

**Additional file 1 for: “Expanded Mosaic Chromosomal Alterations, Frailty and Risks of All-Cause and Cause-Specific Mortality among Chinese and the UK Adults: Evidence from Two Prospective Cohorts”**

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**Table S1 List of 28 frailty index items included in the CKB baseline questionnaire.**

<b>Item</b>	<b>Variables</b>	<b>Coding</b>	<b>Number (%) of the highest deficit<sup>a</sup></b>
1	Hypertension	Yes = 1; No = 0	40,166 (40.07%)
2	Self-reported heart disease	Yes = 1; No = 0	3,075 (3.07%)
3	Self-reported stroke or transient ischaemic attack	Yes = 1; No = 0	1,393 (1.39%)
4	Self-reported emphysema or chronic bronchitis	Yes = 1; No = 0	3,818 (3.81%)
5	Self-reported tuberculosis	Yes = 1; No = 0	1,696 (1.69%)
6	Self-reported asthma	Yes = 1; No = 0	729 (0.73%)
7	Self-reported peptic ulcer	Yes = 1; No = 0	3,993 (3.98%)
8	Self-reported gallstone disease, with or without cholecystitis	Yes = 1; No = 0	6,178 (6.16%)
9	Self-reported rheumatoid arthritis	Yes = 1; No = 0	2,290 (2.28%)
10	Self-reported fracture	Yes = 1; No = 0	6,585 (6.57%)
11	Self-reported neurasthenia	Yes = 1; No = 0	1,162 (1.16%)
12	Diabetes	Yes = 1; No = 0	6,744 (6.73%)
13	Self-reported cancer	Yes = 1; No = 0	420 (0.42%)
14	Self-reported chronic kidney disease	Yes = 1; No = 0	1,500 (1.5%)
15	Walk difficulty or walk slow because of chest discomfort	Yes = 1; No = 0	8,004 (7.99%)
16	Insomnia/early waking/difficulty concentrating in last month	Yes = 1; No = 0	17,770 (17.73%)
17	Bowel movements each week	Lower than 3 times per week = 1; Other = 0	4,534 (4.52%)
18	Pain or discomfort lasting $\geq 3$ months in last year	Yes = 1; No = 0	1,251 (1.25%)
19	Frequent cough in last year	Yes, for $\geq 3$ months = 1; Yes, for $< 3$ months = 0.5; No = 0	4,792 (4.78%)
20	Brush teeth rarely or never, or have false teeth	Yes = 1; No = 0	10,442 (10.42%)
21	Physical activity in last year	Lowest quintile stratified by sex = 1; Other = 0	16,368 (16.33%)
22	Lost weight ( $\geq 2.5$ kg) despite not trying to intentionally lose weight in last year	Yes = 1; No = 0	10,595 (10.57%)

23	Feel sadder or more depressed than usual for $\geq 2$ weeks in last year	Yes = 1; No = 0	3,387 (3.38%)
24	General health status	Poor = 1; Fair = 0.5; Good = 0.25; Excellent = 0	11,577 (11.55%)
25	Body-mass index ( $\text{kg}/\text{m}^2$ )	$<18.5$ or $\geq 28.0 = 1$ ; $\geq 24.0$ and $<28.0 = 0.5$ ; $\geq 18.5$ and $<24.0 = 0$	16,410 (16.37%)
26	Waist circumference (cm) to hip circumference ratio	$\geq 0.95$ for male or $\geq 0.90$ for female = 1; $\geq 0.90$ and $<0.95$ for male or $\geq 0.85$ and $<0.90$ for female = 0.5; $<0.90$ for male or $<0.85$ for female = 0	30,488 (30.42%)
27	Measured heart rate, beats per min	$<60$ or $>100 = 1$ ; $\geq 60$ and $\leq 100 = 0$	8,127 (8.11%)
28	The ratio of forced expiratory volume in 1 s to the forced vital capacity measured to be $<0.7$	Yes = 1; No = 0	7,251 (7.23%)

<sup>a</sup> Proportions were calculated in the study population (n=100,237)

**Table S2 List of 49 frailty index items included in the UK Biobank baseline questionnaire.**

<b>Item</b>	<b>Variables</b>	<b>Coding</b>	<b>Number (%) of the highest deficit<sup>a</sup></b>
1	Self-reported glaucoma	Yes = 1; No = 0	6,775 (1.49%)
2	Self-reported cataracts	Yes = 1; No = 0	15,231 (3.34%)
3	Hearing difficulty	Yes = 1; No = 0	111,645 (25.47%)
4	Self-reported migraine	Yes = 1; No = 0	13,090 (2.87%)
5	Dental problems	Yes = 1; No = 0	179,713 (39.51%)
6	Self-rated health	Poor = 1; Fair = 0.5; Good = 0.25; Excellent = 0	19,415 (4.27%)
7	Fatigue: frequency of tiredness / lethargy in last two weeks	Nearly every day = 1; More than half = 0.5; Several days = 0.25; Not at all = 0	27,623 (6.24%)
8	Sleep: experience of sleeplessness/insomnia	Usually = 1; Sometimes = 0.5; Never/rarely = 0	127,474 (27.96%)
9	Depressed feelings: frequency in last two weeks	Nearly every day = 1; More than half = 0.75; Several days = 0.5; Not at all = 0	8,172 (1.87%)
10	Self-described nervous personality	Yes = 1; No = 0	103,964 (23.39%)
11	Self-reported severe anxiety/ panic attacks	Yes = 1; No = 0	6,058 (1.33%)
12	Common to feel loneliness	Yes = 1; No = 0	81,571 (18.16%)
13	Sense of misery (ever/never)	Yes = 1; No = 0	190,460 (42.46%)
14	Infirmity: long-standing illness or disability	Yes = 1; No = 0	142,592 (31.95%)
15	Falls in last year	More than one fall = 1; Only one fall = 0.5; No falls = 0	29,144 (6.40%)
16	Fractures/broken bones in last five years	Yes = 1; No = 0	42,819 (9.43%)
17	Self-reported diabetes	Yes = 1; No = 0	23,678 (5.20%)
18	Self-reported myocardial infarction	Yes = 1; No = 0	10,455 (2.29%)
19	Self-reported angina	Yes = 1; No = 0	14,560 (3.20%)
20	Self-reported stroke	Yes = 1; No = 0	7,306 (1.60%)
21	Self-reported high blood pressure	Yes = 1; No = 0	124,506 (27.32%)
22	Self-reported hypothyroidism	Yes = 1; No = 0	21,578 (4.73%)
23	Self-reported deep-vein thrombosis	Yes = 1; No = 0	9,204 (2.02%)
24	Self-reported high cholesterol	Yes = 1; No = 0	78,609 (17.35%)

25	Breathing: wheeze in last year	Yes = 1; No = 0	92,686 (20.71%)
26	Self-reported pneumonia	Yes = 1; No = 0	6,229 (1.37%)
27	Self-reported chronic bronchitis/emphysema	Yes = 1; No = 0	10,810 (2.37%)
28	Self-reported asthma	Yes = 1; No = 0	53,283 (11.69%)
29	Self-reported rheumatoid arthritis	Yes = 1; No = 0	5,019 (1.10%)
30	Self-reported osteoarthritis	Yes = 1; No = 0	36,497 (8.00%)
31	Self-reported gout	Yes = 1; No = 0	6,356 (1.39%)
32	Self-reported osteoporosis	Yes = 1; No = 0	7,165 (1.57%)
33	Self-reported hayfever, allergic rhinitis or eczema	Yes = 1; No = 0	110,902 (24.33%)
34	Self-reported psoriasis	Yes = 1; No = 0	5,042 (1.11%)
35	Self-reported any cancer diagnosis	Yes = 1; No = 0	37,361 (8.20%)
36	Multiple cancers diagnosed (number reported)	Multiple cancers = 1; No cancer or single cancer = 0	2,432 (0.53%)
37	Chest pain	Yes = 1; No = 0	72,192 (15.98%)
38	Head and/or neck pain	Yes = 1; No = 0	160,757 (35.27%)
39	Back pain	Yes = 1; No = 0	116,937 (25.66%)
40	Stomach/abdominal pain	Yes = 1; No = 0	39,072 (8.57%)
41	Hip pain	Yes = 1; No = 0	50,475 (11.07%)
42	Knee pain	Yes = 1; No = 0	97,510 (21.39%)
43	Whole-body pain	Yes = 1; No = 0	7,566 (1.66%)
44	Facial pain	Yes = 1; No = 0	8,339 (1.83%)
45	Self-reported sciatica	Yes = 1; No = 0	4,222 (0.93%)
46	Self-reported gastric reflux	Yes = 1; No = 0	18,925 (4.15%)
47	Self-reported hiatus hernia	Yes = 1; No = 0	9,983 (2.19%)
48	Self-reported gall stones	Yes = 1; No = 0	7,342 (1.61%)
49	Self-reported diverticulitis	Yes = 1; No = 0	4,796 (1.05%)

