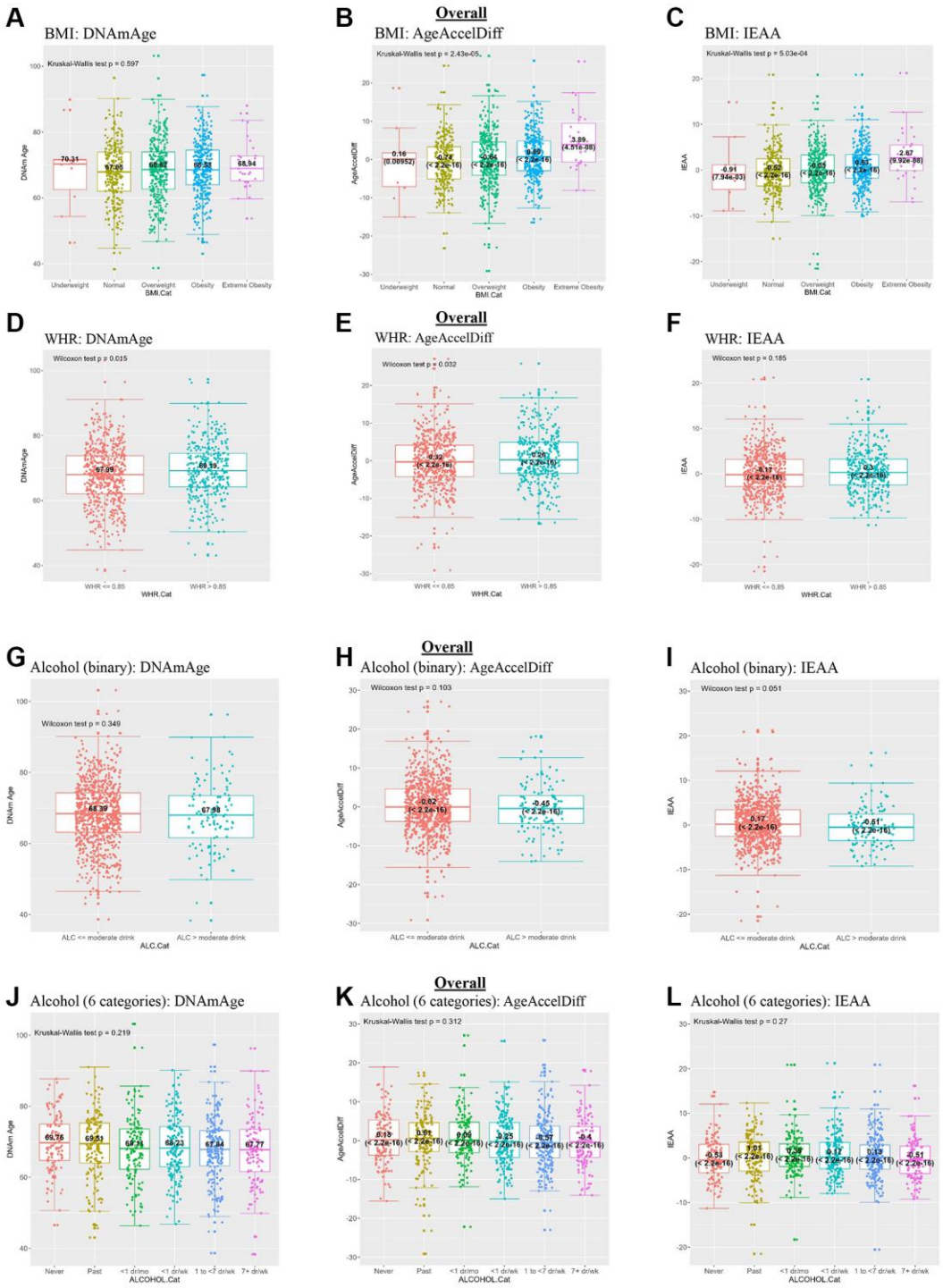
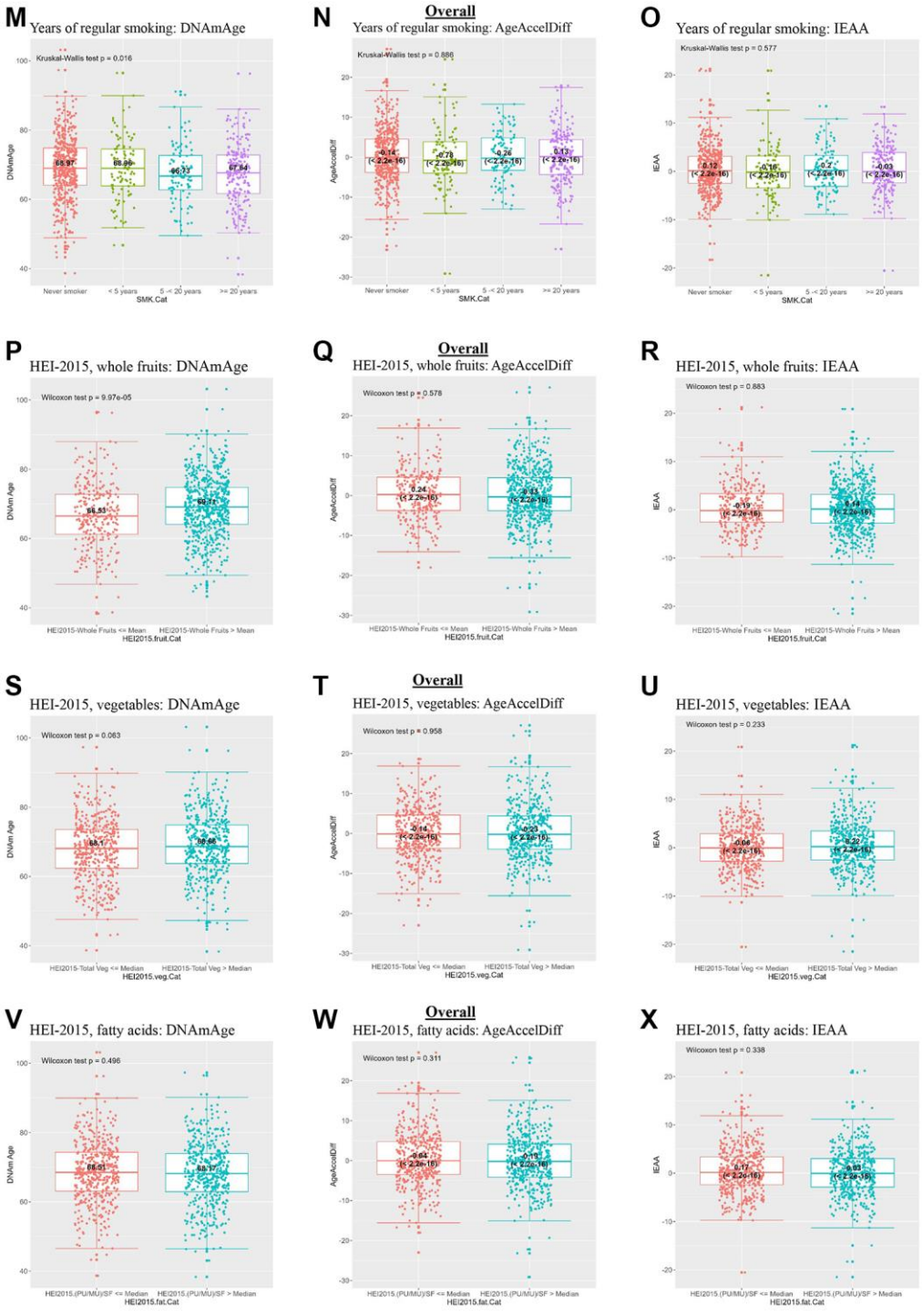
