SUPPLEMENTARY FIGURES AND TABLES

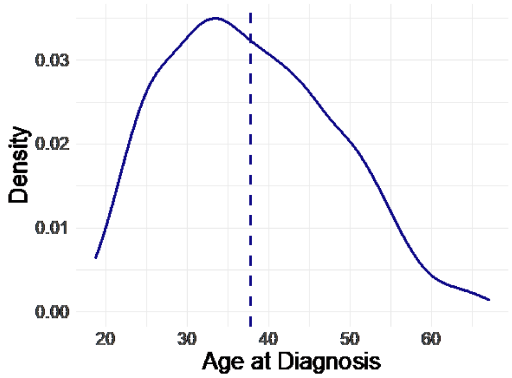

Figure S1. Age at diagnosis profile of the FutureMS participants. Demonstrating monomodal distribution and truncation at extremes of age (particularly <18) due to inclusion criteria. Dotted line is the mean age at diagnosis.

ASSESSMENT	Baseline	Year 1	Year 5
Informed Consent	**X**		**X**
Demographics	**X**		
Medical History	**X**	**X**	**X**
Social History	**X**	**X**	**X**
Family History	**X**	**X**	**X**
Migration History			**X**
Relapse/Progression History	**X**	**X**	**X**
Medication History	**X**	**X**	**X**
Infectious Mononucleosis History			**X**
Structured Neurological Examination	**X**	**X**	**X**
BMI, Height, Weight, BP	**X**	**X**	**X**
Measures of Physical Disability (EDSS, T25FTWT, 9HPT)	**X**	**X**	**X**
Cognitive tests (PASAT-3, SDMT)	**X**	**X**	**X**
PHQ-9 and GAD-7	**X**	**X**	**X**
MSIS-29	**X**	**X**	**X**
Fatigue Severity Score	**X**	**X**	**X**
Patient Derived Disease Severity Score	**X**	**X**	**X**
Visual Acuity	**X**	**X**	**X**
Standard MRI Protocol	**X**	**X**	**X**
Disease Modifying Therapy History	**N/A**	**X**	**X**
Lymphocyte subsets stored (CD3+CD4+, CD3+CD8+, CD19+, CD14+)	**X**		
Serum stored	**X**		**X**
Saliva stored			**X**
DNA Genotyping	**X**		
Advanced MRI Imaging (SS3)	**X**	**X**	**X**
Optical Coherence Tomography (SS4)	**X**	**X**	**X**

Table S1. Summary of measures at each study visit. SS3 = Substudy 3. SS4 = Substudy 4.

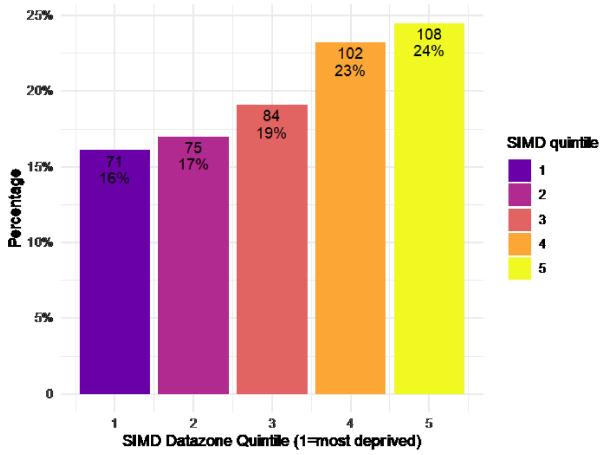

Figure S2. Scottish Index of Multiple Deprivation (SIMD) quintile of study participants.

	Parent/Grandparent	% of Parent				% of Grandparent			
		Mean	SD	LQ10	UQ10	Mean	SD	LQ10	UQ10
Single cells	Events	56.05	15.98	35.60	75.00				
Viable (7AAD -ve)	Single cells	91.77	10.11	97.80	84.93.				
CD14+ Monocyes	CD3-/viable cells	22.03	11.67	34.30	10.40				
CD19+ B cells	CD3-/viable cells	8.11	3.69	4.08	12.9				
CD4+ T cells	CD3+/viable cells	69.44	11.67	81.47	57.00	38.97	10.48	51.27	26.56
CD8+ T cells	CD3+/viable cells	20.27	8.31	30.37	11.22	20.27	8.31	30.37	11.22

Table S2. Proportion of PBMCs expressing markers for monocytes (CD14+), B/plasma cells (CD19+), helper (CD3+CD4+) and cytotoxic (CD3+CD8+) t cells in the peripheral blood mononuclear cells donated by patients to the study.

