

Supplemental eTable 1. UK Biobank field IDs used to extract data for this project.

Field	Field ID	Instance	ICD codes
Creatinine	30700	Baseline	
Cystatin C	30720	Baseline	
Hand grip strength (left)	46	Imaging	
Hand grip strength (right)	47	Imaging	
Total thigh fat-free muscle volume	22409	Imaging	
Arms lean mass	23258	Imaging	
Legs lean mass	23275	Imaging	
Height	12144	Imaging	
Body mass index (BMI)	21001	Baseline Imaging	
Age	21003	Baseline	
Sex	31	Baseline	
Date of attending assessment centre	53	Baseline Imaging	
Ethnicity	21000	Baseline	
Education	6138	Baseline	
Townsend deprivation index at recruitment	189	Baseline	
Smoking status	20116	Baseline	
IPAQ physical activity group	22032	Baseline	
Alcohol intake frequency	1558	Baseline	
Cancer excluding non-melanoma skin cancer	40005 41280 41281		ICD-10: C00-C97 excluding C44 ICD-9: 140-209 excluding 172
Diabetes	130706 130708 130710 130712 130714		E10 E11 E12 E13 E14
Myocardial infarction	131298 131300 131302 131304 131306		I21 I22 I23 I24 I25
Stroke	131360 131362 131364 131366 131368		I60 I61 I62 I63 I64
Heart failure	131354		I50
Chronic kidney disease	132032		N18

Supplemental eTable 2. Shows the prevalence of low FFMV, low ALM/BMI, low ALM/height² and low grip strength using age- and sex-specific normative values.

Outcome and Cutpoint		Low ($<$ Cutpoint)	High (\geq Cutpoint)
Grip Strength			
T-score -2 in a 4-90-year Great British cohort	Women (<19 kg)	15,212 (20.11%)	60,421 (79.89%)
	Men (<32 kg)	10,644 (14.37%)	63,430 (85.64%)
T-score -2.5 in a 4-90-year Great British cohort 20 th percentile among the included sample	Women (<16 kg)	5,783 (7.65%)	69,850 (92.35%)
	Men (<27 kg)	3,857 (5.21%)	70,217 (94.79%)
	Women (<18 kg)	9,591 (12.68%)	66,042 (87.32%)
	Men (<33 kg)	14,541 (19.63%)	59,533 (80.37%)
FFMV			
T-score -2 in middle-aged adults in the UK Biobank	Women (<6.21 liters)	200 (4.66%)	4,093 (95.34%)
	Men (<9.61 liters)	426 (7.83%)	5,012 (92.17%)
T-score -2.5 in middle-aged adults (45-59 years) in the UK Biobank 20 th percentile among the included samples	Women (<5.62 liters)	40 (0.93%)	4,254 (99.07%)
	Men (<8.75 liters)	120 (2.21%)	5,318 (97.79%)
	Women (<6.97 liters)	859 (20.01%)	3,434 (79.99%)
	Men (<10.40 liters)	1,088 (20.01%)	4,350 (79.99%)
ALM/BMI			
T-score -2	Women (<0.512 kg/kg/m ²)	162 (3.60%)	4,342 (96.40%)
	Men (<0.789 kg/kg/m ²)	615 (10.68%)	5,141 (89.32%)
20 th percentile among the included samples	Women (<0.582 kg/kg/m ²)	901 (20.00%)	3,603 (80.00%)
	Men (<0.830 kg/kg/m ²)	1,151 (20.00%)	4,605 (80.00%)
ALM/Height²			

T-score -2	Women (<5.50 kg/m ²)	543 (11.75%)	4,078 (88.25%)
	Men (<7.00 kg/m ²)	911 (15.54%)	4,952 (84.46%)
20 th percentile among the included samples	Women (<5.71 kg/m ²)	924 (20.00%)	3,697 (80.00%)
	Men (<7.13 kg/m ²)	1,173 (20.01%)	4,690 (79.99%)

Age-and sex-specific normative values are from population studies using grip strength (19), FFMV (20), ALM/Height² (1) and ALM/BMI (21).

Supplemental eTable 3. Unadjusted associations of the outcomes across quartile groups of Cr:Cys.

