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RESEARCH BRIEF

Scaling Up vs. Starting High: Treatment Approaches Vary Widely for Patients Diagnosed With Multiple Sclerosis

Patients were equally likely to undergo escalation and induction approaches to MS treatment with disease modifying therapies.

KEY FINDINGS:

- Approximately 930,000 patients in Komodo's Healthcare Map™ had two or more claims for MS between January 2016 and June 2023.
- An escalation treatment regime was utilized almost as often as an induction regime to deliver disease modifying therapies (DMTs) (48% vs. 52%).
- Nearly three in four patients (74%) undergoing an escalation approach remained on a recommended lower-efficacy drug for at least two years.
- Patients on an induction treatment regime were 15% more likely to be commercially insured than those on an escalation regime and 35% more likely to be male.

EXECUTIVE SUMMARY:

Experts agree that early treatment with a disease-modifying therapy (DMT) can slow the progression of multiple sclerosis (MS) and reduce the number of relapses. However, there is no consensus on the best approach to treatment, and there is no standard protocol for DMT selection. In cases of relapsing-remitting multiple sclerosis (RRMS) — the most common form of MS — providers generally advocate for one of two strategies: "escalation" or "induction" (also referred to as "early-intense"). An escalation approach begins with lower-risk and lower-efficacy DMTs, escalating if needed, while an induction approach starts with higher-risk, higher-efficacy medications.

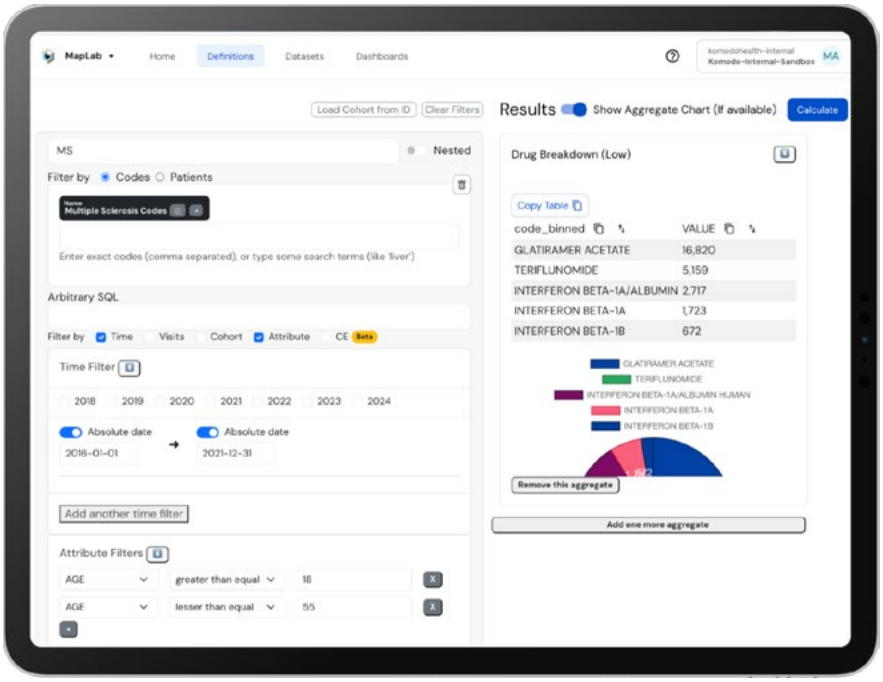
Komodo's analysis assessed the use of the top recommended DMTs for RRMS in both treatment regimes. As highlighted in our recent "Fast Facts," newly diagnosed MS patients who undergo either regime represent a wide variety of patient-specific considerations and treatment journeys. Here, we expand that snapshot to dive deeper into the data on escalation and induction approaches to treatment. As clinical research evolves, this analysis highlights the current state of affairs for the treatment of newly diagnosed MS.

