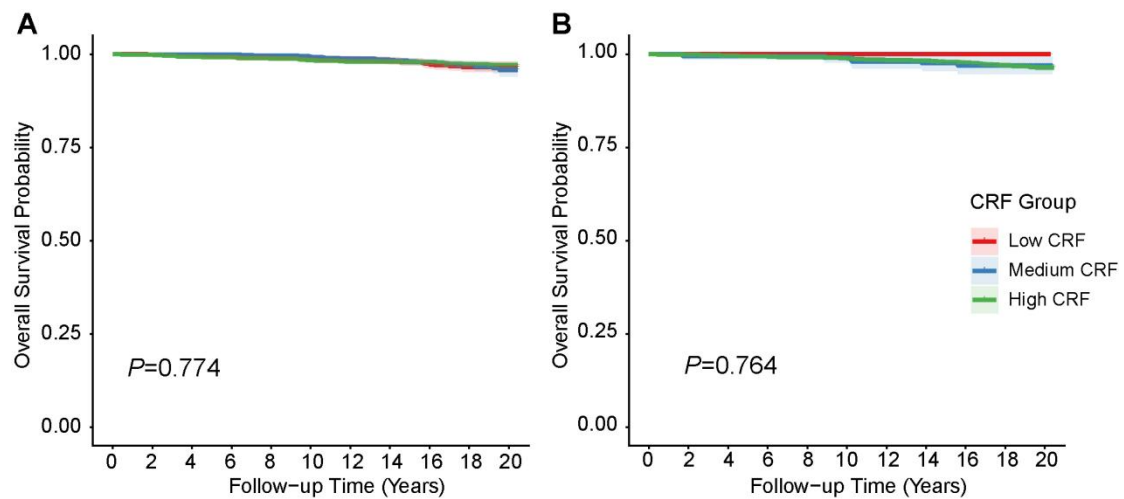
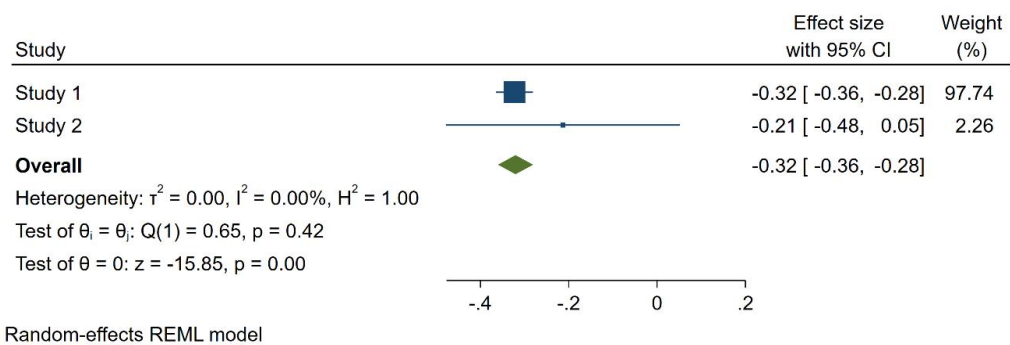
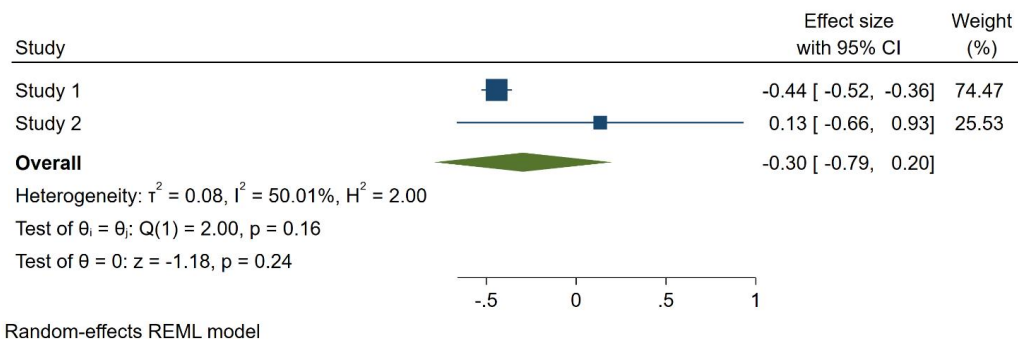




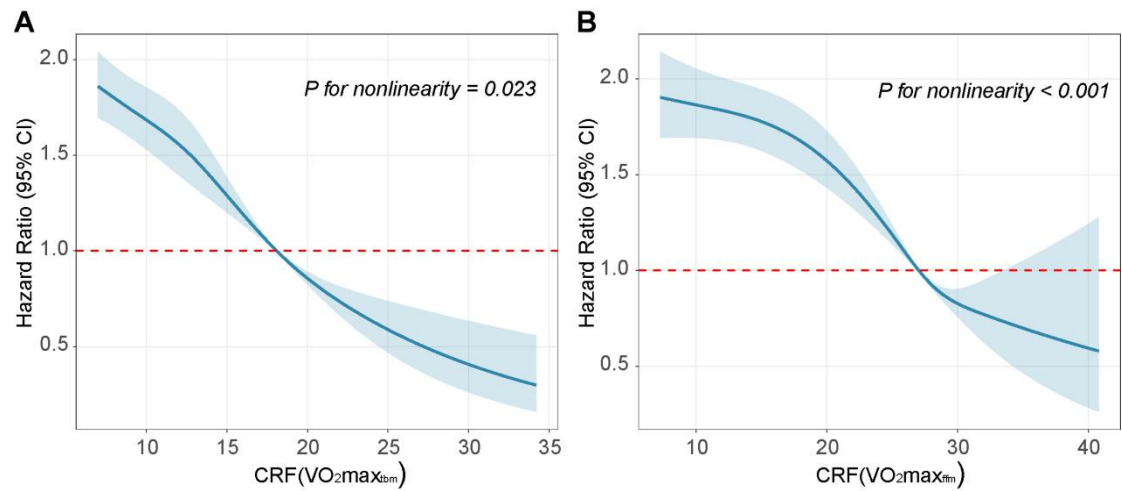
Supplementary Figure S1. Kaplan-Meier survival curves of the association between CRF and all-cause mortality in the NHANES cohort based on (A) $VO_{2max_{tbm}}$ and (B) $VO_{2max_{ffm}}$.