<sup>a</sup> Proportions were calculated in the study population (n=456,283)

**Table S3 The distribution of death causes among CKB (n=100,237) and UKB (n=456,283) population.**

Cause of deaths	CKB		UKB	
	N	Proportion	N	Proportion
Circulatory diseases	13,641	52.5%	8,257	20.9%
Cancers	5,484	21.1%	19,117	48.5%
Respiratory diseases	3,194	12.3%	2,814	7.1%
Other reasons	3,647	14.0%	9,230	23.4%
<b>Total</b>	<b>25,966</b>	<b>100.0%</b>	<b>39,418</b>	<b>100.0%</b>

CKB, China Kadoorie Biobank; UKB, UK Biobank

**Table S4 The number (prevalence) of carriers and expanded mCAs carriers among CKB and UKB population.**

	<b>No. of carriers (Prevalence, %)</b>	<b>No. of expanded carriers (Prevalence, %)</b>	<b>Proportions of expanded mCAs, %</b>
<b>CKB</b>			
Any mCAs	5,804 (5.79)	2,152 (2.15)	37.08
Autosomal mCAs	2,623 (2.62)	1,370 (1.37)	52.23
LOY	2,454 (5.73)	826 (1.93)	33.66
LOX	849 (1.48)	24 (0.04)	2.83
<b>UKB</b>			
Any mCAs	68,373 (14.98)	15,443 (3.38)	22.59
Autosomal mCAs	16,178 (3.55)	3,325 (0.73)	20.51
LOY	42,432 (20.29)	11,849 (5.67)	27.92
LOX	12,808 (5.18)	462 (0.19)	3.60

mCAs, mosaic chromosomal alterations; CKB, China Kadoorie Biobank; UKB, UK Biobank; LOY, loss of Y chromosomes; LOX, loss of X chromosomes

**Table S5 Associations of expanded mCAs with frailty status among CKB and UKB population.**

	<b>CKB</b>	<b>UKB</b>
<b>Robust</b>	ref	ref
<b>Prefrail</b>	1.00 (0.91, 1.10)	1.00 (0.96, 1.03)
<b>Frail</b>	1.01 (0.81, 1.25)	0.94 (0.88, 1.01)

Multinomial logistic regression models were adjusted for age, gender (male and female), region (10 regions in CKB and 3 assessment centers in UKB), ethnicity (only in UKB), genotyping sampling group (only in CKB), genotyping array, top 10 principal components, sociodemographic characteristics (occupation, highest education and household income in CKB, multiple deprivation index in UKB), tobacco smoking, alcohol consumption and diet habits.

mCAs, mosaic chromosomal alterations; CKB, China Kadoorie Biobank; UKB, UK Biobank

**Table S6 Baseline characteristics of CKB participants (n=100,237) by frailty status.**

	Frailty status			<i>P</i>
	Robust	Prefrail	Frail	
	(N=53,975) n (%)	(N=42,617) n (%)	(N=3,645) n (%)	
Age, mean±sd	50.3±10.3	57.2±10.5	62.7±9.1	< 2E-16
Gender				
Male	22,971 (53.6)	18,387 (42.9)	1,468 (3.4)	< 2E-16
Female	31,004 (54.0)	24,230 (42.2)	2,177 (3.8)	
Region				
North area	21,279 (49.8)	19,596 (45.9)	1,820 (4.3)	
South area	32,696 (56.8)	23,021 (40.0)	1,825 (3.2)	< 2E-16
Highest education				
Primary school or lower	25,285 (47.5)	25,396 (47.7)	2,561 (4.8)	
Middle or high school	24,917 (60.7)	15,177 (37.0)	943 (2.3)	< 2E-16
College or higher	3,773 (63.3)	2,044 (34.3)	141 (2.4)	< 2E-16
Occupation				
Agricultural or industrial	31,355 (59.4)	20,109 (38.1)	1,292 (2.4)	
Retirement	7,239 (37.7)	10,853 (56.5)	1,129 (5.9)	< 2E-16
Non-agricultural or industrial	11,291 (52.8)	9,064 (42.3)	1,048 (4.9)	< 2E-16
Others	4,090 (59.6)	2,591 (37.8)	176 (2.6)	< 2E-16
Household income				
<10,000 yuan	14,281 (45.9)	15,039 (48.4)	1,768 (5.7)	
10,000-19,999 yuan	16,210 (53.8)	12,918 (42.9)	996 (3.3)	< 2E-16
≥20,000 yuan	23,484 (60.2)	14,660 (37.6)	881 (2.3)	< 2E-16
Smoking status				
Non-smoker	36,087 (54.9)	27,480 (41.8)	2,224 (3.4)	
Former smoker	1,501 (46.6)	1,588 (49.3)	129 (4.0)	0.070
Current smoker	16,387 (52.5)	13,549 (43.4)	1,292 (4.1)	1.29E-07
Alcohol consumption				
Non-drinker	43,653 (54.4)	33,636 (41.9)	2,908 (3.6)	
Former drinker	1,657 (35.9)	2,575 (55.7)	388 (8.4)	< 2E-16
Weekly drinker but not daily	3,434 (58.7)	2,299 (39.3)	115 (2.0)	0.007
Daily drinker	5,231 (54.6)	4,107 (42.9)	234 (2.4)	0.045
Healthy diet				
No	19,420 (56.0)	14,230 (41.0)	1,044 (3.0)	
Yes	34,555 (52.7)	28,387 (43.3)	2,601 (4.0)	1.08E-05

Models and variable definitions were the same as in Table 1.

CKB, China Kadoorie Biobank; mCAs, mosaic chromosomal alterations

**Table S7 Baseline characteristics of UKB participants (n=456,283) by frailty status.**

	Frailty status			<i>P</i>
	Robust	Prefrail	Frail	
	(N=255,589) n (%)	(N=168,865) n (%)	(N=31,829) n (%)	
Age, mean±sd	55.7±8.1	57.5±8.0	58.5±7.5	<2E-16
Gender				
Male	121,310 (58.0)	74,651 (35.7)	13,153 (6.3)	<2E-16
Female	134,279 (54.3)	94,214 (38.1)	18,676 (7.6)	
Assessment center				
England	225,652 (55.9)	149,895 (37.2)	27,934 (6.9)	
Scotland	19,841 (58.8)	11,607 (34.4)	2,277 (6.8)	<2E-16
Wales	10,096 (52.9)	7,363 (38.6)	1,618 (8.5)	<2E-16
Ethnicity				
White	242,716 (56.3)	159,068 (36.9)	29,479 (6.8)	
Mixed	1,354 (52.7)	991 (38.6)	224 (8.7)	1.13E-12
Asian	4,967 (51.0)	3,843 (39.5)	928 (9.5)	<2E-16
Black	3,577 (52.1)	2,668 (38.8)	626 (9.1)	<2E-16
Others	2,975 (50.9)	2,295 (39.3)	572 (9.8)	<2E-16
Multiple deprivation index, mean±sd	15.4±12.7	18.3±14.5	24.4±17.3	<2E-16
Smoking status				
Non-smoker	151,962 (60.7)	85,282 (34.0)	13,294 (5.3)	
Former smoker	78,387 (53.7)	57,528 (39.4)	9,985 (6.8)	<2E-16
Current smoker	25,240 (42.2)	26,055 (43.5)	8,550 (14.3)	<2E-16
Alcohol consumption				
Non-drinker	59,771 (48.8)	49,865 (40.7)	12,779 (10.4)	
Former drinker	5,903 (36.7)	7,195 (44.8)	2,965 (18.5)	<2E-16
Weekly drinker but not daily	134,627 (60.0)	78,335 (34.9)	11,428 (5.1)	<2E-16
Daily drinker	55,288 (59.2)	33,470 (35.8)	4,657 (5.0)	<2E-16
Healthy diet				
No	5,910 (44.5)	5,612 (42.3)	1,759 (13.2)	
Yes	249,679 (56.4)	163,253 (36.9)	30,070 (6.8)	<2E-16

Models and variable definitions were the same as in Table 2.

