

VANTAGGI E LIMITI DELLA TERAPIA INIETTIVA: NUOVE STRATEGIE PER VECCHI PROBLEMI



DOTT.SSA MAURA FRIGO
Clinica Neurologica
MONZA
CAM 9 Aprile 2014

Aderenza: problematiche

- ❑ Non esiste un gold standard né esistono sistemi standardizzati per misurarla
- ❑ C'è eterogeneità nella valutazione del concetto di aderenza (interruzione al trattamento, persistenza, missing dose, durata della valutazione) nei dati disponibili
- ❑ Di solito si utilizzano misurazioni indirette del fenomeno perché più semplici (dati spesso retrospettivi ricavati dal paziente, conteggio pillole residue, dati ricavati dal dispensatore, ecc.)
- ❑ La determinazione del fenomeno è estremamente dipendente dal soggetto e quindi imprecisa

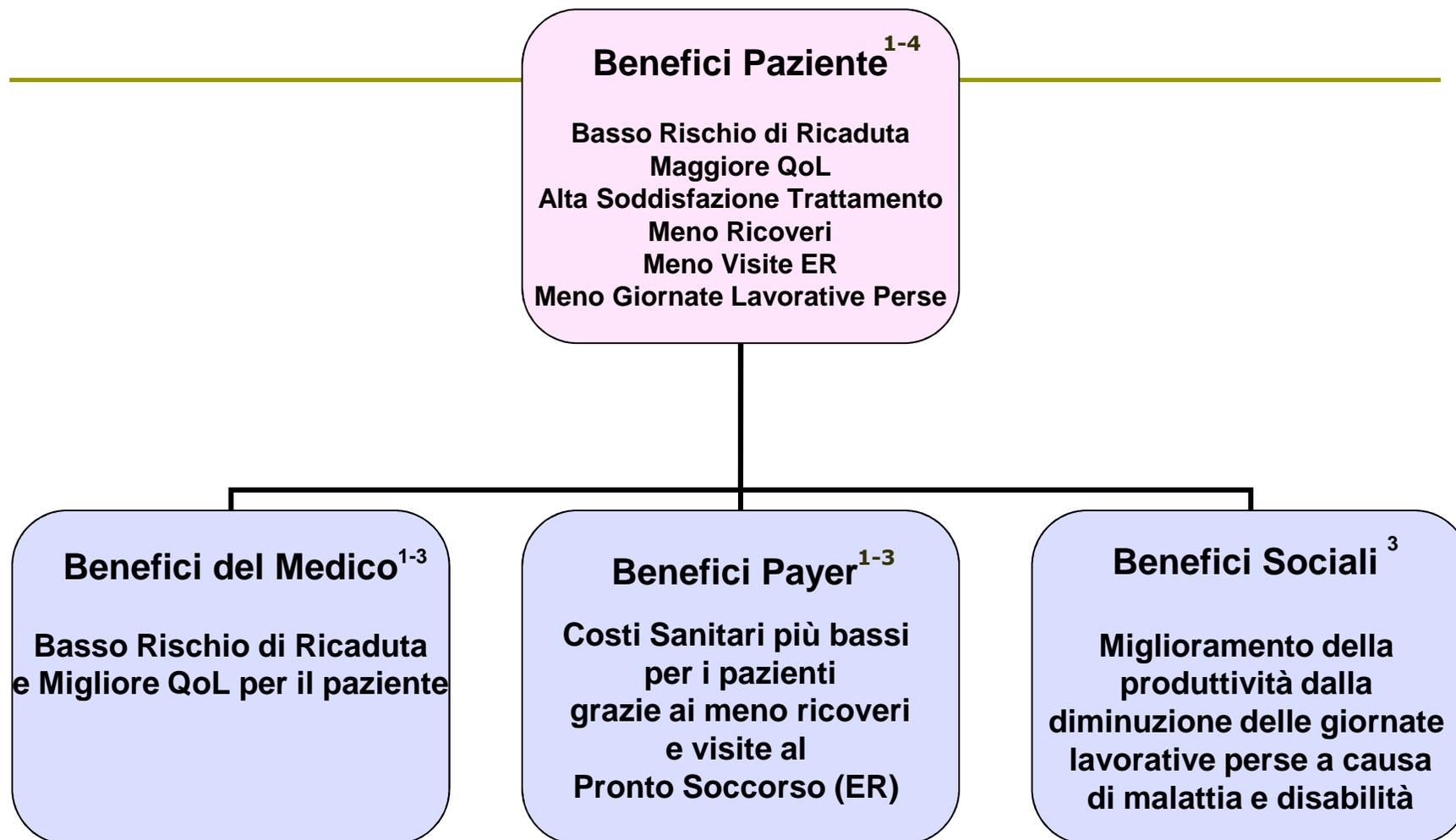
Fattori che influenzano l'aderenza





Perchè è importante essere aderenti al
trattamento?

