Supplementary Materials

Accelerated biological aging drives the progression from MASLD to cirrhosis

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Supplementary Tables and Figures

Supplementary Table 1. ICD-10 codes used to define baseline liver disease

Diagnosis	ICD-10
Acute hepatitis B	B16.0, B16.9
Other acute viral hepatitis	B17.0, B17.1, B17.2, B17.8, B17.9
Chronic viral hepatitis	B18.0, B18.1, B18.2, B18.8, B18.9,
Chronic viral hepatitis	B19.9
Hepatocellular carcinoma	C22.0
Alcoholic liver disease	K70.1, K70.2, K70.3, K70.4, K70.9
Toxic liver disease	K71.0, K71.1, K71.2, K71.3, K71.5, K71.6, K71.7, K71.8, K71.9
Hepatic failure, not elsewhere classified	K72.0, K72.1, K72.9
Chronic hepatitis, not elsewhere classified	K73.0, K73.1, K73.2, K73.8, K73.9
Fibrosis and cirrhosis of liver	K74.0, K74.1, K74.2, K74.3, K74.4, K74.5, K74.6
Other inflammatory liver diseases	K75.0, K75.1, K75.2, K75.3, K75.4, K75.8, K75.9
Other diseases of liver	K76.0, K76.1, K76.2, K76.3, K76.4, K76.5, K76.6, K76.7, K768, K76.9
Liver disorders in diseases classified elsewhere	K77.0, K77.8
Oesophageal varices	I85.0, I85.9
Ascites	R18

Supplementary Table 2. Definition of metabolic dysfunction-associated steatotic liver disease

Definition items	Corresponding items in the UK Biobank	
Hepatic steatosis	Fatty liver index ≥60	$(e^{0.953*\ln(TG) + 0.139*BMI + 0.718*\ln(GGT) + 0.053*WC - 15.745}) / (1 + e^{0.953*\ln(TG) + 0.139*BMI + 0.718*\ln(GGT) + 0.053*WC - 15.745}) \times 100$
Met one of five		
Overweight or obesity	Met one of two	BMI≥25 kg/m^2 WC >94 cm(M) 80 cm(F)
Type 2 diabetes mellitus	Met one of three	Glycated hemoglobin A1c > 47 mmol/mol ICD-10 codes of E11 Regularly took medication for diabetes
Hypertension	Met one of two	systolic ≥130 or diastolic ≥85 mmHg use of antihypertensive medication
Plasma triglycerides	Met one of two	Plasma triglycerides > 1.70 mmolL [150 mg/dl] lipid lowering treatment
Plasma HDL-cholesterol	Met one of two	Plasma HDL-cholesterol < 1.0mmol/L [40 mg/dl] (M) and < 1.3 mmolL [50 mg/dl] (F) lipid lowering treatment
Exclude the following individuals (Met one of four):		
Excessive alcohol consumption		Alcohol consumption>210g/week (M) 140g/week (F)
Had other liver diseases at baseline		Excluded participants who had other chronic liver diseases at baseline
Abnormal liver function indicators		Aspartate transaminase or alanine aminotransferase > 500 U/L.
History of use of fat-raising drugs		Used valproic acid, tamoxifen, methotrexate and amiodarone drugs

Abbreviations: BMI,body mass index; WC,Waist circumference; HDL, high density lipoprotein.

Supplementary Table 3. Information on SNPs used to build polygenic risk scores for cirrhosis

SNP ID	Mapped gene	Location	Reference allele	Risk allele	Beta
rs2642438	*MARC1*	1:220970028	G	A	-0.094
rs12904	*EFNA1*	1:155106697	G	A	-0.105
rs6834314	*HSD17B13*	4:88213808	A	G	-0.163
rs888655	*ARHGEF28*	5:72917439	A	G	-0.073
rs9398804	*CENPW*	6:126703390	T	A	-0.073
rs7029757	*TOR1B*	9:132566666	G	A	-0.163
rs1799992	*HMBS*	11:118957246	C	T	0.207
rs28929474	*SPRPINA1*	14:94844947	T	C	0.708
rs58542926	*TM6SF2*	19:19379549	C	T	0.365
rs429358	*APOE*	19:45411941	T	C	-0.163
rs1883711	*MAFB*	20:39179822	C	G	0.191
rs738409	*PNPLA3*	22:44324727	C	G	0.489

Abbreviations: SNP, single nucleotide polymorphisms; ID, identity.

