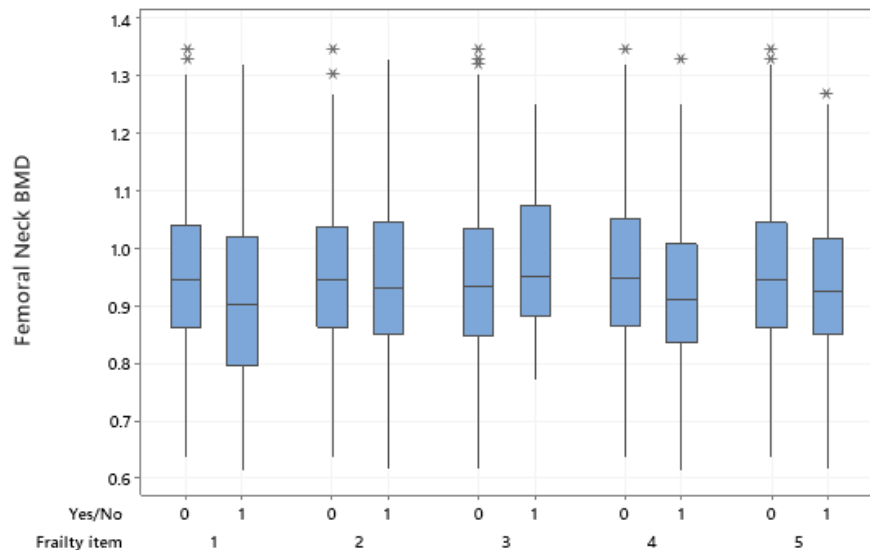
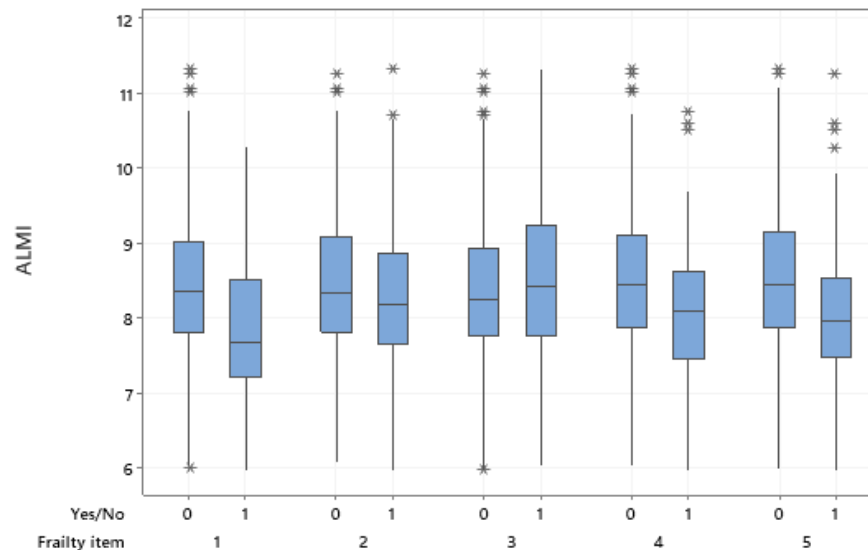