UKB, UK Biobank; mCAs, mosaic chromosomal alterations

**Table S8 Associations of expanded mCAs categories with all-cause and cause-specific deaths among CKB and UKB population.**

	No. mCAs /N	All-cause deaths		Cancers		Circulatory diseases		Respiratory diseases	
		No. deaths (Crude mortality)	HRs (95% CIs)	No. deaths (Crude mortality)	HRs (95% CIs)	No. deaths (Crude mortality)	HRs (95% CIs)	No. deaths (Crude mortality)	HRs (95% CIs)
<b>Autosomal mCAs</b>									
CKB	1,370/ 100,237	25,966 (16.77)	<b>1.20 (1.09, 1.32)</b>	5,484 (3.54)	1.07 (0.87, 1.33)	13,641 (8.81)	<b>1.24 (1.09, 1.41)</b>	3,194 (2.06)	1.19 (0.91, 1.56)
UKB	3,325/ 456,283	39,418 (6.45)	<b>1.78 (1.65, 1.93)</b>	19,117 (3.13)	<b>2.04 (1.84, 2.27)</b>	8,257 (1.35)	<b>1.28 (1.05, 1.56)</b>	2,814 (0.46)	<b>1.46 (1.07, 2.01)</b>
Combined	—	—	1.46 (0.99, 2.16)	—	1.49 (0.79, 2.80)	—	<b>1.25 (1.12, 1.39)</b>	—	<b>1.30 (1.06, 1.59)</b>
<i>P</i> for heterogeneity	—	—	1.75E-10	—	1.26E-07	—	0.808	—	0.333
<b>LOY</b>									
CKB	826/ 42,826	14,414 (22.89)	<b>1.18 (1.08, 1.29)</b>	3,153 (5.01)	<b>1.39 (1.16, 1.67)</b>	7,346 (11.67)	<b>1.15 (1.02, 1.30)</b>	1,950 (3.10)	1.16 (0.93, 1.44)
UKB	11,849/ 209,114	23,300 (8.41)	<b>1.10 (1.05, 1.15)</b>	10,342 (3.73)	<b>1.11 (1.05, 1.18)</b>	5,705 (2.06)	1.05 (0.96, 1.14)	1,753 (0.63)	<b>1.29 (1.13, 1.47)</b>
Combined	—	—	<b>1.13 (1.05, 1.21)</b>	—	1.22 (0.98, 1.52)	—	1.09 (0.99, 1.19)	—	<b>1.25 (1.12, 1.41)</b>
<i>P</i> for heterogeneity	—	—	0.136	—	0.022	—	0.212	—	0.416

<b>LOX</b>									
CKB	24/ 57,411	11,552 (12.57)	1.20 (0.54, 2.68)	2,331 (2.54)	1.48 (0.37, 5.96)	6,295 (6.85)	0.42 (0.06, 2.98)	1,244 (1.35)	— <sup>a</sup>
UKB	462/ 247,169	16,118 (4.83)	<b>1.50 (1.15, 1.95)</b>	8,775 (2.63)	<b>1.73 (1.23, 2.42)</b>	2,552 (0.76)	1.28 (0.64, 2.56)	1,061 (0.32)	0.38 (0.05, 2.72)
Combined	—	—	<b>1.47 (1.14, 1.88)</b>	—	<b>1.71 (1.24, 2.38)</b>	—	1.08 (0.50, 2.36)	—	—
<i>P</i> for heterogeneity	—	—	0.610	—	0.835	—	0.293	—	—

The crude mortality rates referred to the number of deaths in the given population per 1,000 person-years. Adjusted covariates in the models were consistent with models in Table 3, as appropriate. The combined HRs were derived from meta-analysis using random effect models. <sup>a</sup> There were no participants death from respiratory diseases among expanded LOX carriers in the CKB female population.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank; LOY, loss of Y chromosomes; LOX, loss of X chromosomes

**Table S9 Associations of expanded mCAs on 22 autosomes with all-cause and cause-specific deaths among CKB (n=100,237) and UKB (n=456,283) population.**

	No. expanded mCAs, % Proportion	All-cause deaths	Cancers	Circulatory diseases	Respiratory diseases
		HRs (95% CIs)	HRs (95% CIs)	HRs (95% CIs)	HRs (95% CIs)
<b>Chr1</b>					
CKB	110, 7.6%	<b>1.61 (1.14, 2.27)</b>	1.54 (0.73, 3.23)	1.46 (0.89, 2.40)	1.92 (0.71, 5.17)
UKB	225, 5.7%	<b>2.16 (1.64, 2.85)</b>	<b>2.60 (1.81, 3.74)</b>	1.20 (0.54, 2.66)	2.27 (0.85, 6.04)
Combined	—	<b>1.90 (1.42, 2.53)</b>	<b>2.22 (1.38, 3.56)</b>	1.38 (0.91, 2.11)	<b>2.08 (1.04, 4.19)</b>
<i>P</i> for heterogeneity	—	0.190	0.213	0.675	0.813
<b>Chr2</b>					
CKB	56, 3.9%	1.43 (0.98, 2.09)	1.99 (0.99, 4.00)	1.28 (0.72, 2.26)	1.75 (0.72, 4.26)
UKB	196, 5.0%	<b>1.68 (1.19, 2.36)</b>	<b>2.29 (1.51, 3.48)</b>	1.23 (0.51, 2.96)	1.36 (0.34, 5.44)
Combined	—	<b>1.56 (1.21, 2.01)</b>	<b>2.21 (1.54, 3.16)</b>	1.27 (0.79, 2.04)	1.63 (0.77, 3.44)
<i>P</i> for heterogeneity	—	0.548	0.734	0.943	0.764
<b>Chr3</b>					
CKB	94, 6.5%	1.22 (0.79, 1.87)	1.23 (0.55, 2.75)	1.01 (0.50, 2.03)	1.38 (0.34, 5.56)
UKB	133, 3.4%	<b>2.31 (1.65, 3.24)</b>	<b>2.44 (1.52, 3.93)</b>	1.90 (0.85, 4.23)	1.90 (0.47, 7.60)
Combined	—	1.70 (0.91, 3.20)	1.88 (0.98, 3.60)	1.34 (0.73, 2.48)	1.62 (0.61, 4.33)
<i>P</i> for heterogeneity	—	0.021	0.152	0.244	0.753
<b>Chr4</b>					
CKB	94, 6.5%	1.11 (0.77, 1.60)	0.62 (0.20, 1.92)	<b>1.50 (1.00, 2.25)</b>	0.39 (0.05, 2.78)
UKB	152, 3.9%	<b>2.01 (1.44, 2.80)</b>	<b>2.78 (1.85, 4.18)</b>	1.60 (0.72, 3.57)	0.82 (0.12, 5.84)
Combined	—	1.50 (0.84, 2.69)	1.44 (0.33, 6.22)	<b>1.52 (1.06, 2.18)</b>	0.57 (0.14, 2.27)
<i>P</i> for heterogeneity	—	0.019	0.014	0.883	0.597
<b>Chr5</b>					
CKB	50, 3.4%	1.02 (0.65, 1.59)	1.28 (0.48, 3.44)	1.07 (0.62, 1.85)	0.48 (0.07, 3.41)
UKB	115, 2.9%	<b>2.14 (1.42, 3.23)</b>	1.71 (0.89, 3.28)	<b>2.71 (1.22, 6.04)</b>	1.27 (0.18, 9.00)

