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Shifting from the treat-to-target to the early highly effective treatment approach in patients with multiple sclerosis – real-world evidence from Germany

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Steffeni Papukchieva, Ann-Sophie Stratil, Maria Kahn, Nils-Henning Neß, Maike Hollnagel-Schmitz, Vivien Gerencser, Julia Rustemeier, Markus Eberl, Benjamin Friedrich and Tjalf Ziemssen

Abstract

Background: While evidence highlights the effectiveness of initiating disease-modifying therapy with a high-efficacy medication for multiple sclerosis (MS) patients with poor prognostic factors, it remains unclear whether this approach has been adopted by a broad range of MS providers in Germany yet.

Objective: To assess the adoption of the early highly effective treatment (EHT) compared to the treat-to-target treatment approach with the option of escalating treatment efficacy over time in Germany based on real-world evidence data.

Design: Patient-level pharmacy dispensing data from the Permea platform were analysed from 2020 to 2022.

Methods: In total, 29,529 therapy beginners (>18 years) were included to analyse shifts in treatment approaches over time and switching behaviour. Medication classification adhered to the German Society of Neurology guidelines and designated fumarates, glatiramer acetate, teriflunomide and interferons as low-efficacy category 1 medications; cladribine and S1P-modulators as medium-efficacy category 2 medications; and alemtuzumab, natalizumab, ocrelizumab, ofatumumab and rituximab (off-label) as high-efficacy category 3 medications.

Results: Our results show that 70.0% of patients redeemed their first prescription for category 1 medication, 16.3% for category 2 and 13.7% for category 3 medications. The proportion of prescriptions filled shifted from 2020 to 2022 with a decrease of 14.7% for category 1 drugs and an increase of 12.5% for category 3 drugs. 93.2% of patients stayed on their initially prescribed medication category. 3.2% of category 1 and 3.7% of category 2 therapy beginners escalated to category 3 medication. 3.4% of category 3 medication users de-escalated their treatment to category 1 or category 2.

Conclusion: While most individuals started their treatment according to the treat-to-target approach and remained on their initially prescribed medication category, there has been a steadily increasing shift towards the EHT approach since 2020. These insights demonstrate that, while not officially recommended by German guidelines, MS providers increasingly adopt the EHT approach.

Keywords: early high-efficacy treatment, treatment escalation, multiple sclerosis, real-world evidence, treat-to-target

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Correspondence to:
Benjamin Friedrich
Temedica GmbH, Landsberger Straße 300, 80687 München, Munich, Germany
benjamin.friedrich@temedica.com

Steffeni Papukchieva
Ann-Sophie Stratil
Maria Kahn
Markus Eberl
Temedica GmbH, Munich, Germany

Nils-Henning Neß
Maike Hollnagel-Schmitz
Vivien Gerencser
Julia Rustemeier
Hexal AG, Holzkirchen, Germany

Tjalf Ziemssen
Center of Clinical Neuroscience, Department of Neurology, University Hospital Carl Gustav Carus, Dresden University of Technology, Dresden, Germany

Introduction

Multiple sclerosis (MS) is a chronic and progressive neurological autoimmune disease affecting the central nervous system, defined as a pathophysiological mixture of neurodegeneration and neuroinflammation.[1,2] MS is one of the most common neurological diseases worldwide, affecting approximately 2.8 million people across the globe in 2020.[3,4] In Germany, more than 280,000 people had an MS diagnosis in 2019, and the condition may have a profound impact on the quality of life and employment.[5,6]

Over the past 25 years, the treatment and management of MS have changed significantly.[7] Recently, the optimal treatment approach for MS is being revised with a growing emphasis on personalized treatment approaches dependent on a patient's age, individual preferences, disease activity and progression.[8] However, a comprehensive strategy for personalized MS treatment practice and treatment algorithms based on prognostic factors and treatment response is still lacking.[8,9] Besides maintaining patients' quality of life, a frequently proposed goal of disease-modifying therapy (DMT) is to achieve no evidence of disease activity (NEDA) within a defined timeframe as indicated by relapse occurrences, disability progression or the presence of new or enlarged T2 lesions or gadolinium-enhancing inflammatory lesions.[5,10] To achieve this, traditionally, treatment is initiated with lower-efficacy treatment and only proceeds to higher-efficacy treatment if the ongoing approach fails.[5] This treat-to-target approach has been shown comparatively safe and effective in reducing annual relapse rate (ARR), inflammatory activities and disability progression.[11] A growing body of evidence emphasizes the importance of prompt intervention following diagnosis, alongside the early optimization of treatment when the disease remains active despite treatment with DMTs.[12,13] At the core of this approach lies the 'window of opportunity', where research has demonstrated that treatment is most effective during the initial stages of the disease, particularly when patients are younger and exhibit more pronounced clinical and magnetic resonance imaging (MRI) and biomarker-detected inflammatory activity, and when they show other poor prognostic factors, for example, a high relapse rate or short time intervals between first and second relapses.[8,14] However, it has also been associated with an increased risk for adverse events including increased risk of hematologic abnormalities, infections, malignancy, secondary autoimmunity, neurovascular events and teratogenicity.[15–17] Treating MS patients with high-efficacy forms of medication early after diagnosis (early highly effective treatment, EHT) has shown higher effectiveness in terms of achieving NEDA, delayed relapses, lower levels of disability after onset and lower risk of transitioning to secondary progressive MS (SPMS) compared to initiating treatment with low-efficacy medications.[13,15,18–26] These insights are primarily based on observational studies. Results from randomized controlled trials (RCTs) assessing the effectiveness of the EHT approach will only be available beyond 2025.[5] High-efficacy medication often also requires less frequent administration, making it a preferred option regarding patient tolerance and adherence.[1] Cost–benefit considerations of starting MS patients on high-efficacy drugs showed that higher costs in EHT are compensated by lower costs for patient care and productivity loss.[27]

