Diabetes in Asia
Epidemiology, Risk Factors, and Pathophysiology

Juliana C. N. Chan, MBChB, MD
Vasanti Malik, MSc
Weiping Jia, MD, PhD
Takashi Kadowaki, MD, PhD
Chittaranjan S. Yajnik, MD, PhD
Kun-Ho Yoon, MD
Frank B. Hu, MD, PhD

Context With increasing globalization and East-West exchanges, the increasing epidemic of type 2 diabetes in Asia has far-reaching public health and socioeconomic implications.

Objective To review recent data in epidemiologic trends, risk factors, and complications of type 2 diabetes in Asia.

Evidence Acquisition Search of MEDLINE using the term *diabetes* and other relevant keywords to identify meta-analyses, systematic reviews, large surveys, and cohort studies. Separate searches were performed for specific Asian countries. The review was limited to English-language articles published between January 1980 and March 2009; publications on type 1 diabetes were excluded.

Evidence Synthesis The prevalence of diabetes in Asian populations has increased rapidly in recent decades. In 2007, more than 110 million individuals in Asia were living with diabetes, with a disproportionate burden among the young and middle aged. Similarly, rates of overweight and obesity are increasing sharply, driven by economic development, nutrition transition, and increasingly sedentary lifestyles. The "metabolically obese" phenotype (ie, normal body weight with increased abdominal adiposity) is common in Asian populations. The increased risk of gestational diabetes, combined with exposure to poor nutrition in utero and overnutrition in later life in some populations, may contribute to the increasing diabetes epidemic through "diabetes begetting diabetes" in Asia. While young age of onset and long disease duration place Asian patients with diabetes at high risk for cardiorenal complications, cancer is emerging as an important cause of morbidity and mortality.

Conclusions Type 2 diabetes is an increasing epidemic in Asia, characterized by rapid rates of increase over short periods and onset at a relatively young age and low body mass index. Prevention and control of diabetes should be a top public health priority in Asian populations.

JAMA. 2009;301(20):2129-2140 www.jama.com

Once considered a disease of the West, type 2 diabetes is now a global health priority.[1] The International Diabetes Federation has predicted that the number of individuals with diabetes will increase from 240 million in 2007 to 380 million in 2025, with 80% of the disease burden in low- and middle-income countries.[2] More than 60% of the world's population with diabetes will come from Asia, because it remains the world's most populous region. The number of individuals with diabetes and impaired glucose tolerance (IGT) in each Asian country will increase substantially in coming decades (TABLE 1).[1] Unlike in the West, where older populations are most affected, the burden of diabetes in Asian countries is disproportionately high in young to middle-aged adults (FIGURE).[2]

Asia has undergone marked economic and epidemiologic transition in recent decades. Increasing globalization and East-West exchanges have been accompanied by increasing population movements, changes in food supply and dietary patterns, technology transfer, and cultural admixtures. In the recent World Economics Forum Report, the increasing burden of chronic diseases including diabetes was highlighted as a major global risk predicted to cause substantial financial loss resulting from increased health care expenditure and lost productivity.[3] However, there is considerable heterogeneity in ethnicity, cultures, and stages of socioeconomic development within Asia, all of which affect clinical presentation, management, and prevention of diabetes. In this article, we review epidemiologic trends and complications of type 2 diabetes in Asian populations and discuss risk factors implicated in this epidemic.

EVIDENCE ACQUISITION

We searched MEDLINE using the term *diabetes* and other relevant keywords (*diabetes mellitus*, *metabolic syndrome*,

Author Affiliations: Hong Kong Institute of Diabetes and Obesity, Department of Medicine, and Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China (Dr Chan); Departments of Nutrition and Epidemiology, Harvard School of Public Health, and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, Massachusetts (Drs Malik and Hu); Department of Endocrinology and Metabolism, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, China (Dr Jia); Department of Metabolic Diseases, Graduate School of Medicine, University of Tokyo, Tokyo, Japan (Dr Kadowaki); Diabetes Unit, KEM Hospital Research Center, Pune, India (Dr Yajnik); and Department of Endocrinology and Metabolism, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea (Dr Yoon).
Corresponding Authors: Juliana C. N. Chan, MBChB, MD, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, The Prince of Wales Hospital, Shatin, Hong Kong SAR, China (jchan@cuhk.edu.hk) and Frank B. Hu, MD, PhD, Departments of Nutrition and Epidemiology, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115 (frank.hu@channing.harvard.edu).