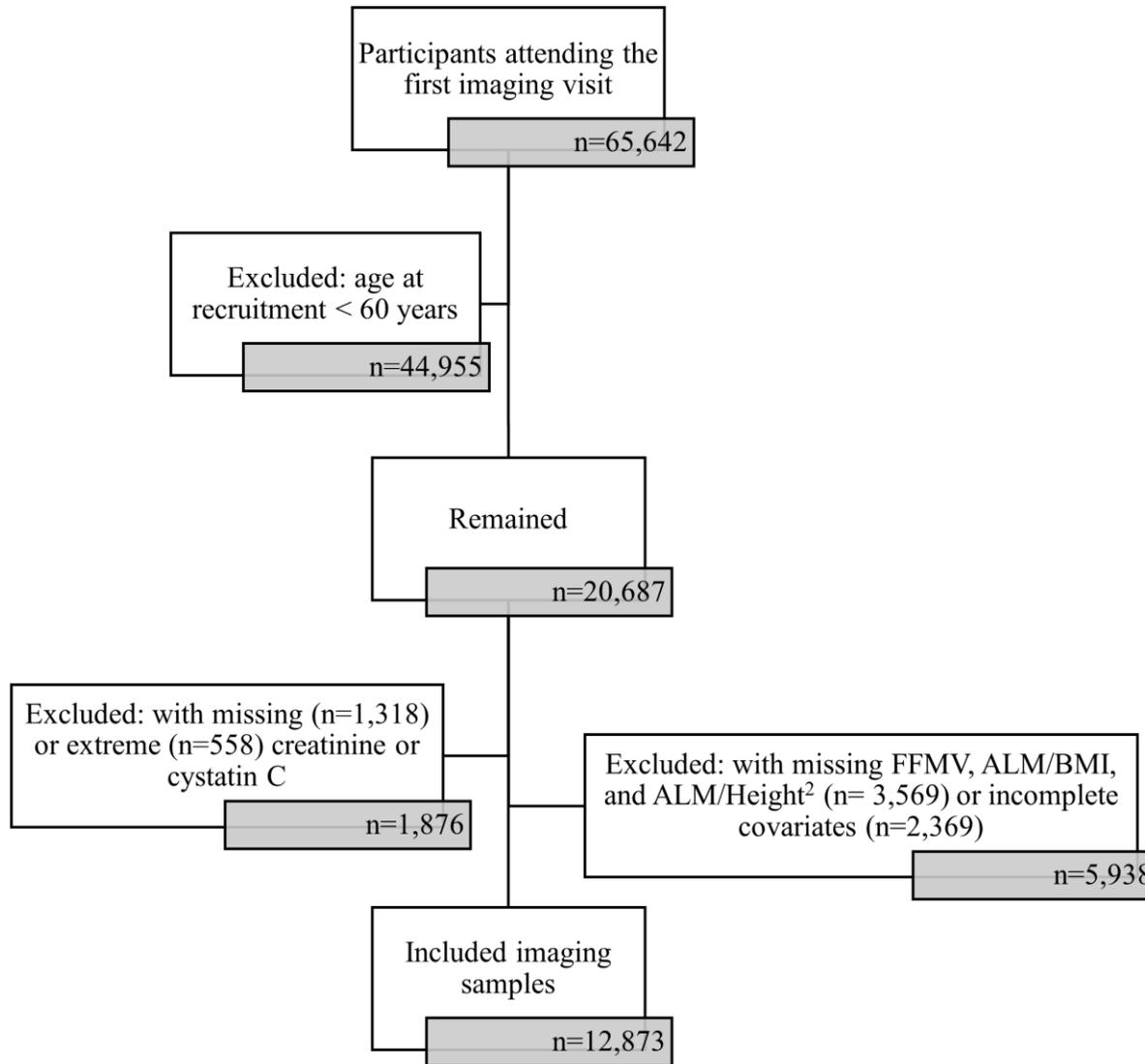
Imaging	All	Q1	Q2	Q3	Q4	P-Value
		<0.81	0.81 to <0.91	0.91 to <1.01	≥1.01	
	(n = 9,731)	(n = 2,433)	(n = 2,433)	(n = 2,433)	(n = 2,433)	
FFMV (liters)	9.95 ± 2.32	8.25 ± 1.72	9.52 ± 2.2	10.66 ± 2.10	11.38 ± 1.93	<0.001
Imaging	All	Q1	Q2	Q3	Q4	P-Value
		<0.81	0.81 to <0.91	0.91 to <1.01	≥1.01	
	(n = 10,260)	(n = 2,565)	(n = 2,565)	(n = 2,565)	(n = 2,565)	
ALM/BMI (kg/kg/m²)	0.8 ± 0.16	0.68 ± 0.13	0.78 ± 0.15	0.85 ± 0.15	0.91 ± 0.13	<0.001
ALM (kg)	20.97 ± 4.71	17.85 ± 3.73	20.29 ± 4.68	22.20 ± 4.42	23.55 ± 3.89	<0.001
BMI at the imaging visit (kg/m²)	26.28 ± 3.99	26.61 ± 4.68	26.21 ± 4.02	26.17 ± 3.74	26.14 ± 3.38	0.19
Imaging	All	Q1	Q2	Q3	Q4	P-Value
		<0.81	0.81 to <0.91	0.91 to <1.01	≥1.01	
	(n = 10,484)	(n = 2,261)	(n = 2,261)	(n = 2,261)	(n = 2,261)	
ALM/Height² (kg/m²)	7.18 ± 1.11	6.59 ± 0.99	7.01 ± 1.10	7.4 ± 1.06	7.72 ± 0.96	<0.001
ALM (kg)	20.96 ± 4.72	17.85 ± 3.74	20.25 ± 4.69	22.20 ± 4.42	23.55 ± 3.9	<0.001
Height (m)	1.70 ± 0.09	1.64 ± 0.08	1.69 ± 0.1	1.72 ± 0.09	1.74 ± 0.08	<0.001
	All	Q1	Q2	Q3	Q4	P-Value
		<0.77	0.77 to <0.87	0.87 to <0.98	≥0.98	
Baseline	(n = 149,707)	(n = 37,426)	(n = 37,427)	(n = 37,427)	(n = 37,427)	
Grip strength (kg)	31.41 ± 10.8	24.29 ± 7.79	28.94 ± 9.65	34.08 ± 10.3	38.3 ± 9.77	<0.001

Supplemental eTable 4. Fully-adjusted associations (predicted values and their 95% confidence intervals) for outcomes across quartile groups of the biomarker difference between Creatinine and Cystatin C.