Despite this evidence and a growing number of experts advocating this approach as part of personalized treatment options for MS, treatment strategies still differ substantially between countries. For example in Denmark, the predominant practice is for patients to initiate treatment with a conventional first-line DMT, while one-third of Swedish patients start their treatment with a highly effective DMT.[28] The 2023 German guideline for the treatment of MS follows the treat-to-target approach, where patients receive medications of different efficacy levels based on disease activity, and mentions the EHT approach as a recent approach of interest while criticizing the lack of prospective randomized studies confirming its effectiveness.[5]

It is unclear whether the EHT approach has reached a broad range of MS patients yet. Our real-world evidence analysis of German prescription sales data for MS medication presents the first insights into whether the EHT approach is becoming increasingly more relevant in Germany and delivers valuable insights into patient care reality.

Methods

Data source and collection of German prescription sales data

The data for this analysis were provided by the Permea platform (Temedica GmbH, Munich,

Germany) and encompasses the patient-level pharmacy dispensing data from 8246 pharmacies across Germany, covering approximately 44% of community pharmacy dispensing in Germany. All data related to the treatment of MS were collected between January 2019 and December 2022. The data were stored in the Permea platform in a General Data Protection Regulation (GDPR) compliant manner, and no personal information that might allow the identification of individuals was revealed. The age of the individual was only available if there was a minimum of seven persons related to the data source.

Data processing and analysis

A total of 785,414 transactions related to MS medication were observed in the period from 2019 to 2022. Only individuals over the age of 18 and individuals who redeemed at least two prescriptions with MS-specific DMTs during the observation period were included in this analysis. Records without prescription dates were excluded. To approximate that only new therapy beginners were included in the dataset, we introduced a 'cleaning' period of 1 year. Specifically, we excluded all individuals in the observation period of 2020–2022 who had filled a prescription for a DMT in the year 2019, resulting in 29,529 unique individuals with 215,354 DMT purchases. Medication categories 1, 2 and 3 were assigned to each international non-proprietary name (INN) based on the German Society of Neurology (DGN) classification of drugs.[5] The classification is based on the relative efficacy of drugs in reducing the ARR. Drugs assigned to category 1 (dimethyl fumarate, diroximel fumarate, glatiramer acetate, teriflunomide, interferon beta-1a, interferon beta-1b, peginterferon beta-1a) are recommended when disease activity is low and show a relative reduction of ARR of 30–50% compared to placebo. Category 2 (cladribine and S1P-modulators fingolimod, ozanimod, ponesimod and siponimod) and category 3 [alemtuzumab, natalizumab, ocrelizumab, ofatumumab and rituximab (off-label)] medications are both indicated for highly active MS and show a relative reduction of ARR of 50–60% and >60% compared to placebo, respectively. For this analysis, category 3 medications were considered high-efficacy medications. The data were further processed and analysed with Python 3.9. Statistical tests were conducted with Prism 9.3.1. Figure 3(a), (c) and (f) were generated using Sankeymatic. χ^2 tests were performed to detect significant differences in the relative frequencies over time. A p value less than 0.05 was considered statistically significant.

Therapy shift over time. To analyse the shift over time, therapy beginners were grouped based on the date of medication purchase into 2020 (1 January 2020–31 December 2020), 2021 (1 January 2021–31 December 2021) and 2022 (1 January 2022–31 December 2022). Differences were calculated based on the proportion of patients who received a prescription for medications of category 1, 2 or 3.

Medication switches. To analyse the switch between medication categories and selected INNs, we looked at the first and second prescriptions of all therapy beginners between 2020 and 2022 based on INNs. A therapy switch was defined as a customer who filled a prescription of a different INN than the previous INN. The average number of days until the switch to a different INN was calculated as the time between the first prescription sales dates.

