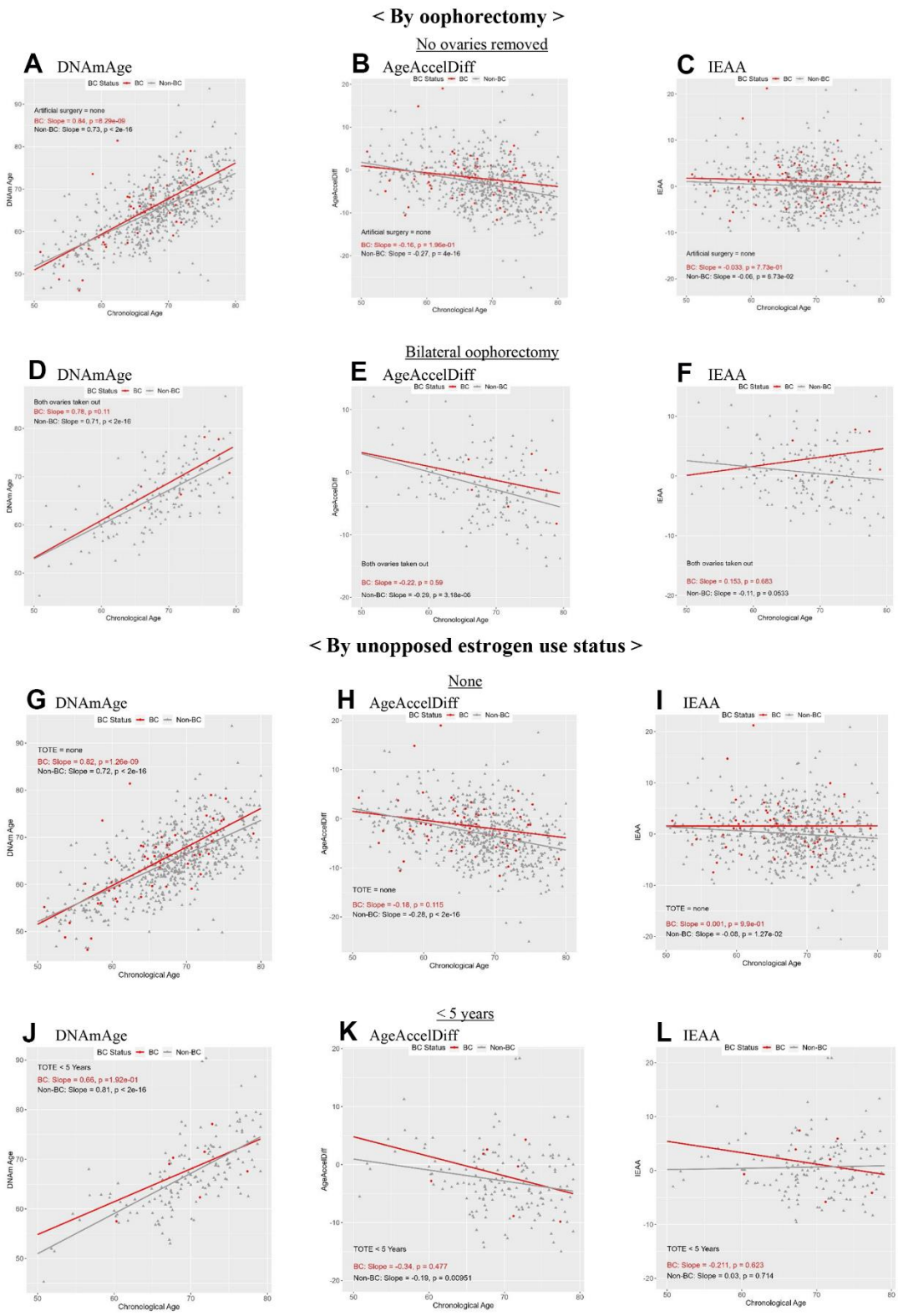
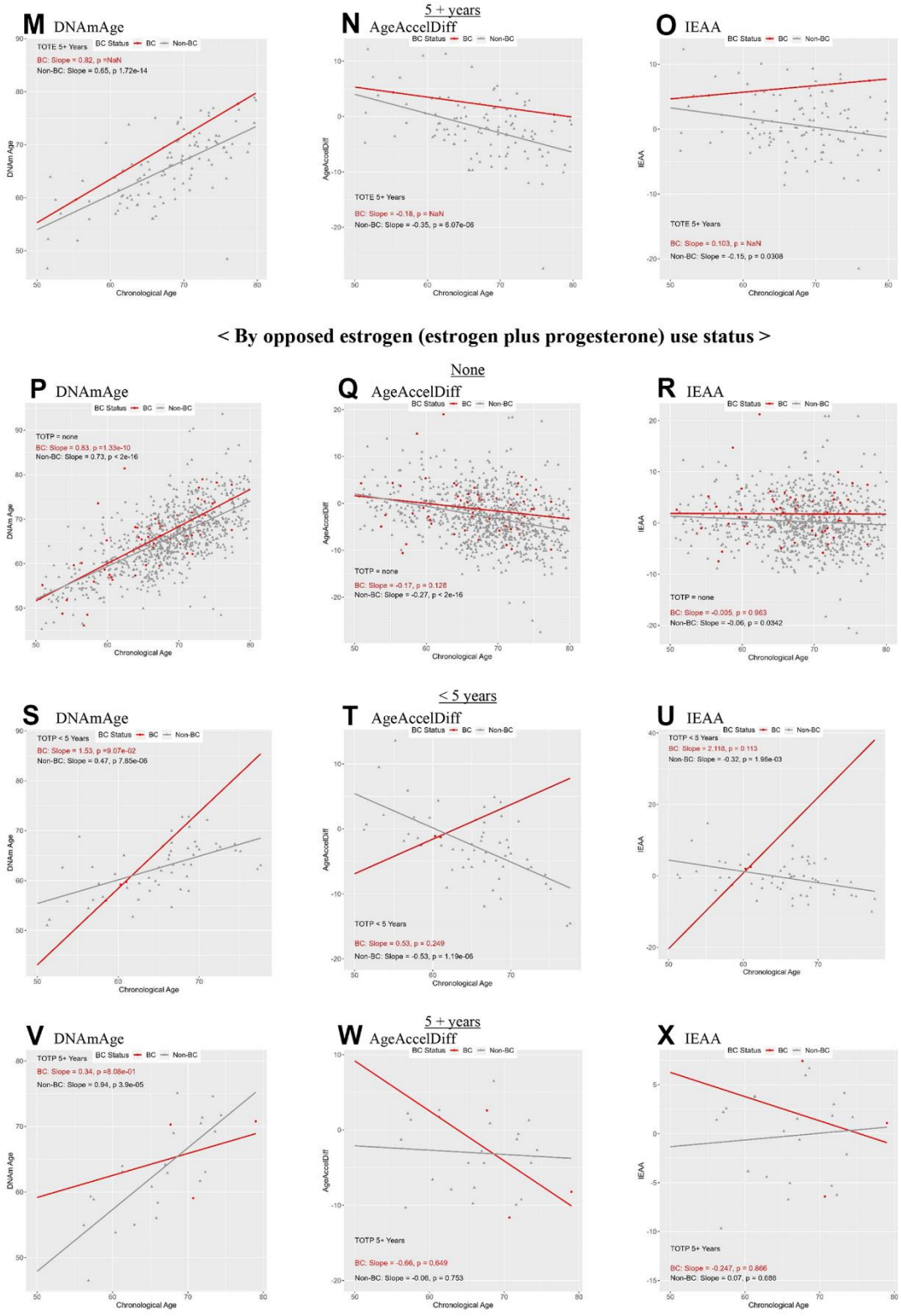
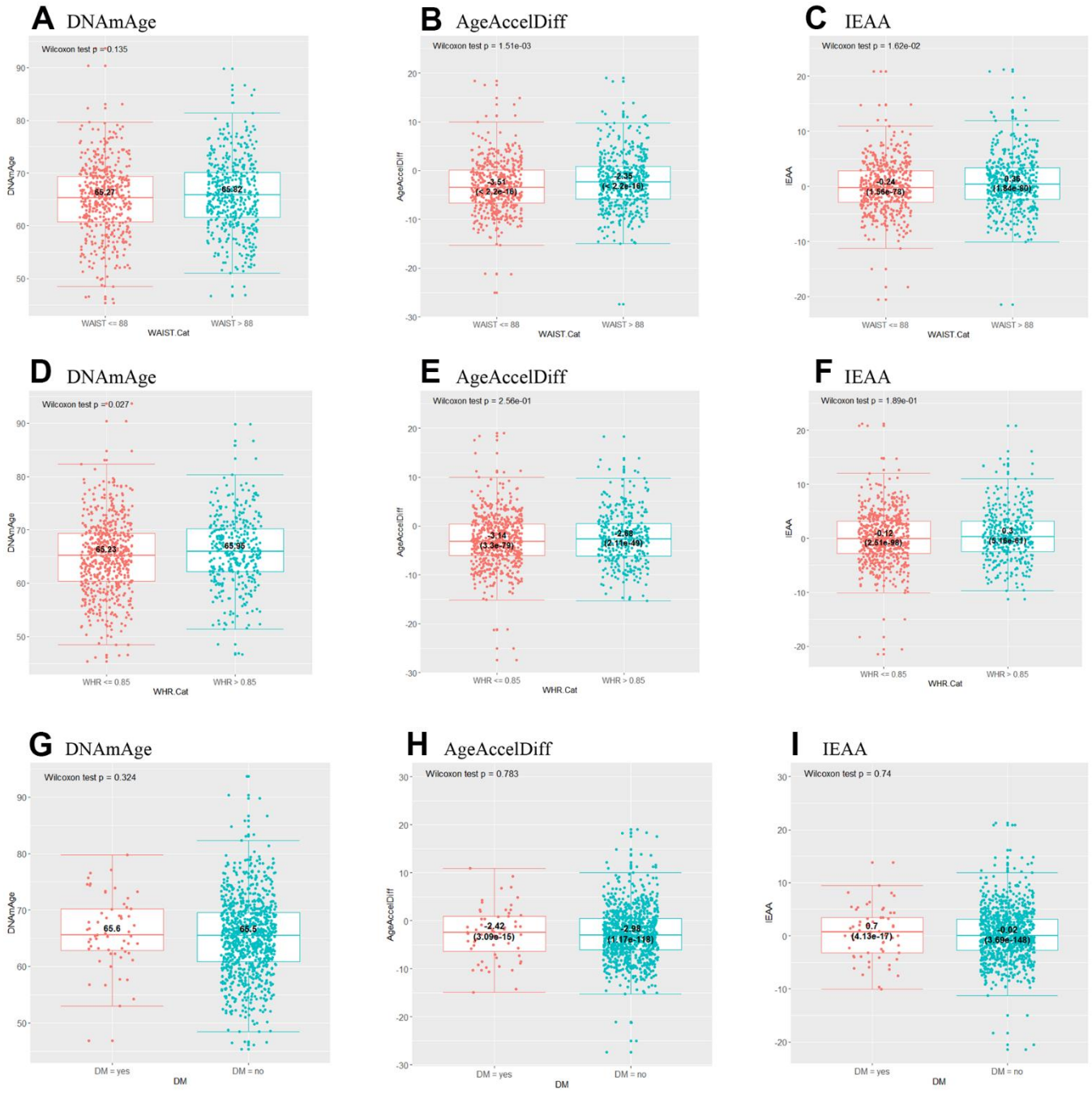
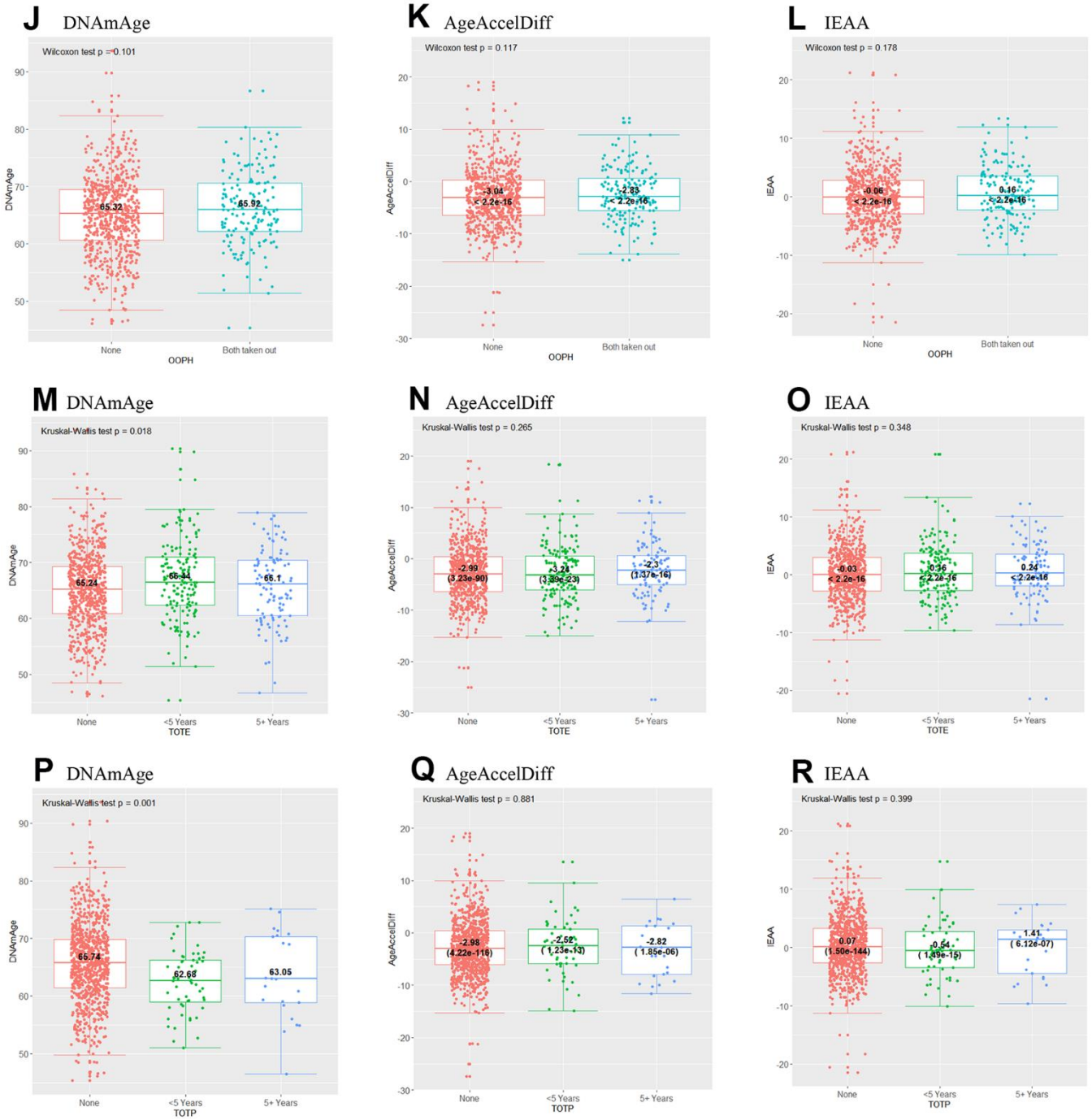
SUPPLEMENTARY FIGURES