I BENEFICI DELL'ADERENZA SI ESTENDONO OLTRE IL PAZIENTE



1. Steinberg S et al. Clin Drug Investig 2010;30:89-100

2. Treadaway K et al. J Neurol 2009;256:568-76

3. Phillips A et al. AAN, Toronto, Canada, Apr 10-17, 2010

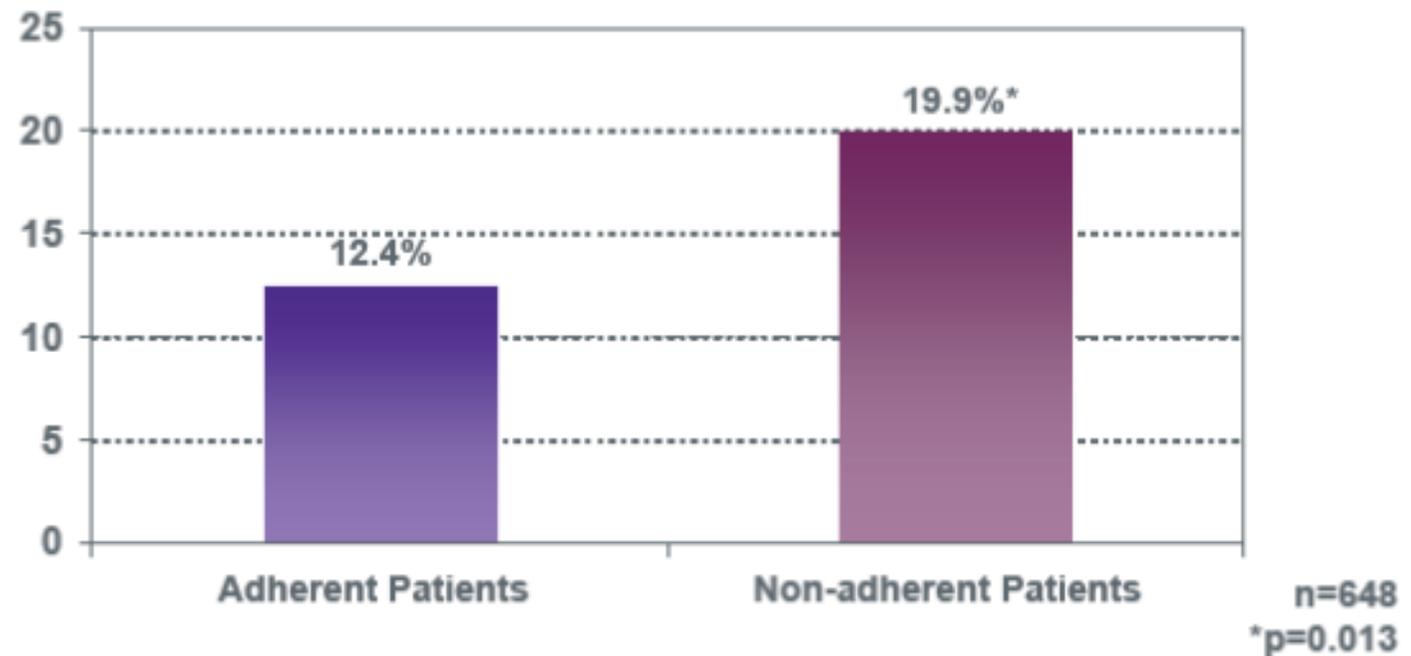
4. Tan H et al. AAN, Toronto, Canada, Apr 10-17, 2010

UNA MIGLIORE ADERENZA RIDUCE IL RISCHIO DI RICADUTE GRAVI

I pazienti “aderenti” (MPR \geq 80%) hanno una quota significativamente più bassa di gravi ricadute in 2 anni rispetto ai pazienti “non aderenti”

L’Aderenza riduce il Rischio di Gravi Ricadute *

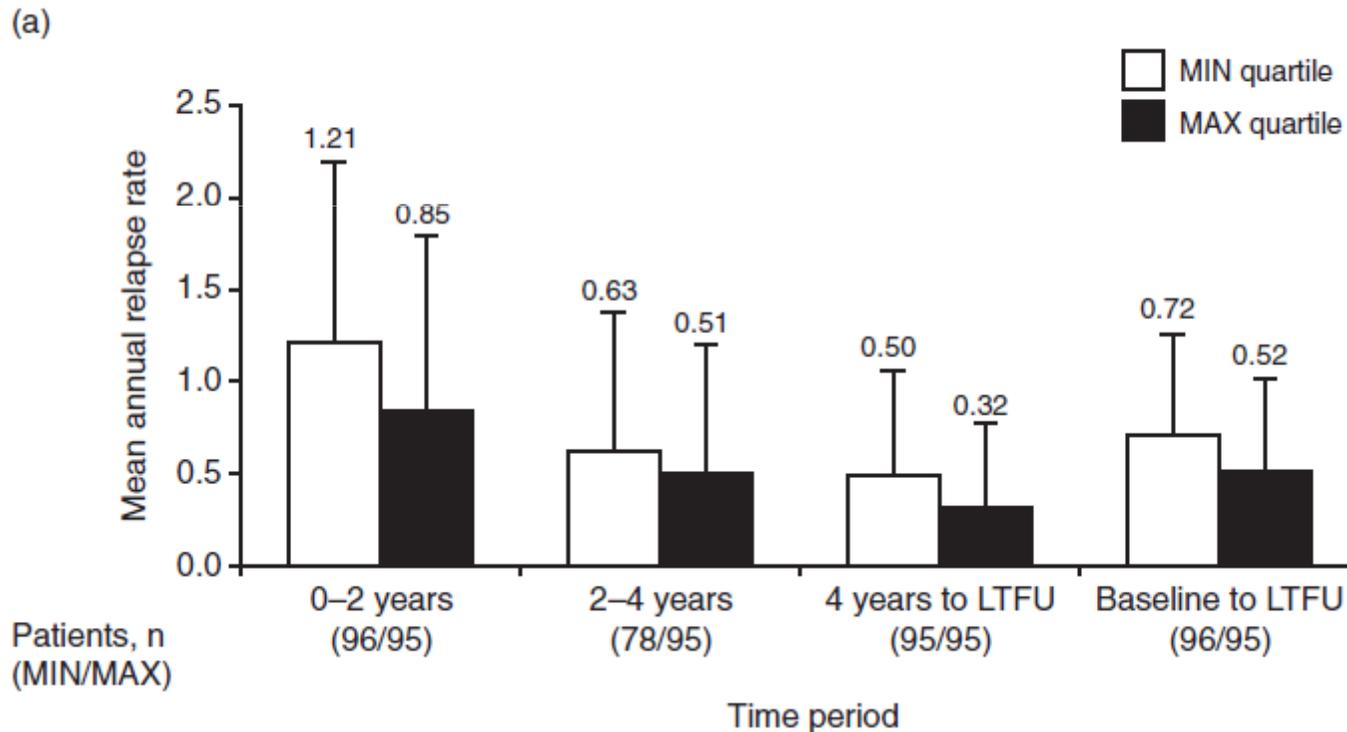
Pazienti con Gravi Ricadute (%)



* Grave Ricaduta: è definita come una ricaduta che necessita di una visita al pronto soccorso o un ricovero

Impatto della esposizione all'interferon beta

L'alta esposizione all'interferon beta è risultata associata ad un migliore outcome clinico rispetto alla bassa esposizione