Results

MS therapy approach is shifting

To understand whether the approach to treating MS patients changed over time, we analysed a total of 29,529 individuals who received a prescription for their first DMT between 2020 and 2022. As seen in Figure 1(a), for the whole observation period, 70.0% of patients received a prescription for a drug from category 1, of which dimethyl fumarate (33.3%) and glatiramer acetate (24.7%) accounted for the largest proportions. 16.3% of patients started on a category 2 medication, of which fingolimod (48.2%) and siponimod (20.0%) were the most prescribed medications. 13.7% of all patients purchased a category 3 medication. In this category, ocrelizumab (39.1%) and natalizumab (35.5%) accounted for the largest proportions of all DMT sales. Share of INNs among all therapy beginners is found in Supplemental Figure S1.

Between 2020 and 2022, the proportions of patients starting with medication of category 1 declined from 75.3% (2020), 68.5% (2021) to 60.6% (2022) representing a 14.7% decrease over 3 years [Figure 1(b)]. The proportion of

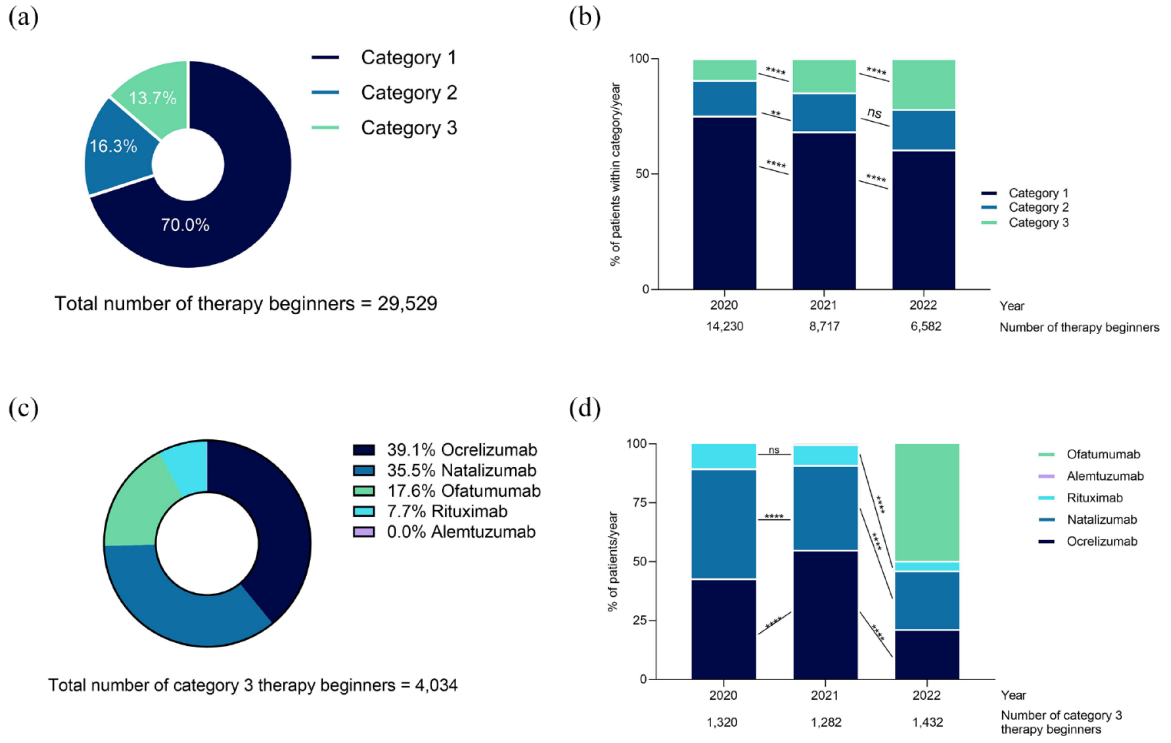

Figure 1. MS therapy approach shifted over time. From 1 January 2020 to 31 December 2022, data from 29,529 individuals were analysed based on their first MS-specific prescription medication. Proportions were calculated according to DGN classification of MS medication: category 1 (dimethyl fumarate, diroximel fumarate, glatiramer acetate, teriflunomide and interferons), category 2 (cladribine, S1P-modulators) and category 3 (alemtuzumab, natalizumab, ocrelizumab, ofatumumab and rituximab). (a) Proportion of medications over the entire observation period by medication category. (b) Therapy shift over time by medication category. The distribution of each first prescription medication within categories 1, 2 and 3 was calculated for each calendar year. (c) The proportion of category 3 medications over the entire observation period by INN. (d) Therapy shift over time for category 3 medication. The distribution of each first prescription medication within category 3 by INN was calculated for each calendar year.
$^{**}p < 0.01$, $^{****}p < 0.0001$.
DGN, German Society of Neurology; INN, international non-proprietary name; MS, multiple sclerosis; ns, not significant.

patients purchasing medications of category 2 increased by 2.2% over 3 years, from 15.4% (2020), 16.8% (2021) to 17.6% (2022). In 2020, 9.3% of all patients who purchased DMTs for the first time purchased category 3 medication. The proportion increased to 14.7% in 2021 and 21.8% in 2022, representing a total increase of 12.5% over 3 years. Furthermore, we also assessed which INN was most prevalent within the group of individuals who started therapy with a category 3 medication in each calendar year. The proportions of individuals starting with ocrelizumab first increased by 12.2% in 2021 and then decreased by 33.7% in 2022 [Figure 1(d)]. Proportions of natalizumab as a first-time prescription decreased by 10.7% in 2021, and another 11.1% in 2022. Rituximab decreased by 1.7% in 2021 and another 4.7% in 2022. Alemtuzumab was only used in 0.2% of category 3 therapy beginners in 2021. The share of category 3 therapy beginners starting their treatment with ofatumumab was 49.7% after market introduction in 2022.