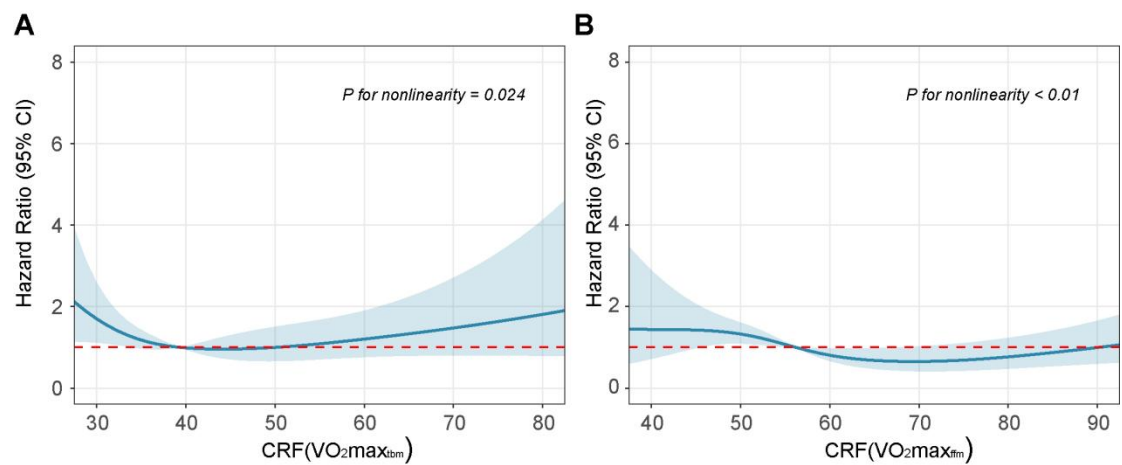
Supplementary Figure S2. Meta-analysis forest plot of association between CRF ($VO_{2max_{tbm}}$) and all-cause mortality. Study1: all-cause mortality from the UKB database; Study2: all-cause mortality outcome from the NHANES database. Model was adjusted for age, sex.



Supplementary Figure S3. Meta-analysis forest plot of association between CRF ($VO_{2max_{ffm}}$) and all-cause mortality. Study1: all-cause mortality from the UKB database; Study2: all-cause mortality outcome from the NHANES database. Model was adjusted for age, sex.



Supplementary Figure S4. Restricted cubic spline curves of the association between CRF and all-cause mortality in the UKB cohort based on (A) $\text{VO}_{2\text{max}_{\text{tbm}}}$ and (B) $\text{VO}_{2\text{max}_{\text{ffm}}}$.



Supplementary Figure S5. Restricted cubic spline curves of the association between CRF and all-cause mortality in the NHANES cohort based on (A) $\text{VO}_{2\text{max}_{\text{tbm}}}$ and (B) $\text{VO}_{2\text{max}_{\text{ffm}}}$.

Supplementary Table S1. Baseline characteristics of participants according to CRF ($\text{VO}_{2\text{max}_{\text{tbn}}}$) estimates from exercise testing. (UKB and NHANES cohort)

Variables	Lower fitness	Mid fitness	Higher fitness	<i>P</i>
UKB				
N	7941	429	63412	
Age(y) (mean $\pm$ SD)	58.97 $\pm$ 7.59	55.21 $\pm$ 7.84	56.49 $\pm$ 8.13	< 0.001
Gender, n (%)				< 0.001
Female	4941(62.20)	66(15.40)	34654(54.60)	
Male	3000(37.80)	363(84.60)	28758(45.40)	
Weight (kg)	79.00(68.10,91.40)	103.90(92.85,111.70)	75.90(66.00,86.90)	< 0.001
Fat-free mass (kg)	49.10(43.10,60.60)	68.70(62.60,74.40)	50.20(43.30,62.30)	< 0.001
BMI ($\text{kg} \cdot \text{m}^{-2}$)	28.31(25.21,32.35)	32.97(29.22,36.74)	26.48(23.95,29.46)	< 0.001
$\text{VO}_{2\text{max}_{\text{tbn}}}(\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1})$	7.00(7.00,7.00)	11.19(10.71,11.66)	18.66(16.39,20.83)	< 0.001
$\text{VO}_{2\text{max}_{\text{ffm}}}(\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1})$	10.77(9.77,12.01)	16.44(15.82,17.34)	27.54(25.21,29.50)	< 0.001
TDI	16.87(9.72,29.29)	17.95(10.12,31.96)	13.42(7.89,22.91)	< 0.001
Smoking, n (%)				< 0.001
Never	4155(52.30)	199(46.40)	35824(56.50)	
Previous	2758(34.70)	172(40.10)	21838(34.40)	
Current	1028(13.00)	58(13.50)	5750(9.10)	
Alcohol consumption, n (%)				< 0.001
Never or previous	2488(31.30)	114(26.60)	12248(19.30)	
At most 2 per week	2823(35.50)	160(37.30)	23007(36.30)	
3 or more per week	2630(33.10)	155(36.10)	28157(44.40)	
Education, n (%)				< 0.001
Lower level	5456(68.70)	314(73.20)	37005(58.40)	
Higher level	2485(31.30)	115(26.80)	26407(41.60)	
Race, n (%)				< 0.001
Asian or Asian British	356(4.50)	13(3.00)	3342(5.30)	