Supplementary Table 4. Associations between polygenic risk scores and risk of incident cirrhosis among individuals with MASLD

Polygenic risk score	No. of incident cases/total participants	Model 1		Model 2	
		HR(95%CI)	*P* value	HR(95%CI)	*P* value
Low	73/18355	Reference		Reference	
Intermediate	272/53919	1.26(0.97-1.63)	0.081	1.24(0.96-1.61)	0.097
High	174/17661	2.46(1.87-3.24)	<0.001	2.43(1.85-3.19)	<0.001
P for trend	519/89935	1.66(1.45-1.91)	<0.001	1.65(1.44-1.90)	<0.001

Model 1：Adjusted for age at recruitment and sex.

Model 2：Further adjusted for ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 5. Joint association of polygenic risk score and biological age indicators with incident cirrhosis among individuals with MASLD

Biological age indicators	Polygenic risk score	No. of incident cases/total participants	HR(95%CI)	*P* value
KDM-BA acceleration				
Younger	Low	39/9997	Reference	
Older		34/8358	1.11(0.70-1.76)	0.668
Younger	Intermediate	143/29929	1.20(0.84-1.71)	0.318
Older		129/23990	1.44(1.01-2.07)	0.047
Younger	High	94/10053	2.38(1.64-3.45)	<0.001
Older		80/7608	2.76(1.88-4.08)	<0.001
PhenoAge acceleration				
Younger	Low	42/16170	Reference	
Older		31/2185	4.14(2.59-6.64)	<0.001
Younger	Intermediate	194/47443	1.55(1.11-2.17)	0.010
Older		78/6476	3.44(2.34-5.05)	<0.001
Younger	High	118/15616	2.87(2.02-4.08)	<0.001
Older		56/2045	7.65(5.08-11.52)	<0.001
Leukocyte telomere length				
Longer	Low	26/8755	Reference	
Shorter		47/9600	1.46(0.91-2.37)	0.119
Longer	Intermediate	94/25671	1.22(0.79-1.89)	0.366
Shorter		178/28248	1.84(1.22-2.77)	0.004
Longer	High	58/8279	2.32(1.46-3.69)	<0.001
Shorter		116/9382	3.63(2.37-5.56)	<0.001

Adjusted for age at recruitment and sex, ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

Biological age acceleration >0 was defined as biological age older than chronological age; and <0 was defined as biological age younger than chronological age.

Standardized leukocyte telomere length >0 was defined as longer; and <0 was defined as shorter.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 6. Interactions between polygenic risk score and biological age indicators on the risk of incident cirrhosis among individuals with MASLD

Subgroup	Additive interaction				Multiplicative interaction	
	Intermediate genetic risk		High genetic risk			
	RERI (95%CI)	AP (95%CI)	RERI (95%CI)	AP (95%CI)	HR(95%CI)	*P*-value
KDM-BA acceleration					1.01(0.76-1.33)	0.613
older	0.14(-0.54,0.66)	0.10(-0.32, 0.47)	0.32(-0.67, 1.19)	0.11(-0.25, 0.39)		
PhenoAge acceleration					0.85(0.63-1.14)	0.282
older	-1.31(-3.53,0.49)	-1.03(-3.24, 0.12)	1.98(-0.76,5.06)	0.24(-0.11, 0.47)		
Leukocyte telomere length					1.04(0.78-1.39)	0.774
shorter	0.15(-0.70,0.69)	0.08(-0.31, 0.42)	0.86(-0.23, 1.93)	0.23(-0.06, 0.47)		

Adjusted for age, sex, ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, history of heart disease.

Biological age acceleration >0 was defined as biological age older than chronological age; and <0 was defined as biological age younger than chronological age

Leukocyte telomere length >0 was defined as longer; and <0 was defined as shorter

To estimate RERI and AP, younger KDM-BA acceleration, younger PhenoAge acceleration, longer telomere length and low genetic risk groups were the reference categories.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; KDM-BA, Klemera-Doubal method biological age; RERI, Relative Excess Risk of Interaction; AP, Attributable Proportion; HR, hazard ratio; 95%CI, 95% confidence interval

Supplementary Table 7. Biological aging indicators on cirrhosis in different subgroups among the MASLD population

