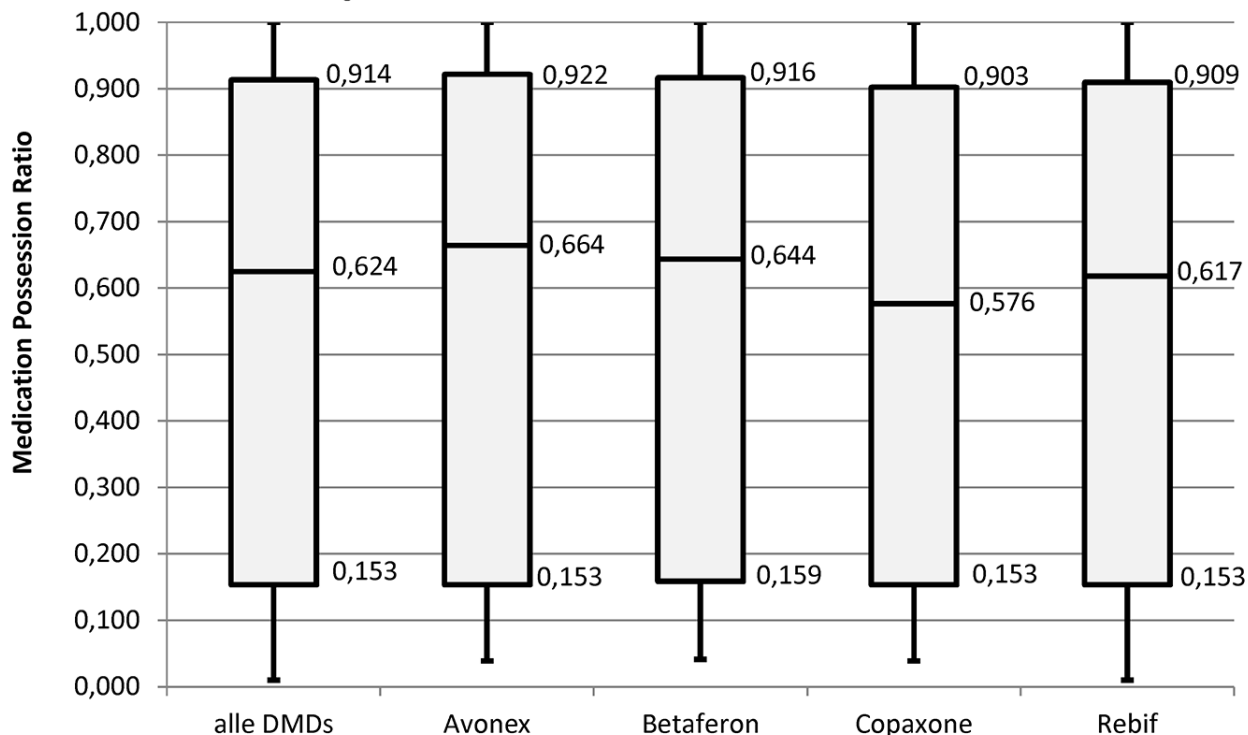
50,057 patients (**Avonex®**, **Betaferon®**, **Copaxone®**, **Rebif®**)

No clinically relevant differences between cohorts

**Overall persistence 24 months: 32.3%**

**Overall MPR  $\geq$  0.8: 39.9%**

### Boxplot of Median MPRs of DMDs



#### MPR $\geq 0.70$

All DMDs	46.1%
Avonex	48.2%
Betaferon	47.1%
Rebif	45.6%
Copaxone	43.5%

#### Characteristics

DMD (%)	52516 (100.0)								
Medical specialist (%)	<table border="1"> <tbody> <tr> <td>Neurologist</td> <td>42602 (81.1)</td> </tr> <tr> <td>General practitioner</td> <td>5236 (10.0)</td> </tr> <tr> <td>Institutions</td> <td>2615 (5.0)</td> </tr> <tr> <td>Others/not specified</td> <td>2063 (3.9)</td> </tr> </tbody> </table>	Neurologist	42602 (81.1)	General practitioner	5236 (10.0)	Institutions	2615 (5.0)	Others/not specified	2063 (3.9)
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#### Overall

RESEARCH

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# Glatiramer acetate treatment persistence - but not adherence - in multiple sclerosis patients is predicted by health-related quality of life and self-efficacy: a prospective web-based patient-centred study (CAIR study)

Peter Joseph Jongen<sup>1,2\*</sup>, Wim A. Lemmens<sup>3</sup>, Erwin L. Hoogervorst<sup>4</sup> and Rogier Donders<sup>3</sup>

Jongen PJ, Lemmens WA, Hoogervorst EL, Donders R. Glatiramer acetate treatment persistence - but not adherence - in multiple sclerosis patients is predicted by health-related quality of life and self-efficacy: a prospective web-based patient-centred study (CAIR study). *Health Qual Life Outcomes*. 2017;15:50. doi: 10.1186/s12955-017-0622-z.

Persistence and adherence in multiple sclerosis patients starting glatiramer acetate treatment: assessment of relationship with care received from multiple disciplines

**12-month persistence: 62%**

**85% of persistent patients were 95% adherent**

99.2% were 85% adherent; 92.7% were 90% adherent

**No associations with care given by neurologist, nurse, psychologist, pharmacist or rehabilitation doctor**

Patients discontinuing in Q4: less-frequent and shorter **psychological care** in Q3 ( $p = 0.0018$  and  $p = 0.0022$ )

Adherent patients: more frequent and longer **home care** and **informal care** ( $p = 0.0074$ ;  $p = 0.0198$ ) ( $p = 0.0074$ ;  $p = 0.0318$ )

# Comparative analysis of first-year fingolimod and natalizumab drug discontinuation among Swedish patients with multiple sclerosis

**1-year persistence; 2011-2013; NTZ (n = 640) or FGL (n = 876)**

FGL older than NTZ cohort (44% had used FGL)

**NTZ 87% vs. FGL-NTZ-naïve 83% vs. FGL-after-NTZ 76%**

**Adverse events most frequent reason for discontinuing FGL (FGL-NTZ-naïve 9%, FGL-after-NTZ 12%); higher than NTZ 3%**

**Patients stopping treatment due to lack of effect:**

NTZ 4%, FGL-NTZ-naïve 3%, FGL-after-NTZ 8%

The Global Adherence Project (GAP): a multicenter observational study on adherence to disease-modifying therapies in patients with relapsing-remitting multiple sclerosis

**2009:** IM IFNb-1a, SC IFNb-1a, IFNb-1b, GA ('**ABCR**')  
n = 2648; mean treatment duration 31 months

**Adherence: not missing a single injection in 4 weeks < study**

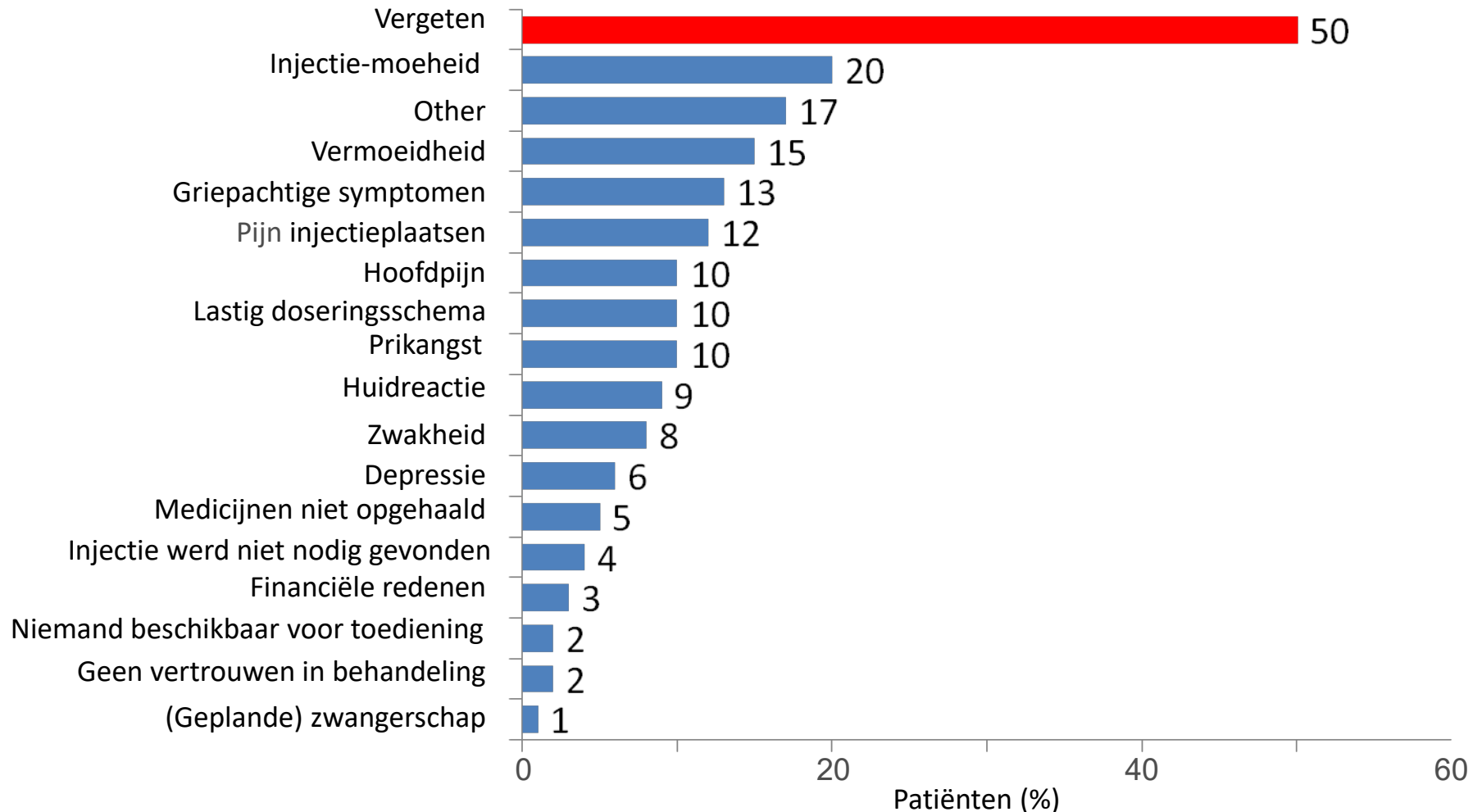
**75% were adherent to therapy**

Most common **reasons for non-adherence:**

- **forgetting to administer (50.2%)**
- **injection-related reasons (32.0%)**

**Adherent patients:** - **better quality of life**  
- **fewer neuropsychological issues**

# Redenen voor non-adherentie in GAP-studie

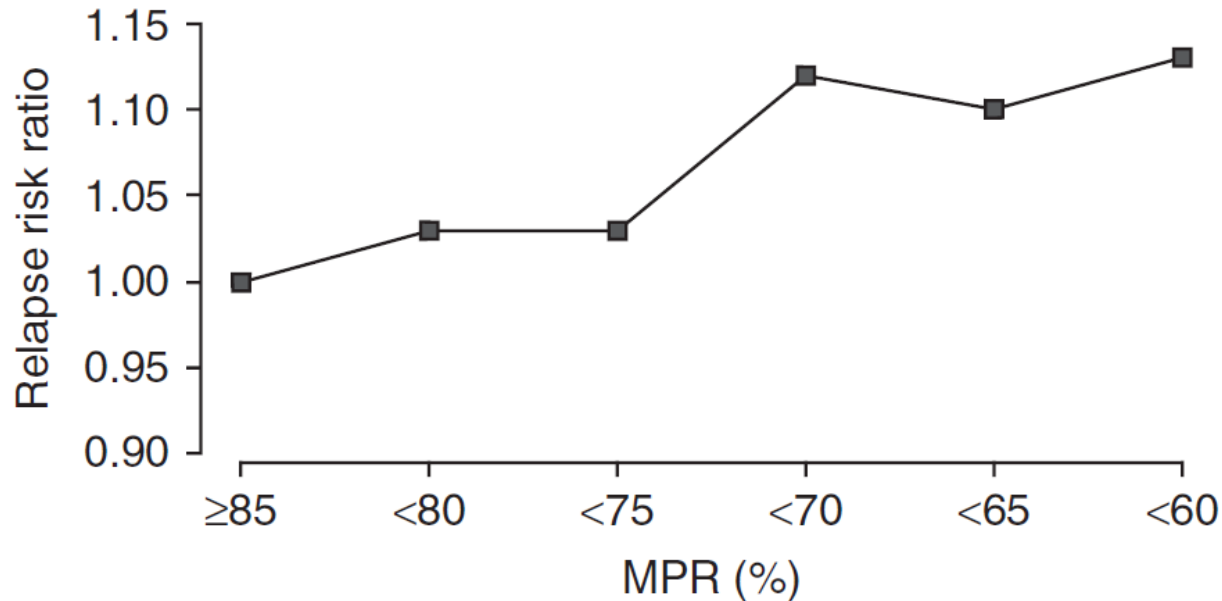


## Gevolgen van therapieontrouw

- **Meer ziekteactiviteit** morbiditeit
- **Verminderde kwaliteit van leven**
- **Ziekenhuisopnames** zorgkosten
- **Vroegtijdig overlijden** mortaliteit