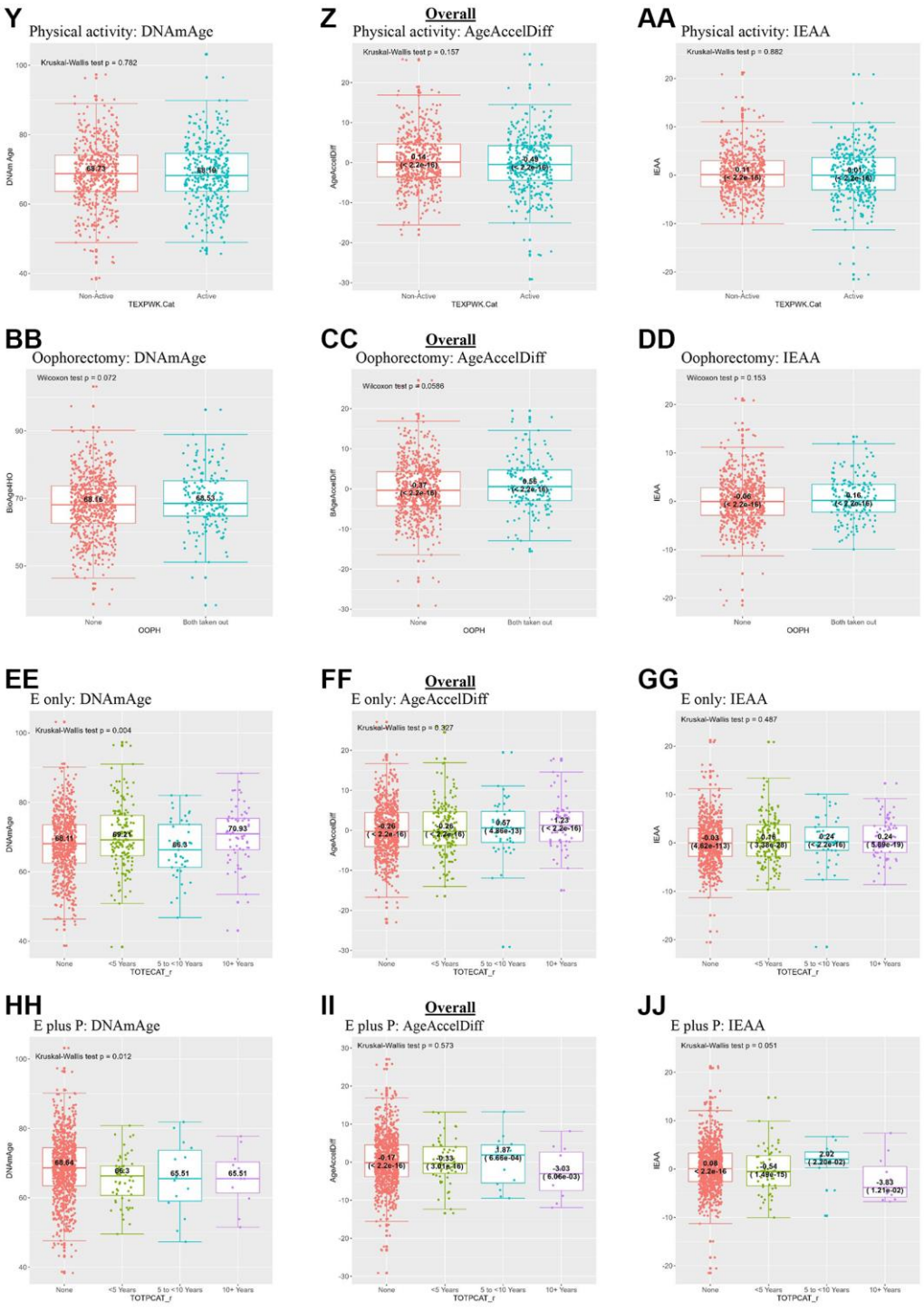
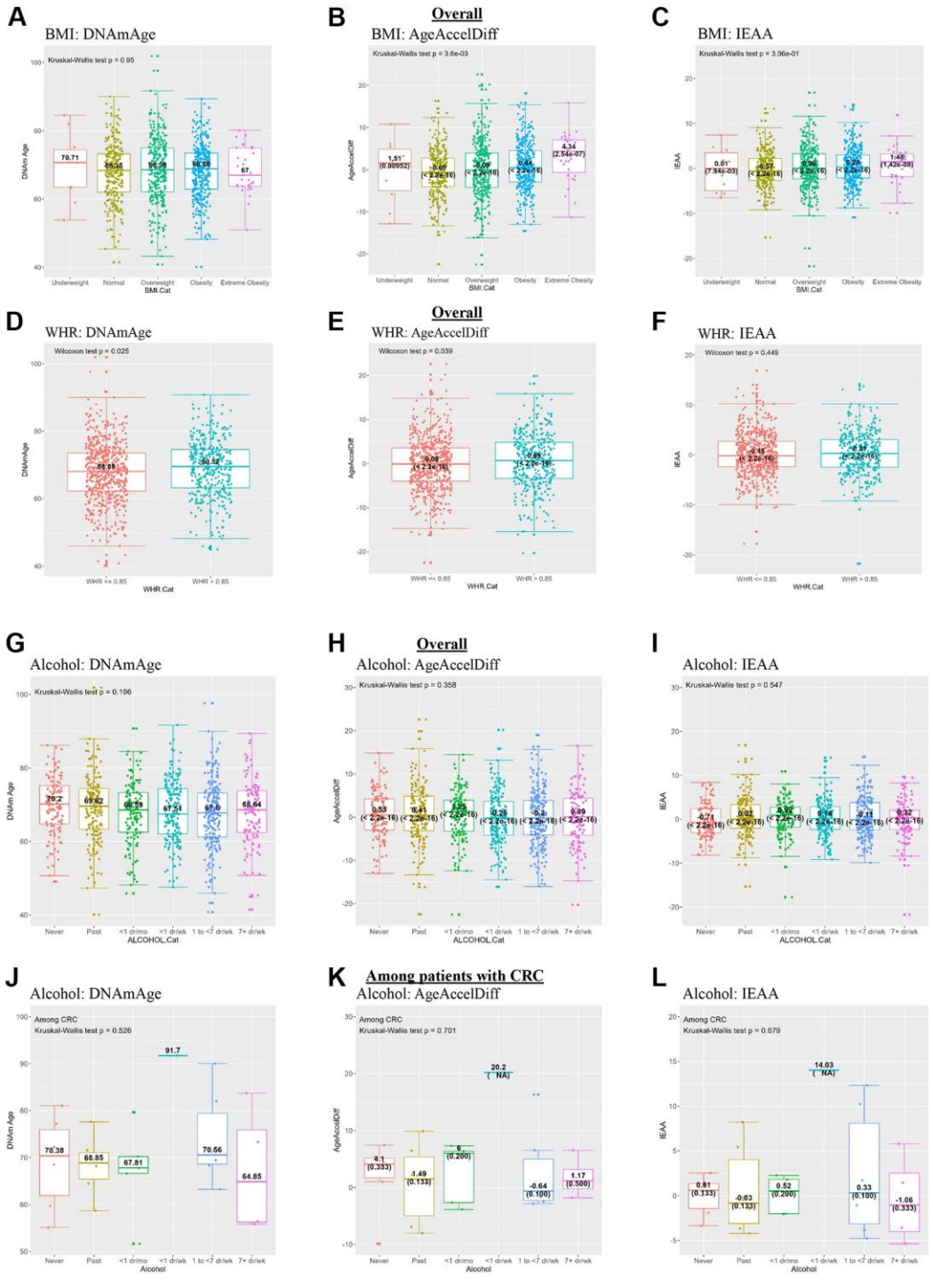
SUPPLEMENTARY FIGURES

