Figures and figure supplements

Associations of combined phenotypic aging and genetic risk with incident cancer: A prospective cohort study

Lijun Bian and Zhimin Ma *et al*.

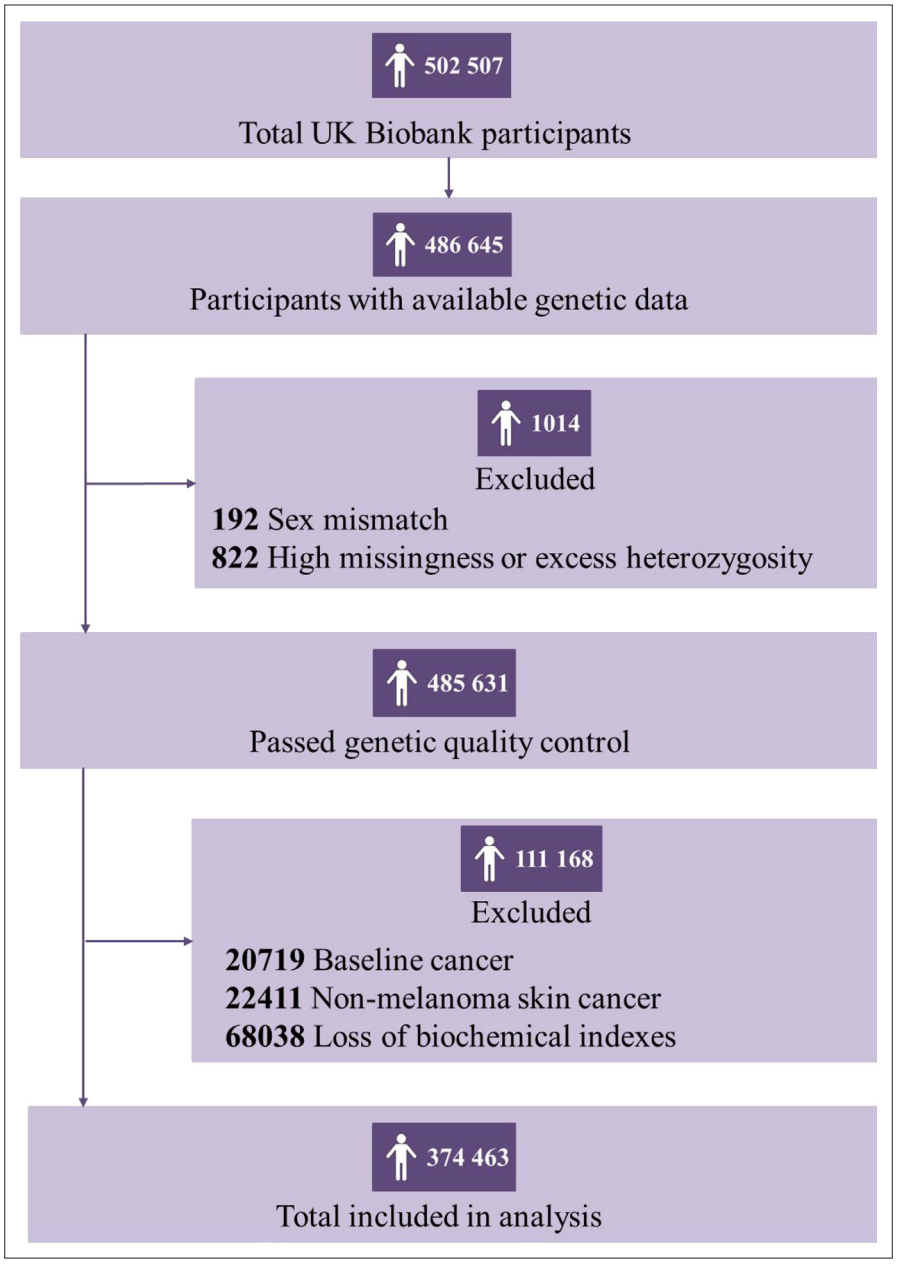

Figure 1. Flowchart for filtering participants from the UK Biobank cohort. Participants who had withdrawn their consent, had been diagnosed with cancer before baseline, failed to be genotyped, reported a mismatch sex with genetic data, or with missing data on Phenotypic Age (PhenoAge) were excluded.

