MS Relapse Treatments and Relapse Resolution: Retrospective Study Results from a US Health Plan

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Introduction

Multiple sclerosis (MS) affects an estimated 400,000 people in the United States (US) and 2.5 million people worldwide.[1] MS is characterized by relapses, which may indicate disease progression.[2] Relapses have a high cost burden and adversely impact health-related quality of life and functional ability.[2]

Corticosteroids [CS; oral (OCS) and intravenous methyl prednisolone (IVMP)], are considered first-line treatment[3]; OCS are often used first due to convenience. Other options which may be considered include repository corticotropin injection (RCI or H.P. Acthar® Gel; approved in the US), plasmapheresis (PMP; procedure), and intravenous immunoglobulin (IVIG; not approved). Limited data supports IVIG's efficacy.[3]

Little information exists on the real-world use of relapse treatments and their effectiveness beyond CS. Relapse methodology using claims data does not usually account for inter-related events. We evaluate relapse episodes and unresolved relapses to do so: 1) 'relapse episode' uses a standardized 30-day[3] window to inter-relate relapse events, 2) 'unresolved relapse' uses a subsequent event occurring within 30 days[3] of a prior event to inter-relate relapse events. These may be used to infer lack of resolution and treatment effectiveness.

Humana, a US health and wellness company, has a coverage policy which requires experience of an acute MS relapse, and contraindications or intolerance to CS in order to receive second-line relapse treatment. CS trial and failure is not required.

Objective

To evaluate the prevalence of MS relapse, use of relapse treatments, and rate of unresolved relapse per treatment. Unresolved relapses were not evaluated when the index treatment was OCS or IVMP.

Methods

Study Design:

- Retrospective, observational, cohort study (unrestricted enrollment)
- Study period: January 1, 2008 to July 31, 2015
- Patients ages >18 and < 90 years†

Key Definitions & Measures:

- MS relapse event = inpatient admission or outpatient claim with a diagnosis of MS (ICD-9-CM code 340.xx) followed by receipt of a relapse therapy or procedure (OCS, IVMP, RCI, PMP, or IVIG) within 30 days[5].
- OCS = oral forms of dexamethasone, methylprednisolone, prednisolone, and prednisone

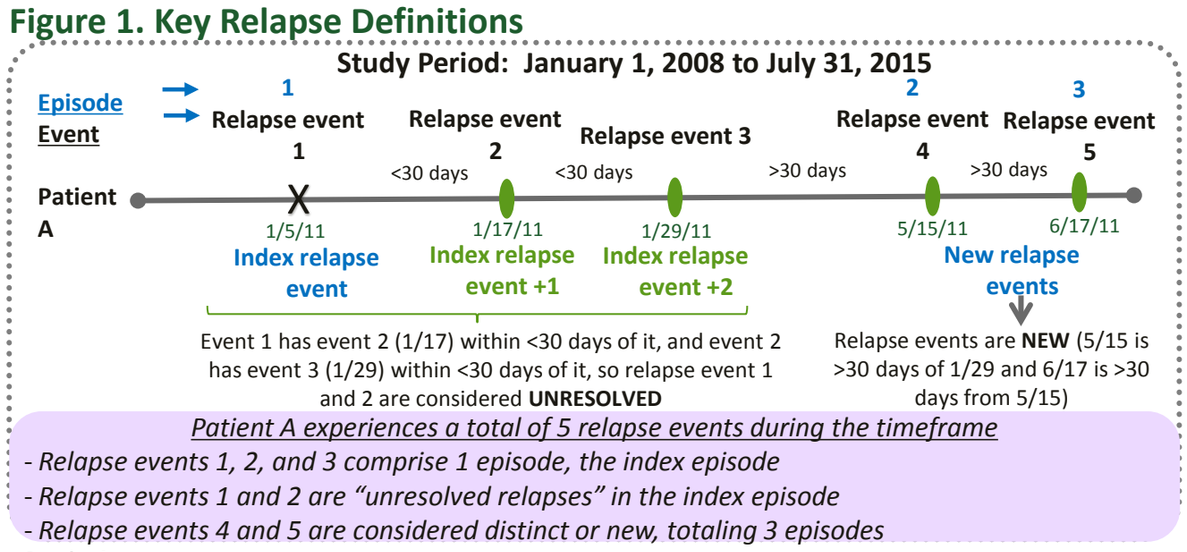
Methods (continued)

- The relapse event date was designated the date of treatment
- The first relapse event observed = index relapse event; its date = index date
- A relapse episode comprised all relapse events (i.e. >=1) occurring within 30 days of the first relapse event.
- A relapse event was called an 'unresolved relapse' event if the next relapse occurred within 30 days (and 'new' if it occurred >30 days) of the prior event.

Data Source:

- Humana provides Medicare Advantage, stand-alone prescription drug plan, and commercial health insurance across the US.
- Humana Commercial and Medicare Advantage administrative claims data, comprised of integrated medical, pharmacy, and eligibility files, were used.
- This study was approved by the Schulman Institutional Review Board.

