



Brief Original Report

Diabetes, body mass index and the excess risk of coronary heart disease, ischemic and hemorrhagic stroke in the Asia Pacific Cohort Studies Collaboration

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ABSTRACT

Objective. To examine the effects of diabetes on coronary heart disease, ischemic and hemorrhagic stroke and cardiovascular disease according to category of body mass index.

Methods. Data on 161,161 men and women from 31 cohorts (baseline years, 1966–99; mean follow-up, 2–24 years) from the Asia Pacific Cohort Studies Collaboration were analyzed using Cox regression, stratified by sex and study and adjusted for age, systolic blood pressure and smoking. Diabetes was self-reported in all but one study. Body mass index was divided into five categories according to the World Health Organization Asian criteria.

Results. The hazard ratio (diabetes v. not) for cardiovascular disease was 1.83 (95% confidence interval, 1.66–2.01). Across body mass index categories, this hazard ratio did not change significantly ($p = 0.19$). Similar lack of difference across body mass index groups was found for coronary heart disease ($p = 0.33$), ischemic stroke ($p = 0.97$) and hemorrhagic stroke ($p = 0.98$).

Conclusions. Body mass index does not modify the effect of diabetes on major cardiovascular outcomes.

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Introduction

It is widely accepted that excess body weight is a major risk factor for diabetes (Fu, 2008). It is currently unknown, however, whether the cardiovascular risks associated with diabetes are the same in obese compared with relatively non-obese individuals. If not, then this will have implications for how individuals with diabetes are managed. In order to examine this issue reliably, a large population

sample comprising individuals with a wide range of body mass index (BMI) values is required. Furthermore, this should include many lean or normal weight people with diabetes, a phenotype that is more typical of Asian than Western populations (Chan et al., 2009; Sairenchi et al., 2008). Thus, we used individual-participant data from the Asia Pacific Cohort Studies Collaboration (APCSC) to determine whether the cardiovascular hazards associated with diabetes are equivalent in individuals across categories of BMI.

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Research design and methods

Methods of study identification, and characteristics of studies included have been reported elsewhere (Asia Pacific Cohort Studies Collaboration, 2003, 2004; Woodward et al., 2006). All studies were independently instigated and conducted. Studies were eligible for inclusion in APCSC if they satisfied the following criteria: 1) a study population from the Asia Pacific region; 2) prospective study design; 3) at least 5000 person-years of follow-up recorded; 4) date of birth (or age), sex and blood pressure at baseline; 5) date of death (or the age at death) recorded during follow-up. For this report, only those aged ≥ 30 years at study entry, with information recorded on diabetes status, BMI and smoking status at baseline were included.

The baseline diabetes status of participants was determined by self-reported history except in one study where an oral glucose tolerance test was used. In most studies, blood pressure was measured at rest in the seated position using a standard mercury sphygmomanometer. BMI was calculated as weight (kg) divided by height squared (m²). Smokers were classified into current, former and never smokers. All studies reported deaths by underlying cause and a subset of studies also reported non-fatal cardiovascular disease (CVD) events; fatal and non-fatal events were combined. Most studies used database linkages to identify deaths, while others also included scheduled follow-up visits or examined hospital records, particularly to identify non-fatal events, defined as those that did not result in death within 28 days. Outcomes were classified according to the Ninth Revision of International Classification of Disease (ICD-9). The outcomes analyzed were:

coronary heart disease (CHD) (ICD-9: 410–414), hemorrhagic stroke (ICD-9: 431.0–432.9), ischemic stroke (ICD-9: 433.0–434.9) and CVD (ICD-9: 390–459).

Sex- and study-stratified Cox proportional hazard models, adjusted for age, systolic blood pressure and smoking status, were used to examine the relationships between diabetes, BMI and CVD. BMI was categorized into five groups according to WHO Asia criteria (WHO/IASO/IOTF, 2000): underweight: BMI < 18.5 kg/m²; normal weight: 18.5 < BMI < 23 kg/m²; high-normal: 23 < BMI < 25 kg/m²; overweight: 25 < BMI < 30 kg/m²; obese: BMI > 30 kg/m². The hazard ratios (HRs) and 95% confidence intervals (95% CI) for diabetes compared with no diabetes within each category of BMI were estimated, and effect modification by BMI was assessed using likelihood ratio tests (Woodward, 2005). For total CVD (where numbers were sufficient to achieve reliable results), subgroup analyses were performed by age (<65 years v ≥ 65 years); region (Asia v Australia and New Zealand) and sex. We further estimated HRs (95% CI) after left-censoring the data, removing the first 2 years of follow-up, to explore the effect of reverse causation (Flegal et al., 2011). Analyses were conducted using SAS version 9.2.