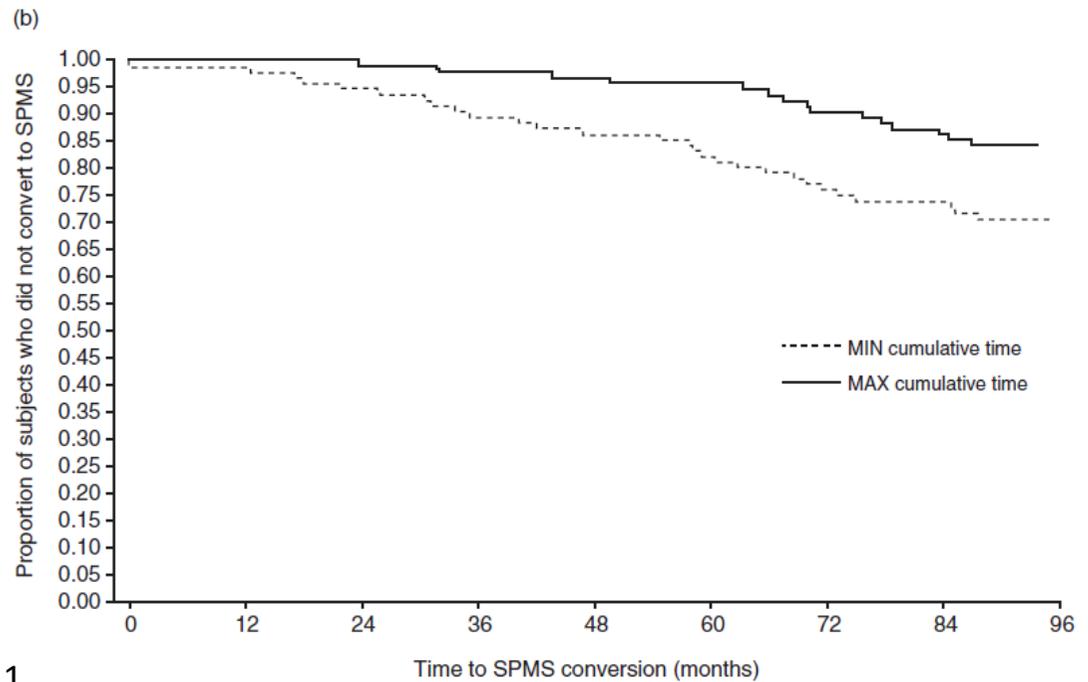
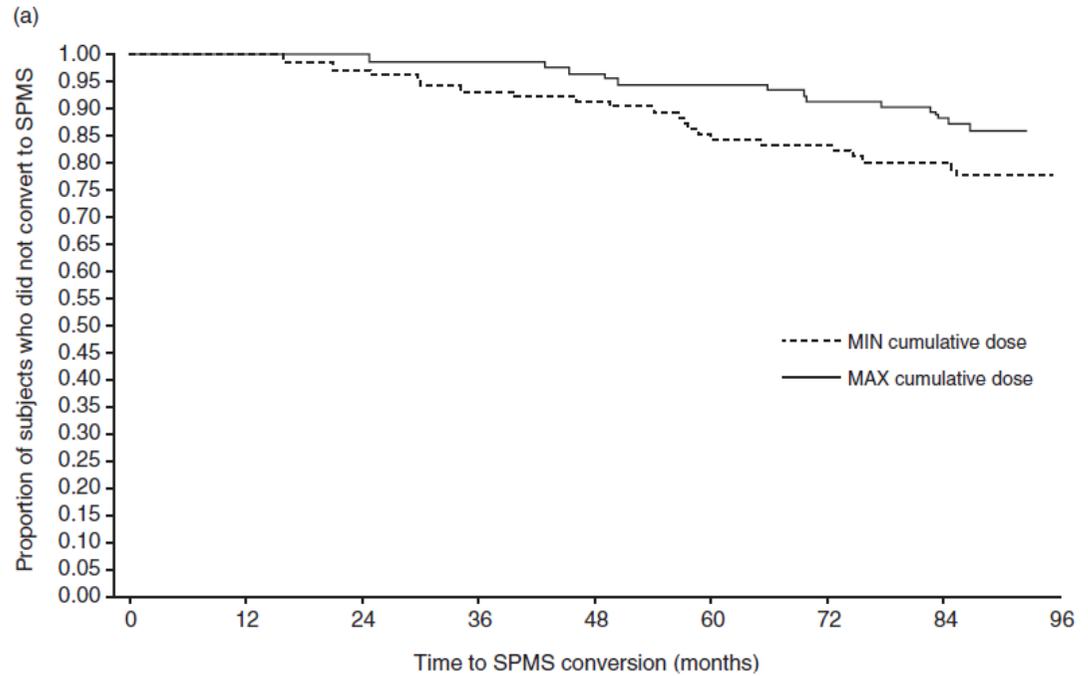
Dose cumulativa Max e Min a confronto