Figure 1. Key Relapse Definitions



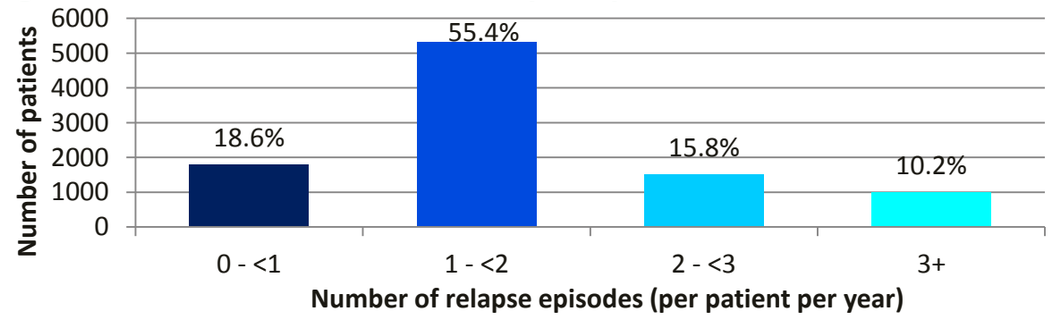
Analysis:

- CHI managed all data and conducted all analyses using SAS Enterprise Guide 7.1
- The annualized rate of relapse episodes were calculated in addition to treatments used for relapse episodes and total unresolved relapses.
- Subsequent relapse episodes were calculated and the number and distribution of unresolved relapse events within the index relapse episode was assessed.
- Counts below 10 had to be suppressed or combined†

Results

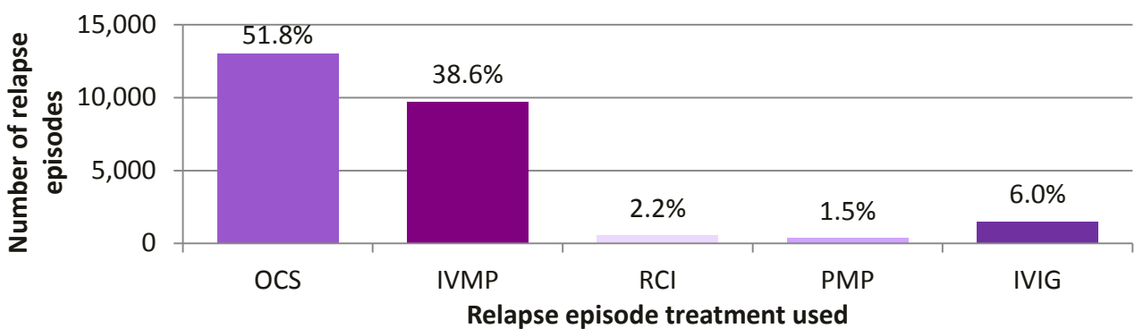
9,574 patients with relapse episodes and 25,162 relapse episodes were identified. The mean±SD follow-up time per patient was 2.7±2.1 years.

Figure 1a. Annualized rates of relapse episodes



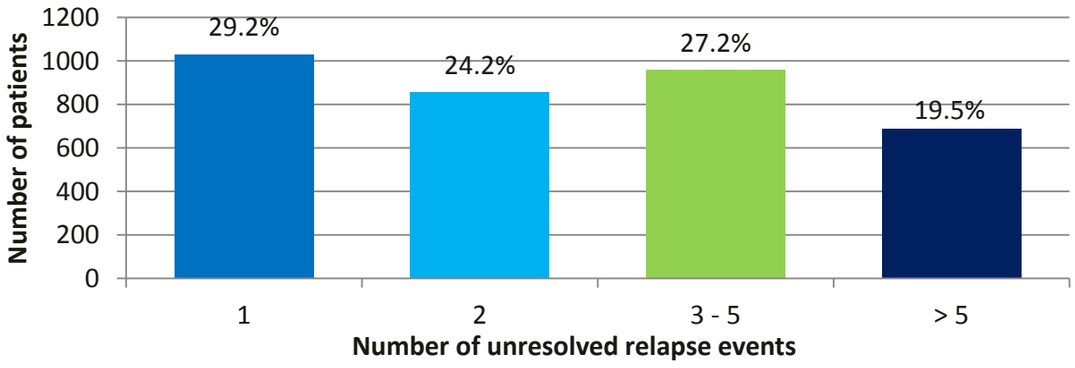
The majority of patients (74.0%) had <2 relapse episodes and 26.0% had ≥2 relapses per year ***[Figure 1a]***. CS were used to treat 90.4% of index relapse events (OCS 51.8%, IVMP 38.6%) within the index relapse episode ***[Figure 1b].***

Figure 1b. Index relapse event treatments used in index relapse episodes



Of patients experiencing relapse episodes, 36.9% (n=3,532) of patients had >=1 unresolved relapse event, for a total 16,707 unresolved relapse events during the study period [mean (SD) = 4.7 (8.9) unresolved relapse events per patient] ***[Data not shown]***. The distribution of unresolved relapse events in patients with >=1 unresolved relapse event is provided in ***[Figure 2].***

