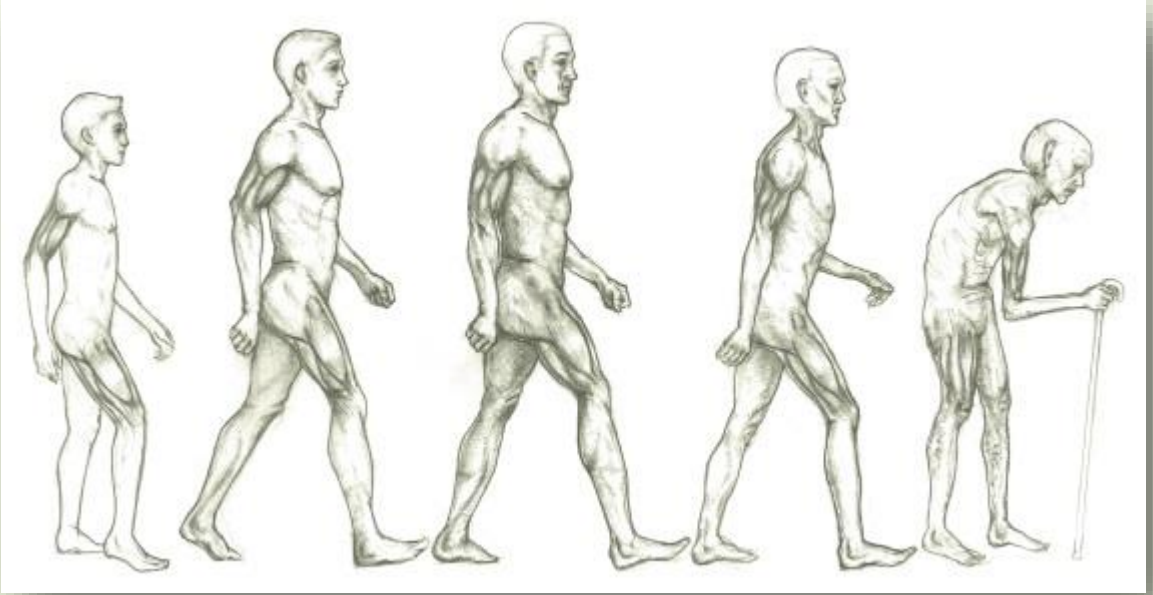
The Association between Different Skeletal Muscle Indices of Low Muscle Mass and its Dysfunction



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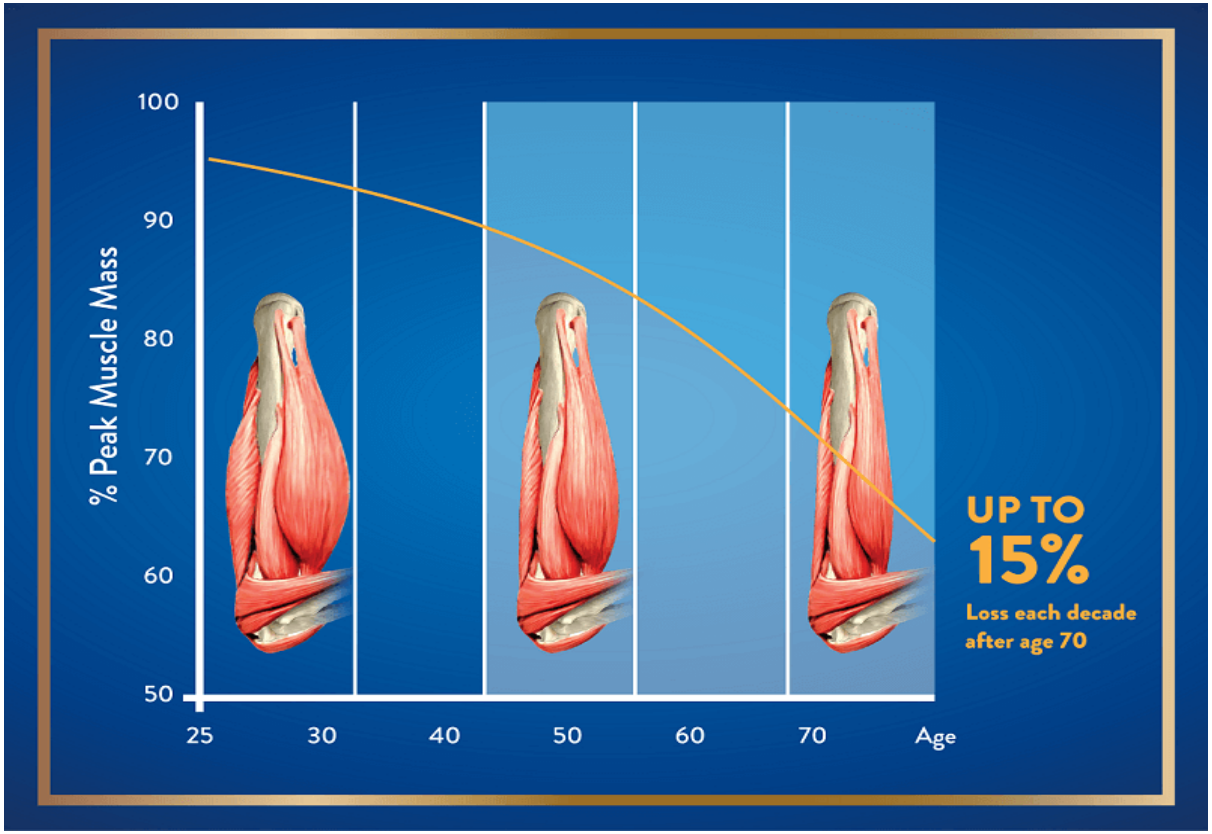
Background

Sarcopenia = Age-related loss of muscle mass

- 3-8% loss of muscle mass per decade after 30-year-old
- 0.5-1.0% loss of muscle mass per year after 70-year-old



Loss of muscle mass

↓ strength

↓ function

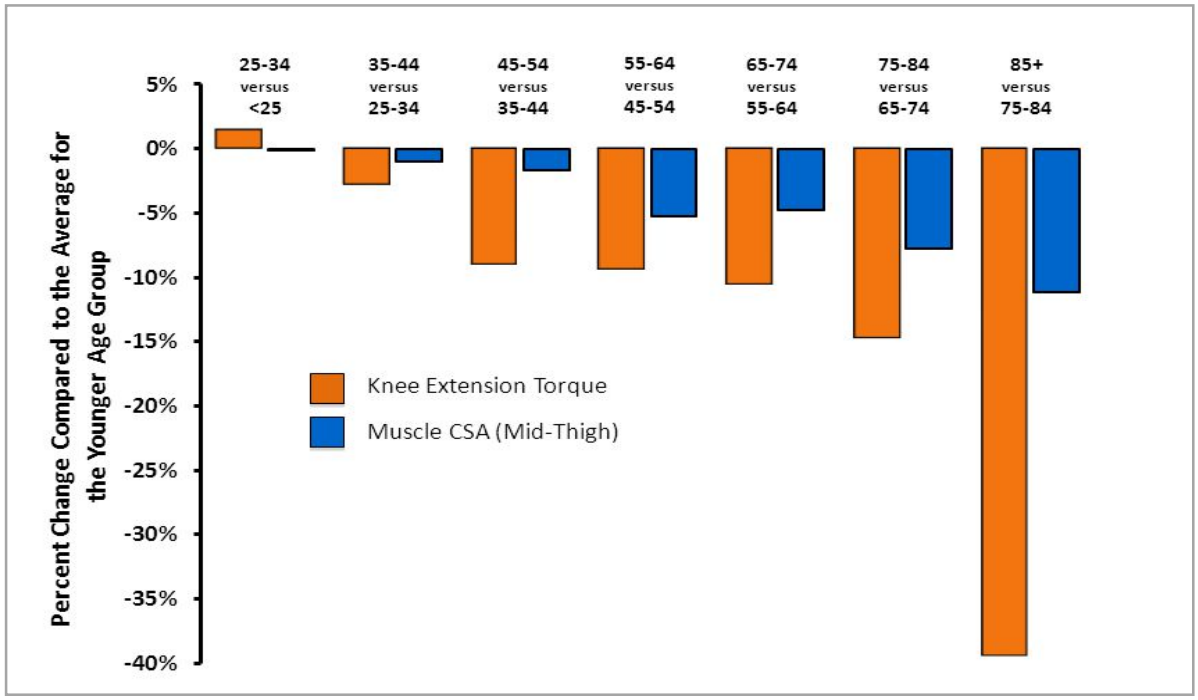
Rosenberg I. Am J Clin Nutr. 1989
Holloszy JO. Mayo Clin Proc. 2000
Baumgartner et al. 1998

Von Haehling S (2010)

- Muscle strength declines by 1.5% between ages 50-60 and by 3% thereafter

Baltimore Longitudinal Study of Aging (BLSA) to estimate age-related change of muscle strength every 10 years

- isokinetic dynamometry
- dual-energy X-ray absorptiometry(DXA)



Dynapenia

= Age-related loss of muscle Strength

Stages of Sarcopenia (EWGSOP 2010)

Stage	Muscle Mass	Muscle Function
Pre-sarcopenia	↓	Normal
Sarcopenia	↓	↓ Muscle strength or ↓ Physical Performance
Severe Sarcopenia	↓	↓ Muscle strength and ↓ Physical Performance