# Relatie tussen MPR en relapse risico



pharmacy and medical claims data, n = 1606, 2006-2008, RRMS

4% van de patiënten heeft een MPR van  $\geq 85\%$  (3-jaar studie)

Lagere MPR: hoger gebruik gezondheidsvoorzieningen

# Gevolgen van therapieontrouw

Een betere therapietrouw aan **antihypertensieve medicatie** kan naar schatting in de **VS** jaarlijks het **vroegtijdig overlijden van 89.000 patiënten** voorkomen

Osterberg and Blaschke. Adherence to Medication. N Engl J Med. 2005;353:487-97.

Adherence to long term therapies: evidence for action. World Health Organization (WHO) .

Cutler, Long, Berndt et al. The value of antihypertensive drugs: a perspective on medical innovation. Health Aff (Millwood) 2007;26:97-110.

# Therapietrouw bij chronisch zieken

NED TIJDSCHR GENEESKD. 2009;153:A420

PATIËNTGERICHTE BENADERING IS NOODZAKELIJK

Ted Klok, Eric J. Sulkers, Ad A. Kaptein, Eric J. Duiverman, Paul L.P. Brand

KLINISCHE PRAKTIJK

## TABEL 1 Belangrijke voorspellers van therapieontrouw<sup>3</sup>

psychische problemen, met name depressie  
verminderd cognitief functioneren  
asymptomatische ziekte  
onvoldoende follow-up  
bijwerkingen van medicatie  
patiënt heeft onvoldoende geloof in het voordeel van de behandeling  
patiënt heeft onvoldoende inzicht in zijn of haar ziekte  
slechte arts-patiëntrelatie  
niet verschijnen op afspraken  
complexiteit en duur van behandeling

# Factoren niet-intentionele en intentionele therapieontrouw

Niet-intentionele factoren	intentionele factoren
vergeetachtigheid (bv. door complexe doseerschema's, polyfarmacie)	patiënt ervaart behandeling als niet-noodzakelijk (bv. asymptomatische aandoening)
beperkt vermogen om de behandeling te begrijpen	negatieve attitude ten aanzien van specifiek voorgeschreven geneesmiddel
onherkenbaarheid geneesmiddel	zorgen om geneesmiddel (bijwerkingen, afhankelijkheid, verslaving)
kosten behandeling (bijbetaling)	gebrek aan vertrouwen in behandeling
analfabetisme	kennisgebrek
slechtziendheid	aandoening wordt als stigmatiserend gezien

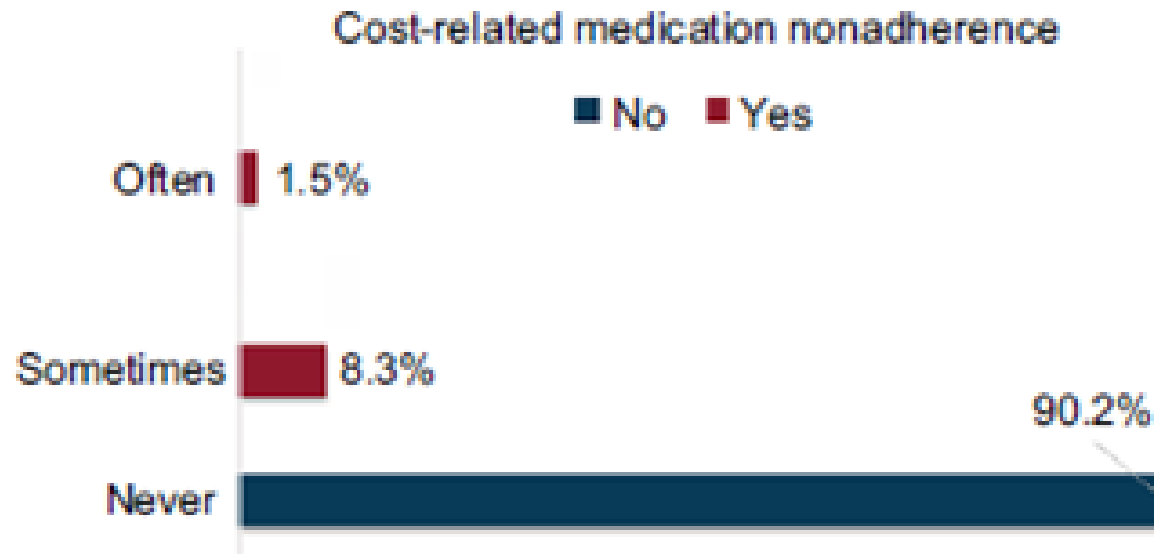
Van Onzenoort 2012. <http://genesmiddelenbulletin.com/artikel/therapietrouw-2/>

Osterberg and Blaschke. Adherence to Medication. N Engl J Med 2005;353:487-97.

Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking. London: National Co-ordinating Centre for NHS Service Delivery and Organisation (NCCSDO), 2005

[http://www.netscc.ac.uk/hsdr/files/project/SDO\\_FR\\_08-1412-076\\_V01.pdf](http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf)

# Patient-reported financial barriers to adherence to treatment in neurology



... the magnitude of **financial barriers** to medication adherence ... **varies across** ... **demographic characteristics**

## Wijze van toediening

- Intramusculaire injectie
- Intraveneuze infusie
- Onderhuidse injectie
- Oraal

# Doseerschema



**Figure 1. Adherence to Medication According to Frequency of Doses.**

Vertical lines represent 1 SD on either side of the mean rate of adherence (horizontal bars). Data are from Claxton et al.<sup>7</sup>

Osterberg and Blaschke. Adherence to Medication. *N Engl J Med.* 2005;353:487-97.

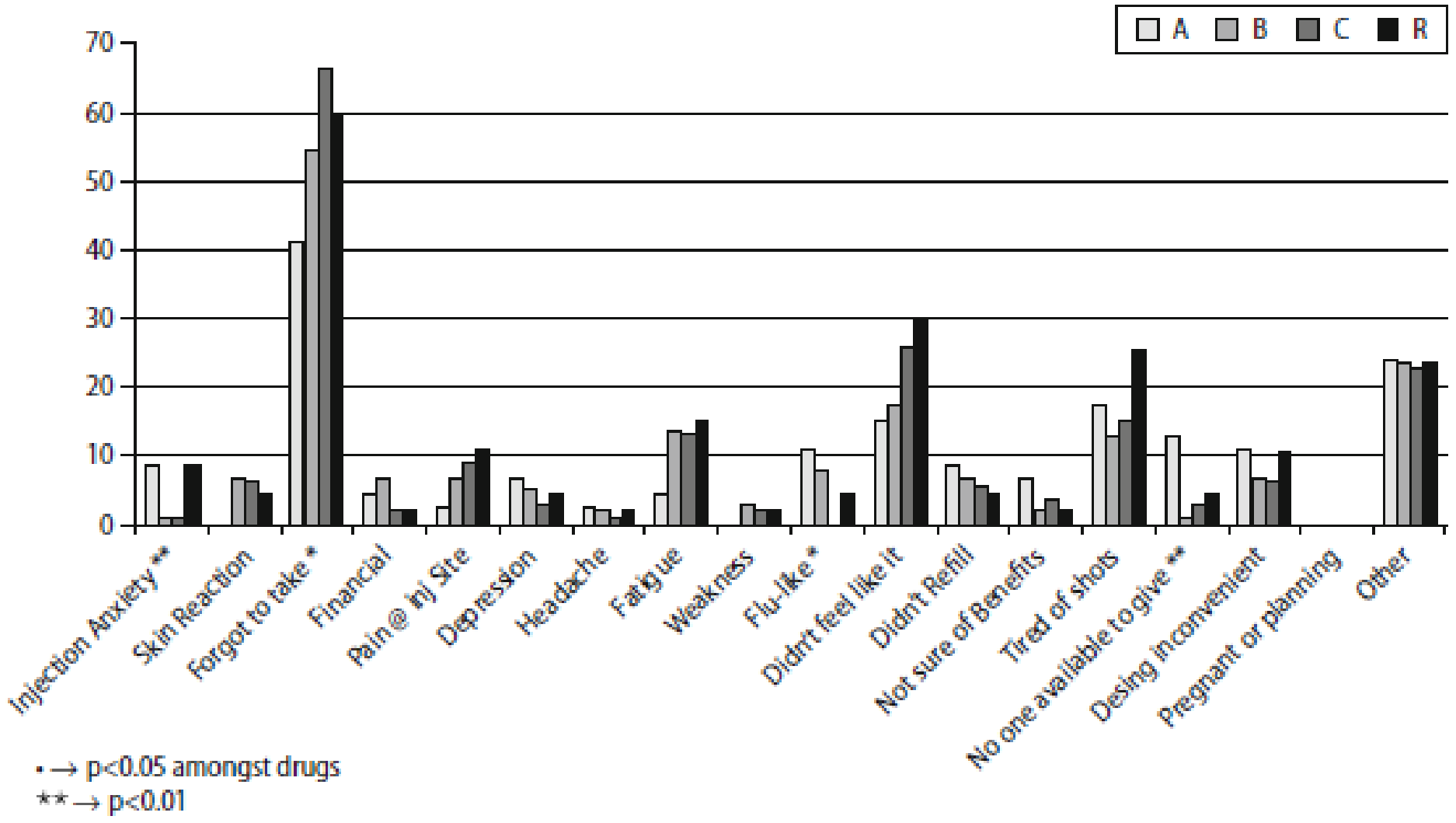
Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther.* 2001;23:1296-310.

# Bijwerkingen

Verschillen tussen middelen

Afhankelijk van werkingsmechanisme en  
toedieningswijze





Reasons for **Avonex**, **Betaferon**, **Copaxone** and **Rebif** non-adherence

Treadaway K, Cutter G, Salter A, et al. Factors that influence adherence with disease-modifying therapy in MS. J Neurol. 2009;256:568-76.