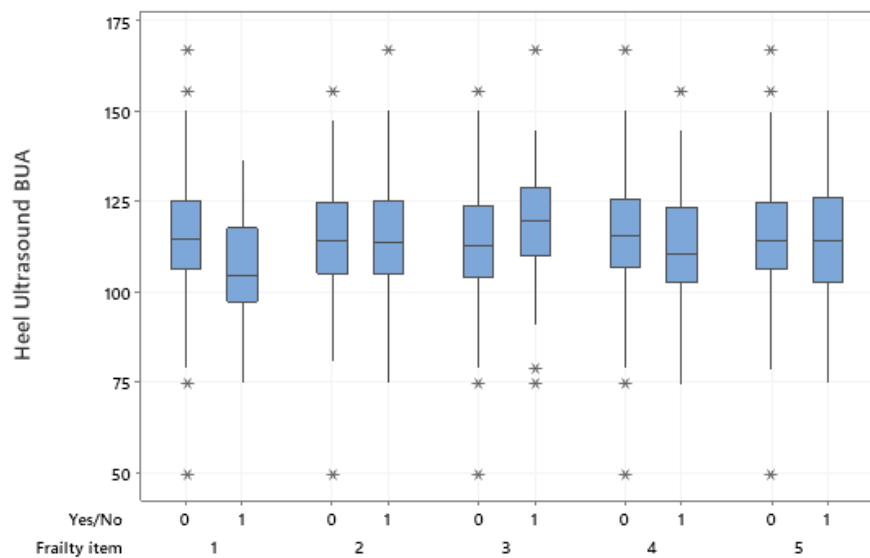
Boxplot of Femoral Neck BMD



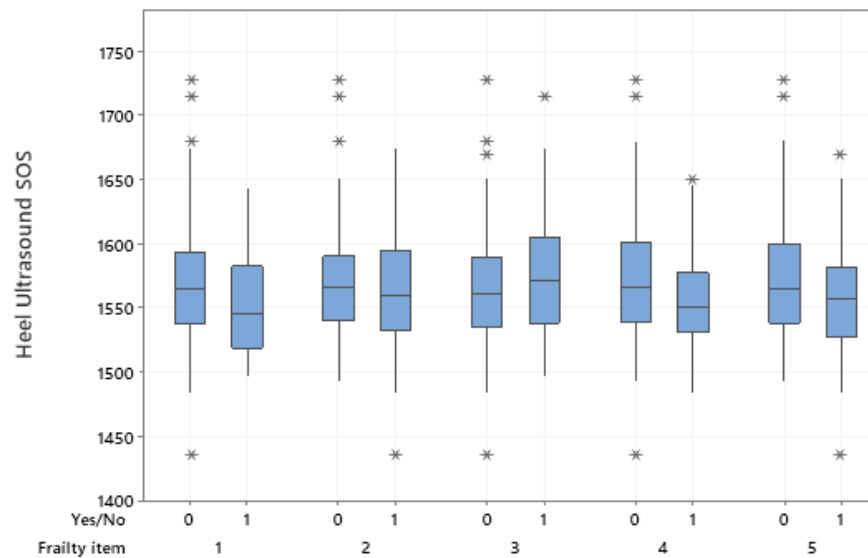
Boxplot of ALMI

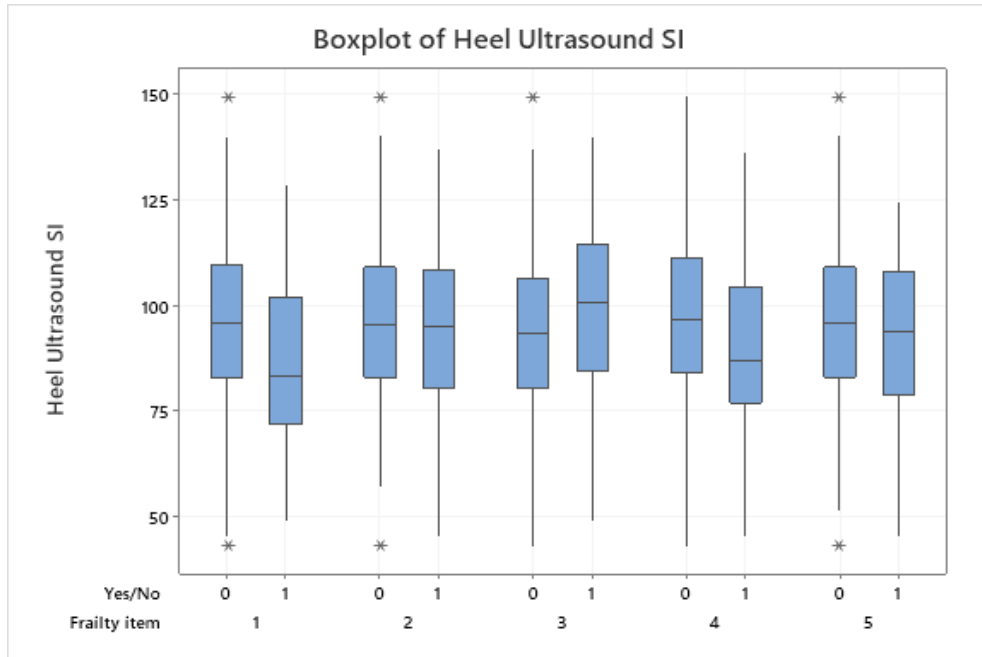


Boxplot of Heel Ultrasound BUA