Black or Black British	100(1.30)	7(1.60)	562(0.90)	
White	6830(86.00)	362(84.40)	55204(87.10)	
Mixed	470(5.90)	38(8.90)	3145(5.00)	
Other	185(2.30)	9(2.10)	1159(1.80)	
Hypertension, n (%)				< 0.001
Not hypertensive	3116(39.20)	166(38.70)	32370(51.00)	
Hypertensive	4825(60.80)	263(61.30)	31042(49.00)	
Diabetes, n (%)				< 0.001
Not diabetic	7132(89.80)	368(85.80)	60427(95.30)	
Diabetic	809(10.20)	61(14.20)	2985(4.70)	
NHANES				
N	763	1210	1418	
Age(years) (mean $\pm$ SD)	26.15 $\pm$ 9.17	29.02 $\pm$ 9.70	31.74 $\pm$ 9.64	< 0.001
Gender, n (%)				< 0.001
Female	411(53.90)	542(44.80)	640(45.10)	
Male	352(46.10)	668(55.20)	778(54.90)	
Weight (kg)	78.20(65.00,94.10)	75.00(62.68,87.33)	73.15(63.08,85.80)	< 0.001
Fat-free mass (kg)	51.30(41.50,62.20)	52.60(42.30,63.50)	53.00(42.90,63.62)	0.126
BMI ($\text{kg} \cdot \text{m}^{-2}$)	27.66(23.21,32.69)	25.49(22.46,29.35)	25.13(22.22,29.19)	< 0.001
$\text{VO}_{2\text{max}}_{\text{tbm}}(\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1})$	31.52(27.87,34.54)	37.60(33.50,41.53)	46.10(41.45,52.40)	< 0.001
$\text{VO}_{2\text{max}}_{\text{ffm}}(\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1})$	47.69(42.94,52.14)	53.75(49.28,58.64)	64.44(58.37,72.99)	< 0.001
PIR	2.00(0.95,3.59)	2.33(1.13,4.09)	2.49(1.19,4.52)	< 0.001
Smoking, n (%)				< 0.001
Never	661(96.60)	987(81.60)	1080(76.20)	
Previous	25(3.30)	54(4.50)	88(6.20)	
Current	77(10.10)	169(14.00)	250(17.60)	
Alcohol consumption, n (%)				< 0.001
Yes	288(37.70)	649(53.60)	932(65.70)	
No	123(16.10)	196(16.20)	256(18.10)	

Other	352(46.20)	365(30.20)	230(16.20)	
Education, n (%)				< 0.001
Lower level	353(46.30)	388(32.10)	292(20.60)	
Medium level	180(23.60)	337(27.90)	447(31.50)	
Higher level	230(30.10)	485(40.10)	679(47.90)	
Race, n (%)				< 0.001
White	523(69.50)	897(74.10)	1126(79.40)	
Black	206(27.00)	261(21.60)	253(17.80)	
Other	34(4.50)	52(4.30)	39(2.80)	
Hypertension, n (%)				0.532
Not hypertensive	726(95.20)	1141(94.30)	1350(95.20)	
Hypertensive	37(4.80)	69(5.70)	68(4.80)	
Diabetes, n (%)				0.364
Not diabetic	748(98.00)	1195(98.80)	1387(97.80)	
Diabetic	11(1.40)	9(0.70)	23(1.60)	
Other	4(0.50)	6(0.50)	8(0.60)	

Note. The *P* value was derived from the Kruskal–Wallis test and the chi-square test. CRF, cardiorespiratory fitness; PIR, poverty-to-income ratio; BMI, body mass index; SD, standard deviation.

* *P* < 0.05, the result is statistically significant.

Supplementary Table S2. Baseline characteristics of participants according to CRF (VO₂max_{ffm}) estimates from exercise testing. (UKB and NHANES cohort)