# Understanding Patients' Adherence-Related Beliefs about Medicines Prescribed for Long-Term Conditions: A Meta-Analytic Review of the Necessity-Concerns Framework

**Higher adherence** was associated with

**1) stronger perceptions of necessity of treatment**

(OR 1.74, 95% CI [1.57, 1.93], p,0.0001)

**2) fewer concerns about treatment**

(OR 0.50, 95% CI [0.45, 0.56], p,0.0001)

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# Persistence and adherence in multiple sclerosis patients starting glatiramer acetate treatment: assessment of relationship with care received from multiple disciplines

**1-year, online self-reports**, 203 patients, GA 20 mg sc daily

To study persistence and adherence in relation to duration and frequency of care received from neurologist, nurse, psychologist, pharmacist, rehabilitation,

and general practitioners, occupational therapists, physiotherapists, social workers, dieticians, home caregivers, informal caregivers, other medical specialists, and other caregivers

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**Adherent patients: more frequent and longer home care and informal care** ( $p = 0.0074$ ;  $p = 0.0198$ ) ( $p = 0.0074$ ;  $p = 0.0318$ )

# Methoden om therapietrouw te monitoren

- **Directe methoden**
- **Indirecte methoden**

Methodie om therapietrouw te meten	voordelen	nadelen
vragenlijsten/patiëntenrapportages	eenvoudige en goedkope methode	resultaten zijn eenvoudig te manipuleren
patiëntendagboek	aanvullende inzichten bij therapieontrouw	resultaten zijn eenvoudig te manipuleren
tabletten tellen	objectieve methode, kwantificeerbaar en eenvoudig uit te voeren	resultaten zijn eenvoudig te manipuleren
aflevergegevens van openbare apotheek	objectieve en eenvoudig uit te voeren methode	aflevering betekent niet dat doseerschema wordt gevolgd, vereist een gesloten apotheekstelsel.
bepaling van klinische respons	eenvoudig uit te voeren methode	factoren anders dan therapieontrouw kunnen klinische respons beïnvloeden
meten van fysiologische parameters (bv. bloeddruk)	eenvoudig uit te voeren methode	factoren anders dan therapieontrouw kunnen parameter beïnvloeden
elektronische meet-systemen	precies, eenvoudig kwantificeerbaar en kan innamepatronen onderscheiden, direct interveniëren is mogelijk	relatief kostbare methode, vereist infrastructuur

## Indirecte methoden om therapieontrouw te monitoren

Van Onzenoort 2012.

<http://geneesmiddelenbulletin.com/artikel/therapieontrouw-2/>

Osterberg and Blaschke. Adherence to Medication. N Engl J Med. 2005;353:487-97.

# Zelfrapportage

## **‘Patients’ self-reports can simply and effectively measure adherence’\***

\* Osterberg and Blaschke. Adherence to Medication. N Engl J Med. 2005;353:487-97.

Walsh, Mandalia, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS. 2002;16:269-77.

Haynes, Taylor, Sackett, Gibson, Bernholz, Mukherjee. Can simple clinical measurements detect patient noncompliance? Hypertension. 1980;2:757-64.



# Disease-Modifying Therapies and Adherence in Multiple Sclerosis: Comparing Patient Self-Report with Pharmacy Records

Self reported missed DMT doses in the previous 30 days consecutive MS patients attending an (n = 1) MS clinic  
135 reported using an injectable DMT  
MPR < 80% defined non-adherence

**Non-adherence** estimated

13% self-reported

30% MPR year pre-clinic visit

43% MPR year post-clinic visit

**Moderate to fair agreement**

$\kappa = 0.41$ ; 95% CI 0.22-0.59 (pre-clinic visit)

$\kappa = 0.22$ ; 95% CI 0.09-0.36 (post-clinic visit)

# Subjective patient-reported versus objective adherence to subcutaneous interferon $\beta$ -1a in multiple sclerosis using RebiSmart<sup>®</sup>: the CORE study

## 53 patients: **objective vs. self-reported adherence**

Mean objective adherence was higher in self-reported adherent (**100%** [IQR 98.8-100%], n = 33) than in self-reported non-adherent patients (**93.4%** [77.2-97.5%], n = 20)





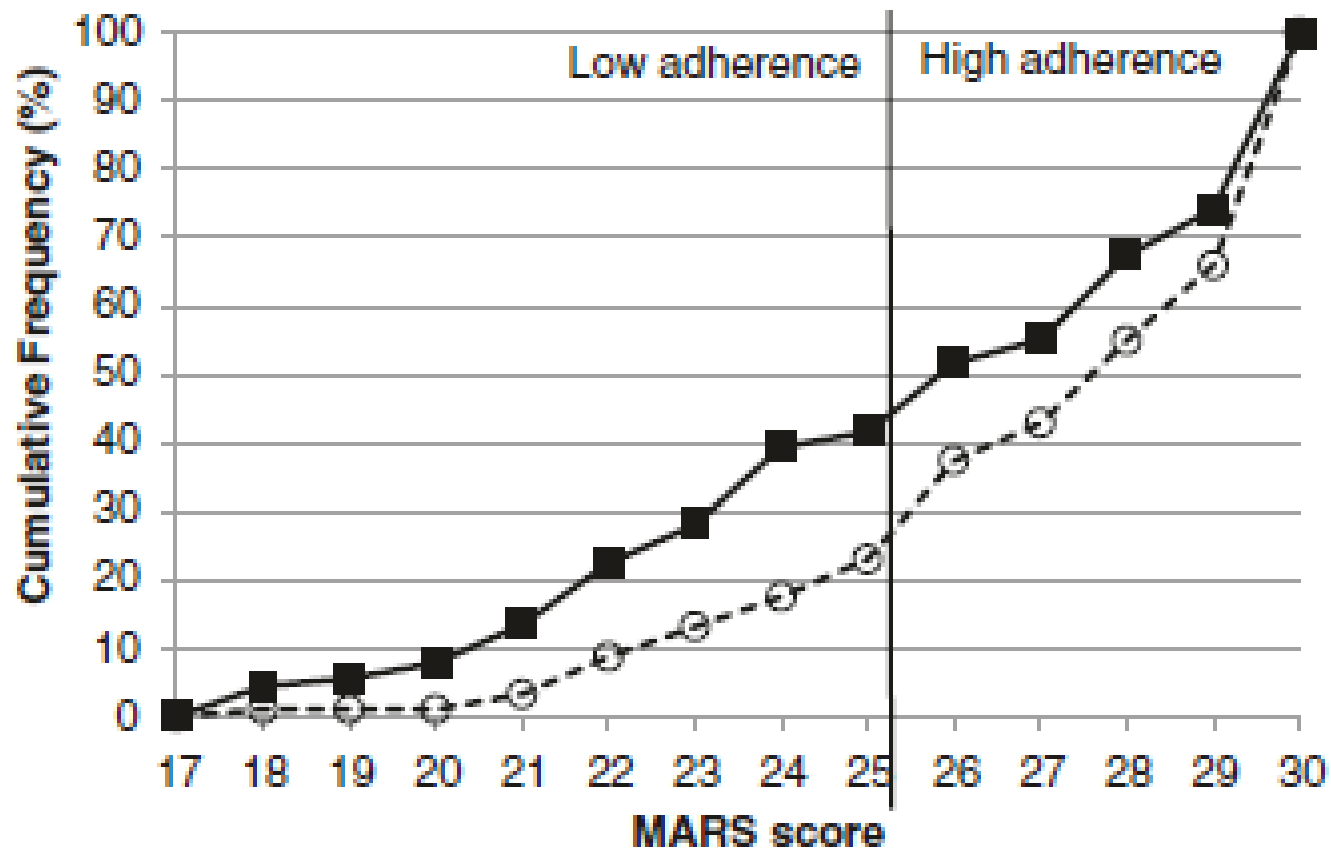
# Medication Adherence Report Scale (MARS)

**6 items** assessing **unintentional** (e.g. 'I forgot') and **intentional** (e.g. 'I decided to miss a dose') non-adherent behaviors

5-point Likert type scale

Higher scores indicating higher reported adherence

Dichotomization of scores: **Score  $\geq 26$  high adherer**  
**Score  $\leq 25$  low adherer**



**Fig 1** Showing vertical line of the dichotomous MARS. (Square = South Asian patients, circles = White British)

# Morisky Medication Adherence Scale (MMAS)

1. Do you sometimes forget to take your high blood pressure pills?
2. Over the past 2 weeks, were there any days when you did not take your high blood pressure medicine?
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?
4. When you travel or leave home, do you sometimes forget to bring along your medications?
5. Did you take your high blood pressure medicine yesterday?
6. When you feel like your blood pressure is under control, do you sometimes stop taking your medicine?
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your blood pressure treatment plan?
8. How often do you have difficulty remembering to take all your blood pressure medication?

Voorbeeld: toepassing bij antihypertensiva

Morisky et al. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. J Clin Hypertens. (Greenwich) 2008;10:348-54.

# What are validated self-report adherence scales really measuring?: a systematic review

**Thi-My-Uyen Nguyen, Adam La Caze & Neil Cottrell**

*Pharmacy Australia Centre of Excellence – School of Pharmacy, The University of Queensland,  
Woolloongabba, Queensland 4102, Australia*



# What are self-report scales measuring?

- 1) **Medication-taking behavior** and/or
- 2) **Barriers** to good medication-taking behavior or
- 3) **Beliefs** associated with adherence

Greater focus on measuring medication-taking behavior

To select the 'right' adherence scale(s) consider:

- **What needs to be measured?**
- **How (and in whom) the scale has been validated?**

# Coming full circle in the measurement of medication adherence: opportunities and implications for health care

Elizabeth Whalley Buono<sup>1</sup>

Bernard Vrijens<sup>2</sup>

Hayden B Bosworth<sup>3</sup>

Larry Z Liu<sup>4</sup>

Leah L Zullig<sup>5,6</sup>

Bradi B Granger<sup>7,8</sup>

## ... measurement of medication adherence ...

Most robust medication adherence measures are often **ill suited for large-scale use**

Less robust measures were commonly **misapplied**

**Adherence assessment and measurement were rarely integrated into standard patient care practice patterns**

Successful strategies to improve medication adherence will depend on **how to efficiently and effectively measure adherence**

# Monitoring medication adherence in multiple sclerosis using a novel web-based tool: A pilot study

**MS HAT:** internet-based module for *self-management, communication and education*

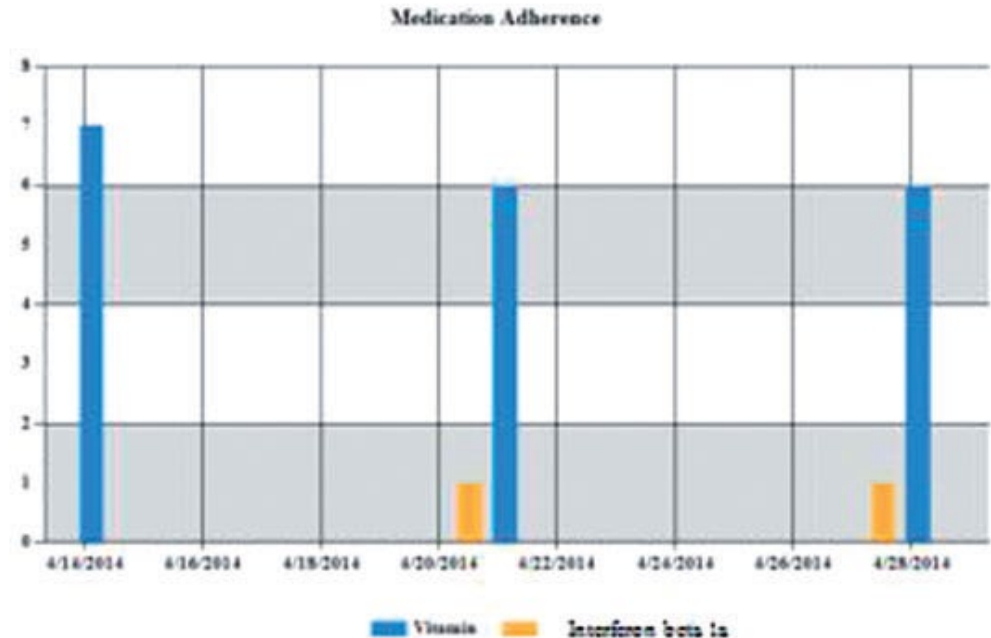
N = 30; randomized to **MS Home Automated Telehealth (MS HAT)** or routine care; weekly IM INFb-1a; 6 months

- Adherence
- Self-reported
  - Diaries
  - Pharmacy refill rates
  - Blood serum levels
  - MS HATalerts

**IM INFb-1a adherence highly correlated across measures**



Start Date: 04/14/2014    End Date: 04/28/2014



Patients with more preserved **cognitive function** appeared to benefit more from use of the MS HAT system



# MSmonitor

The interactive web-based program MSmonitor for self-management and multidisciplinary care in multiple sclerosis: concept, content, and pilot results

Jongen PJ, Sinnige LG, van Geel BM, et al. The interactive web-based program MSmonitor for self-management and multidisciplinary care in multiple sclerosis: concept, content, and pilot results. *Patient Prefer Adherence*. 2015;9:1741-50.

