SUPPLEMENTARY DATA

Fasting Glucose and All-cause Mortality by Age in Diabetes: A Prospective Cohort Study.

Sang-Wook Yi, MD, PhD, Department of Preventive Medicine and Public Health, Catholic Kwandong University College of Medicine, Republic of Korea; **Sangkyu Park**, MD, PhD, Department of Biochemistry, Catholic Kwandong University College of Medicine, Republic of Korea; **Yong-ho Lee**, MD, PhD, Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea; **Beverley Balkau**, PhD, Center for Research in Epidemiology and Population Health (CESP), Team 5 (EpReC, Renal and cardiovascular Epidemiology), INSERM U-1018, France; **Jee-Jeon Yi**, PhD, Institute for Occupational and Environmental Health, Catholic Kwandong University, Republic of Korea

Correspondence: Sang-Wook Yi, MD, PhD, Department of Preventive Medicine and Public Health, Catholic Kwandong University College of Medicine, Bumil-ro 579, Gangneung, Gangwon-do, 25601, Republic of Korea; Tel: +82-33-649-7468; Fax +82-33-641-1074. e-mail: flyhigh@cku.ac.kr

Categorical and spline analyses

Fasting serum glucose concentrations were categorized into 10 groups (<65, 65-74, 75-84, 85-99 [Reference], 100-109, 110-125, 126-139, 140-169, 170-199, ≥200 mg/dL) and a restricted cubic spline transformation of fasting glucose with 5 knots (5th, 27.5th, 50th, 72.5th, and 95th percentiles in each group analyzed) was used in individuals with known prevalent diabetes to evaluate non-linear associations, including each subgroup analysis. In people without known diabetes, the same 5 knots (70, 85, 100, 120, and 140 mg/dL) was used to our previous study, which provided more detailed information on the corresponding associations (1).

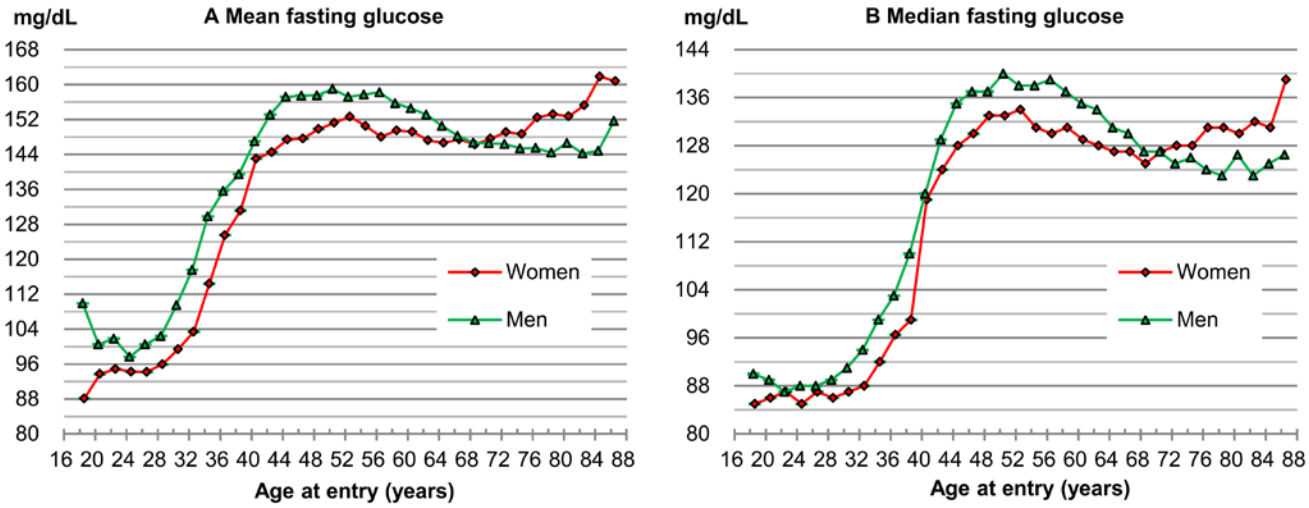
Optimal fasting glucose ranges associated with the lowest mortality

Apparent optimal ranges of fasting glucose were determined by general inspection of the curvilinear association using similar methods to our previous study (2). In general, the ranges with an excess risk below 5%, relative to the lowest potential risk (the lowest unweighted geometric mean of hazard ratios (HRs) in two consecutive fasting glucose categories in the categorical analysis, and the lowest hazard ratios in the spline analysis), were considered the optimal ranges. For example, in diabetic persons, the lowest potential risk was 0.98 (the geometric mean of HRs at fasting glucose of 85-99 [HR=1.00], and 100-109 mg/dL [0.96]; Table S2). The relative hazard at 126-139 mg/dL (HR=1.02) was 1.04 (1.02/0.98), and the excess risk was 4%. Thus, in diabetic individuals, a fasting glucose of 126-139 mg/dL was considered a part of the optimal range in the categorical analysis. In the spline analysis, in diabetic persons, the lowest potential risk was 0.999 at fasting glucose of 107 mg/dL, compared to 110 mg/dL. The relative hazard at 90 (HR=1.050), 91(1.044), 127 (1.045), 128 (1.048), and 129 (1.053) mg/dL was 1.051 (1.050/0.999), 1.045 (1.044/0.999), 1.046 (1.045/0.999), 1.049 (1.048/0.999), and 1.054 (1.053/0.999), respectively. Thus, a fasting glucose of 91-128, or “approximately” 90-130 mg/dL (when the range of nearest 5 or 10 mg/dL was used) was considered the optimal range in the spline analysis.