METHODOLOGY:

This patient journey analysis used Komodo's Healthcare Map™, the industry's largest and most complete database of de-identified real-world patient journeys in the U.S. MS prevalence rates were calculated among medically insured patients of all ages in the Map using ICD-9-CM and ICD-10-CM codes.* Patients with established MS — defined as any patient with two or more MS-related visits within a 180-day period — were included in this rate. DMT treatment rates were calculated for newly diagnosed adult patients between ages 18 and 55. A new diagnosis of MS was defined as patients with no prior MS diagnosis who had two or more MS-related visits within six months. Patients were not filtered for RRMS diagnostic

criteria, but those who underwent either of the two DMT treatment regimes (escalation or induction) are likely to have RRMS. DMTs were defined using National Drug Codes of recommended agents listed by UpToDate and categorized as high efficacy, intermediate efficacy, and lower efficacy.** It should be noted that the classification of high-efficacy DMTs can vary depending on specific clinical guidelines and updates in medical research.

DMT treatments were tracked for two years following an MS diagnosis. Patients who were initially prescribed a lower-efficacy DMT after diagnosis were included in the escalation treatment regime cohort. Patients who were initially prescribed a high-efficacy DMT with no prescription for lower- or intermediate-efficacy DMTs were included in the induction cohort.



This analysis was produced using Komodo's MapLab™ solution, which rapidly generates high-value insights and leverages out-of-the-box healthcare-specific analytics on a unified platform. We used the following MapLab templates, which create easily digestible patient breakdowns using key variables: Incidence and Prevalence to explore the number of patients for a given time frame; Cohort Report to find proportions of patients by gender, age, payer channel, and prescribed drugs; and Patient Event Pathways to understand the sequence and timing of events experienced by patients from diagnosis through treatment. Additional binning criteria were added to drug breakdowns to group drugs into specific lower-, intermediate-, and high-efficacy DMT categories.

RESULTS:

Approximately 930,000 patients in Komodo's Healthcare Map had two or more claims for MS between January 2016 and June 2023.

Because MS is sometimes misdiagnosed, prevalence can be difficult to quantify accurately, as demonstrated by the wide range of figures in previously published literature. Most estimates since the 1970s have hovered around 400,000 U.S. patients; however, more recent research suggests the number of patients living with MS is at least twice that. Komodo identified likely MS patients based on those with two or more health claims* for MS in that time period. Among the patients identified in this analysis, the five most common symptoms were: fatigue (47%), weakness (42%), dizziness (32%), skin tingling (29%), and constipation (29%).

An escalation treatment regime was utilized almost as often as an induction regime for the delivery of DMTs.

Among patients treated with either an escalation or induction regime, 48% underwent an escalation approach and 52% underwent an induction approach.

Patients undergoing an escalation regime were initially treated with a recommended lower-efficacy DMT: glatiramer acetate (63%), teriflunomide (19%), or interferon beta-1a/albumin human (10%). Patients undergoing an induction regime were initially treated with a recommended high-efficacy DMT: ocrelizumab (63%), natalizumab (34%), or ofatumumab (5%).

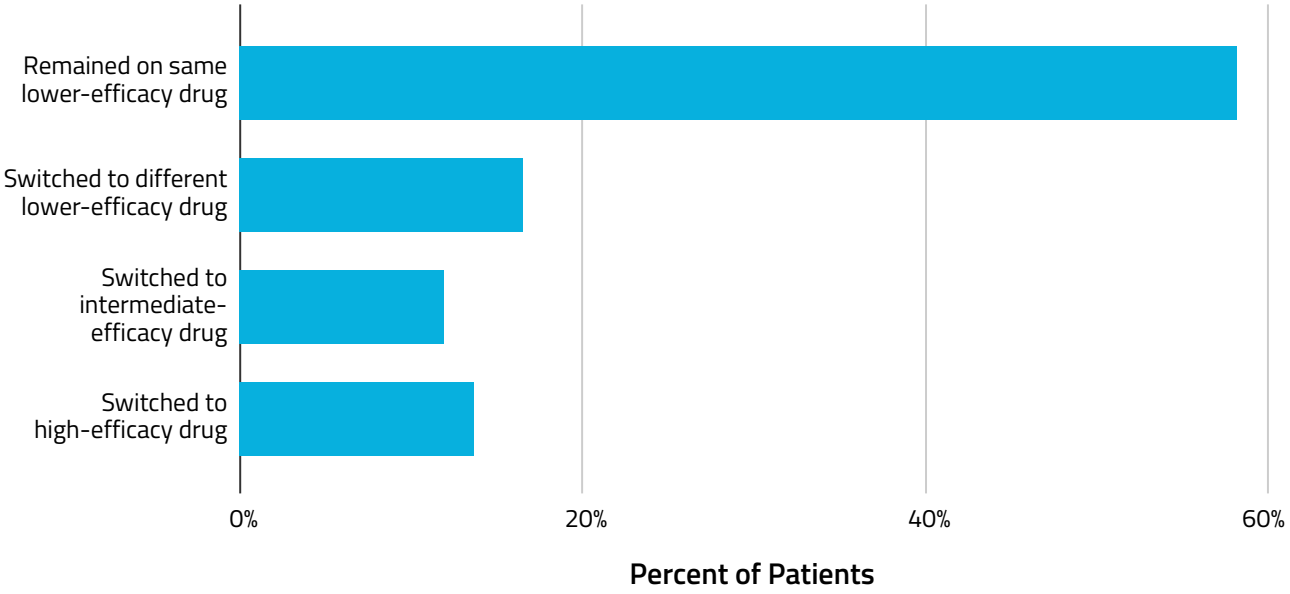
Among escalation patients, 74% remained on a lower-efficacy drug for at least two years.

