

Supplementary material

Effectiveness of disease-modifying treatment on spinal cord lesion formation in relapse-onset multiple sclerosis. An MSBase registry study.

Daniel Kreiter, Tomas Kalincik, Raymond Hupperts, Francesco Patti, Daniele Spitaleri, Matteo Foschi, Andrea Surcinelli, Davide Maimone, Bassem Yamout, Samia J. Khoury, Jeannette Lechner-Scott, Serkan Ozakbas, Oliver Gerlach on behalf of the MSBase Study Group

Corresponding Author

Daniel Kreiter

Academic MS center Zuyd, Department of Neurology

Zuyderland MC, Sittard-Geleen, The Netherlands

d.kreiter@zuyderland.nl

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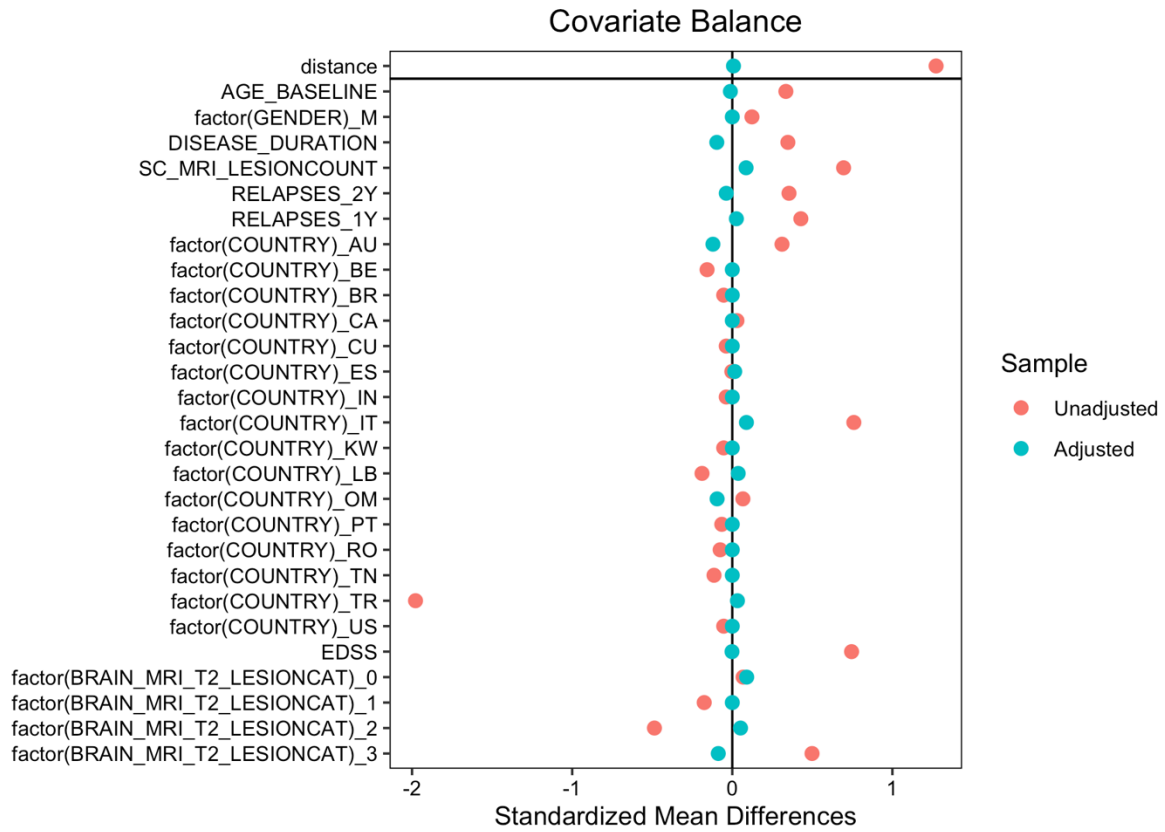
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S1 - Data quality procedure