The interactive web-based program MSmonitor for self-management and multidisciplinary care in multiple sclerosis: utilization and valuation by patients

Jongen PJ, Sinnige LG, van Geel BM, et al. The interactive web-based program MSmonitor for self-management and multidisciplinary care in multiple sclerosis: utilization and valuation by patients. *Patient Prefer Adherence*. 2016;10:243-50.

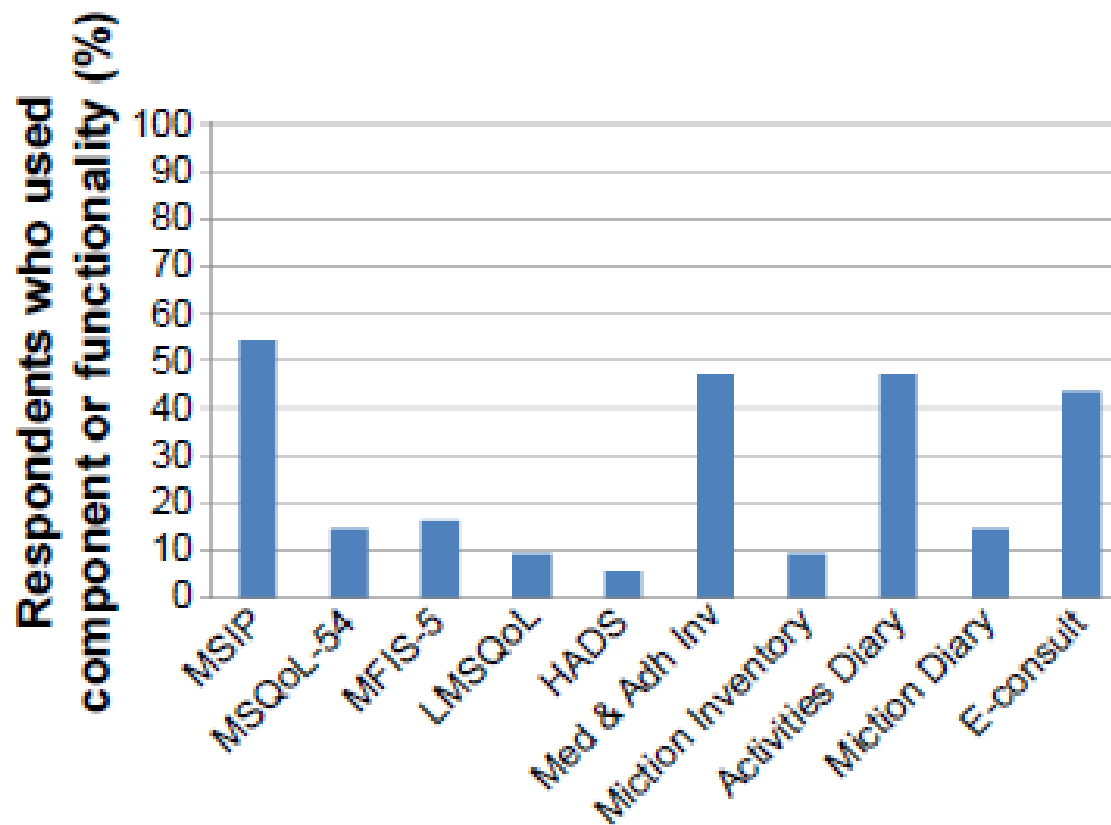


Figure 1 The percentages of respondents who used a specific component or functionality.

Abbreviations: e-consult, electronic consultation; HADS, Hospital Anxiety and Depression Scale; LMSQoL, Leeds Multiple Sclerosis Quality of Life; Med & Adh Inv, Medication and Adherence Inventory; MFIS-5, Modified Fatigue Impact Scale-5 Item Version; MSIP, Multiple Sclerosis Impact Profile; MSQoL-54, Multiple Sclerosis Quality of Life-54.

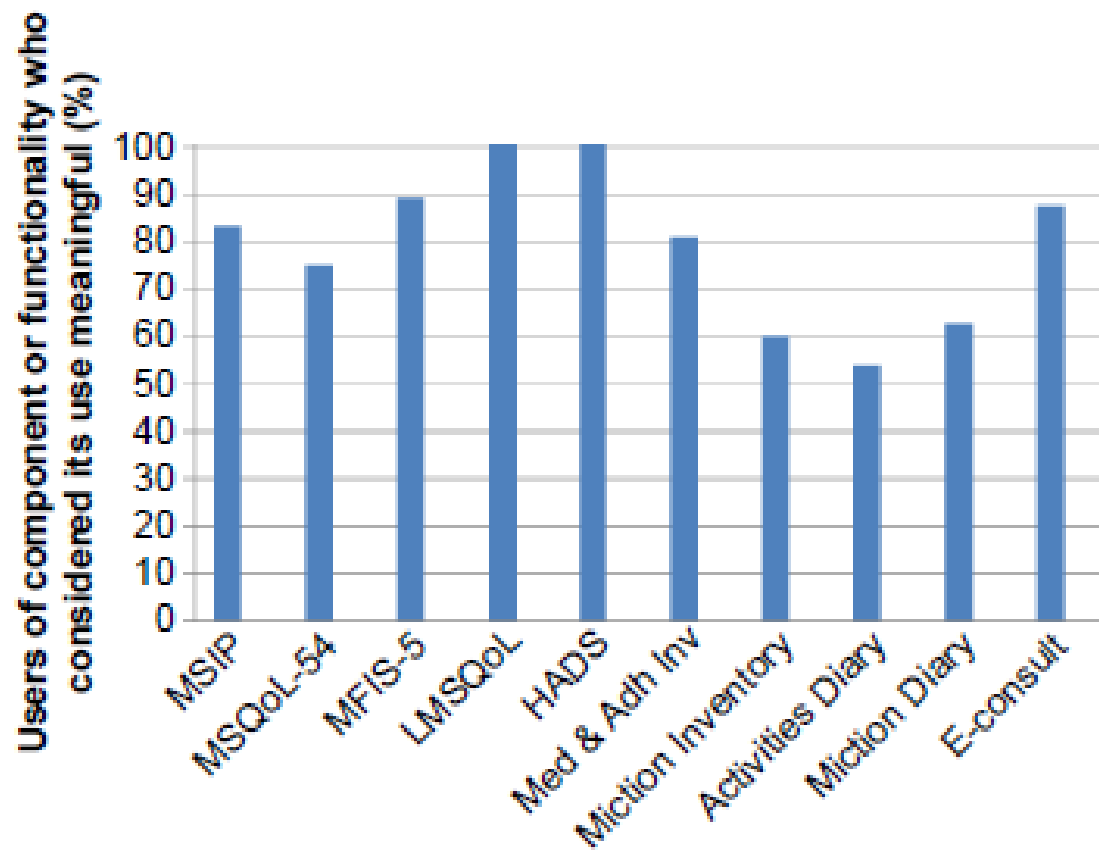


Figure 2 The percentages of users of a component or functionality who considered its use meaningful.

**Abbreviations:** e-consult, electronic consultation; HADS, Hospital Anxiety and Depression Scale; LMSQoL, Leeds Multiple Sclerosis Quality of Life; Med & Adh Inv, Medication and Adherence Inventory; MFIS-5, Modified Fatigue Impact Scale-5 Item Version; MSIP, Multiple Sclerosis Impact Profile; MSQoL-54, Multiple Sclerosis Quality of Life-54.



## NEUROLOGIE

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**drs. Okke Sinnige**

neuroloog, afdeling Neurologie Medisch Centrum Leeuwarden, Leeuwarden

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MS-PATIËNTEN REGISTREREN ONLINE GEGEVENS OVER HUN ZIEKTE

# MSmonitor blijkt zinvolle e-healthtoepassing

Bij de zorg voor multiple sclerose zijn veel disciplines betrokken. Met het onlineprogramma MSmonitor kunnen patiënten zelf ontwikkelingen vastleggen en daar doen veel zorgverleners hun voordeel mee.

The logo for MEDISCH CONTACT, featuring the words "MEDISCH" and "CONTACT" stacked vertically in a white, serif font, set against a solid blue rectangular background.

## **6. Interventies om therapietrouw te bevorderen**

Published Online: 20 NOV 2014



Cochrane Database of Systematic Reviews

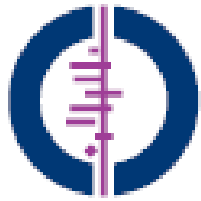
## Interventions for enhancing medication adherence (Review)

Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C, Haynes RB

Effects were **inconsistent** from study to study

Only a minority of lowest risk of bias RCTs improved both **adherence and clinical outcomes**

Current methods of improving medication adherence for chronic health problems are mostly **complex and not very effective**, so that the full benefits of treatment cannot be realized



**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

**7 September 2011**

## **Reminder packaging for improving adherence to self-administered long-term medications (Review)**

Mahtani KR, Heneghan CJ, Glasziou PP, Perera R

Effectief bij: - hypertensie (2 studies): bloeddrukdaling  
- diabetes (2 studies): daling HbA1c

### TABEL 1 Belangrijke voorspellers van therapieontrouw<sup>3</sup>

psychische problemen, met name depressie  
verminderd cognitief functioneren  
asymptomatische ziekte  
onvoldoende follow-up  
bijwerkingen van medicatie  
patiënt heeft onvoldoende geloof in het voordeel van de behandeling  
patiënt heeft onvoldoende inzicht in zijn of haar ziekte  
slechte arts-patiëntrelatie  
niet verschijnen op afspraken  
complexiteit en duur van behandeling

**Table 3. Strategies for Improving Adherence to a Medication Regimen.\***

Identify poor adherence

Look for markers of nonadherence: missed appointments (“no-shows”), lack of response to medication, missed refills

Ask about barriers to adherence without being confrontational

Emphasize the value of the regimen and the effect of adherence

Elicit patient’s feelings about his or her ability to follow the regimen, and if necessary, design supports to promote adherence

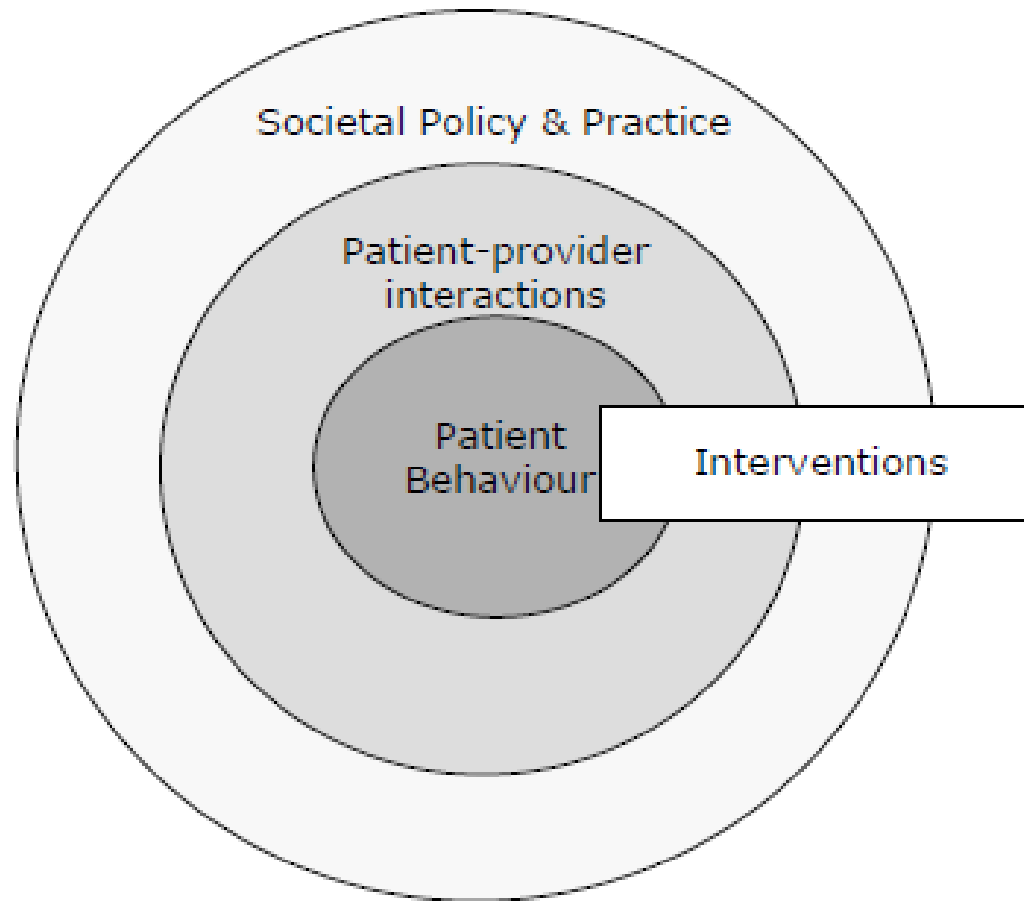
Provide simple, clear instructions and simplify the regimen as much as possible