Combined	—	1.49 (0.72, 3.08)	1.56 (0.91, 2.70)	1.62 (0.66, 4.02)	0.78 (0.19, 3.12)
<i>P</i> for heterogeneity	—	0.016	0.634	0.061	0.491
<b>Chr6</b>					
CKB	53, 3.7%	1.28 (0.82, 1.99)	1.52 (0.68, 3.39)	0.82 (0.37, 1.83)	1.74 (0.56, 5.43)
UKB	112, 2.9%	1.55 (0.98, 2.46)	1.64 (0.85, 3.16)	1.62 (0.61, 4.33)	1.26 (0.18, 8.94)
Combined	—	<b>1.40 (1.02, 1.93)</b>	1.59 (0.96, 2.64)	1.09 (0.56, 2.10)	1.61 (0.60, 4.29)
<i>P</i> for heterogeneity	—	0.555	0.879	0.292	0.779
<b>Chr7</b>					
CKB	57, 3.9%	1.07 (0.63, 1.81)	0.34 (0.05, 2.43)	1.37 (0.73, 2.55)	0.81 (0.11, 5.75)
UKB	110, 2.8%	<b>2.71 (1.87, 3.93)</b>	<b>3.00 (1.81, 4.98)</b>	0.88 (0.22, 3.53)	<b>4.26 (1.37, 13.22)</b>
Combined	—	1.73 (0.70, 4.32)	1.26 (0.16, 10.12)	1.27 (0.72, 2.25)	2.27 (0.47, 11.03)
<i>P</i> for heterogeneity	—	0.004	0.036	0.572	0.150
<b>Chr8</b>					
CKB	48, 3.3%	1.40 (0.81, 2.41)	1.70 (0.64, 4.56)	0.97 (0.40, 2.35)	2.74 (0.68, 11.03)
UKB	117, 3.0%	<b>3.47 (2.49, 4.84)</b>	<b>4.83 (3.24, 7.21)</b>	0.95 (0.24, 3.82)	<b>6.25 (2.34, 16.69)</b>
Combined	—	2.26 (0.93, 5.51)	<b>3.17 (1.16, 8.65)</b>	0.97 (0.46, 2.04)	<b>4.76 (2.13, 10.61)</b>
<i>P</i> for heterogeneity	—	0.005	0.054	0.98	0.342
<b>Chr9</b>					
CKB	76, 5.2%	<b>1.63 (1.15, 2.29)</b>	0.74 (0.24, 2.29)	<b>1.77 (1.16, 2.70)</b>	2.07 (0.66, 6.48)
UKB	230, 5.9%	<b>3.01 (2.37, 3.83)</b>	<b>3.07 (2.18, 4.32)</b>	1.50 (0.71, 3.15)	1.32 (0.33, 5.27)
Combined	—	<b>2.24 (1.23, 4.10)</b>	1.67 (0.42, 6.67)	<b>1.70 (1.17, 2.45)</b>	1.73 (0.72, 4.17)
<i>P</i> for heterogeneity	—	0.004	0.018	0.707	0.620
<b>Chr10</b>					
CKB	127, 8.7%	0.89 (0.64, 1.23)	0.64 (0.27, 1.54)	0.90 (0.59, 1.39)	0.76 (0.28, 2.04)
UKB	78, 2.0%	1.53 (0.87, 2.70)	1.31 (0.55, 3.15)	<b>3.03 (1.26, 7.29)</b>	— <sup>a</sup>
Combined	—	1.11 (0.65, 1.88)	0.92 (0.45, 1.85)	1.56 (0.48, 5.06)	—
<i>P</i> for heterogeneity	—	0.100	0.257	0.015	—
<b>Chr11</b>					
CKB	103, 7.1%	0.80 (0.54, 1.18)	0.80 (0.33, 1.93)	0.85 (0.51, 1.42)	0.87 (0.28, 2.70)
UKB	269, 6.9%	<b>1.83 (1.41, 2.38)</b>	<b>2.62 (1.90, 3.62)</b>	0.86 (0.39, 1.92)	1.56 (0.59, 4.17)
Combined	—	1.22 (0.54, 2.77)	1.56 (0.49, 4.94)	0.86 (0.56, 1.31)	1.21 (0.58, 2.55)

<i>P</i> for heterogeneity	—	0.001	0.013	0.979	0.441
<b>Chr12</b>					
CKB	56, 3.9%	<b>2.14 (1.44, 3.18)</b>	2.02 (0.91, 4.52)	<b>2.15 (1.24, 3.72)</b>	2.31 (0.74, 7.22)
UKB	246, 6.3%	<b>2.69 (2.11, 3.43)</b>	<b>3.01 (2.17, 4.17)</b>	1.38 (0.66, 2.90)	<b>2.97 (1.24, 7.16)</b>
Combined	—	<b>2.52 (2.05, 3.10)</b>	<b>2.84 (2.10, 3.85)</b>	<b>1.84 (1.18, 2.86)</b>	<b>2.71 (1.35, 5.43)</b>
<i>P</i> for heterogeneity	—	0.338	0.369	0.347	0.731
<b>Chr13</b>					
CKB	40, 2.8%	1.29 (0.76, 2.19)	<b>2.65 (1.26, 5.57)</b>	1.41 (0.67, 2.96)	— <sup>a</sup>
UKB	469, 11.9%	<b>2.04 (1.69, 2.45)</b>	<b>3.24 (2.61, 4.01)</b>	0.82 (0.44, 1.53)	1.00 (0.38, 2.68)
Combined	—	<b>1.74 (1.14, 2.66)</b>	<b>3.19 (2.59, 3.92)</b>	1.03 (0.61, 1.74)	—
<i>P</i> for heterogeneity	—	0.110	0.609	0.274	—
<b>Chr14</b>					
CKB	94, 6.5%	<b>1.56 (1.15, 2.10)</b>	<b>1.88 (1.01, 3.50)</b>	1.37 (0.89, 2.11)	1.41 (0.58, 3.41)
UKB	243, 6.2%	<b>1.91 (1.46, 2.51)</b>	<b>1.96 (1.34, 2.89)</b>	1.55 (0.81, 2.98)	1.61 (0.52, 4.99)
Combined	—	<b>1.74 (1.43, 2.13)</b>	<b>1.94 (1.40, 2.69)</b>	1.42 (0.99, 2.04)	1.48 (0.74, 2.97)
<i>P</i> for heterogeneity	—	0.322	0.906	0.752	0.858
<b>Chr15</b>					
CKB	23, 1.6%	0.72 (0.34, 1.52)	0.68 (0.10, 4.83)	0.63 (0.20, 1.97)	0.62 (0.15, 2.54)
UKB	90, 2.3%	1.42 (0.88, 2.28)	1.61 (0.84, 3.10)	1.88 (0.78, 4.53)	— <sup>a</sup>
Combined	—	1.08 (0.56, 2.06)	1.48 (0.80, 2.75)	1.16 (0.40, 3.37)	—
<i>P</i> for heterogeneity	—	0.134	0.411	0.135	—
<b>Chr16</b>					
CKB	42, 2.9%	1.02 (0.60, 1.72)	0.91 (0.23, 3.65)	0.93 (0.46, 1.86)	1.20 (0.29, 4.94)
UKB	219, 5.6%	1.41 (0.98, 2.04)	1.28 (0.74, 2.20)	1.90 (0.95, 3.81)	0.63 (0.09, 4.49)
Combined	—	1.27 (0.94, 1.72)	1.22 (0.74, 2.03)	1.33 (0.66, 2.69)	0.96 (0.30, 3.03)
<i>P</i> for heterogeneity	—	0.314	0.655	0.153	0.606
<b>Chr17</b>					
CKB	45, 3.1%	1.25 (0.82, 1.90)	1.81 (0.81, 4.05)	1.17 (0.66, 2.07)	— <sup>a</sup>
UKB	181, 4.6%	<b>1.79 (1.28, 2.51)</b>	<b>2.19 (1.41, 3.40)</b>	1.49 (0.67, 3.32)	0.70 (0.10, 5.01)
Combined	—	1.53 (1.08, 2.17)	<b>2.10 (1.43, 3.09)</b>	1.27 (0.80, 2.02)	—
<i>P</i> for heterogeneity	—	0.189	0.684	0.634	—