Variable	Cardiorespiratory fitness			P
	Lower fitness	Mid fitness	Higher fitness	
UKB				
N	1163	2214	68405	
Age(y) (mean ± SD)	53.03 ± 7.30	61.29 ± 6.51	56.67 ± 8.11	< 0.001
Gender, n (%)				< 0.001
Female	3(0.30)	575(26.00)	39083(57.10)	
Male	1160(99.70)	1639(74.00)	29322(42.90)	
Weight (kg)	81.60(72.60,90.40)	83.40(65.20,95.20)	76.10(66.20,87.10)	< 0.001
Fat-free mass (kg)	62.70(56.80,68.00)	59.80(47.50,66.90)	49.50(43.20,61.80)	< 0.001
BMI (kg · m ⁻²)	26.34(24.19,28.97)	27.80(23.87,31.22)	26.66(24.08,29.77)	< 0.001
VO ₂ max _{t_{bm}} (ml · min ⁻¹ · kg ⁻¹)	7.00(7.00,7.00)	7.00(7.00,7.00)	18.33(15.72,20.63)	< 0.001
VO ₂ max _{ffm} (ml · min ⁻¹ · kg ⁻¹)	9.13(8.79,9.55)	9.84(9.48,10.19)	27.24(24.18,29.32)	< 0.001
TDI	18.27(9.80,31.97)	15.96(9.34,28.85)	13.69(8.03,23.37)	< 0.001
Smoking, n (%)				< 0.001
Never	574(49.30)	963(43.50)	38641(56.50)	
Previous	322(27.70)	939(42.40)	23507(34.40)	
Current	267(23.00)	312(14.10)	6257(9.10)	
Alcohol consumption, n (%)				0.001
Never or previous	258(22.20)	536(24.20)	14056(20.50)	
At most 2 per week	410(35.30)	756(34.10)	24824(36.30)	
3 or more per week	495(42.50)	922(41.60)	29525(43.20)	
Education, n (%)				< 0.001
Lower level	762(65.50)	1491(67.30)	40522(59.20)	
Higher level	401(34.50)	723(32.70)	27883(40.80)	
Race, n (%)				< 0.001

Asian or Asian British	68(5.80)	92(4.20)	3551(5.20)	
Black or Black British	20(1.70)	20(0.90)	629(0.90)	
White	948(81.60)	1942(87.70)	59506(87.00)	
Mixed	100(8.60)	104(4.70)	3449(5.00)	
Other	27(2.30)	56(2.50)	1270(1.90)	
Hypertension, n (%)				< 0.001
Not hypertensive	514(44.20)	819(37.00)	34319(50.20)	
Hypertensive	649(55.80)	1395(63.00)	34086(49.80)	
Diabetes, n (%)				< 0.001
Not diabetic	1085(93.30)	1923(86.90)	64919(94.90)	
Diabetic	78(6.70)	291(13.10)	3486(5.10)	
NHANES				
N	19	206	3166	
Age (years), mean $\pm$ SD	26.15 $\pm$ 9.17	29.02 $\pm$ 9.70	31.74 $\pm$ 9.64	< 0.001
Gender, n (%)				< 0.001
Female	1(5.30)	26(12.60)	1566(49.50)	
Male	18(94.70)	180(87.40)	1600(50.50)	
Weight (kg)	78.20(65.00,94.10)	75.00(62.68,87.33)	73.15(63.08,85.80)	< 0.001
Fat-free mass (kg)	51.30(41.50,62.20)	52.60(42.30,63.50)	53.00(42.90,63.62)	0.126
BMI ($\text{kg} \cdot \text{m}^{-2}$)	27.66(23.21,32.69)	25.49(22.46,29.35)	25.13(22.22,29.19)	< 0.001
$\text{VO}_2\text{max}_{\text{tbn}}$ ($\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$)	31.52(27.87,34.54)	37.60(33.50,41.53)	46.10(41.45,52.40)	< 0.001
$\text{VO}_2\text{max}_{\text{ffm}}$ ($\text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$)	47.69(42.94,52.14)	53.75(49.28,58.64)	64.44(58.37,72.99)	< 0.001
PIR	2.00(0.95,3.59)	2.33(1.13,4.09)	2.49(1.19,4.52)	< 0.001
Smoking, n (%)				0.003
Never	18(94.70)	185(89.80)	2525(79.80)	
Previous	1(5.30)	4(1.90)	162(5.10)	
Current	0(0.00)	17(8.30)	479(15.10)	
Alcohol consumption, n (%)				< 0.001

Yes	1(5.30)	54(26.20)	1814(57.30)	
No	1(5.30)	13(6.30)	561(17.70)	
Other	17(89.40)	139(67.50)	791(25.00)	
Education, n (%)				< 0.001
Lower level	16(84.20)	139(67.50)	878(27.70)	
Medium level	2(10.50)	34(16.50)	928(29.30)	
Higher level	1(5.30)	33(16.00)	1360(43.00)	
Race, n (%)				0.057
White	11(57.90)	140(68.00)	2395(75.60)	
Black	7(36.80)	56(27.20)	657(20.80)	
Other	1(5.30)	10(4.90)	114(3.60)	
Hypertension, n (%)				0.294
Not hypertensive	17(89.50)	199(96.60)	3001(94.80)	
Hypertensive	2(10.50)	7(3.40)	165(5.20)	
Diabetes, n (%)				0.410
Not diabetic	19(100.00)	204(99.00)	3107(98.10)	
Diabetic	0(0.00)	0(0.00)	43(1.40)	
Other	0(0.00)	2(1.00)	16(0.50)	

Note. The *P*-value is derived from the Kruskal-Wallis test and the chi-square test. CRF, cardiorespiratory fitness; TDI, Townsend deprivation index; PIR, poverty to income ratio; BMI, body mass index; SD, standard deviation.

* *P* < 0.05, the result is statistically significant.