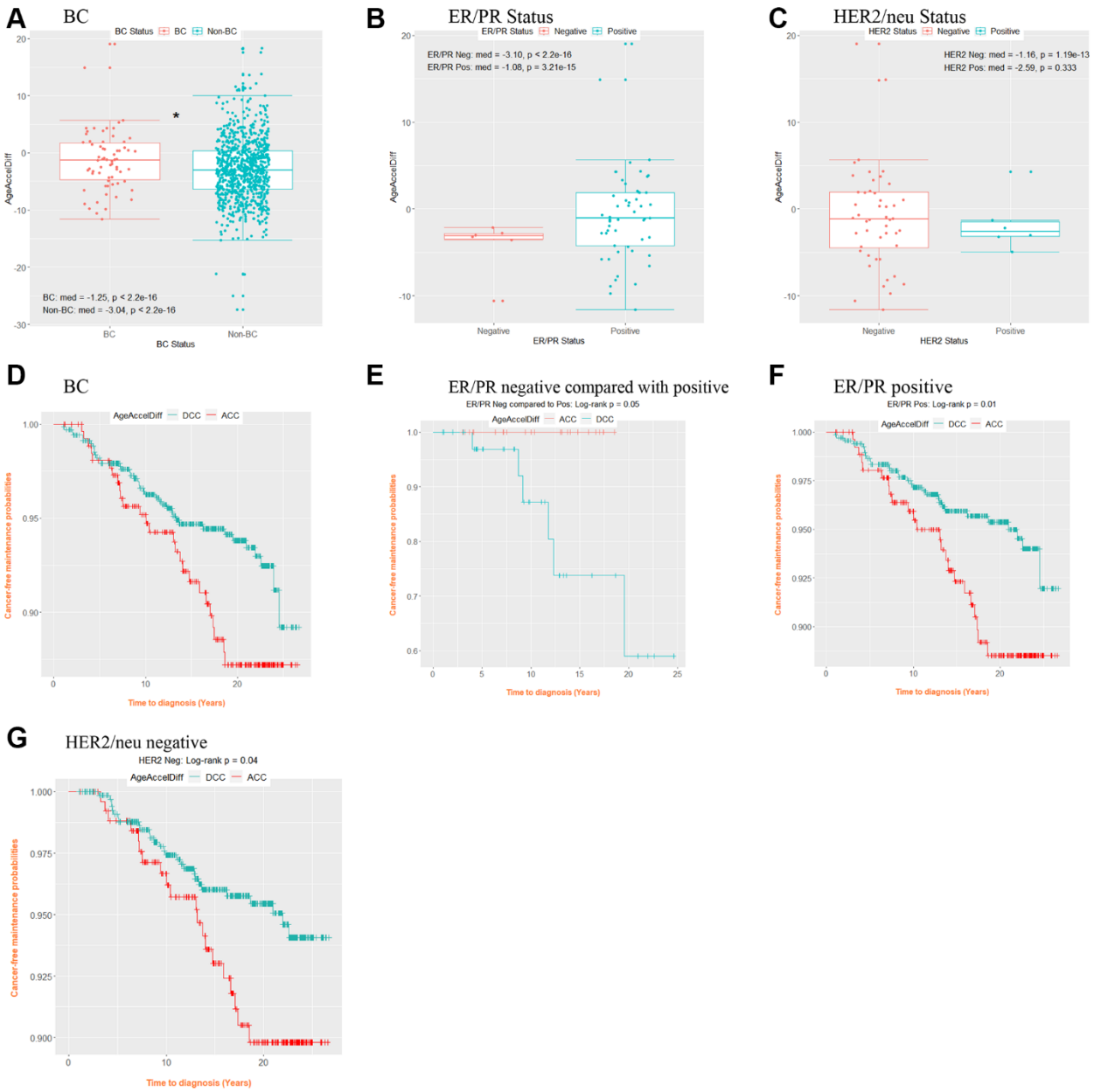


Supplementary Figure 1. Correlation between DNAmAge/AgeAccelDiff/IEAA and chronologic age by BC status. By oophorectomy, (**A**–**C**) no ovaries removed, (**D**–**F**) bilateral. By unopposed estrogen use status, (**G**–**I**) none, (**J**–**L**) < 5 years, (**M**–**O**) 5 + years. By opposed estrogen (estrogen plus progesterone) use status, (**P**–**R**) none, (**S**–**U**) < 5 years, (**V**–**X**) 5 +years. (AgeAccelDiff, epigenetic age acceleration measured as departure of DNAmAge from chronologic age; IEAA, intrinsic epigenetic age acceleration measured as residuals by regressing DNAmAge on chronologic age, adjusted for cell composition; BC, breast cancer; DNAmAge, DNA methylation–based marker of aging).