diabetic complications, *clinical studies*, *registry*, *prospective cohorts*, *cross-sectional cohorts*, *case-control*, *cohorts*, *epidemiology*, *prevalence*, *incidence*, *causes*, *causation*, *diagnosis*, *prognosis*, *socioeconomic status*, *ethnicity*, *depression*, *psychosocial stress*, *smoking*, *haemoglobinopathy*, *thalassaemia*, *visceral fat*, *hepatitis*, *C reactive proteins*, *infections*, *tobacco*, *alcohol*, *dietary factors*, *persistent organic pollutants*, *environmental toxins*, *pollutants*, *urbanization*, *acculturation*, *iron*, *iron overload*, *birthweight*, *body mass index*, *waist circumference*, *central obesity*, *waist hip ratio*, *exercise*, *physical activity*, *risk score*, *risk equation*, *risk prediction*, *adolescent obesity*, *gestational diabetes*, *inflammation*, *nutritional transition*, *sleep*, *television watching*).

Separate searches were performed for specific Asian countries. We limited the searches to English-language articles published between January 1980 and March 2009; non–English-language studies were excluded, because the quality of these studies is difficult to evaluate. Publications on type 1 diabetes were excluded. High-priority articles included meta-analyses, systematic reviews, large surveys, and cohort studies.

Table 1. Top 10 Countries in Asia With the Highest Number of Persons With Type 2 Diabetes and Impaired Glucose Tolerance in the Age Group 20 to 79 Years in 2007 and Projected Data in 2025[a]

Country	Diabetes 2007	Diabetes 2025	Impaired Glucose Tolerance 2007	Impaired Glucose Tolerance 2025
India	40 850	69 882	35 906	56 228
China	39 809	59 270	64 323	79 058
Japan	6978	7171	12 891	12 704
Bangladesh	3848	7416	6819	10 647
Korea	3074	4163	3224	4240
Thailand	3162	4660	1896	2399
Philippines	3055	5572	4410	7582
Indonesia	2887	5129	14 144	20 597
Malaysia	1530	2743	2915	4442
Vietnam	1294	2500	1175	1902
Subtotal[b]				
Western Pacific	66 993	99 401	111 898	142 693
Southeast Asia	46 543	80 341	45 169	70 525
Grand total Asia[b]	113 536	179 742	157 067	213 218

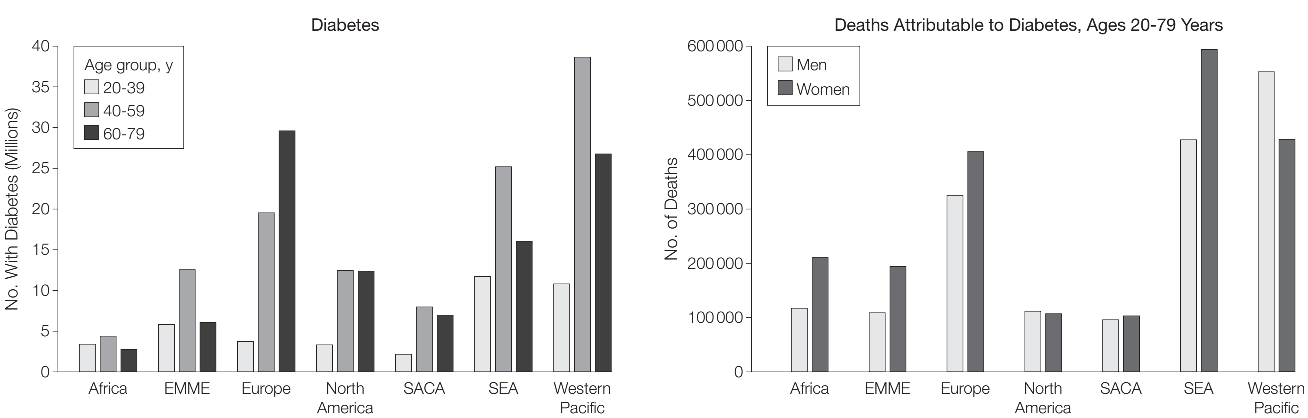
[a] Source: International Diabetes Federation.[2] All values are in thousands.
[b] Includes numbers from Asian countries not shown here.