Share of category 3 therapy beginners varies across age and regions

We assessed the distribution of age groups among therapy beginners for each respective medication category. 8.4% of category 3 therapy beginners were 18–25-year-olds compared to 6.3% and 6.9% of category 1 and 2 therapy beginners, respectively. 6.8% of category 3 therapy beginners were 66+-year-olds compared to 4.1% and 3.3% of category 1 and 2 therapy beginners, respectively [Figure 2(a)]. Within category 3, rituximab was notably prescribed as

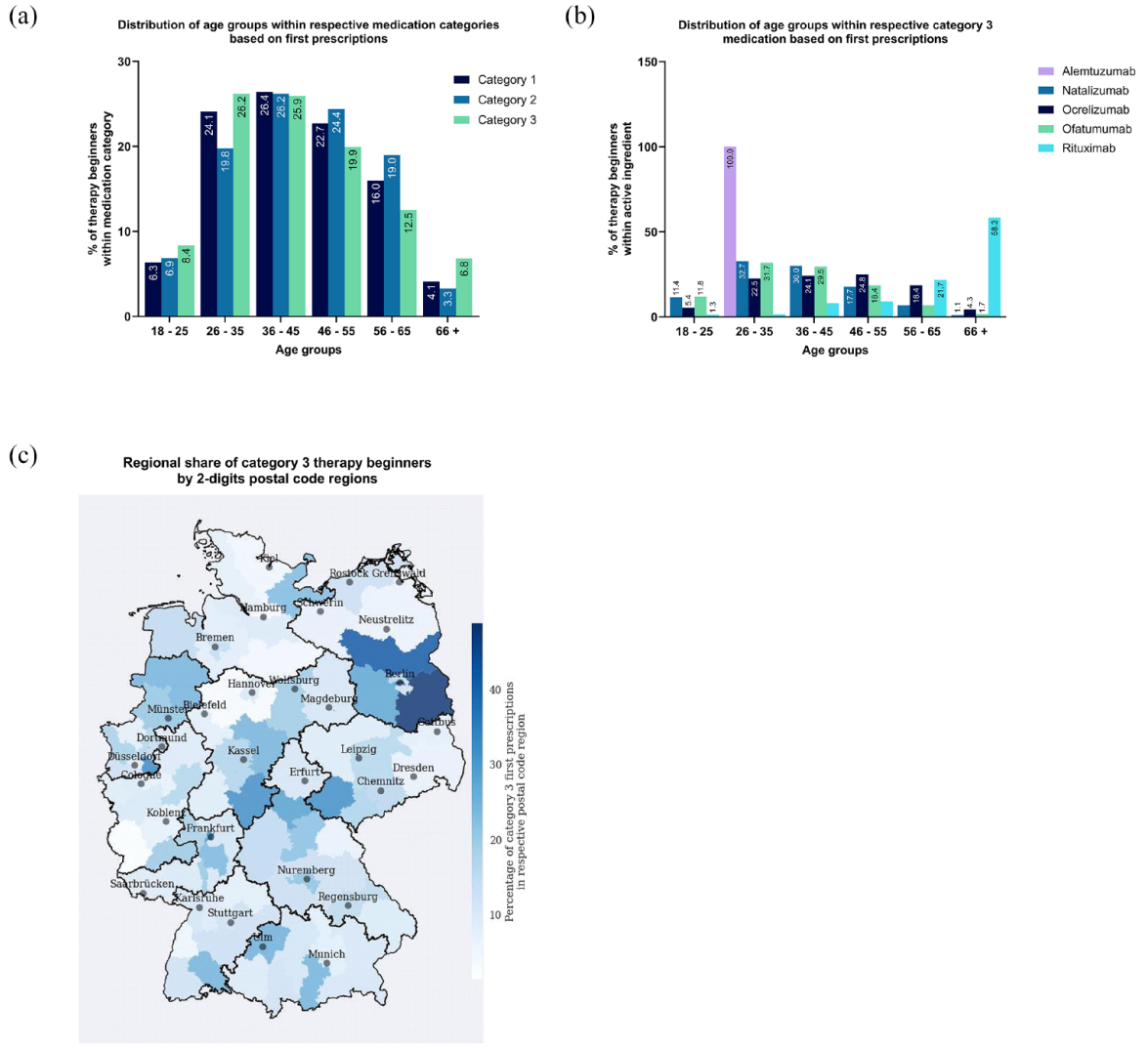

Figure 2. (a, b) Age distribution of first-time DMT prescriptions. Age distribution of therapy beginners at their first prescription by (a) medication category and (b) INN of category 3. (c) Regional distribution of first-time DMT prescriptions. The distribution of therapy beginners who started on category 3 medications was calculated for each two-digit postal code region of the pharmacy where the purchase was processed. (c) Share of category 3 therapy beginners among all therapy beginners by two-digit postal code region.
DMT, disease-modifying therapy; INN, international non-proprietary name.