<b>Chr18</b>					
CKB	25, 1.7%	<b>3.91 (2.34, 6.52)</b>	<b>9.83 (4.62, 20.92)</b>	1.43 (0.46, 4.44)	<b>3.65 (1.11, 12.03)</b>
UKB	90, 2.3%	1.47 (0.89, 2.44)	<b>2.04 (1.10, 3.80)</b>	1.41 (0.45, 4.37)	— <sup>a</sup>
Combined	—	2.40 (0.92, 6.25)	4.41 (0.95, 20.59)	1.42 (0.64, 3.16)	—
<i>P</i> for heterogeneity	—	0.008	0.002	0.989	—
<b>Chr19</b>					
CKB	119, 8.2%	1.15 (0.80, 1.67)	0.72 (0.30, 1.74)	1.28 (0.74, 2.21)	<b>2.95 (1.47, 5.95)</b>
UKB	84, 2.1%	<b>1.68 (1.01, 2.78)</b>	<b>2.13 (1.11, 4.10)</b>	2.01 (0.75, 5.36)	— <sup>a</sup>
Combined	—	1.33 (0.93, 1.91)	1.29 (0.45, 3.73)	1.43 (0.89, 2.30)	—
<i>P</i> for heterogeneity	—	0.243	0.052	0.432	—
<b>Chr20</b>					
CKB	83, 5.7%	1.14 (0.83, 1.56)	1.47 (0.79, 2.74)	1.24 (0.82, 1.87)	0.69 (0.26, 1.85)
UKB	302, 7.7%	<b>1.60 (1.24, 2.07)</b>	1.32 (0.88, 1.99)	1.29 (0.71, 2.33)	1.34 (0.50, 3.58)
Combined	—	1.37 (0.98, 1.91)	1.37 (0.97, 1.92)	1.25 (0.89, 1.76)	0.96 (0.48, 1.93)
<i>P</i> for heterogeneity	—	0.095	0.784	0.914	0.348
<b>Chr21</b>					
CKB	12, 0.8%	1.70 (0.81, 3.58)	1.27 (0.18, 9.08)	1.80 (0.74, 4.36)	— <sup>a</sup>
UKB	51, 1.3%	<b>1.93 (1.04, 3.59)</b>	1.58 (0.59, 4.22)	1.81 (0.45, 7.22)	2.57 (0.36, 18.27)
Combined	—	<b>1.83 (1.14, 2.95)</b>	1.52 (0.63, 3.65)	1.80 (0.85, 3.80)	—
<i>P</i> for heterogeneity	—	0.794	0.845	0.996	—
<b>Chr22</b>					
CKB	45, 3.1%	1.45 (0.90, 2.33)	1.20 (0.39, 3.73)	1.77 (0.98, 3.22)	0.83 (0.12, 5.89)
UKB	215, 5.5%	<b>1.91 (1.46, 2.50)</b>	<b>1.91 (1.29, 2.82)</b>	1.34 (0.67, 2.67)	<b>2.88 (1.37, 6.05)</b>
Combined	—	<b>1.78 (1.41, 2.26)</b>	<b>1.81 (1.25, 2.63)</b>	<b>1.57 (1.00, 2.47)</b>	2.18 (0.79, 6.04)
<i>P</i> for heterogeneity	—	0.326	0.449	0.544	0.244

Adjusted covariates in the models were consistent with models in Table 3, as appropriate. The combined HRs were derived from meta-analysis using random effect models. Proportion (%) = Number of mCAs per chromosome / Total number of mCAs across all autosomes in the corresponding population. <sup>a</sup> There were no participants death from respiratory diseases among corresponding group.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank

**Table S10 Associations of expanded autosomal mCAs subtypes with all-cause and cause-specific deaths among CKB (n=100,237) and UKB (n=456,283) population.**

	No. expanded mCAs, % Proportion	All-cause deaths	Cancers	Circulatory diseases	Respiratory diseases
		HRs (95% CIs)	HRs (95% CIs)	HRs (95% CIs)	HRs (95% CIs)
<b>CN-LOH</b>					
CKB	929, 67.1%	<b>1.17 (1.04, 1.32)</b>	1.12 (0.86, 1.46)	<b>1.20 (1.02, 1.42)</b>	1.32 (0.93, 1.88)
UKB	1156, 32.5%	<b>1.64 (1.43, 1.88)</b>	<b>1.82 (1.50, 2.19)</b>	1.16 (0.82, 1.64)	0.84 (0.42, 1.67)
Combined	—	1.39 (0.99, 1.93)	1.44 (0.90, 2.31)	<b>1.19 (1.03, 1.39)</b>	1.16 (0.78, 1.74)
<i>P</i> for heterogeneity	—	2.90E-04	0.003	0.853	0.250
<b>Gain</b>					
CKB	91, 6.6%	<b>1.52 (1.12, 2.07)</b>	1.52 (0.72, 3.19)	1.31 (0.87, 1.97)	1.16 (0.37, 3.61)
UKB	653, 18.4%	<b>2.38 (2.04, 2.79)</b>	<b>2.65 (2.14, 3.28)</b>	<b>1.70 (1.14, 2.54)</b>	<b>2.58 (1.47, 4.56)</b>
Combined	—	<b>1.94 (1.26, 3.01)</b>	<b>2.25 (1.37, 3.70)</b>	<b>1.50 (1.13, 1.99)</b>	2.02 (0.98, 4.18)
<i>P</i> for heterogeneity	—	0.011	0.158	0.367	0.215
<b>Loss</b>					
CKB	365, 26.4%	<b>1.24 (1.06, 1.45)</b>	1.16 (0.81, 1.66)	<b>1.30 (1.06, 1.60)</b>	0.93 (0.59, 1.47)
UKB	1745, 49.1%	<b>1.80 (1.62, 2.00)</b>	<b>2.14 (1.86, 2.46)</b>	1.29 (0.99, 1.69)	1.37 (0.88, 2.13)
Combined	—	<b>1.50 (1.05, 2.16)</b>	1.61 (0.88, 2.94)	<b>1.30 (1.10, 1.53)</b>	1.13 (0.78, 1.66)
<i>P</i> for heterogeneity	—	1.14E-04	0.002	0.962	0.229

Adjusted covariates in the models were consistent with models in Table 3, as appropriate. The combined HRs were derived from meta-analysis using random effect models. Proportion (%) = Number of mCAs per subtype / Total number of mCAs across all autosomes in the corresponding population.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank; CN-LOH, copy-neutral loss of heterozygosity

**Table S11 Associations of expanded mCAs with solid cancers and hematological malignancies by frailty status among CKB and UKB population.**

	Solid cancers			Hematological malignancies		
	No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>	No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>
<b>CKB</b>						
<b>Total</b>	<b>5,213 (3.37)</b>	<b>1.20 (1.04, 1.39)</b>	<b>0.116</b>	<b>271 (0.18)</b>	<b>2.28 (1.35, 3.85)</b>	<b>0.708</b>
Robust	2,234 (2.53)	0.97 (0.75, 1.25)		133 (0.15)	1.90 (0.86, 4.22)	
Prefrail	2,675 (4.28)	1.30 (1.07, 1.57)		127 (0.20)	2.99 (1.47, 6.06)	
Frail	304 (7.32)	1.58 (0.91, 2.74)		11 (0.26)	-- <sup>a</sup>	
<b>UKB</b>						
<b>Total</b>	<b>17,343 (2.84)</b>	<b>1.17 (1.10, 1.24)</b>	<b>0.978</b>	<b>1,774 (0.29)</b>	<b>2.42 (2.10, 2.80)</b>	<b>0.026</b>
Robust	7,787 (2.25)	1.17 (1.06, 1.28)		815 (0.24)	2.00 (1.61, 2.49)	
prefrail	7,517 (3.35)	1.18 (1.08, 1.29)		774 (0.34)	2.75 (2.22, 3.41)	
Frail	2,039 (5.01)	1.19 (1.00, 1.41)		185 (0.45)	3.58 (2.31, 5.57)	
<b>Combined</b>						
<b>Total</b>	—	<b>1.17 (1.11, 1.24)</b>	<b>0.650</b>	—	<b>2.41 (2.10, 2.77)</b>	<b>0.019</b>
Robust	—	1.11 (0.94, 1.30)		—	1.99 (1.61, 2.46)	
prefrail	—	1.20 (1.11, 1.30)		—	2.77 (2.25, 3.40)	
Frail	—	1.22 (1.03, 1.44)		—	3.58 (2.31, 5.57)	

The crude mortality rates referred to the number of deaths in the given population per 1,000 person-years.

