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Figure 1: Dependency of variability in rates of change on follow-up time. Illustration of the relationship between the estimated standard deviation of a rate of change computed from two time points according to the time interval between the two points. Each standard deviation is scaled by the estimated difference in mean rates of change between early-HD subjects and controls (the latter assumed to be zero for UHRDS-TMS and UHDRS-TFC) for comparison purposes. Formulae for the estimated standard deviations of rates of change are given in equations (5) and (12) in the statistical appendix.

Figure 2: Clinical trial design recommendations. Illustration (in grey) of the most generally recommendable clinical trial design considering the gains in efficiency given by the various strategies considered. As an example, for a clinical trial with caudate atrophy (expressed as a percentage of baseline) as the outcome variable increasing follow-up from one to two years is estimated to reduce sample size requirements by 55%: introducing six-monthly interim visits further relatively reduces these by 9%: stratification by age, CAG, disease burden and baseline caudate volume further relatively reduces these by 42% and enrichment by restriction to patients with CAG >43 further relatively reduces these by 55% (all in the absence of dropouts).