**Table 3. Strategies for Improving Adherence to a Medication Regimen.\***

- Encourage the use of a medication-taking system
- Listen to the patient, and customize the regimen in accordance with the patient's wishes
- Obtain the help from family members, friends, and community services when needed
- Reinforce desirable behavior and results when appropriate
- Consider more “forgiving” medications when adherence appears unlikely†
  - Medications with long half-lives
  - Depot (extended-release) medications
  - Transdermal medications

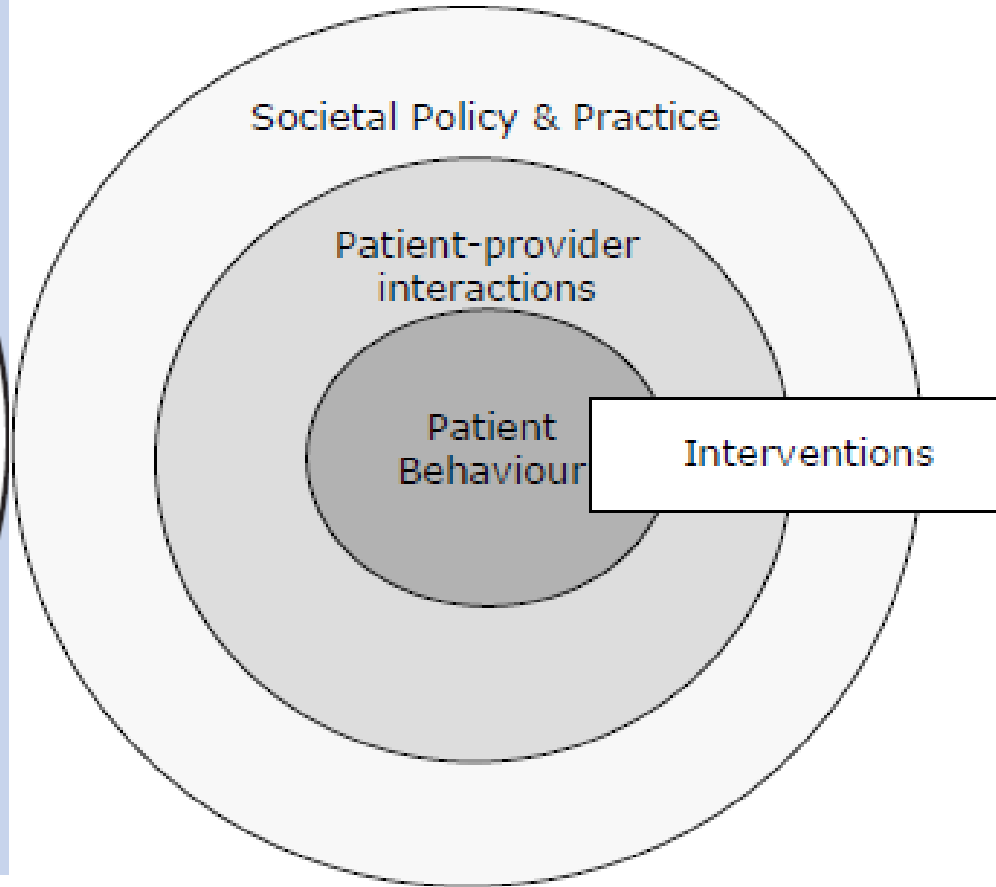
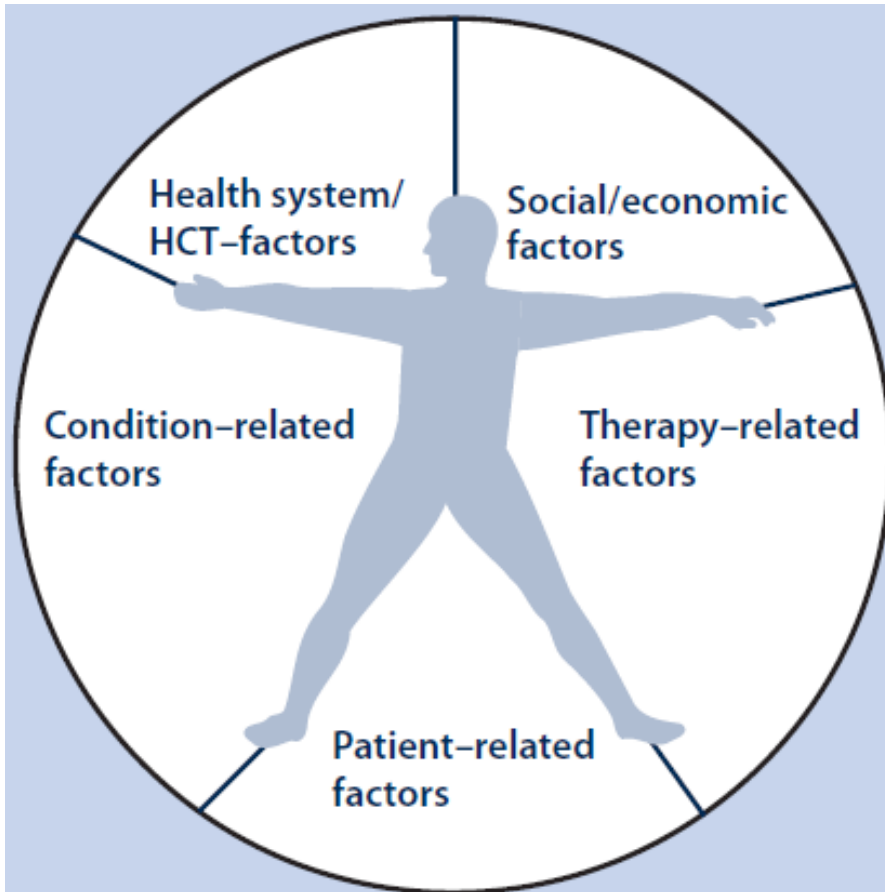
\* Information in this table was adapted from Osterberg and Rudd.<sup>83</sup>

† Forgiving medications are drugs whose efficacy will not be affected by delayed or missed doses.



Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking. London: National Co-ordinating Centre for NHS Service Delivery and Organisation (NCCSDO), 2005  
[http://www.netscc.ac.uk/hsdr/files/project/SDO\\_FR\\_08-1412-076\\_V01.pdf](http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf)





WHO. Adherence to Long-Term Therapies: Evidence for Action. 2003  
Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking. London: National Co-ordinating Centre for NHS Service Delivery and Organisation (NCCSDO), 2005  
[http://www.netscc.ac.uk/hsdr/files/project/SDO\\_FR\\_08-1412-076\\_V01.pdf](http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf)

# **7. Interventies om therapietrouw te bevorderen**

**- Patiënt**

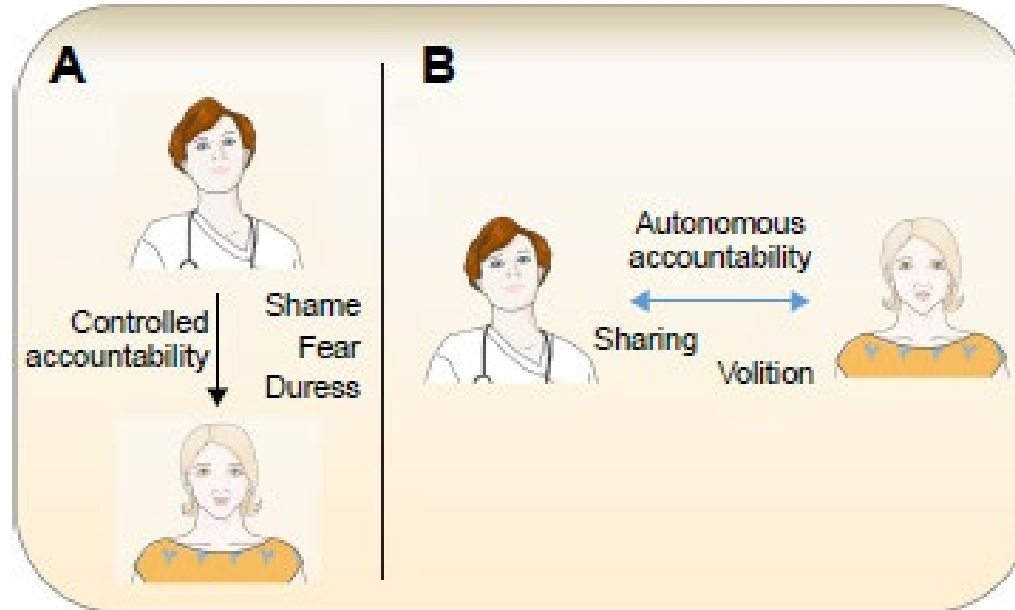
# Patients' conceptions of their own influence on good treatment response: Self-Awareness

Interviews with 25 patients on biological therapy in chronic inflammatory arthritis (low disease activity or in remission)

**Patients conceived that they had a responsibility for adhering** to the treatment as well as achieving balance in life in order to ensure good treatment response.

**Self-awareness was essential for maintaining a good treatment response**, and this reflected the patients' awareness of the complexity of living their lives with a chronic illness.

# Accountability: a missing construct in models of adherence behavior and in clinical practice



Piano lessons and out-patient visits have in common an accountability that encourages people to follow a course of action

The concept '**accountability**' is not found in adherence models and is rarely employed in medical practice

# Belief about Medicines Questionnaire (BMQ)

Deel 1: **geloof in het belang** van geneesmiddelen

Deel 2: **bezorgdheid** over geneesmiddelengebruik  
(bv. bijwerkingen)

Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res.* 1999;47:555-67.

Horne R, Weinman J, Hankins. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Journal Psychology & Health.* 19:14:1-24.