the first medication to older age groups, while natalizumab and ofatumumab were primarily prescribed to younger patients. Alemtuzumab was only prescribed to patients between 26 and 35 years but only made up 0.01% of all prescriptions ($n = 2$) [Figure 2(b)].

To assess whether the choice to initiate patients on category 3 medication was distributed evenly across regions, we estimated the share of category 3 therapy beginners among all therapy beginners for each one-digit postal code [Supplemental Figure S2(a)] and two-digit postal code regions [Figure 2(c)]. Assessing one-digit postal code regions, between 10.1% (postal code 5, includes Cologne) and 30.6% (postal code 1, includes Berlin) of therapy beginners started on category 3 medication [Supplemental Figure S2(a)]. We also assessed the distribution of therapy beginners on medication category 3 INNs by one-digit postal code region, showing that the choice of which category 3 DMT was prescribed also differed between regions [Supplemental Figure S2(b)].

Therapy journey

To gain a better understanding of the therapy journey in MS patients, we first analysed how consistently and for how long patients persisted on their first prescribed therapy during our observation period. As seen in Figure 3(a), most therapy beginners stayed on the medication category they had started on. Among the 29,529 therapy beginners, 93.2% stayed on their first prescribed respective medication category (84.2% did not switch from the first prescribed DMT) and 6.8% switched to another medication category throughout the observation period [Figure 3(a)]. 92.4% of category 1 therapy beginners stayed on category 1 medication (80.8% did not show a switch to another DMT and 11.6% first switched to another category 1 medication). The remaining 7.6% escalated to category 2 (4.3%) and category 3 (3.2%) DMTs after an average of 411 [standard deviation (SD) 247] days and 441 (SD 245) days, respectively [Figure 3(b)]. 93.6% of category 2 therapy beginners stayed on category 2 medication (91.1% did not show a switch from their first INN, 2.6% first switched to another category 2 INN). 2.7% de-escalated to category 1 after an average of 258 (SD 243) days and 3.7% escalated to category 3 after an average of 457 (SD 252) days. 96.6% of category 3 therapy beginners stayed on category 3 medication (93.4% did not show a switch to another INN and 3.2% first switched to another category 3 medication). The remaining 3.4% de-escalated either to category 1 DMTs (1.7%) or category 2 DMTs (1.7%) after an average of 191 (SD 216) days and 409 (SD 246) days, respectively.

Next, we wanted to understand switching behaviour among patients who changed medication categories as the first switch. Among the 847 patients [Figure 3(c) and (e)] who switched to category 3 from category 1 and 2, most patients previously took fumarates (30.9%), followed by glatiramer acetate (22.0%) and S1P-modulators (18.2%) and switched primarily to ofatumumab (51.2%) and natalizumab (26.1%). Before switching to category 3 medication, patients stayed the longest on cladribine for 558 (SD 234) days, followed by teriflunomide for 477 (SD 237) days [Figure 3(d) and (f)]. It took patients the longest to switch to ofatumumab [502 (SD 246) days], followed by ocrelizumab [427 (SD 234) days]. Among the 136 patients [Figure 3(c) and (e)] who switched from category 3 to category 1 and 2, the largest proportion switched from natalizumab (65.4%), followed by ocrelizumab (22.8%) and ofatumumab (11.8%) and primarily to S1P-modulators (29.4%), followed by fumarates (22.1%) and cladribine (21.3%). Before switching to category 1 and 2 medications, patients stayed the longest on natalizumab for 346 (SD 259) days, followed by ocrelizumab for 283 (SD 253) days. It took patients the longest to switch to S1P-modulators [416 (SD 255) days] and cladribine [399 (SD 237) days] [Figure 3(d) and (f)].

Discussion

Currently, there are over 15 INNs approved for the treatment of MS. Over the past 25 years, the treatment approaches used and disease management in general have changed significantly.[7] In Germany, to date, there is little information available as to what percentage of MS patients are treated according to the treat-to-target *versus* EHT (sometimes referred to as hit hard and early) therapy approach. Previous studies have shown that about one-quarter of patients qualify for therapy escalation to a high-efficacy medication in line with the treat-to-target approach and that there has been a trend towards early treatment optimization.[29,30] In our analysis, we focused on understanding how and to what extent the recently defined EHT approach has been adopted in Germany.