1. Yi SW, Park S, Lee YH, Park HJ, Balkau B, Yi JJ: Association between fasting glucose and all-cause mortality according to sex and age: a prospective cohort study. Sci Rep 2017;7:8194
2. Yi SW, Ohrr H, Shin SA, Yi JJ. Sex-age-specific association of body mass index with all-cause mortality among 12.8 million Korean adults: a prospective cohort study. Int J Epidemiol 2015;44:1696-1705

SUPPLEMENTARY DATA

Supplementary Figure S1. Mean and median concentrations of fasting glucose in individuals with known prevalent diabetes at baseline. To convert glucose from mg/dL to mmol/L, multiply by 0.0555.



SUPPLEMENTARY DATA

Supplementary Table S1. Characteristics of participants with and without known prevalent diabetes at baseline

		Total participants	Participants without known diabetes	Participants with known prevalent diabetes
Characteristics	**Classification**	**n = 12,815,006**	**n = 12,455,361**	**n = 359,645**
Age, years		44.4 (±14.2)	44.0 (±14.1)	56.8 (±12.1)
Fasting serum glucose, mg/dL		94.9 (±31.0)	93.4 (±27.5)	148.5 (±71.1)
BMI, kg/m^2		23.5 (±3.2)	23.5 (±3.2)	24.5 (±3.2)
Systolic blood pressure, mmHg		124.1 (±17.3)	123.9 (±17.2)	131.5 (±18.8)
Total cholesterol, mg/dL		194.2 (±49.0)	194.0 (±48.7)	201.2 (±58.3)
Sex	Men	7,292,064 (56.9)	7,090,089 (56.9)	201,975 (56.2)
	Women	5,522,942 (43.1)	5,365,272 (43.1)	157,670 (43.8)
Fasting serum glucose,	<65	112,618 (0.9)	110,963 (0.9)	1,655 (0.5)
mg/dL	65-74	1,165,357 (9.1)	1,155,098 (9.3)	10,259 (2.9)
	75-84	3,115,065 (24.3)	3,090,107 (24.8)	24,958 (6.9)
	85-99	5,100,173 (39.8)	5,047,726 (40.5)	52,447 (14.6)
	100-109	1,655,984 (12.9)	1,622,511 (13.0)	33,473 (9.3)
	110-125	935,017 (7.3)	882,724 (7.1)	52,293 (14.5)
	126-139	228,613 (1.8)	195,850 (1.6)	32,763 (9.1)
	140-169	232,256 (1.8)	177,790 (1.4)	54,466 (15.1)
	170-199	103,694 (0.8)	70,377 (0.6)	33,317 (9.3)
	≥200	166,229 (1.3)	102,215 (0.8)	64,014 (17.8)
Smoking status	Current smoker	3,653,334 (28.5)	3,565,515 (28.6)	87,819 (24.4)
	Never smoker	7,425,581 (57.9)	7,200,954 (57.8)	224,627 (62.5)
	Former smoker	1,099,436 (8.6)	1,061,104 (8.5)	38,332 (10.7)
	Missing	636,655 (5.0)	627,788 (5.0)	8,867 (2.5)
Alcohol use	3-7 days/week	1,237,846 (9.7)	1,197,771 (9.6)	40,075 (11.1)
	2/week-2/month	4,980,284 (38.9)	4,883,807 (39.2)	96,477 (26.8)
	Monthly or less	6,102,884 (47.6)	5,886,404 (47.3)	216,480 (60.2)
	Missing	493,992 (3.9)	487,379 (3.9)	6,613 (1.8)
Physical activity, at least once a week	Yes	5,158,300 (40.3)	4,989,114 (40.1)	169,186 (47.0)
Age, years	18-44	6,986,508 (54.5)	6,926,721 (55.6)	59,787 (16.6)
	45-64	4,580,410 (35.7)	4,379,009 (35.2)	201,401 (56.0)
	65-99	1,248,088 (9.7)	1,149,631 (9.2)	98,457 (27.4)

SUPPLEMENTARY DATA

Data were expressed as mean (± SD) or n (%).
Abbreviations: BMI, body-mass index; SD, standard deviation.
To convert glucose from mg/dL to mmol/L, multiply by 0.0555.
To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

SUPPLEMENTARY DATA

Supplementary Table S2. Hazard ratios* for mortality by 10 categories of fasting serum glucose, according to known prevalent diabetes status at baseline.