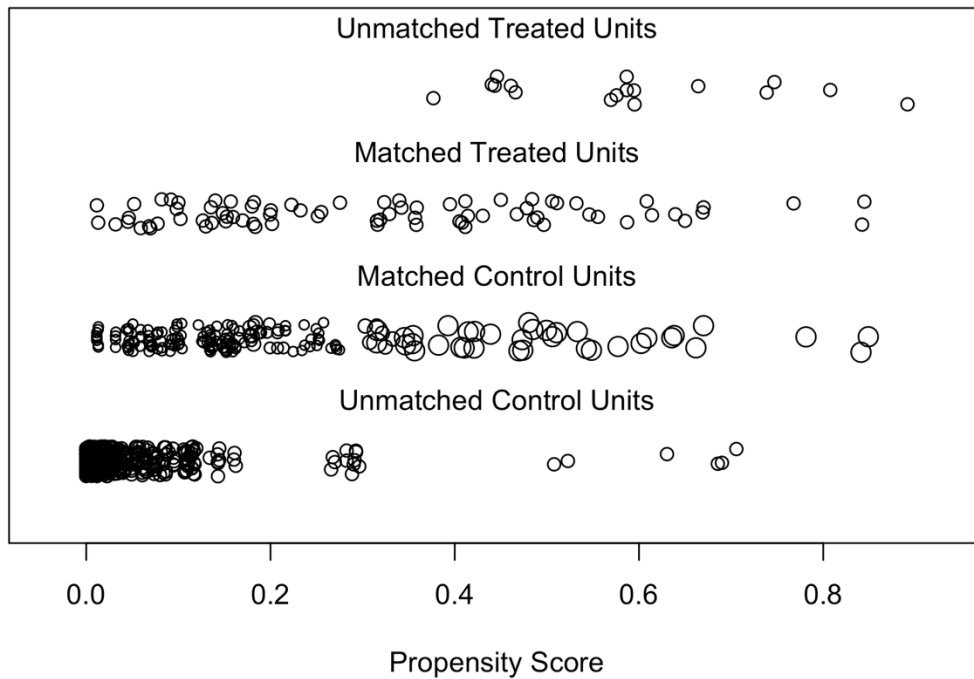
- Duplicate patients were removed.
- Patients with missing date of birth, date of first symptoms and date of diagnosis were excluded.
- Patients with onset dates after MSBase data extraction were removed.
- A logical MS course (e.g. clinically isolated syndrome, relapsing- remitting MS, secondary progressive MS) was assured.
- MRI investigations with insufficient data (e.g. missing information on whether there were new lesions) were removed.
- Duplicate MS relapses, EDSS scores, MRI investigations, visits and treatment entries were merged
- EDSS scores outside the possible EDSS range were removed.
- Relapses occurring within 30 days of each other were merged.
- MS disease modifying therapies were identified and labelled.
- Invalid treatment entries were removed (e.g. start date > end date, initiation after the MSBase data extract date).

S2 - Propensity score matching



Covariate balance before and after matching in the primary analysis.

Distribution of Propensity Scores



Propensity score matching of hDMT and IDMT groups in the primary analysis

S3 - Country of treatment of matched patients

| Characteristic | Unmatched | | | Matched | | |
|----------------|---------------------------|----------------------------|------------------|---------------------------|----------------------------|------------------|
| | hDMT, N = 94 ¹ | IDMT, N = 783 ¹ | SMD ² | hDMT, N = 77 ¹ | IDMT, N = 184 ¹ | SMD ² |
| Country | | | | | | |
| AU | 17 (18%) | 48 (6.1%) | 0.31 | 13 (17%) | 28 (15%) | 0.12 |
| BE | 0 (0%) | 17 (2.2%) | 0.16 | 0 (0%) | 0 (0%) | 0.00 |
| BR | 0 (0%) | 2 (0.3%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| CA | 3 (3.2%) | 21 (2.7%) | 0.03 | 3 (3.9%) | 8 (4.3%) | 0.00 |
| CU | 0 (0%) | 1 (0.1%) | 0.04 | 0 (0%) | 0 (0%) | 0.00 |
| ES | 2 (2.1%) | 17 (2.2%) | 0.00 | 2 (2.6%) | 7 (3.8%) | 0.01 |
| IN | 0 (0%) | 1 (0.1%) | 0.04 | 0 (0%) | 0 (0%) | 0.00 |
| IT | 64 (68%) | 256 (33%) | 0.76 | 52 (68%) | 115 (63%) | 0.09 |
| KW | 0 (0%) | 2 (0.3%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| LB | 3 (3.2%) | 51 (6.5%) | 0.19 | 3 (3.9%) | 10 (5.4%) | 0.04 |
| OM | 1 (1.1%) | 3 (0.4%) | 0.07 | 0 (0%) | 2 (1.1%) | 0.09 |
| PT | 0 (0%) | 3 (0.4%) | 0.07 | 0 (0%) | 0 (0%) | 0.00 |
| RO | 0 (0%) | 4 (0.5%) | 0.08 | 0 (0%) | 0 (0%) | 0.00 |
| TN | 0 (0%) | 9 (1.1%) | 0.11 | 0 (0%) | 0 (0%) | 0.00 |
| TR | 4 (4.3%) | 346 (44%) | 1.98 | 4 (5.2%) | 14 (7.6%) | 0.03 |
| US | 0 (0%) | 2 (0.3%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |

¹Median (IQR); n (%); Mean (SD)

²Standardized mean difference

AU = Australia, BE = Belgium, BR = Brazil, CA = Canada, CU = Cuba, ES = Spain, IN = India, IT = Italy, KW = Kuwait, LB = Libanon, OM = Oman, PT = Portugal, RO = Romania, TN = Tunisia, TR = Turkey, US = United States

S4 - Patient characteristics and treatments for sensitivity analysis (broad caliper, 80% cutoff)

Characteristics of patients included in this sensitivity analysis

| Characteristic | Unmatched | | | Matched | | |
|------------------------------|----------------------------|----------------------------|------------------|----------------------------|----------------------------|------------------|
| | hDMT, N = 116 ¹ | IDMT, N = 917 ¹ | SMD ² | hDMT, N = 113 ¹ | IDMT, N = 441 ¹ | SMD ² |
| Age | 37 (29, 45) | 32 (26, 40) | 0.28 | 37 (29, 46) | 35 (28, 42) | 0.04 |
| Gender | | | | | | |
| F | 78 (67%) | 650 (71%) | 0.08 | 76 (67%) | 303 (69%) | 0.06 |
| M | 38 (33%) | 267 (29%) | 0.08 | 37 (33%) | 138 (31%) | 0.06 |
| EDSS | 2.5 (2.0, 4.0) | 2.0 (1.0, 2.5) | 0.71 | 2.5 (2.0, 4.0) | 2.0 (1.5, 3.0) | 0.08 |
| Baseline brain lesions | | | | | | |
| 0 | 3 (2.6%) | 9 (1.0%) | 0.10 | 2 (1.8%) | 6 (1.4%) | 0.01 |
| 1-2 | 1 (0.9%) | 24 (2.6%) | 0.19 | 1 (0.9%) | 7 (1.6%) | 0.03 |
| 3-8 | 10 (8.6%) | 224 (24%) | 0.56 | 10 (8.8%) | 91 (21%) | 0.07 |
| 9+ | 102 (88%) | 660 (72%) | 0.49 | 100 (88%) | 337 (76%) | 0.05 |
| Baseline spinal cord lesions | 3.0 (1.0, 5.3) | 1.0 (0.0, 2.0) | 0.67 | 3.0 (1.0, 5.0) | 2.0 (1.0, 3.0) | 0.07 |
| Relapses in past year | 1.0 (1.0, 2.0) | 1.0 (1.0, 1.0) | 0.38 | 1.0 (1.0, 2.0) | 1.0 (1.0, 2.0) | 0.07 |
| Relapses in past 2 years | 2.0 (1.0, 2.0) | 1.0 (1.0, 2.0) | 0.32 | 2.0 (1.0, 2.0) | 1.0 (1.0, 2.0) | 0.08 |
| Years since first symptoms | 5.4 (7.1) | 3.2 (5.2) | 0.31 | 5.5 (7.2) | 3.8 (6.2) | 0.06 |
| Follow-up in years | 2.5 (1.6, 3.4) | 3.1 (1.6, 5.9) | | 2.5 (1.6, 3.4) | 3.3 (1.7, 6.2) | |
| Country | | | | | | |
| AU | 22 (19%) | 60 (6.5%) | 0.32 | 21 (19%) | 55 (12%) | 0.02 |