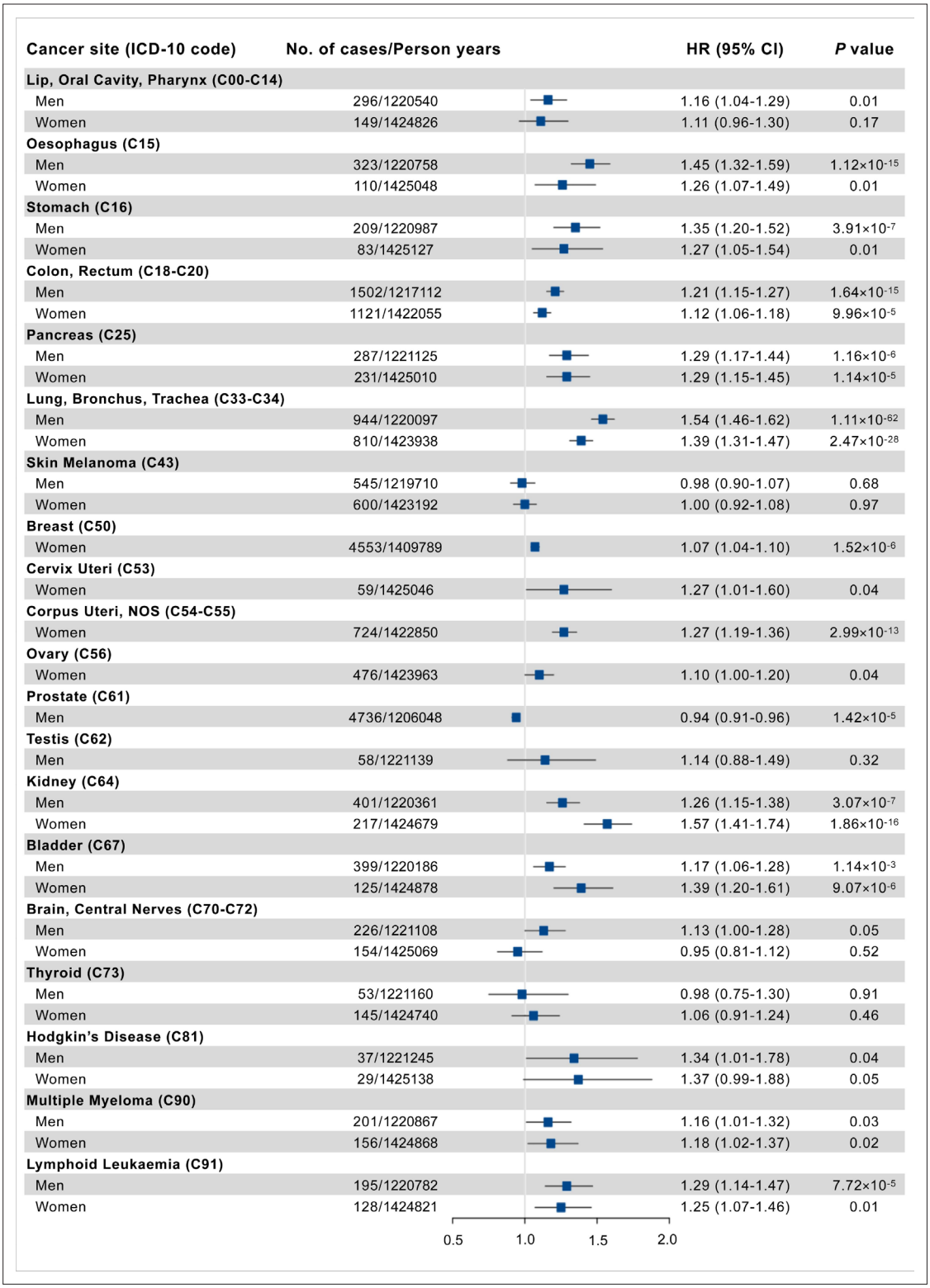

Figure 2. Association results of Phenotypic Age Acceleration (PhenoAgeAccel) with site-specific cancer risk per 5 years increased. Cox proportional hazards regression adjusted for age, height, cancer family history, Townsend deprivation index at recruitment, and the first 10 principal components of ancestry. Error bars are 95% confidence intervals (CIs).