Subgroup	N_{case}/N_{total}	KDM-BA acceleration		$P_{interaction}$	Leukocyte telomere length		$P_{interaction}$
		HR (95% CI)	P_{trend}		HR (95% CI)	P_{trend}	
Age				0.640			0.586
<60	215/47978	1.04(0.91-1.17)	0.591		0.85(0.75-0.96)	0.009	
≥60	304/41957	1.13(1.02-1.25)	0.018		0.83(0.74-0.92)	0.001	
Sex				0.691			0.499
Male	332/53722	1.08(0.94-1.24)	0.261		0.85(0.75-0.97)	0.017	
Female	187/36213	1.10(1.00-1.21)	0.059		0.83(0.75-0.92)	<0.001	
Ethnic				0.932			0.618
White	497/84285	1.09(1.01-1.18)	0.033		0.84(0.77-0.91)	<0.001	
Others	22/5650	1.07(0.70-1.62)	0.764		0.83(0.57-1.21)	0.325	
BMI				0.603			0.974
<25	21/1788	1.11(0.75-1.64)	0.603		0.82(0.55-1.23)	0.337	
≥25	498/88147	1.09(1.00-1.18)	0.044		0.84(0.77-0.91)	<0.001	
Smoking status				0.570			0.600
No	225/48006	1.06(0.94-1.20)	0.349		0.85(0.76-0.96)	0.011	
Yes	294/41929	1.11(1.00-1.24)	0.045		0.83(0.74-0.92)	0.001	
Alcohol status				0.603			0.202
No	29/5242	1.09(0.78-1.54)	0.610		0.98(0.7-1.37)	0.884	
Yes	490/84693	1.09(1.01-1.19)	0.033		0.83(0.76-0.9)	<0.001	
Physical activity				0.510			0.780
Low or Moderate	395/66673	1.12(1.02-1.22)	0.019		0.84(0.77-0.93)	<0.001	
High	124/23262	1.02(0.87-1.20)	0.824		0.82(0.69-0.97)	0.018	
History of hypertension				0.737			0.657
No	307/59847	1.08(0.97-1.20)	0.156		0.82(0.74-0.91)	<0.001	
Yes	212/30088	1.11(0.98-1.26)	0.095		0.86(0.76-0.98)	0.021	
History of diabetes				0.191			0.487
No	383/80771	1.06(0.96-1.16)	0.262		0.82(0.75-0.9)	<0.001	
Yes	136/9164	1.20(1.03-1.40)	0.018		0.89(0.76-1.04)	0.136	
History of heart				0.611			0.742
No	433/82239	1.09(1.00-1.19)	0.064		0.85(0.78-0.92)	<0.001	
Yes	86/7696	1.13(0.93-1.37)	0.205		0.79(0.64-0.97)	0.024	

Adjusted for age at recruitment and sex, ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; KDM-BA, Klemera-Doubal method biological age; BMI,body mass index; HR: hazard ratio; 95%CI: 95% confidence interval.

Supplementary Table 8. Benefit of the relative risk reduction of incident cirrhosis in the MASLD population with KDM-BA acceleration across genetic risk groups

	Older-P1/P2	Younger-P1/P2	Older-P3	Younger-P3
Person years	388135	483560	90767	121225
Number of cases	163	182	80	94
Adjusted HR(95%CI)	Ref	0.82 (0.66, 1.03)	Ref	0.86 (0.63, 1.17)
10-year absolute risk (per 1000 person years)	4.03 (3.37, 4.68)	3.61 (3.04, 4.17)	8.60 (6.60, 10.60)	7.58 (5.93, 9.22)
10-year absolute risk Reduction (per 1000 person years)	Ref	0.42 (-0.43,1.21)	Ref	1.02 (-1.20, 3.33)

KDM-BA acceleration >0 was defined as biological age older than chronological age; and <0 was defined as biological age younger than chronological age.

Genetic risk categories defined according to a polygenic risk score as P1 (quintile 1), P2 (quintiles 2 to 4), and P3 (quintile 5).

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; Ref, reference; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 9. Benefit of the relative risk reduction of incident cirrhosis in the MASLD population with leukocyte telomere length across genetic risk groups

	Shorter-P1/P2	Longer-P1/P2	Shorter-P3	Longer-P3
Person years	453815	417920	111879	3100113
Number of cases	225	120	116	58
Adjusted HR(95%CI)	Ref	0.67 (0.53, 0.84)	Ref	0.63 (0.46, 0.87)
10-year absolute risk (per 1000 person years)	4.75 (4.08, 5.43)	2.75 (2.23, 3.27)	10.13 (8.13, 12.14)	5.65 (4.12, 7.17)
10-year absolute risk Reduction (per 1000 person years)	Ref	2.00 (1.22,2.77)	Ref	4.48 (2.04, 6.76)

Standardized leukocyte telomere length >0 was defined as longer; and <0 was defined as shorter

Genetic risk categories defined according to a polygenic risk score as P1 (quintile 1), P2 (quintiles 2 to 4), and P3 (quintile 5).