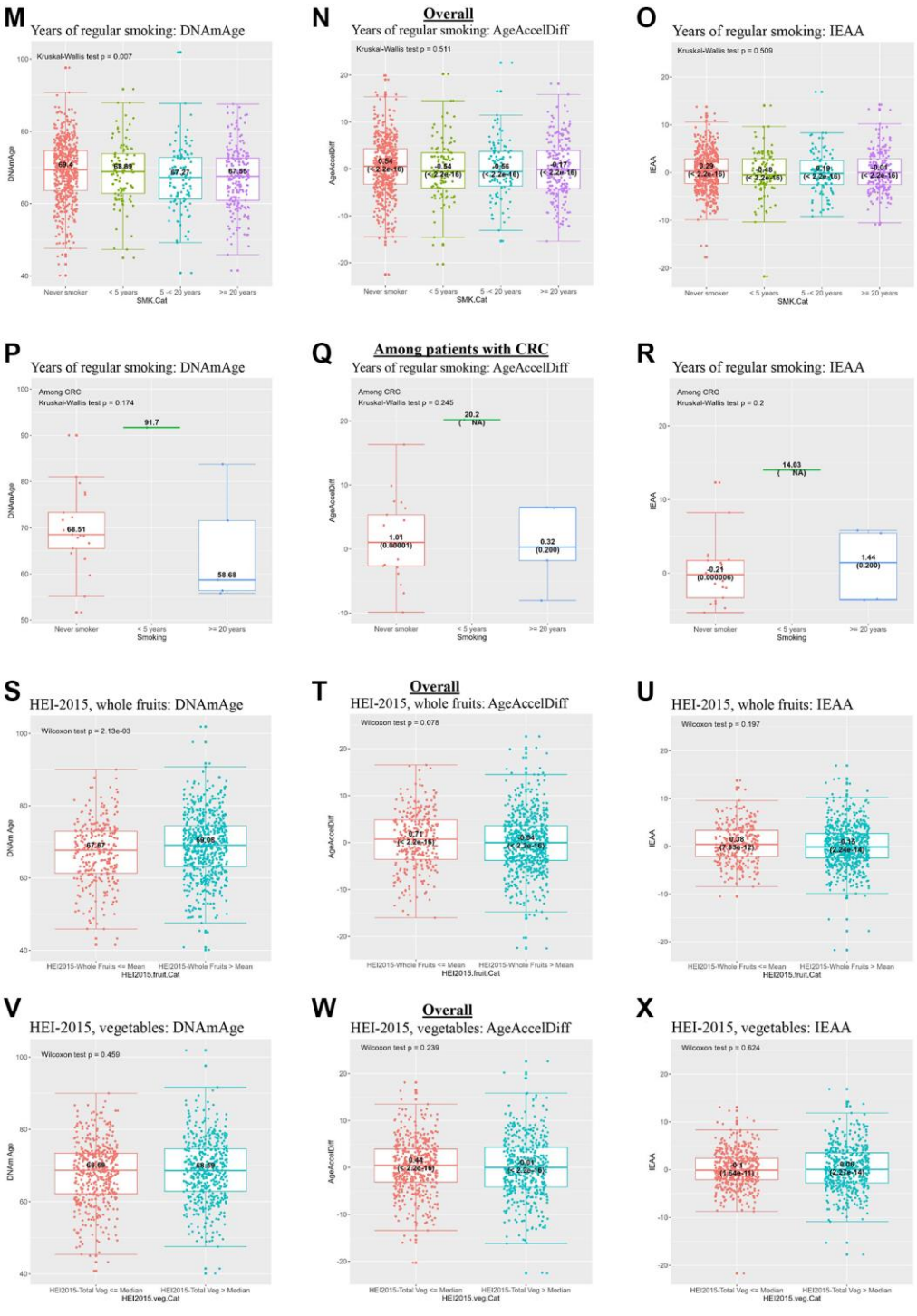


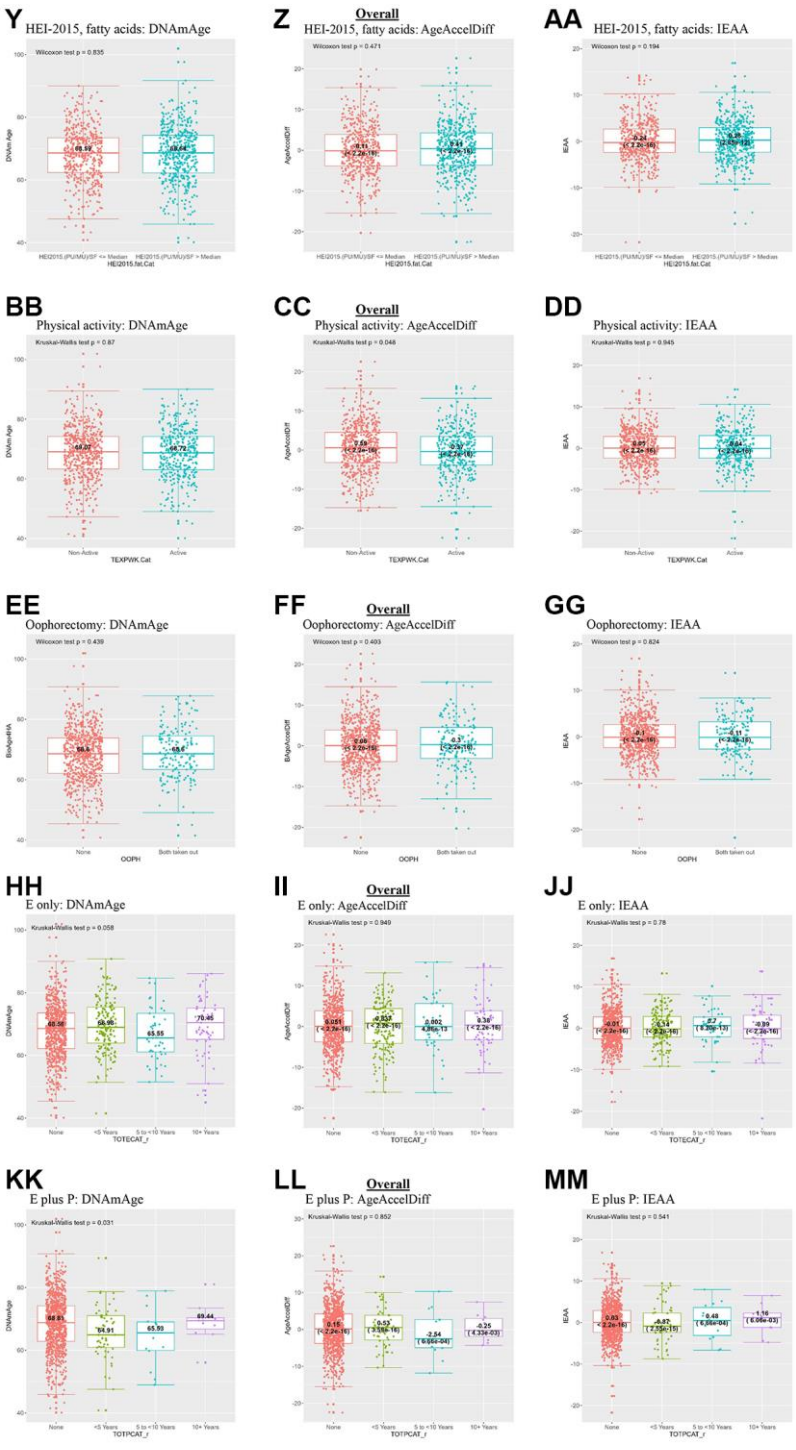

M
Years of regular smoking: DNAmAge
Kruskal-Wallis test p = 0.016
DNAmAge
SMK.Cat
Never smoker
< 5 years
5 -< 20 years
>= 20 years
N
Overall
Years of regular smoking: AgeAccelDiff
Kruskal-Wallis test p = 0.886
AgeAccelDiff
O
Years of regular smoking: IEAA
Kruskal-Wallis test p = 0.577
IEAA
P
HEI-2015, whole fruits: DNAmAge
Wilcoxon test p = 9.97e-05
HEI2015-Whole Fruits <= Mean
HEI2015-Whole Fruits > Mean
HEI2015.fruit.Cat
Q
Overall
HEI-2015, whole fruits: AgeAccelDiff
Wilcoxon test p = 0.578
R
HEI-2015, whole fruits: IEAA
Wilcoxon test p = 0.883
S
HEI-2015, vegetables: DNAmAge
Wilcoxon test p = 0.063
HEI2015-Total Veg <= Median
HEI2015-Total Veg > Median
HEI2015.veg.Cat
T
Overall
HEI-2015, vegetables: AgeAccelDiff
Wilcoxon test p = 0.958
U
HEI-2015, vegetables: IEAA
Wilcoxon test p = 0.233
V
HEI-2015, fatty acids: DNAmAge
Wilcoxon test p = 0.496
HEI2015.(PUFA/MUFA)/SF <= Median
HEI2015.(PUFA/MUFA)/SF > Median
HEI2015.fat.Cat
W
Overall
HEI-2015, fatty acids: AgeAccelDiff
Wilcoxon test p = 0.311
X
HEI-2015, fatty acids: IEAA
Wilcoxon test p = 0.338



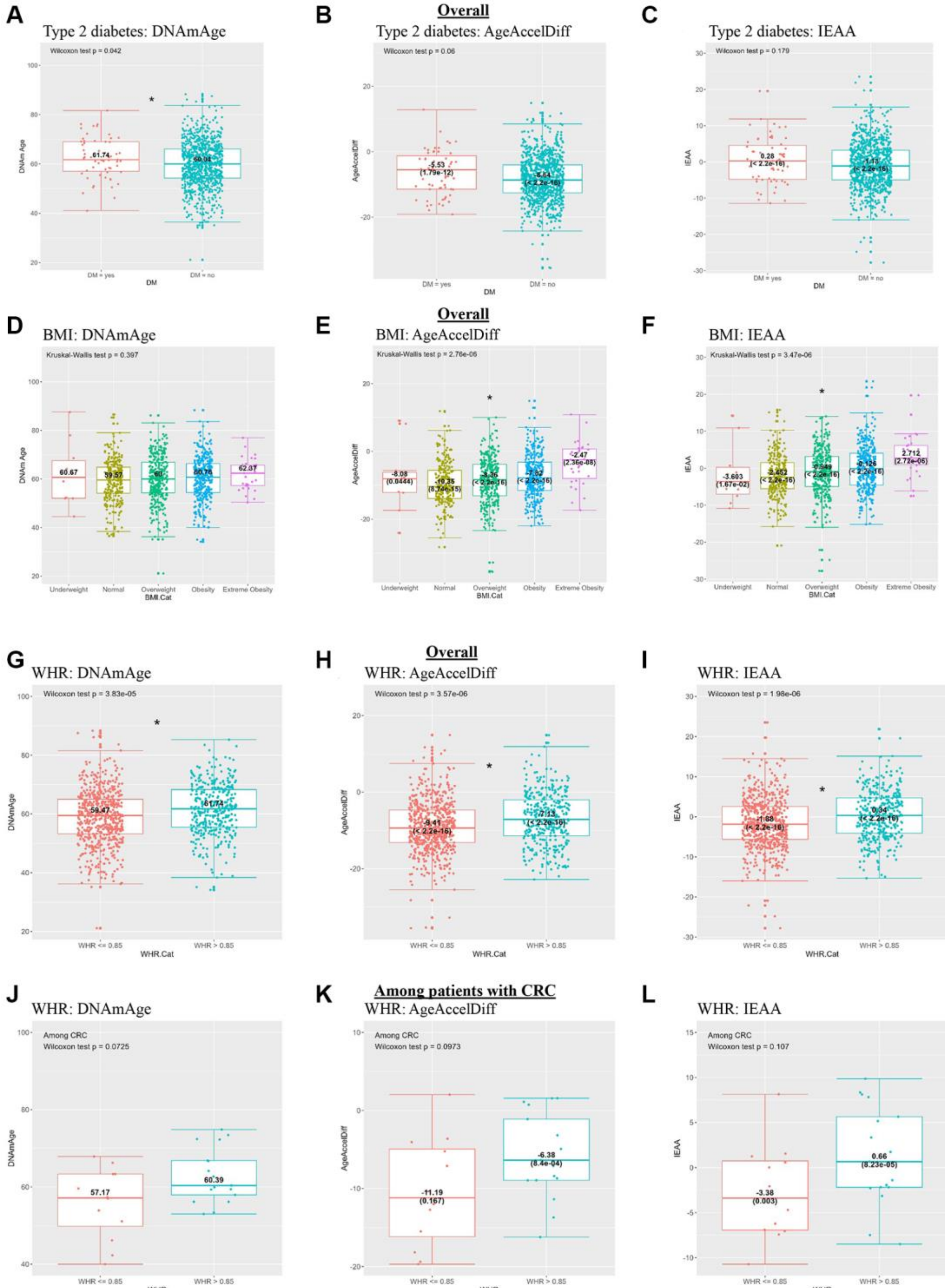
Supplementary Figure 1. Horvath's clock: distribution of DNAmAge, AgeAccelDiff, and IEAA by selected CRC risk factors in overall participants. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; BMI: body mass index; CRC: colorectal cancer; DNAmAge: DNA methylation-based marker of aging; E only: exogenous estrogen only; E plus P: E plus progestin; HEI-2015: Healthy Eating Index-2015; IEAA: intrinsic epigenetic age acceleration as residuals adjusted for cell composition; WHR: waist-to-hip ratio.