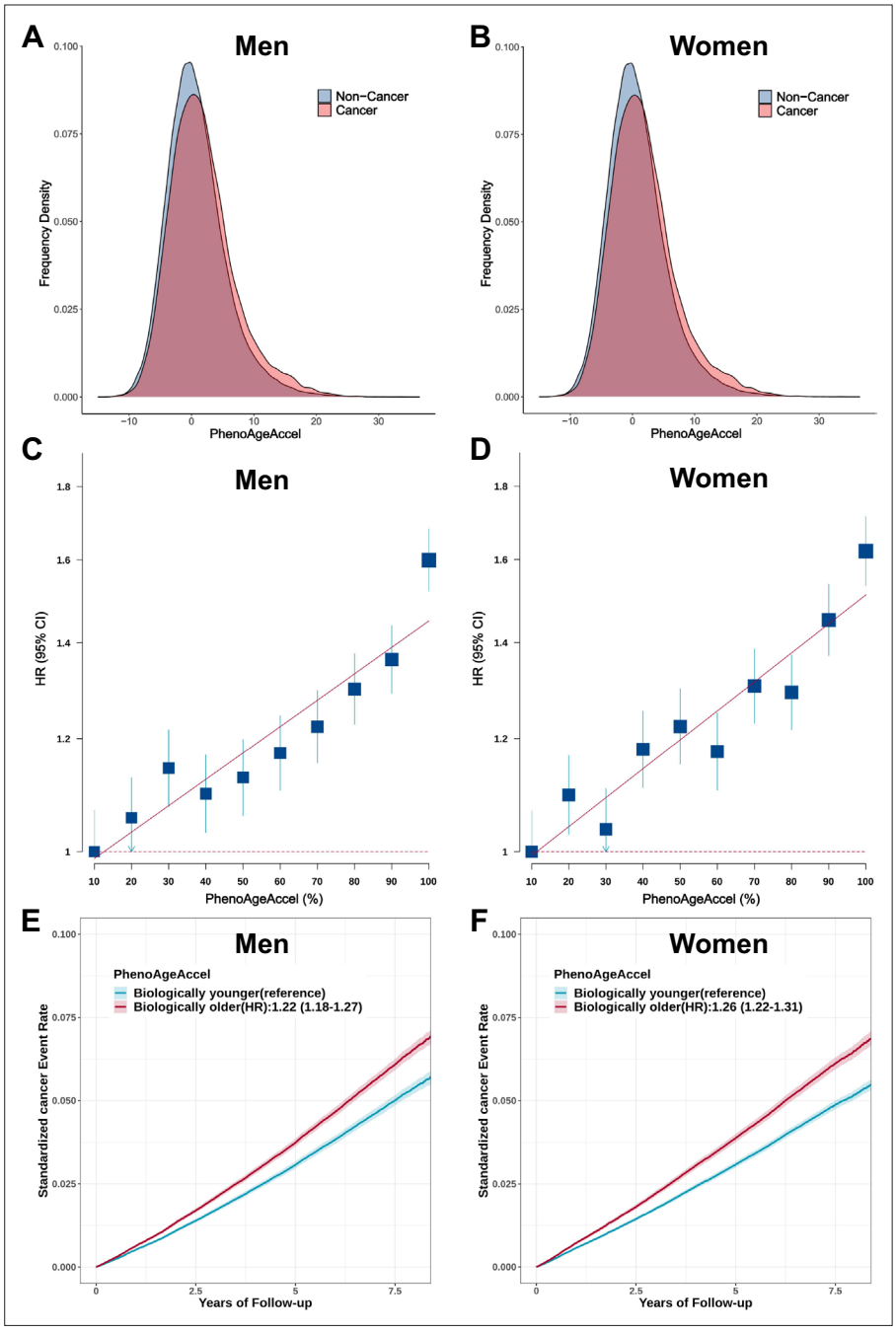

Figure 3. Effect of Phenotypic Age Acceleration (PhenoAgeAccel) on the risk of incident cancer in the UK Biobank. The distribution of PhenoAgeAccel between participants with incident cancer and those without incident cancer in the UK Biobank for men(A) and women (**B**). Participants in the UK Biobank were divided into ten equal groups according to the PhenoAgeAccel for men (**C**) and women (**D**), and the hazard ratios (HRs) of each group were compared with those in the bottom decile of PhenoAgeAccel. Error bars are 95% confidence intervals (CIs). Standardized rates of cancer events in younger and older PhenoAge groups in the UK Biobank for men (**E**) and women (**F**). HRs and 95% CIs were estimated using Cox proportional hazard models with adjustment for age, height, family history of cancer, Townsend deprivation index, and the first 10 principal components of ancestry. Shaded areas are 95% CIs.

A

Subgroup	No. of cases/ Total no.	Incidence/ 100,000 py	HR (95% CI)	*P* value
Low genetic risk				
Biologically younger	668/16458	581.06	Reference	Reference
Biologically older	1031/18229	827.94	1.30 (1.18-1.43)	1.22×10^{-7}
Intermediate genetic risk				
Biologically younger	2606/48636	768.85	1.29 (1.18-1.40)	6.45×10^{-9}
Biologically older	4012/55421	1064.81	1.64 (1.51-1.78)	1.02×10^{-31}
High genetic risk				
Biologically younger	1375/16148	1239.78	2.11 (1.92-2.31)	1.09×10^{-55}
Biologically older	1840/18539	1477.89	2.29 (2.10-2.51)	1.33×10^{-74}

B

Subgroup	No. of cases/ Total no.	Incidence/ 100,000 py	HR (95% CI)	*P* value
Low genetic risk				