This included patients who remained on the same lower-efficacy drug exclusively for two years following initial treatment

(58%) and those who switched to another lower-efficacy drug (16%). During the same time period, 26% of escalation patients switched to a recommended intermediate- (12%) or high-efficacy (14%) drug.

Of those patients who switched from a lower- to an intermediate- or high-efficacy drug, 29% switched within zero to six months, 54% switched within six months to one year, and 87% switched within one to two years. Patients who were prescribed a recommended intermediate-efficacy drug received dimethyl fumarate (70%), fingolimod hcl (26%), or diroximel fumarate (13%).

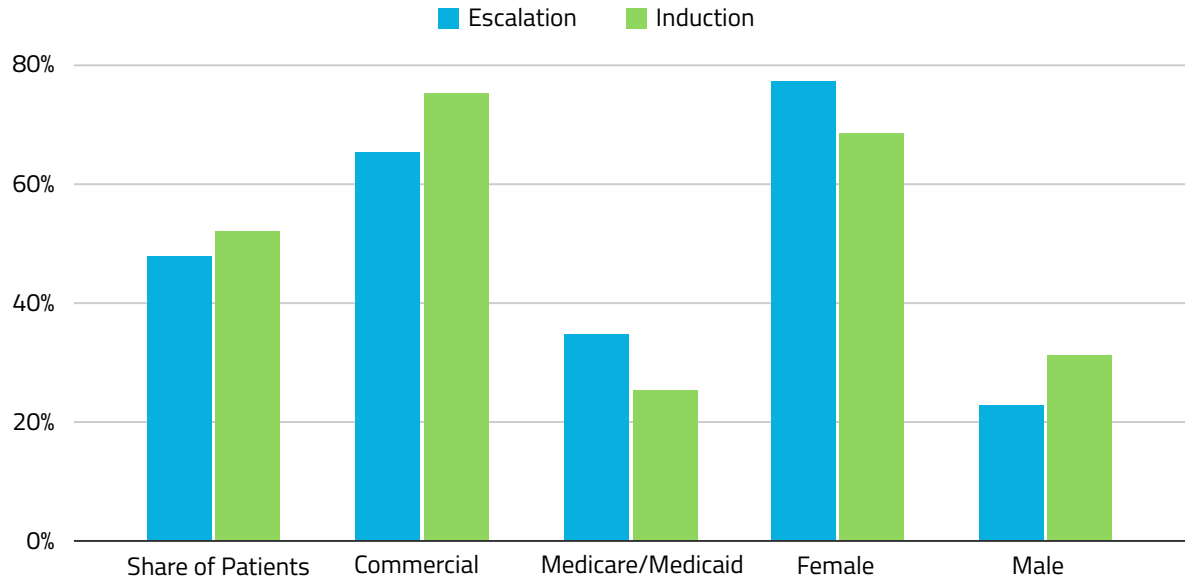
DRUG SWITCHES AMONG ESCALATION PATIENTS



Patients on an induction treatment regime were 15% more likely to be commercially insured than those on an escalation regime and 35% more likely to be male.