	With PBMCs	**FACs sorted**	**Total**
Edinburgh (01)	184	184	185
Glasgow (02)	163	137	165
Dundee (03)	46	46	46
Aberdeen (04)	35	32	35
Inverness (05)	8	6	8
Controls	100	78	103
Totals (patients only)	**436**	**405**	**439**
Totals	**536**	**483**	**542**

Table S3: Summary of numbers of FutureMS study subjects and controls with peripheral blood mononuclear cells available for analysis.

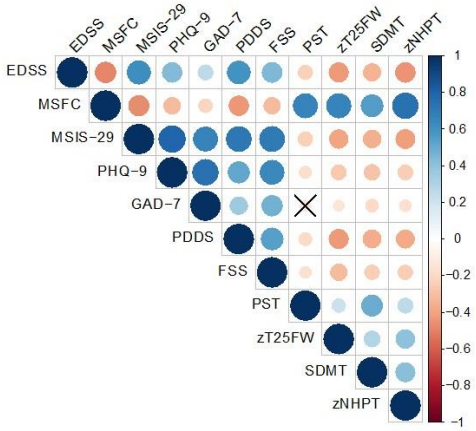

Figure S3. Correllelogram of clinical measures at baseline visit. zT25FW is the z-score of the timed 25-foot walk test. zNHPT is the z-score of the 9-hole peg test. Other acronyms as defined in the main text.

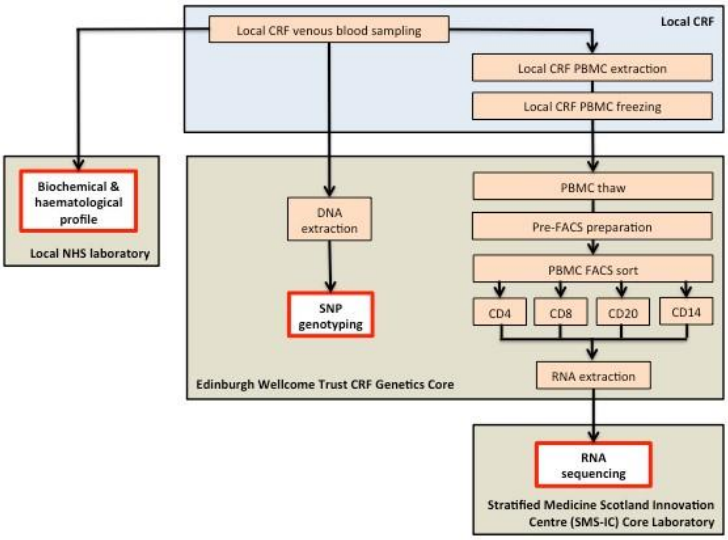

Figure S4: Schematic explaining laboratory pathway for tissue collection for biomarker processing.

