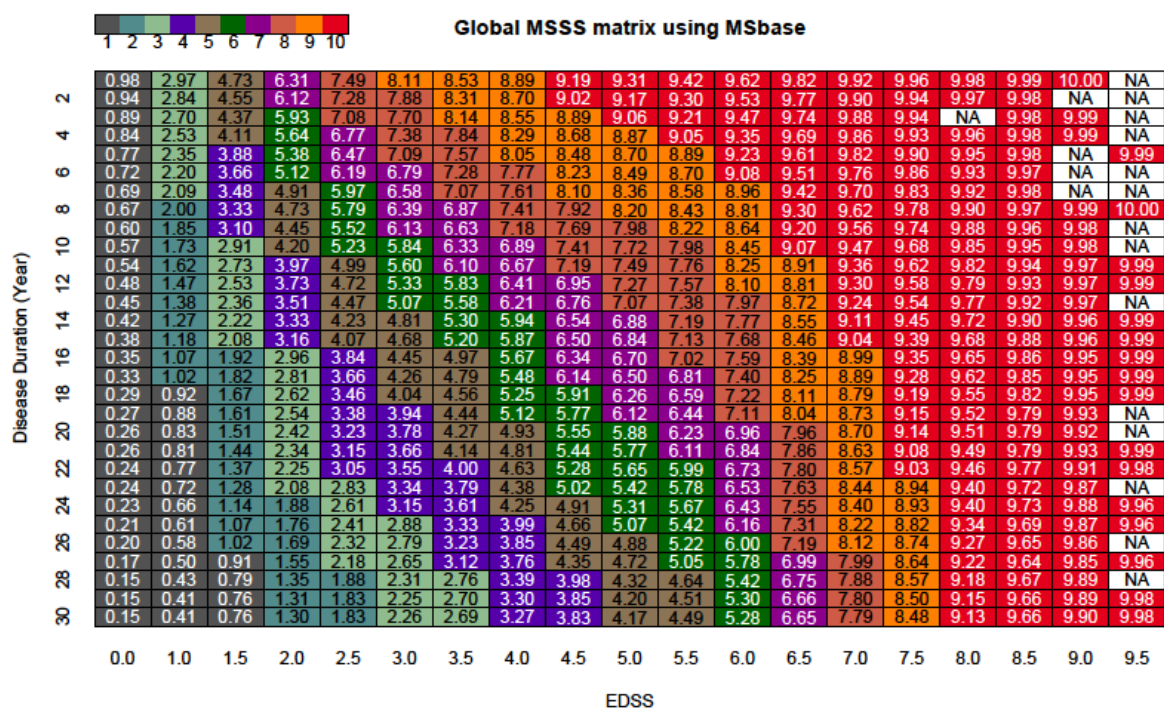


Supplementary Materials

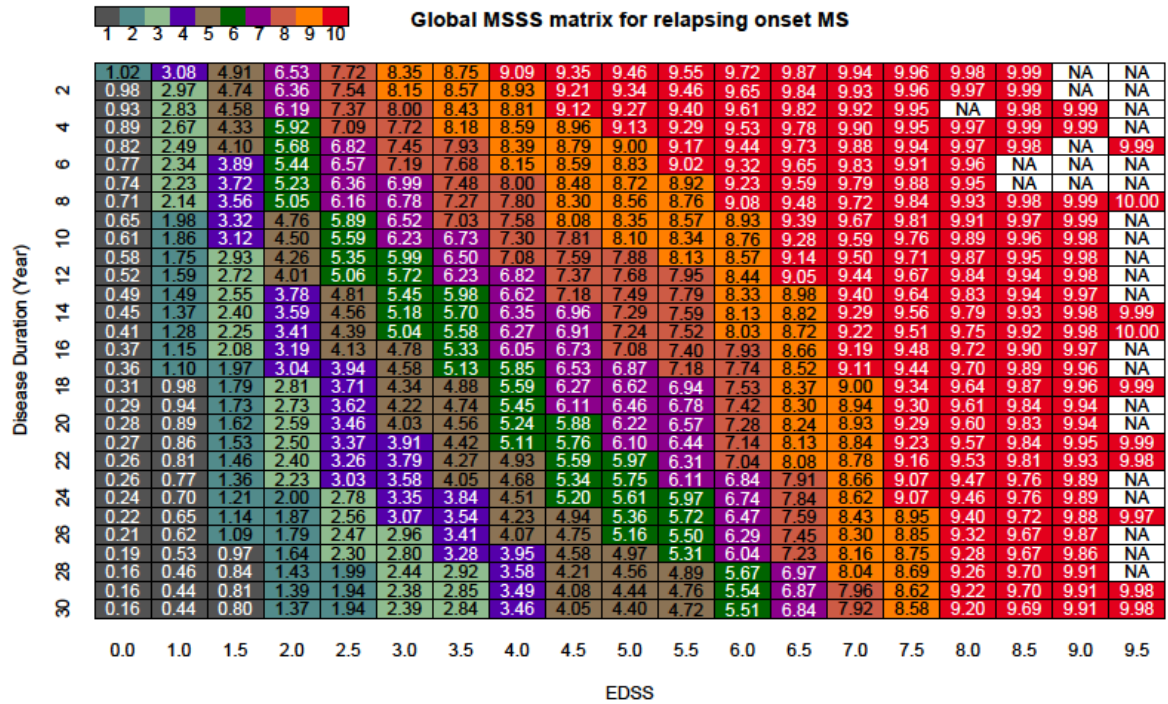
Appendix 1: Further detail on the development of the MSSS matrices.

