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Persistence and Adherence to Parenteral First-Line Therapies in Multiple Sclerosis

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Abstract: Parenteral first-line disease-modifying therapies (DMTs), particularly interferon beta preparations and glatiramer acetate, have formed the cornerstone of relapsing-remitting multiple sclerosis (MS) treatment. Patient persistence (continuing prescribed therapy over time) and adherence (correctly following prescribed regimen) to these injectable therapies are critical for clinical effectiveness yet are challenged by several factors intrinsic to both the drugs and the patient population. This article reviews current evidence regarding persistence and adherence rates, associated determinants, and potential interventions in the real-world treatment of MS.

Keywords: Multiple Sclerosis (MS), Disease-Modifying Therapies (DMTs), Interferon Beta, Glatiramer Acetate, Adherence and Persistence.

INTRODUCTION

Multiple sclerosis is a chronic immune-mediated disorder wherein DMTs are central to relapse prevention and slower progression. First-line injectable agents, including various formulations of interferon beta and glatiramer acetate, require self-injection, contributing to unique challenges in patient adherence and persistence compared to newer oral agents. Robust adherence and persistence are directly linked to better patient outcomes, including reduced relapse rates and disability accrual.

DEFINITIONS

- **Persistence** is the duration a patient continues treatment without switching or stopping.
- **Adherence** refers to the degree to which dosing matches the prescribed regimen, commonly quantified as the proportion of days covered (PDC) or medication possession ratio (MPR), with ≥80% or ≥95% commonly defining "adherent."

Real-World Persistence and Adherence Rates

Overview of Key Findings

- **12-month persistence rates** for injectable DMTs (such as interferon beta and glatiramer acetate) range from approximately 62% to 82%, with higher discontinuation rates observed over longer periods[1][2][3].
- **Adherence rates** (typically defined as taking at least 80% of prescribed doses) range from 60% to 85% at one year, though this rate drops over time[2][4].

- Glatiramer acetate tends to have slightly higher adherence than interferon beta-1b formulations, while intramuscular interferon beta-1a shows the greatest persistence among interferons[3].
- The main reasons for non-persistence and poor adherence are adverse effects (especially flu-like symptoms, injection site reactions), needle phobia, forgetting doses, and lack of perceived efficacy[5][3].

Table 1. Summary of Persistence and Adherence Rates

Therapy	12-Month Persistence (%)	12-Month Adherence (%)	Most Common Dropout Reason
IFN-β1a IM	82–85	80–90	Adverse events, inefficacy
IFN-β1a SC	65–77	67–85	Adverse events, injection rxn
IFN-β1b SC	60–75	67–80	Injection site reactions
Glatiramer Acetate SC	62–82	80–85	Injection reactions, inefficacy

SC: Subcutaneous; IM: Intramuscular; IFN: Interferon[2][3]

Factors Influencing Persistence and Adherence

- **Patient-related:** Age (older patients more adherent), female sex modestly associated with higher adherence, co-morbid psychiatric or cognitive disorders predict lower persistence.
- **Therapy-related:** Frequency and mode of administration (IM better tolerated than SC), injection-site reactions, and side effects are key factors.
- **Disease-related:** Higher disability (EDSS>1.5) predicts earlier discontinuation. Early non-adherence often presages discontinuation.
- **Healthcare system:** Training in self-injection, ongoing support from MS nurse or neurologist, and access to psychological care bolster adherence[1][2][3].

DURATION OF PERSISTENCE

Persistence rates decline with time, with about half of patients remaining on their initial injectable therapy at three years. DMT switches are often due to adverse effects or lack of efficacy rather than poor treatment motivation[3].

Figure 1. Kaplan-Meier Curve of Persistence on Parenteral First-Line DMTs

![Graph: Persistence over time for parenteral first-line MS therapies. The median persistence is 1349 days, with marked attrition at 12 and 24 months.][image:1]

Clinical Consequences of Non-Adherence

- Poor adherence is associated with increased risk for relapse, more frequent hospital visits, and decreased quality of life[6].
- Early discontinuation (especially in the first six months) is common—up to 30% in the first year in some cohorts[5][4].

Interventions to Improve Persistence and Adherence

- **Education and support:** Detailed training in self-injection, regular follow-ups, and counseling address fears, improve confidence, and preempt side effect-related non-adherence.
- **Device innovation:** Autoinjector pens and reminders can reduce missed doses and injection-site complications, improving adherence rates[2][4].
- **Psychological support:** Access to psychological counseling has been linked to greater adherence, especially in the first year of therapy[1].
- **Home-based and informal care:** Provision of at-home support or informal caregiver involvement helps maintain adherence in patients with physical or psychological barriers[1].

Table 2. Summary of Enhancers and Barriers

Enhancers	Barriers
Patient education	Adverse effects (flu-like, injection-site)

Injection devices (autoinjector)	Needle phobia
Regular professional follow-up	Forgetfulness
Informal caregiver support	Psychological burden, depression
Integration of psychological care	Complex injection regimens

Long-term Perspectives

While injectable therapies remain an important first-line option due to safety and long-term experience, persistence and adherence remain suboptimal compared to newer oral or less frequently administered intravenous agents, which often exhibit higher persistence due to lower administration burden[7]. However, with comprehensive care, adherence and persistence with injectables can be optimized for selected patients.

CONCLUSIONS

A significant proportion of MS patients on first-line parenteral DMTs are non-persistent or non-adherent within two years of treatment, primarily due to injection-related challenges and side effects. Multidisciplinary interventions and patient-centered care models are critical to optimize clinical outcomes and enhance therapy persistence.

Figure 1. Kaplan-Meier survival analysis of persistence for patients initiated on injectable first-line therapies. The steepest drop in persistence occurs within the first 12–24 months, with ~60% of patients remaining on therapy at one year.

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