| Characteristic | Unmatched | | | Matched | | |
|----------------|----------------------------|----------------------------|------------------|----------------------------|----------------------------|------------------|
| | hDMT, N = 116 ¹ | IDMT, N = 917 ¹ | SMD ² | hDMT, N = 113 ¹ | IDMT, N = 441 ¹ | SMD ² |
| BE | 0 (0%) | 18 (2.0%) | 0.15 | 0 (0%) | 0 (0%) | 0.00 |
| BR | 0 (0%) | 2 (0.2%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| CA | 3 (2.6%) | 25 (2.7%) | 0.01 | 3 (2.7%) | 16 (3.6%) | 0.02 |
| CU | 0 (0%) | 2 (0.2%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| EG | 0 (0%) | 1 (0.1%) | 0.04 | 0 (0%) | 0 (0%) | 0.00 |
| ES | 2 (1.7%) | 23 (2.5%) | 0.06 | 2 (1.8%) | 14 (3.2%) | 0.04 |
| GR | 0 (0%) | 2 (0.2%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| IN | 2 (1.7%) | 1 (0.1%) | 0.12 | 2 (1.8%) | 1 (0.2%) | 0.07 |
| IT | 76 (66%) | 300 (33%) | 0.69 | 74 (65%) | 261 (59%) | 0.00 |
| KW | 0 (0%) | 2 (0.2%) | 0.05 | 0 (0%) | 0 (0%) | 0.00 |
| LB | 5 (4.3%) | 69 (7.5%) | 0.16 | 5 (4.4%) | 38 (8.6%) | 0.01 |
| OM | 1 (0.9%) | 3 (0.3%) | 0.06 | 1 (0.9%) | 3 (0.7%) | 0.02 |
| PT | 0 (0%) | 4 (0.4%) | 0.07 | 0 (0%) | 0 (0%) | 0.00 |
| RO | 0 (0%) | 5 (0.5%) | 0.08 | 0 (0%) | 0 (0%) | 0.00 |
| TN | 0 (0%) | 10 (1.1%) | 0.11 | 0 (0%) | 0 (0%) | 0.00 |
| TR | 5 (4.3%) | 387 (42%) | 1.87 | 5 (4.4%) | 53 (12%) | 0.01 |
| US | 0 (0%) | 3 (0.3%) | 0.06 | 0 (0%) | 0 (0%) | 0.00 |

¹Median (IQR); n (%); Mean (SD)

²Standardized mean difference

BE = Belgium, BR = Brazil, CA = Canada, CU = Cuba, EG = Egypt, ES = Spain, GR = Greece, IN = India, IT = Italy, KW = Kuwait, LB = Libanon, OM = Oman, PT = Portugal, RO = Romania, TN = Tunisia, TR = Turkey, US = United States

S5 – List of contributors

From Brain and Mind Centre, Sydney, Australia, Michael Barnett

From Barwon Health, University Hospital Geelong, Geelong, Australia, Cameron Shaw

From Monash University, Clayton, Australia, Nevin John

From Box Hill Hospital, Box Hill, Australia, Katherine Buzzard

From Box Hill Hospital, Melbourne, Australia, Olga Skibina

From Westmead Hospital, Sydney, Australia, Justin Garber

From University of Queensland, Brisbane, Australia, Pamela McCombe

From Royal Hobart Hospital, Hobart, Australia, Bruce Taylor

From The Alfred Hospital, Melbourne, Australia, Anneke van der Walt

From The Alfred Hospital, Melbourne, Australia, Helmut Butzkueven

From Royal Brisbane and Women's Hospital, Brisbane, Australia, Pamela McCombe

From CISSS Chaudière-Appalache, Levis, Canada, Pierre Grammond

From Neuro Rive-Sud, Quebec, Canada, Francois Grand'Maison

From Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Canada, Emmanuelle Lapointe

From Galdakao-Usansolo University Hospital, Osakidetza-Basque Health Service, Galdakao, Spain, Jose Luis Sanchez-Menoyo

From Hospital Universitari MútuaTerrassa, Barcelona, Spain, Sarah Besora

From Università di Bologna, Bologna, Italia, Alessandra Lugaresi

From University G. d'Annunzio, Chieti, Italy, Marco Onofri

From University of Florence, Florence, Italy, Maria Pia Amato

From Royal Hospital, Muscat, Oman, Jabir Alkhaboori

From Sultan Qaboos University, Al-Khodh, Oman, Abdullah Al-Asmi

From KTU Medical Faculty Farabi Hospital, Trabzon, Turkey, Cavit Boz

From Bakirkoy Education and Research Hospital for Psychiatric and Neurological Diseases, Istanbul, Turkey, Aysun Soysal

From Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey, Recai Turkoglu

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