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; Ref, reference; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 10. Biological age indicators and risk of cirrhosis in MASLD participants with < 1 years of follow-up

Exposures	No. of incident cases/total participants	Model 1		Model 2	
		HR(95%CI)	*P* value	HR(95%CI)	*P* value
KDM-BA acceleration[a]	497/89913	1.14(1.04-1.25)	0.003	1.10(1.01-1.20)	0.031
KDM-BA acceleration[b]					
Q1	130/22483	Reference		Reference	
Q2	117/22481	0.99(0.77-1.27)	0.948	1.01(0.78-1.30)	0.951
Q3	112/22477	1.00(0.78-1.29)	0.990	1.00(0.77-1.29)	0.971
Q4	138/22472	1.30(1.01-1.66)	0.040	1.20(0.93-1.54)	0.152
PhenoAge acceleration[a]	497/89913	1.48(1.41-1.55)	<0.001	1.38(1.30-1.46)	<0.001
PhenoAge acceleration[b]					
Q1	59/22483	Reference		Reference	
Q2	95/22481	1.60(1.15-2.21)	0.005	1.52(1.10-2.10)	0.012
Q3	109/22481	1.83(1.33-2.51)	<0.001	1.63(1.18-2.24)	0.003
Q4	234/22468	4.06(3.05-5.40)	<0.001	2.96(2.20-3.99)	<0.001
Leukocyte telomere length[a]	497/89913	0.83(0.76-0.91)	<0.001	0.85(0.78-0.93)	<0.001
Leukocyte telomere length[b]					
Q1	174/22474	Reference		Reference	
Q2	130/22476	0.78(0.62-0.98)	0.036	0.81(0.64-1.02)	0.070
Q3	103/22482	0.65(0.51-0.83)	<0.001	0.68(0.53-0.87)	0.002
Q4	90/22481	0.60(0.47-0.78)	<0.001	0.64(0.49-0.83)	<0.001

Model 1：Adjusted for age at recruitment and sex.

Model 2：Further adjusted for ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

[a]Variables were continuous.

[b]Variables were classified by quartile. quartile1, Q1; quartile2, Q2; quartile3, Q3; quartile4, Q4.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 11. Biological age indicators and risk of cirrhosis in MASLD participants with < 2 years of follow-up

Exposures	No. of incident cases/total participants	Model 1		Model 2	
		HR(95%CI)	*P* value	HR(95%CI)	*P* value
KDM-BA acceleration[a]	478/89894	1.14(1.04-1.25)	0.004	1.10(1.01-1.21)	0.030
KDM-BA acceleration[b]					
Q1	122/22475	Reference		Reference	
Q2	114/22478	1.03(0.80-1.33)	0.819	1.05(0.81-1.35)	0.720
Q3	110/22475	1.05(0.81-1.36)	0.732	1.04(0.80-1.35)	0.758
Q4	132/22466	1.32(1.02-1.70)	0.034	1.22(0.95-1.58)	0.124
PhenoAge acceleration[a]	478/89894	1.47(1.40-1.55)	<0.001	1.37(1.29-1.46)	<0.001
PhenoAge acceleration[b]					
Q1	58/22482	Reference		Reference	
Q2	89/22475	1.53(1.10-2.12)	0.013	1.45(1.04-2.01)	0.029
Q3	106/22478	1.81(1.31-2.49)	<0.001	1.61(1.17-2.22)	0.004
Q4	225/22459	3.98(2.98-5.32)	<0.001	2.88(2.13-3.90)	<0.001
Leukocyte telomere length[a]	478/89894	0.84(0.77-0.92)	<0.001	0.86(0.79-0.94)	0.001
Leukocyte telomere length[b]					
Q1	164/22464	Reference		Reference	
Q2	127/22473	0.81(0.64-1.03)	0.081	0.84(0.67-1.06)	0.143
Q3	100/22479	0.67(0.52-0.86)	0.002	0.70(0.54-0.90)	0.005
Q4	87/22478	0.62(0.48-0.81)	<0.001	0.66(0.51-0.86)	0.002

Model 1：Adjusted for age at recruitment and sex.

Model 2：Further adjusted for ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

[a]Variables were continuous.

[b]Variables were classified by quartile. quartile1, Q1; quartile2, Q2; quartile3, Q3; quartile4, Q4.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 12. Biological age indicators and risk of cirrhosis in MASLD participants with < 3 years of follow-up