Our data show that overall, more than two-thirds of people used DMTs of mild to moderate efficacy (category 1 and 2) as a first-time prescription. One of the most used drugs of mild efficacy was interferons, which were first approved in 1996.[31] Notably, 3.3% of all therapy beginners initiated treatment with siponimod, a moderate efficacy drug approved for active SPMS.[32] This seems unexpected, given the anticipation of prior treatment in the context of a secondary progressive disease course. However, in recent phase III trials, 22–27% of SPMS patients had not received any DMT treatment prior to study enrolment.[33] Natalizumab was approved in 2006 as the first high-efficacy (category 3) DMT,[34] followed by others in the following years. Although a substantial proportion of people began their MS therapy with mild to moderate medication, the proportions changed over time. From 2020 to 2022, the proportion of patients who started their therapy on a category 1 drug decreased by 14.7%, whereas the percentage of patients starting their therapy with a high-efficacy drug increased by 12.5%

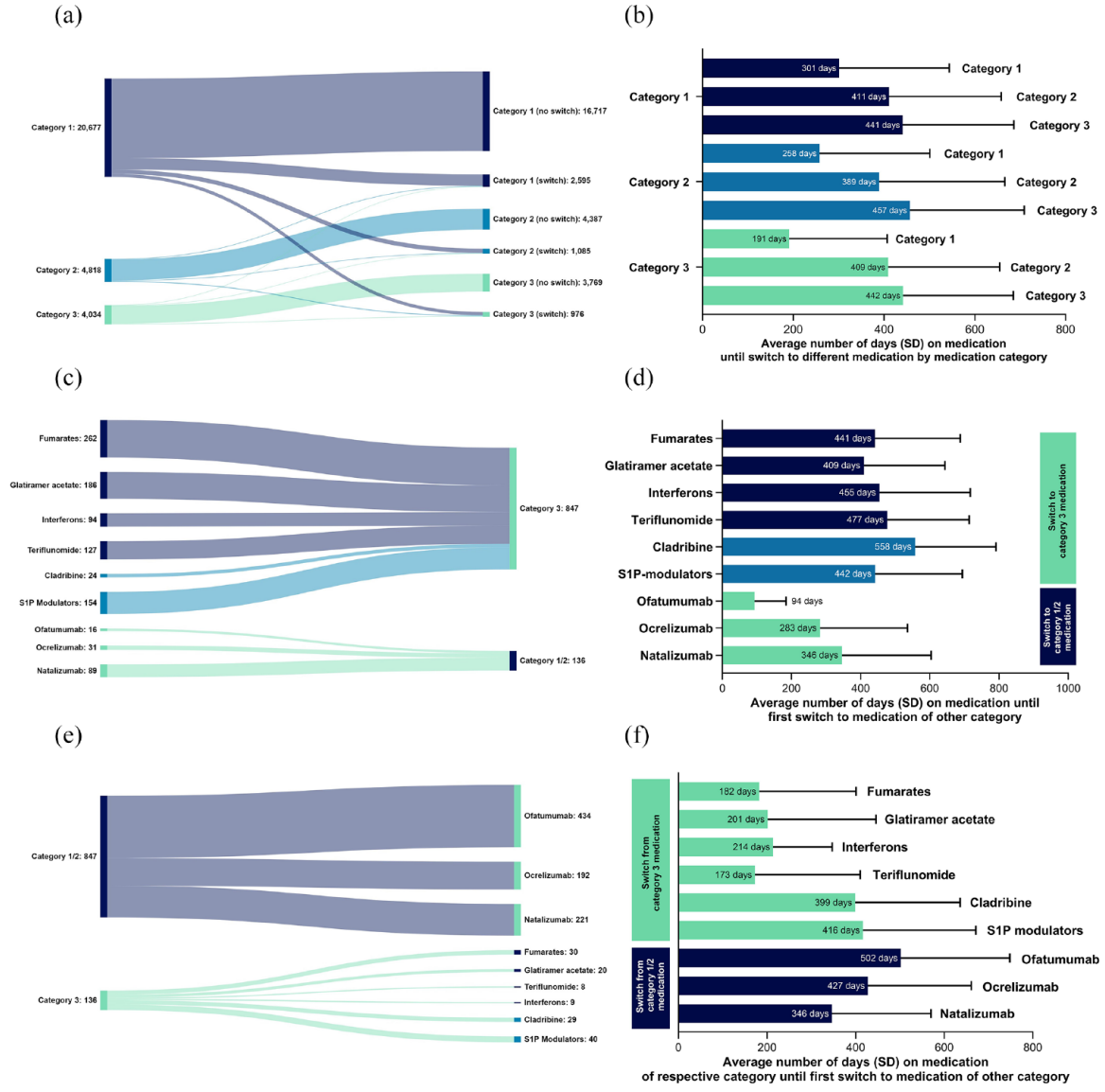

Figure 3. (a, b) Therapy journey. (a) A number of patients who maintained their first prescribed medication based on INN or had a first medication switch between the first two prescriptions of INNs grouped by medication category. (b) The average number of days until the switch between the first two prescriptions of INNs grouped by medication category. (c–f) Medication switches between categories. We selected all therapy beginners who had a first medication switch between the first two prescriptions of differing categories based on INNs. (c) A number of patients switched from their first prescribed INN to another medication category based on INN. (d) The average number of days until the switch from the first prescribed INN to another medication category is based on INN. (e) A number of patients switched from the first prescribed medication category based on INN to an INN of another medication category. (f) The average number of days until the switch from the first prescribed medication category based on INN to an INN of another category.
INN, international non-proprietary name.