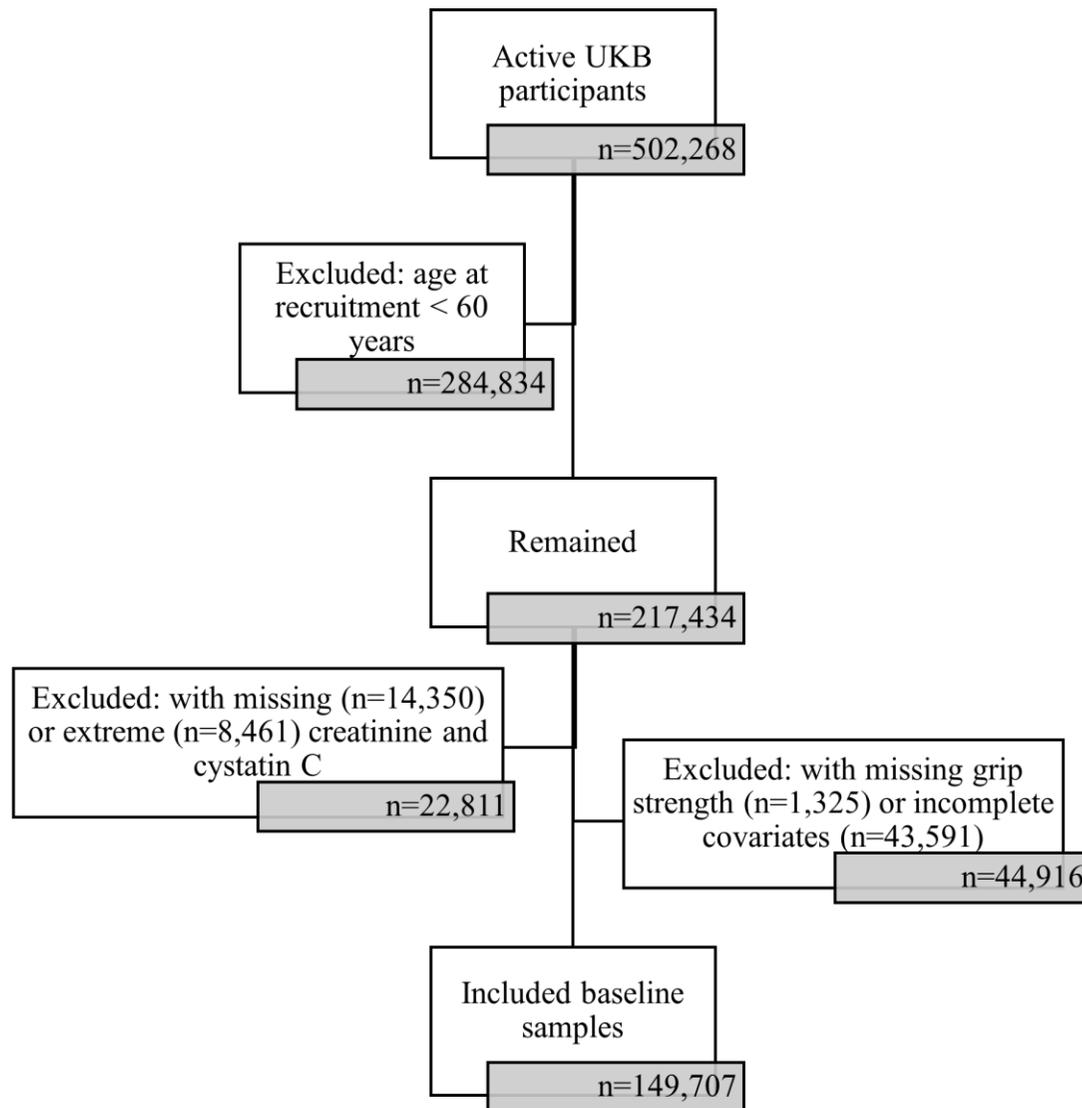
	Group	Q1	Q2	Q3	Q4	Non-linearity P-Value	Association P-Value
Grip Strength	All	29.789 (29.68, 29.897)	31.328 (31.224, 31.427)	31.516 (31.412, 31.617)	32.989 (32.883, 33.098)	< 1e-323	7.53E-25
	Women	22.255 (22.172, 22.334)	23.036 (22.975, 23.103)	23.606 (23.543, 23.669)	24.391 (24.314, 24.465)	5.32E-269	1.33E-08
	Men	37.903 (37.788, 38.015)	39.534 (39.44, 39.631)	40.232 (40.142, 40.317)	40.968 (40.867, 41.077)	7.45E-278	1.55E-24
	Group	Q1	Q2	Q3	Q4	Non-linearity P-Value	Association P-Value
FFMV	All	9.781 (9.69, 9.87)	9.965 (9.876, 10.064)	9.894 (9.797, 9.99)	10.176 (10.09, 10.268)	1.73E-80	3.58E-13
	Women	7.742 (7.68, 7.808)	7.747 (7.698, 7.799)	7.761 (7.711, 7.809)	7.974 (7.915, 8.033)	4.46E-49	9.19E-09
	Men	11.47 (11.391, 11.546)	11.68 (11.613, 11.746)	11.703 (11.635, 11.771)	11.747 (11.668, 11.833)	8.08E-39	2.99E-09
	Group	Q1	Q2	Q3	Q4	Non-linearity P-Value	Association P-Value
ALM/BMI	All	0.773 (0.767, 0.779)	0.802 (0.796, 0.808)	0.806 (0.8, 0.812)	0.833 (0.827, 0.839)	2.36E-37	1.57E-03
	Women	0.63 (0.625, 0.635)	0.65 (0.646, 0.655)	0.665 (0.661, 0.669)	0.682 (0.677, 0.687)	1.05E-21	7.02E-03
	Men	0.892 (0.887, 0.898)	0.916 (0.911, 0.92)	0.924 (0.92, 0.929)	0.939 (0.934, 0.945)	2.84E-18	2.36E-03
	Group	Q1	Q2	Q3	Q4	Non-linearity P-Value	Association P-Value