EVIDENCE SYNTHESIS

Epidemiologic Trends of Diabetes in Asia

In this global epidemic of diabetes, Asian countries undergoing economic and nutritional transitions have experienced a particularly notable increase (TABLE 2).[4-46] In China, the prevalence of diabetes increased from 1% in 1980 to 5.5% in 2001,[7] with much higher rates in urban areas such as Shanghai.[51] Nearly 10% of Chinese adults residing in affluent regions such as Hong Kong and Taiwan have diabetes.[52] Among individuals with diabetes, two-thirds in Mainland China and one-half in Hong Kong and Taiwan remain undiagnosed.[52]

Figure. Number of Persons With Diabetes in Different Age Groups and Number of Deaths Attributable to Diabetes in Different Regions of the World in 2007



Source: International Diabetes Federation.[2] EMME indicates Eastern Mediterranean/Middle East; SACA, South America/Central America; SEA, Southeast Asia (comprises Bangladesh, Bhutan, India, Maldives, Mauritius, Nepal, and Sri Lanka [total population, 770 350 000; estimated prevalence of diabetes in the region, 6%]). Western Pacific comprises Australia, Brunei Darussalam, Cambodia, China, Hong Kong, Macau, Cook Islands, Fiji, French Polynesia, Guam, Indonesia, Japan, Kiribati, Korea (Democratic People's Republic of), Korea (Republic of), Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federal States of), Mongolia, Myanmar, Nauru, New Caledonia, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Samoa, Singapore, Solomon Islands, Taiwan, Thailand, Timor-Leste, Tokelau, Tonga, Tuvalu, Vanuatu, and Vietnam (total population, 1 468 598,000; estimated prevalence of diabetes in the region, 7.6%).

Table 2. Trend of Prevalence of Type 2 Diabetes in Asia in Comparison With That in the United States During the Last 2 to 3 Decades

Country	Sample	Age, y	Women, %	Mean BMI in Survey Population	Diabetes: Diagnosis Method	Diabetes: Criteria[a]	Diabetes: Prevalence, %	Age Adjusted
United States[4-6]								
1976-1980	National	20-74	51.9	25.3	FPG	ADA 1997	5.3	Yes
1999-2000	National	20-74	50.4	28.0	FPG	ADA 1997	8.2	Yes
2005-2006	National	20-74	51.07	28.7	FPG/ OGTT	ADA 1997	12.6	Yes
Mainland China[7-9]								
1980	14 provinces	NA	Male/Female	NA	FPG/ OGTT	>130/>200 mg/dL	≈ 1	Yes
1994-1995	19 provinces	25-64	44.8	23.8 (NGT) 25.2 (diabetes)	FPG/ OGTT	WHO 1985	2.5	Yes
2000/2001	31 provinces	35-74	51.4	24.3 (urban) 23.3 (rural) 24.8 (North) 22.8 (South)	FPG	ADA 1997	5.5	No
Hong Kong[10,11]								
1993	Employees[b]	30-64	39.8	NA	FPG/ OGTT	WHO 1985	7.7	No
1995-1996	Entire region	25-74	Men/Women	23.5 (NGT) 26.6 (impaired fasting glucose [ADA criteria])	FPG/ OGTT	WHO 1999	9.8	
Taiwan[12,13]								
1987-1988	Pu-Li	≥30	52.1	23.0 (NGT) 23.7 (diabetes; 23.0 (previous, 24.6 (new)	FPG/ OGTT	WHO 1985 (modified)	6.9 (previous) 4.4 (new)	Yes
1996	Tainan city	≥20	48.7	Not reported	OGTT	WHO 1985	9.2	Yes
Japan[14-16]								
1981-1982	Tokyo	≥30	21.6	Not reported	FPG/ OGTT	WHO 1980	3.6	No
1988	Hisayama, suburban	40-79	54.2	22.9 (men) 23 (women)	OGTT	WHO 1985	10.2	Yes
1990-1992	Fungata, rural	≥40	56.3	Not reported	OGTT	WHO 1985	10.1	No
Korea[17-19]								
1991	Yonchon County, South Korea	30-64	56.3	Not reported	OGTT	WHO 1985	7.2	Yes
1997	Chongup-rural	>30	41.4	23.6 (NGT) 25.5 (IGT)	OGTT	ADA 1997	6.9	Yes
2001	Nationwide	>20	57	23.3 (NGT men) 24.2 (IGT men) 22.8 (NGT women) 24.4 (IGT women)	FPG	ADA 1997	7.6	Yes
2003	Chongup-rural	≥30	40.8	22.9 (NGT, men) 24.4 (diabetes, men) 24.3 (NGT, women) 26.2 (diabetes, women)	OGTT	ADA 1997	11.7	Yes
India[20-22]								
1979	Multicenter	NA	NA	NA	NA	NA	3 (urban) 1.3 (rural)	No
1999-2002	Nationwide	≥25	50.8	Not reported	OGTT	WHO 1999	4.3 5.6 (urban) 2.7 (rural)	Yes
2003-2005	Nationwide	15-64	51	23.1 (urban males) 24 (urban females) 20.3 (rural males) 20.8 (rural females)	Self-report	NA	4.5 7.3 (urban) 3.1 (rural)	Yes
Pakistan[23]								
1994-1999	Nationwide	≥25	65.2	22.4 (urban men) 24.5 (urban women) 22.6 (rural men) 25 (rural women)	OGTT	WHO 1985	6 (urban men) 3.5 (urban women) 3.3 (rural men) 2.5 (rural women)	No