indicating that the EHT approach is gradually gaining ground in Germany, with more pronounced adoption in certain regions, mainly around Berlin. While German claims data analyses for 2010–2017[35] and 2012–2019[36] showed that prescriptions for interferons (category 1 medication) decreased over time, the increase in category 3 medication was not yet detectable in the observed periods.

DMT treatment aims to prevent disease activity and accumulation of disability which may, in turn,

lead to a secondary progressive course.[21,37,38] However, this goal does not accurately reflect the current unmet need in MS treatment to address compartmentalized inflammation and, in turn, progression independent of relapse activity.[39] Initiating an effective treatment early on in the disease may reduce relapse rates and the underlying inflammatory process could delay irreversible neurological damage and conversion to SPMS.[40,41] Several observational studies suggest that EHT provides a greater benefit compared to the treat-to-target approach, thereby reducing the risk of developing SPMS and disability accrual, at least in the medium–long term of 5–10 years.[22,23,42–46] The approach is especially recommended for patients with poor prognostic features, but there are also suggestions that EHT might be beneficial for all relapsing-remitting MS patients.[8,17,25] Over the past 25 years, the number of high-efficacy drugs approved for relapsing-remitting MS has increased, with over 10 new medications approved in the last decade.[47] These drugs exert their anti-inflammatory effects through various immunomodulating mechanisms.[48] The most used high-efficacy drugs were ocrelizumab and natalizumab. In phase III trials, both have shown good efficacy concerning relapse rates and disability progression.[15,34,49] Our data show that the proportion of people starting with ocrelizumab increased slightly in 2021 but then dropped by a third in 2022. This is mostly likely due to the approval of ofatumumab in 2021.[50] Since ofatumumab, like ocrelizumab, is an anti-CD20 antibody, it provides comparable efficacy while offering subcutaneous administration,[50] unlike ocrelizumab which requires IV administration every 6 months,[51] typically in a clinic or out-patient centre. Ofatumumab, unlike ocrelizumab, also does not require premedication.[50,51] These may be the reasons many practitioners prefer to prescribe ofatumumab over ocrelizumab. Natalizumab also saw a 20% decrease in first prescriptions between 2020 and 2022, which could also be explained by practitioners shifting to ofatumumab. While both ofatumumab and natalizumab show a good safety profile overall, natalizumab, similarly to ocrelizumab, requires IV administration every 4 weeks,[52] and is associated with the risk of progressive multifocal leukoencephalopathy, which is the main reason patients discontinue the drug.[53] Since rituximab is an off-label MS therapy that requires IV administration every 6 months,[54] it is most likely not prescribed extensively. Alemtuzumab is not indicated as a first-line treatment by the European Medicines Agency.[55] Therefore, it is unlikely for any individuals to initiate MS therapy with alemtuzumab.

The options for patients are broadening and developing towards a more personalized structure, which could be one of the reasons we see a shift towards the EHT approach to treatment. At the same time, the range of treatment options leads to challenges concerning patient preference and adherence. Patient preference is a fundamental part of medication selection.[47] Patients with longer disease duration seem to prefer efficacious therapies and tend to underestimate therapy risks and overestimate benefits.[56,57] In some countries, the cost or coverage of a certain therapy might pose a challenge in administering an expensive high-efficacy drug. Globally, 72% of countries state there are barriers to accessing DMTs, mainly due to the cost to the government, healthcare system or insurance provider.[58] In the United States, over 6% of patients do not receive treatment due to financial concerns and insurance barriers.[59] In Germany, the insurance system does not impose restrictions on the choice of therapy, but there are region-specific systems imposed by the Association of Statutory Health Insurance Physicians that encourage treatment with specific medications, for example, teriflunomide and dimethyl fumarate. Hence, treating physicians would base their treatment recommendation not only on the patient's preference and guideline references alone but also on additional regulations and subjective experiences. This could also be a reason that a substantial proportion of therapy beginners are continuing to start therapy on a mild to moderate drug as shown in our data. Our data also show that especially around the Berlin area, physicians followed the EHT approach more frequently than in other German regions, possibly due to a higher affinity for more innovative treatment approaches. Choosing a specific medication is a multifactorial process and warrants further investigation to better understand therapy choices.