ALM/Height²	All	7.215 (7.171, 7.259)	7.185 (7.145, 7.224)	7.102 (7.062, 7.146)	7.22 (7.179, 7.259)	2.03E-76	3.75E-05
	Women	6.475 (6.427, 6.529)	6.326 (6.284, 6.372)	6.265 (6.227, 6.305)	6.324 (6.284, 6.366)	6.38E-29	5.39E-04
	Men	7.839 (7.792, 7.886)	7.84 (7.802, 7.882)	7.815 (7.774, 7.856)	7.853 (7.815, 7.897)	6.53E-47	2.42E-04

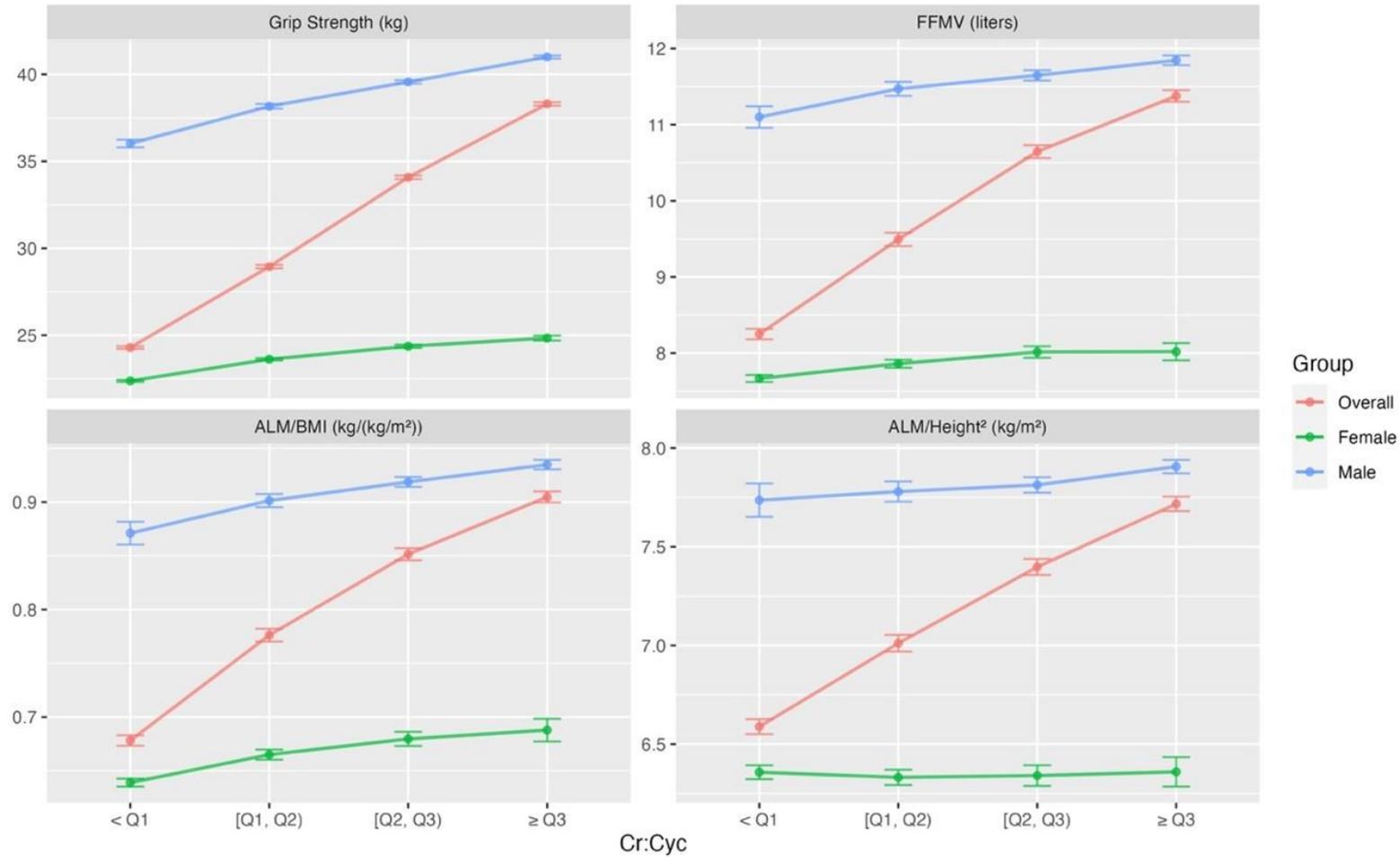
Supplemental eFigure 1. Flow chart of the final analytical sample in the imaging cohort for FFMV, ALM/BMI and ALM/Height².