Boxplot of Heel Ultrasound SOS

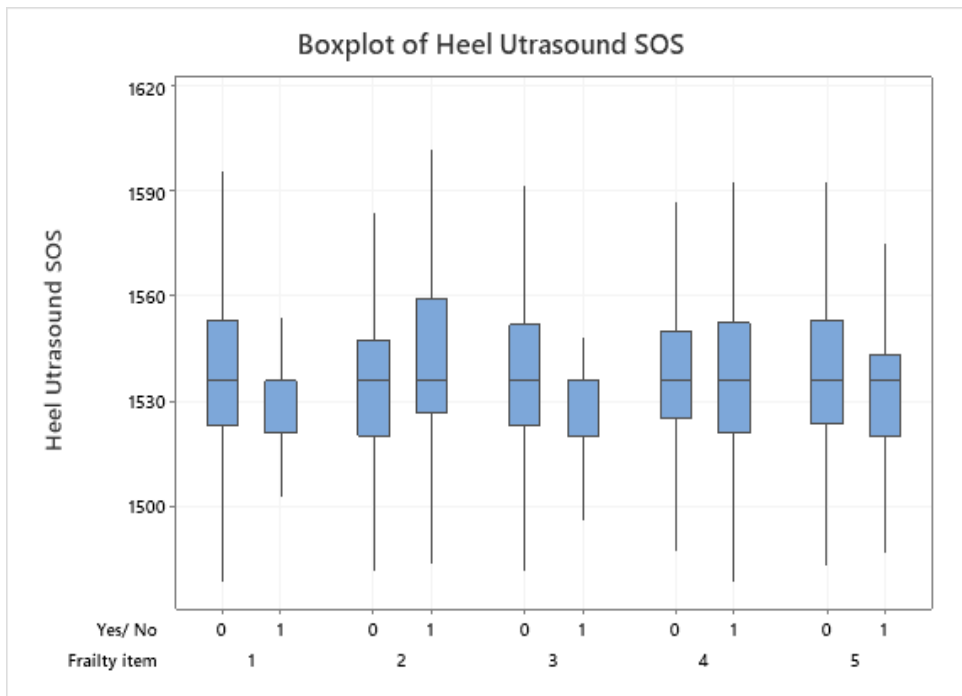
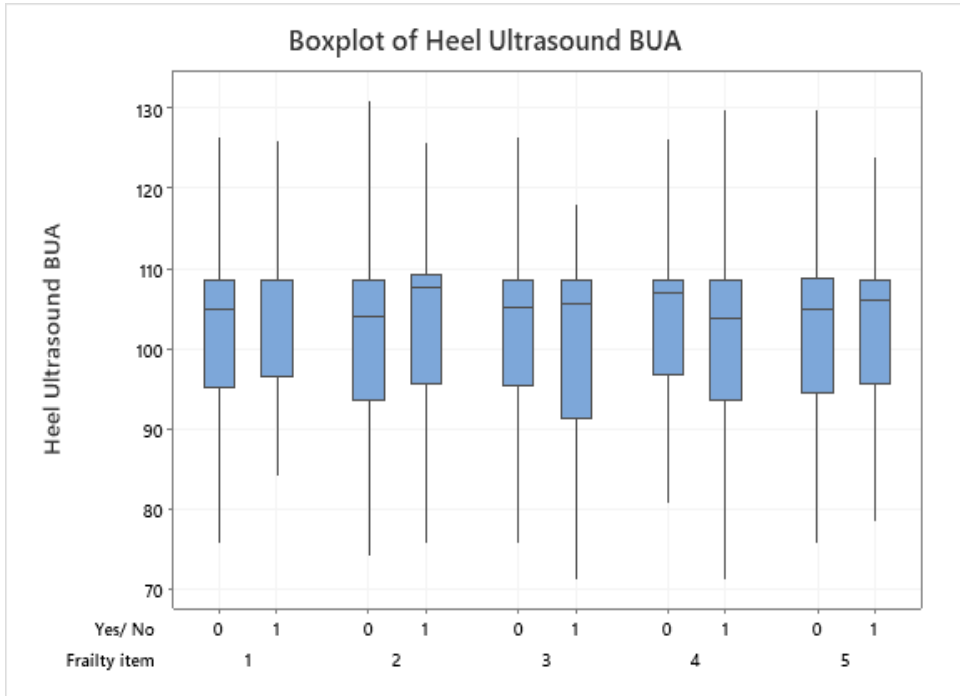
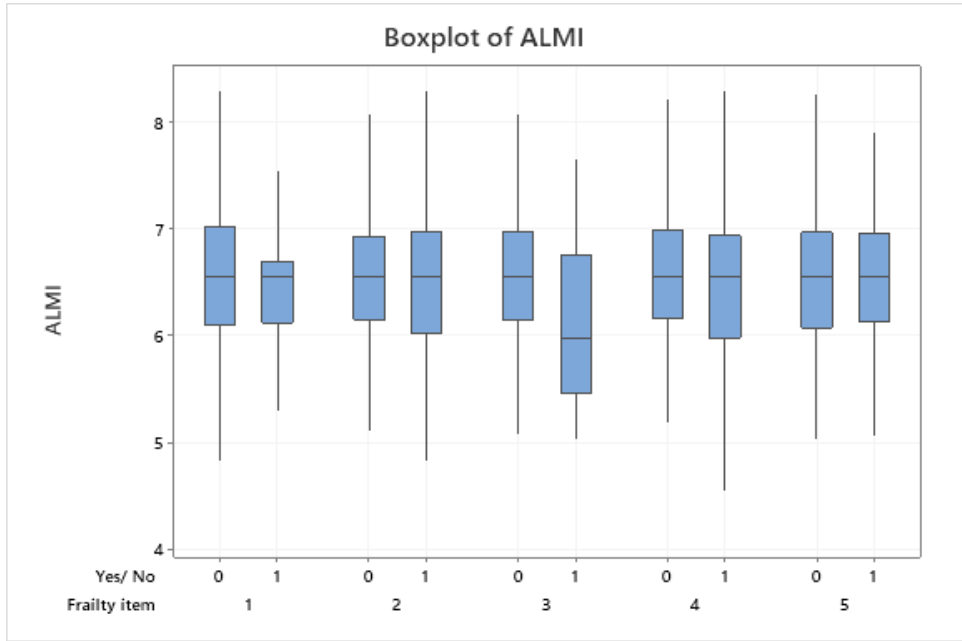
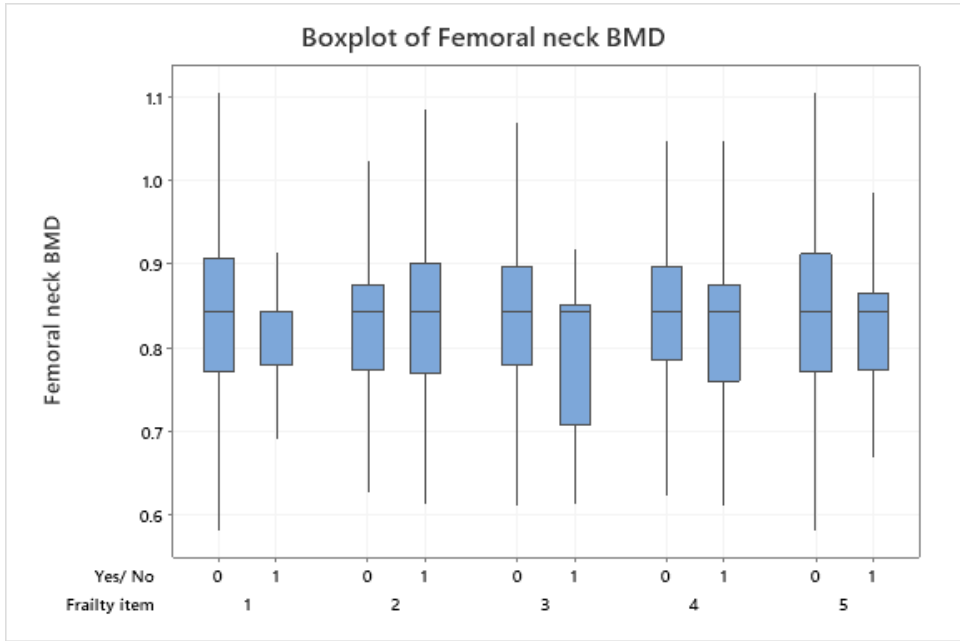