Exposures	No. of incident cases/total participants	Model 1		Model 2	
		HR(95%CI)	*P* value	HR(95%CI)	*P* value
KDM-BA acceleration[a]	448/89864	1.15(1.05-1.26)	0.003	1.11(1.01-1.22)	0.026
KDM-BA acceleration[b]					
Q1	114/22467	Reference		Reference	
Q2	108/22472	1.04(0.80-1.36)	0.758	1.06(0.81-1.38)	0.683
Q3	102/22467	1.03(0.79-1.35)	0.820	1.02(0.78-1.34)	0.872
Q4	124/22458	1.31(1.01-1.71)	0.044	1.21(0.93-1.58)	0.156
PhenoAge acceleration[a]	448/89864	1.45(1.38-1.53)	<0.001	1.34(1.26-1.44)	<0.001
PhenoAge acceleration[b]					
Q1	58/22482	Reference		Reference	
Q2	85/22471	1.46(1.05-2.04)	0.026	1.38(0.99-1.93)	0.058
Q3	102/22474	1.75(1.27-2.42)	<0.001	1.55(1.12-2.15)	0.008
Q4	203/22437	3.61(2.70-4.84)	<0.001	2.61(1.92-3.54)	<0.001
Leukocyte telomere length[a]	448/89864	0.84(0.76-0.92)	<0.001	0.86(0.78-0.94)	0.001
Leukocyte telomere length[b]					
Q1	153/22453	Reference		Reference	
Q2	122/22468	0.84(0.66-1.06)	0.141	0.86(0.68-1.10)	0.227
Q3	91/22470	0.65(0.50-0.85)	0.001	0.68(0.52-0.88)	0.004
Q4	82/22473	0.62(0.48-0.82)	<0.001	0.66(0.50-0.87)	0.003

Model 1：Adjusted for age at recruitment and sex.

Model 2：Further adjusted for ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

[a]Variables were continuous.

[b]Variables were classified by quartile. quartile1, Q1; quartile2, Q2; quartile3, Q3; quartile4, Q4.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 13. Biological age indicators and risk of cirrhosis in individuals with MASLD after filling in missing values

Exposures	No. of incident cases/total participants	Model 1		Model 2	
		HR(95%CI)	*P* value	HR(95%CI)	*P* value
KDM-BA acceleration[a]	645/103581	1.14(1.06-1.23)	<0.001	1.10(1.02-1.19)	0.012
KDM-BA acceleration[b]					
Q1	165/25896	Reference		Reference	
Q2	157/25895	1.05(0.84-1.30)	0.680	1.07(0.86-1.34)	0.521
Q3	148/25895	1.04(0.83-1.31)	0.704	1.04(0.83-1.31)	0.704
Q4	175/25895	1.31(1.05-1.63)	0.018	1.22(0.98-1.53)	0.077
PhenoAge acceleration[a]	645/103581	1.51(1.45-1.57)	<0.001	1.40(1.33-1.47)	<0.001
PhenoAge acceleration[b]					
Q1	68/25896	Reference		Reference	
Q2	129/25895	1.88(1.40-2.52)	<0.001	1.81(1.35-2.43)	<0.001
Q3	135/25895	1.96(1.47-2.63)	<0.001	1.78(1.33-2.38)	<0.001
Q4	313/25895	4.74(3.64-6.16)	<0.001	3.46(2.64-4.54)	<0.001
Leukocyte telomere length[a]	645/103581	0.83(0.77-0.89)	<0.001	0.85(0.78-0.91)	<0.001
Leukocyte telomere length[b]					
Q1	225/25896	Reference		Reference	
Q2	171/25895	0.79(0.65-0.97)	0.024	0.82(0.67-1.00)	0.051
Q3	132/25895	0.64(0.51-0.79)	<0.001	0.67(0.54-0.83)	<0.001
Q4	117/25895	0.60(0.48-0.75)	<0.001	0.63(0.50-0.80)	<0.001

Model 1：Adjusted for age at recruitment and sex.

Model 2：Further adjusted for ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

[a]Variables were continuous.

[b]Variables were classified by quartile. quartile1, Q1; quartile2, Q2; quartile3, Q3; quartile4, Q4.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

Supplementary Table 14. Biological age indicators and risk of cirrhosis in individuals with MASLD: analysis with further adjustment for C-reactive protein and self-reported overall health status

