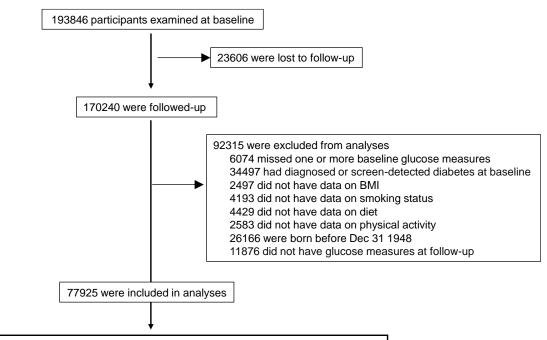
Online Supplementary Materials

- 1. Supplementary Figure 1. Flowchart of the analysis
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Supplementary Figure 1. Participant Flow Diagram of the China Cardiometabolic Disease and Cancer Cohort (4C) Study



Participants were classified into three groups according to birth date:

- 1) Born between January 1, 1959 to December 31, 1962: fetal exposed (n=13195);
- 2) Born between January 1, 1949 to December 31, 1958: childhood exposed (n=41148);
- 3) Born between January 1, 1963 to December 31, 1974: non-exposed (n=23582).

Supplementary Table 1. Definitions of 6 ideal cardiovascular health metrics in participants without diabetes at baseline $^{\rm a}$

Cardiovascular health metrics	Ideal level		
Smoking	Never or quit >12 months		
Body mass index	$< 24 \text{ kg/m}^2$		
Physical activity	\geq 150 min/week moderate intensity or \geq 75		
	min/week vigorous intensity or ≥ 150		
	min/week moderate + vigorous intensity		
Healthy diet	Dietary score ≥3 (including the following 4		
	items: fruits and vegetables ≥ 4.5 cups/d; fish		
	≥198 g/wk; sweets/sugar-sweetened beverages		
	≤ 450 kcal/wk; soy protein ≥25 g/d.		
Total cholesterol	< 200 mg/dL (untreated)		
Blood pressure	< 120/80 mm Hg (untreated)		

^a Definitions were adapted from the recommendations of the Goals and Metrics Committee of the Strategic Planning Task Force of the American Heart Association.

Reference:

1. Lloyd-Jones DM, Hong Y, Labarthe D, et al; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 2010; 121:586-613.

Supplementary Table 2. RRs (95% CIs) for incident type 2 diabetes according to famine exposure in early life among 77925 participants by age-balanced analysis.

	Pre-famine and post-famine	Famine Exposure	
Case/Number	4050/64730 792/13195		
%	6.26	6.00	
Model 1	1.00 (ref)	0.96 (0.89-1.03)	
Model 2	1.00 (ref)	1.11 (1.03-1.20)	
Model 3	1.00 (ref)	1.14 (1.05-1.23)	
Model 4	1.00 (ref)	1.11 (1.03-1.19)	

Model 1 was unadjusted; Model 2 was adjusted for age and sex; Model 3 included model 2 plus education attainment (less than high school or high school or greater), drinking status (current drinker or not) and family history of diabetes (yes or no). Model 4 included model 3 plus individual cardiovascular health metrics. RRs, risk ratios; CIs, confidence intervals; BMI, body mass index.

	Case/n (%)	Non-exposed	Famine Exposure		P for	
			Fetal	Childhood	interaction	
Diet pattern					0.4357	
Non-ideal	2219/33651 (6.59)	1.00 (ref)	1.32, 1.12-1.55	1.26, 1.00-1.57		
Ideal	2623/44274 (5.92)	1.00 (ref)	1.09, 0.94-1.26	0.99, 0.80-1.22		
Physical activity					0.7508	
Non-ideal	4181/66912 (6.25)	1.00 (ref)	1.18, 1.05-1.32	1.05, 0.89-1.24		
Ideal	661/11013 (6.00)	1.00 (ref)	1.27, 0.92-1.75	1.51, 0.99-2.31		
Smoking Status					0.0013	
Non-ideal	1110/15836 (7.01)	1.00 (ref)	1.26, 1.01-1.57	0.99, 0.72-1.37		
Ideal	3732/62089 (6.01)	1.00 (ref)	1.17, 1.03-1.33	1.14, 0.96-1.36		
BMI					0.0003	
Non-ideal	3307/40399 (8.19)	1.00 (ref)	1.21, 1.06-1.38	1.10, 0.92-1.32		
Ideal	1535/37526 (4.09)	1.00 (ref)	1.12, 0.91-1.37	1.18, 0.89-1.56		
TC					0.1854	
Non-ideal	2222/30799 (7.21)	1.00 (ref)	1.14, 0.96-1.36	1.14, 0.91-1.43		
Ideal	2620/47126 (5.56)	1.00 (ref)	1.18, 1.02-1.36	1.03, 0.83-1.26		
BP					0.8310	
Non-ideal	3920/53046 (7.39)	1.00 (ref)	1.23, 1.08-1.39	1.17, 0.99-1.39		
Ideal	922/24879 (3.71)	1.00 (ref)	0.99, 0.78-1.25	0.86, 0.60-1.22		
Number of ICVHMs					0.0005	
≤1	947/9703 (9.76)	1.00 (ref)	1.62, 1.24-2.11	1.30, 0.90-1.88		
2	1553/19978 (7.77)	1.00 (ref)	1.02, 0.83-1.24	0.97, 0.74-1.27		
3	1452/23598 (6.15)	1.00 (ref)	1.01, 0.83-1.23	1.06, 0.81-1.39		
4	658/16579 (3.97)	1.00 (ref)	1.24, 0.94-1.64	1.31, 0.89-1.94		
≥5	232/8067 (2.88)	1.00 (ref)	0.93, 0.60-1.43	0.64, 0.34-1.22		