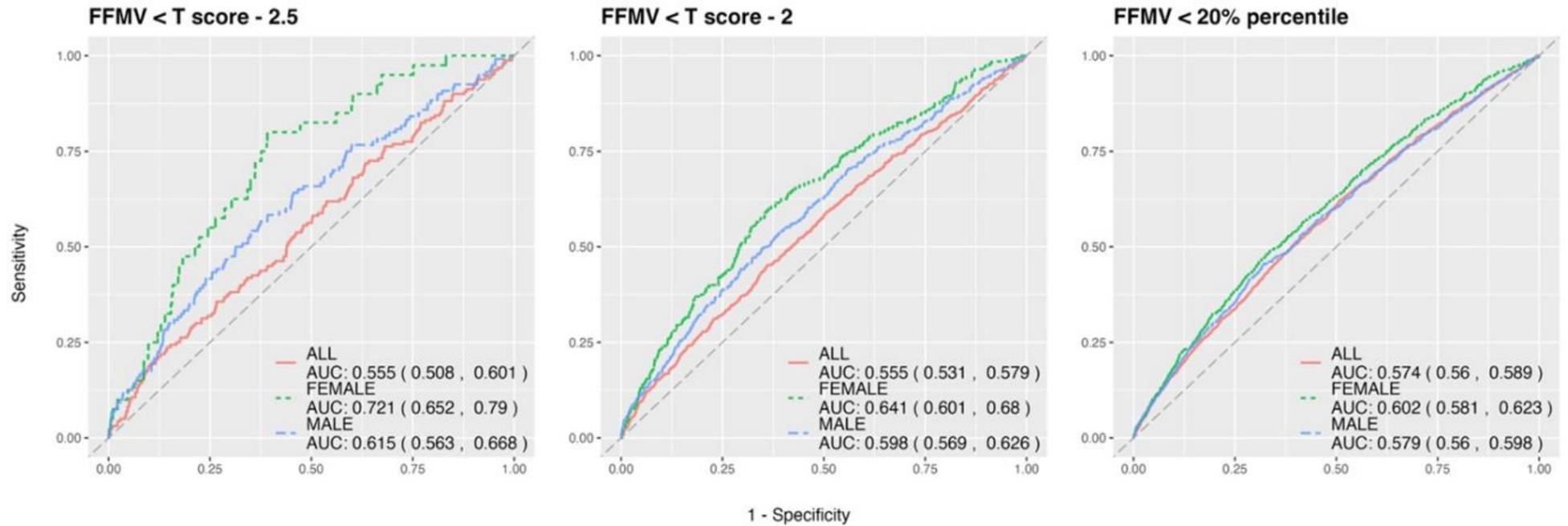
Supplemental eFigure 2. Flow chart of the final analytical sample in the baseline cohort for grip strength.



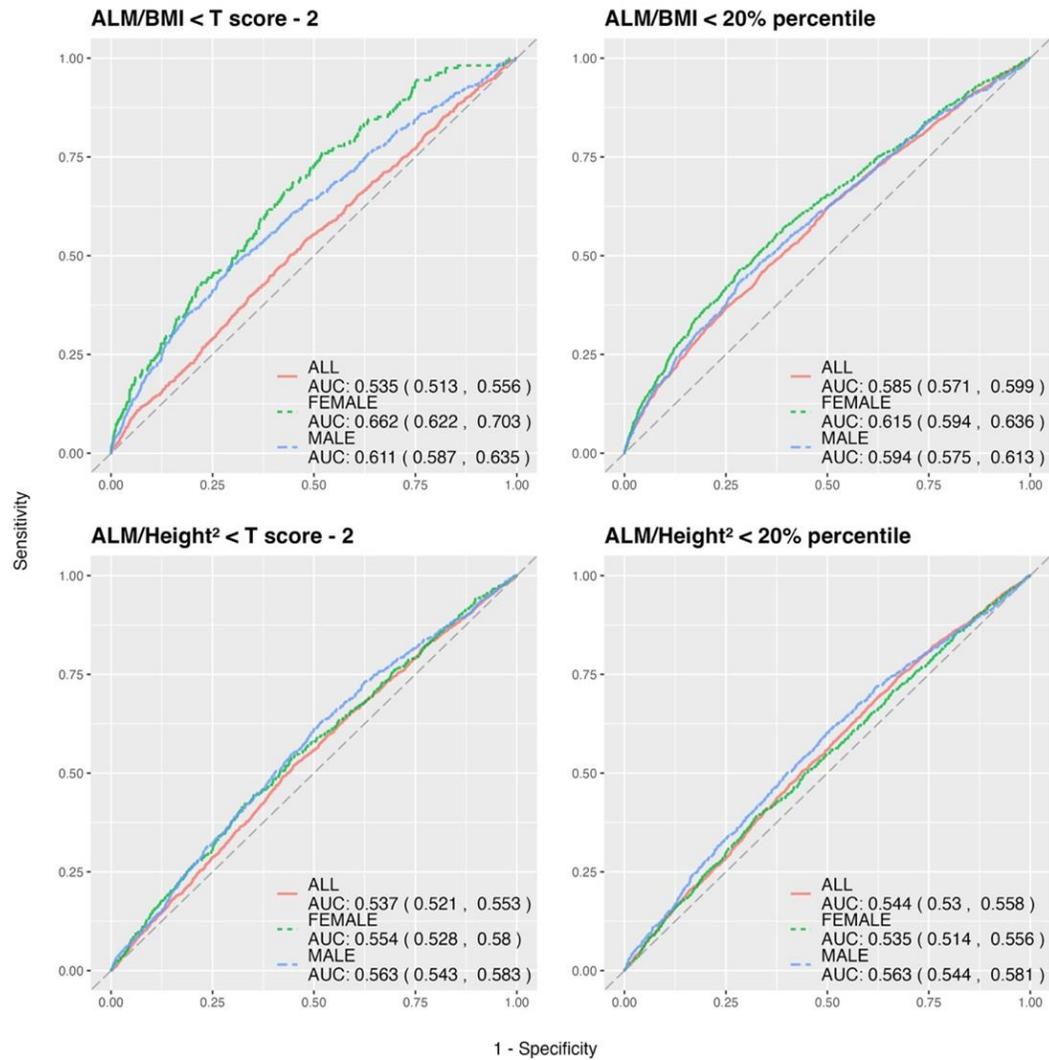
Supplemental eFigure 3. Means and their 95% confidence intervals for different outcomes across the quartile groups of Cr:Cyc, overall and by sex adjusting for covariates.