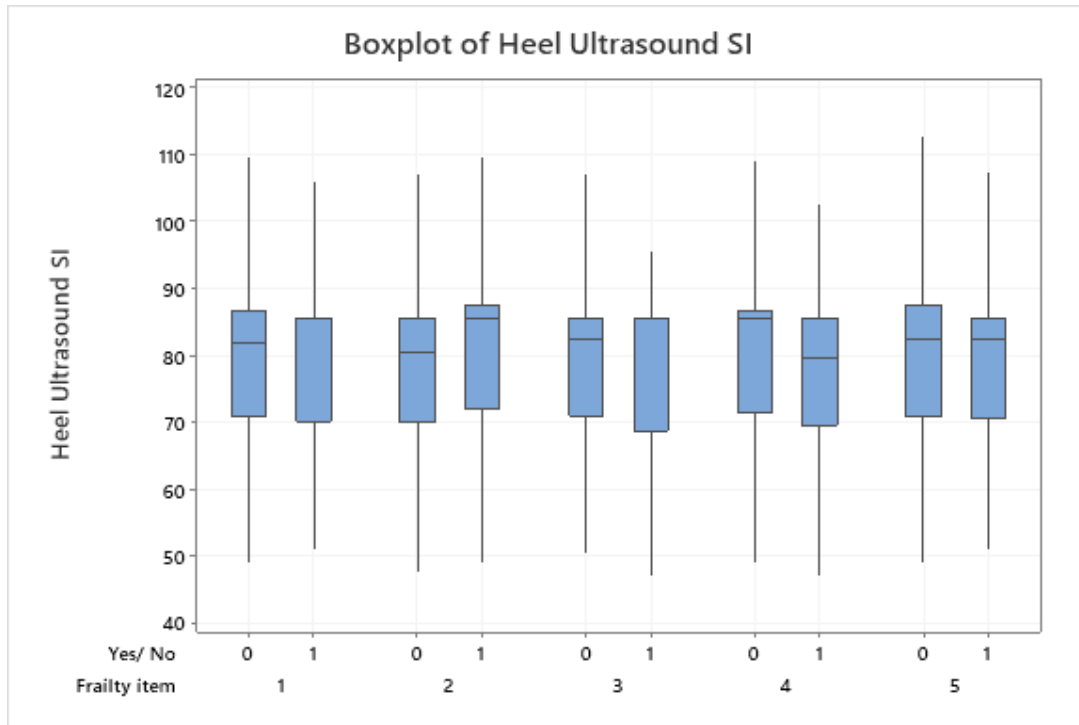


Supplementary Figure 1 Association between frailty items in the Fried frailty phenotype and musculoskeletal parameters in men.

Frailty items; 1= Low physical activity, 2=fatigue, 3= weight loss, 4= slowness, 5= low handgrip strength

Heel Ultrasound measures; BUA= broadband ultrasound attenuation, SOS= speed of sound, SI= stiffness index





Supplementary Figure 2 Association between frailty items in the Fried frailty phenotype and musculoskeletal parameters in women.

Frailty items; 1= Low physical activity, 2=fatigue, 3= weight loss, 4= slowness, 5= low handgrip strength

Heel Ultrasound measures; BUA= broadband ultrasound attenuation, SOS= speed of sound, SI= stiffness index

Supplementary Table 1 Spearman correlation of frailty items with frailty in men

	Frailty	Low physical activity	Weight loss	Fatigue	Slowness
Low physical activity	0.460				
Weight loss	0.384	0.085			
Fatigue	0.598	0.176	0.273		
Slowness	0.570	0.330	-0.004	0.083	
Low HGS*	0.547	0.250	0.051	-0.015	0.361

*HGS= Handgrip strength

Supplementary Table 2 Spearman correlation of frailty items with frailty in women

	Frailty	Weight loss	Fatigue	Low physical activity	Slowness
Weight Loss	0.316				
Fatigue	0.554	0.204			
Low physical activity	0.572	0.212	0.101		
Slowness	0.652	0.103	0.106	0.295	
HGS	0.617	0.078	0.020	0.257	0.261

Men Logistic regression models including all covariates

Table 3 Model 1 Femoral BMD

Covariate	Odds Ratio	P-value	95% Confidence Interval
Femoral Neck BMD	0.92	0.68	0.63-1.34
Age	1.05	0.009	1.01-1.09
BMI	1.12	0.004	1.04-1.22
Fracture	2.03	0.08	0.93-4.46
SES	0.90	0.80	0.39-2.04
Alcohol	1.18	0.74	0.46-3.03
Smoking	1.02	0.98	0.27-3.90
CCI	1.25	0.79	0.26-6.07

Table 4 Model 2 BUA

Covariate	Odds Ratio	P-value	95% Confidence Interval
BUA	0.85	0.29	0.63-1.14
Age	1.05	0.01	1.01-1.09
BMI	1.12	0.002	1.04-1.21
Fracture	1.64	0.22	0.74-3.63
SES	0.83	0.64	0.37-1.85
Alcohol	1.11	0.83	0.43-2.82
Smoking	1.01	1.00	0.27-3.90
CCI	1.15	0.86	0.25-5.40