La qualità di esposizione al trattamento modifica il decorso della malattia

Dose cumulativa



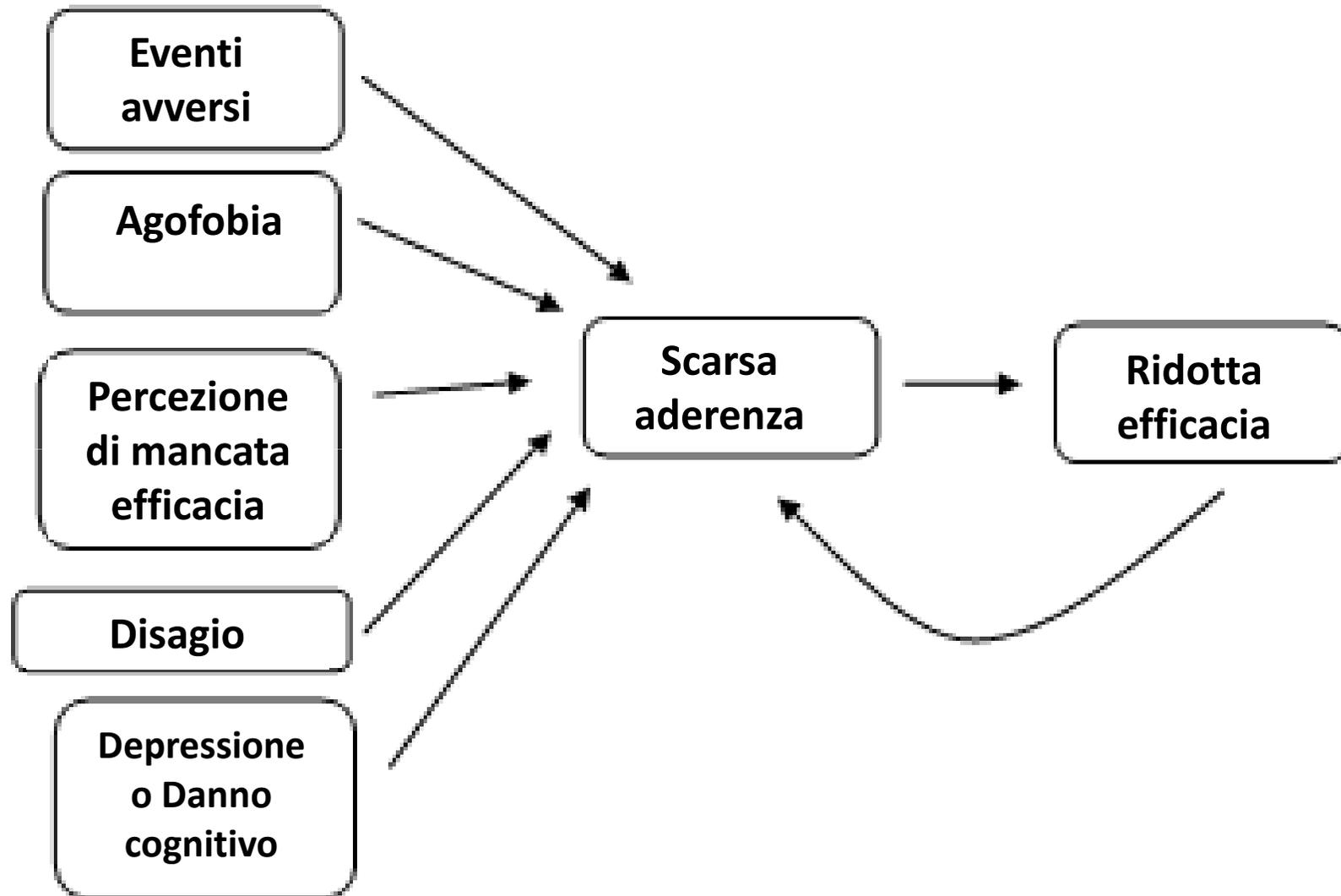
Tempo di esposizione cumulativo



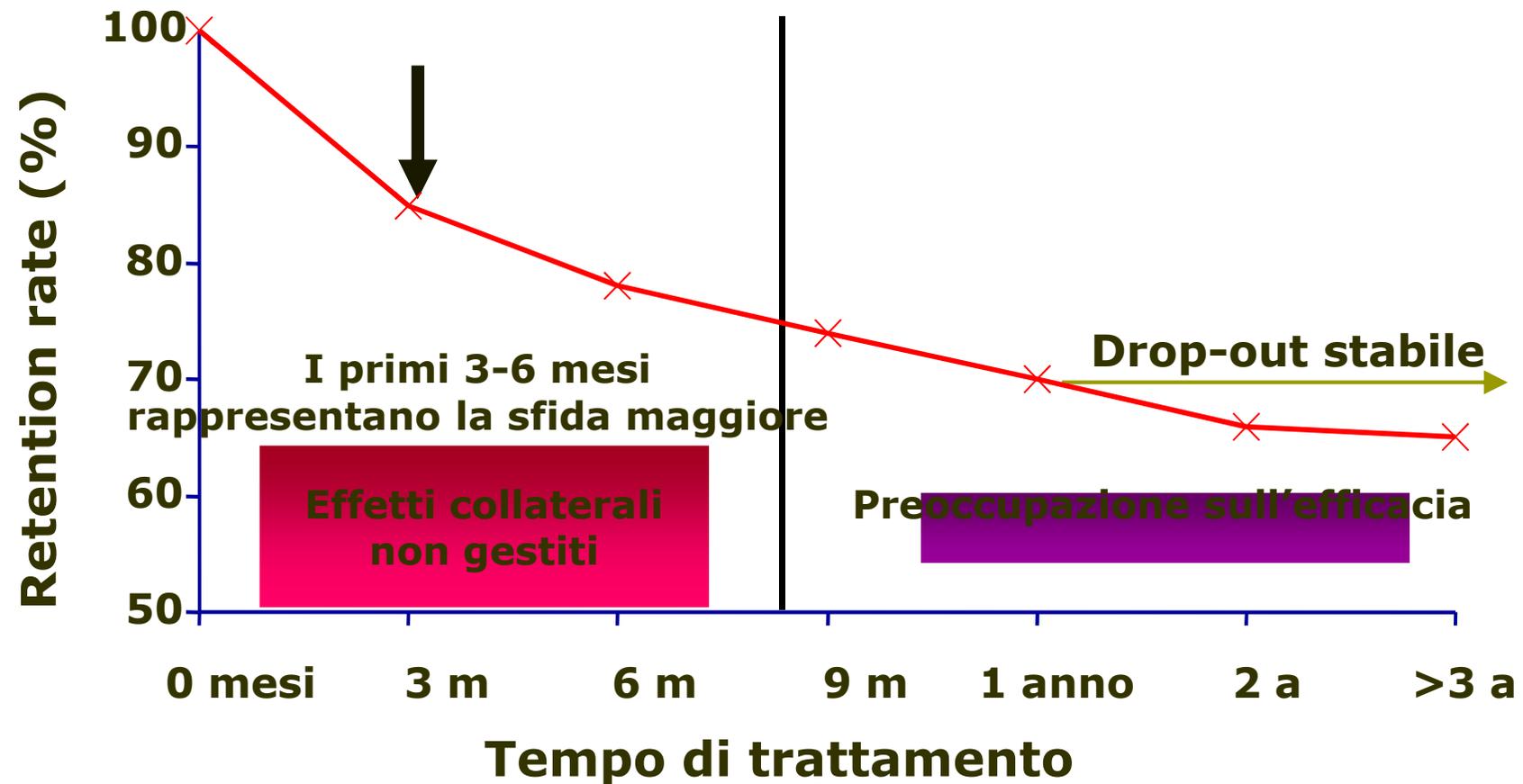


Quali sono le cause di non aderenza al trattamento?

