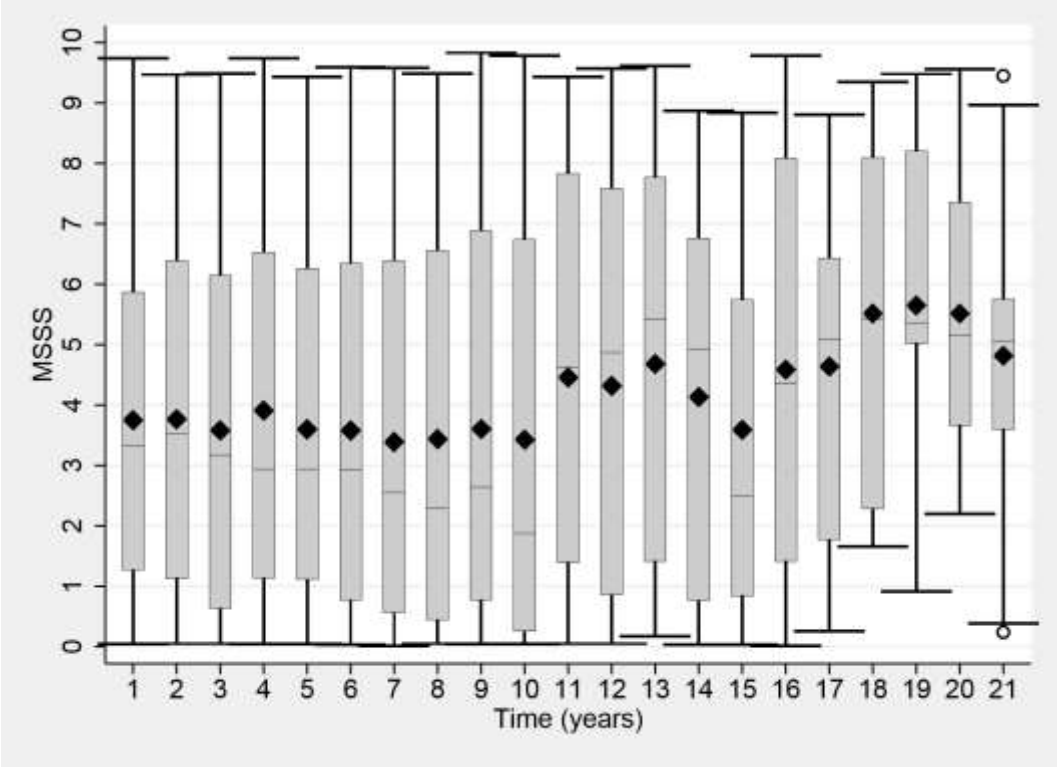
Supplementary Materials



Distribution of MSSS by years of follow-up

The boxplot shows the distribution of the raw MSSS values, group by year of follow up. The diamond is the mean, the line in the middle of the box is the median, and the box is the interquartile range, between the 25% and 75% percentiles. The whiskers extend from the box out to 1.5 times the interquartile range, or to the minimum and maximum observations if no observation are than 1.5 times the interquartile range away from the 25th or 75th quartiles. Observation beyond the range of the whiskers are denoted with hollow circles to indicate outliers.

Time (years)	Estimated Mean	Standard Error	Denominator Degrees of Freedom	95% Confidence Interval	
[0, 1]	3.8155	0.1762	648	3.4696	4.1615
(1, 2]	3.8076	0.1994	733	3.4162	4.199
(2, 3]	3.6184	0.2079	729	3.2102	4.0265
(3, 4]	3.4792	0.1987	714	3.0891	3.8692
(4, 5]	3.4499	0.201	727	3.0554	3.8445
(5. 6]	3.438	0.2043	737	3.0369	3.839
(6, 7]	3.2848	0.1913	730	2.9093	3.6603
(7, 8]	3.333	0.2092	760	2.9224	3.7437
(8, 9]	3.2934	0.2	716	2.9007	3.6861
(9, 10]	3.2544	0.2168	759	2.8288	3.6799
(10, 11]	3.3192	0.2375	784	2.8529	3.7855
(11, 12]	3.6098	0.2456	786	3.1278	4.0919
(12, 13]	3.6111	0.2852	826	3.0514	4.1709
(13, 14]	3.3924	0.3134	808	2.7773	4.0075
(14, 15]	3.3474	0.3457	658	2.6686	4.0261
(15, 16]	3.3898	0.3891	694	2.6258	4.1537

Contrast	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F Statistic	p value
Time Overall	15	334	1.59	0.0739
Time Overall: [0, 1], (7, 9], (14, 16]	2	209	5.65	0.0041

Categorical model of MSSS over time

A longitudinal regression model was fit with each year of follow up being a categorical variable. To make fitting the longitudinal covariance matrix manageable, MSSS observations for each subject were averaged for each follow up year, and the number of observations was incorporated into the model as a weight. The table presents model estimated MSSS means for each follow up year, along with standard error, degrees of freedom for the standard error (denominator degrees of freedom), and 95% confidence intervals. The table below performs F tests using the model estimates to simultaneously test whether the means differ over follow up years. The first F test is for whether there is any difference among any follow up years. The second F test averages follow up years 7-8

and 8-9, and averages follow up years 14-15 and 15-16, and tests whether either differs from the first year of follow up.

Label	Estimate	Standard Error	Denominator Degrees of Freedom	95% Confidence Interval		T Statistic	p value
Baseline	3.8226	0.2461	133	3.3359	4.3094		
8 Years	3.2817	0.2408	186	2.8067	3.7568		
15 Years	3.5297	0.3611	54	2.8058	4.2536		
Change 8 Years vs Baseline	-0.5409	0.2364	97.1	-1.0101	-0.0717	-2.29	0.0243
Change 15 Years vs Baseline	-0.2929	0.3854	53.5	-1.0659	0.4800	-0.76	0.4506
Change 15 vs 8 Years	0.2480	0.3095	29.1	-0.3849	0.8808	0.80	0.4295

Contrast	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F Statistic	p value
Overall Time Effect	2	55.4	2.90	0.0634

Categorical model evaluating change from baseline to year 8 and year 15, and between year 8 and 15

MSSS observations in the first year of follow up were selected, along with observations between 7 and 9 years and 14 and 16 years of follow up. For each subject the MSSS observations within each of the three periods were averaged to create a MSSS observation representing baseline, 8 years of follow up, and 15 years of follow up. The compressed MSSS observations were then used to fit a longitudinal regression model with categorical time. Mean MSSS was estimated for each time, the times were pair-wise compared, and omnibus F test was performed for mean MSSS differences among the times. Standard errors, degrees of freedom, 95% confidence intervals, T statistics, and p values were presented along with the estimates as applicable.

Label	Estimate	Standard Error	Denominator Degrees of Freedom	95% Confidence Interval		T Statistic	p value
1 Year Change	-0.04691	0.01655	118	-0.07969	-0.01413	-2.83	0.0054

Linear mixed model of MSSS

A longitudinal regression model was fit to the MSSS data, with the explanatory variable time of follow up. Time was treated as continuous, and a linear slope was fit.