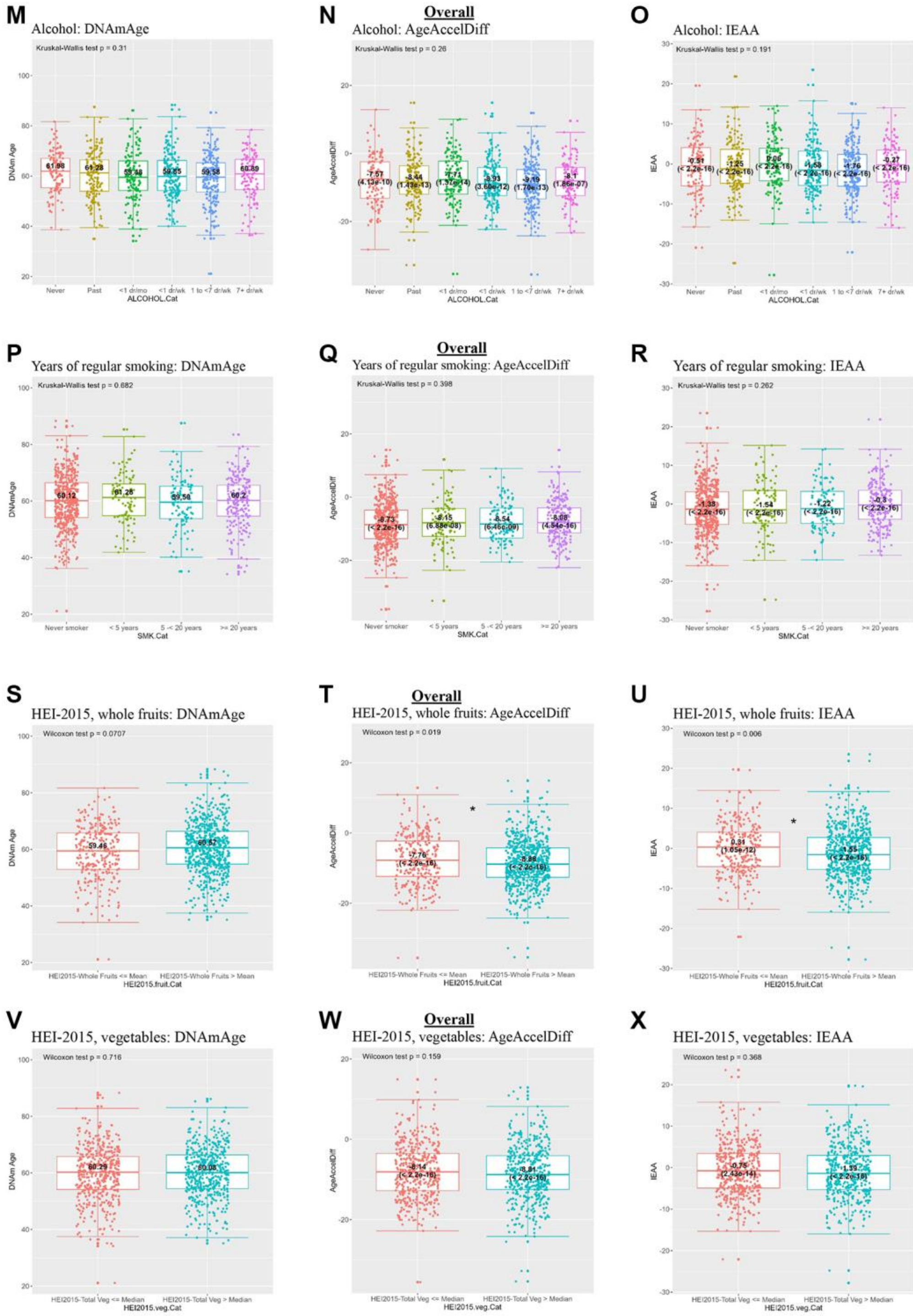

A
BMI: DNAmAge
Kruskal-Wallis test p = 0.95
DNAm Age
BMI.Cat
Underweight
Normal
Overweight
Obesity
Extreme Obesity
B
Overall
BMI: AgeAccelDiff
Kruskal-Wallis test p = 3.6e-03
AgeAccelDiff
C
BMI: IEAA
Kruskal-Wallis test p = 3.06e-01
IEAA
D
WHR: DNAmAge
Wilcoxon test p = 0.025
WHR.Cat
WHR <= 0.85
WHR > 0.85
E
Overall
WHR: AgeAccelDiff
Wilcoxon test p = 0.039
F
WHR: IEAA
Wilcoxon test p = 0.449
G
Alcohol: DNAmAge
Kruskal-Wallis test p = 0.196
ALCOHOL.Cat
Never
Past
<1 dr/mo
<1 dr/wk
1 to <7 dr/wk
7+ dr/wk
H
Overall
Alcohol: AgeAccelDiff
Kruskal-Wallis test p = 0.358
I
Alcohol: IEAA
Kruskal-Wallis test p = 0.547
J
Alcohol: DNAmAge
Among CRC
Kruskal-Wallis test p = 0.526
Alcohol
K
Among patients with CRC
Alcohol: AgeAccelDiff
Among CRC
Kruskal-Wallis test p = 0.701
L
Alcohol: IEAA
Among CRC
Kruskal-Wallis test p = 0.679