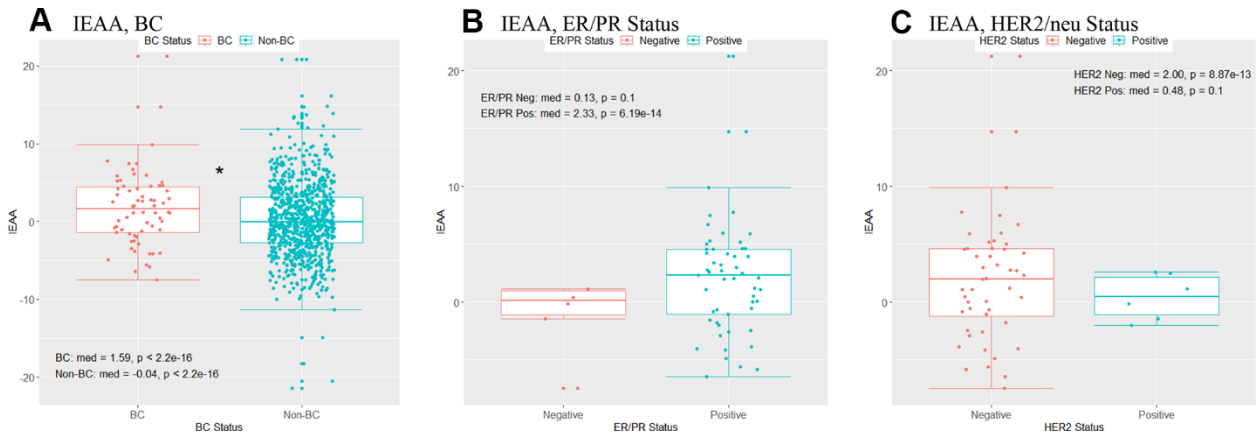

A DNAmAge
Wilcoxon test p = 0.135
DNAmAge
65.27
65.82
WAIST <= 88
WAIST > 88
WAIST.Cat
B AgeAccelDiff
Wilcoxon test p = 1.51e-03
AgeAccelDiff
-3.51
(< 2.2e-16)
2.35
(< 2.2e-16)
WAIST <= 88
WAIST > 88
WAIST.Cat
C IEAA
Wilcoxon test p = 1.62e-02
IEAA
-0.24
(1.56e-78)
0.36
(1.84e-90)
WAIST <= 88
WAIST > 88
WAIST.Cat
D DNAmAge
Wilcoxon test p = 0.027
DNAmAge
65.23
65.95
WHR <= 0.85
WHR > 0.85
WHR.Cat
E AgeAccelDiff
Wilcoxon test p = 2.56e-01
AgeAccelDiff
-3.14
(3.3e-79)
2.69
(2.11e-49)
WHR <= 0.85
WHR > 0.85
WHR.Cat
F IEAA
Wilcoxon test p = 1.89e-01
IEAA
-0.12
(2.51e-98)
0.3
(5.18e-67)
WHR <= 0.85
WHR > 0.85
WHR.Cat
G DNAmAge
Wilcoxon test p = 0.324
DNAmAge
65.6
65.5
DM = yes
DM = no
DM
H AgeAccelDiff
Wilcoxon test p = 0.783
AgeAccelDiff
-2.42
(3.09e-15)
2.38
(1.17e-118)
DM = yes
DM = no
DM
I IEAA
Wilcoxon test p = 0.74
IEAA
0.7
(4.13e-17)
-0.02
(3.69e-148)
DM = yes
DM = no
DM



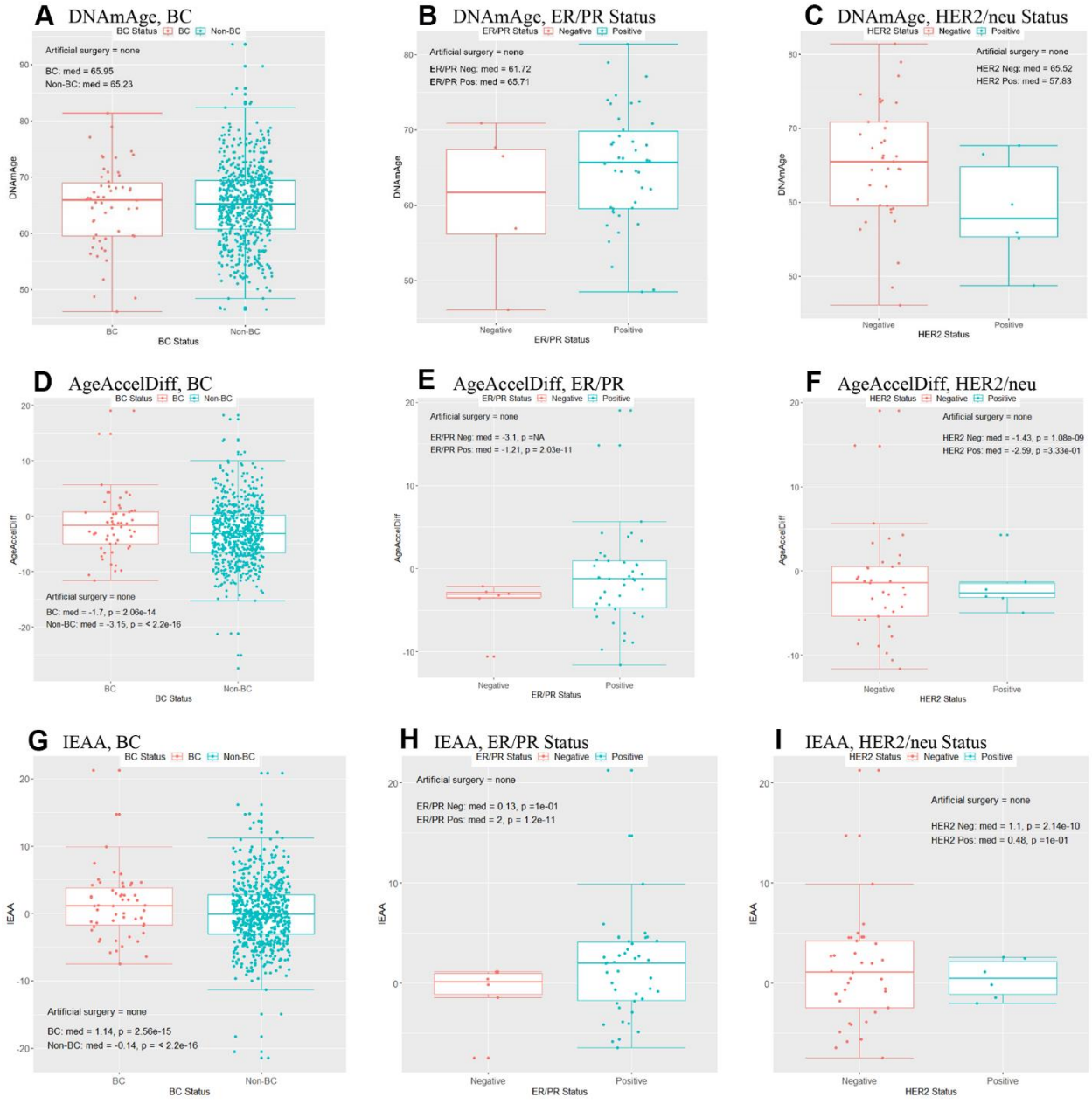
Supplementary Figure 2. Distribution of DNAmAge/AgeAccelDiff/IEAA by BC-risk factors (except body mass index, diet, smoking, and alcohol). By waist circumference, (**A**–**C**); WHR, (**D**–**F**); DM, (**G**–**I**); OOPH, (**J**–**L**); TOTE, (**M**–**O**); TOTP, (**P**–**R**). (AgeAccelDiff, epigenetic