Supplementary Table S3. Overall and subgroup associations of CRF (VO₂max_{ffm}) with all-cause mortality in the UKB and NHANES cohorts

	<i>HR (95%CI)</i>		
	Model 1	Model 2 ^{a,b}	Model 3
UKB			
All-cause mortality	0.64(0.59,0.69)	0.70(0.64,0.76)	0.69(0.64,0.75)
Subgroup			
Age			
≤ 56 (n = 31825)	0.60(0.51,0.70)	0.69(0.59,0.80)	0.68(0.58,0.80)
56-65 (n = 25704)	0.64(0.56,0.73)	0.70(0.61,0.80)	0.70(0.61,0.80)
≥ 65 (n = 14391)	0.67(0.57,0.77)	0.71(0.61,0.83)	0.71(0.61,0.82)
Sex			
Male (n = 32246)	0.64(0.59,0.70)	0.70(0.64,0.77)	0.70(0.64,0.76)
Female (n = 39674)	0.58(0.42,0.79)	0.60(0.44,0.82)	0.59(0.43,0.81)
CVD			
Yes	0.63 (0.49,0.82)	0.68 (0.52,0.89)	0.68 (0.52,0.88)
No	0.64 (0.59,0.70)	0.70 (0.64,0.76)	0.69 (0.63,0.75)
NHANES			
All-cause mortality	1.14(0.51,2.53)	1.07(0.48,2.37)	1.11(0.50,2.46)
Subgroup			
Age			
≤ 29 (n = 1818/42)	1.66(0.62,4.47)	1.56(0.58,4.20)	1.55(0.57,4.17)
30-39 (n = 876/18)	-	-	-
40-49 (n = 697/36)	0.30(0.07,1.29)	0.24(0.05,1.05)	0.24(0.05,1.09)
Sex			
Male (n = 1798/68)	1.18(0.53,2.63)	1.09(0.49,2.41)	1.16(0.52,2.59)
Female (n = 1593/28)	-	-	-

Note. Model 1 adjusted for age and sex. Model 2^a indicates that Model2 of UKB was adjusted for age, sex, smoking status, history of diabetes, history of hypertension, and TDI. Model 2^b indicates that Modle2 of NHANES was adjusted for age, sex, smoking status, history of diabetes, history of hypertension, and PIR. Model 3 was further adjusted for obesity based on Model 2. *CI*,

confidence interval; *HR*, hazard ratio; CRF, cardiorespiratory fitness; TDI, Townsend deprivation index; PIR, poverty to income ratio.

Supplementary Table S4. Overall and subgroup associations of CRF ($VO_{2max_{tbm}}$) with all-cause mortality in the UKB cohorts after excluding participants with events during the first 2 years of follow-up

	<i>HR (95%CI)</i>		
	Model 1	Model 2	Model 3
All-cause mortality	0.73(0.70,0.76)	0.78(0.75,0.82)	0.79(0.76,0.83)
Subgroup			
Age			
≤ 56 (n = 32356)	0.63(0.57,0.70)	0.71(0.64,0.79)	0.72(0.65,0.80)
56-65 (n = 26174)	0.71(0.67,0.76)	0.76(0.71,0.82)	0.77(0.72,0.83)
≥ 65 (n = 14639)	0.79(0.74,0.84)	0.83(0.78,0.89)	0.84(0.78,0.89)
Sex			
Male (n = 32755)	0.71(0.67,0.75)	0.77(0.73,0.82)	0.78(0.74,0.83)
Female (n = 40414)	0.76(0.71,0.81)	0.80(0.75,0.85)	0.80(0.75,0.85)

Note. Model 1 adjusted for age and sex. Model 2 indicates that Model2 of UKB was adjusted for age, sex, smoking status, history of diabetes, history of hypertension, and TDI. Model 3 was further adjusted for obesity based on Model 2.

CI, confidence interval; *HR*, hazard ratio; CRF, cardiorespiratory fitness; TDI, Townsend deprivation index.

Supplementary Table S5. Total life expectancy and life expectancy with or without CVD by CRF ($VO_{2max_{tbm}}$) group, by Sex

Age group	LE without CVD, years	LE with CVD, years	Total LE, years
Female			
Overall Population			
40-49	32.40(32.09,32.71)	3.29(3.05,3.56)	35.59(35.23,35.95)