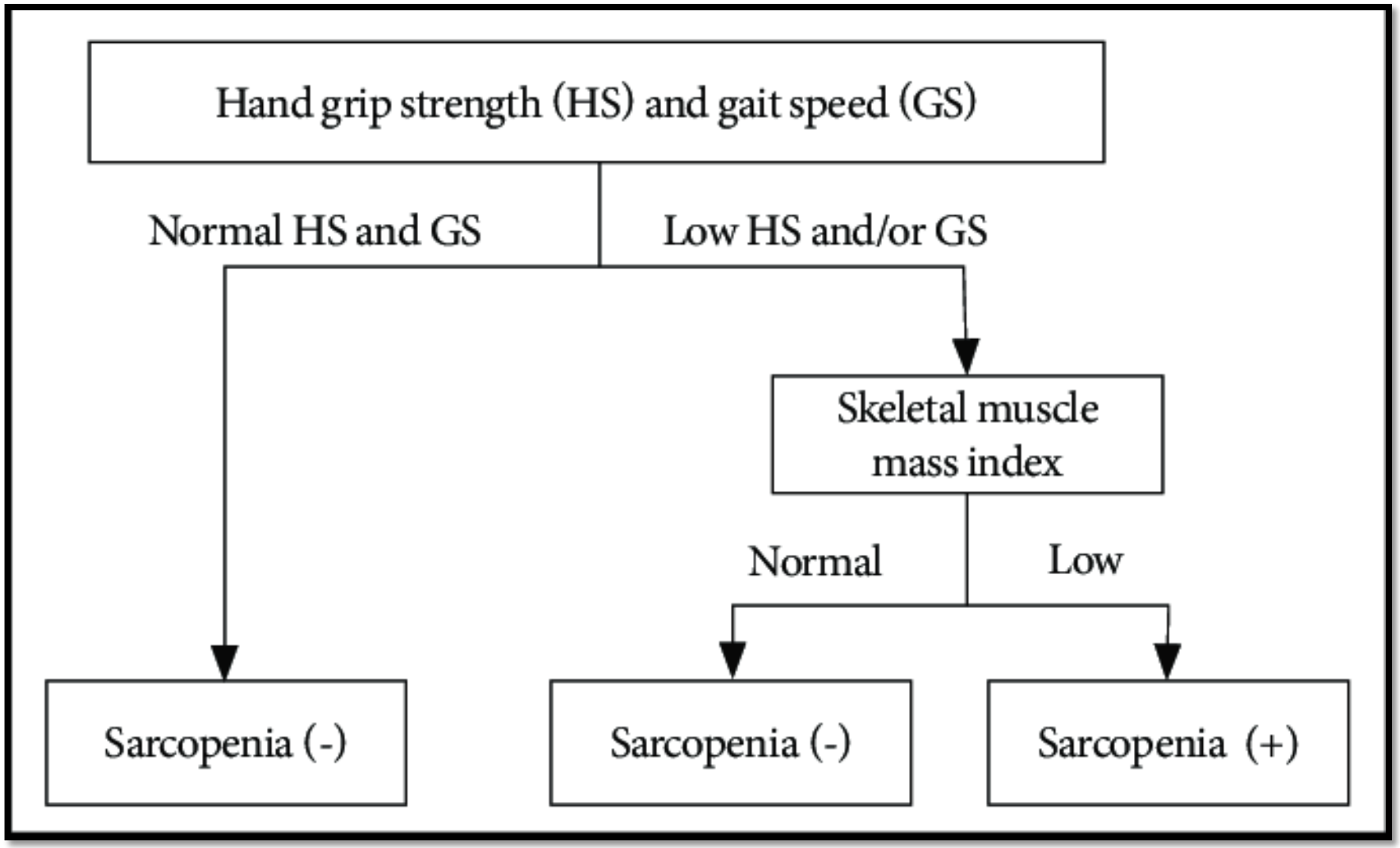
Cruz-Jentoft AJ , Age Ageing. 2010 Jul;39

Recommended cut-off values for Sarcopenia diagnosis

Measure	Technique	Cut-off value	
		Asia(2014)	(Europe2010)
Muscle Mass	DXA (ASM/height^2)	Men: 7.0 kg/m^2 Women: 5.4 kg/m^2	Men: 7.26 kg/m^2 Women: 5.50 kg/m^2
	BIA (ASM/height^2)	Men: 7.0 kg/m^2 Women: 5.7 kg/m^2	Men: 8.87 kg/m^2 Women: 6.42 kg/m^2
Muscle strength	Handgrip strength	Men: < 26 kg Women: < 18 kg	Men: < 30 kg Women: < 20 kg
Physical performance	Gait speed	≤ 0.8 m/s	≤ 0.8 m/s

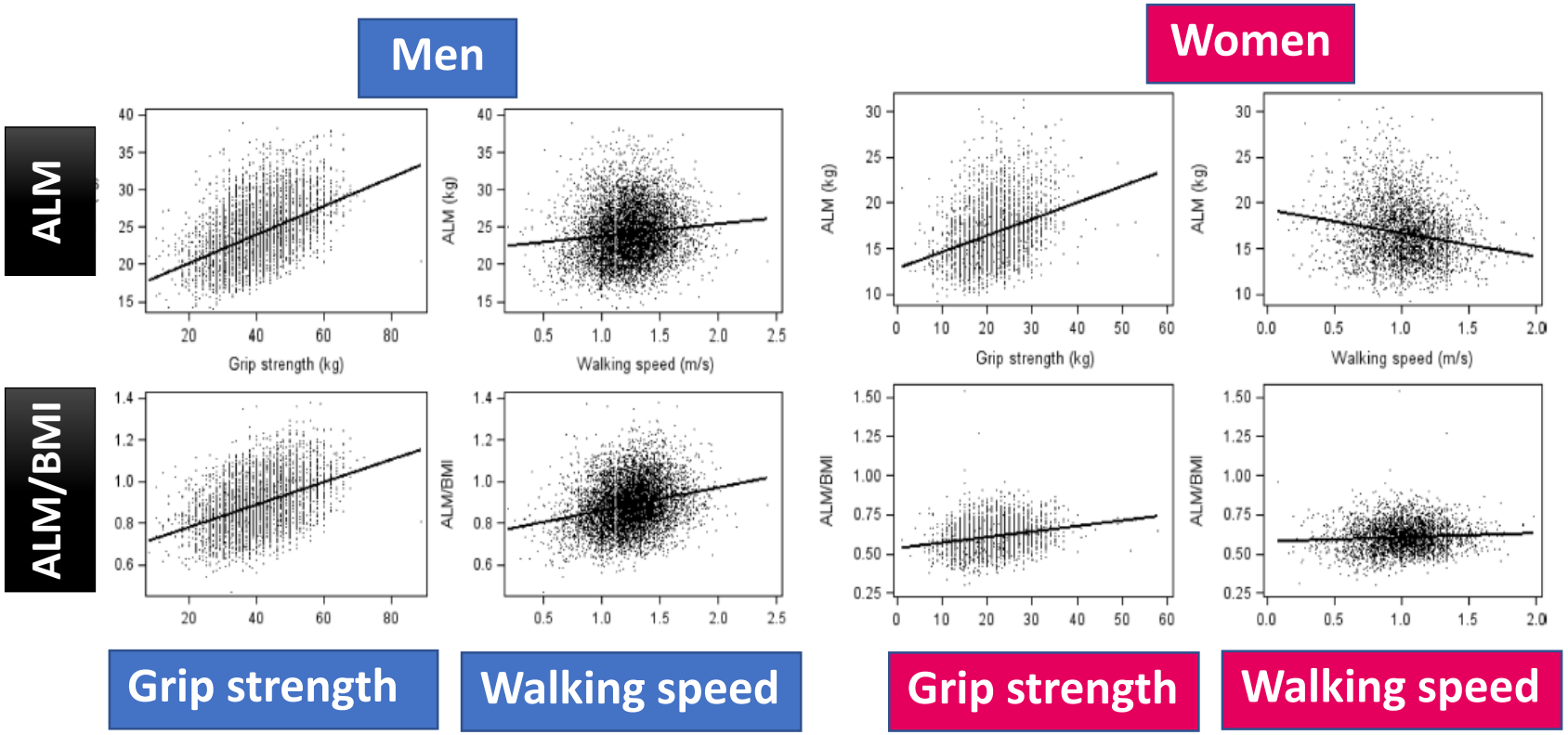
- ASM =Appendicular Skeletal Mass or ALM = Appendicular Lean Mass
  - Summation of skeletal muscle mass from both arms and legs
- BIA=Bioelectrical Impedance Analyzer
- DXA=dual X-ray absorptiometry

Asian Working Group for Sarcopenia (AWGS 2014) according to the definition of elderly (≥ 60 or 65 years)



Previous studies

Low Appendicular Lean Mass With Clinically Significant Weakness



Only ALM/BMI and ALM as potential discriminators of weakness

Foundation for the National Institutes of Health (FNIH) Sarcopenia Project
J Gerontol A Biol Sci Med Sci. 2014

Waist to Height Ratio(WHtR)

- **Indicator of central obesity**
- **Superior to BMI in detecting several outcomes including**
  - **incident cardiovascular disease**
  - **cardiovascular disease mortality**
  - **all-cause mortality**

Ashwell M, Obes Rev 2012
Savva SC, Diabetes Metab Syndr Obes. Ocy 24 ,2013

Adjusted ALM with BMI, Body surface Area and WHtR more associated with muscle strength and performance than ALM/height2

Jae Seung Chang, Geriatrics Geront Int 2017;17

Objective

- **Primary outcomes**
  - To compared cutoff values of various muscle mass indices to muscle function
  - Prevalence of Sarcopenia and impaired muscle function
- **Secondary outcomes**
  - To evaluate factors associated with muscle dysfunction