Adjusted for age, sex, education attainment (less than high school or high school or greater), drinking status (current drinker or not) and family history of diabetes (yes or no). BMI, body mass index; TC, total cholesterol; BP, blood pressure.

Supplementary Table 4. Multivariable-adjusted RRs (95% CIs) for incident type 2 diabetes according to famine exposure and combined ICVHMs by multiple testing via FDR

	Case/n	Cumulative Incidence, %	Non-exposed		Fetal famine Exposure		Childhood famine Exposure	
		,		RR (95%CI)	P value	RR (95%CI)	P value	
Diet pattern								0.5392
Non-ideal	2219/33651	6.59	1.00 (ref)	1.29 (1.10-1.52)	0.0017**	1.25 (1.00-1.56)	0.0499	
Ideal	2623/44274	5.92	1.00 (ref)	1.07 (0.93-1.25)	0.3486	1.01 (0.82-1.25)	0.8933	
Physical activity								0.5766
Non-ideal	4181/66912	6.25	1.00 (ref)	1.16 (1.03-1.30)	0.0140*	1.06 (0.90-1.25)	0.4526	
Ideal	661/11013	6.00	1.00 (ref)	1.25 (0.91-1.72)	0.1729	1.52 (0.996-2.31)	0.0523	
Smoking Status								0.0621
Non-ideal	1110/15836	7.01	1.00 (ref)	1.28 (1.02-1.59)	0.0296	1.03 (0.75-1.42)	0.8482	
Ideal	3732/62089	6.01	1.00 (ref)	1.14 (1.01-1.30)	0.0384	1.14 (0.96-1.36)	0.1272	
BMI								0.0018**
Non-ideal	3307/40399	8.19	1.00 (ref)	1.20 (1.05-1.36)	0.0063*	1.09 (0.91-1.31)	0.3381	
Ideal	1535/37526	4.09	1.00 (ref)	1.10 (0.90-1.35)	0.3614	1.17 (0.88-1.54)	0.2768	
TC								0.4103
Non-ideal	2222/30799	7.21	1.00 (ref)	1.15 (0.97-1.37)	0.0980	1.17 (0.93-1.46)	0.1770	
Ideal	2620/47126	5.56	1.00 (ref)	1.17 (1.01-1.35)	0.0358	1.06 (0.86-1.30)	0.5808	
BP								0.9710
Non-ideal	3920/53046	7.39	1.00 (ref)	1.22 (1.08-1.38)	0.0015**	1.18 (1.00-1.40)	0.0517	
Ideal	922/24879	3.71	1.00 (ref)	0.97 (0.76-1.23)	0.7946	0.87 (0.61-1.23)	0.4318	
Number of ICVHMs								0.0005**
≤1	947/9703	9.76	1.00 (ref)	1.59 (1.24-2.04)	0.0003**	1.28 (0.90-1.80)	0.1659	
2	1553/19978	7.77	1.00 (ref)	1.03 (0.85-1.26)	0.7533	1.02 (0.78-1.33)	0.8933	
3	1452/23598	6.15	1.00 (ref)	1.00 (0.83-1.22)	0.9656	1.01 (0.77-1.32)	0.9552	
4	658/16579	3.97	1.00 (ref)	1.14 (0.84-1.55)	0.3949	1.26 (0.82-1.93)	0.3000	
≥5	232/8067	2.88	1.00 (ref)	1.09 (0.67-1.78)	0.7147	0.79 (0.39-1.60)	0.5070	

Adjusted for age, sex, education attainment (less than high school or high school or greater), drinking status (current drinker or not) and family history of diabetes (yes or no). Individual cardiovascular health metrics were mutually adjusted. RRs, risk ratios; CIs, confidence intervals; BMI, body mass index; TC, total cholesterol; BP, blood pressure; ICVHMs, ideal cardiovascular health metrics. * FDR < 0.05; ** FDR < 0.01

Supplementary Table 5. Multivariable-adjusted ORs (95% CIs) for type 2 diabetes according to famine exposure and combined ICVHMs with further adjustment of area (rural/urban), marriage status, occupation, economic status.