Adjusted covariates in the models were consistent with models in Table 3, as appropriate. *P*-values reflected the heterogeneity test results between different frailty status groups. <sup>a</sup> There were no expanded mCAs carriers among frail participants death from hematological malignancies.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank

**Table S12 The HRs and 95% CIs of all-cause and cause-specific mortality associated with expanded mCAs by frailty status among CKB and UKB population.**

	All-cause deaths		Cancers		Circulatory diseases		Respiratory diseases	
	No. deaths	HRs (95% CIs)	No. deaths	HRs (95% CIs)	No. deaths	HRs (95% CIs)	No. deaths	HRs (95% CIs)
<b>CKB</b>								
Robust	8,278	1.05 (0.93, 1.19)	2,367	1.02 (0.80, 1.30)	3,993	1.02 (0.85, 1.21)	652	1.49 (1.05, 2.11)
Prefrail	15,293	1.25 (1.15, 1.35)	2,802	1.35 (1.13, 1.63)	8,477	1.26 (1.13, 1.41)	1,971	1.08 (0.86, 1.35)
Frail	2,395	1.32 (1.05, 1.66)	315	1.56 (0.90, 2.70)	1,171	1.07 (0.76, 1.52)	571	1.52 (0.95, 2.45)
<b>UKB</b>								
Robust	15,543	1.18 (1.11, 1.26)	8,602	1.25 (1.15, 1.36)	2,855	1.09 (0.96, 1.25)	653	1.34 (1.05, 1.72)
Prefrail	17,612	1.25 (1.18, 1.32)	8,291	1.30 (1.20, 1.41)	3,778	1.08 (0.96, 1.21)	1,356	1.39 (1.17, 1.65)
Frail	626	1.18 (1.07, 1.30)	2,224	1.33 (1.13, 1.56)	1,624	1.11 (0.93, 1.34)	805	1.11 (0.85, 1.45)
<b>Combined</b>								
Robust	—	1.13 (1.01, 1.27)	—	1.17 (0.97, 1.41)	—	1.06 (0.96, 1.18)	—	1.39 (1.14, 1.70)
Prefrail	—	1.25 (1.19, 1.31)	—	1.31 (1.22, 1.41)	—	1.17 (1.00, 1.36)	—	1.24 (0.96, 1.59)
Frail	—	1.20 (1.10, 1.32)	—	1.35 (1.16, 1.57)	—	1.10 (0.94, 1.30)	—	1.22 (0.91, 1.62)

Adjusted covariates in the models were consistent with models in Table 3, as appropriate. The combined HRs were derived from meta-analysis using random effect models.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank

**Table S13 Associations of expanded mCAs with all-cause, cancer and cause-specific cancer mortality by frailty status in a subcohort of the CKB (n=81,064).**

	No. mCAs /N	All-cause deaths			Cancers			Solid cancers			Hematological malignancies		
		No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>	No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>	No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>	No. deaths (Crude mortality)	HRs (95% CIs)	<i>P</i>
<b>Total</b>	<b>1,655/ 81,064</b>	<b>15,075 (11.39)</b>	<b>1.17 (1.08, 1.27)</b>	<b>0.573</b>	<b>4,497 (3.40)</b>	<b>1.24 (1.07, 1.45)</b>	<b>0.136</b>	<b>4,280 (3.23)</b>	<b>1.19 (1.02, 1.40)</b>	<b>0.090</b>	<b>217 (0.16)</b>	<b>2.36 (1.34, 4.16)</b>	<b>0.958</b>
Robust	814/ 46,908	5,235 (6.63)	1.09 (0.94, 1.27)		2,031 (2.57)	1.00 (0.77, 1.31)		1,924 (2.44)	0.93 (0.70, 1.24)		107 (0.14)	2.31 (1.02, 5.26)	
Prefrail	772/ 31,930	8,591 (17.00)	1.18 (1.06, 1.32)		2,228 (4.41)	1.34 (1.09, 1.65)		2,123 (4.20)	1.30 (1.05, 1.60)		105 (0.21)	2.75 (1.23, 6.13)	
Frail	69/ 2,226	1,249 (42.79)	1.28 (0.93, 1.75)		238 (8.15)	1.68 (0.92, 3.09)		233 (7.98)	1.70 (0.93, 3.13)		5 (0.17)	— <sup>a</sup>	

The CKB subcohort excluded participants (n=19,173) who were selected for genotyping as COPD or CVD cases. The crude mortality rates referred to the number of deaths in the given population per 1,000 person-years. Adjusted covariates in the models were consistent with models in Table 3, as appropriate. *P*-values reflected the heterogeneity test results between different frailty status groups. <sup>a</sup> There were no expanded mCAs carriers among frail participants death from hematological malignancies.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease

**Table S14 The HRs and 95% CIs of all-cause and cause-specific deaths according to joint groups of frailty status and expanded mCAs among CKB and UKB population.**

	No. deaths / N	All-cause deaths	Cancers	Circulatory diseases	Respiratory diseases
<b>CKB</b>					
<b>Robust</b>					
expanded mCAs-	7,991 / 53,004	ref	ref	ref	ref
expanded mCAs+	287 / 971	1.13 (1.00, 1.27)	1.04 (0.82, 1.33)	1.12 (0.94, 1.32)	1.63 (1.17, 2.28)
<b>Prefrail</b>					
expanded mCAs-	14,680 / 41,546	1.48 (1.43, 1.52)	1.08 (1.02, 1.14)	1.60 (1.53, 1.66)	2.05 (1.86, 2.26)
expanded mCAs+	613 / 1,071	1.82 (1.67, 1.98)	1.46 (1.21, 1.75)	2.00 (1.78, 2.24)	2.22 (1.76, 2.82)
<b>Frail</b>					
expanded mCAs-	2,302 / 3,535	2.45 (2.33, 2.57)	1.37 (1.21, 1.56)	2.46 (2.29, 2.64)	4.21 (3.71, 4.78)
expanded mCAs+	93 / 110	3.27 (2.66, 4.03)	2.27 (1.40, 3.67)	3.04 (2.21, 4.17)	5.69 (3.70, 8.76)
<b>UKB</b>					
<b>Robust</b>					
expanded mCAs-	14,301 / 247,671	ref	ref	ref	ref
expanded mCAs+	1,242 / 7,918	1.20 (1.13, 1.28)	1.26 (1.16, 1.37)	1.14 (1.00, 1.30)	1.51 (1.19, 1.92)
<b>Prefrail</b>					
expanded mCAs-	16,046 / 162,619	1.39 (1.35, 1.42)	1.21 (1.17, 1.24)	1.61 (1.53, 1.70)	2.26 (2.04, 2.50)
expanded mCAs+	1,566 / 6,246	1.75 (1.66, 1.85)	1.57 (1.44, 1.70)	1.77 (1.58, 1.99)	3.18 (2.65, 3.81)
<b>Frail</b>					
expanded mCAs-	5,782 / 30,550	2.21 (2.14, 2.28)	1.48 (1.40, 1.55)	3.04 (2.84, 3.25)	5.29 (4.71, 5.93)
expanded mCAs+	481 / 1,279	2.48 (2.26, 2.72)	1.94 (1.67, 2.25)	3.08 (2.58, 3.68)	5.12 (3.93, 6.66)
<b>Combined</b>					
<b>Robust</b>					
expanded mCAs-	—	ref	ref	ref	ref
expanded mCAs+	—	1.19 (1.13, 1.25)	1.19 (1.00, 1.42)	1.13 (1.02, 1.25)	1.55 (1.28, 1.88)
<b>Prefrail</b>					
expanded mCAs-	—	1.43 (1.34, 1.52)	1.14 (1.02, 1.28)	1.60 (1.55, 1.65)	2.15 (1.95, 2.36)
expanded mCAs+	—	1.77 (1.69, 1.85)	1.55 (1.44, 1.67)	1.88 (1.67, 2.11)	2.68 (1.89, 3.80)
<b>Frail</b>					
expanded mCAs-	—	2.32 (2.10, 2.57)	1.46 (1.38, 1.54)	2.73 (2.22, 3.36)	4.73 (3.78, 5.91)
expanded mCAs+	—	2.80 (2.14, 3.67)	1.96 (1.70, 2.26)	3.07 (2.63, 3.58)	5.27 (4.20, 6.60)

Adjusted covariates in the models were consistent with models in Table 3, as appropriate.

HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; UKB, UK Biobank; mCAs, mosaic chromosomal alterations

**Table S15 Additive and multiplicative interactions between frailty status and expanded mCAs on all-cause and cause-specific deaths among CKB and UKB population.**

	Prefrail		Frail		<i>P</i> for multiplicative interactions
	RERIs (95% CIs)	APs (95% CIs)	RERIs (95% CIs)	APs (95% CIs)	
<b>CKB</b>					
All-cause deaths	<b>0.22 (0.02, 0.41)</b>	<b>0.12 (0.01, 0.21)</b>	<b>0.70 (0.07, 1.46)</b>	<b>0.21 (0.01, 0.35)</b>	0.292
Cancers	0.34 (-0.03, 0.70)	0.23 (-0.04, 0.41)	0.86 (-0.07, 2.28)	0.38 (-0.15, 0.54)	0.123
Circulatory diseases	0.29 (-0.01, 0.57)	0.14 (-0.01, 0.26)	0.46 (-0.39, 1.61)	0.15 (-0.21, 0.36)	0.526
Respiratory diseases	-0.46 (-1.24, 0.26)	-0.21 (-0.65, 0.08)	0.85 (-1.23, 3.90)	0.15 (-0.36, 0.42)	0.135
<b>UKB</b>					
All-cause deaths	<b>0.16 (0.05, 0.27)</b>	<b>0.09 (0.03, 0.15)</b>	0.07 (-0.16, 0.32)	0.03 (-0.08, 0.11)	0.082
Cancers	0.10 (-0.06, 0.25)	0.06 (-0.04, 0.15)	0.20 (-0.09, 0.52)	0.10 (-0.07, 0.22)	0.861
Circulatory diseases	0.02 (-0.22, 0.27)	0.01 (-0.14, 0.13)	-0.09 (-0.62, 0.52)	-0.03 (-0.25, 0.13)	0.587
Respiratory diseases	0.40 (-0.21, 1.04)	0.13 (-0.08, 0.28)	-0.69 (-1.95, 0.84)	-0.13 (-0.49, 0.11)	<b>0.019</b>

Additive interactions were estimated using RERIs and APs with their 95% CIs (estimated by variance recovery method) by fitting cox hazard models with an interaction term for frailty status and expanded mCAs on all-cause and cause-specific deaths. Multiplicative interactions were tested by comparing the multivariate-adjusted models with and without cross-product interaction terms using likelihood-ratio tests. Adjusted covariates in the models were consistent with models in Table 3, as appropriate.

mCAs, mosaic chromosomal alterations; CKB, China Kadoorie Biobank; UKB, UK Biobank; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; CI, confidence interval

**Table S16 Adjusted 10-year all-cause, circulatory diseases and respiratory diseases mortality rates and 95% CIs by frailty status and frailty-mCAs joint groups among CKB and UKB population.**

Groups		All-cause		Circulatory diseases		Respiratory diseases		
		Adjusted mortality (95% CIs)		Adjusted mortality (95% CIs)		Adjusted mortality (95% CIs)		
<b>CKB</b>								
Robust	mCAs-	10.07% (10.30%,	10.02% (10.26%, 9.79%)	5.22% (5.05%,	5.19% (5.02%, 5.37%)	0.85% (0.78%,	0.83% (0.76%, 0.91%)	
	mCAs+	9.84%)	11.43% (12.50%, 10.36%)	5.40%)	6.12% (5.24%, 7.00%)	0.92%)	1.28% (0.88%, 1.69%)	
Prefrail	mCAs-	15.40% (15.67%,	15.32% (15.59%, 15.06%)	8.85% (8.63%,	8.81% (8.59%, 9.02%)	1.90% (1.80%,	1.89% (1.79%, 2.00%)	
	mCAs+	15.14%)	17.60% (18.61%, 16.59%)	9.06%)	10.04% (9.14%, 10.93%)	2.00%)	2.02% (1.60%, 2.45%)	
Frail	mCAs-	24.20% (24.88%,	24.10% (24.79%, 23.41%)	11.89% (11.31%,	11.89% (11.30%, 12.48%)	4.92% (4.50%,	4.89% (4.47%, 5.32%)	
	mCAs+	23.52%)	27.22% (30.35%, 24.09%)	12.47%)	11.98% (9.00%, 14.95%)	5.34%)	5.76% (3.64%, 7.88%)	
<b>UKB</b>								
Robust	mCAs-	3.52% (3.58%,	3.44% (3.50%, 3.38%)	0.63% (0.61%,	0.62% (0.59%, 0.65%)	0.14% (0.13%,	0.13% (0.12%, 0.15%)	
	mCAs+	3.46%)	4.70% (4.96%, 4.45%)	0.66%)	0.79% (0.69%, 0.89%)	0.15%)	0.26% (0.20%, 0.31%)	
Prefrail	mCAs-	5.44% (5.53%,	5.30% (5.39%, 5.21%)	1.15% (1.10%,	1.13% (1.09%, 1.17%)	0.39% (0.37%,	0.37% (0.35%, 0.40%)	
	mCAs+	5.35%)	7.55% (7.91%, 7.19%)	1.19%)	1.38% (1.23%, 1.52%)	0.42%)	0.65% (0.55%, 0.76%)	
Frail	mCAs-	10.01% (10.25%,	9.86% (10.10%, 9.62%)	2.59% (2.46%,	2.57% (2.43%, 2.71%)	1.20% (1.11%,	1.19% (1.09%, 1.28%)	
	mCAs+	9.77%)	12.29% (13.25%, 11.32%)	2.73%)	2.86% (2.39%, 3.33%)	1.29%)	1.38% (1.03%, 1.72%)	

Cause-specific Cox regression models were developed for cause-specific deaths, to account for competing risks. Model adjustments were the same as models in Figure 3. Adjusted 10-year mortality rates were estimated using direct standardization by frailty status and frailty-mCAs joint groups, respectively.

mCAs, mosaic chromosomal alterations; CKB, China Kadoorie Biobank; UKB, UK Biobank; CI, confidence interval

**Table S17 Adjusted 10-year cancer mortality rates and 95% CIs by frailty status and frailty-mCAs joint groups in a subcohort of the CKB (n=81,064).**

Groups		Any cancers		Solid cancers		Hematological malignancies	
		Adjusted mortality (95% CIs)		Adjusted mortality (95% CIs)		Adjusted mortality (95% CIs)	
Robust	mCAs-	2.57% (2.44%,	2.57% (2.43%, 2.71%)	2.46% (2.33%,	2.46% (2.33%, 2.60%)	0.11% (0.08%,	0.11% (0.08%, 0.14%)
	mCAs+	2.71%)	2.63% (1.98%, 3.28%)	2.60%)	2.32% (1.71%, 2.94%)	0.14%)	0.30% (0.07%, 0.53%)
Prefrail	mCAs-	2.74% (2.60%,	2.71% (2.57%, 2.85%)	2.62% (2.48%,	2.59% (2.46%, 2.73%)	0.12% (0.09%,	0.11% (0.09%, 0.14%)
	mCAs+	2.88%)	3.61% (2.92%, 4.29%)	2.76%)	3.35% (2.69%, 4.01%)	0.15%)	0.26% (0.06%, 0.46%)
Frail	mCAs-	3.78% (3.30%,	3.68% (3.20%, 4.16%)	3.70% (3.22%,	3.60% (3.12%, 4.08%)	0.08% (0.01%,	0.08% (0.01%, 0.15%)
	mCAs+	4.26%)	6.19% (3.48%, 8.90%)	4.17%)	6.14% (3.45%, 8.82%)	0.15%)	<0.01%