Table 5 Model 3 SI

Covariate	Odds Ratio	P-value	95% Confidence Interval
SI	0.77	0.14	0.55-1.09
Age	1.04	0.02	1.01-1.08
Weight	1.03	0.002	1.01-1.06
Height	0.94	0.01	0.89-0.99
Fracture	1.51	0.31	0.68-3.34
SES	0.88	0.77	0.39-1.99
Alcohol	1.09	0.86	0.43-2.75
Smoking	0.94	0.93	0.25-3.62
CCI	1.23	0.80	0.26-5.89

Table 6 Model 4 SOS

Covariate	Odds Ratio	P-value	95% Confidence Interval
SOS	0.93	0.48	0.76-1.14
Age	1.05	0.02	1.01-1.08
Weight	1.04	0.004	1.01-1.06
Height	0.94	0.01	0.89-0.99
Fracture	1.69	0.19	0.78-3.68
SES	0.85	0.70	0.38-1.92
Alcohol	1.11	0.82	0.44-2.81
Smoking	0.99	0.99	0.26-3.78
CCI	1.22	0.81	0.252-5.88

Table 7 Model 5 ALMI

Covariate	Odds Ratio	P-value	95% Confidence Interval
ALMI	0.46	0.000	0.32-0.66
Age	1.03	0.10	0.99-1.07
Fracture	2.40	0.04	1.06-5.42
SES	0.89	0.79	0.38-2.07
Alcohol	1.01	0.99	0.38-2.68
Smoking	0.67	0.58	0.17-2.69
CCI	2.30	0.31	0.47-11.30
FMI	1.32	0.000	1.18-1.48

Table 8 Model 6 HGS

Covariate	Odds Ratio	P-value	95% Confidence Interval
HGS	0.19	0.000	0.11-0.32
Age	1.00	0.83	0.96-1.05
Height	1.02	0.26	0.98-1.08
Fracture	1.77	0.19	0.75-4.17
SES	0.83	0.69	0.34-2.04
Alcohol	0.98	0.96	0.36-2.63
Smoking	0.76	0.73	0.17-3.38
CCI	2.90	0.22	0.54-15.65

**BMD= Bone mineral density, BMI= Body mass index, SES= Socioeconomic status, CCI= Charlson comorbidity index, BUA=Broadband ultrasound attenuation, SI= Stiffness index, SOS= Speed of sound, ALMI= Appendicular lean mass index, FMI= Fat mass index, HGS= Hand grip strength

Women Logistic regression models including all covariates

Table 9 Model 1 Femoral BMD

Covariate	Odds Ratio	P-value	95% Confidence Interval
Femoral Neck BMD	0.75	0.20	0.48-1.17
Age	1.10	0.000	1.05-1.16
BMI	1.09	0.02	1.01-1.18
Fracture	1.25	0.59	0.56-2.79
SES	0.84	0.68	0.36-1.95
Alcohol	*	*	*
Smoking	1.84	0.40	0.45-7.59
CCI	2.2	0.55	0.17-29.12

Table 10 Model 2 BUA

Covariate	Odds Ratio	P-value	95% Confidence Interval
BUA	0.92	0.59	0.68-1.24
Age	1.12	0.000	1.06-1.18
BMI	1.08	0.02	1.01-1.15
Fracture	0.93	0.87	0.37-2.31
SES	1.02	0.97	0.43-2.39
Alcohol	*	*	*
Smoking	1.95	0.35	0.48-7.91
CCI	5.30	0.02	1.30-21.56

Table 11 Model 3 SI

Covariate	Odds Ratio	P-value	95% Confidence Interval
SI	0.73	0.19	0.45-1.17
Age	1.12	0.000	1.05-1.17
BMI	1.07	0.03	1.01-1.15
Fracture	0.73	0.51	0.29-1.86
SES	0.98	0.96	0.42-2.30
Alcohol	*	*	*
Smoking	1.76	0.43	0.44-7.10
CCI	3.69	0.06	0.94-14.49

Table 12 Model 4 SOS

Covariate	Odds Ratio	P-value	95% Confidence Interval
SOS	0.81	0.15	0.60-1.08
Age	1.11	0.00	1.05-1.17
Weight	1.03	0.03	1.00-1.06
Height	0.93	0.03	0.87-0.99
Fracture	0.80	0.64	0.32-2.01
SES	1.03	0.94	0.32-2.01
Alcohol	*	*	*
Smoking	1.71	0.46	0.41-7.21
CCI	5.69	0.02	1.39-23.32

Table 13 Model 5 ALMI

Covariate	Odds Ratio	P-value	95% Confidence Interval
ALMI	0.02	0.01	0.00-0.42
Age	1.13	0.000	1.07-1.18
Fracture	1.04	0.92	0.47-2.27
SES	1.10	0.82	0.47-2.56
Alcohol	*	*	*
Smoking	2.00	0.33	0.50-7.96
CCI	3.20	0.37	0.25-40.44
FMI	1.16	0.005	1.04-1.28

Table 14 Model 6 HGS

Covariate	Odds Ratio	P-value	95% Confidence Interval
HGS	0.49	0.000	0.36-0.66
Age	1.05	0.05	1.00-1.09
Height	0.96	0.14	0.90-1.01
Fracture	1.00	1.00	0.47-2.13
SES	0.75	0.48	0.33-1.68
Alcohol	*	*	*
Smoking	0.88	0.86	0.21-3.66
CCI	4.57	0.27	0.31-68.39

