**SUPPLEMENTARY DATA**

**Table e-1:** **Study variables.**

|  |  |  |  |
| --- | --- | --- | --- |
| Type of variable | Variable | Units, values | Type |
| Demographic data | Date of birth | Date/time | Date |
| Gender | Males/Female | Binomial |
| Anthropometric data (measured at diagnosis and at 4, 6 and 8 years of age for some patients (n=8) | Weight | Kilograms | Quantitative |
| Height | Meters | Quantitative |
| BMI | Weight(kg)/height(m)² | Quantitative |
| International Obesity Task Force (IOTF) categories | Normal (<25), overweight (between 25 and 30), obesity (>30). | Ordered factor |
| Diagnosis of multiple sclerosis | Age at diagnosis | Date of diagnosis-date of birth expressed in number of years | Duration (quantitative) |
| Brain and spinal lesions at initial MRI | Contrast or no contrast | Binomial |
| Initial cerebrospinal fluid (CSF) analysis | Oligoclonal bands (OCB) | Presence/absence | Binomial |
| Cellularity significant for age according to Bicêtre laboratory standards | Presence/absence | Binomial |
| Proteinorachy | Greater or lower than 0.4 g/L | Binomial |
| Other biological data at the time of diagnosis | CRP level, | Positive/Non positive (considered positive if ≥10 mg/l) | Binomial |
| 25 OH vitamin D level | Normal/anormal (considered normal if ≥30 ng/ml) | Binomial |
| Data on the severity of the disease | Time to second relapse |  | Duration (quantitative) |
| Number of clinical relapses | Total number of relapses counted during the patient's follow-up | Count |
| Annualized relapses rate | Mean number of relapses per year | Estimated by including the duration between two relapses as an offset in the model. |

**Table e-2:** **Reasons for consulting: NNC**

|  |  |
| --- | --- |
| Reasons for consultation | Number of patients |
| anxiety or mild depression without somatic syndrome | 18 |
| social difficulties | 18 |
| psychosomatic disorders | 17 |
| voluntary drug intoxication | 11 |
| non-severe lower respiratory infection | 6 |
| advices | 5 |
| suicide attempts | 5 |
| mental retardation | 4 |
| dermatological pathologies | 5 |
| anemia | 2 |
| behavioral disorder | 2 |
| constipation | 2 |
| domestic accidents | 3 |
| gallstone without cholecystitis | 2 |
| gynecological problems | 2 |
| isolated cough | 2 |
| isolated fever | 2 |
| isolated headaches | 2 |
| nausea | 2 |
| influenza | 1 |
| isolated fatigue | 1 |

**Table e-3:** **Statistical models**. This table represents the generalized additive models that we used to study the effect of children age (smooth term), children type, and sex on BMI (A, full model, in B and C we report the specific contrasts to test for differences between the three children types, for each sex given that the type\*sex interaction of model A was significant). Effects and their interactions are tested with F test anova. Means values (estimates) of the effect are reported in brackets for some effects.

|  |  |  |  |
| --- | --- | --- | --- |
| Factors | F statistics | Df | p-value |
| **(A) BMI as a function of age (smooth term), sex and children type (gam model).** |  |  |  |
| Age (smooth term) | 3088 | 9 | <0.0001 |
| Sex (Girls, Boys) | 4.1 | 1 | 0.04 |
| Children type (POMS, NNC, HC) | 17.3 | 2 | <0.0001 |
| Sex\*Type | 9.1 | 2 | 0.0001 |
| **Submodel BMI (gam model, Boys only, contrasts between the different children types)** |  |  |  |
| Children type (overall difference) | 19.1 | 2 | <0.0001 |
| Children type (NNC < HC) (-0.90) | 11 | 1 | 0.0008 |
| Children type (POMS > HC) (+2.04) | 26.5 | 1 | <0.0001 |
| Children type (POMS > NCC) (+2.9) | 10.1 | 1 | 0.0002 |
| **Submodel BMI (gam model, Girls only, contrasts between the different children types)** |  |  |  |
| Children type (overall difference) | 5.2 | 2 | 0.005 |
| Children type (NNC = HC) | 1.6 | 1 | 0.199 |
| Children type (POMS > HC) (+0.989) | 8.7 | 1 | 0.003 |
| Children type (POMS = NNC) | 0.76 | 1 | 0.399 |
|  | | | |
| (B) **rBMI as a function of children sex and type (gaussian glm model)** | Likelihood ratio Chisquare test | Df | p-value |
| Sex (Girls, Boys) | 1.99 | 1 | 0.15 |
| Children type (POMS, NNC) | 9.15 | 4 | 0.0025 \*\* |
| Sex\*Type | 3.73 | 1 | 0.053 |
| Submodel Children type (POMS > NNC) for boys (+2.95) | 10.2 | 1 | 0.0013 |
| Submodel Children type (POMS, NNC) for girls | 0.58 | 1 | 0.44 |
| Specific contrasts to test if the mean rBMI of each category differ from zero. | t-value |  | p-value |
| Submodel POMS boys (+2.19)  NNC boys | 2.71  -1.38 |  | 0.0073  0.167 |
| Submodel POMS girls  NNC girls | 1.31  0.42 |  | 0.19  0.69 |
|  |  |  |  |
| (C) **z-scores as a function of children sex and type (gaussian glm model)** | LR Chisq | Df | p-value |
| Sex (Girls, Boys) | 2.04 | 1 | 0.1531 |
| Children type (POMS, NNC) | 9.05 | 1 | 0.0026 |
| Sex\*Type | 3.84 | 1 | 0.049 |
| Submodel (C1): Children type (POMS > NNC) for boys (+0.84) | 10.4 | 1 | 0.0012 |
| Submodel (C2): Children type (POMS, NNC) for girls | 0.47 | 1 | 0.49 |
|  |  |  |  |
| (D) **IOTF categories (quasibinomial glm model) >30** | LR Chisq | Df | p-value |
| Sex | 0.01 | 1 | 0.91 |
| Patient type (POMS versus NNC) | 6.22 | 1 | 0.012 |
| Sex\*Type | 4.23 | 1 | 0.039 |
| Submodel: Patient type for boys (POMS > NNC) | 14.3 | 1 | 0.0001 |
| Submodel: Patient type for girls (POMS = NNC) | 0.26 | 1 | 0.61 |
|  |  |  |  |
| (E) **IOTF categories (quasibinomial glm model) >25** |  |  |  |
| Sex | 1.11 | 1 | 0.29 |
| Patient type (POMS > NNC) | 6.28 | 1 | 0.012 |
| Sex\*Type | 2.23 | 1 | 0.135 |
| **Simplified model (sex effects dropped)** |  |  |  |
| Patient type (POMS NNC) | 6.09 | 1 | 0.013 |