Biologically younger	1030/24736	594.71	Reference	Reference
Biologically older	761/15471	711.64	1.25(1.14-1.38)	2.14×10^{-6}
Intermediate genetic risk				
Biologically younger	3579/74310	690.11	1.17(1.09-1.25)	9.55×10^{-6}
Biologically older	2704/46308	848.31	1.52(1.41-1.63)	4.61×10^{-30}
High genetic risk				
Biologically younger	1620/24602	954.27	1.63(1.51-1.77)	1.03×10^{-34}
Biologically older	1144/15605	1076.17	1.94(1.78-2.11)	1.85×10^{-53}

Figure 4. Risk of incident cancer according to genetic and Phenotypic Age Acceleration (PhenoAgeAccel) categories in the UK Biobank for men (**A**) and women (**B**). The hazard ratios (HRs) were estimated using Cox proportional hazard models with adjustment for age, height, family history of cancer, Townsend deprivation index, and the first 10 principal components of ancestry. Participants were divided into younger and older PhenoAge under different genetic risk groups. Error bars are 95% confidence intervals (CIs).

A

Subgroup	No. of cases/ Total no.	Incidence/ 100,000 py	HR (95% CI)	*P* value
Low genetic risk				
Low	256/7190	505.92	Reference	Reference
Intermediate	946/20619	662.79	1.23(1.07-1.41)	3.46×10^{-3}
High	497/6878	1076.74	1.80(1.55-2.09)	2.70×10^{-14}
Intermediate genetic risk				
Low	1041/20627	720.46	1.37(1.19-1.57)	6.63×10^{-6}
Intermediate	3845/62570	890.97	1.62(1.42-1.84)	1.14×10^{-13}
High	1732/20860	1239.89	2.03(1.78-2.31)	6.58×10^{-26}
High genetic risk				
Low	567/6870	1195.52	2.33(2.01-2.70)	3.68×10^{-29}
Intermediate	1877/20869	1321.54	2.41(2.11-2.75)	1.70×10^{-39}
High	771/6948	1677.93	2.81(2.43-3.23)	4.94×10^{-46}