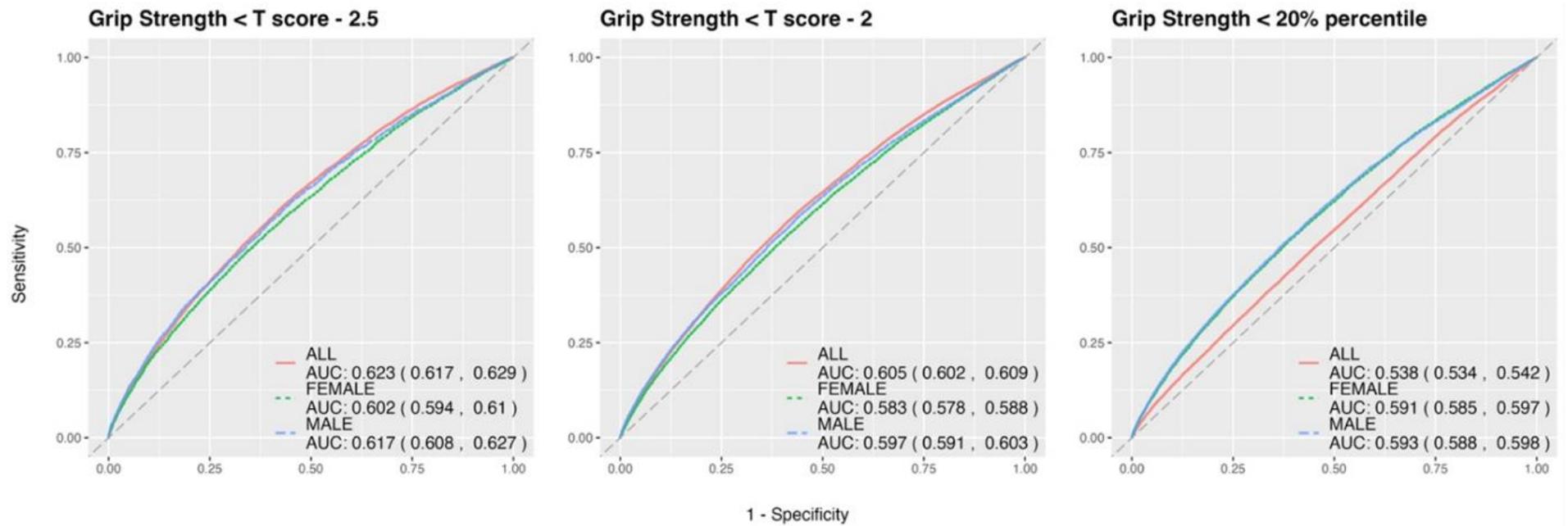
Supplemental eFigure 4. Receiver operator characteristic curves shows the diagnostic power of Cr:Cyc for identifying low FFMV using cutpoints. Models are unadjusted.