(continued)

Table 2. Trend of Prevalence of Type 2 Diabetes in Asia in Comparison With That in the United States During the Last 2 to 3 Decades (continued)

					Diabetes			
Country	Sample	Age, y	Women, %	Mean BMI in Survey Population	Diagnosis Method	Criteria[a]	Prevalence, %	Age Adjusted
Bangladesh[24-26]								
1997	Dhaka city-suburban	30-64	35.2	20.17 (NGT, men) 21.6 (diabetes, men) 19.7 (NGT, women) 23 (diabetes, women)	FPG/OGTT	WHO 1985	4.5	Yes
1999	Chandra region-rural	≥20	57.2	20.2	FPG/OGTT	WHO 1999	2.3	No
2004	Chandra region-rural	≥20	59.8	20.7	FPG/OGTT	WHO 1999	6.8	No
2005	Dhaka city-urban	≥20	52.9	19.4	FPG/OGTT	WHO 1999	8.1	No
Nepal[27-29]								
1990	Kathmandu/Kabhre	≥20	52	19.5 (suburban men) 20 (rural men) 19.6 (suburban women) 20.4 (rural women)	FPG	ADA 1997 (post hoc)	1.4 (suburban) 0.3 (rural)	No
1999-2001	Urban/rural	≥20	53.7	Not reported	FPG	ADA 1997	14.6 (urban) 2.5 (rural)	No
2007	Semi-urban	21-94	60	NA	NA		9.5	NA
Sri Lanka[30,31]								
1994[c]	Suburban	30-64	50.7	Not reported	OGTT	WHO 1985	5.0	Yes
2005-2006	National	>20	60	21.2 (NGT) 23.8 (diabetes)	FPG/OGTT	ADA 1997	10.3	Yes
Indonesia[32,33]								
1981-1982	Jakarta-urban	≥15	52.8	NA	OGTT	WHO 1980	1.63	No
1995	Jakarta-urban	NA	Male/Female	NA	NA	NA	5.7	NA
Malaysia[34-36]								
1982	National	NA	Male/Female	NA	NA	NA	2.1	NA
1992-1995	Kelantan-Malay/rural	≥30	Men/Women	NA	FPG/OGTT	WHO 1980	10.5	NA
2005-2006	National	25-64	Men/Women	NA	FPG	≥7 mmol/L	11	NA
Thailand[37-39]								
1991	National	≥30	56.5	22 (men) 23.5 (women)	FPG	≥7.8 mmol/L	2.4 (men) 3.7 (women)	Yes
2000	National	≥35	Men/Women	23.8 (NGT) 25.4 (diabetes)	FPG	≥7 mmol/L	9.6	Yes
2004	National	≥15	Male/Female	22.3 (NGT) 28.3 (diagnosed diabetes)	FPG	≥7 mmol/L	6.7	Yes
Vietnam[40,41]								
1990	Hanoi	30-64	53.5	19.3 (men) 20.1 (women) (subset of 116 with new diabetes)	OGTT	WHO 1985	1.4	Yes
2001	Ho Chi Minh	≥15	74.4	21.1 (NGT, males) 21.8 (NGT, females) 22.7 (diabetes, men) 23.3 (diabetes, women)	FPG	ADA	3.8	Yes
Cambodia[42]								
2004	Rural/suburban	30-64	63.6	20.4 (men) 21.3 (women)	OGTT	WHO 1999	9.7 (suburban) 5.6 (rural)	Yes
Philippines[43]								
1982-1983	Luzon-urban	Adults	Men/Women	NA	OGTT	≥11.1 mmol/L	3.3	No
2002	Luzon-urban	20-65	63.5	22.9 (men) 23.3 (women)	OGTT	WHO 1999	4.8	Yes
							5.1	No