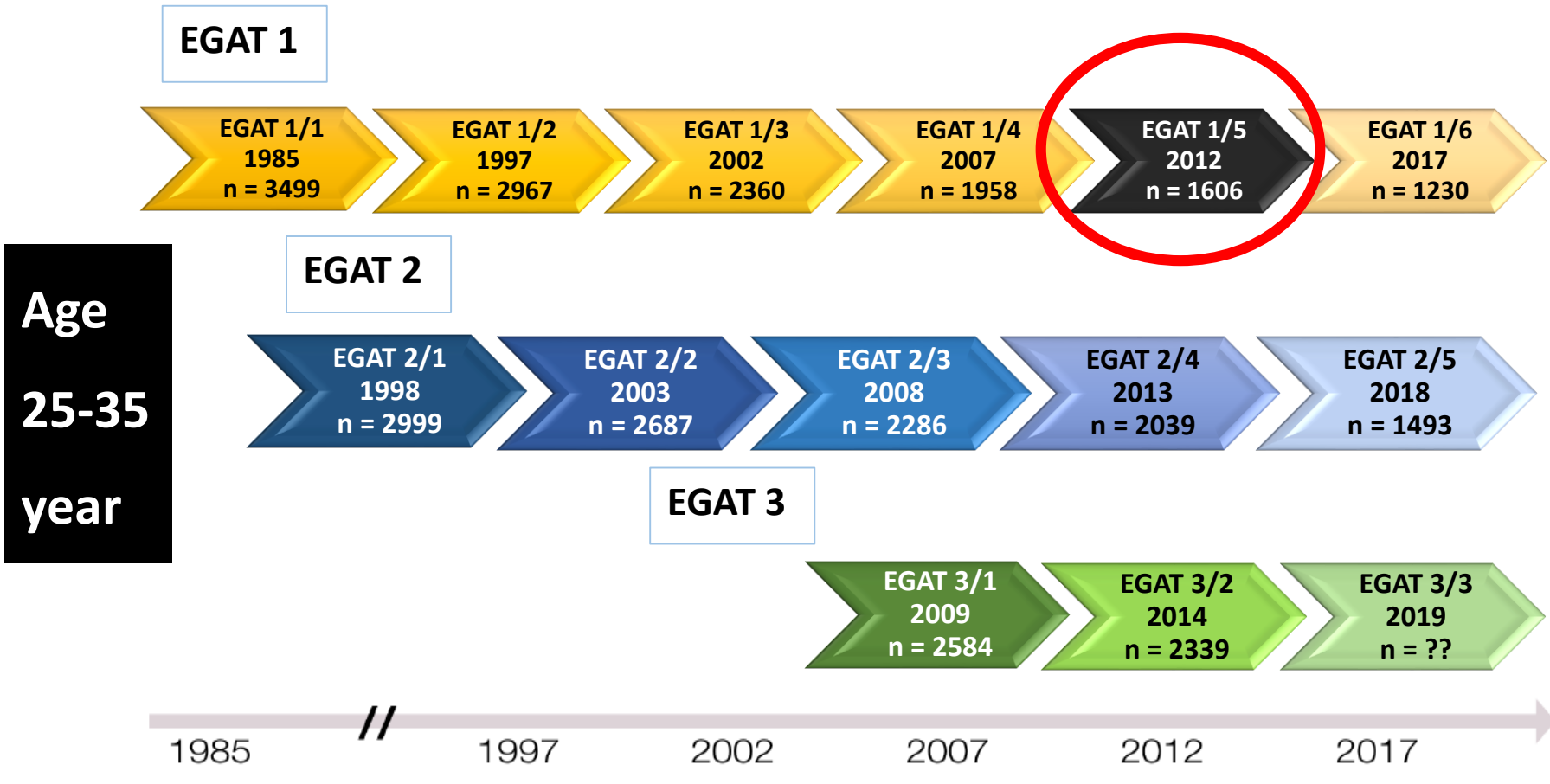
Material and Methods

- **Retrospective cross-sectional study**
- **Obtained data from Electricity Generating Authority of Thailand (EGAT1/5) between June to August 2012**

- **Exclusion criteria**
  - **Age under 60 years**
  - **Incomplete all examination of hand grip strength, 4-metre walk test and body composition analysis with bioelectrical impedance analyzer (BIA)**
- **1256 older participants**
  - **Demographic data of age, gender and comorbid disease**
  - **Cognitive assessment : 3-item recall and clock drawing test**

Background of study population

- **EGAT1 study started in 1985**
  - **Cross-sectional design in cohort study**
  - **Mainly covered details of CVD risk**
  - **The 5 years interval of follow up**



Muscle Strength and Physical performance

- **Handgrip strength (HGS)**
  - **Maximum value was selected for evaluation**
  - **Low HGS : Male <26 kg , Female <18 kg**

- **Gait speed (GS) from 4-m walk test**
  - **Low GS : < 0.8 m/s**

Material and Methods (Cont.)

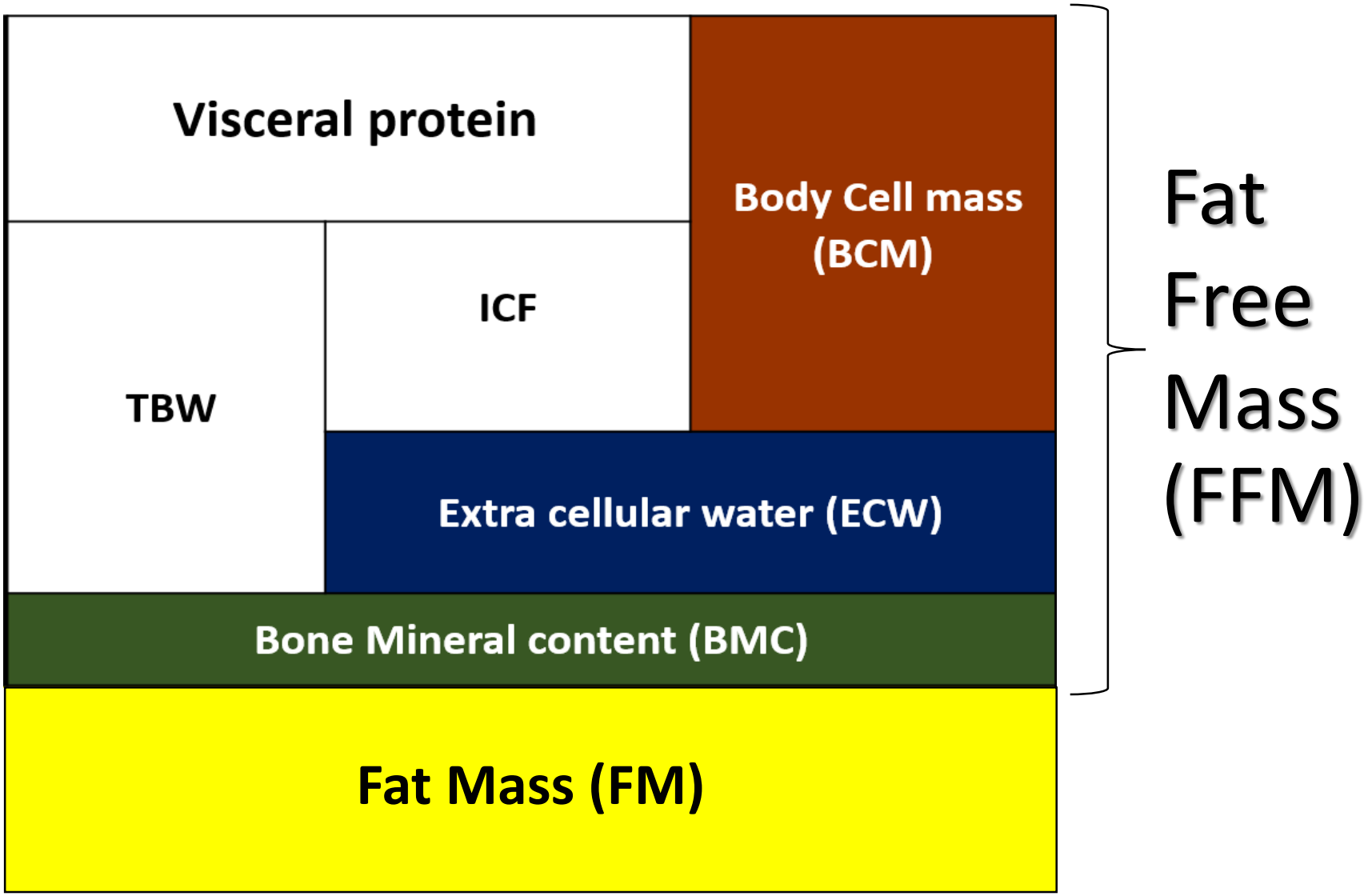
Anthropometry

- Body Weight (BW)
- Height (H)
- Waist Circumference (WC)
- Body Mass Index (BMI)
- Waist to Height Ratio (WHtR)