Fattori che portano alla scarsa aderenza alla terapia per la SM



Aderenza nei DMT



DMT= disease modifying treatment

Factors related with treatment adherence to interferon β and glatiramer acetate therapy in multiple sclerosis

Jordi Río*, Joana Porcel, Nieves Téllez, Angela Sánchez-Betancourt, Mar Tintoré, M Jesús Arévalo, Carlos Nos and Xavier Montalban
Unitat de Neuroimmunologia Clínica, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Il 17% (107) dei pazienti ha interrotto il trattamento

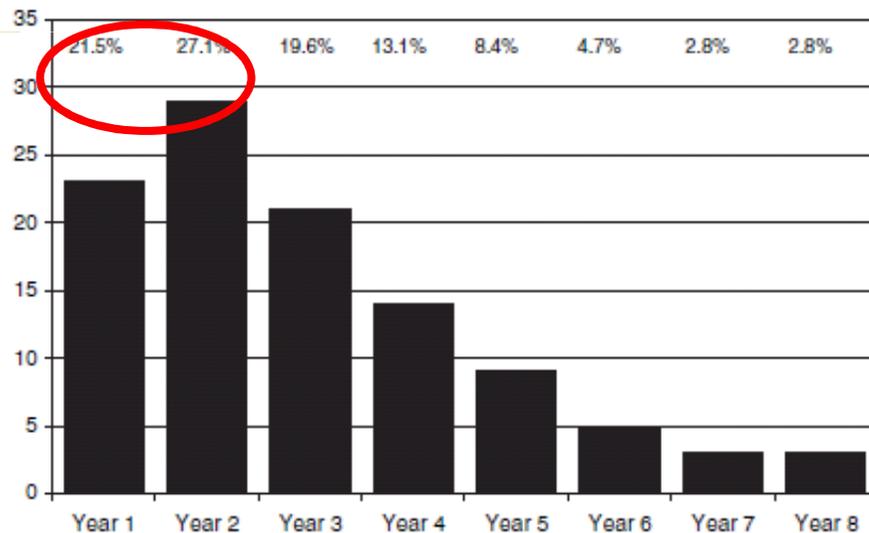


Figure 1 In the cohort of patients who stopped therapy, the graph shows the number and proportion of patients who stopped therapy in different timepoints during the follow-up period. x axis: number of patients.

Table 1 Reasons for stopping treatment with IMD not related with efficacy

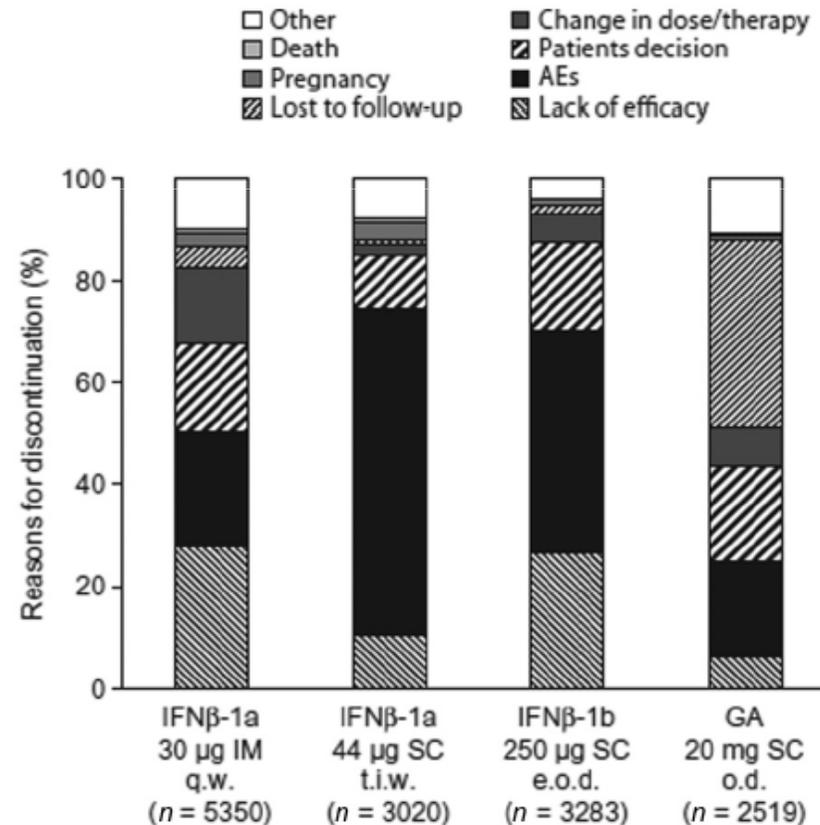
Reason for stopping therapy	Number (Percentage)
Own will decision	27 (25%)
Flu symptoms	7 (6.5%)
Pregnancy	7 (6.5%)
Death	5 (4.7%)
Cerebral haemorrhage	1 (1%)
Allergic reaction	1 (1%)
Aplastic anaemia	1 (1%)
Gastrointestinal bleeding	1 (1%)
Autoimmune hepatitis	1 (1%)

Systematic review of disease-modifying therapies to assess unmet needs in multiple sclerosis: tolerability and adherence

G Giovannoni¹, E Southam² and E Waubant³

Discontinuation of treatment ranged from 17% (IFN β -1a SC) to 36% (GA SC) with the most common reasons for discontinuation reported to be the occurrence of adverse events and lack of treatment efficacy.

