

## SUPPLEMENTARY DATA

**Table S1.** Correlations (Pearson correlation coefficient r) between plasma biomarker concentrations [ $\mu\text{mol/L}$ ] or ratios and study characteristics among 360 participants from the 3-City Bordeaux and AMI cohorts involved in the Frailomic initiative

Biomarker	Age [years]	BMI [kg/m <sup>2</sup> ]	Medication [servings/d]	Meat [servings/d]	Fish [servings/d]
3-MH	0.149*	0.109	0.198**	-0.029	0.004
1-MH	0.089	0.055	0.137*	0.027	0.111*
Crea	0.175**	-0.007	0.155*	-0.002	-0.007
3-MH/Crea	-0.014	0.143*	0.120*	-0.003	-0.005
1-MH/Crea	0.020	0.055	0.093	0.040	0.112*
eGFR	-0.488**	0.080	-0.231**	0.129*	-0.089
3-MH/eGFR	0.292**	0.039	0.228**	-0.063	0.033
3-MH/1-MH	-0.026	-0.008	-0.055	-0.041	-0.116*

eGFR in [ml/min/1,73 m<sup>2</sup>]. \* p < 0.05 and \*\* p ≤ 0.001 display statistical significant correlations.

**Table S2.** Quintiles of 3-MH concentrations and, 3-MH/Crea, 3-MH/eGFR and 3-MH/1-MH ratios among 360 participants from the 3-City Bordeaux and AMI cohorts involved in the Frailomic initiative

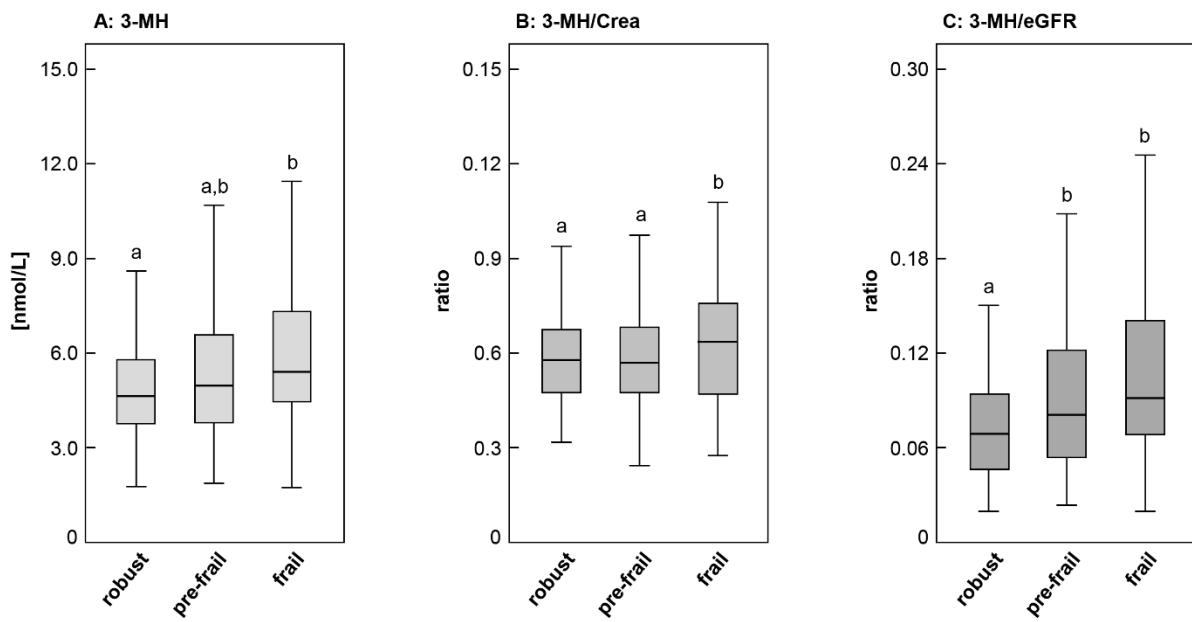
Biomarker quintiles	3-MH [ $\mu\text{mol/L}$ ]	3-MH/Crea	3-MH/eGFR	3-MH/1-MH
Q1	3.04 (1.74; 3.67)	0.039 (0.024; 0.045)	0.038 (0.019; 0.048)	0.255 (0.111; 0.386)
Q2	4.09 (3.69 ; 4.52)	0.049 (0.046; 0.052)	0.057 (0.049; 0.067)	0.554 (0.387; 0.737)
Q3	4.92 (4.54 ; 5.37)	0.058 (0.053; 0.062)	0.078 (0.068; 0.088)	0.994 (0.741; 1.267)
Q4	6.09 (5.39; 6.93)	0.067 (0.063; 0.072)	0.105 (0.088; 0.129)	1.719 (1.277; 2.342)
Q5	10.03 (6.97; 39.13)	0.091 (0.073; 0.193)	0.297 (0.130; 1.880)	3.490 (2.351; 7.817)

Values are displayed as mean (minimum; maximum).

**Table S3.** Prevalence of frailty criteria among 360 participants from the 3-City Bordeaux and AMI cohorts involved in the Frailomic initiative

Frailty criteria, % (n)	total	robust	pre-frail	frail
Sedentarity <sup>1</sup>	40.8 (147)	0.0 (0)	55.5 (86)	88.4 (61)
Weakness <sup>2</sup>	22.2 (80)	0.0 (0)	20.6 (32)	69.6 (48)
Shrinking <sup>3</sup>	13.9 (50)	0.0 (0)	18.1 (28)	31.9 (22)
Slowness <sup>4</sup>	27.8 (100)	0.0 (0)	25.8 (40)	87.0 (60)
Fatigue <sup>5</sup>	16.4 (59)	0.0 (0)	14.8 (23)	52.2 (36)

Data are shown as % (n). BMI = body mass index. 1 Sedentarity: low energy expenditure or physical activity; 2 Weakness: low grip strength or chair stand test; 3 Shrinking: unintentional weight loss; 4 Slowness: walking distance or gait speed; 5 Fatigue: self-reported exhaustion.



**Figure S1. (A) plasma 3-methylhistidine concentrations, (B) 3-methylhistidine-to-creatinine ratios, and (C) 3-methylhistidine-to-eGFR ratios by frailty status among 360 participants of the 3-City Bordeaux and AMI cohorts involved in the Frailomic initiative**

Results are shown as boxplots. Robust: n = 136; pre-frail: n = 155; frail: n = 69 (3-MH) and n = 68 (3-MH/Crea and 3-MH/eGFR). <sup>a,b</sup> Differences between frailty groups determined by simple GLM, p < 0.05.