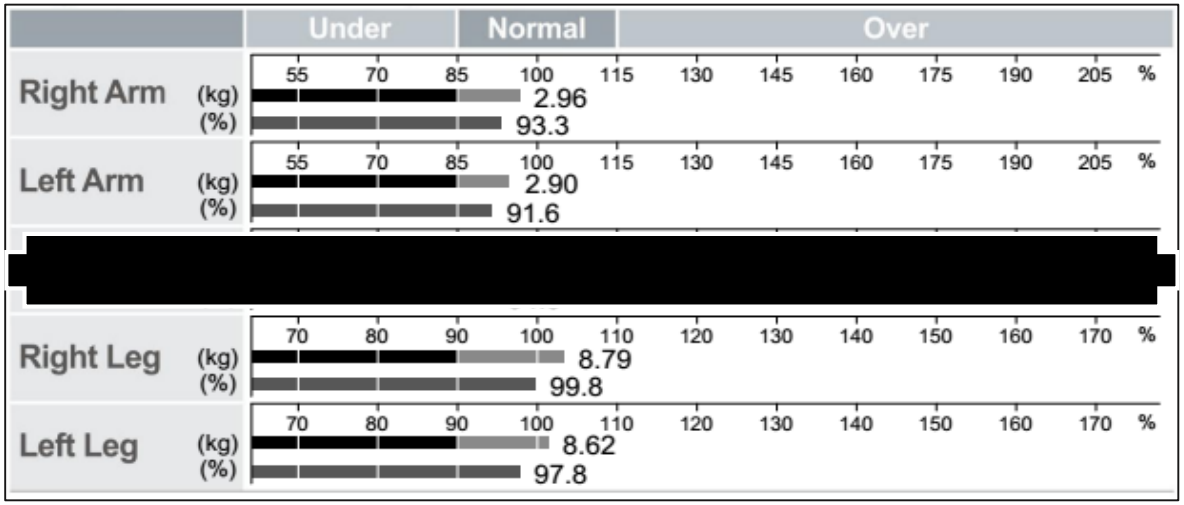
Body composition analysis

- Fat Mass (FM)
- Percentage of Body Fat (%BF)
- Lean Body Mass or Body Cell Mass (BCM)
- Extracellular Water (ECW)
- Body Mineral Content (BMC)
- Appendicular Skeletal Mass (ASM)

Body composition compartments



Segmental analysis from BIA

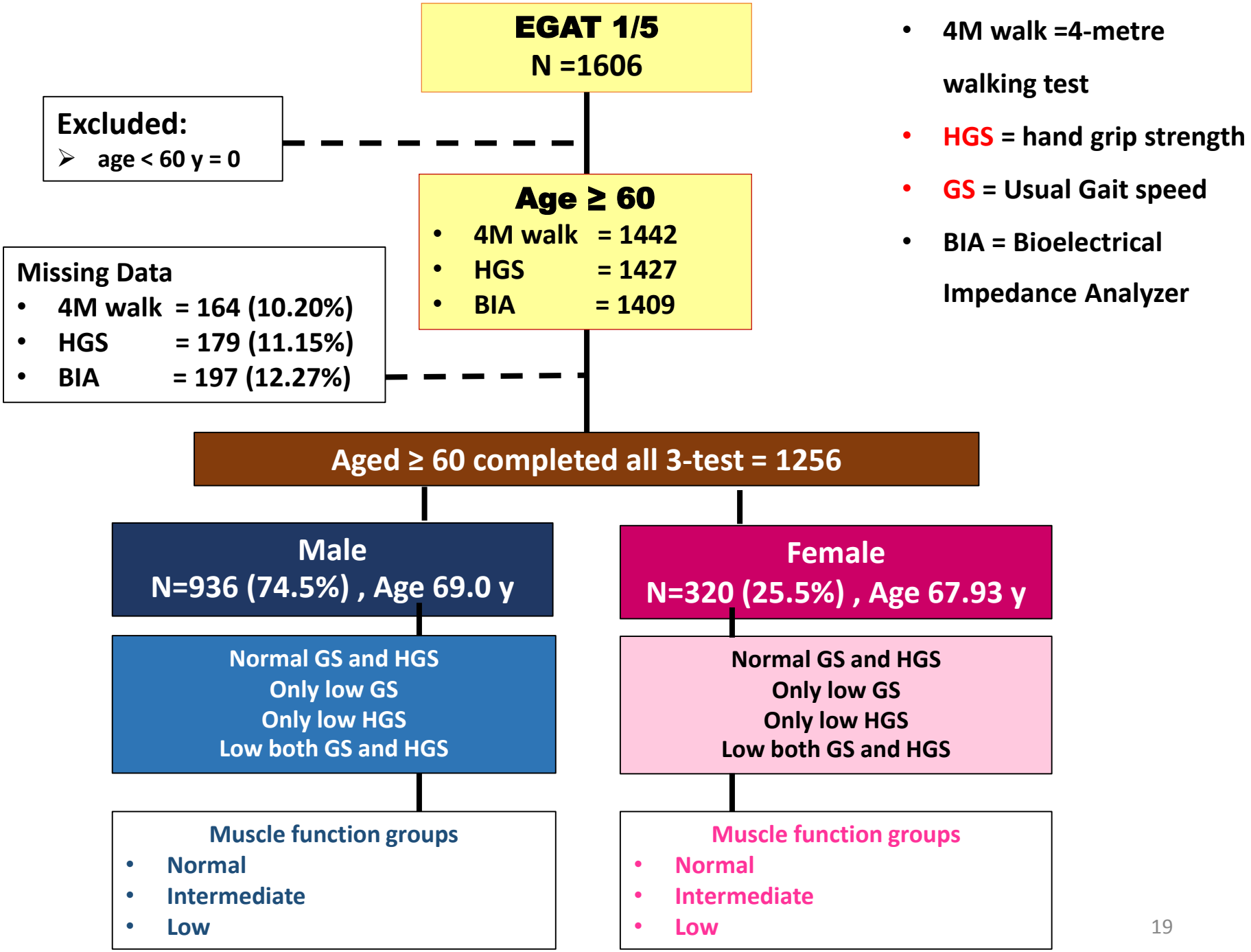


- **ASM** =Appendicular Skeletal Mass or **ALM** = Appendicular Lean Mass
  - Summation of skeletal muscle mass <u>from both arms and legs</u>
- **BIA**=Bioelectrical Impedance Analyzer

Adjusted skeletal muscle indices

- ASM/ height2 (ASM/H2)
  - Low muscle mass (kg/m2) : Male < 7.0 , Female < 5.7
- Percentage of ASM/ body weight (%ASM)
- ASM/ BMI
- ASM/ WHtR

- ASM =Appendicular Skeletal Mass
  - Summation of skeletal muscle mass from both arms and leg
- BMI =Body Mass Index (kg/m2)
- WHtR = Waist to Height Ratio


EGAT 1/5
N =1606
Excluded:
age < 60 y = 0
Age ≥ 60
4M walk = 1442
HGS = 1427
BIA = 1409
Missing Data
4M walk = 164 (10.20%)
HGS = 179 (11.15%)
BIA = 197 (12.27%)
Aged ≥ 60 completed all 3-test = 1256
Male
N=936 (74.5%) , Age 69.0 y
Female
N=320 (25.5%) , Age 67.93 y
Normal GS and HGS
Only low GS
Only low HGS
Low both GS and HGS
Normal GS and HGS
Only low GS
Only low HGS
Low both GS and HGS
Muscle function groups
Normal
Intermediate
Low
Muscle function groups
Normal
Intermediate
Low
4M walk =4-metre walking test
HGS = hand grip strength
GS = Usual Gait speed
BIA = Bioelectrical Impedance Analyzer

Statistical analysis

- All statistical analyses were carried out using SPSS 18.0 (IBM Corporation, Armonk, NY, USA)
- Descriptive data were presented as mean (±SD) for quantitative variables and as frequency or percentage for categorical variables
- One-way analysis of variance (ANOVA) with Bonferroni method was used for multiple comparisons
- p-value <0.05 was considered statistically significant

Statistical analysis (Cont.)

- Cut-off values to discriminate muscle mass for muscle dysfunction
  - Receiver operating characteristic (ROC) analyses
  - Maximizing Sensitivity and Specificity using the Youden index
- Univariate logistic regression analyses
  - To determine predictors of muscle dysfunction
- Chi-Square test
  - To determine presence or absence of disease to muscle function

Results

Baseline characteristics of older men

	Male (N=936)				
	Normal both GS and HGS	Only low GS	Only low HGS	Low both GS and HGS	P-value
N (%)	637 (68.06)	100 (10.68)	159 (16.99)	40 (4.27)	
Age (y)	67.96±4.82	70.53±4.75*	71.25±4.73*	72.83±4.53*	<0.001
Height (Cm.)	165.04±0.44	165.21±5.25	162.16±5.49*$_x$	160.87±4.88*	<0.001
BW (Kg.)	67.50±9.65	67.77±10.28	63.55±11.21*$_x$	63.92±9.31	<0.001
WC (Cm.)	89.83±10.48	91.47±9.77	88.35±10.56	88.81±9.83	0.121
BMI	24.76±3.17	24.82±3.52	24.12±3.85	24.72±3.57	0.177
WHtR	0.54±0.06	0.55±0.06	0.54±0.06	0.55±0.06	0.464

p< 0.05 ,significant compared between groups; * significant compared to normal GS and HGS; $_x$ significant between only low HGS to only low GS group

BW=body weight; WC= waist circumference; BMI=body mass index; WHtR=waist to height ratio

Baseline characteristics of older men (Cont.)