Multiple Sclerosis Journal
0(0) 1–15
© The Author(s) 2012
Reprints and permission:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1352458511433302
msj.sagepub.com
SAGE



TOLLERANZA CUTANEA

Le iniezioni sottocutanee creano possono dare problemi di tolleranza cutanea (pomfi, retrazione cutanea, lipodistrofia).



“Missing dose”

J Neurol (2009) 256:568–576
DOI 10.1007/s00415-009-0096-y

ORIGINAL COMMUNICATION

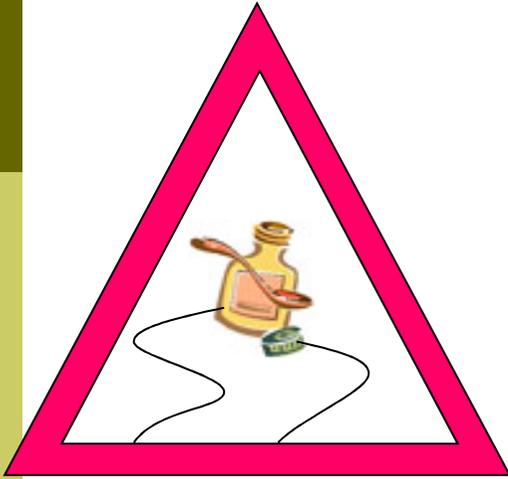
Katherine Treadaway
Gary Cutter
Amber Salter
Sharon Lynch
James Simsarian
John Corboy
Douglas Jeffery
Bruce Cohen
Ken Mankowski
Joseph Guarnaccia
Lawrence Schaeffer
Roy Kanter

David Brandes
Charles Kaufman
David Duncan
Ellen Marder
Arthur Allen
John Harney
Joanna Cooper
Douglas Woo
Olaf Stüve
Michael Racke
Elliot M. Frohman

Factors that influence adherence with disease-modifying therapy in MS

I fattori che determinano le “missing dose” sembrano essere differenti da quelli che determinano l’interruzione al trattamento e non sembrano motivati da una reale necessità medica, ma più che altro condizionati da aspetti motivazionali e psicologici

... i cui risultati sono...



- In sei mesi un paziente affetto da sclerosi multipla su dieci, manca l'assunzione di dieci dosi di farmaco
- Almeno $\frac{3}{4}$ dei pazienti affetti da Sclerosi Multipla mancano l'assunzione di dosi di farmaco
- L'88% dei pazienti si somministra almeno l'80 % delle dosi previste

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

V. Devonshire^a, Y. Lapierre^b, R. Macdonell^c, C. Ramo-Tello^d, F. Patti^e, P. Fontoura^f, L. Suchet^g, R. Hyde^h, I. Balla^h, E. M. Frohmanⁱ and B. C. Kieseier^j, for the GAP Study Group*

^aUniversity of British Columbia Hospital MS Clinic, Vancouver, BC; ^bHopital Neurologique de Montreal, Montreal, QC, Canada; ^cAustin Hospital, Heidelberg, Vic., Australia; ^dHospital Universitario Germans Trias i Pujol Servicio De Neurologia, Badalona (Barcelona), Spain; ^eUniversity of Catania, Catania, Italy; ^fNew University of Lisbon, Lisbon, Portugal; ^gCabinet Medical, Marseille, France; ^hBiogen Idec International GmbH, Zug, Switzerland; ⁱUniversity of Texas Southwestern Medical Center, Dallas, TX, USA; and ^jHeinrich-Heine University, Düsseldorf, Germany

Keywords:

adherence, disease-modifying therapy, glatiramer acetate, interferon, multiple sclerosis

Received 5 November 2009
Accepted 9 March 2010

Background: Most disease-modifying therapies (DMTs) for multiple sclerosis (MS) are self-injectable medications that must be taken on an ongoing basis to reduce disease activity. Thus, adherence to therapy becomes an important challenge that must be addressed to maximize benefits of therapy. This study evaluated rates of adherence to prescribed treatment and explored factors affecting adherence amongst patients with relapsing-remitting MS.

Methods: This was an observational, multicenter, multinational, phase 4 study. Patients and physicians received paper questionnaires regarding adherence to DMTs approved at the time of the study, including intramuscular interferon beta-1a (IFN β -1a), subcutaneous IFN β -1a, IFN β -1b, and glatiramer acetate. Quality of life and cognition data also were collected. Multivariate analysis was conducted to identify factors associated with adherence to long-term DMTs.

Results: Two thousand six hundred and forty-eight patients were studied, revealing an average treatment duration of 31 months. Seventy-five percent of patients ($n = 1923$) were adherent to therapy. The most common reasons for non-adherence were forgetting to administer the injection (50.2%) and other injection-related reasons (32.0%). Adherent patients reported better quality of life ($P < 0.05$) and fewer neuropsychological issues ($P < 0.001$) than non-adherent patients. Adherent patients had significantly shorter duration of disease ($P < 0.001$) and shorter duration of therapy ($P = 0.005$) than non-adherent patients. Women were more likely than men to adhere to treatment.

Conclusion: Identifying factors that affect adherence to prescribed treatments is the first step in improving adherence of patients with MS to therapy, thereby helping maximize the benefits of long-term DMTs.



Si può incrementare l'Aderenza?

SCELTA DEL FARMACO

- AGOFOBIA
- MANUALITA'
- COMORBIDITA'
- STILE DI VITA



Strategie per incrementare l'aderenza

- **Supporto medico specialistico**
- **Programmi educativi e di supporto**
- **Azione sulla formulazione del farmaco**
- **Dispositivi autoiniettivi**



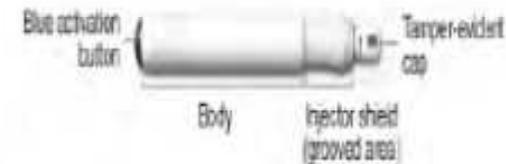
L'EVOLUZIONE DELLA SPECIE



Strategie per migliorare aderenza e persistenza: auto-iniettori

An open-label, multicenter study to evaluate the safe and effective use of the single-use autoinjector with an Avonex[®] prefilled syringe in multiple sclerosis subjects *BMC Neurology* 2011, 11:126