		N7 .	Famine Exposure		De
	Case/n	Non-exposed	Fetal	Childhood	P for interaction
Diet pattern					0.5334
Non-ideal	2219/33651	1.00 (ref)	1.26, 1.07-1.48	1.21, 0.97-1.51	
Ideal	2623/44274	1.00 (ref)	1.06, 0.91-1.23	1.01, 0.82-1.24	
Physical activity					0.5256
Non-ideal	4181/66912	1.00 (ref)	1.14, 1.01-1.28	1.05, 0.89-1.24	
Ideal	661/11013	1.00 (ref)	1.23, 0.89-1.70	1.52, 0.997-2.31	
Smoking Status					0.0569
Non-ideal	1110/15836	1.00 (ref)	1.22, 0.98-1.52	0.99, 0.72-1.36	
Ideal	3732/62089	1.00 (ref)	1.13, 0.997-1.28	1.14, 0.96-1.35	
BMI					0.0018
Non-ideal	3307/40399	1.00 (ref)	1.18, 1.03-1.34	1.08, 0.90-1.29	
Ideal	1535/37526	1.00 (ref)	1.08, 0.88-1.33	1.16, 0.88-1.53	
TC					0.3412
Non-ideal	2222/30799	1.00 (ref)	1.14, 0.96-1.35	1.15, 0.92-1.44	
Ideal	2620/47126	1.00 (ref)	1.15, 0.99-1.32	1.05, 0.85-1.29	
BP					0.8845
Non-ideal	3920/53046	1.00 (ref)	1.20, 1.06-1.35	1.16, 0.98-1.37	
Ideal	922/24879	1.00 (ref)	0.97, 0.76-1.23	0.87, 0.62-1.24	
Number of ICVHMs					0.0003
≤1	947/9703	1.00 (ref)	1.51, 1.18-1.94	1.20, 0.85-1.69	
2	1553/19978	1.00 (ref)	1.01, 0.83-1.23	1.00, 0.76-1.30	
3	1452/23598	1.00 (ref)	0.99, 0.81-1.21	1.00, 0.76-1.30	
4	658/16579	1.00 (ref)	1.13, 0.84-1.54	1.27, 0.83-1.95	
≥5	232/8067	1.00 (ref)	1.07, 0.66-1.74	0.78, 0.39-1.59	

Adjusted for age, sex, education attainment (less than high school or high school or greater), drinking status (current drinker or not) and family history of diabetes (yes or no), area (rural/urban), marriage status, occupation, economic status. Individual cardiovascular health metrics were mutually adjusted. ORs, odds ratios; CIs, confidence intervals; BMI, body mass index; TC, total cholesterol; BP, blood pressure; ICVHMs, ideal cardiovascular health metrics.

Supplementary Table 6. Age-balanced analysis of the ICVHMs' influence on famine exposure and diabetes risk.

	Case/n	Cumulative Incidence, %	Non-exposed + childhood- exposed	Fetal-exposed	P interaction
Diet pattern					0.1231
Non-ideal	2219/33651	6.59	1.00 (ref)	1.16, 1.03-1.29	
Ideal	2623/44274	5.92	1.00 (ref)	1.07, 0.96-1.18	
Physical activity					0.2527
Non-ideal	4181/66912	6.25	1.00 (ref)	1.12, 1.03-1.22	
Ideal	661/11013	6.00	1.00 (ref)	1.00, 0.80-1.25	
Smoking Status					0.0165
Non-ideal	1110/15836	7.01	1.00 (ref)	1.26, 1.08-1.46	
Ideal	3732/62089	6.01	1.00 (ref)	1.07, 0.98-1.17	
BMI					0.0320
Non-ideal	3307/40399	8.19	1.00 (ref)	1.15, 1.05-1.25	
Ideal	1535/37526	4.09	1.00 (ref)	1.01, 0.88-1.17	
TC					0.8370
Non-ideal	2222/30799	7.21	1.00 (ref)	1.06, 0.95-1.19	
Ideal	2620/47126	5.56	1.00 (ref)	1.13, 1.02-1.26	
BP					0.5756
Non-ideal	3920/53046	7.39	1.00 (ref)	1.12, 1.03-1.22	
Ideal	922/24879	3.71	1.00 (ref)	1.04, 0.88-1.23	
Number of ICVHMs					0.0041
≤1	947/9703	9.76	1.00 (ref)	1.40, 1.19-1.65	
2	1553/19978	7.77	1.00 (ref)	1.02, 0.89-1.18	
3	1452/23598	6.15	1.00 (ref)	1.00, 0.87-1.15	
4	658/16579	3.97	1.00 (ref)	1.02, 0.82-1.25	
≥5	232/8067	2.88	1.00 (ref)	1.24, 0.88-1.74	

Adjusted for age, sex, education attainment (less than high school or high school or greater), drinking status (current drinker or not) and family history of diabetes (yes or no). Individual cardiovascular health metrics were mutually adjusted. RRs, risk ratios; CIs, confidence intervals; BMI, body mass index; TC, total cholesterol; BP, blood pressure; ICVHMs, ideal cardiovascular health metrics.