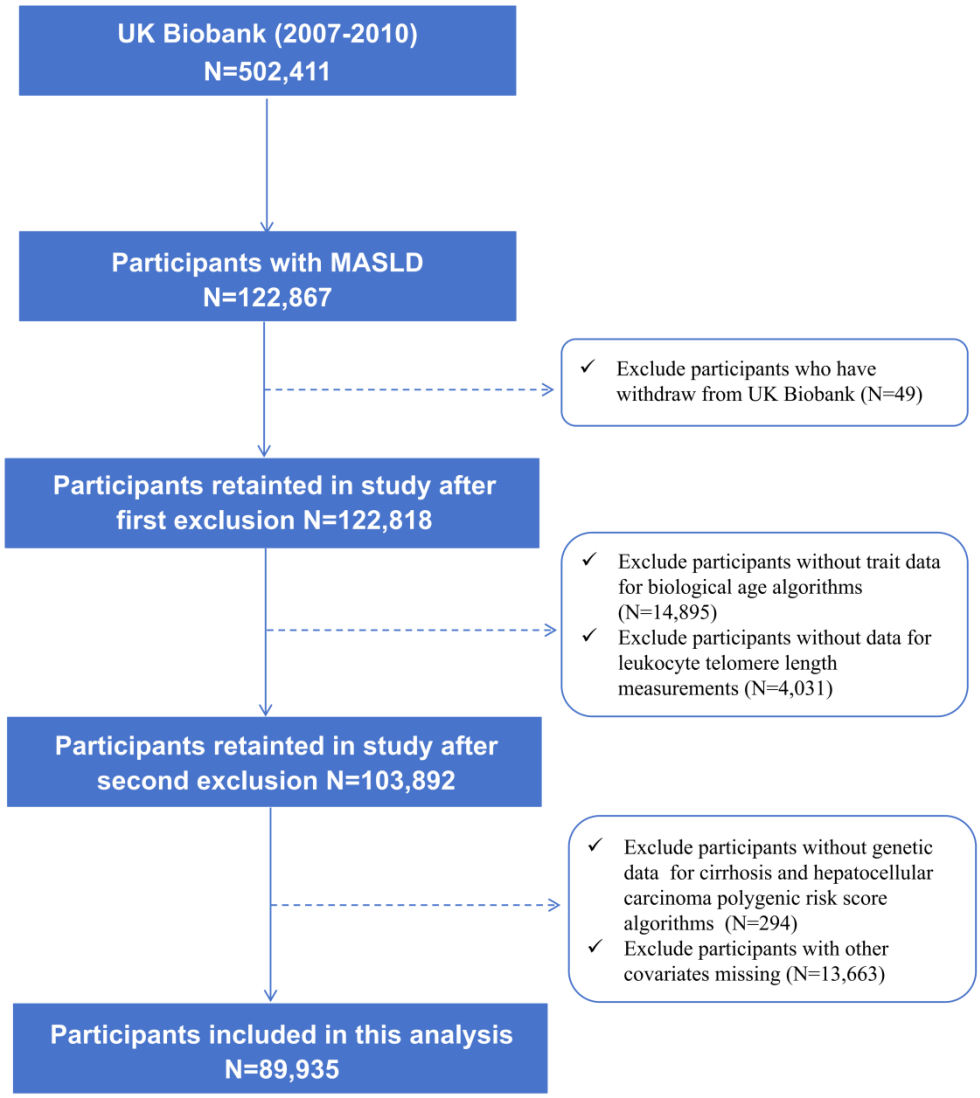
Exposures	No. of incident cases/total participants	HR(95%CI)	*P* value
KDM-BA acceleration[a]	519/89935	1.10(1.01-1.19)	0.034
KDM-BA acceleration[b]			
Q1	131/22484	Reference	
Q2	120/22484	1.05(0.84-1.30)	0.680
Q3	118/22483	1.04(0.83-1.31)	0.704
Q4	150/22484	1.31(1.05-1.63)	0.018
PhenoAge acceleration[a]	519/89935	1.35(1.27-1.43)	<0.001
PhenoAge acceleration[b]			
Q1	60/22484	Reference	
Q2	98/22484	1.51(1.10-2.09)	0.012
Q3	111/22483	1.57(1.14-2.15)	0.005
Q4	250/22484	2.80(2.07-3.78)	<0.001
Leukocyte telomere length[a]	519/89935	0.84(0.77-0.91)	<0.001
Leukocyte telomere length[b]			
Q1	184/22484	Reference	
Q2	138/22484	0.81(0.65-1.02)	0.069
Q3	104/22483	0.65(0.51-0.82)	<0.001
Q4	93/22484	0.62(0.48-0.80)	<0.001

Adjusted for age at recruitment, sex, ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, C-reactive protein, self-reported overall health status, history of hypertension, history of diabetes, and history of heart disease.