	Male (N=936)				
	Normal both GS and HGS	Only low GS	Only low HGS	Low both GS and HGS	P-value
FM(Kg.)	18.09±6.27	19.24±7.06	18.17±7.44	18.58±6.45	0.424
%BF	26.22±6.29	27.16±6.93	27.66±8.41	28.32±7.33	0.055
BCM (Kg.)	31.89±3.50	31.24±3.40	29.20±3.52*$_x$	29.08±3.09*	<0.001
BMC (Kg.)	2.70±0.31	2.67±0.30	2.51±0.30*	2.49±0.29*	<0.001
ECW (Kg.)	14.82±1.76	14.61±1.58	13.66±1.62*$_x$	13.76±1.44*	<0.001
ASM (Kg.)	20.76±2.64	20.42±2.60	18.76±2.78*$_x$	18.71±2.12*	<0.001
HGS (Kg.)	33.72±5.02	31.49±3.91*	22.49±2.97*$_x$	22.58±3.43*	<0.001
4M walk (sec)	3.87±0.58	5.86±1.04*	4.05±0.58*$_x$	6.02±1.18*	<0.001
GS (m/sec)	1.06±0.17	0.70±0.09*	1.01±0.16*$_x$	0.68±0.10*	<0.001

p< 0.05 ,significant compared between groups; * significant compared to normal GS and HGS; $_x$ significant between only low HGS to only low GS group

FM=fat mass; %BF=percentage of body fat; BCM=body cell mass; BMC=body mineral content; ECW=extracellular water; ASM=appendicular skeletal mass; HGS=hand grip strength; 4M walk, 4 metre walk test ; GS=gait speed

Baseline characteristics of older women

	Female (N=320)				
	Normal both GS and HGS	Only low GS	Only low HGS	Low both GS and HGS	P-value
N (%)	168 (52.50)	54 (16.88)	65 (20.31)	33 (10.31)	
Age (y)	67.08±3.26	68.50±4.11	68.71±4.18*	69.80±5.07*	<0.001
Height (Cm.)	153.58±4.48	153.64±4.27	151.93±4.80	151.34±4.89	0.009
BW (Kg.)	59.31±10.75	59.73±8.91	54.53±8.59*$_x$	54.03±8.31*	<0.001
WC (Cm.)	85.98±10.37	87.22±8.86	84.07±9.25	84.75±9.91	0.337
BMI	25.13±4.33	25.35±3.96	23.64±3.66	23.59±3.38	0.018
WHtR	0.56±0.07	0.57±0.06	0.55±0.07	0.56±0.06	0.739

p< 0.05 ,significant compared between groups; * significant compared to normal GS and HGS; $_x$ significant between only low HGS to only low GS group

BW=body weight; WC= waist circumference; BMI=body mass index; WHtR=waist to height ratio

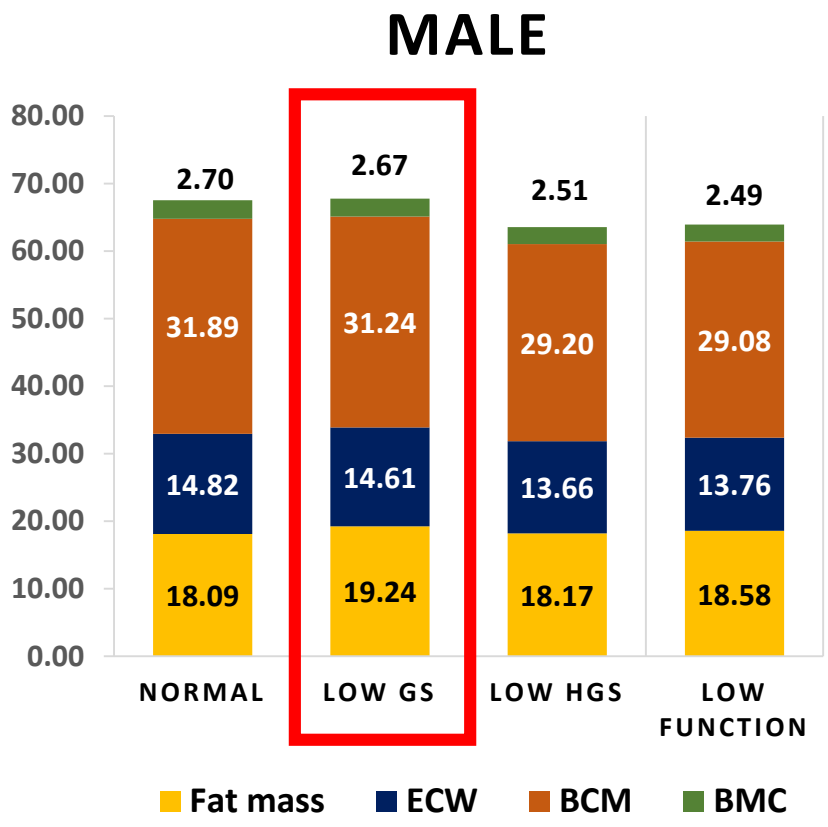
Baseline characteristics of older women (Cont.)

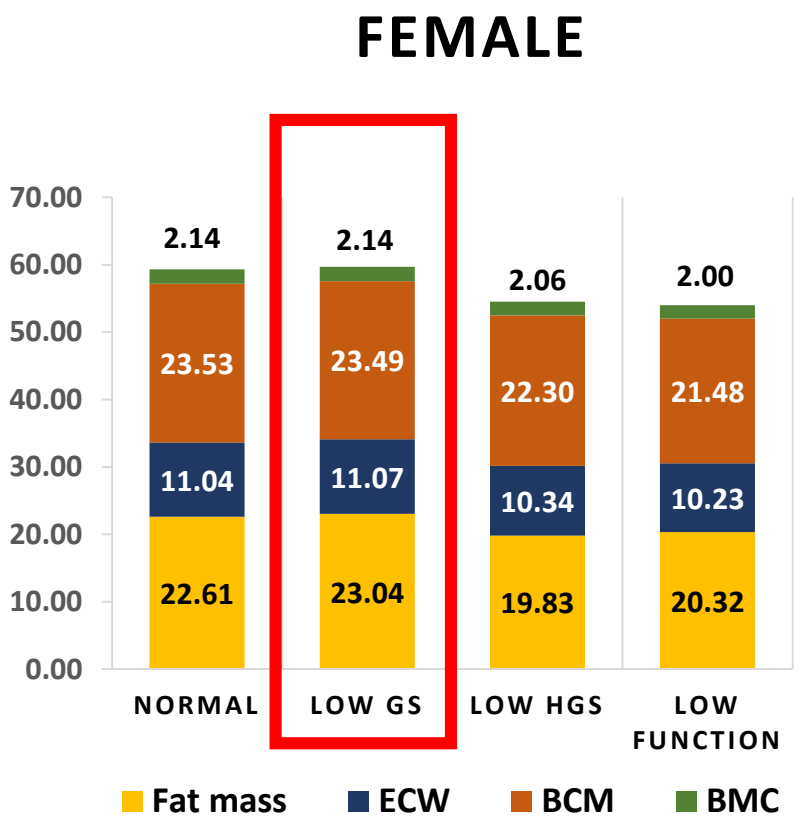
	Female (N=320)				
	Normal both GS and HGS	Only low GS	Only low HGS	Low both GS and HGS	P-value
FM(Kg.)	22.61±8.15	23.04±6.96	19.83±6.28$_x$	20.32±6.38	0.027
%BF	37.01±7.51	37.84±6.87	35.58±7.03	36.74±8.03	0.390
BCM (Kg.)	23.53±2.42	23.49±2.41	22.30±2.87*	21.48±2.37*	<0.001
BMC (Kg.)	2.14±0.24	2.14±0.19	2.06±0.21	2.00±0.23	0.002
ECW (Kg.)	11.04±1.16	11.07±1.18	10.34±1.58*$_x$	10.23±1.06*	<0.001
ASM (Kg.)	14.58±2.15	14.47±2.01	13.33±2.10*$_x$	12.99±1.68*	<0.001
HGS (Kg.)	22.03±2.92	21.42±2.89	15.32±2.30*$_x$	14.73±2.06*	<0.001
4M walk (sec)	3.97±0.54	5.84±0.85*	4.02±0.58$_x$	6.11±1.20*	<0.001
GS (m/sec)	1.03±0.15	0.70±0.08*	1.01±0.13$_x$	0.67±0.10*	<0.001

p< 0.05 ,significant compared between groups; * significant compared to normal GS and HGS; $_x$ significant between only low HGS to only low GS group

FM=fat mass; %BF=percentage of body fat; BCM=body cell mass; BMC=body mineral content; ECW=extracellular water; ASM=appendicular skeletal mass; HGS=hand grip strength; 4M walk, 4 metre walk test ; GS=gait speed