(continued)

Table 2. Trend of Prevalence of Type 2 Diabetes in Asia in Comparison With That in the United States During the Last 2 to 3 Decades (continued)

Country	Sample	Age, y	Women, %	Mean BMI in Survey Population	Diabetes: Diagnosis Method	Diabetes: Criteria[a]	Diabetes: Prevalence, %	Age Adjusted
Singapore[44-46]								
1984-1985	National	18-69	Men/Women	25.8 (Chinese) 27 (Malay) 24.1 (Indian)[d]	OGTT	WHO 1985	4.7[e]	Yes
1992	National	18-69	49.5	22.3 (Chinese men) 22.8 (Malay men) 23.6 (Indian men) 21.3 (Chinese women) 23.8 (Malay women) 23.7 (Indian women)	OGTT	WHO 1985	8.4[f]	Yes
2004	National	18-69	Men/Women	NA	FPG/OGTT	WHO 1985	8.9 (men) 7.6 (women)[g]	NA

Abbreviations: ADA, American Diabetes Association; BMI, body mass index; FPG, fasting plasma glucose; IGT, impaired glucose tolerance; NA, not available; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; WHO, World Health Organization.
SI conversion factor: To convert glucose values to mg/dL, divide by 0.0555.
[a] ADA 1997[47]: fasting plasma glucose level 7.0 mmol/L or greater; WHO 1980[48]: fasting plasma glucose level 7.8 mmol/L or greater or 2-hour plasma glucose level 11.1 mmol/L or greater; WHO 1985[49]: fasting plasma glucose level 7.8 mmol/L or greater or 2-hour plasma glucose level 11.1 mmol/L or greater; WHO 1998[50]: fasting plasma glucose level 7.0 mmol/L or greater or 2-hour plasma glucose level 11.1 mmol/L or greater.
[b] Employees from 2 work sites of a major public utility company and regional hospital.
[c] Publication year.
[d] Mean BMI among individuals with diabetes.
[e] Age-standardized prevalence of diabetes was 4.2 in Chinese men, 4 in Chinese women, 9.1 in Malay men, 6.4 in Malay women, 12.3 in Indian men, and 5.5 in Indian women.
[f] Age-standardized prevalence of diabetes was 12.2 in Asian Indians, 10.1 in Malays, and in 7.8 in Chinese.
[g] Prevalence of diabetes was 7.1 in Chinese, 15.3 in Indians, and 11 in Malays (unsure if age-standardized).