# Treatment Satisfaction Questionnaire for Medication (TSQM)

MULTIPLE  
SCLEROSIS  
JOURNAL

MSJ

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*Original Research Paper*

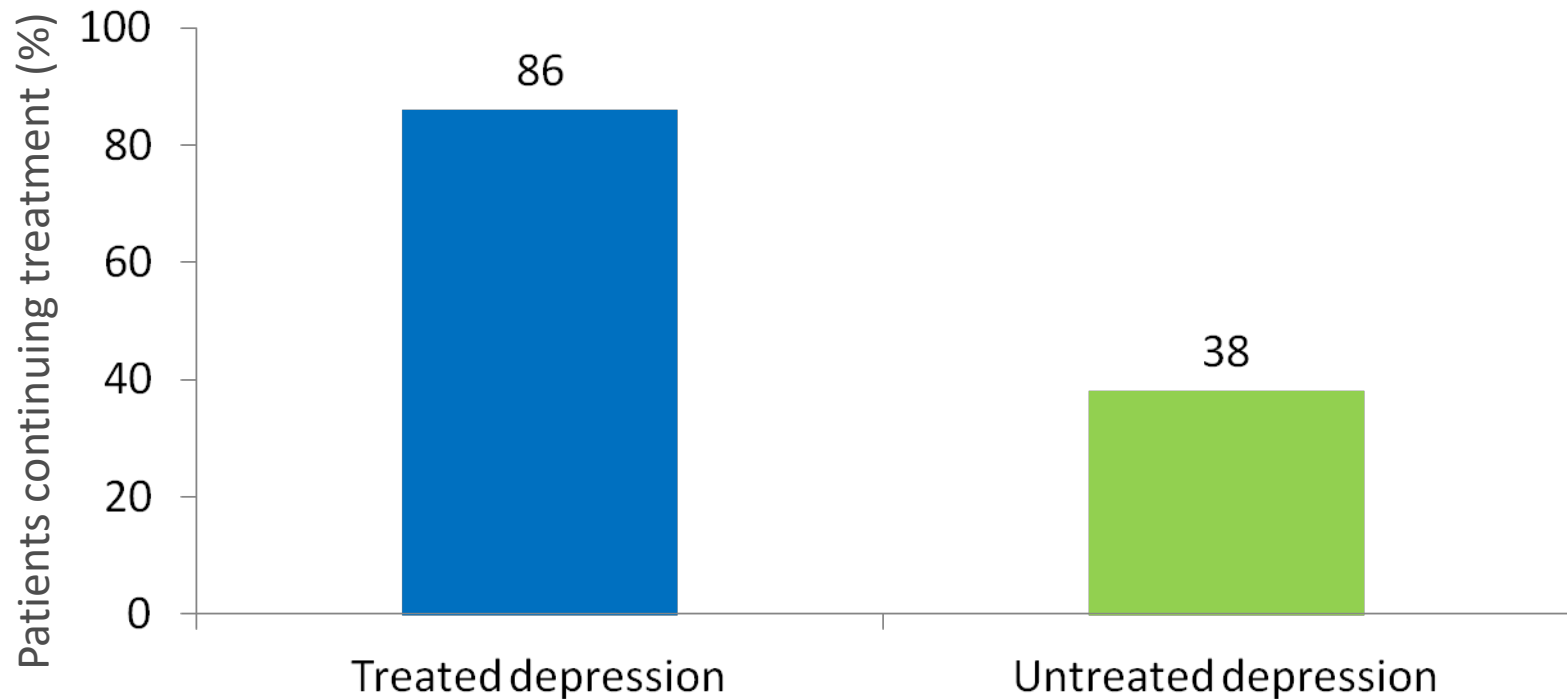
## Measuring treatment satisfaction in MS: Is the Treatment Satisfaction Questionnaire for Medication fit for purpose?

**YES**

**Conclusion:** This investigation found the TSQM to be a useful tool, exhibiting good psychometric measurement properties in patients with relapsing MS in the TENERE study.

# Treatment of depression: higher persistence

Psychotherapy and/or antidepressants  
85 relapsing MS patients on IFNB-1b, 6 month of follow-up



## **7. Interventies om therapietrouw te bevorderen**

**-Interactie patiënt-zorgverlener**

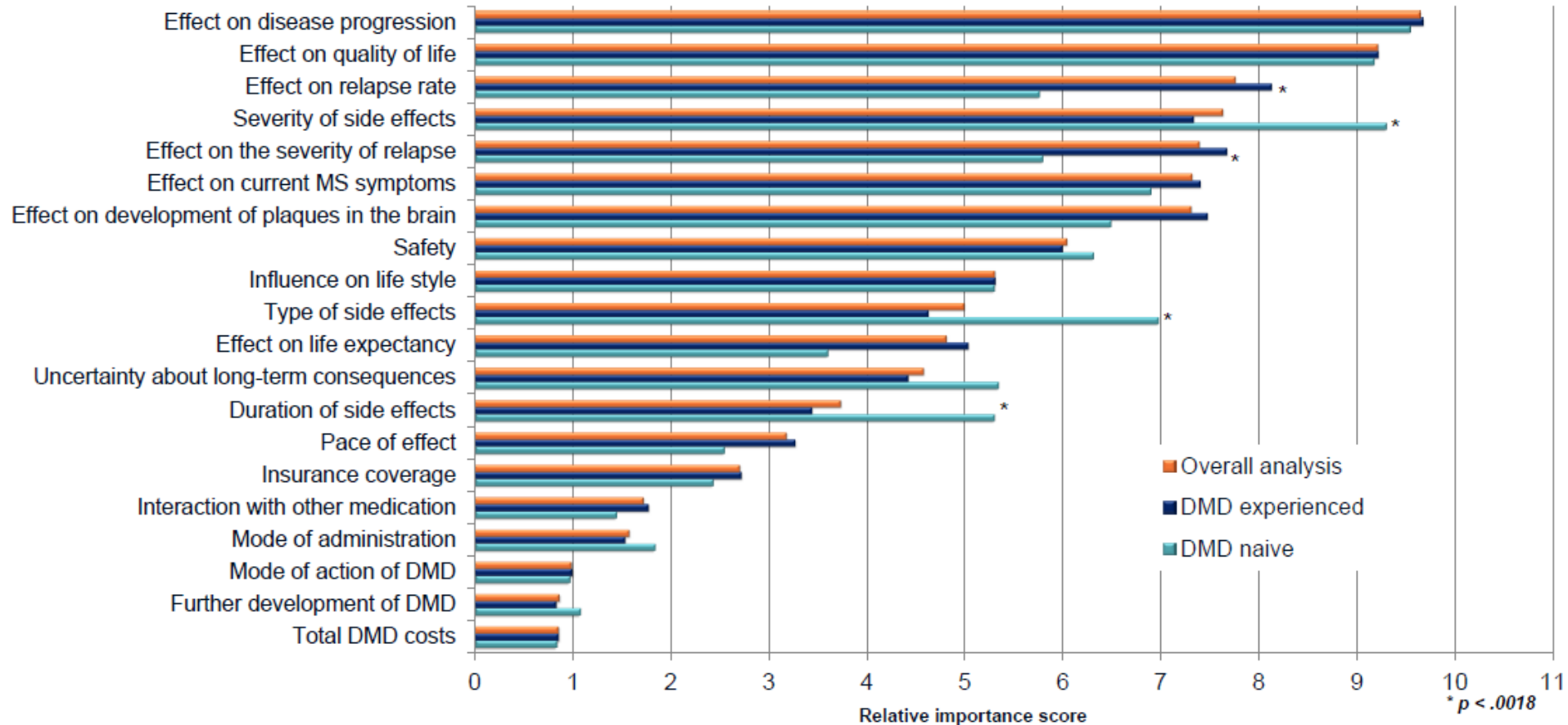


## WHO and NICE

The guidelines developed by the World Health Organization and National Institute for Clinical Excellence (NICE) recommend that **health care professionals explore patient's beliefs, concerns and attitudes toward medication** as these are considered the most important drivers of non-adherence among chronic disease patients

# Shared decision making – patients' preferences

Attributes' relative importance score: Overall analysis vs. DMD naive patients (n=27) vs. DMD experienced patients (n=157)



\*DMD = disease modifying drug

# Overwegingen ter preventie van niet-intentionele therapieontrouw

Is de behandeling **haalbaar**?

Past de behandeling bij **dagelijkse routine** van patiënt?

Past de behandeling bij diens **verwachtingen en voorkeuren**?

# Overwegingen ter preventie van intentionele therapieontrouw

Bij chronische behandeling de **afweging** tussen **noodzaak** om het geneesmiddel te gebruiken en **zorgen** om mogelijke bijwerkingen (bv. door de bijsluiter, social media) en nadelige effecten van de behandeling

# “My patients are better than yours”: optimistic bias about patients’ medication adherence by European health care professionals

Cross-sectional online survey of physicians (855), nurses (1,294), and pharmacists (1,047) in 10 European countries

**Health care professionals (HCP) perceived their own patients to be more likely to initiate and more likely to persist with treatment than other patients**

... reported significantly lower prevalence of adherence for their own patients than for patients in general

**Optimistic bias** by HCPs about their patients’ behavior

# Taking Our Medicine — Improving Adherence in the Accountability Era

Lisa Rosenbaum, M.D., and William H. Shrank, M.D.

At the heart of this problem lie essential questions about **human motivation** and **physician hood**

... the multi-factorial nature of non-adherence ... makes **solutions at the individual and practice levels** most promising

# Could Physician Use of Realistic Previews Increase Treatment Adherence and Patient Satisfaction?

... businesses face challenges in minimizing employee turnover

One of the best methods for increasing employee retention and job satisfaction is to provide a **realistic preview** of what the job will be like, especially if that description **includes unpleasant aspects** of the job

... suggest that the best way **to encourage behavior maintenance** is to acknowledge fully and clearly the challenges that patients will face

Focella ES, Zikmund-Fisher BJ, Shaffer VA. Could Physician Use of Realistic Previews Increase Treatment Adherence and Patient Satisfaction? *Med Decis Making*. 2016;36:683-5.

Phillips JM. Effects of realistic job previews on multiple organizational outcomes: a meta-analysis. *Acad Manage J*. 1998;41:673-90.

# Treatment adherence in multiple sclerosis: a survey of Belgian neurologists

Survey among 41 neurologists

mean time spent on the **treatment-adherence discussion during the initial consultation 11 minutes**