**Table e-4: Statistical models for the analysis of the characteristics of the disease.**

|  |  |  |  |
| --- | --- | --- | --- |
| Factors | LR Chisq | Df | p-value |
| (F) **The presence of OCB in the CSF at diagnosis (glm quasibinomial)** |  |  |  |
| Age | 9.6 | 1 | 0.0018 |
| Sex | 0.75 | 1 | 0.38 |
| rBMI | 10.1 | 1 | 0.0015 |
| rBMI\*Age | 9.8 | 1 | 0.0017 |
|  |  |  |  |
| **(G) Protein levels in the CSF (****hyperproteinorachia, glm quasibinomial)** |  |  |  |
| Age | 0.25 | 1 | 0.61 |
| Sex | 0.06 | 1 | 0.79 |
| rBMI | 1.30 | 1 | 0.25 |
| rBMI\*Sex | 6.88 | 1 | 0.009 |
| Submodel rBMI (for boys) | 1.22 | 1 | 0.27 |
| Submodel rBMI (for girls) | 9.34 | 1 | 0.002 |
|  |  |  |  |
| **(**H**) Observing any of the three markers of inflammation (hyperproteinorrachia, and/or pleiocytosis and/or OCB, glm quasibinomial)** |  |  |  |
| Age | 7.1 | 1 | 0.0077 |
| Sex | 0.003 | 1 | 0.95 |
| rBMI | 6.9 | 1 | 0.008 |
| rBMI\*Age | 6.6 | 1 | 0.01 |
| Submodel. rBMI for child under 14. | 7.17 | 1 | 0.007 |
| Submodel. rBMI for child above 14. | 0.001 | 1 | 0.96 |
|  |  |  |  |
| **(**I**) Mean vitamin D level** |  |  |  |
| Age | 0.34 |  | 0.55 |
| Sex | 2.28 |  | 0.13 |
| rBMI | 4.89 | 1 | 0.027 |
| rBMI\*Sex | 4.29 | 1 | 0.038 |
| Submodel: rBMI for boys | 5.75 | 1 | 0.016 |
| Submodel: rBMI for girls | 0.24 | 1 | 0.62 |
|  |  |  |  |
| (J) **Probability to observe more than 6 T2 lesions as a function of POMS patient’s sex, age and corpulence (quasibinomial glm model)** |  |  |  |
| Age | 0.05 | 1 | 0.82 |
| Sex | 1.99 | 1 | 0.16 |
| rBMI | 0.40 | 1 | 0.52 |
|  |  |  |  |
| **(K) Probability to have a gadolinium enhancement on initial MRI as a function of POMS patient’s sex, age and corpulence** |  |  |  |
| Age | 0.71 | 1 | 0.39 |
| Sex | 0.00060 | 1 | 0.98 |
| rBMI | 0.21 | 1 | 0.64 |
|  |  |  |  |
| **(L) Time interval between the first two relapses (years) as a function of POMS patient’s sex, age and corpulence** |  |  |  |
| Age | 2.43 | 1 | 0.12 |
| Sex | 0.14 | 1 | 0.71 |
| rBMI | 0.52 | 1 | 0.47 |