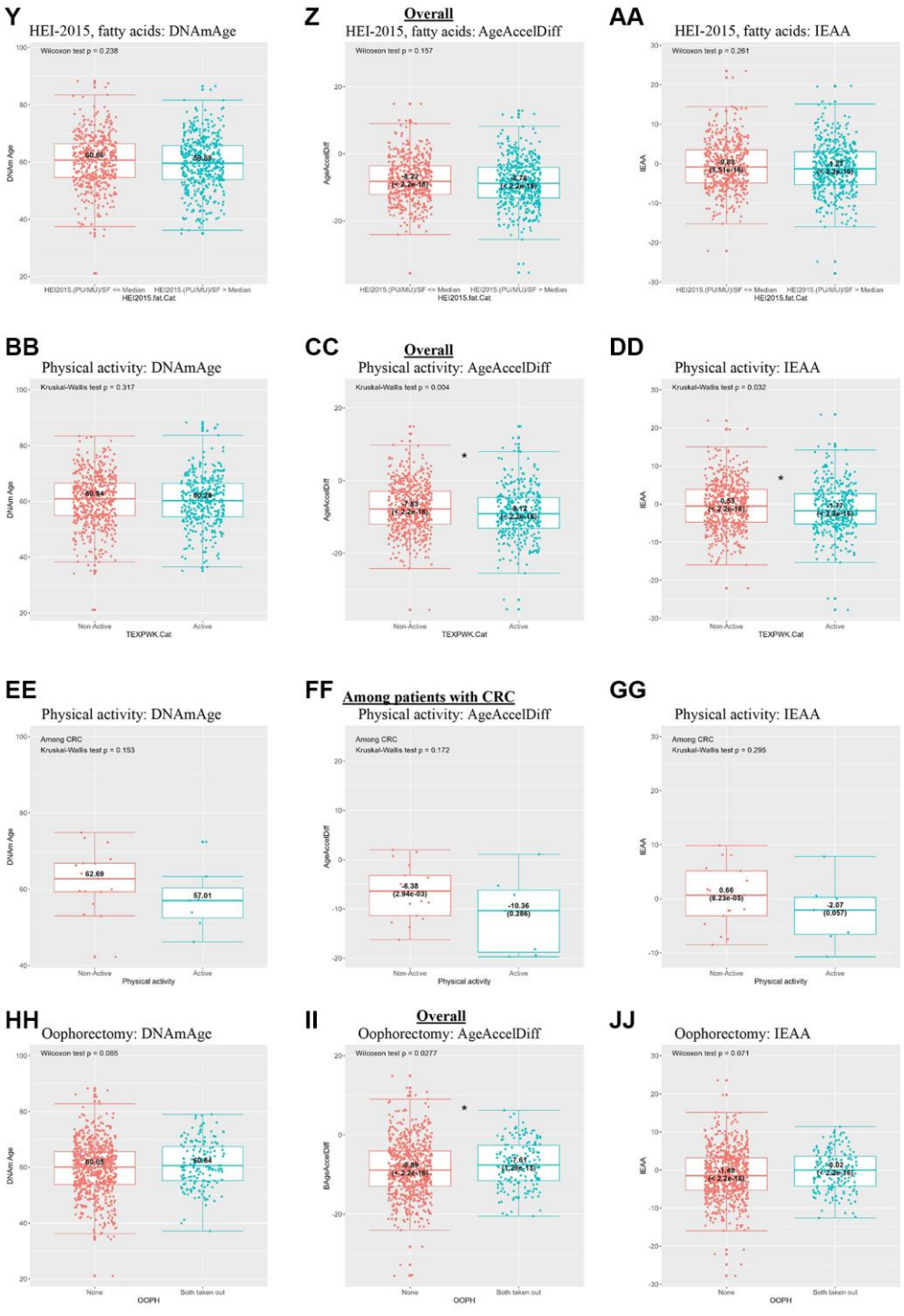

M
Years of regular smoking: DNAmAge
Kruskal-Wallis test p = 0.007
DNAmAge
SMK.Cat
Never smoker
< 5 years
5 -< 20 years
>= 20 years
N
Overall
Years of regular smoking: AgeAccelDiff
Kruskal-Wallis test p = 0.511
AgeAccelDiff
O
Years of regular smoking: IEAA
Kruskal-Wallis test p = 0.509
IEAA
P
Years of regular smoking: DNAmAge
Among CRC
Kruskal-Wallis test p = 0.174
91.7
68.51
58.68
Smoking
Q
Among patients with CRC
Years of regular smoking: AgeAccelDiff
Among CRC
Kruskal-Wallis test p = 0.245
20.2
(NA)
1.01
(0.00001)
0.32
(0.200)
R
Years of regular smoking: IEAA
Among CRC
Kruskal-Wallis test p = 0.2
14.03
(NA)
-0.21
(0.000106)
1.44
(0.200)
S
HEI-2015, whole fruits: DNAmAge
Wilcoxon test p = 2.13e-03
DNAm Age
HEI2015-Whole Fruits <= Mean
HEI2015-Whole Fruits > Mean
HEI2015.fruit.Cat
T
Overall
HEI-2015, whole fruits: AgeAccelDiff
Wilcoxon test p = 0.078
U
HEI-2015, whole fruits: IEAA
Wilcoxon test p = 0.197
V
HEI-2015, vegetables: DNAmAge
Wilcoxon test p = 0.459
HEI2015-Total Veg <= Median
HEI2015-Total Veg > Median
HEI2015.veg.Cat
W
Overall
HEI-2015, vegetables: AgeAccelDiff
Wilcoxon test p = 0.239
X
HEI-2015, vegetables: IEAA
Wilcoxon test p = 0.624

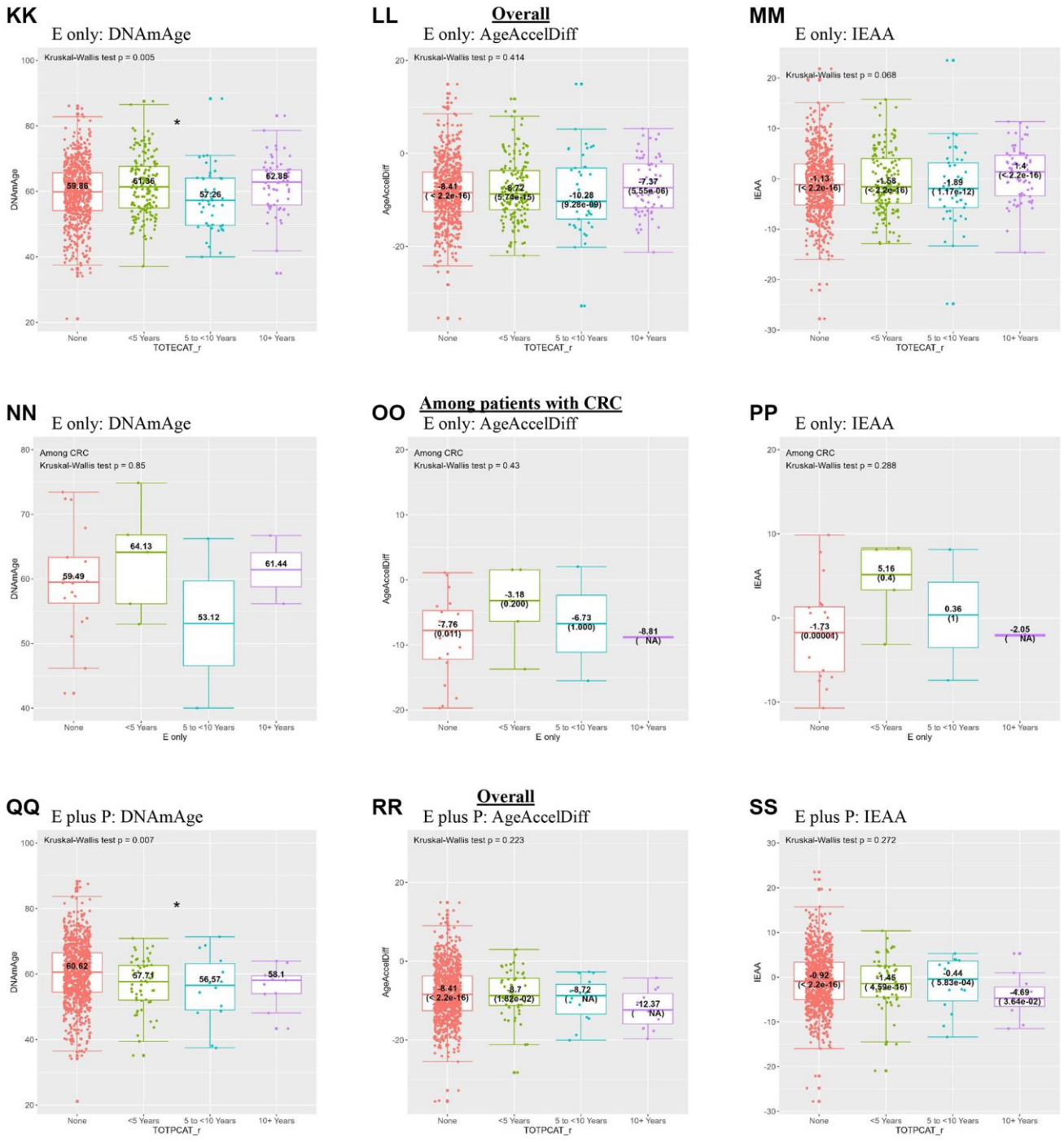


Supplementary Figure 2. Hannum's clock: distribution of DNAmAge, AgeAccelDiff, and IEAA by selected CRC risk factors. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; BMI: body mass index; CRC: colorectal cancer; DNAmAge: DNA methylationbased marker of aging; E only: exogenous estrogen only; E plus P: E plus progestin; HEI-2015: Healthy Eating Index-2015; IEAA: intrinsic epigenetic age acceleration as residuals adjusted for cell composition; WHR: waist-to-hip ratio.