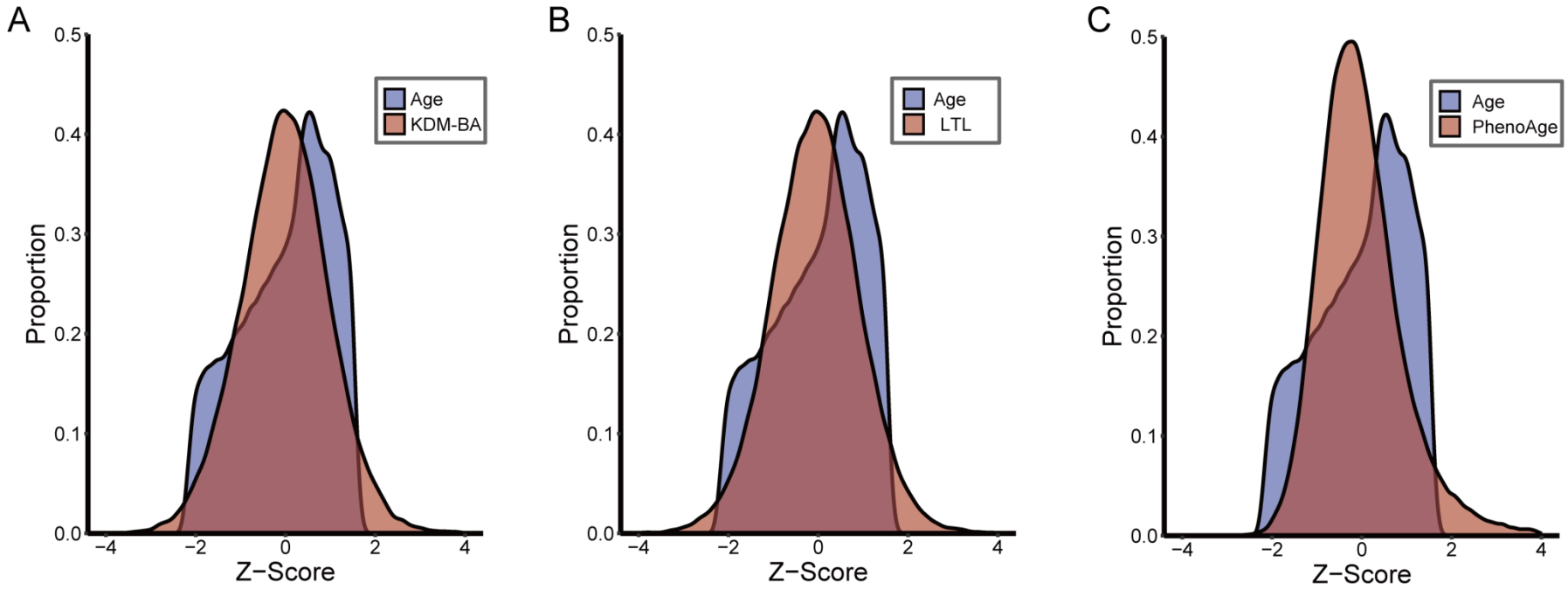
[a] Variables were continuous.

[b] Variables were classified by quartile. quartile1, Q1; quartile2, Q2; quartile3, Q3; quartile4, Q4.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; No., number; KDM-BA, Klemera-Doubal method biological age; HR, hazard ratio; 95% CI, 95% confidence interval.