J. Theodore Phillips¹, Edward Fox², William Grainger³, Dianne Tuccillo⁴, Shifang Liu⁴ and Aaron Deykin^{4*}



Supportive strategies to improve adherence to IFN beta-1b in Multiple Sclerosis – Results of the BetaPlus observational cohort study

Carlo Pozzilli^{a,*}, Bernd Schweikert^b, Ugo Ecarl^c, Wolfgang Oentrich^d and for the BetaPlus Study group¹ *Journal of the Neurological Sciences* 307 (2011) 120-126



Patient adherence to and tolerability of self-administered interferon β -1a using an electronic autoinjection device: a multicentre, open-label, phase IV study

Alessandra Lugaresi^{1,11*}, Ciro Florio², Vincenzo Brescia-Morra³, Salvatore Cottone⁴, Paolo Bellantonio⁵, Marinella Clerico⁶, Diego Centonze⁷, Antonio Uccelli⁸, Maria di Iorio¹, Giovanna De Luca¹, Andrea Marcellusi⁹ and Andrea Paolillo¹⁰, for the BRIDGE study group

Lugaresi et al. *BMC Neurology* 2012, 12:7



BRIDGE Study

RESEARCH ARTICLE

Open Access

Patient adherence to and tolerability of self-administered interferon β -1a using an electronic autoinjection device: a multicentre, open-label, phase IV study

Overall, 35.6% of missed injections (31/87) were due to medical reasons (patients experienced AEs that precluded injection), 20.7% (18/87) due to forgetfulness and 27.6% (24/87) due to 'other reasons'. Pain at the injection site and 'problems using the autoinjection device'/'device unusable' accounted for 3.4% (3/87) and 6.9% (6/87) of missed injections, respectively. At Weeks 4 and 8, most injections were missed due to medical reasons (42.3% [11/26] and 40.1% [11/27], respectively), while at Week 12 most were due to 'other' reasons (42.4% [14/33]) and medical reasons accounted for 27.3% [9/33] of missed injections.

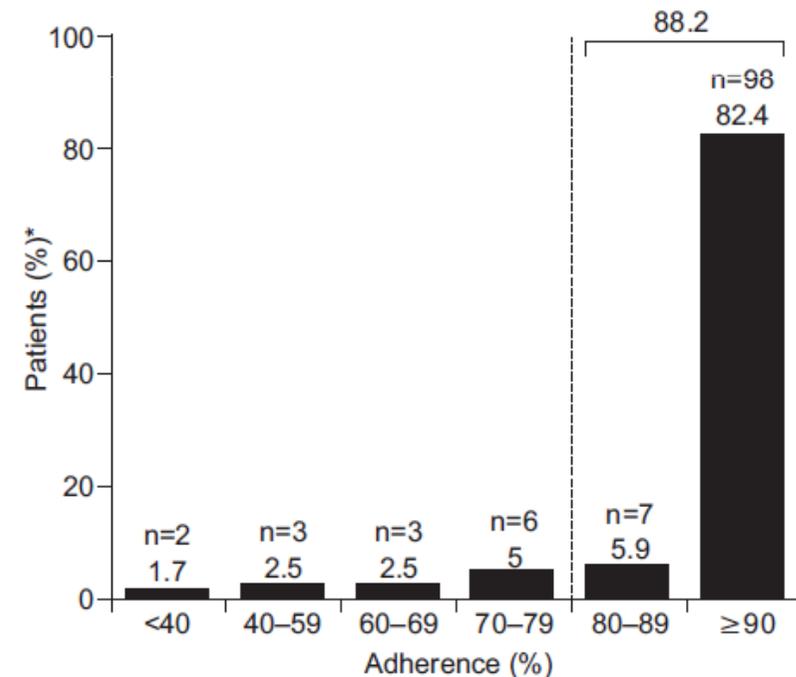


Figure 2 Patient adherence at Week 12 in the intent-to-treat population (n = 119). *Percentages may not add up to 100 due to rounding.

I nuovi autoiniettori per INF beta-1a sc possono incidere sull'aderenza nei pazienti con SM?

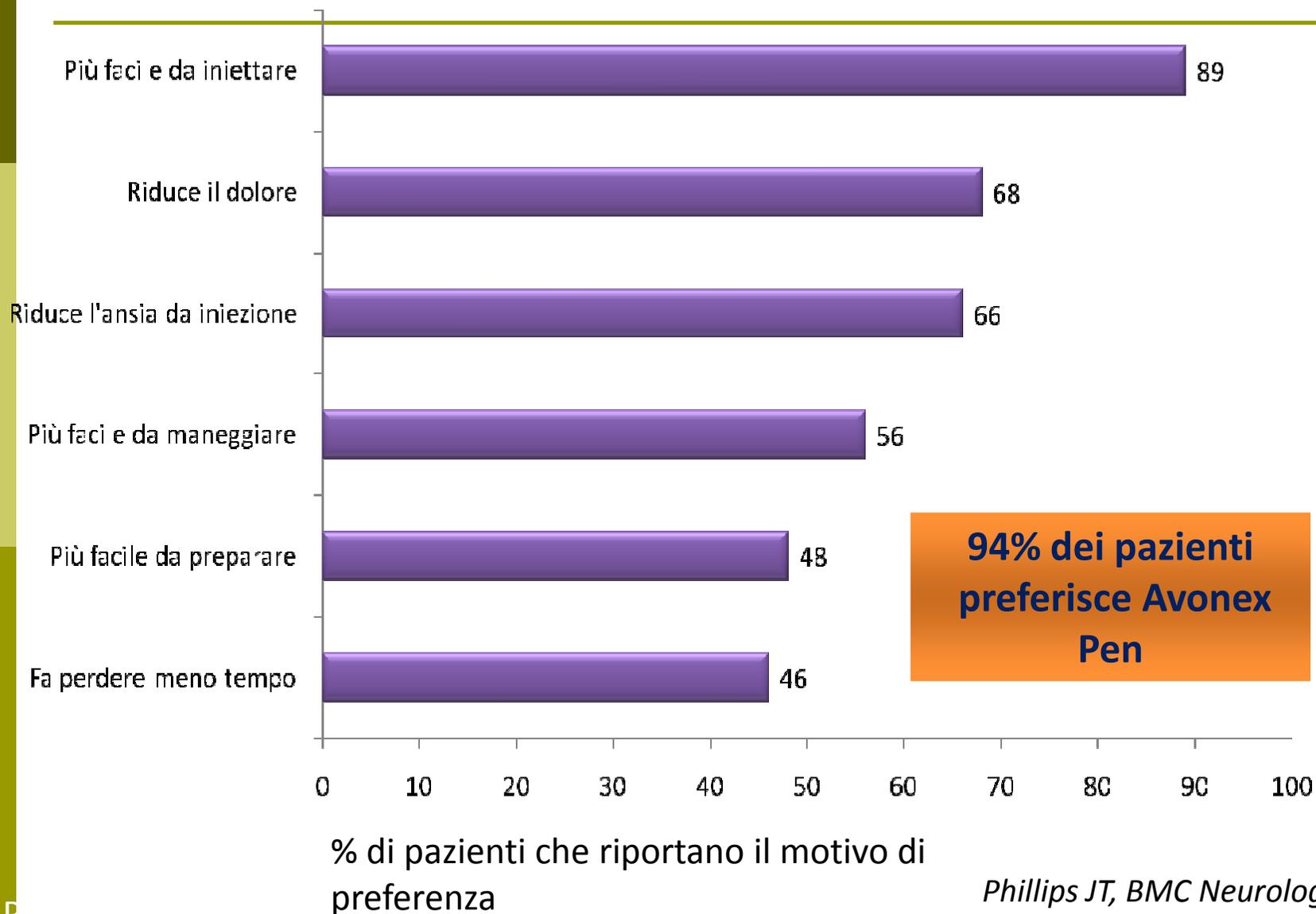
Will New Injection Devices for Interferon Beta-1a s.c. Affect Treatment Adherence in Patients With Multiple Sclerosis? An Expert Opinion in the Middle East