Body composition model between muscle function group

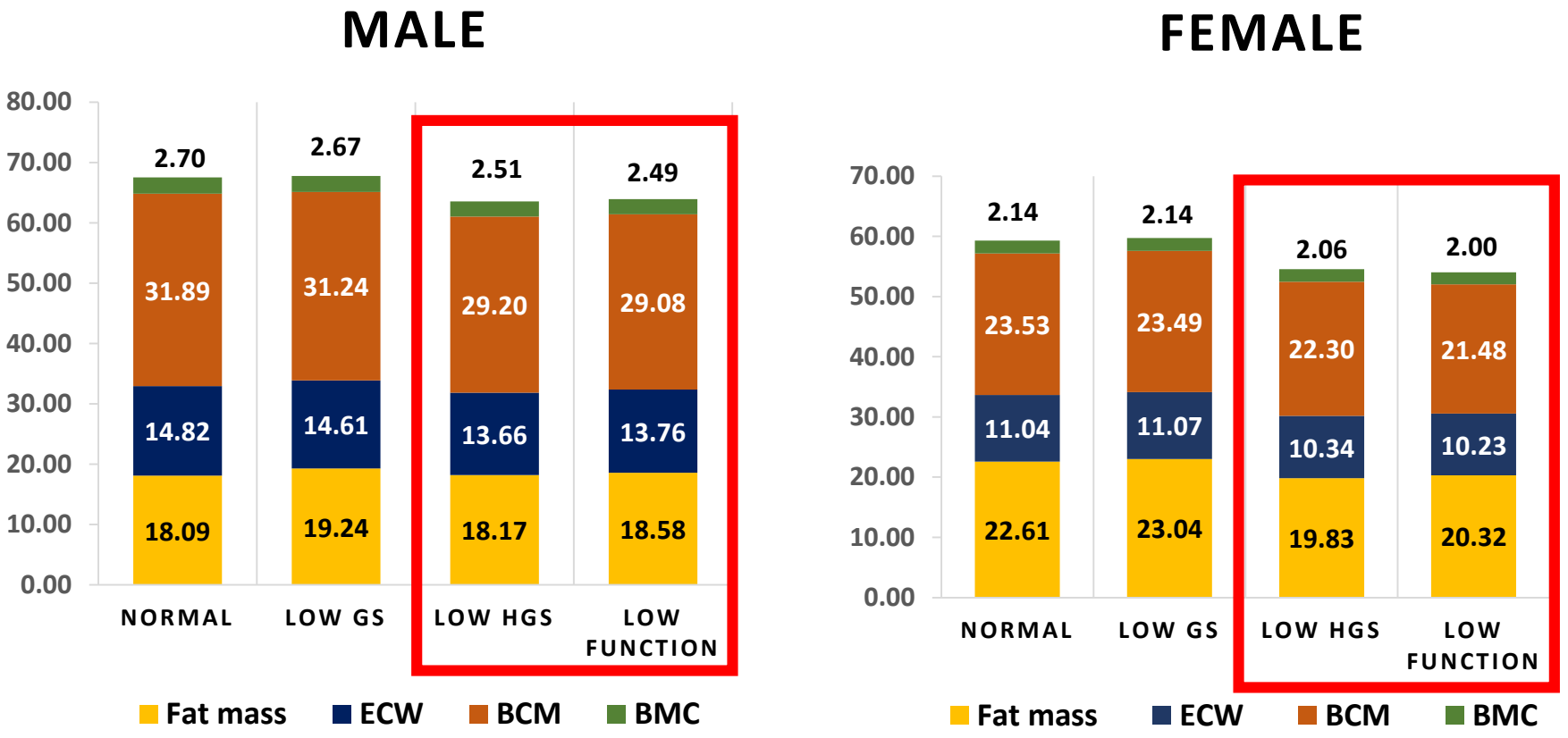




- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Low GS / Low HGS = Low gait speed , Low hand grip strength
- ❑ Low = Low both gait speed and hand grip strength

• BMC= body mineral contents; BMC = body cell mass; ECW = extracellular water

Body composition model between muscle function group



- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Low GS / Low HGS = Low gait speed , Low hand grip strength
- ❑ Low = Low both gait speed and hand grip strength

• BMC= body mineral contents; BMC = body cell mass; ECW = extracellular water

Skeletal muscle indices and Muscle function

Male Muscle function (N=936)				
Muscle Index	Normal (637)	Low GS/HGS (259)	Low both (40)	p-value
ASM /H2	7.60±0.69	7.24±0.78*	7.22 ±0.69*	<0.001
%ASM	30.93±2.64	30.03 ±3.02*	29.58±3.31*	<0.001
ASM /BMI	0.85±0.12	0.81±0.13*	0.77±0.11*	<0.001
ASM /WHtR	38.19±5.14	35.60±5.21*	34.21±4.69*	<0.001

- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Low GS/HGS = Low gait speed or Low hand grip strength
- ❑ Low both = Low both gait speed and hand grip strength

*p < 0.05,significant between groups; *significant compared with Normal group*

Skeletal muscle indices and muscle function

Female Muscle function (N=320)				
Muscle Index	Normal (168)	Low GS/HGS (119)	Low both (33)	p-value
ASM /H2	6.17±0.83	5.92±0.77*	5.66 ±0.53*	<0.001
%ASM	24.87±2.85	24.52±2.84	24.29±2.64	0.411
ASM /BMI	0.59±0.09	0.57±0.09	0.56±0.08	0.216
ASM /WHtR	26.22±3.81	24.87±3.99*	23.36±3.01*	<0.001

- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Low GS/HGS = Low gait speed or Low hand grip strength
- ❑ Low both = Low both gait speed and hand grip strength

*p < 0.05,significant between groups; *significant compared with Normal group*

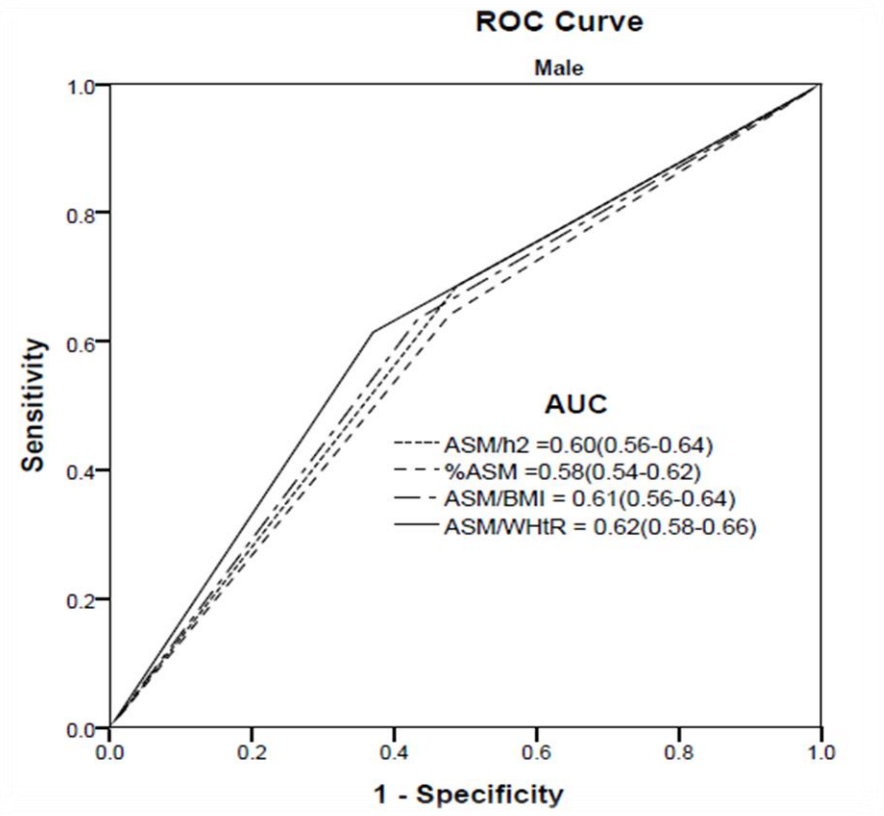
Cutoff values of skeletal muscle mass indices for muscle dysfunction

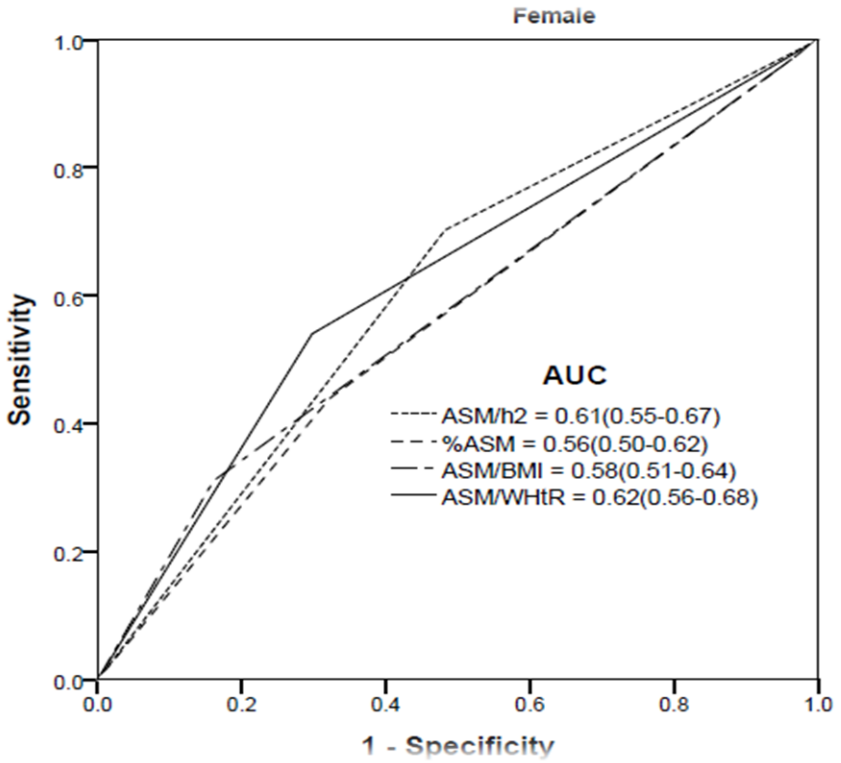
Male	Cut off	Sensitivity	Specificity	AUC	95%CI	P-value
ASM / H2	7.60	69	51	0.599	0.56-0.64	<0.001
%ASM	30.56	64	52	0.582	0.54-0.62	<0.001
ASM/ BMI	0.82	64	57	0.601	0.56-0.64	<0.001
ASM/ WHtR	36.06	61	63	0.622	0.58-0.66	<0.001

Female	Cut off	Sensitivity	Specificity	AUC	95%CI	P-value
ASM / H2	6.19	70	52	0.610	0.55-0.67	0.001
%ASM	23.80	44	68	0.559	0.50-0.62	0.071
ASM/BMI	0.52	31	84	0.575	0.51-0.64	0.021
ASM/ WHtR	24.57	54	70	0.621	0.60-0.68	<0.001

Low muscle mass by AWGS 2014 sarcopenia criteria using ASM / H2: Male < 7.0 , Female < 5.7