In urban Indian adults, diabetes prevalence increased from 3% in the early 1970s to 12% in 2000, with a narrowing rural-urban gradient.[20] In 2006, the rate of type 2 diabetes in rural South India was 9.2%, compared with an increase in urban South India from 13.9% in 2000 to 18.6% in 2006.[53]

In rural Bangladesh, prevalence of diabetes increased from 2.3% to 6.8% between 1999 and 2004.[24] In a national survey in 2001, 8% of Korean adults had diabetes, with little difference between urban and rural areas.[17] In a nationwide survey in Singapore in 1998, Indians had the highest prevalence of diabetes (12.8%), followed by Malays (11.3%) and Chinese (8.4%).[54] Similarly, 11% of Malays living in Malaysia have diabetes.[34,35] Other Asian countries including Japan, Sri Lanka, Indonesia, Thailand, and Vietnam also have experienced a marked increase in prevalence of diabetes (Table 2). While some Asian countries like China and India have a very large number of patients with diabetes, the prevalence of diabetes can be as high as 40% in some Pacific Island populations.[55]

Risk Factors for the Diabetes Epidemic in Asia

Increasing Overall and Abdominal Obesity. Asians have lower rates of overweight and obesity than their Western counterparts, using conventional definitions (body mass index [BMI] ≥25 for overweight and ≥30 for obesity, calculated as weight in kilograms divided by height in meters squared). Despite lower BMI, some Asian countries have similar or even higher prevalence of diabetes than Western countries.[56] These data confirm that the risk of type 2 diabetes starts at a lower BMI for Asians than for Europeans.[57]

In China, the prevalence of overweight (BMI ≥25) in adults increased from 14.6% to 21.8% between 1992 and 2002.[58] In a cross-sectional survey of 15 540 Chinese adults aged 35 to 74 years in 2000-2001, the age-standardized prevalence of overweight was 26.9% in men and 31.1% in women, with higher rates in northern than in southern China as well as higher rates in urban than in rural residents.[59] In India, between 2003 and 2005, the prevalence of overweight ranged from 9.4% in rural men to 38.8% in urban women.[21] Using the same BMI cutpoint, 28.6% of adults living in urban Pakistan were overweight.[23] In developing countries, obesity in adults is not necessarily a disease of the socioeconomic elite, as is commonly believed.[60] In fact, the burden of obesity and diabetes tends to shift toward lower socioeconomic status groups as a country's gross national product increases.[61]

The increasing trend of childhood obesity in Asia places many young individuals at high risk for type 2 diabetes in early adulthood. In China, based on the 2000 reference values from the US Centers for Disease Control and Prevention, 22.9% of boys and 10.4% of girls attending urban schools were overweight.[62] Among schoolchildren in urban South India, 17.8% of boys and 15.8% of girls were overweight.[20] Similar rates have been reported in Malaysia,[36] Korea,[63,64] and Thailand.[65] In Hong Kong, 2.3% of adolescents have the metabolic syndrome, with family history of diabetes, BMI, and low academic performance as independent predictors.[66]

Asian populations, especially those of South Asian descent, are more prone to abdominal obesity and low muscle mass with increased insulin resistance compared with their Western counterparts.[20,67-73] Thus, waist circumference reflecting central obesity is a useful measure of obesity-related risk of type 2 diabetes, especially in individuals with normal BMI values.[67,74] In Singapore, for the same age, sex, and BMI, Indians had the highest body fat percentage, followed by Malays and Chinese. All 3 groups had a higher body fat percentage than whites.[70]

Using imaging technology (such as computed tomography scan) to measure total body fat and specific depots of fat, healthy Chinese and South Asian individuals were found to have a greater amount of visceral adipose tissue than Europeans with the same BMI or waist circumference.[75] These data suggest that the increased risk of type 2 diabetes in Asian populations may be attributed to increased abdominal and visceral adiposity for a given BMI. Despite having a lower body weight, Indian infants have higher subcutaneous fat, leptin, and insulin levels than white infants.[76] This "metabolically obese" phenotype (eg, normal weight by conventional BMI standards but increased abdominal adiposity) has been associated with increased risk of insulin resistance and diabetes.[77] In Asian populations, the amount of visceral fat (including mesenteric fat) and fatty liver was significantly associated with subclinical atherosclerosis.[78] In addition, increased waist circumference has been associated with substantially increased risk of developing diabetes[67,79,80] as well as increased risk of cardiovascular and all-cause mortality, independent of BMI.[81-84]

