

# **SUPPLEMENTAL MATERIAL**

## Data S1.

### Supplemental Methods

The  $CV_i$  was defined as the median value of the CVs of the repeated measurements in individual subjects ( $CV_{\text{subject}}$ ), adjusted for the analytical variation:

$$CV_i = \sqrt{\text{median}(CV_{\text{subject}}^2) - CV_a^2}$$

Finally,  $CV_g$  was determined as 100% times the standard deviation ( $sd_{\bar{X}_{\text{subject}}}$ ) of the mean values of the repeated measurements in individual subjects ( $\bar{X}_{\text{subject}}$ ) by the (unweighted) mean of these means ( $\bar{X}_{\text{group}}$ ):

$$CV_g = 100\% * sd_{\bar{X}_{\text{subject}}} / \bar{X}_{\text{group}}$$

The *Index of Individuality (II)* is the ratio of the combined within-subject and analytical variation relative to the between-subject variation:

$$II = \sqrt{CV_i^2 + CV_a^2} / CV_g$$

When the  $II < 0.6$ , it is agreed that subjects should have their own reference values, based on previous samples.<sup>17</sup> When the  $II > 1.4$ , a population-based reference is preferred.

The *Reference Change Value (RCV)* reflects the limit of (relative) change in biomarker values in individual subjects that can be explained by the combined within-subject and analytical variation. For biomarkers with a normal distribution, the RCV can be calculated as follows:

$$RCV = Z_{\alpha/2} * \sqrt{2(CV_i^2 + CV_a^2)}$$

where  $Z_{\alpha/2}$  represents the critical value of the normal distribution for  $100\% * (1 - \alpha)/2$  confidence. For biomarkers with a skewed distribution a log-normal approach has been described,<sup>18</sup> and the RCV limits can be determined as follows:

$$\text{RCV}_{\text{downward}} = e^{-Z_{\alpha/2} * \sqrt{2 \ln(\text{CV}_w^2 + \text{CV}_a^2 + 1)}} - 1$$
$$\text{RCV}_{\text{upward}} = e^{Z_{\alpha/2} * \sqrt{2 \ln(\text{CV}_w^2 + \text{CV}_a^2 + 1)}} - 1$$

We used  $\alpha = 0.05$  (for 95% confidence), thus  $Z_{0.025} = 1.96$ .

**Table S1. Association between baseline characteristics and inter-individual variation of high-sensitivity troponin.**

	hsTnI		hsTnT	
	estimate (95%CI)	P-value	estimate (95%CI)	P-value
Male sex	0.002 (-0.686, 0.691)	0.994	-0.064 (-0.669, 0.541)	0.834
Age, y	-0.01 (-0.04, 0.02)	0.503	-0.022 (-0.048, 0.003)	0.088
Current Smoking, yes	0.072 (-0.501, 0.645)	0.804	-0.15 (-0.652, 0.352)	0.555
Diabetes, yes	-0.53 (-1.269, 0.209)	0.158	-0.213 (-0.867, 0.441)	0.519
Hypertension, yes	-0.01 (-0.576, 0.556)	0.972	0.192 (-0.303, 0.688)	0.443
Hypercholesterolemia, yes	0.094 (-0.474, 0.662)	0.744	-0.17 (-0.668, 0.328)	0.5
Family history of CAD, yes	-0.061 (-0.633, 0.511)	0.832	0.193 (-0.379, 0.765)	0.503
BMI	-0.029 (-0.108, 0.05)	0.467	-0.032 (-0.101, 0.038)	0.368
Heart Rate	0.004 (-0.013, 0.021)	0.637	-0.005 (-0.02, 0.009)	0.485
Systolic blood pressure, mmHg	-0.001 (-0.012, 0.009)	0.842	-0.002 (-0.011, 0.007)	0.702
Killip-class	0.782 (-0.859, -2.544)	0.947	0.52 (-0.92, -2.254)	0.717
Aspirin	0.516 (-1.122, 2.153)	0.533	0.556 (-0.881, 1.992)	0.445
BetaBlocker	-0.726 (-1.497, 0.045)	0.065	0.088 (-0.601, 0.777)	0.8
ACE inhibitor	0.059 (-0.555, 0.672)	0.85	-0.04 (-0.579, 0.498)	0.882
ARB	0.294 (-0.599, 1.188)	0.515	0.088 (-0.698, 0.874)	0.824
Statin	-1.864 (-3.827, 0.099)	0.062	-0.326 (-2.081, 1.428)	0.713

Betas for increase/decrease in Cvi for the different baseline characteristics

95%CI: 95% confidence interval; Y: year; CAD: coronary artery disease; BMI: body Mass Index; ARB: angiotensin renin blocker