Conclusioni

Studi sugli autoiniettori per SM hanno mostrato che i dispositivi (Rebitect II™ o Betaject®) hanno una miglior tollerabilità delle siringhe. Il nuovo RebiSmart™, autoiniettore che utilizza IFN beta-1a s.c. e ha diverse funzioni progettate per renderlo più semplice da usare e ben tollerato, anche dai pazienti che vivono con ansia l'autoiniezione. Il gruppo ha ritenuto che questo nuovo dispositivo potrebbe promuovere l'adesione del paziente alla IFN beta-1a, terapia sc.

International Journal of Neuroscience, 121, 171–175, 2011

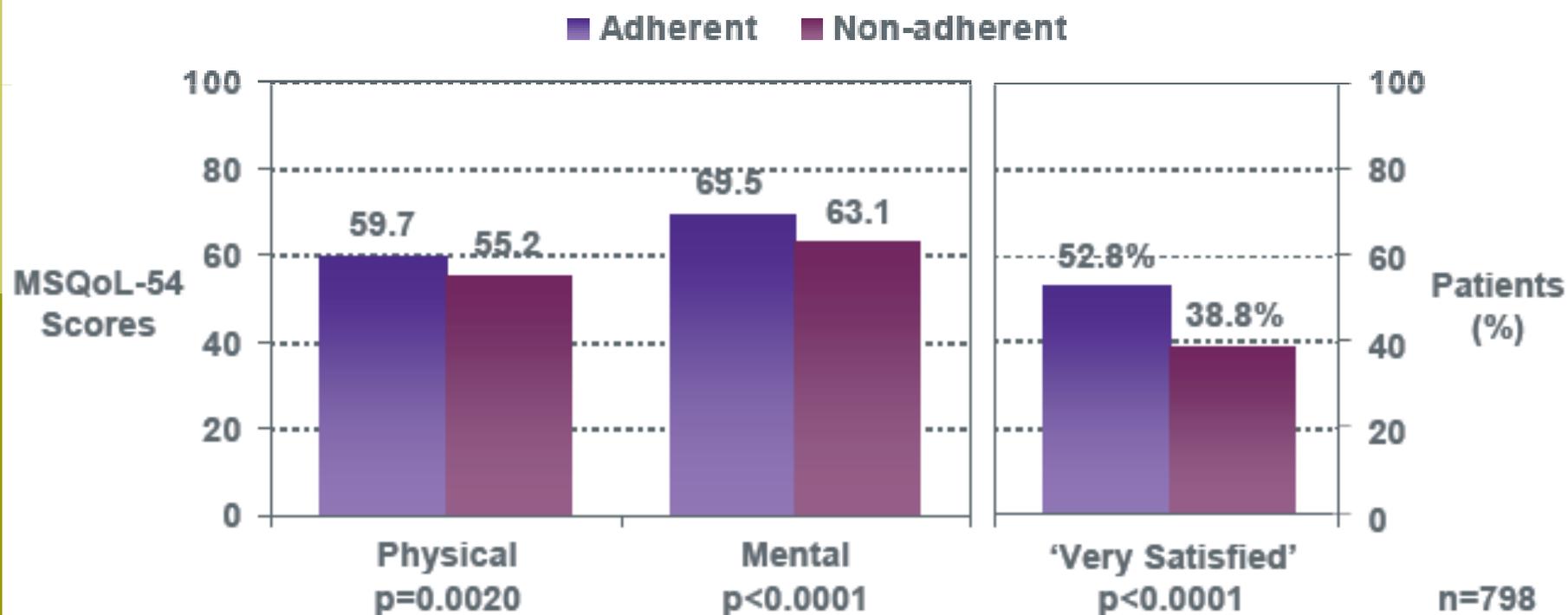
Motivi di preferenza dell'Avonex Pen



Phillips JT, BMC Neurology 2011

QUALITA' DELLA VITA E SODDISFAZIONE DAL TRATTAMENTO

Pazienti aderenti hanno riferito di avere una migliore qualità di vita e sono più soddisfatti della terapia.



Componenti dell'aderenza



**L' Aderenza alla terapia è un problema multidimensionale che
può
essere influenzato dai diversi Operatori Sanitari**

