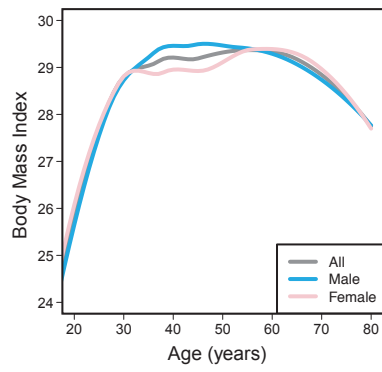


**Supplementary Figure 1. DE-SWAN age effect when stratifying the analysis per cohort and accounting for subcohort in the modeling**

(a) DE-SWAN results when stratifying the analysis per cohort ( $n=3,301$  for Interval cohort and 962 for LonGenity). The 3 local peaks identified at age 34, 60 and 78y are indicated by colored vertical lines.

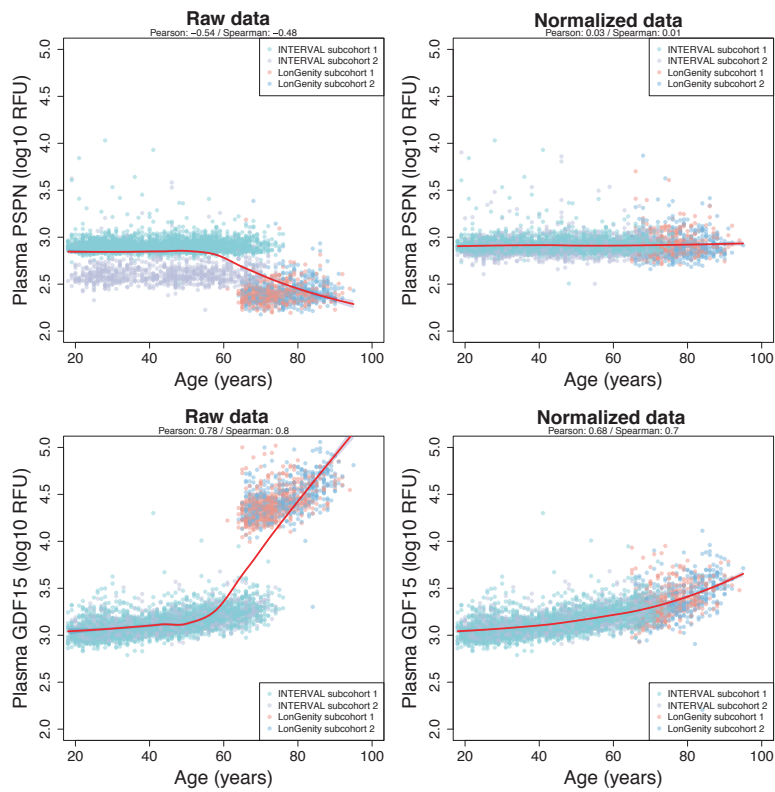
(b) Comparison of DE-SWAN results when adjusting for subcohort or not ( $n=4,263$ ).

(c-e) Age effect at 34, 60 and 78y when adjusting for subcohort or not ( $n=4,263$ ).



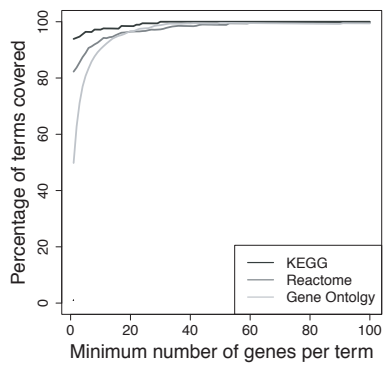
**Supplementary Figure 2. Age related changes of BMI.**

Changes during aging are estimated using LOESS curves, fitted for all subjects and for male and female separately. Data from the R NANHES package (Pruim, R. NHANES: Data from the US National Health and Nutrition Examination Study. 2015)



### Supplementary Figure 3. Normalization examples.

Representative examples of the normalization process in the INTERVAL and LonGenity cohorts. For each protein, the average of the subjects in the 60-70y range within each subcohort was used as a normalization factor. LOESS regression curves are fitted. Note that this normalization is needed when fitting aging trajectories (Fig. 2) but does not affect the results when “subcohort” is included as covariate in the statistical modeling



**Supplementary Figure 4. Pathways covered by the 2,925 proteins measured in this study.**

The 2,925 proteins measured in this study cover 90% of the human GO, Reactome and KEGG terms containing more than 8 genes. Coverage for pathways with 1+ to 100+ genes is represented.