50-59	23.65(23.34,23.97)	2.89(2.63,3.15)	26.54(26.18,26.91)
60-69	15.81(15.51,16.12)	2.43(2.17,2.70)	18.25(17.88,18.61)
70-79	9.27(9.01,9.54)	1.79(1.56,2.02)	11.06(10.75,11.38)
80+	5.41(5.24,5.59)	1.16(1.01,1.33)	6.58(6.38,6.77)
Lower fitness			
40-49	28.45(1.13,55.77)	3.72(0.14,7.30)	32.17(1.27,63.07)
50-59	20.18(0.81,39.56)	3.33(0.11,6.54)	23.51(0.93,46.09)
60-69	13.11(0.65,25.57)	2.78(0.12,5.44)	15.89(0.78,31.00)
70-79	7.56(0.39,14.72)	2.08(0.10,4.05)	9.63(0.50,18.76)
80+	4.49(0.22,8.76)	1.42(0.06,2.78)	5.90(0.28,11.53)
Mid fitness			
40-49	31.05(2.09,60.00)	3.47(0.22,6.72)	34.52(2.32,66.71)
50-59	22.48(1.70,43.25)	3.13(0.22,6.04)	25.60(1.93,49.28)
60-69	14.94(1.18,28.70)	2.64(0.19,5.08)	17.58(1.38,33.78)
70-79	8.77(0.76,16.77)	1.95(0.17,3.74)	10.72(0.94,20.51)
80+	5.17(0.58,9.76)	1.29(0.14,2.44)	6.46(0.72,12.19)
Higher fitness			
40-49	33.45(33.13,33.76)	3.16(2.91,3.41)	36.61(36.26,36.95)
50-59	24.65(24.33,24.97)	2.87(2.61,3.13)	27.52(27.18,27.87)
60-69	16.70(16.39,17.02)	2.43(2.18,2.68)	19.13(18.79,19.48)
70-79	9.93(9.67,10.18)	1.78(1.57,2.00)	11.71(11.43,11.99)
80+	5.79(5.63,5.96)	1.13(0.99,1.28)	6.93(6.76,7.10)
Male			
Overall Population			
40-49	26.54(26.31,26.78)	5.02(4.73,5.32)	31.57(31.22,31.91)
50-59	18.46(18.21,18.71)	4.48(4.15,4.80)	22.94(22.56,23.32)
60-69	11.65(11.39,11.91)	3.71(3.36,4.07)	15.36(14.94,15.79)
70-79	6.51(6.27,6.75)	2.74(2.41,3.07)	9.24(8.85,9.64)
80+	3.83(3.65,4.00)	1.87(1.63,2.10)	5.70(5.42,5.97)

Lower fitness			
40-49	22.16(0.88,43.43)	5.53(0.20,10.85)	27.69(1.10,54.27)
50-59	14.79(0.66,28.91)	4.83(0.20,9.45)	19.61(0.87,38.35)
60-69	8.93(0.41,17.45)	3.93(0.17,7.70)	12.87(0.59,25.14)
70-79	4.81(0.24,9.39)	2.91(0.12,5.71)	7.73(0.37,15.09)
80+	2.83(0.15,5.52)	2.09(0.10,4.07)	4.92(0.26,9.58)
Mid fitness			
40-49	24.74(1.61,47.88)	5.35(0.33,10.38)	30.09(1.94,58.25)
50-59	16.97(1.17,32.77)	4.74(0.31,9.18)	21.71(1.48,41.94)
60-69	10.59(0.90,20.27)	3.92(0.32,7.53)	14.51(1.23,27.80)
70-79	5.89(0.49,11.29)	2.92(0.23,5.61)	8.81(0.72,16.90)
80+	3.50(0.37,6.63)	2.03(0.20,3.85)	5.52(0.58,10.47)
Higher fitness			
40-49	27.34(27.08,27.60)	5.10(4.80,5.40)	32.44(32.08,32.80)
50-59	19.24(18.98,19.51)	4.57(4.24,4.90)	23.81(23.43,24.20)
60-69	12.37(12.09,12.65)	3.83(3.48,4.17)	16.20(15.78,16.61)
70-79	7.07(6.81,7.32)	2.84(2.53,3.15)	9.91(9.55,10.26)
80+	4.20(4.02,4.38)	1.90(1.68,2.12)	6.10(5.86,6.34)

Note. Participants were divided into low, medium, and high groups according to specific tertiles of maximal oxygen consumption as an indicator of CRF using age and sex in the UK Biobanks online protocol. CVD, cardiovascular disease; CRF, cardiorespiratory fitness; LE, life expectancy.

Supplementary Table S6. CRF ($VO_{2max_{tbm}}$) groups associated with life expectancy without CVD

Age group	Lower fitness		Mid fitness ^a		Higher fitness ^a	
	(Reference) ^a					
	LE HR (95% CI)	LE HR (95% CI)	Difference HR (95% CI) ^b	LE HR (95% CI)	Difference HR (95% CI) ^b	
Female						

40-49	28.45(1.13,55.77)	31.05(2.09,60.00)	2.6(-37.24,42.44)	33.45(33.13,33.76)	5.00(-22.31,32.31)
50-59	20.18(0.81,39.56)	22.48(1.70,43.25)	2.3(-26.11,30.71)	24.65(24.33,24.97)	4.47(-14.91,23.85)
60-69	13.11(0.65,25.57)	14.94(1.18,28.70)	1.83(-16.74,20.40)	16.70(16.39,17.02)	3.59(-8.87,16.05)
70-79	7.56(0.39,14.72)	8.77(0.76,16.77)	1.21(-9.53,11.95)	9.93(9.67,10.18)	2.37(-4.79,9.53)
80+	4.49(0.22,8.76)	5.17(0.58,9.76)	0.68(-5.59,6.95)	5.79(5.63,5.96)	1.3(-2.97,5.57)
Male					
40-49	22.16(0.88,43.43)	24.74(1.61,47.88)	2.58(-28.88,34.04)	27.34(27.08,27.60)	5.18(-15.97,26.33)
50-59	14.79(0.66,28.91)	16.97(1.17,32.77)	2.18(-19.01,23.37)	19.24(18.98,19.51)	4.45(-9.68,18.58)
60-69	8.93(0.41,17.45)	10.59(0.90,20.27)	1.66(-11.24,14.56)	12.37(12.09,12.65)	3.44(-5.08,11.96)
70-79	4.81(0.24,9.39)	5.89(0.49,11.29)	1.08(-11.34,13.50)	7.07(6.81,7.32)	2.26(-2.33,6.85)
80+	2.83(0.15,5.52)	3.50(0.37,6.63)	0.67(-3.45,4.79)	4.20(4.02,4.38)	1.37(-1.32,4.06)

Note. ^a Participants were divided into low, medium, and high groups according to specific tertiles of maximal oxygen consumption as an indicator of CRF using age and sex in the UK Biobanks online protocol.