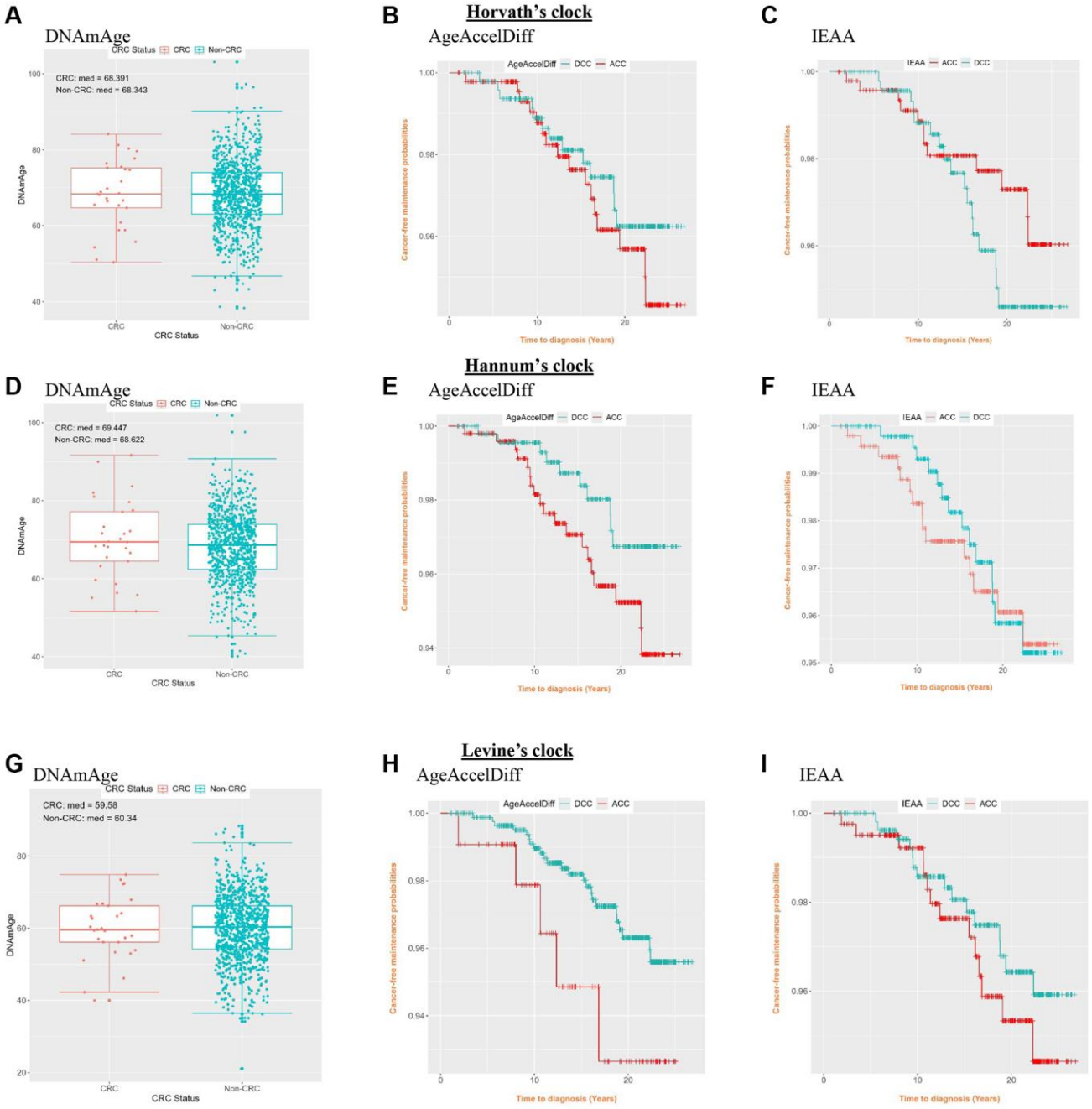

A
Type 2 diabetes: DNAmAge
Wilcoxon test p = 0.042
B
Overall
Type 2 diabetes: AgeAccelDiff
Wilcoxon test p = 0.06
C
Type 2 diabetes: IEAA
Wilcoxon test p = 0.179
D
BMI: DNAmAge
Kruskal-Wallis test p = 0.397
E
Overall
BMI: AgeAccelDiff
Kruskal-Wallis test p = 2.76e-06
F
BMI: IEAA
Kruskal-Wallis test p = 3.47e-06
G
WHR: DNAmAge
Wilcoxon test p = 3.83e-05
H
Overall
WHR: AgeAccelDiff
Wilcoxon test p = 3.57e-06
I
WHR: IEAA
Wilcoxon test p = 1.98e-06
J
WHR: DNAmAge
Among CRC
Wilcoxon test p = 0.0725
K
Among patients with CRC
WHR: AgeAccelDiff
Among CRC
Wilcoxon test p = 0.0973
L
WHR: IEAA
Among CRC
Wilcoxon test p = 0.107


M
Alcohol: DNAmAge
Kruskal-Wallis test p = 0.31
N
Overall
Alcohol: AgeAccelDiff
Kruskal-Wallis test p = 0.26
O
Alcohol: IEAA
Kruskal-Wallis test p = 0.191
ALCOHOL.Cat
P
Years of regular smoking: DNAmAge
Kruskal-Wallis test p = 0.682
Q
Overall
Years of regular smoking: AgeAccelDiff
Kruskal-Wallis test p = 0.398
R
Years of regular smoking: IEAA
Kruskal-Wallis test p = 0.262
SMK.Cat
S
HEI-2015, whole fruits: DNAmAge
Wilcoxon test p = 0.0707
T
Overall
HEI-2015, whole fruits: AgeAccelDiff
Wilcoxon test p = 0.019
U
HEI-2015, whole fruits: IEAA
Wilcoxon test p = 0.006
HEI2015.fruit.Cat
V
HEI-2015, vegetables: DNAmAge
Wilcoxon test p = 0.716
W
Overall
HEI-2015, vegetables: AgeAccelDiff
Wilcoxon test p = 0.159
X
HEI-2015, vegetables: IEAA
Wilcoxon test p = 0.368
HEI2015.veg.Cat

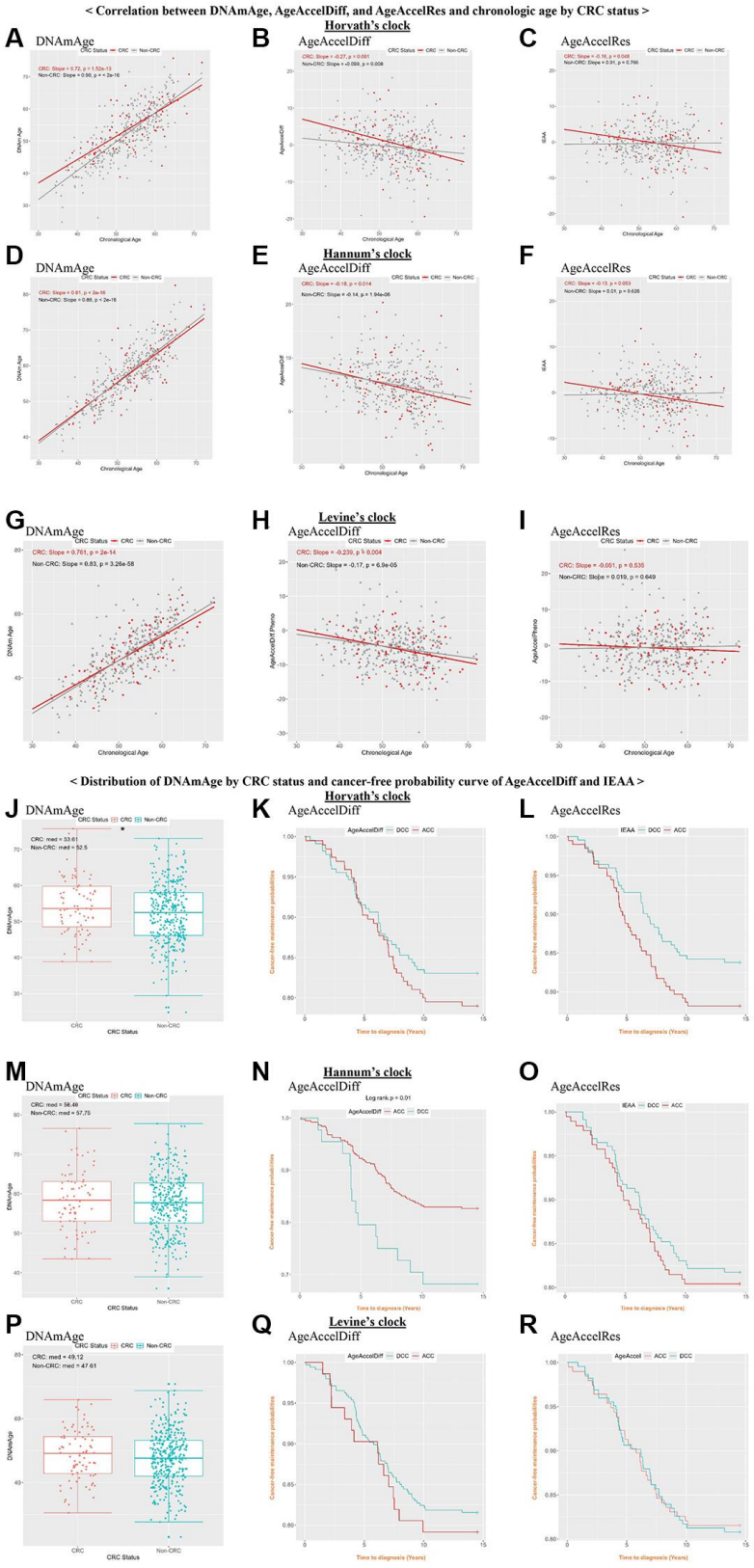

Y
HEI-2015, fatty acids: DNAmAge
Wilcoxon test p = 0.238
DNAm Age
HEI2015.fat.Cat
Z
Overall
HEI-2015, fatty acids: AgeAccelDiff
Wilcoxon test p = 0.157
AgeAccelDiff
HEI2015.fat.Cat
AA
HEI-2015, fatty acids: IEAA
Wilcoxon test p = 0.261
IEAA
HEI2015.fat.Cat
BB
Physical activity: DNAmAge
Kruskal-Wallis test p = 0.317
DNAm Age
Non-Active
Active
TEXPWK.Cat
CC
Overall
Physical activity: AgeAccelDiff
Kruskal-Wallis test p = 0.004
AgeAccelDiff
TEXPWK.Cat
DD
Physical activity: IEAA
Kruskal-Wallis test p = 0.032
IEAA
TEXPWK.Cat
EE
Physical activity: DNAmAge
Among CRC
Kruskal-Wallis test p = 0.153
DNAm Age
Physical activity
FF
Among patients with CRC
Physical activity: AgeAccelDiff
Among CRC
Kruskal-Wallis test p = 0.172
AgeAccelDiff
Physical activity
GG
Physical activity: IEAA
Among CRC
Kruskal-Wallis test p = 0.295
IEAA
Physical activity
HH
Oophorectomy: DNAmAge
Wilcoxon test p = 0.085
DNAm Age
None
Both taken out
OOPH
II
Overall
Oophorectomy: AgeAccelDiff
Wilcoxon test p = 0.0277
BAgeAccelDiff
OOPH
JJ
Oophorectomy: IEAA
Wilcoxon test p = 0.071
IEAA
OOPH