Figure 2. Distribution of unresolved relapse events



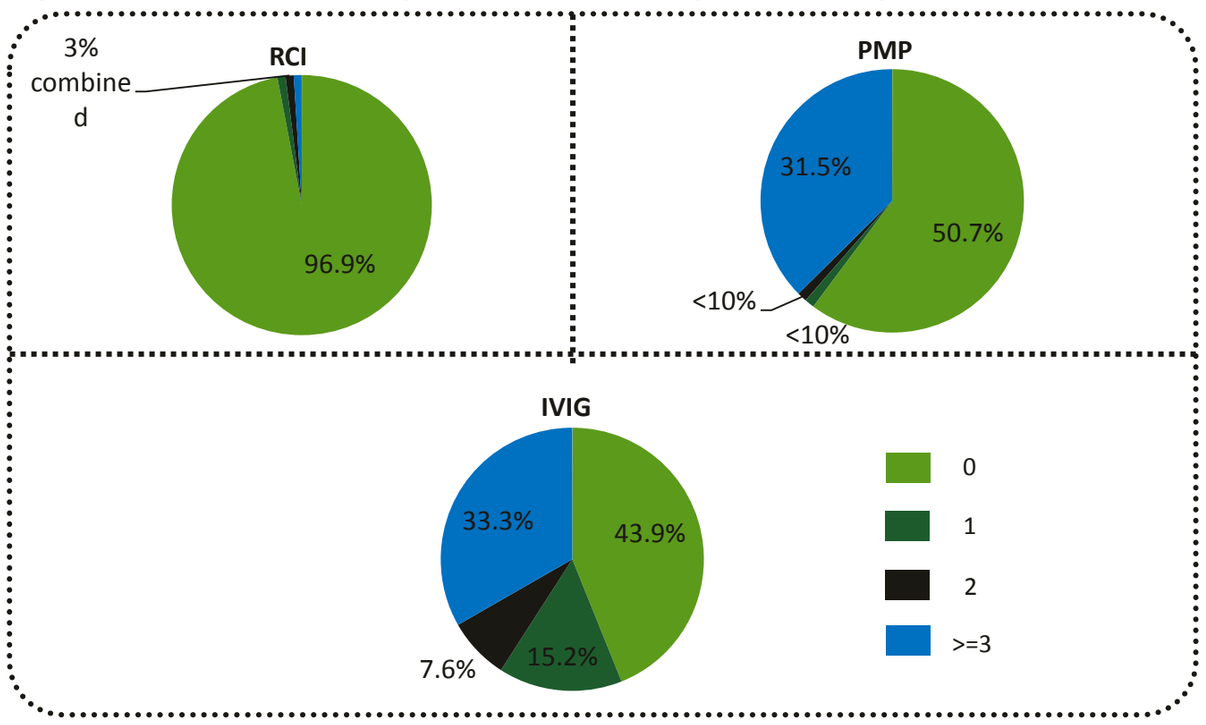
When a relapse episode was first treated with a particular therapy, patients were likely to use the same index therapy again during subsequent episodes ***[Table 1]***.

Table 1. Index and subsequent relapse episode therapy

Index relapse event treatment within episode	RCI n = 195	PMP n = 73	IVIG n = 171	IVMP n= 3,425	OCS n = 5,710
Index event treatment during subsequent relapse episodes:					
RCI	82	0	<10	138	135
PMP	<10	185	<10	42	60
IVIG	<10	<10	971	213	137
IVMP	60	30	84	4,719	1,392
OCS	66	23	56	1,379	5,791

When treated with RCI, 96.9% of patients had 0 unresolved relapses. When treated with PMP and IVIG, 50.7% and 43.9% of patients, respectively, had 0 unresolved relapses. The distribution of unresolved relapses (1,2,>=3) remained lowest with RCI ***[Figure 3]***.*

Figure 3. Unresolved relapses in the index episode analyses



Conclusions

- Study results provide current insight into existing challenges with MS relapse.
- 26% of patients with MS experienced 2 or more relapse episodes per year. Over 1/3 of patients experienced ≥1 unresolved relapse event, requiring additional relapse treatment beyond the initial treatment received.
- Based on index relapse episode analyses, we found unresolved relapse rates differed by treatment. Patients receiving RCI had the lowest unresolved relapse rate; 96.9% (RCI), 43.9% (IVIG), and 50.7% (PMP) experienced 0 unresolved relapses.
- Robust management of MS relapse should reflect timely resolution with appropriate treatment in order to minimize patient burden.

Limitations

- Administrative claims data often lack clinical detail, such as disease severity, reason for prescription, etc.
- Relapses were identified based on treatment-seeking behavior using an established claims-based algorithm[4]; treatment received outside a healthcare visit was not addressed.
- Index relapse events were first observed, but perhaps not the actual first events; however, unresolved relapses evaluate subsequent (vs. prior) relapses.
- Unrestricted enrollment could underestimate unresolved relapses. PMP and IVIG may be administered as courses of therapy, which would lead to an underestimation as well.*

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