Results

Table 1 shows the baseline characteristics of the studies. Overall 161,161 individuals (46% Asian, 46% women) from 31 cohorts contributed data to these analyses. The mean (standard deviation) BMI

Table 1
Baseline characteristics of the studies in Asia Pacific Cohort Studies Collaboration, of which baseline years 1966–99, mean follow-up 2–24 years.

Study	Country	Baseline years	Number of participants	Female (%)	Age (years)		Diabetes (%)	Body mass index (kg/m ²)		Systolic BP (mm Hg)		Current smokers (%)	Mean follow-up (years)	Number of events (fatal and non-fatal)			
					Mean	SD		Mean	SD	Mean	SD			CHD	Isch	Hem	CVD
Beijing Aging	China	1992	2084	51	70	9	4	23	4	141	25	30	4	0	0	0	202
CISCH	China	1992–93	2160	51	44	7	2	25	3	118	17	27	3	14	0	0	23
East Beijing	China	1977–94	833	53	49	12	7	24	3	128	23	27	14	14	10	7	45
Huashan	China	1990–92	1859	52	53	12	0	23	3	126	21	25	2	3	10	6	22
Seven Cities Cohorts	China	1987	10687	54	54	12	1	23	4	130	24	35	6	82	115	180	611
Yunnan	China	1992	6580	3	56	9	1	22	3	124	21	68	4	18	12	93	222
Hong Kong	Hong Kong	1985–91	2816	57	78	7	8	22	4	150	24	19	2	69	4	15	171
Aito Town	Japan	1980–83	1689	57	51	9	3	23	3	136	21	19	15	15	0	5	58
Akabane	Japan	1985–86	1834	56	54	8	1	22	3	125	19	28	11	27	15	5	77
Civil Service Workers	Japan	1990–92	9315	33	47	5	2	22	3	126	18	38	6	1	0	1	12
Konan	Japan	1987–95	1087	56	54	14	3	22	3	131	19	30	6	2	6	3	23
Miyama	Japan	1988–90	1028	55	60	9	5	22	3	132	22	29	6	2	4	0	18
Ohasama	Japan	1992–93	2195	63	59	11	10	23	3	128	17	20	4	5	34	10	66
Saitama	Japan	1986–90	3541	62	55	11	2	22	3	135	20	28	10	24	26	15	118
Shibata	Japan	1977	2329	58	57	11	1	22	3	131	21	33	16	66	75	36	337
Shigaraki Town	Japan	1991–97	3734	59	57	14	5	23	3	132	19	29	4	3	4	2	29
Shirakawa	Japan	1974–79	4391	54	50	11	1	22	3	127	22	35	17	65	39	31	193
Tanno/Soubetsu	Japan	1977	1963	53	51	7	6	24	3	133	21	38	15	24	10	16	73
Singapore Heart	Singapore	1982–97	1727	49	46	11	12	24	4	127	23	22	11	66	21	7	132
Singapore NHS92	Singapore	1992	2469	53	44	10	13	24	4	121	20	18	6	33	13	4	76
CVDFACTS	Taiwan	1988–96	4874	54	51	13	3	24	3	120	19	22	6	13	7	7	59
Kinmen	Taiwan	1993–97	1179	48	63	9	8	23	3	139	22	30	3	7	0	0	31
EGAT	Thailand	1985	3492	23	43	5	2	23	3	121	16	43	10	33	0	0	51
Total Asia			73866	46	53	13	3	23	3	128	22	34	8	586	405	443	2649
Longitudinal Study of Aging	Australia	1992–93	1560	48	78	6	8	26	4	148	22	8	5	74	6	7	194
National Heart Foundation	Australia	1989–90	7587	51	48	11	2	26	4	128	19	23	8	75	2	0	113
Busselton	Australia	1966–81	3908	51	52	14	2	25	4	146	27	34	24	838	153	65	1439
Melbourne	Australia	1990–94	41263	59	55	9	4	27	4	138	20	11	9	323	11	35	550
Newcastle	Australia	1983–94	3376	50	54	11	4	27	5	133	20	18	6	42	0	3	58
Perth	Australia	1978–94	8838	48	48	11	2	25	4	132	20	25	13	193	4	10	311
Western Australia AAA Screenees	Australia	1996–99	12193	0	72	4	12	27	4	157	21	11	3	322	113	31	602
Fletcher Challenge	NZ	1992–94	8570	28	48	13	3	27	4	127	17	22	6	261	67	9	450
Total ANZ			87295	45	56	13	4	27	4	138	22	16	8	2128	356	160	3717
Total			161161	46	54	13	4	25	4	134	23	24	8	2714	761	603	6366

Diabetes was determined based on a reported history of diabetes at baseline, except in the 1992 Singapore National Health Survey, where status was also dependent on diagnosis by an oral glucose tolerance test.

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