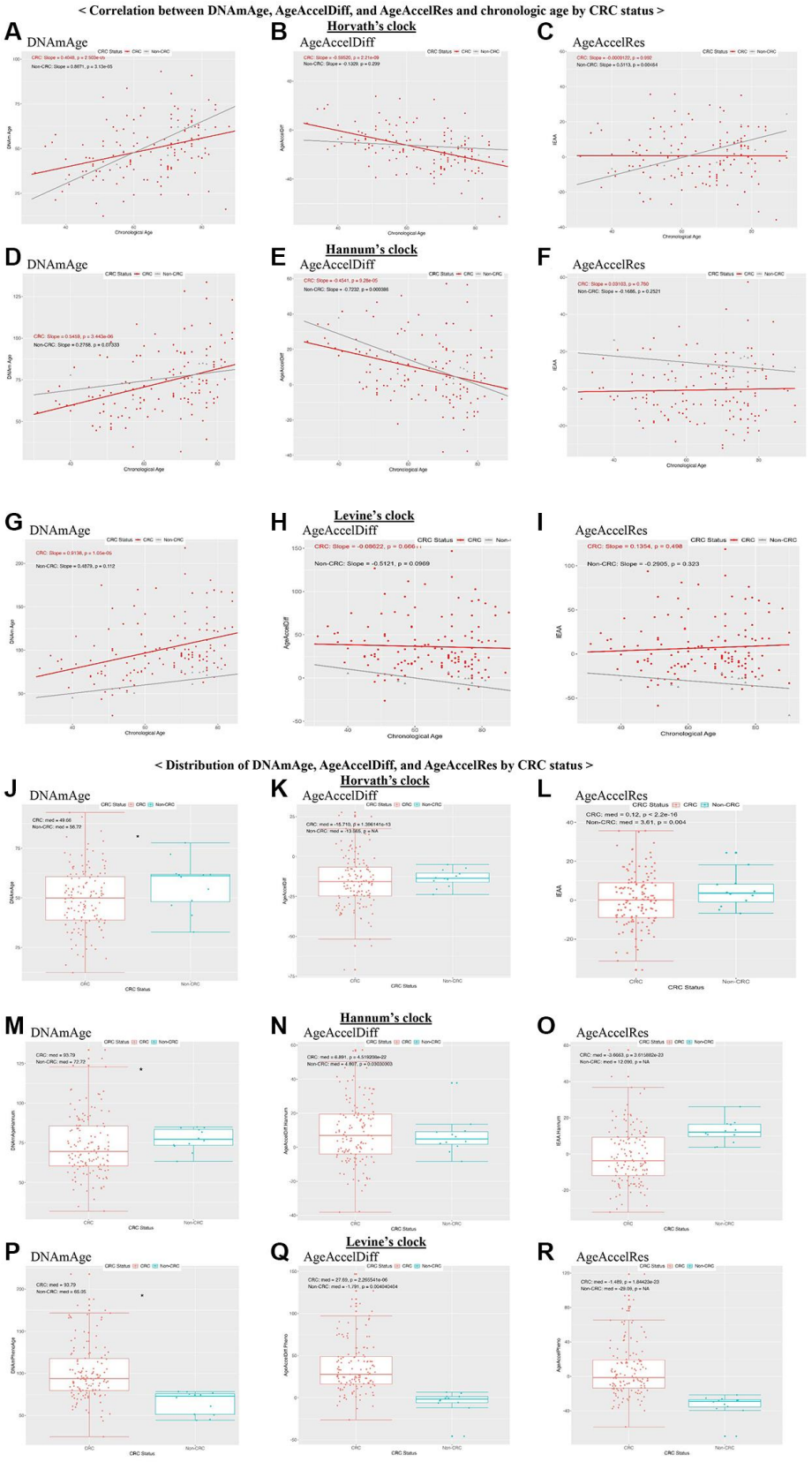
Supplementary Figure 3. Levine's clock: distribution of DNAmAge, AgeAccelDiff, and IEAA by selected CRC risk factors. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; BMI: body mass index; CRC: colorectal cancer; DNAmAge: DNA methylationbased marker of aging; E only: exogenous estrogen only; E plus P: E plus progestin; HEI-2015: Healthy Eating Index-2015; IEAA: intrinsic epigenetic age acceleration as residuals adjusted for cell composition; WHR: waist-to-hip ratio.



Supplementary Figure 4. Distribution of DNAmAge by CRC status and cancer-free probability curve of AgeAccelDiff and IEAA. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; ACC: accelerated age, i.e., positive difference of DNAm age from chronologic age; CRC: colorectal cancer; DNAmAge: DNA methylation-based marker of aging; DCC: decelerated age, i.e., negative difference of DNAm age from chronologic age; IEAA: intrinsic epigenetic age acceleration as residuals adjusted for cell composition.



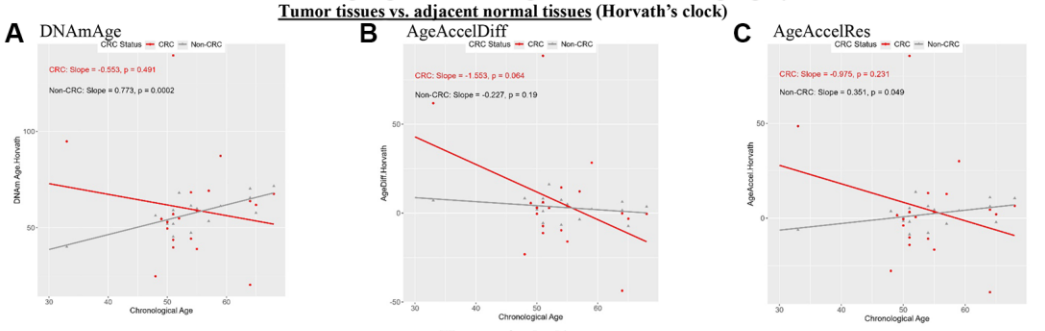
Supplementary Figure 5. GSE51032 women, validation tests. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; ACC: accelerated age, i.e., positive difference of DNAm age from chronologic age; CRC: colorectal cancer; DCC: decelerated age, i.e., negative difference of DNAm age from chronologic age; DNAmAge: DNA methylation-based marker of aging; IEAA, intrinsic epigenetic age acceleration as residuals adjusted for cell composition.



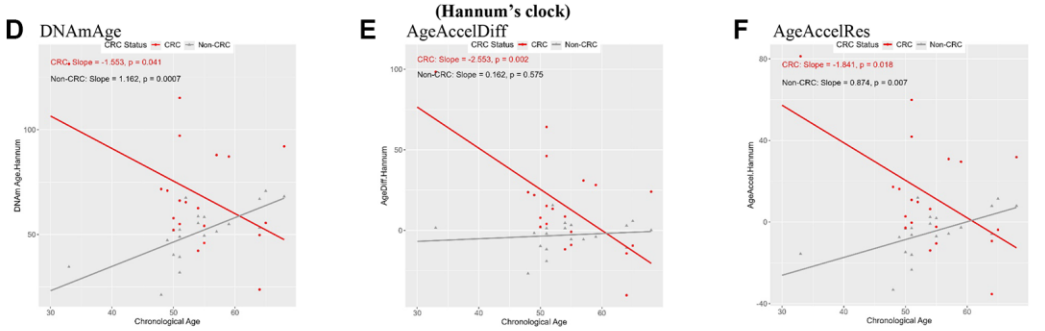
Supplementary Figure 6. TCGA women, validation tests. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; AgeAccelRes: epigenetic age acceleration as residuals by regressing DNAmAge on chronologic age; CRC: colorectal cancer; DNAmAge: DNA methylation-based marker of aging.

< Correlation between DNAmAge, AgeAccelDiff, and AgeAccelRes and chronologic age by CRC status >

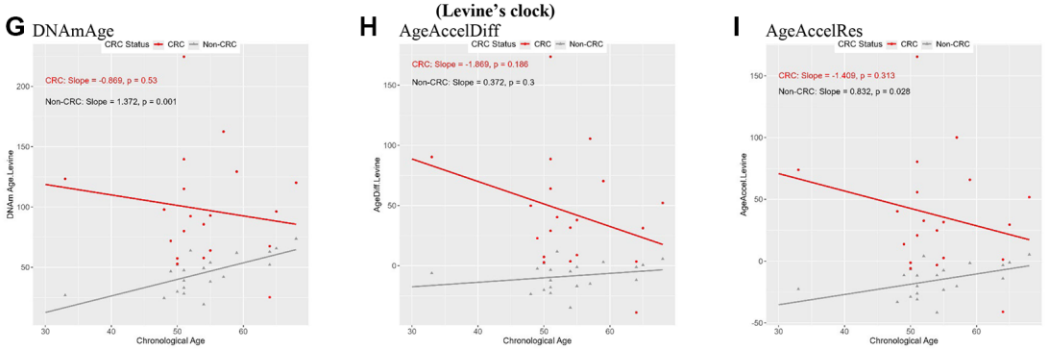
Tumor tissues vs. adjacent normal tissues (Horvath's clock)



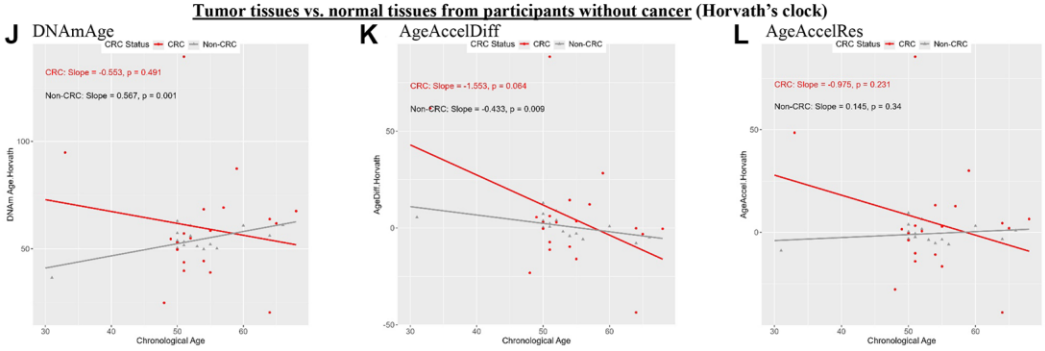
(Hannum's clock)