**24%** of doctors spending **5 minutes**

**24%** of doctors spending **10 minutes** discussing this issue

**56%** perceived the adherence level as good

**12%** perceived it as excellent



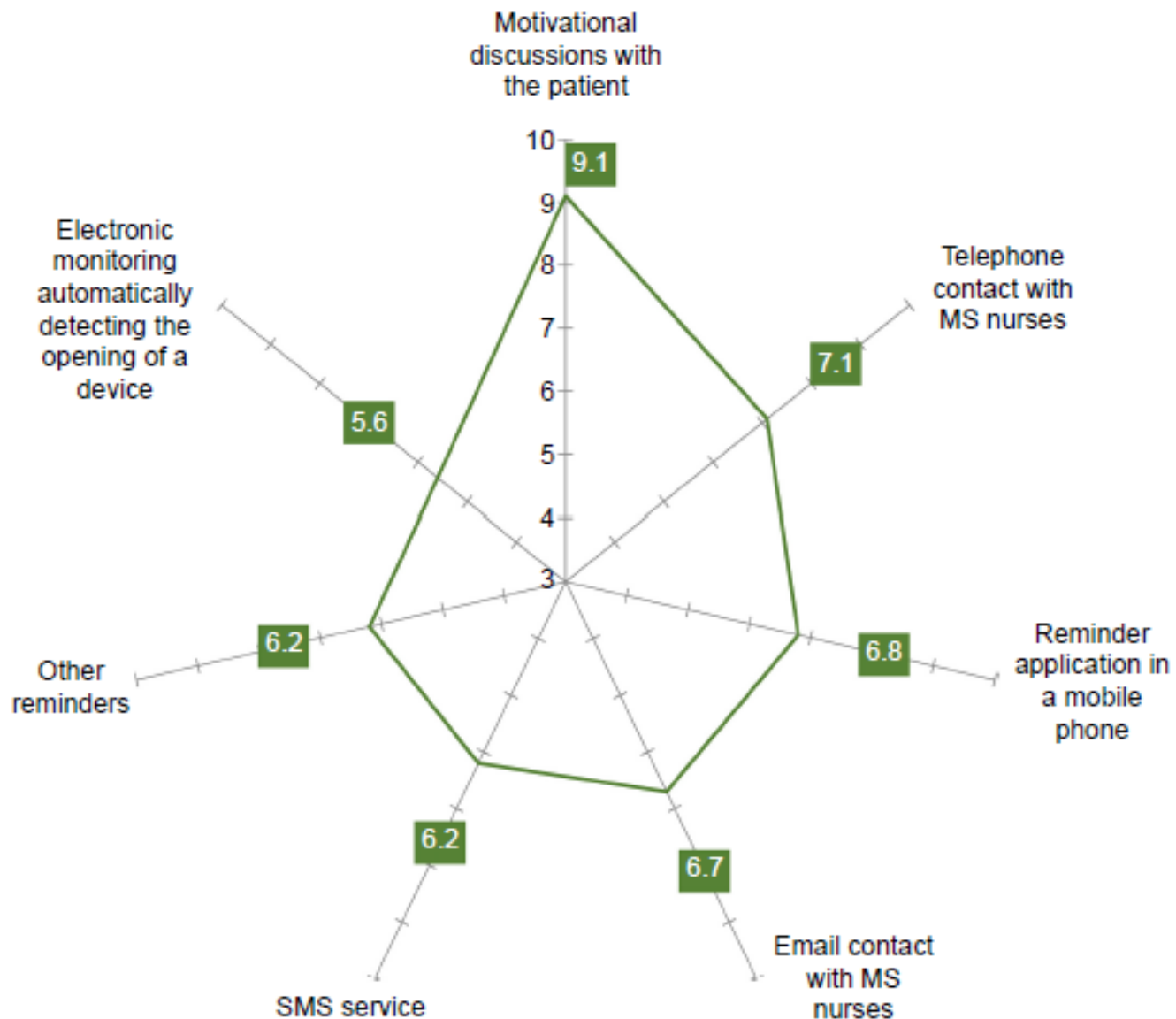
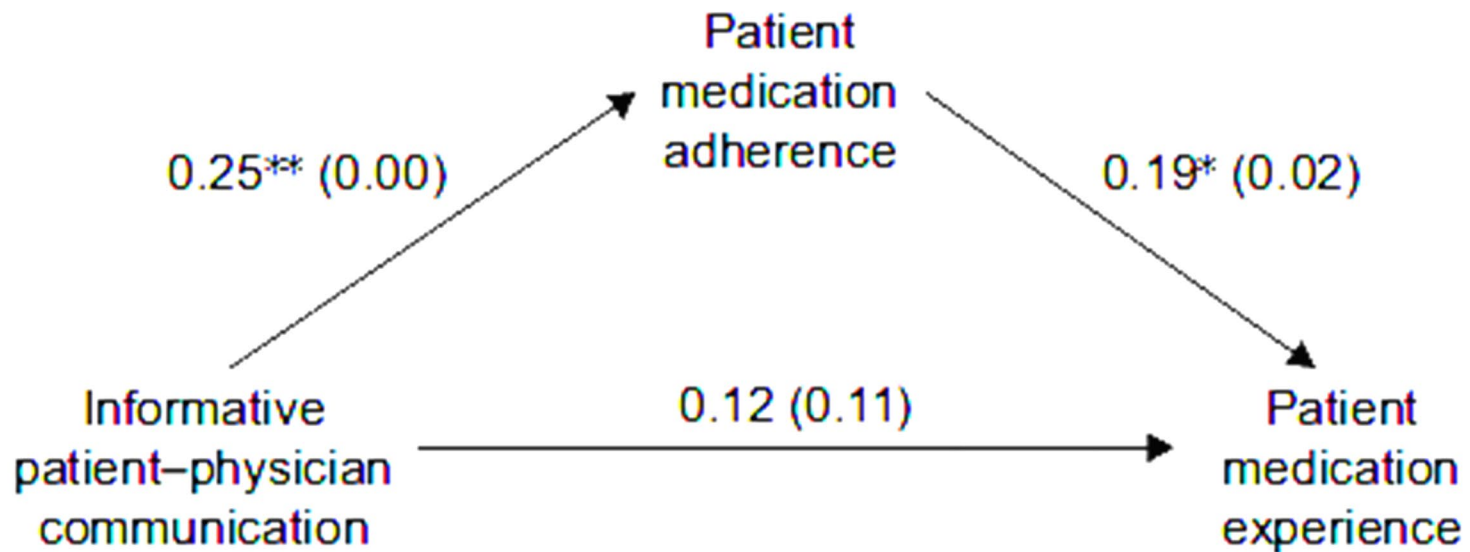


Figure 1 Level of motivational value of potential supports/tools improving patient adherence to multiple sclerosis (MS) treatment.

Notes: Neurologists assessed the extent to which potential tools/supports can improve treatment adherence on a scale of 1–10, where 1= “cannot improve adherence” and 10= “can improve adherence”.



**Figure 1** Mediation effect of patient medication adherence between informative patient-physician communication and patient medication experience.

**Notes:** \* $P < 0.05$ , \*\* $P < 0.001$ . Values before parentheses are standardized beta coefficients and values within parentheses represent  $P$ -values.

# Satisfaction with Information about Medicines Scale (SIMS)

The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research

R Horne, M Hankins, R Jenkins

17-item tool to assess the extent to which patients feel they have received enough information about prescribed medicines.

## **7. Interventies om therapietrouw te bevorderen**

- Medische praktijk en maatschappij**

# Assessing the role of patient support services on adherence rates in patients using glatiramer acetate for relapsing-remitting multiple sclerosis

5,825 RRMS patients taking GA (Copaxone®)

## **Sponsor-provided support:**

70% received manufacturer-provided injection training

75% utilized copayment assistance

**74%** accessing sponsor-provided support had **MPR  $\geq$  80%**

**MPR  $\geq$  80% was 40% more likely if injection training was provided by manufacturer (OR 1.44; 95% CI 1.26-1.64)**

## Hawthorne effect ('observer effect')

“Hawthorne effect (or observer effect) is a type of reactivity in which individuals **modify an aspect of their behavior in response to their awareness of being observed**”

Verklaart deels de hoge therapietrouw in klinische studies

# Telephone Counseling and Home Telehealth Monitoring to Improve Medication Adherence: Results of a Pilot Trial Among Individuals With Multiple Sclerosis

- **Brief telephone counseling (3 sessions; motivational)**
- **Home Telehealth Monitoring (customized text messages)**

Monitors provided reminder alarms:

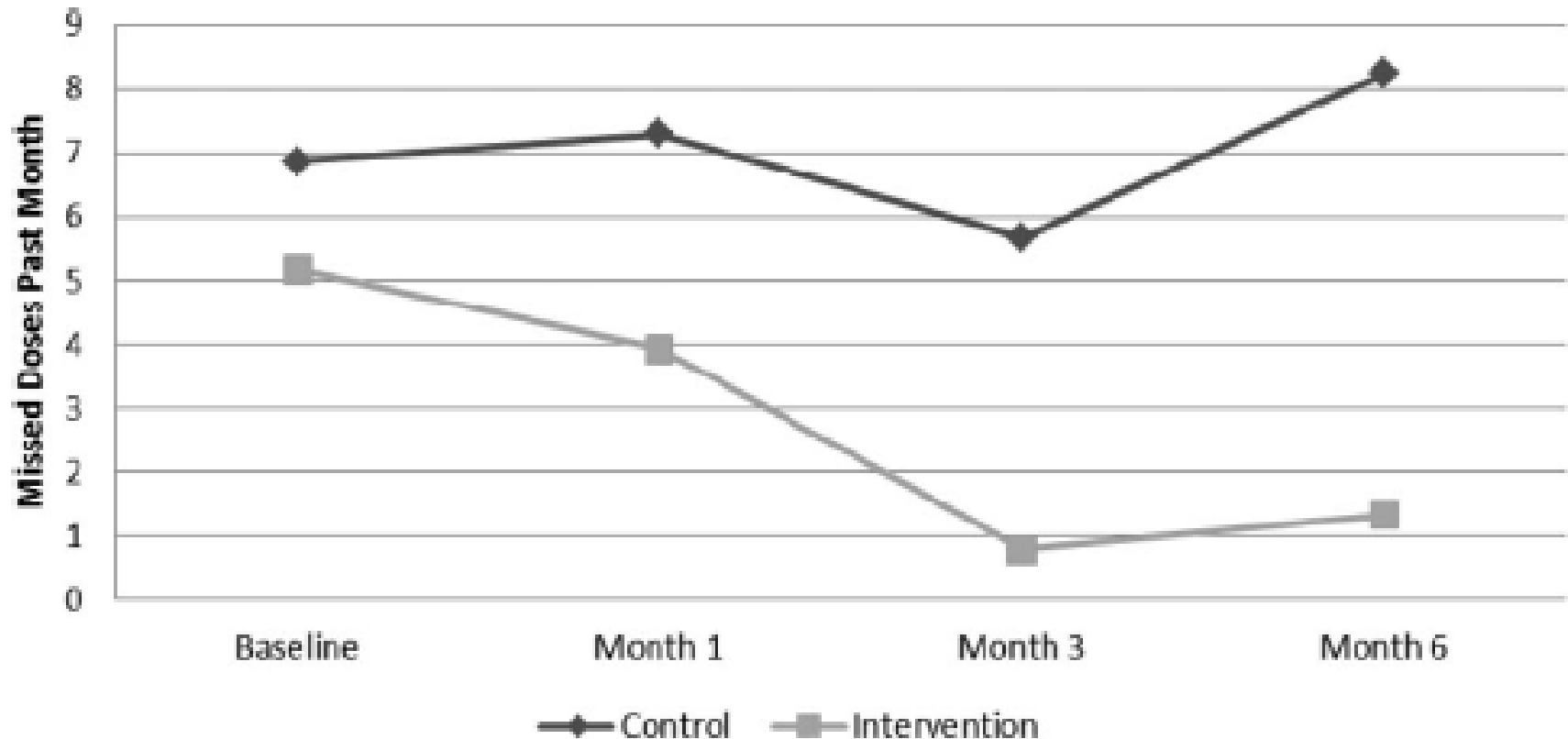
Q: “Did you take your DMT dose as prescribed?”

If ‘yes’ , then encouraging statements

6-months RC pilot trial: 19 patients using DMT  
**missing doses 1.3 (2.1) vs. 8.2 (12.3) in past month**

**90% of patients rated the program as highly successful**

# Telephone Counseling and Home Telehealth Monitoring to Improve Medication Adherence: Results of a Pilot Trial Among Individuals With Multiple Sclerosis



Turner AP, Sloan AP, Kivlahan DR, Haselkorn JK. Telephone counseling and home telehealth monitoring to improve medication adherence: results of a pilot trial among individuals with multiple sclerosis. *Rehabil Psychol.* 2014;59:136-46.



# Predicting medication adherence in multiple sclerosis using telephone-based home monitoring

1-item, via telephone, measure of **adherence expectations**

Q1: *“How confident are you that you will be taking your prescribed DMT one month from now?”* [Note: self-efficacy!]

1-item, via telephone, measure of **adherence**

Q2: *“People often have difficulty taking their medications for one reason or another. How many times have you missed taking your DMT in the past month?”*

89 MS patients; monthly telephone interviews for 6 months

**Adherence expectations predicted adherence** after adjusting for demographic, illness related, and psychosocial factors

# How many injections did you miss last month? A simple question to predict interferon $\beta$ -1a adherence in multiple sclerosis

N = 114      treatment with SC IFNb-1a for  $\geq 6$  months before inclusion  
treatment duration:  $2.94 \pm 3.32$  years; follow-up  $1.55 \pm 0.96$  years

## Electronic auto-injector with real-time recording of adherence

fully adherent:    no doses missed

early missing:    missing 1<sup>st</sup> dose during 1<sup>st</sup> month of observation

late missing:     missing the 1<sup>st</sup> dose later

## Adherence lower in ‘early missing’ than in ‘late missing’

‘Early missing’: fourfold chance of having a relapse

# Farmacologische maatregelen om therapietrouw te verbeteren

**Doseerschema:** hoe eenvoudiger des te beter

Osterberg and Blaschke. Adherence to Medication. N Engl J Med. 2005;353:487-97.

**Verpakkingen:** geneesmiddelenpotten, weekdozen, verpakkingen voor eenmalig gebruik, evt. met onderscheid in dag, dagdeel en tijdstip

Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. Cochrane Database Syst Rev. 2011: CD005025.