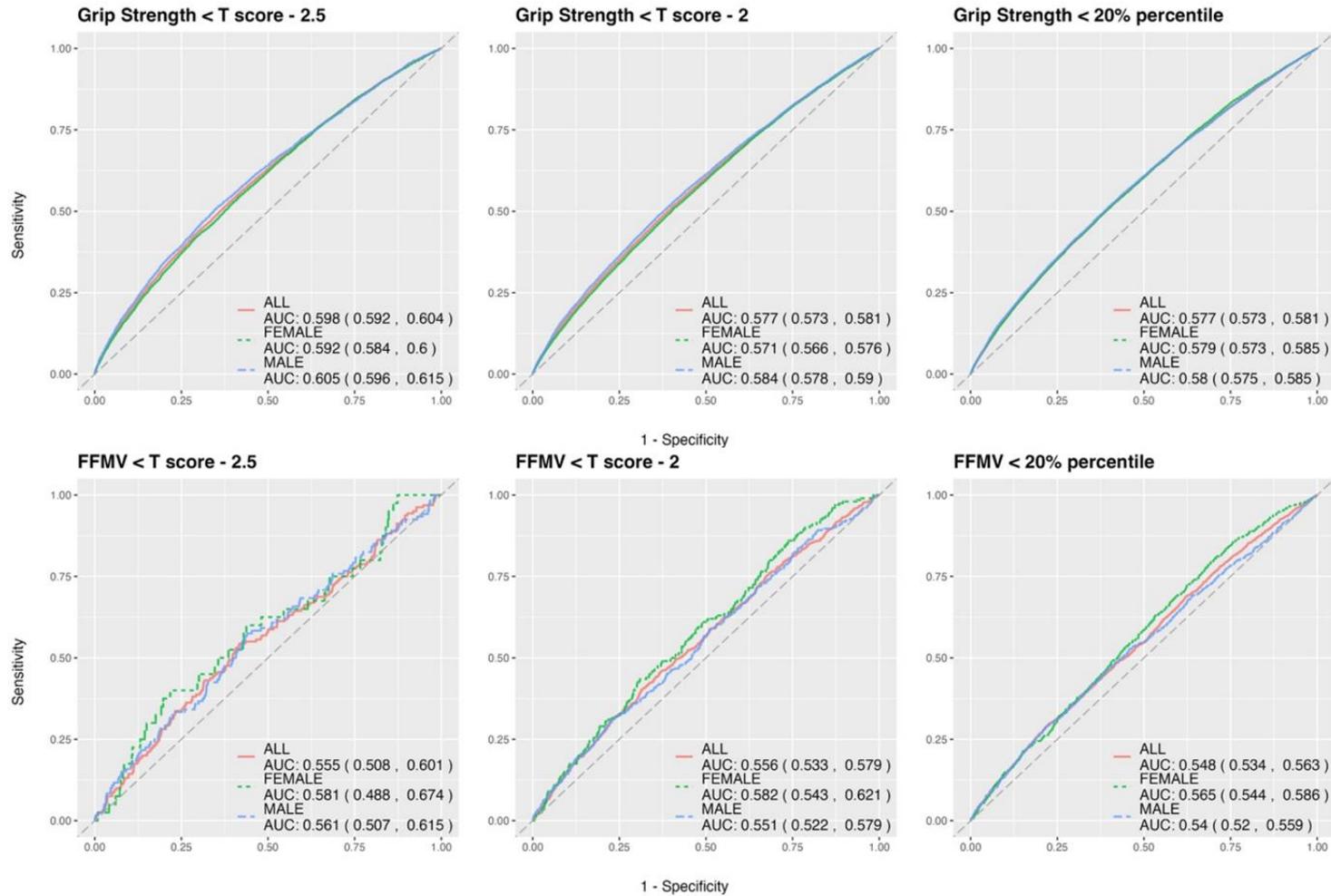
Supplemental eFigure 5. Receiver operator characteristic curves shows the diagnostic power of Cr:Cyc for identifying low ALM/BMI or ALM/Height² using cutpoints. Models are unadjusted.



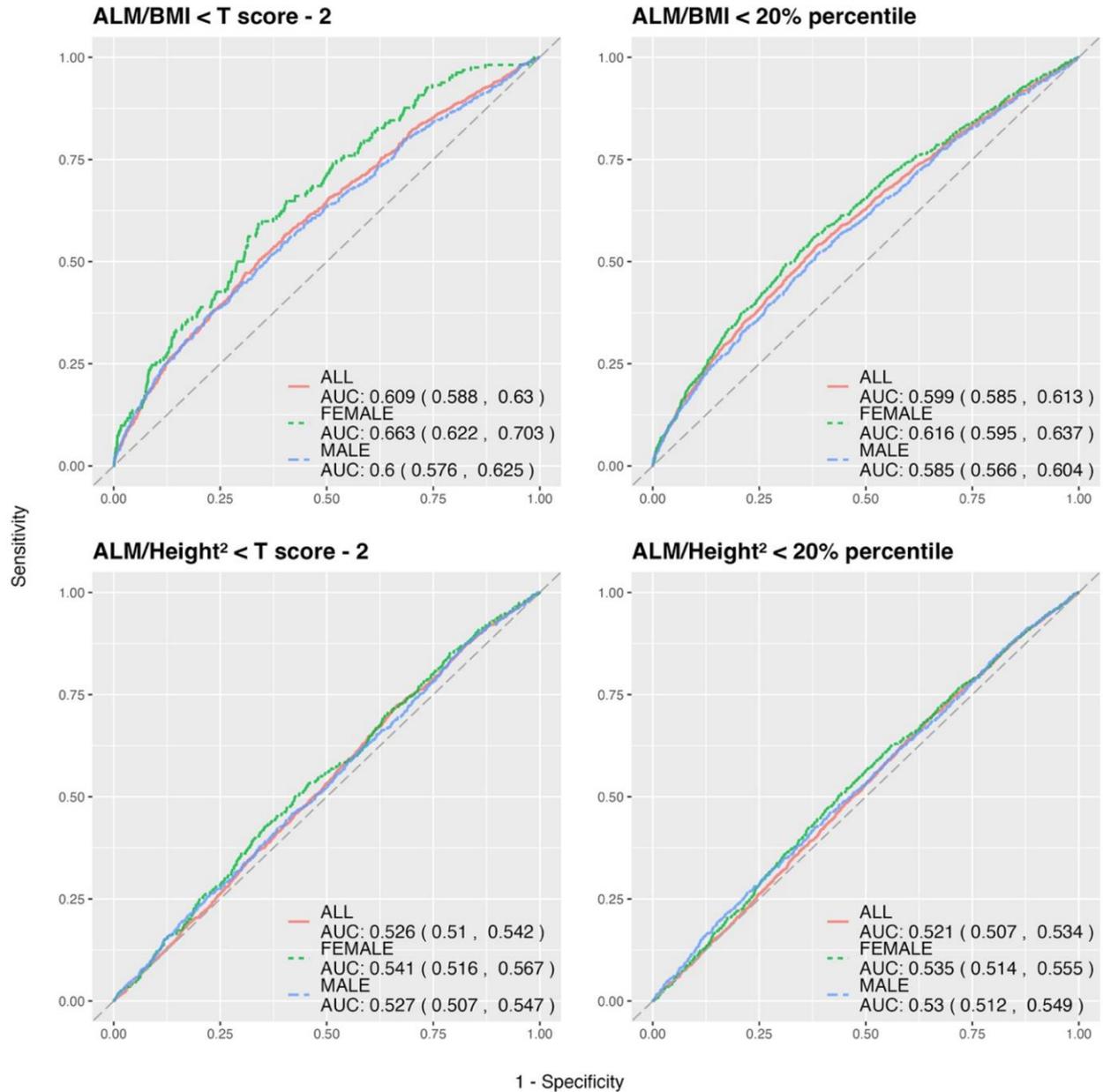
Supplemental eFigure 6. Receiver operator characteristic curves shows the diagnostic power of Cr:Cyc for identifying low grip strength using cutpoints. Models are unadjusted.