*Denotes not enough data to run analysis

**BMD= Bone mineral density, BMI= Body mass index, SES= Socioeconomic status, CCI= Charlson comorbidity index, BUA=Broadband ultrasound attenuation, SI= Stiffness index, SOS= Speed of sound, ALMI= Appendicular lean mass index, FMI= Fat mass index, HGS= Hand grip strength

Men Data

Exposure: ALMI

Step 1: The inclusive logistic model is presented.

```
. logistic frailty_dich rALM Age BMI i.Fracture i.SES i.Smoking i.CharlsonComorbidity Fatmassindex, or  
base
```

Logistic regression

Number of obs = 345

LR chi2(13) = 58.97

Prob > chi2 = 0.0000

Log likelihood = -120.19782

Pseudo R2 = 0.1970

frailty_dich	Odds ratio	Std. err.	z	P> z	[95% conf. interval]	
ALMI	.2983879	.0776547	-4.65	0.000	.1791671	.4969404
Age	1.030198	.0202046	1.52	0.129	.9913489	1.070569
BMI	1.373065	.1594045	2.73	0.006	1.093633	1.723893
Fracture						
0	1	(base)				
1	2.394882	.9984614	2.09	0.036	1.057805	5.422038
SES						
1	1	(base)				
2	.9545276	.4167347	-0.11	0.915	.4056623	2.246013
3	.4963864	.197493	-1.76	0.078	.2275934	1.08263
Smoking						
0	1	(base)				
1	.8226749	.5841438	-0.27	0.783	.2045639	3.308473
CharlsonComor~y						

0		1	(base)				
1		.983323	.4261215	-0.04	0.969	.4205613	2.299127
2		.6630003	.3317627	-0.82	0.411	.2486428	1.767875
3		1.518698	1.028593	0.62	0.537	.4026841	5.727674
4		1.175665	1.108821	0.17	0.864	.1851309	7.46601
5		.768004	.9979386	-0.20	0.839	.0601615	9.804114
6		1	(empty)				
8		1	(empty)				
Fatmassindex		.9517502	.1209597	-0.39	0.697	.7418946	1.220966
_cons		2.05e-06	6.06e-06	-4.43	0.000	6.25e-09	.0006725

Note: _cons estimates baseline odds.

Step 2: The link test.

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs = 345
```

```
LR chi2(2) = 51.55
```

```
Prob > chi2 = 0.0000
```

```
Log likelihood = -123.90637
```

```
Pseudo R2 = 0.1722
```

```
-----+-----
```

frailty_dich	Coefficient	Std. err.	z	P> z	[95% conf. interval]	
* _hat	.6437314	.364733	1.76	0.078	-.0711321	1.358595
** _hatsq	-.1312012	.1259561	-1.04	0.298	-.3780707	.1156683
_cons	-.1192326	.2886283	-0.41	0.680	-.6849336	.4464685

```
-----+-----
```

**The linear predicted value has a low p-value indicating an acceptable predictability.*

***The linear predicted value squared is not significant, indicating no evidence of misspecification.*

Step 3: Including square and cubic terms into the regression model and performing the joint square and cubic terms test.

```
. logistic frailty_dich rALM Age BMI i.Fracture i.SES i.Alcohol i.Smoking i.CharlsonComorbidity  
Fatmassindex xbhsq_rALM xbhcu_rALM, or base
```

```
. test xbhsq_rALM xbhcu_rALM
```

```
( 1) [frailty_dich]xbhsq_rALM = 0
```

```
( 2) [frailty_dich]xbhcu_rALM = 0
```

```
chi2( 2) = 4.15
```

```
Prob > chi2 = 0.1259 (Non-significant, no evidence of misspecification)
```

Exposure: SI

Step 1.

```
. logistic frailty_dich SI Age BMI i.Fracture i.SES i.Smoking i.CharlsonComorbidity Fatmassindex, or base
```

Logistic regression

Number of obs = 343

LR chi2(13) = 30.91

Prob > chi2 = 0.0035

Pseudo R2 = 0.1035

Log likelihood = -133.88401

frailty_dich	Odds ratio	Std. err.	z	P> z	[95% conf. interval]	
SI	.7937888	.1387124	-1.32	0.186	.5635856	1.118021
Age	1.044892	.0194385	2.36	0.018	1.00748	1.083694
BMI	.9884019	.0811789	-0.14	0.887	.84144	1.161031
Fracture						
0	1	(base)				
1	1.703154	.7027375	1.29	0.197	.7586472	3.823558
SES						
1	1	(base)				
2	.823384	.3388971	-0.47	0.637	.3674988	1.844799
3	.477382	.1765616	-2.00	0.046	.2312309	.9855672
Smoking						
0	1	(base)				
1	.8888654	.6160963	-0.17	0.865	.2284786	3.458012
CharlsonComor~y						
0	1	(base)				

1		.7780867	.3280084	-0.60	0.552	.3405631	1.7777
2		.6287387	.2918881	-1.00	0.318	.2531076	1.561835
3		1.131058	.7230809	0.19	0.847	.3230836	3.95963
4		1.669593	1.327067	0.64	0.519	.3515906	7.928369
5		.7488349	.959847	-0.23	0.821	.0607193	9.23518
6		1	(empty)				
8		1	(empty)				
Fatmassindex		1.217612	.135668	1.77	0.077	.9787392	1.514785
_cons		.0020212	.0043929	-2.85	0.004	.0000285	.1430984

Note: _cons estimates baseline odds.

Step 2

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs = 343
```

```
LR chi2(2) = 33.62
```

```
Prob > chi2 = 0.0000
```

```
Pseudo R2 = 0.1126
```

```
Log likelihood = -132.52831
```

```
-----+-----  
frailty_dich | Coefficient Std. err. z P>|z| [95% conf. interval]  
-----+-----  
* _hat | .2168663 .521078 0.42 0.677 -.8044279 1.23816  
** _hatsq | -.2874587 .1828032 -1.57 0.116 -.6457465 .070829  
_cons | -.3557897 .3919846 -0.91 0.364 -1.124065 .4124861  
-----+-----
```