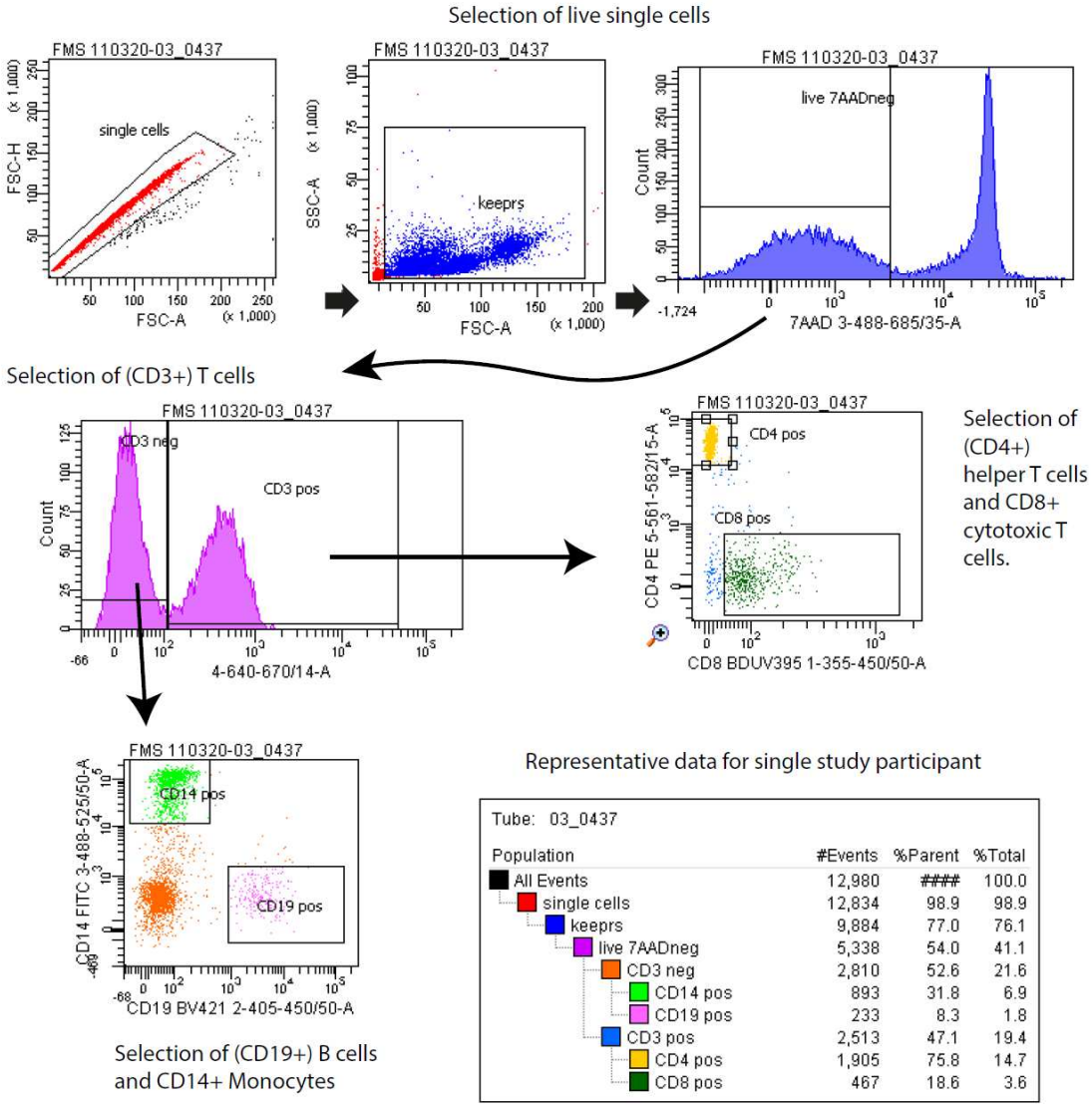

Figure S5. Example of the fluorescence-activated cell sorting undertaken for a representative member of the FMS cohort. CD3 – T cell marker. CD4+ helper T cells, CD8+ cytotoxic T cells. CD19+ B cell marker and CD14+ monocyte marker. 7AAD – 7-Aminoactinomycin D uptake associated with loss of cell viability.