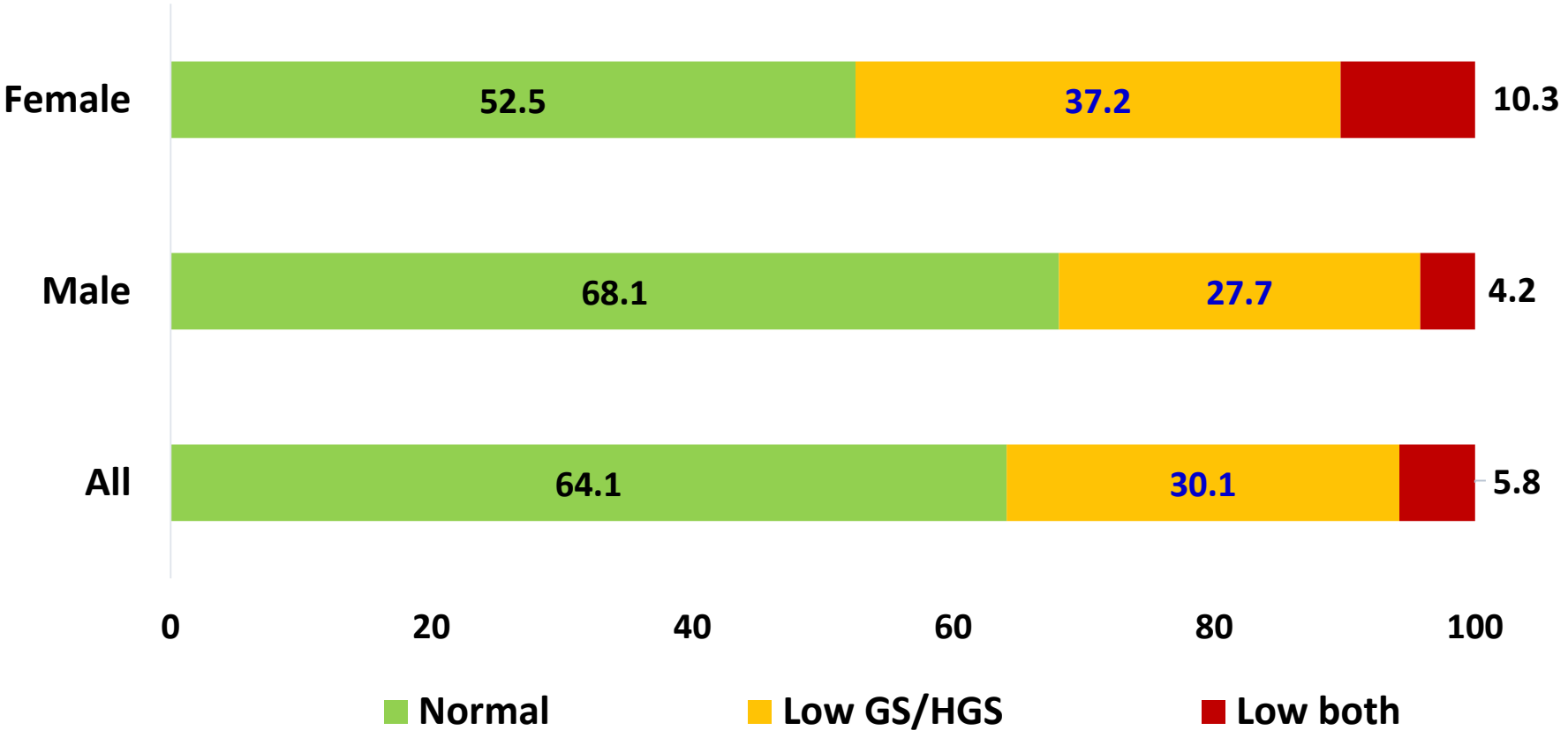
Cutoff values of muscle indices for predicting Muscle Dysfunction





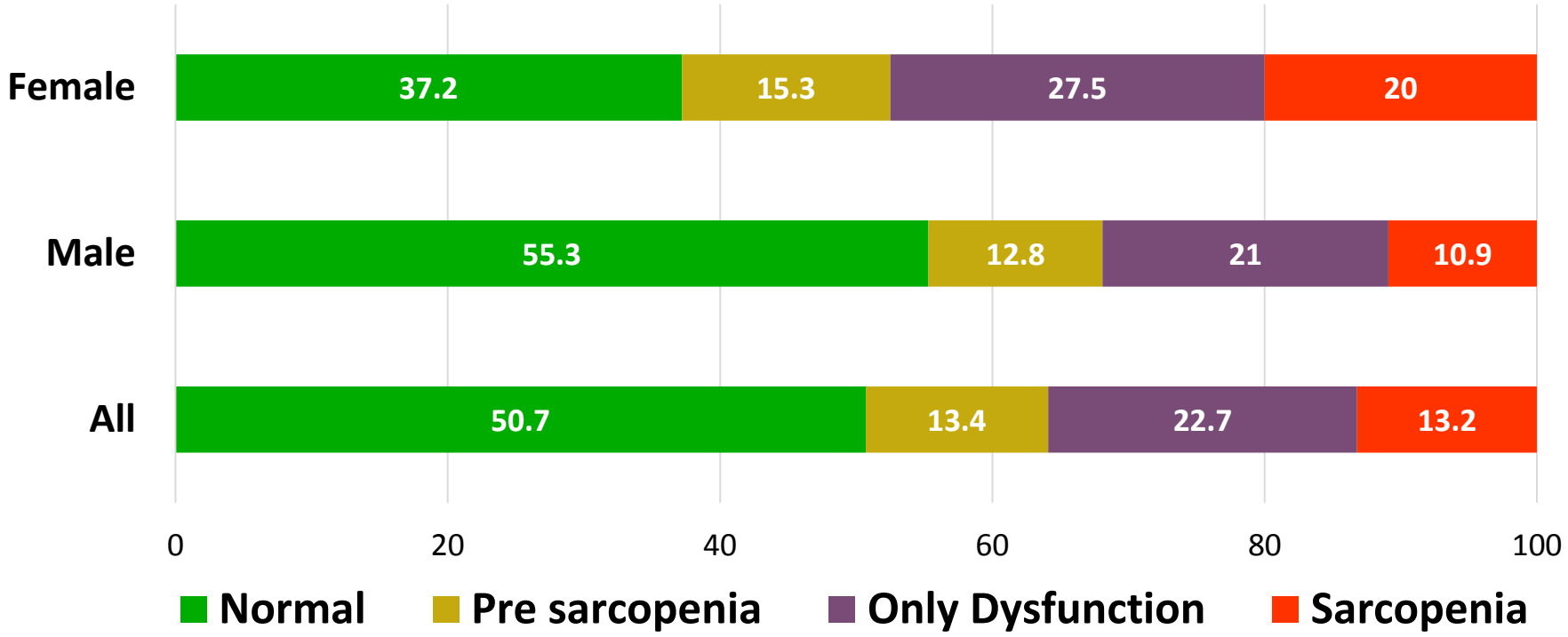
- Muscle dysfunction included
  - Low gait speed **or** Low grip strength
  - Low both gait speed **and** grip strength

Prevalence of older adults with Muscle dysfunction



- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Low GS/HGS = Low gait speed or Low hand grip strength
- ❑ Low both = Low both gait speed and hand grip strength

Prevalence of Sarcopenia by AWGS 2014 criteria (ASM/H2 < 7 in male or < 5.7 in female) with Muscle dysfunction



- ❑ Presarcopenia = Low muscle mass
- ❑ Only Dysfunction = Muscle dysfunction with normal muscle mass
- ❑ Sarcopenia = Low muscle mass and Muscle dysfunction

Risk factors to muscle dysfunction

Variables	Odd Ratio > 1	Odd ratio ≤ 1	95%CI	P-value
Age	1.14		1.11-1.17	<0.001
Female	1.93		1.49-2.50	<0.001
Height		0.94	0.92-0.96	<0.001
Weight		0.97	0.96-0.98	<0.001
BMI		0.96	0.93-1.00	0.025
WC		0.99	0.98-1.00	0.130
WHtR	3.57		0.55-23.07	0.181
ASM		0.86	0.83-0.89	<0.001
FM	1.01		0.99-1.03	0.340
%BF	1.03		1.02-1.05	<0.001

Conclusion

- **Skeletal muscle mass, strength and physical performance declined with age**
  - **mean age of only low gait speed group was less than low grip strength and low both of them , respectively**

- **The most suitable indices compatible with loss of muscle function for both older men and older women in this study were**
  - **ASM/WHtR and ASM/H2 , respectively**

- **Factors associated with muscle dysfunction were**
  - **female , advanced age , short stature**
  - **↓ muscle mass ,body weight and BMI**
  - **↑%BF**

- ASM = Appendicular Skeletal Mass , WHtR = Waist to Height Ratio , H2 = Height2
- %BF = percentage of body fat

Conclusion

- **Total prevalence of muscle dysfunction was much higher than low muscle mass**
  - **Muscle dysfunction = 35.9% , about 1/3 of them were sarcopenia (13.2%)**
  - **Low muscle mass = 26.6%**

- **Prevalence of muscle dysfunction, low muscle mass and sarcopenia was greater in <u>older women</u>**
  - **Muscle dysfunction**
    - **Male = 31.94 , 34.1% of them were sarcopenia**
    - **Female = 47.5% , 42.1% of them were sarcopenia**
  - **Low muscle mass**
    - **Male = 23.6% , Female = 35.3%**

- ASM = Appendicular Skeletal Mass , WHtR = Waist to Height Ratio , H2 = Height2
- %BF = percentage of body fat
- Low muscle mass : ASM/H2 < 7 in male , < 5.7 in female