^b The 95% *CI* for the difference in LE was calculated: the difference in LE $\pm 1.96 * SE$, where the SE of the difference was calculated as the square root of the sum of the squares of the two sets of SE.

CI, confidence interval; *HR*, hazard ratio; SE, standard error; CRF, cardiorespiratory fitness; LE, life expectancy.

Supplementary Table S7 Total life expectancy and life expectancy with or without CVD by CRF ($\text{VO}_2\text{max}_{\text{ffm}}$) group, by sex

Age group	LE without CVD, years	LE with CVD, years	Total LE, years
Female			
Overall Population			
40-49	32.41(32.11,32.72)	3.18(2.93,3.44)	35.60(35.24,35.95)
50-59	23.67(23.35,23.98)	2.89(2.62,3.15)	26.55(26.18,26.92)
60-69	15.82(15.51,16.13)	2.43(2.16,2.70)	18.26(17.89,18.63)
70-79	9.28(9.01,9.55)	1.79(1.56,2.02)	11.07(10.76,11.39)
80+	5.41(5.25,5.58)	1.17(1.01,1.33)	6.58(6.38,6.78)
Lower fitness			
40-49	26.48(25.33,27.63)	3.07(2.53,3.61)	29.55(28.35,30.74)
50-59	18.40(17.58,19.21)	2.70(2.19,3.21)	21.10(20.24,21.96)
60-69	11.59(10.92,12.27)	2.21(1.77,2.66)	13.80(13.07,14.54)
70-79	6.46(5.98,6.95)	1.63(1.26,2.00)	8.09(7.52,8.66)
80+	3.80(3.49,4.10)	1.16(0.89,1.43)	4.96(4.59,5.33)
Mid fitness			
40-49	29.52(28.98,30.05)	3.17(2.82,3.52)	32.69(32.13,33.25)
50-59	21.07(20.57,21.57)	2.84(2.49,3.18)	23.91(23.37,24.45)
60-69	13.71(13.27,14.16)	2.37(2.04,2.69)	16.08(15.58,16.58)
70-79	7.87(7.54,8.21)	1.75(1.47,2.04)	9.63(9.22,10.03)
80+	4.62(4.40,4.85)	1.20(0.99,1.41)	5.82(5.55,6.09)
Higher fitness			
40-49	32.45(32.14,32.76)	3.18(2.92,3.43)	35.63(35.27,35.99)
50-59	23.69(23.37,24.00)	2.88(2.61,3.15)	26.56(26.20,26.93)
60-69	15.83(15.52,16.14)	2.43(2.16,2.69)	18.26(17.89,18.63)
70-79	9.28(9.02,9.54)	1.78(1.55,2.02)	11.06(10.75,11.38)
80+	5.41(5.24,5.58)	1.16(1.00,1.32)	6.57(6.37,6.78)

Male			
Overall Population			
40-49	26.58(26.34,26.82)	5.08(4.77,5.39)	31.66(31.29,32.02)
50-59	18.49(18.24,18.74)	4.53(4.20,4.87)	23.02(22.63,23.42)
60-69	11.67(11.41,11.94)	3.76(3.41,4.12)	15.44(15.01,15.87)
70-79	6.52(6.28,6.77)	2.78(2.45,3.11)	9.30(8.90,9.70)
80+	3.84(3.66,4.02)	1.89(1.66,2.13)	5.73(5.46,6.01)
Lower fitness			
40-49	21.04(20.15,21.94)	4.66(3.96,4.85)	25.71(24.68,26.76)
50-59	13.78(13.11,14.45)	4.00(3.36,4.65)	17.79(16.95,18.62)
60-69	8.08(7.58,8.59)	3.18(2.61,3.74)	11.26(10.55,11.97)
70-79	4.19(3.84,4.54)	2.29(1.82,2.76)	6.48(5.92,7.05)
80+	2.40(2.16,2.64)	1.67(1.31,2.03)	4.07(3.65,4.49)
Mid fitness			
40-49	23.98(23.55,24.40)	4.94(4.52,5.35)	28.91(28.39,29.43)
50-59	16.24(15.86,16.62)	4.34(3.93,4.75)	20.58(20.07,21.09)
60-69	9.92(9.59,10.25)	3.54(3.12,3.95)	13.46(12.96,13.96)
70-79	5.36(5.09,5.64)	2.60(2.23,2.97)	7.96(7.51,8.41)
80+	3.13(2.93,3.32)	1.84(1.56,2.12)	4.97(4.63,5.30)
Higher fitness			
40-49	27.00(26.76,27.25)	5.13(4.80,5.45)	32.13(31.76,32.50)
50-59	18.85(18.59,19.12)	4.59(4.24,4.93)	23.44(23.03,23.85)
60-69	11.95(11.68,12.23)	3.81(3.45,4.18)	15.77(15.33,16.21)
70-79	6.70(6.45,6.95)	2.81(2.48,3.15)	9.51(9.11,9.92)
80+	3.94(3.75,4.12)	1.90(1.66,2.14)	5.84(5.56,6.12)

Note. Participants were divided into low, medium, and high groups according to specific tertiles of maximal oxygen consumption as an indicator of CRF using age and sex in the UK Biobanks online protocol. CVD, cardiovascular disease; CRF, cardiorespiratory fitness; LE, life expectancy.