B

Subgroup	No. of cases/ Total no.	Incidence/ 100,000 py	HR (95% CI)	*P* value
Low genetic risk				
Low	327/8054	576.07	Reference	Reference
Intermediate	1033/24166	613.36	1.11(0.98-1.26)	0.10
High	431/7987	784.35	1.48(1.28-1.71)	8.98×10^{-8}
Intermediate genetic risk				
Low	1127/24217	662.60	1.16(1.03-1.31)	0.02
Intermediate	3691/72343	724.85	1.34(1.20-1.50)	3.37×10^{-7}
High	1465/24058	887.91	1.71(1.51-1.92)	2.70×10^{-18}
High genetic risk				
Low	492/7936	893.57	1.58(1.37-1.82)	1.57×10^{-10}
Intermediate	1627/24109	982.24	1.81(1.61-2.04)	1.66×10^{-22}
High	645/8162	1165.00	2.27(1.99-2.60)	1.61×10^{-33}

Figure 4—figure supplement 1. Risk of incident cancer according to genetic and Phenotypic Age Acceleration (PhenoAgeAccel) categories (quintiles) in the UKB cohort for men (**A**) and women (**B**). The hazard ratios (HRs) were estimated using Cox proportional hazard models with adjustment for age, height, family history of cancer, Townsend deprivation index, and the first 10 principal components of ancestry. Participants were divided into low (the bottom quintile of PhenoAgeAccel), intermediate (quintiles 2–4), and high (the top quintile) accelerated aging under different genetic risk groups. Error bars are 95% confidence intervals (CIs).

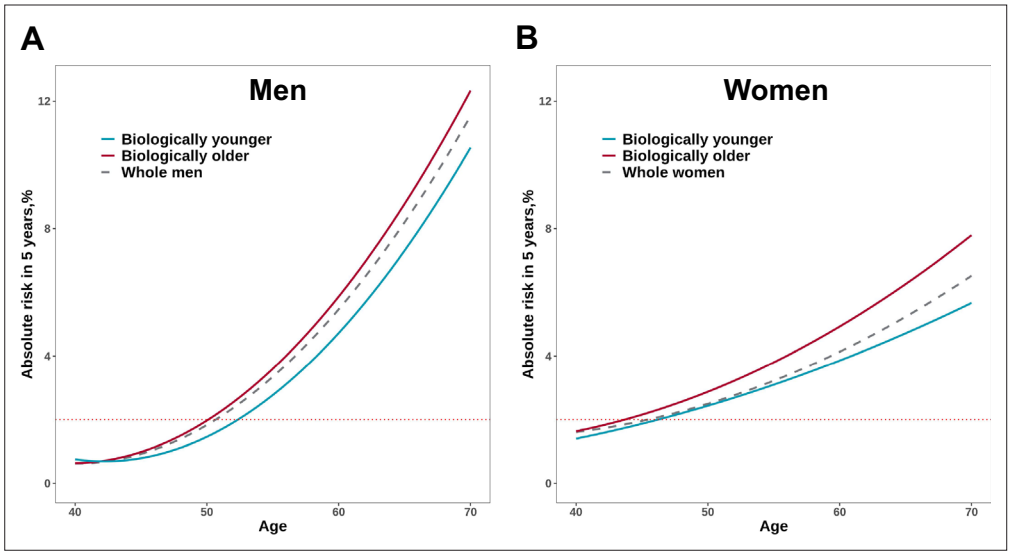

Figure 5. Absolute risk estimates of overall cancer based on the UK Biobank for men (**A**) and women (**B**). The x-axis is chronological age. The curves describe the average risk of participants in younger and older Phenotypic Age (PhenoAge) groups. The dashed curve represents the average risk of the whole population at different ages. The red horizontal dotted line represents 2% of 5 year absolute risks of overall cancer.