Each matrix has 570 cells (19x30). Despite the large overall sample size in our analysis, some cell values could not be calculated using the above method due to small sample sizes for rare cases (those in the lowest and highest deciles of disability progression). As in previous work,⁵ the vacant cells were interpolated after analysis to present a complete matrix (Figures 1, 3 and 4). Values were interpolated from the average of the two neighbouring vertical cells where it was possible to do so, and continuously inward where it was not.

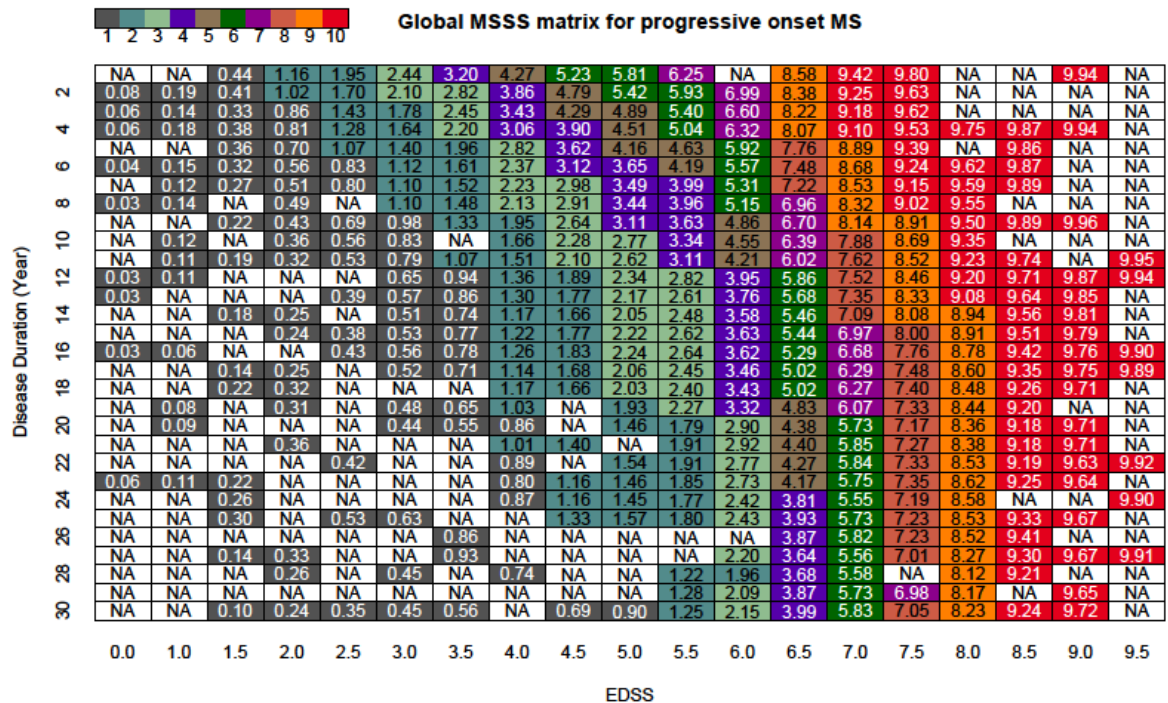
Supplemental Figure 1: Global MSSS matrix calculated using all included cases from the MSBase Registry. The MSSS takes into account both the patient EDSS (x-axis) and disease duration (y-axis). The resulting score is a relative measure of the rate of disability progression, with higher values indicating more rapid disability progression. Cell colours indicate the decile of disability progression. Cooler colours indicate lower deciles and warmer colours indicate higher deciles.



Supplemental Figure 2: Relapsing-onset MSSS matrix. The MSSS takes into account both the patient EDSS (x-axis) and disease duration (y-axis). The resulting score is a relative measure of disability progression of the patient, with higher values indicating more rapid disability progression. Cell colours indicate the decile of disability progression. Cooler colours indicate lower deciles and warmer colours indicate higher deciles.



Supplemental Figure 3: Progressive-onset MSSS matrix. The MSSS takes into account both the patient EDSS (x-axis) and disease duration (y-axis). The resulting score is a relative measure of disability progression of the patient, with higher values indicating more rapid disability progression. Cell colours indicate the decile of disability progression. Cooler colours indicate lower deciles and warmer colours indicate higher deciles.



Supplemental Figure 4: The proportion of MSSS variance explained by the single nucleotide polymorphism (SNP) in various simulated scenarios, indicated by the heading over each graph. For example, M4.5_A0.1 indicates that the simulation used a mean MSSS of 4.5 and minor allele frequency of 0.1. The x-axis represents

the number of PPMS patients in the simulation. The y-axis represents the power change between using the global MSSS and the progressive-onset-specific MSSS.