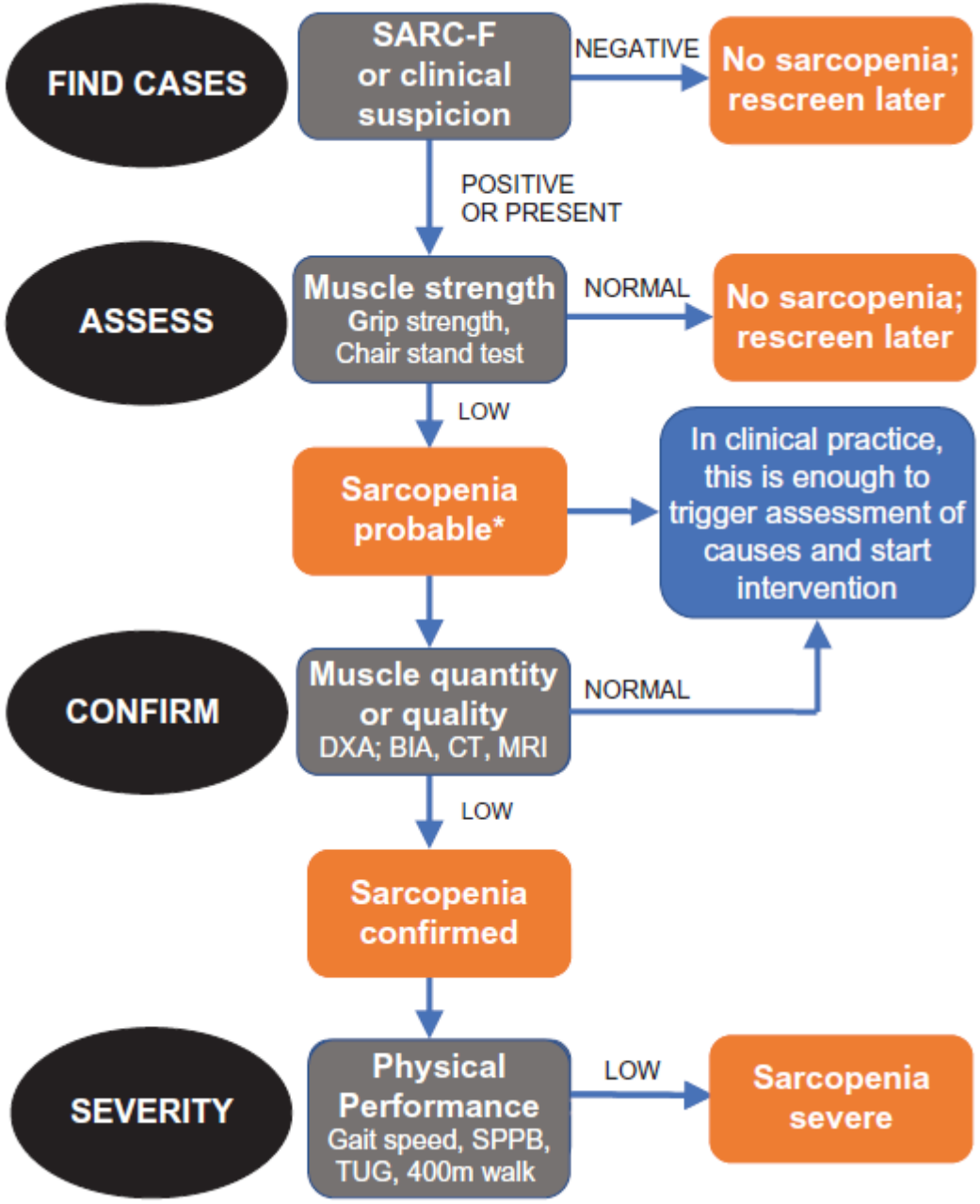
Mini Cognitive assessment and Muscle function

	Male muscle function (N=936)				Female muscle function (N=320)			
	Normal	Intermediate	Low	P-value	Normal	Intermediate	Low	P-value
N	637(%)	259 (%)	40 (%)		168 (%)	119 (%)	33 (%)	
Recall score	624	255	38	0.02	166	119	32	0.247
0	24 (3.8)	23 (9.1)	3 (7.9)		7 (4.2)	6 (5.0)	5 (15.6)	
1	48 (7.7)	22 (8.7)	3 (7.9)		7 (4.2)	8 (6.7)	2 (6.3)	
2	151 (24.2)	64 (25.4)	14 (18.0)		43 (25.9)	29 (24.4)	8 (25.0)	
3	401 (64.3)	143 (56.7)	18 (47.4)		109 (65.7)	76 (63.9)	17 (53.1)	
Mini-Cog				<0.001				0.315
Normal	575 (92.1)	211(83.7)	30(78.9)		141(84.9)	102(85.7)	24(75)	
Impairment	49 (7.9)	41(16.3)	8(21.1)		25(15.1)	17(14.3)	8(25)	

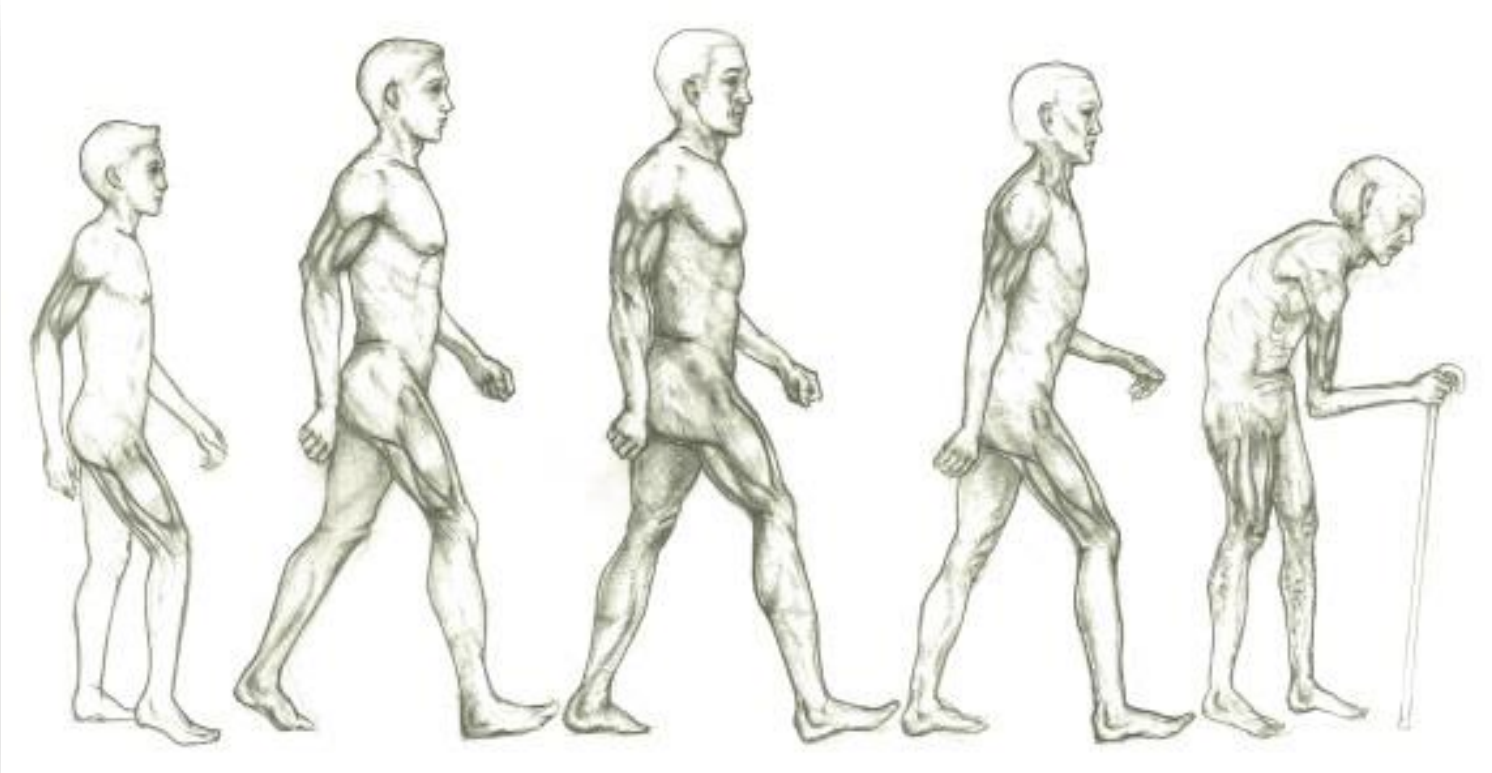
- ❑ Normal = Normal both gait speed and hand grip strength
- ❑ Intermediate = Low gait speed or Low hand grip strength
- ❑ Low = Low both gait speed and hand grip strength

Prevalence of comorbidities in each muscle function group

	Male muscle function (N=936)				Female muscle function (N=320)			
	Normal	Intermediate	Low	P-value	Normal	Intermediate	Low	P-value
N	637(%)	259 (%)	40 (%)		168 (%)	119 (%)	33 (%)	
HT	489 (76.8)	204 (78.8)	31 (77.5)	0.810	103 (61.3)	76 (63.9)	19 (57.6)	0.786
DLP	423 (66.9)	163 (64.7)	28 (70.0)	0.728	115(68.9)	89 (76.1)	19 (57.6)	0.101
DM	131 (20.6)	75 (29.0)	10 (25.0)	0.026	25 (14.9)	22 (18.5)	10 (30.3)	0.103
CVD	43 (6.8)	18 (6.9)	5 (12.5)	0.386	5 (3.0)	7 (5.9)	4 (12.1)	0.076
Osteoarthritis	106 (16.8)	45 (17.4)	8 (20.0)	0.858	54 (32.3)	41 (35.0)	10 (30.3)	0.835
Osteoporosis	14 (2.2)	6 (2.3)	1 (2.5)	0.982	21 (12.6)	24 (20.5)	7 (21.2)	0.151
Parkinsonism	9 (1.4)	4 (1.6)	1 (2.5)	0.861	1 (0.6)	0	0	0.637



EWGSOP2-2019 algorithm of Sarcopenia



Thank you