The CKB subcohort excluded participants (n=19,173) who were selected for genotyping as COPD or CVD cases. Cause-specific Cox regression models were used to account for competing risks. Model adjustments were the same as models in Figure 3. Adjusted 10-year mortality rates were estimated using direct standardization by frailty status and frailty-mCAs joint groups, respectively.

mCAs, mosaic chromosomal alterations; HR, hazard ratios; CI, confidence interval; CKB, China Kadoorie Biobank; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease

**Table S18 Differences and 95% CIs in adjusted 10-year cancer mortality rates between different frailty-mCAs joint groups among CKB and UKB population.**

	Any cancers	Solid cancers	Hematological malignancies
<b>CKB</b>			
Diff <sub>g2 - g3</sub>	0.00% (-0.62%, 0.69%)	-0.16% (-0.74%, 0.44%)	0.16% (-0.02%, 0.40%)
Diff <sub>g4 - g5</sub>	0.31% (-0.38%, 1.02%)	0.16% (-0.53%, 0.87%)	0.17% (-0.03%, 0.42%)
<b>UKB</b>			
Diff <sub>g2 - g3</sub>	<b>0.30% (0.06%, 0.54%)</b>	0.08% (-0.15%, 0.31%)	<b>0.19% (0.11%, 0.28%)</b>
Diff <sub>g4 - g5</sub>	0.31% (-0.05%, 0.69%)	-0.05% (-0.37%, 0.28%)	<b>0.31% (0.19%, 0.43%)</b>

The 95% CIs were estimated using the bootstrap method with 1,000 resampling iterations.

g2: robust participants with mCAs; g3: prefrail participants without mCAs; g4: prefrail participants with mCAs; g5: frail participants without mCAs

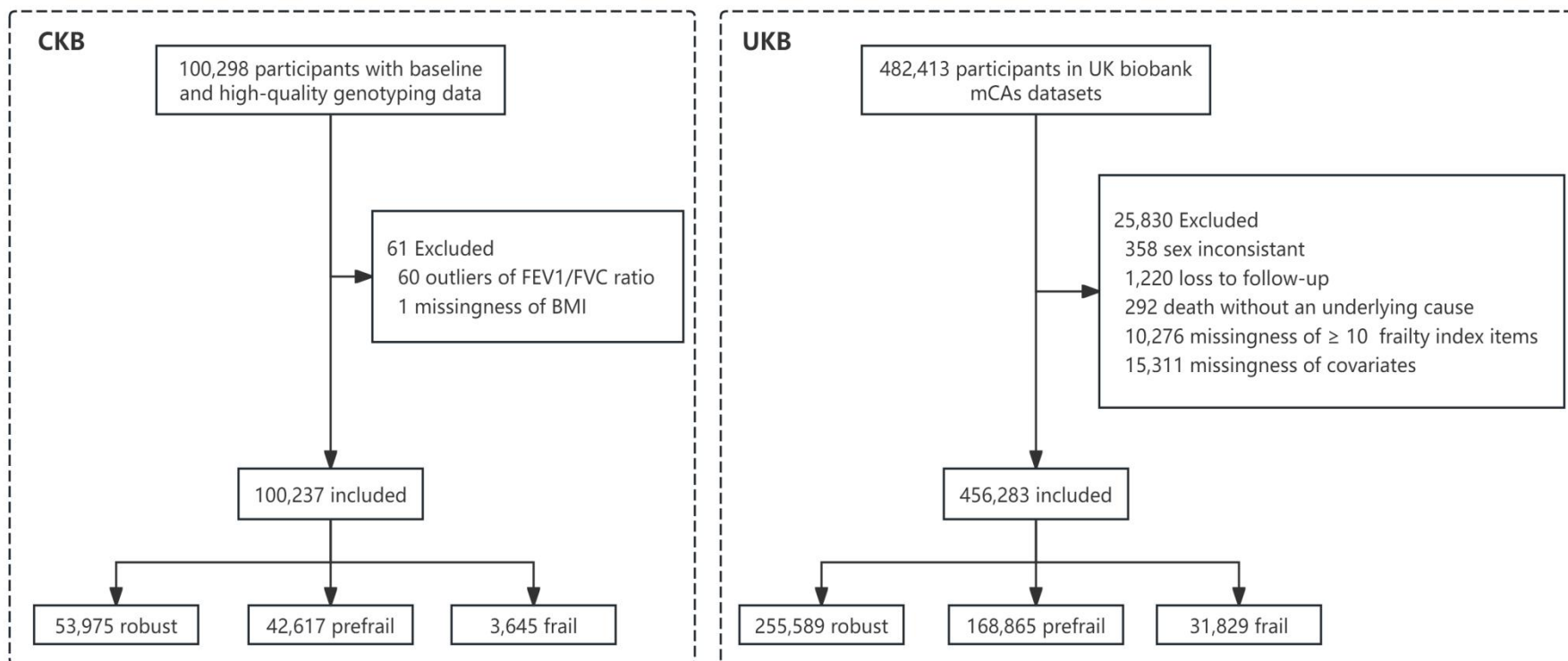
CKB, China Kadoorie Biobank; UKB, UK Biobank; CI, confidence interval; mCAs, mosaic chromosomal alterations

**Table S19 Associations of frailty index with all-cause and cause-specific deaths among CKB and UKB population.**

	CKB		UKB	
	No. deaths (Crude mortality)	HRs (95% CIs)	No. deaths (Crude mortality)	HRs (95% CIs)
<b>All-cause deaths</b>				
robust	8,278 (9.38)	ref	15,543 (4.49)	ref
prefrail	15,293 (24.48)	1.61 (1.56, 1.65)	17,612 (7.85)	1.40 (1.37, 1.43)
frail	2,395 (57.67)	2.79 (2.65, 2.92)	6,263 (15.38)	2.21 (2.14, 2.28)
<b>Cancers</b>				
robust	2,367 (2.68)	ref	8,602 (2.49)	ref
prefrail	2,802 (4.49)	1.09 (1.03, 1.16)	8,291 (3.69)	1.21 (1.17, 1.25)
frail	315 (7.58)	1.43 (1.27, 1.62)	2,224 (5.46)	1.49 (1.42, 1.56)
<b>Solid cancers</b>				
robust	2,234 (2.53)	ref	7,787 (2.25)	ref
prefrail	2,675 (4.28)	1.10 (1.04, 1.17)	7,517 (3.35)	1.21 (1.17, 1.25)
frail	304 (7.32)	1.45 (1.28, 1.64)	2,039 (5.01)	1.48 (1.41, 1.56)
<b>Hematological malignancies</b>				
robust	133 (0.15)	ref	815 (0.24)	ref
prefrail	127 (0.20)	0.98 (0.76, 1.26)	774 (0.34)	1.26 (1.14, 1.39)
frail	11 (0.26)	1.11 (0.59, 2.10)	185 (0.45)	1.54 (1.31, 1.82)
<b>Circulatory diseases</b>				
robust	3,993 (4.53)	ref	2,855 (0.83)	ref
prefrail	8,477 (13.57)	1.79 (1.72, 1.86)	3,778 (1.68)	1.61 (1.53, 1.69)
frail	1,171 (28.19)	2.66 (2.49, 2.85)	1,624 (3.99)	3.02 (2.83, 3.23)
<b>Respiratory diseases</b>				
robust	652 (0.74)	ref	653 (0.19)	ref
prefrail	1,971 (3.15)	2.42 (2.20, 2.65)	1,356 (0.60)	2.26 (2.06, 2.49)
frail	571 (13.75)	6.97 (6.18, 7.87)	805 (1.98)	5.15 (4.62, 5.75)

The crude mortality rates referred to the number of deaths in the given population per 1,000 person-years. Cox proportional hazard models were stratified by age in the 5-year interval, gender (male and female), and regions (10 regions in CKB and 3 assessment centers in UKB), and adjusted for ethnicity (only in UKB), sociodemographic characteristics (occupation, highest education and household income in CKB, multiple deprivation index in UKB), tobacco smoking, alcohol consumption and diet habits.

CKB, China Kadoorie Biobank; UKB, UK Biobank; HR, hazard ratios; CI, confidence interval



**Fig. S1 Flow chart of the study.**

CKB, China Kadoorie Biobank; UKB, UK Biobank; mCAs, mosaic chromosomal alterations; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; BMI, body mass index