age acceleration as departure of DNAmAge from chronologic age; IEAA, intrinsic epigenetic age acceleration as residuals adjusted for cell composition; BC, breast cancer; Cat, Categories; DM, diabetes; DNAmAge, DNA methylation–based marker of aging; OOPH, oophorectomy; TOTE, total duration of unopposed estrogen use; TOTP, total duration of opposed estrogen plus progestin use; WHR, waist-to-hip ratio).



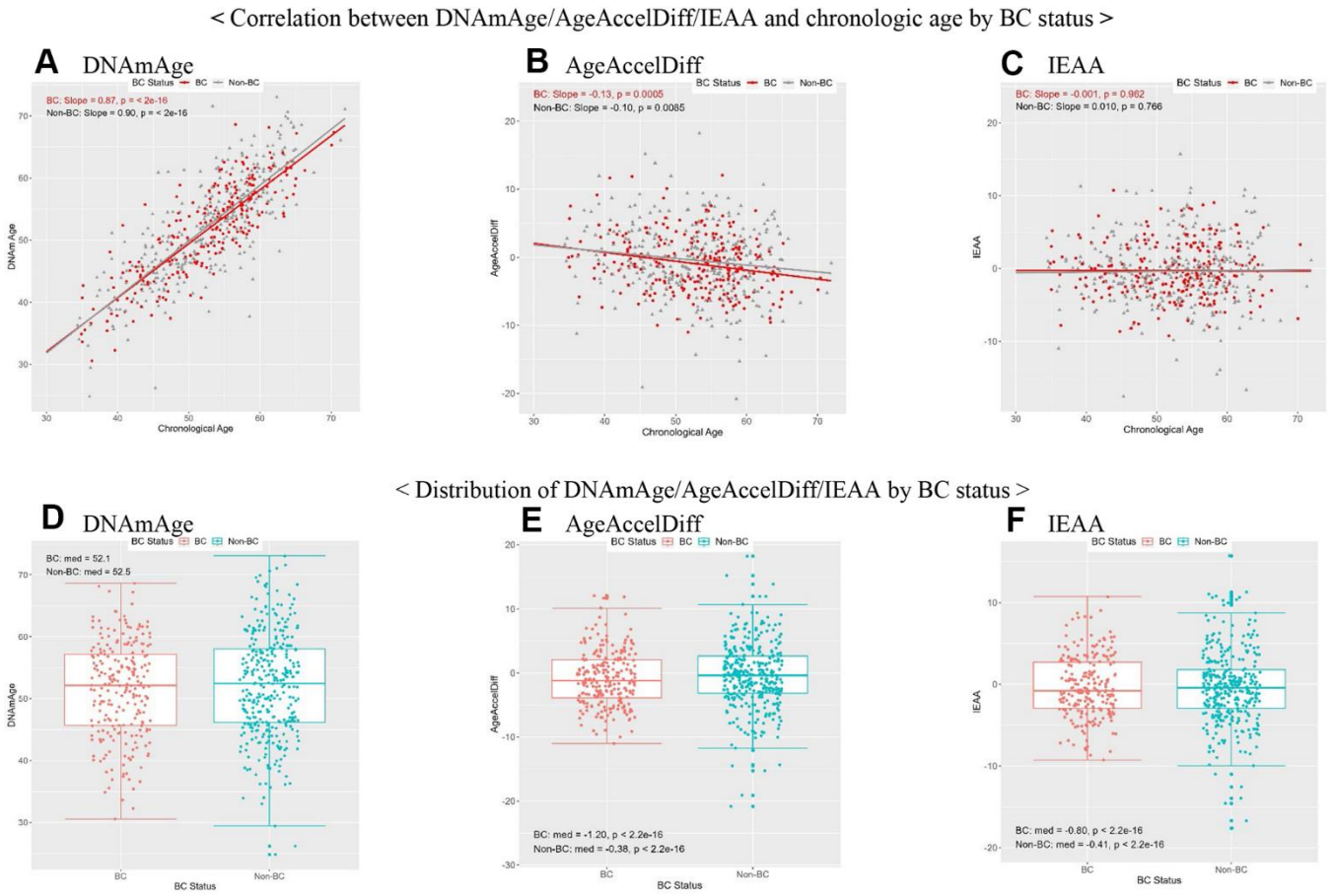
Supplementary Figure 3. Distribution (**A**–**C**) and cancer-free probability curve (**D**–**G**) of AgeAccelDiff by BC status and BC subtype. (AgeAccelDiff, epigenetic age acceleration as departure of DNAmAge from chronologic age; ACC, acceleration, i.e., positive difference of DNAm age from chronologic age; BC, breast cancer; DCC, deceleration, i.e., negative difference of DNAm age from chronologic age; DNAmAge, DNA methylation–based marker of aging; ER/PR, estrogen and progesterone receptor; HER2/neu, human epidermal growth factor receptor 2).



Supplementary Figure 4. Distribution of IEAA by BC status (**A**) and BC subtype (**B**, **C**). (IEAA, intrinsic epigenetic age acceleration as residuals adjusted for cell composition; BC, breast cancer; ER/PR, estrogen and progesterone receptor; HER2/neu, human epidermal growth factor receptor 2).



Supplementary Figure 5. Women without a history of oophorectomy. Distribution of DNAmAge (**A**–**C**)/AgeAccelDiff (**D**–**F**)/IEAA (**G**–**I**) by BC status and BC subtype. (AgeAccelDiff, epigenetic age acceleration measured as departure of DNAmAge from chronologic age; IEAA, intrinsic epigenetic age acceleration as residuals adjusted for cell composition; BC, breast cancer; DNAmAge, DNA methylation–based marker of aging; ER/PR, estrogen and progesterone receptor; HER2/neu, human epidermal growth factor receptor 2).



Supplementary Figure 6. GSE51032: validation tests. Correlation between DNAmAge (**A**)/AgeAccelDiff (**B**)/IEAA (**C**) and chronologic age by BC status. Distribution of DNAmAge (**D**)/AgeAccelDiff (**E**)/IEAA (**F**) by BC status. (AgeAccelDiff, epigenetic age acceleration measured as departure of DNAmAge from chronologic age; IEAA, intrinsic epigenetic age acceleration measured as residuals by regressing DNAmAge on chronologic age, adjusted for cell composition; BC, breast cancer; DNAmAge, DNA methylation–based marker of aging).