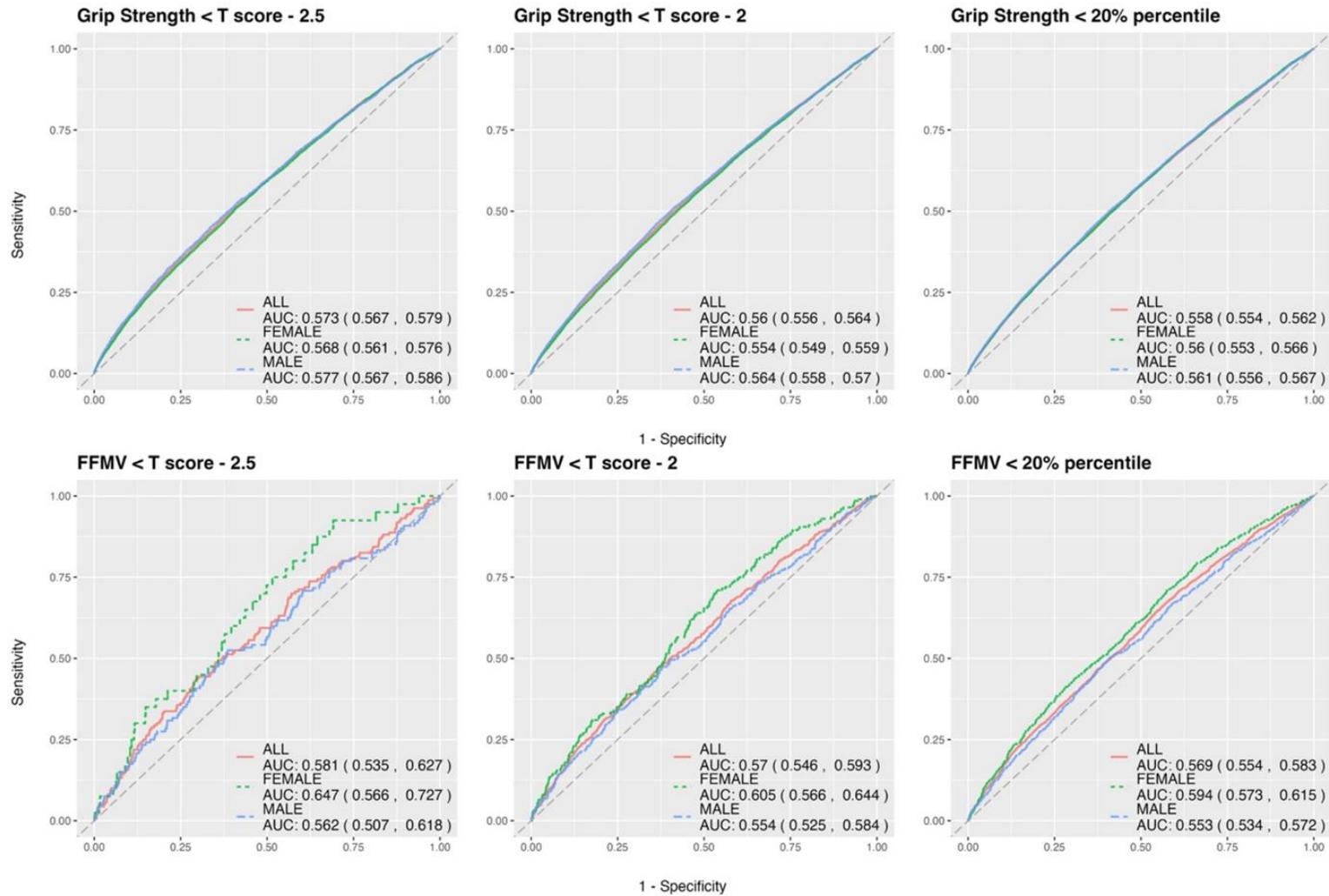
Supplemental eFigure 7. Receiver operator characteristic curves shows the diagnostic power using the biomarker difference between Creatinine and Cystatin C for identifying low grip strength or low FFMV using cutpoints. Models are unadjusted.



Supplemental eFigure 8. Receiver operator characteristic curves shows the diagnostic power using the biomarker difference between Creatinine and Cystatin C for identifying low ALM/BMI or ALM/Height² using cutpoints. Models are unadjusted.



Supplemental eFigure 9. Receiver operator characteristic curves shows the diagnostic power using the biomarker difference between Creatinine and Cystatin C for identifying low grip strength or low FFMV using cutpoints. Models are fully-adjusted.



Supplemental eFigure 10. Receiver operator characteristic curves shows the diagnostic power using the biomarker difference between Creatinine and Cystatin C for identifying low ALM/BMI or ALM/Height² using cutpoints. Models are fully-adjusted.