Among escalation patients, 65% were commercially insured, compared with 75% of patients on an induction treatment regime. Among patients on an escalation treatment regime, 77% were female and 23% were male, compared with 69% and 31% of patients on an induction treatment regime.

PATIENTS: ESCALATION VS. INDUCTION



DISCUSSION:

This analysis assessed the use of top recommended DMTs for RRMS, the most common form of MS, finding a near-even distribution among patients undergoing either an escalation or induction approach to treatment. The use of higher-risk, high-efficacy DMTs has historically been limited to those with highly active disease and a prognosis that suggests a more severe disease course. However, more recent **research suggests** that higher-potency DMTs may offer improvements earlier in disease progression and lower relapse rates. Given the diverse nature of MS and the fact that most individuals initially exhibit milder manifestations of it, the conservative approach may forfeit a window of opportunity for optimal disease control in some patients. Decisions on approach are influenced by such factors as provider education, concerns about side effects, risk tolerance, cost, the need for stringent monitoring with high-efficacy DMTs, and perceived severity of disease. Ongoing **clinical trials** are expected to further inform treatment guidelines for RRMS, balancing efficacy, safety, and patient quality of life.

This analysis found a higher likelihood that commercially insured patients would receive induction treatment than patients on Medicare and Medicaid. This likely reflects underlying socioeconomic disparities and drug cost considerations, as higher-potency drugs tend to cost more. Men were also more likely to receive induction treatment, which may reflect certain gender-based disparities such as provider bias, differences in patient **self-advocacy**, and **risk tolerance**. It may also predominantly reflect the tendency for men to be **diagnosed with MS at more advanced** stages and have a worse prognosis compared to their female counterparts.

These findings underscore the evolving landscape and complexity of managing RRMS and emphasize the need for more research to support a nuanced understanding of patient-specific factors in guiding treatment decisions. Further research should include a comprehensive list of DMTs, evidence of disease activity by treatment type, and patients across varying degrees of disease severity at diagnosis.

As early treatment decisions have significant long-term impact for patients, detailed insights and up-to-date snapshots of MS patient journeys offer an important perspective on the current state of patient care as research remains ongoing. Komodo's near real-time real-world data, combined with tech-enabled analytics, offers the industry's most complete, accurate, and timely view of patient journeys. As our understanding of MS treatment continues to evolve, provider and patient education is crucial to incorporate recent research into treatment decisions and to maximize informed consent. Patients should be supported in weighing regime-specific side effects, costs, monitoring requirements, and current evidence for risks and benefits in the context of their unique situations and goals. Together, these initiatives will optimize patients' outcomes as we move toward our shared goal of reducing the burden of disease.

** MS diagnosis codes: ICD-9: 340, ICD-10: G35*

*** High-efficacy DMTs included intravenous natalizumab, intravenous ocrelizumab, and subcutaneous ofatumumab. Intermediate-efficacy DMTs included oral fumarates (dimethyl fumarate, diroximel fumarate, and monomethyl fumarate) and oral sphingosine 1-phosphate receptor (S1PR) modulators (fingolimod, siponimod, ozanimod, or ponesimod). Lower-efficacy DMTs included oral teriflunomide, intramuscular recombinant human interferon beta-1a, subcutaneous recombinant human interferon beta-1a, subcutaneous pegylated recombinant human interferon beta-1a, subcutaneous recombinant human interferon beta-1b, and subcutaneous glatiramer acetate.*

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About Komodo Health

Komodo Health builds groundbreaking software solutions powered by our Healthcare Map™ — the industry's largest and most comprehensive database of real-world, patient-level data. With access to data from over 330 million patients, Komodo Health's next-generation analytics make it easy to unlock meaningful insights and create more cost-effective, value-driven solutions. We help stakeholders in Life Sciences, patient advocacy groups, and healthcare payers and providers answer healthcare's most complex questions in our mission to reduce the global burden of disease.