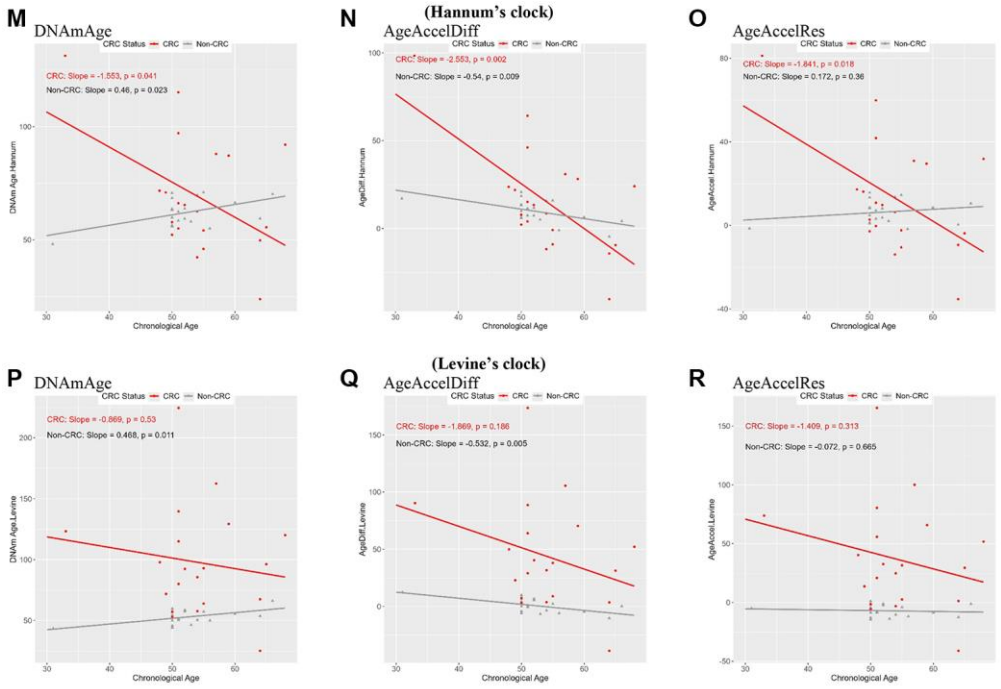


(Levine's clock)



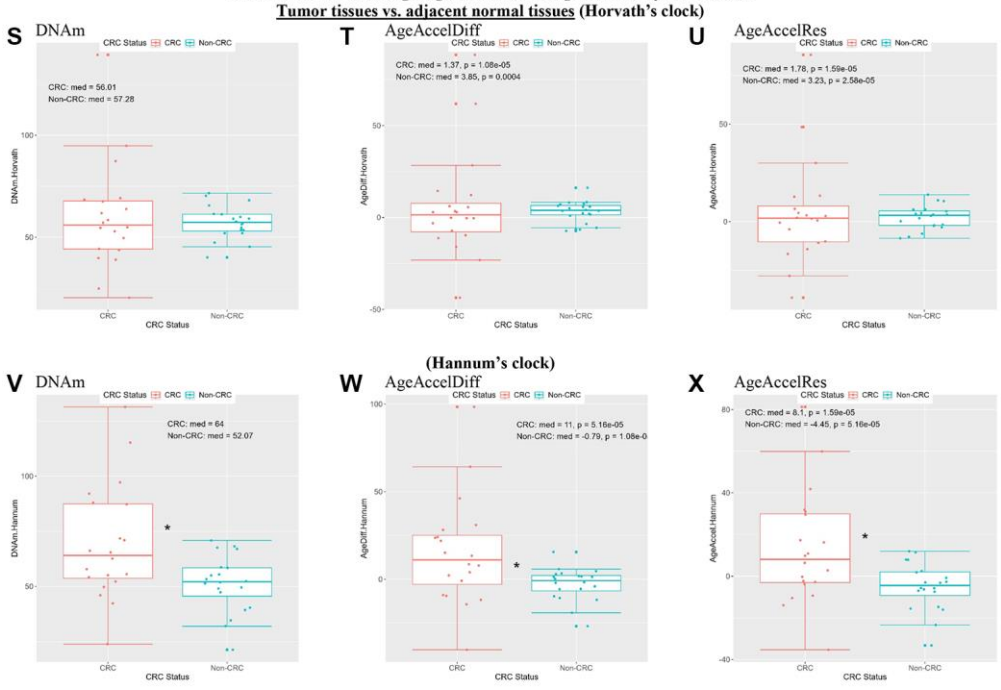
Tumor tissues vs. normal tissues from participants without cancer (Horvath's clock)

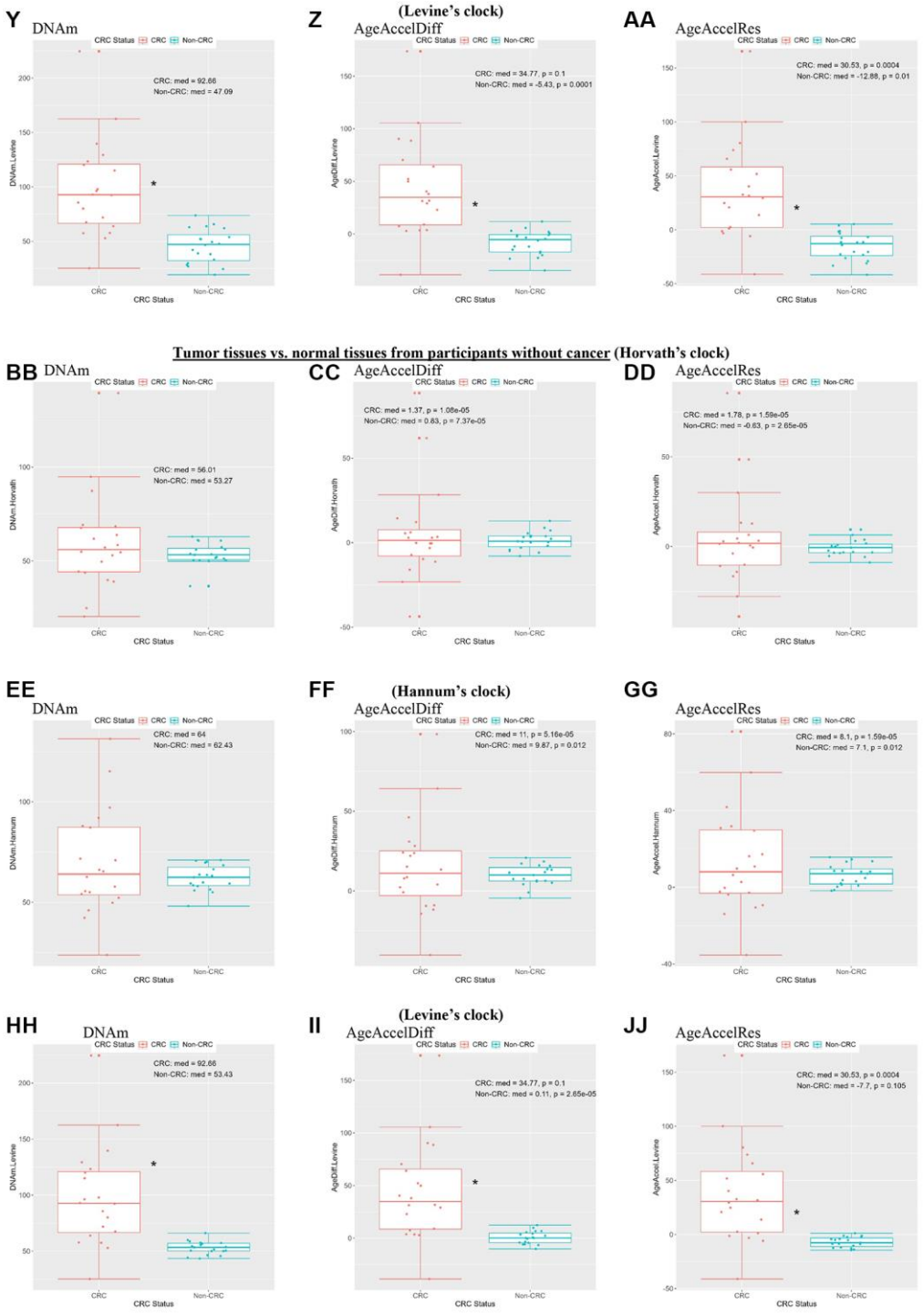




< Distribution of DNAmAge, AgeAccelDiff, and AgeAccelRes by CRC status >

Tumor tissues vs. adjacent normal tissues (Horvath's clock)





Supplementary Figure 7. GSE199057 women, validation tests. Abbreviations: AgeAccelDiff: epigenetic age acceleration as departure of DNAmAge from chronologic age; AgeAccelRes: epigenetic age acceleration as residuals by regressing DNAmAge on chronologic age; CRC: colorectal cancer; DNAmAge: DNA methylation-based marker of aging.