Choosing an escalation path faces other challenges. The most used approach encompasses maintaining the patient on the same DMT until it no longer shows efficacy, tolerability and safety.[60] If these goals are not reached, a therapeutic switch can be considered.[61] A study in 2019 demonstrated that long-term outcomes were more favourable in patients following early intensive therapy *versus* first-line moderate efficacy DMT.[23] Treatment transitions pose an additional

challenge when following the treat-to-target approach. Drugs may be sequenced together too closely, or a therapeutic gap may lead to the loss of nervous system tissue, resulting in potential relapses, MRI activity or disability accrual.[62] Our results show that most patients (>90%) stayed on their initially prescribed medication category and neither escalated nor de-escalated their treatment regimen, which corresponds to findings where most patients were switched between mild to moderate DMTs, and only a small proportion received a subsequent high-efficacy medication.[63] Only 3–4% of category 1 and 2 therapy beginners escalated their treatment to a high-efficacy drug and took an average of 15 months to do so.

A challenge of starting therapy with the EHT approach is the lack of knowledge regarding de-escalation and the question of where patients go after already using high-efficacy medication. Switching from high-efficacy to low-efficacy medications is non-inferior compared to staying on the same medication category regarding relapse rates and disability, but more research is needed.[64] Our results showed that this 'de-escalation' approach is already commonly used but not widely spread: Among category 3 therapy beginners, 3.4% de-escalated their treatment to category 1 or 2 medication and took an average of 6–14 months to do so, respectively. Reasons for switching can vary from non-response or loss of efficacy of current therapy to unbearable side effects or quality of life implications.[63] As variables on comorbidities, relapse rates or adverse events are not included in the dataset, the appropriateness of initial therapy choice and escalating strategies could not be assessed. The comparatively shorter time to de-escalation *versus* escalation might indicate that the de-escalation route is taken due to tolerability issues. The 'de-escalation' approach has been proposed especially for older MS patients who seem to prefer but have shown to benefit less from initiating therapy on high-efficacy medications.[65,66] Our data show that almost 7% of high-efficacy therapy beginners were over 66 years old, while only between 3 and 4% of mild- to moderate-efficacy beginners were in the same age group. The main challenge at present is to understand the long-term implications of the EHT approach as studies show that the mid-term benefits are promising,[22,23,42–45] but long-term outcomes remain unknown. The forthcoming results from the RCTs DELIVER-MS (Determining the effectiveness of early intensive versus escalation approaches for RRMS, NCT03535298) and TREAT-MS (Traditional versus early aggressive therapy for multiple sclerosis trial, NCT03500328) are anticipated to offer additional insights into the efficacy of the EHT approach in comparison to the treat-to-target approach.[5] If these trials demonstrate effectiveness, it may serve as a compelling basis for advocating the integration of the EHT approach into German treatment guidelines and clinical practice.

Limitations

Our data rely on prescription sales data, and due to GDPR, we do not receive information about the coded diagnosis and subtypes of the disease. Since approved MS medications are specifically approved for the disease and only available upon prescription, we are confident that our data represents actual patients. The lack of additional information, especially surrounding the frequency of flare-ups, periods of remission, other types of medications used, comorbidities, etc., limited us from evaluating the suitability of the initial therapeutic approach and escalation strategies. Due to the data structure, we could only analyse the last 3 years of prescription sales data, limiting the possibility of assessing long-term developments. The used dataset covers 44% of community pharmacies and only includes prescriptions of the retail market and not hospitals, thereby limiting the generalizability of our results to all German MS patients.

Conclusion

Real-world evidence data are becoming increasingly important in understanding patient care reality and therapy approaches. While most individuals started their treatment according to the treat-to-target approach and remained on their initially prescribed medication category, there has been a steadily increasing shift towards the EHT approach since 2020. These insights demonstrate that, while not officially recommended by the DGN guideline, MS care providers are increasingly adopting the EHT approach. Further studies and insights are needed to further assess the value of initiating a HET approach early on.

Declarations

Ethics approval and consent to participate

Our study did not require ethical board approval since the data analysed here retrospectively are anonymized prescription sales data.

Consent for publication
Not applicable.

Author contributions
Steffeni Papukchieva: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Ann-Sophie Stratil: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Maria Kahn: Conceptualization; Formal analysis; Methodology; Writing – original draft.

Nils-Henning Neß: Conceptualization; Writing – review & editing.

Maike Hollnagel-Schmitz: Conceptualization; Writing – review & editing.

Vivien Gerencser: Conceptualization; Writing – review & editing.

Julia Rustemeier: Conceptualization; Writing – review & editing.

Markus Eberl: Conceptualization; Writing – review & editing.

Benjamin Friedrich: Conceptualization; Writing – review & editing.

Tjalf Ziemssen: Conceptualization; Writing – review & editing.

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Availability of data and materials
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ORCID iDs
Ann-Sophie Stratil https://orcid.org/0000-0002-8977-6731

Benjamin Friedrich https://orcid.org/0000-0002-2198-9925

Supplemental material
Supplemental material for this article is available online.

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