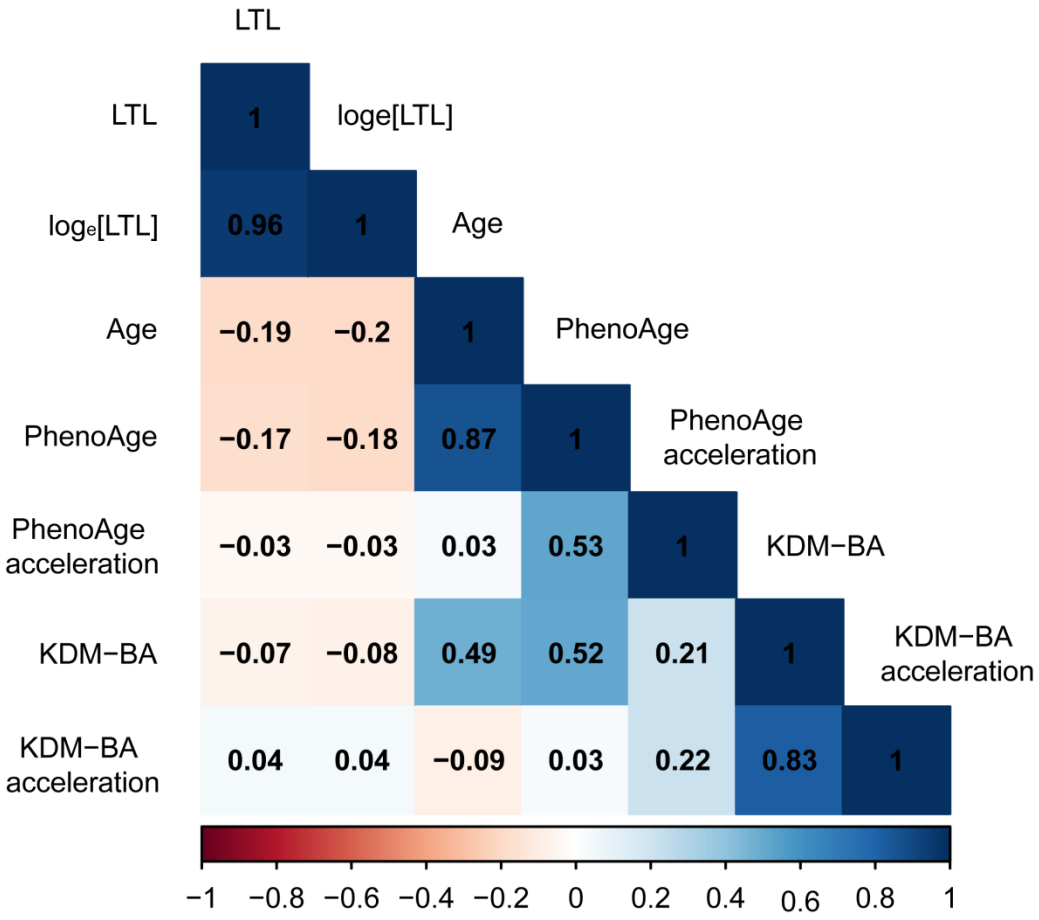


Supplementary Figure 1. The inclusion and exclusion process of participants in this study.



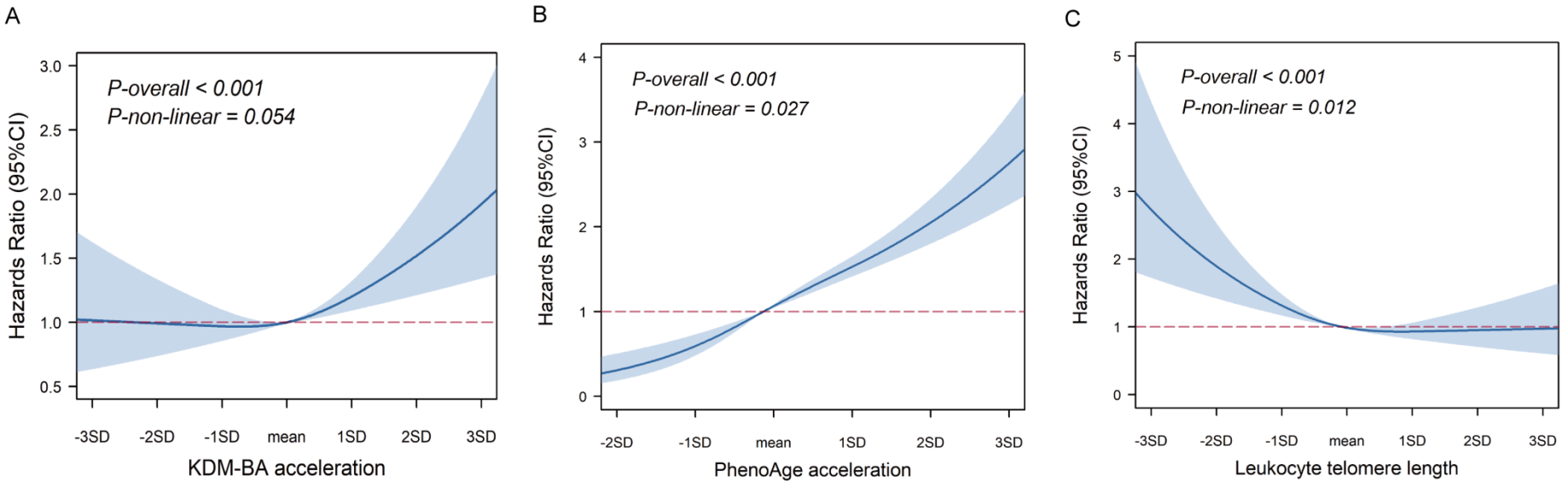
Supplementary Figure 2. The distributions of biological age and chronological age for all included participants. (A) The distributions of KDM-BA acceleration and chronological age for all included participants. (B) The distributions of LTL and chronological age for all included participants. (C) The distributions of PhenoAge acceleration and chronological age for all included participants.

Abbreviations: KDM-BA, Klemera-Doubal method biological age; LTL, leukocyte telomere length.



Supplementary Figure 3. Correlation matrix of chronological age, biological ages, and age accelerations indicators (Pearson correlation).

Abbreviations: KDM-BA, Klemera-Doubal method biological age; LTL, leukocyte telomere length.



Supplementary Figure 4. Non-linear relationships between biological age indicators and cirrhosis risk among individuals with MASLD. Estimates were adjusted for age, sex, ethnicity, Townsend deprivation index, body mass index, alcohol status, smoking status, physical activity, history of hypertension, history of diabetes, and history of heart disease.

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; 95% CI, 95% confidence interval; KDM-BA, Klemera-Doubal method biological age