# Nadeel van betere therapietrouw

Betere therapietrouw: meer kans op dosisgerelateerde bijwerkingen

## **7. Praktijk en perspectief**

## **7. Praktijk en perspectief**

### **- Praktijk**

### Trefwoorden

- Therapietrouw
- Multiple Sclerose (MS)
- Eerstelijnsinjectiebehandeling
- Onderzoek
- Delphi-methode

# Consensus over beïnvloeden therapietrouw bij MS

Professionals in de MS-zorg krijgen vaak veel en diverse informatie. Daarnaast blijken de adviezen die ze aan hun patiënten geven ook niet altijd eenduidig. De **digitale Delphi-methode** hielp consensus te bereiken over de factoren die de therapietrouw van MS-patiënten beïnvloeden, als **het gaat om de eerstelijnsbehandeling met injecties.**

# 2015

## Richtlijn therapietrouw eerstelijns injectiebehandelingen multiple sclerose



2016 CMSC Annual Meeting

June 1 - 4

Gaylord National Resort & Convention Center  
National Harbor, Maryland

[www.msca.org/2016](http://www.msca.org/2016)

A.E.J. Slettenaar<sup>a</sup>, M.C.M.Booy<sup>b</sup>, L. Trommelen<sup>c</sup>, T. Kempkens<sup>d</sup>, K.Harrison<sup>e</sup>, N.J.M. Arts<sup>f</sup>, A. Baars<sup>g</sup>, L.H. Visser<sup>o,h</sup>

<sup>a</sup>Medisch Spectrum Twente – Enschede, <sup>b</sup>Amphia Ziekenhuis – Breda, <sup>c</sup>TweeSteden Ziekenhuis – Tilburg/Waalwijk, <sup>d</sup>Zuyderland Ziekenhuis – Sittard,

<sup>e</sup>Tergooi – Blaricum, <sup>f</sup>Winkler Kliniek, Pro Persona – Wolfheze, <sup>g</sup>Ziekenhuis Rijnstate – Arnhem, <sup>h</sup>St. Elisabeth Ziekenhuis – Tilburg



# Dutch Guideline Adherence First-Line Injection Therapy MS

1. Regular visits
2. Identify if **flu-like symptoms, injection-site reactions, fatigue, depression, (injection) anxiety or cognitive dysfunction** have an effect on adherence
3. Ask **open questions** without reproachful undertone
4. Use instruments, e.g. **MMAS**
5. Use additional instruments: **HADS, MFIS, Cognitive Failure Questionnaire**

A.E.J. Slettenaar<sup>a</sup>, M.C.M.Booy<sup>b</sup>, L. Trommelen<sup>c</sup>, T. Kempkens<sup>d</sup>, K.Harrison<sup>e</sup>, N.J.M. Arts<sup>f</sup>, A. Baars<sup>g</sup>, L.H. Visser<sup>o,h</sup>

<sup>a</sup>Medisch Spectrum Twente – Enschede, <sup>b</sup>Amphia Ziekenhuis – Breda, <sup>c</sup>TweeSteden Ziekenhuis – Tilburg/Waalwijk, <sup>d</sup>Zuyderland Ziekenhuis – Sittard,

<sup>e</sup>Tergooi – Blaricum, <sup>f</sup>Winkler Kliniek, Pro Persona – Wolfheze, <sup>g</sup>Ziekenhuis Rijnstate – Arnhem, <sup>h</sup>St. Elisabeth Ziekenhuis – Tilburg

# Voorstel: 12-puntenplan Therapietrouw Ziektemodificerende behandeling MS

1. Screen op psychologische problemen
2. Screen op depressie
3. Screen op cognitieve problemen
4. Zorg voor adequate follow-up
5. Informeer over, voorkom en behandel bijwerkingen
6. Screen op geloof van patiënt in behandeling
7. Let op ziekte-inzicht
8. Zorg voor goede arts-patiëntrelatie
9. Let op logistieke of andere drempels
10. Let op gemiste afspraken
11. Voorkom zo veel mogelijk complexe behandeling
12. Let op financiële aspecten (medicatie, vervoer)

# Recommendations for a Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)

## Recommendation

If only **5 min** available use Symbol Digit Modalities Test (**SDMT**) to assess attention and processing speed

If **additional 10 min** available also use California Verbal Learning Test-II (**CVLT-II**), first five recall trials, to assess verbal memory - immediate recall  
Brief Visuospatial Memory Test-revised (**BVLT-r**), first three recall trials, to assess visual memory – immediate recall

# SDMT

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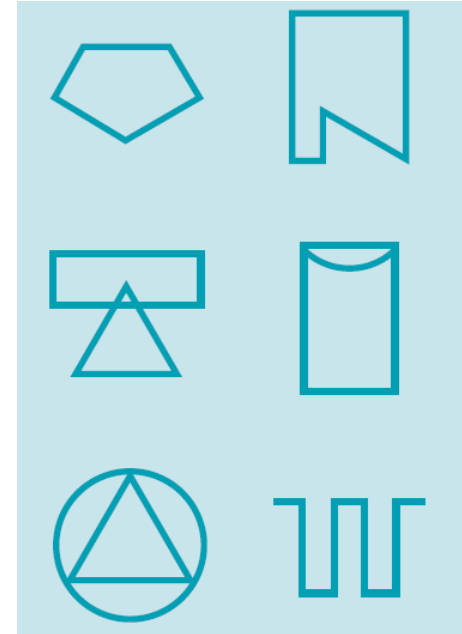
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# BICAMS tests

## CVLT-II

- Carrot
- Sweater
- Hammer
- Baseball
- Football
- Chisel
- Pants
- Beans
- Shoes
- Screwdriver
- Basketball
- Corn
- Saw
- Golf
- Dress
- Lettuce

## BVMT-R



# 12-puntenplan Therapietrouw

## Item

## 'Instrument'

1. Psychologische aspecten

Gesprek, MSSES

2. Depressie, angst

HADS

3. Cognitieve problemen

Cognitive Failure Quest  
SDMT, BICAMS

4. Follow-up

Organisatie

5. Bijwerkingen

Gesprek, TSQM

6. Geloof van patiënt in behandeling

BMQ

7. Ziekte-inzicht

Gesprek

8. Arts-patiëntrelatie

!

9. Logistieke of andere drempels

Gesprek

10. Gemiste afspraken

Organisatie

11. Eenvoudig mogelijke behandeling

Kennis

12. Financiële aspecten

Gesprek

# 12-puntenplan Therapietrouw

## Instrumenten

Kennis

Gesprek met patiënt

Vragenlijsten

Organisatie

## 'Randvoorwaarden'

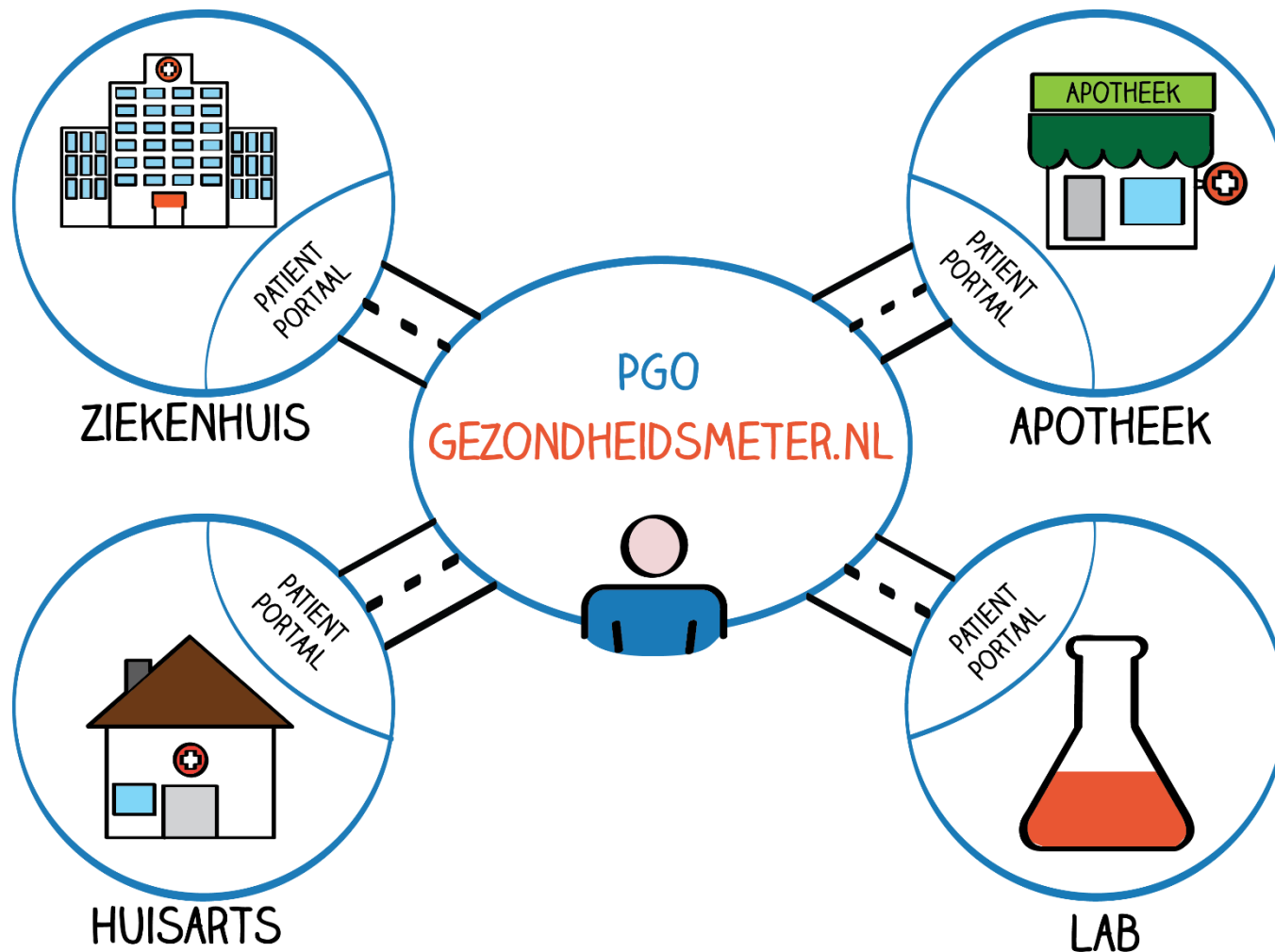
Scholing

Arts-patiëntrelatie  
Tijd

Online platform

MS-verpleegkundige  
Cognitieve testen

# Online Screenen, Monitoren en Zelfrapportage



# Online Screenen, Monitoren en Zelfrapportage

**MS monitor**  
Mijn persoonlijk dossier online

HOME PATIËNT PROFESSIONAL MIJN ZIEKENHUIS PUBLICATIES NIEUWS LINKS MEER DOSSIERS

**Ik ben zorgverlener**  
Meer weten...

**Ik heb MS**  
Nieuwsgierig...

**Direct inloggen**  
U heeft al een account.

Gebruikersnaam:

Wachtwoord:

**Inloggen**  
[Inloggegevens kwijt? Klik hier](#)

**Zorgverlener:**  
Meld patiënt aan

**Patiënt:**  
Ik meld mij aan

**APP's**  
Snel inloggen met 5 cijfers?  
Voor tablet en smartphone

Download on the App Store

**Beschikbaar**

- Adherentielijst
- HADS
- MFIS-5
- MSSSES



## **7. Praktijk en perspectief**

### **- Perspectief**

# Focus of future research

1. Efficacy of interventions on **long-term adherence/persistence**
2. **Role of (in)formal caregivers**
3. **Improve health literacy**
4. Methods to **monitoring adherence**
5. **New interventions** to improve adherence
6. **Implementation** of research studies in clinical practice
7. **Integrated care in relation to cost-effectiveness**

# Belang therapietrouw in de praktijk

*“Increasing the effectiveness of adherence interventions might have a far greater impact on the health of the population than any improvement in specific medical treatments”*

# Disclaimer

Verreweg de meeste onderzoeken naar therapietrouw bij MS zijn geïnitieerd, gefinancierd, geconcipieerd, uitgevoerd of gerapporteerd door farmaceutische bedrijven.