Supplementary Table S8. CRF (VO₂max_{ffm}) groups associated with life expectancy without CVD

Age group	Lower fitness		Mid fitness ^a		Higher fitness ^a	
	(Reference) ^a					
	LE	LE	Difference	LE	Difference	
	<i>HR (95% CI)</i>	<i>HR (95% CI)</i>	<i>HR (95% CI)^b</i>	<i>HR (95% CI)</i>	<i>HR (95% CI)^b</i>	
Female						
40-49	26.48(25.33,27.63)	29.52(28.98,30.05)	3.04(1.71,4.37)	32.45(32.14,32.76)	5.97(4.72,7.22)	
50-59	18.40(17.58,19.21)	21.07(20.57,21.57)	2.67(1.71,3.63)	23.69(23.37,24.00)	5.29(4.40,6.18)	
60-69	11.59(10.92,12.27)	13.71(13.27,14.16)	2.12(1.30,2.94)	15.83(15.52,16.14)	4.24(3.49,4.99)	
70-79	6.46(5.98,6.95)	7.87(7.54,8.21)	1.41(0.82,2.00)	9.28(9.02,9.54)	2.82(2.27,3.37)	
80+	3.80(3.49,4.10)	4.62(4.40,4.85)	0.82(0.44,1.20)	5.41(5.24,5.58)	1.61(1.26,1.96)	
Male						
40-49	21.04(20.15,21.94)	23.98(23.55,24.40)	2.94(1.96,3.92)	27.00(26.76,27.25)	5.96(5.04,6.88)	
50-59	13.78(13.11,14.45)	16.24(15.86,16.62)	2.46(1.69,3.23)	18.85(18.59,19.12)	5.07(4.35,5.79)	
60-69	8.08(7.58,8.59)	9.92(9.59,10.25)	1.84(1.23,2.45)	11.95(11.68,12.23)	3.87(3.29,4.45)	
70-79	4.19(3.84,4.54)	5.36(5.09,5.64)	1.17(0.73,1.61)	6.70(6.45,6.95)	2.51(2.09,2.93)	
80+	2.40(2.16,2.64)	3.13(2.93,3.32)	0.73(0.42,1.04)	3.94(3.75,4.12)	1.54(1.24,1.84)	

Note. ^a Participants were divided into low, medium, and high groups according to specific tertiles of maximal oxygen consumption as an indicator of CRF using age and sex in the UK Biobanks online protocol.

^b The 95% CI for the difference in LE was calculated: the difference in LE $\pm 1.96 \times$ SE, where the SE of the difference was calculated as the square root of the sum of the squares of the two sets of SE.

CI, confidence interval; HR, hazard ratio; SE, standard error; CRF, cardiorespiratory fitness; LE, life expectancy.

Supplementary Table S9. Results of IVW analysis for the associations of CRF with longevity

Outcome	Method	SNP (N)	OR (95% CI)	P
Longevity 90th/60th	IVW	128	1.003(0.971,1.037)	0.857
	WM	128	1.001(0.958,1.046)	0.965
	PWM	128	1.001(0.958,1.047)	0.951

Longevity 99th/60th	MR-Egger	128	0.963(0.897,1.034)	0.296
	IVW	127	0.999(0.947,1.053)	0.965
	WM	127	0.996(0.924,1.074)	0.918
	PWM	127	0.996(0.927,1.070)	0.914
	MR-Egger	127	0.864(0.773,0.967)	0.012

P-values are derived from the IVW, WM, PWM, and MR-Egger methods. Beta is the estimated effect size; IVW, inverse variance weighted; WM, weighted median method; PWM, penalized weighted median method; MR-Egger, Egger regression method; SNP, single-nucleotide polymorphism; *OR*, odds ratio; *CI*, confidence intervals; SE, standard error; CRF, cardiorespiratory fitness.

**P* < 0.05, the result is statistically significant.

Supplementary Table S10 .The results of horizontal pleiotropy and heterogeneity tests for CRF with longevity

Outcome	Pleiotropy test		Heterogeneity test	
	MR-Egger	<i>P</i> ^a	Q-statistic	<i>P</i> ^b
	Intercept			
Longevity90th/60th	0.007	0.203	179.966	0.001
Longevity99th/60th	0.024	0.005	184.132	0.001

Note. *P*^a is the value of *P* for the MR-Egger intercept.

P^b is the value of *P* for heterogeneity tests according to the inverse-variance weighted method.

**P* < 0.05, the result is statistically significant.

Supplementary Methods

Detailed calculation methods for socioeconomic indicators: The Townsend Deprivation Index (TDI) was derived from residential postcode-level census data in the UK Biobank, integrating four key indicators: employment status (unemployment), car ownership (non-car ownership), home ownership (non-home ownership), and household overcrowding. The Poverty Income Ratio (PIR) in NHANES was calculated by dividing the reported annual family income by the poverty threshold specified by the U.S. Department of Health and Human Services, adjusting for family size, composition, and age [S1].

References for Supplementary Methods:

[S1] Johnson CL, et al. National Health and Nutrition Examination Survey: Analytic guidelines, 1999–2010. *Vital Health Stat 2*. 2013;(161):1–24.