		Participants without known diabetes (n=12,455,361)			Participants with known prevalent diabetes (n=359,645)		
Age group	Fasting serum glucose (mg/dL)	No. of deaths	*P*-value	HR (95% CI)	No. of deaths	*P*-value	HR (95% CI)
All ages	<65	5,635	<.001	1.21 (1.18-1.24)	392	<.001	1.46 (1.32-1.61)
	65-74	46,605	<.001	1.06 (1.05-1.07)	1,628	<.001	1.12 (1.06-1.19)
	75-84	119,482	<.001	1.02 (1.01-1.03)	3,463	<.001	1.09 (1.04-1.13)
	85-99	219,095		1.00 (Reference)	6,944		1.00 (Reference)
	100-109	95,925	<.001	1.07 (1.07-1.08)	4,846	.027	0.96 (0.92-1.00)
	110-125	73,600	<.001	1.22 (1.21-1.23)	8,257	.127	1.03 (0.99-1.06)
	125-139	21,310	<.001	1.35 (1.33-1.37)	5,139	.290	1.02 (0.98-1.06)
	140-169	22,938	<.001	1.51 (1.49-1.53)	9,094	<.001	1.12 (1.09-1.16)
	170-199	10,236	<.001	1.74 (1.71-1.77)	6,311	<.001	1.31 (1.27-1.36)
	≥200	17,563	<.001	2.29 (2.25-2.32)	15,960	<.001	1.78 (1.73-1.83)
18-44 years	<65	703	<.001	1.20 (1.11-1.29)	8	.462	1.30 (0.64-2.64)
	65-74	6,342	.005	1.04 (1.01-1.07)	44	.570	1.10 (0.79-1.52)
	75-84	16,123	.657	1.00 (0.98-1.02)	122	.334	1.12 (0.89-1.40)
	85-99	25,538		1.00 (Reference)	208		1.00 (Reference)
	100-109	8,678	<.001	1.09 (1.06-1.12)	116	.009	1.35 (1.08-1.70)
	110-125	5,334	<.001	1.33 (1.29-1.37)	139	<.001	1.48 (1.19-1.84)
	126-139	1,233	<.001	1.53 (1.45-1.62)	104	<.001	1.96 (1.55-2.50)
	140-169	1,228	<.001	1.76 (1.66-1.86)	188	<.001	1.87 (1.53-2.29)
	170-199	535	<.001	1.98 (1.82-2.16)	166	<.001	2.35 (1.90-2.89)
	≥200	1,248	<.001	3.10 (2.93-3.28)	640	<.001	3.57 (3.03-4.21)
45-64 years	<65	1,825	<.001	1.23 (1.17-1.28)	133	<.001	1.76 (1.48-2.10)
	65-74	15,851	<.001	1.07 (1.05-1.08)	515	.002	1.16 (1.06-1.28)
	75-84	42,463	<.001	1.02 (1.01-1.03)	1,159	<.001	1.18 (1.10-1.27)
	85-99	79,397		1.00 (Reference)	2,277		1.00 (Reference)
	100-109	34,769	<.001	1.08 (1.07-1.09)	1,747	.577	1.02 (0.96-1.08)
	110-125	25,853	<.001	1.23 (1.21-1.25)	2,954	.205	1.04 (0.98-1.09)
	126-139	7,501	<.001	1.42 (1.38-1.45)	1,890	.508	1.02 (0.96-1.09)
	140-169	8,224	<.001	1.61 (1.57-1.65)	3,435	<.001	1.10 (1.04-1.16)
	170-199	3,919	<.001	1.82 (1.77-1.88)	2,548	<.001	1.32 (1.25-1.39)
	≥200	7,650	<.001	2.53 (2.47-2.59)	7,067	<.001	1.91 (1.82-2.00)
65-99 years	<65	3,107	<.001	1.19 (1.15-1.24)	251	<.001	1.33 (1.17-1.51)
	65-74	24,412	<.001	1.07 (1.05-1.08)	1,069	.004	1.10 (1.03-1.18)
	75-84	60,896	<.001	1.02 (1.01-1.03)	2,182	.094	1.04 (0.99-1.10)
	85-99	114,160		1.00 (Reference)	4,459		1.00 (Reference)
	100-109	52,478	<.001	1.06 (1.05-1.07)	2,983	<.001	0.91 (0.87-0.95)
	110-125	42,413	<.001	1.18 (1.17-1.19)	5,164	.930	1.00 (0.96-1.04)
	126-139	12,576	<.001	1.29 (1.26-1.31)	3,145	.702	0.99 (0.95-1.04)
	140-169	13,486	<.001	1.42 (1.39-1.44)	5,471	<.001	1.11 (1.07-1.16)
	170-199	5,782	<.001	1.64 (1.60-1.69)	3,597	<.001	1.27 (1.21-1.33)
	≥200	8,665	<.001	2.00 (1.95-2.04)	8,253	<.001	1.61 (1.55-1.67)

SUPPLEMENTARY DATA

Abbreviations: CI, confidence interval; HR, hazard ratio.
*HRs were calculated by Cox models stratified by age (baseline age, years: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85-99), after adjusting for age at baseline, sex (if applicable), smoking status, alcohol use, physical activity, body mass index, systolic blood pressure, and total cholesterol.
To convert glucose from mg/dL to mmol/L, multiply by 0.0555.