**The linear predicted value has a ? p-value indicating an acceptable predictability.*

***The linear predicted value squared is not significant, indicating no evidence of misspecification.*

Step 3.

```
. logistic frailty_dich SI Age BMI i.Fracture i.SES i.Alcohol i.Smoking i.CharlsonComorbidity  
Fatmassindex xbhsq_SI xbhcu_SI, or base
```

```
. test xbhsq_SI xbhcu_SI
```

```
( 1) [frailty_dich]xbhsq_SI = 0
```

```
( 2) [frailty_dich]xbhcu_SI = 0
```

```
chi2( 2) = 2.61
```

```
Prob > chi2 = 0.2710 (Non-significant, no evidence of misspecification)
```

Exposure: HGS

Step 1.

```
. logistic frailty_dich HGS_std Age BMI i.Fracture i.SES i.Alcohol i.Smoking i.CharlsonComorbidity  
Fatmassindex, or base
```

Logistic regression

Number of obs = 344

LR chi2(14) = 85.05

Prob > chi2 = 0.0000

Pseudo R2 = 0.2844

Log likelihood = -106.98399

frailty_dich	Odds ratio	Std. err.	z	P> z	[95% conf. interval]	
HGS_std	.1204	.041146	-6.19	0.000	.0616217	.2352445
Age	1.009655	.0213531	0.45	0.650	.9686593	1.052386
BMI	1.036798	.0741246	0.51	0.613	.9012365	1.192751
Fracture						
0	1	(base)				
1	1.740556	.7764358	1.24	0.214	.726072	4.172498
SES						
1	1	(base)				
2	.7858692	.3650619	-0.52	0.604	.3161836	1.953265
3	.4020963	.1699814	-2.16	0.031	.175588	.9208
Alcohol						
0	1	(base)				
1	1.072841	.5483383	0.14	0.891	.3939844	2.921406
Smoking						
0	1	(base)				
1	.9275245	.7357721	-0.09	0.924	.1959285	4.390896

CharlsonComor~y						
0		1	(base)			
1		1.17331	.5410034	0.35	0.729	.4752599 2.896641
2		1.004698	.5279366	0.01	0.993	.3587209 2.813939
3		1.155243	.8552937	0.19	0.845	.2706943 4.930233
4		2.956017	2.784631	1.15	0.250	.4665055 18.73083
5		.5043338	.6802902	-0.51	0.612	.0358544 7.09405
6		1	(empty)			
8		1	(empty)			

Fatmassindex		1.116072	.1062991	1.15	0.249	.9260201 1.345129
_cons		.0006583	.0014785	-3.26	0.001	8.07e-06 .0537112

Note: _cons estimates baseline odds.

Step 2.

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs = 344
```

```
LR chi2(2) = 85.44
```

```
Prob > chi2 = 0.0000
```

```
Pseudo R2 = 0.2857
```

```
Log likelihood = -106.79109
```

```
-----+-----  
frailty_dich | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]  
-----+-----  
    *_hat |   .8574051   .2671087     3.21  0.001     .3338817    1.380929  
   **_hatsq | -.0534168   .0887053    -0.60  0.547    -.2272759    .1204423  
    _cons |  -.013089   .2298274    -0.06  0.955    -.4635424    .4373645  
-----+-----
```

**The linear predicted value has a low p-value indicating an acceptable predictability.*

***The linear predicted value squared is not significant, indicating no evidence of misspecification.*

Step 3.

```
. logistic frailty_dich HGS_std Age BMI i.Fracture i.SES i.Smoking i.CharlsonComorbidity Fatmassindex  
xbhsq_HGS xbhcu_HGS, or base
```

```
. test xbhsq_HGS xbhcu_HGS
```

```
( 1)  [frailty_dich]xbhsq_HGS = 0
```

```
( 2)  [frailty_dich]xbhcu_HGS = 0
```

```
chi2( 2) = 2.73
```

```
Prob > chi2 = 0.2553 (Non-significant, no evidence of misspecification)
```

Women Data

Exposure: ALMI

Step 1.