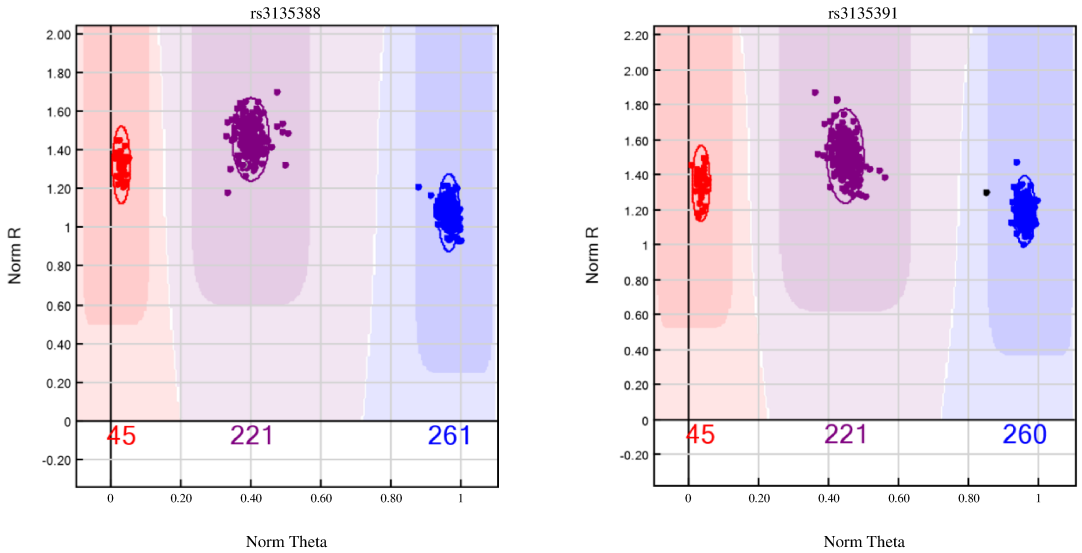

*Figure S6. Demonstration of two SNPs in linkage disequilibrium from the FutureMS cohort demonstrating clear separation of clusters resulting in high confidence of genotype calls. These two SNPs mark HLA-DRB1*15:01, which contributes the largest single gene effect for multiple sclerosis.*

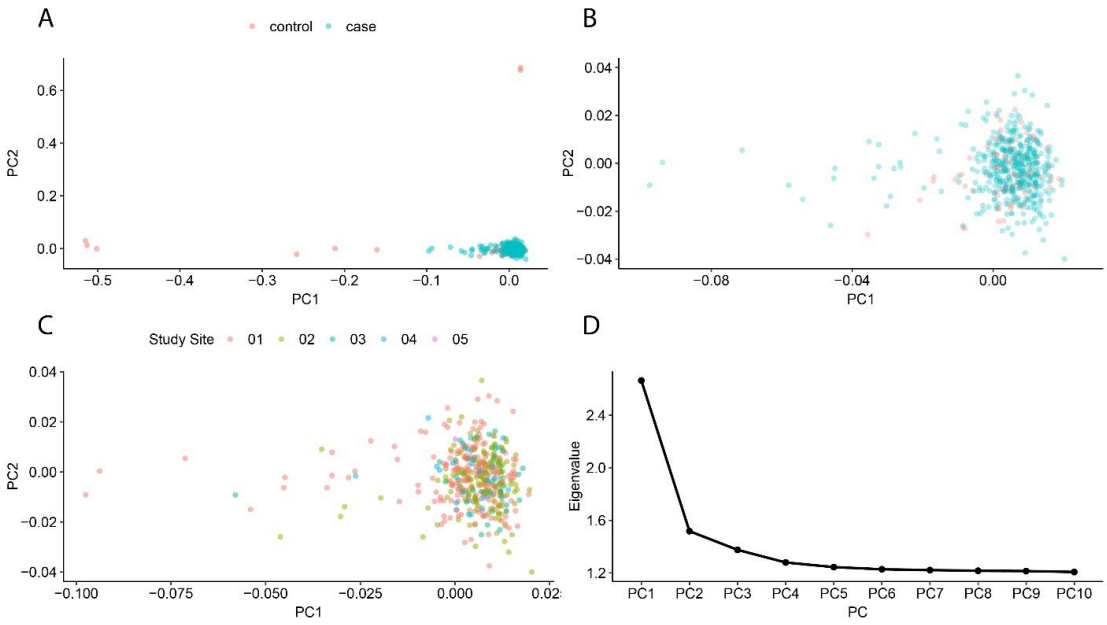

Figure S7. Genetic stratification analysis of the FutureMS cohort and controls. A – plot of first two principal components, comparing cases and controls. B – enlarged region of A with most cases and controls tightly clustered. Note difference of scale in PCs in A&B and A&C. C – Cases demonstrate little evidence of genetic stratification within the cohort based on the study site they were recruited from (scaled as in B). D – Scree plot of Eigenvalues of first ten principal components.