```
. logistic frailty_dich rALM Age BMI i.Fracture i.SES i.Smoking i.CharlsonComorbidity Fatmassindex, or base
```

Logistic regression

Number of obs = 311

LR chi2(13) = 44.44

Prob > chi2 = 0.0000

Pseudo R2 = 0.1683

Log likelihood = -109.84726

frailty_dich	Odds ratio	Std. err.	z	P> z	[95% conf. interval]	
ALMI	.0032756	.0088914	-2.11	0.035	.000016	.6696394
Age	1.126256	.0282492	4.74	0.000	1.072227	1.183007
BMI	1.195011	.2576796	0.83	0.409	.7831187	1.823543
Fracture						
0	1	(base)				
1	.951251	.3793142	-0.13	0.900	.4353875	2.078329
SES						
1	1	(base)				
2	1.112307	.4792872	0.25	0.805	.4780207	2.588231
3	1.180736	.5723954	0.34	0.732	.4565716	3.053494
Smoking						
0	1	(base)				
1	1.799923	1.299834	0.81	0.416	.4370688	7.412388
CharlsonComor~y						
0	1	(base)				

1		.9460996	.439805	-0.12	0.905	.3804051	2.35303
2		1.116951	.5642338	0.22	0.827	.4149969	3.006237
3		2.273709	1.70004	1.10	0.272	.5251656	9.844044
4		3.39875	4.381638	0.95	0.343	.2716175	42.52856
5		5.283059	7.930614	1.11	0.268	.2786841	100.1518
Fatmassindex		.9619163	.224255	-0.17	0.868	.609107	1.519081
_cons		3.53e-07	1.29e-06	-4.07	0.000	2.78e-10	.0004478

Note: _cons estimates baseline odds.

Step 2.

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs = 311
```

```
LR chi2(2) = 44.45
```

```
Prob > chi2 = 0.0000
```

```
Pseudo R2 = 0.1683
```

```
Log likelihood = -109.84515
```

```
-----+-----  
frailty_dich | Coefficient  Std. err.      z    P>|z|     [95% conf. interval]  
-----+-----  
      *_hat |    1.023776   .4031116    2.54   0.011    .2336915    1.81386  
     **_hatsq |   .0082841   .1274166    0.07   0.948   -.241448    .2580161  
      _cons |   .0081902   .3187208    0.03   0.979   -.6164911    .6328715  
-----+-----
```

**The linear predicted value has a low p-value indicating an acceptable predictability.*

***The linear predicted value squared is not significant, indicating no evidence of misspecification.*

Step 3.

```
. logistic frailty_dich rALM Age BMI i.Fracture i.SES i.Smoking i.CharlsonComorbidity Fatmassindex  
xbhsq_rALM xbhcu_rALM, or base
```

```
. test xbhsq_rALM xbhcu_rALM
```

```
( 1) [frailty_dich]xbhsq_rALM = 0
```

```
( 2) [frailty_dich]xbhcu_rALM = 0
```

```
chi2( 2) = 1.67
```

```
Prob > chi2 = 0.4337 (Non-significant, no evidence of misspecification)
```

Exposure: HGS

Step 1.

logistic frailty_dich SDunitsHGS Age BMI Height i.Fracture i.SES i.Smoking i.CharlsonComorbidity
Fatmassindex, or base

Logistic regression

Number of obs = 319

LR chi2(14) = 61.16

Prob > chi2 = 0.0000

Pseudo R2 = 0.2208

Log likelihood = -107.93872

frailty_dich	Odds ratio	Std. err.	z	P> z	[95% conf. interval]
SDunitsHGS	.4854853	.0760159	-4.62	0.000	.3571885 .6598644
Age	1.071296	.0270878	2.72	0.006	1.019499 1.125724
BMI	1.075025	.0436194	1.78	0.075	.9928432 1.164008
Height	.966749	.0305275	-1.07	0.284	.9087301 1.028472
Fracture					
0	1	(base)			
1	.9696297	.3929142	-0.08	0.939	.4382089 2.14551
SES					
1	1	(base)			
2	.8676334	.3738528	-0.33	0.742	.3728755 2.018872
3	.9938547	.4908102	-0.01	0.990	.3775385 2.616282
Smoking					
0	1	(base)			
1	1.180606	.8879975	0.22	0.825	.2703153 5.156316
CharlsonComor~y					
0	1	(base)			

1		.8316095	.3878905	-0.40	0.693	.3333424	2.074667
2		.9029777	.4660296	-0.20	0.843	.3283744	2.483046
3		3.060282	2.317286	1.48	0.140	.6937778	13.49903
4		3.816273	5.798852	0.88	0.378	.1941928	74.99734
5		2.635381	3.903227	0.65	0.513	.1445906	48.03376
Fatmassindex		.9835912	.0468997	-0.35	0.729	.8958341	1.079945
_cons		.3646237	2.179019	-0.17	0.866	2.99e-06	44533.81

Note: _cons estimates baseline odds.

Step 2.

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs = 274
```

```
LR chi2(2) = 35.46
```

```
Prob > chi2 = 0.0000
```

```
Pseudo R2 = 0.1533
```

```
Log likelihood = -97.920926
```

```
-----+-----  
frailty_dich | Coefficient Std. err. z P>|z| [95% conf. interval]  
-----+-----  
* _hat | .7894532 .388664 2.03 0.042 .0276858 1.551221  
** _hatsq | -.0785075 .1320186 -0.59 0.552 -.3372592 .1802442  
_cons | -.0685285 .341574 -0.20 0.841 -.7380013 .6009442  
-----+-----
```

**The linear predicted value has a low p-value indicating an acceptable predictability.*

***The linear predicted value squared is not significant, indicating no evidence of misspecification.*

Step 3.

```
. logistic frailty_dich SDunitsHGS Age BMI Height i.Fracture i.SES i.Smoking i.CharlsonComorbidity  
Fatmassindex xbhsq_HGS xbhcu_HGS, or base
```

```
. test xbhsq_HGS xbhcu_HGS
```

```
( 1) [frailty_dich]xbhsq_HGS = 0
```

```
( 2) [frailty_dich]xbhcu_HGS = 0
```

```
chi2( 2) = 0.69
```

```
Prob > chi2 = 0.7097 (Non-significant, no evidence of misspecification)
```