Nutrition Transition and Changes in Diet and Lifestyle. In many Asian countries, rapid socioeconomic development has led to a concurrent shift in infrastructure, technology, and food supply that promotes overnutrition and sedentary lifestyles. Traditional dietary patterns are disappearing as Asians adapt to increasingly industrial and urban conditions resulting from globalization. Rapid nutrition transition has left many countries facing coexisting problems of overnutrition and undernutrition.[60,85]

In China between 1992 and 2002, the proportion of energy intake from animal foods increased from 9.3% to 13.7% and that from fats from 22% to 29.8%.[58] In India the change was more pronounced among urban residents, who consumed 32% of energy from fat compared with 17% in rural residents.[86] Substantial increases in animal fat intake also have been reported in Vietnam,[40] Japan,[87] Korea,[64,88] and Thailand.[89] Vegetable ghee, such as *Dalda*—a clarified butter commonly used in cooking in India and other southeastern Asian countries—contains *trans* fatty acid levels as high as 50%.[90] Higher intake of *trans* fatty acids has been associated with weight gain, increased cardiometabolic risk, and insulin resistance.[91-93]

Polished rice and refined wheat form the basis of most Asian diets with high glycemic index and glycemic load values.[94] The glycemic index of Vietnamese rice ranges from 86 to 109.[72] In a prospective cohort study of middle-aged Chinese women, a high intake of foods with a high glycemic index or glycemic load, especially rice, is associated with a 2-fold increased risk of type 2 diabetes,[95] especially in overweight and obese individuals. Similar findings have been reported in Japan.[96] Consumption of sugar-sweetened beverages, an important contributor of dietary glycemic load and excess calories, has increased rapidly worldwide, particularly in Asia.[97]

Increased urbanization and universal use of automobiles has caused many Asians to shift from a physically active, agrarian lifestyle marked by energy scarcity to a sedentary lifestyle marked by energy surplus. In developing countries, a rapid uptake of technologies has been accompanied by increasing shifts from agriculture and increasing employment in manufacturing and services.[90] In Asia, automobiles are rapidly replacing bicycles as the primary mode of transportation. In China, an average of 1 in 10 Beijing permanent residents owns a car.[58] In the past decade, the annual rate of increase in motor vehicle ownership in India was approximately 11%.[85]

Psychosocial stress, depression, and short sleeping hours, which have become increasingly common in developing countries undergoing rapid economic developments, have been associated with higher risk of the metabolic syndrome and diabetes in Asian populations.[98-101] In a meta-analysis, depression was associated with a 60% increased risk of type 2 diabetes, while the latter was associated with a 15% increased risk of depression.[102] The coexistence of diabetes and depression was associated with a 50% to 100% increased risk of all-cause mortality.[103]

Cigarette Smoking. In a recent meta-analysis, current smoking was associated with 44% increased risk of developing diabetes.[104] A similar positive association has been reported in Korea,[105] Taiwan,[106] and China.[107] Smoking is known to induce insulin resistance and inadequate compensatory insulin secretion responses. Among individuals with normal BMI, smokers were more likely to have abdominal obesity than nonsmokers.[104]

In many Asian countries, between 50% and 60% of adult men are regular smokers.[105-107] China, followed by India, is the greatest producer and consumer of cigarettes in the world. Almost 1 of 3 cigarettes produced worldwide is consumed in China.[108] Most Indians use smokeless tobacco products, such as betel quid, and 40% smoke bidis—small, often flavored, nontaxable cigarettes—the production of which provides employment for many urban poor.[109]

Pancreatic Beta Cell Function. In the 1980s, Japanese researchers first unraveled that reduced early insulin response was an independent predictor for diabetes.[110] Fukushima et al[111] found that at all stages of glucose intolerance, Japanese individuals had reduced early and late phases of insulin responses. In Japanese men with normal glucose tolerance, even a small increase in BMI produced a decrease in beta cell function disproportionate to that in insulin sensitivity.[112] In a sample of Chinese patients with type 2 diabetes, 50% were of normal weight, with low BMI correlating with low levels of fasting plasma C-peptide (a marker of decreased insulin secretion) and high glycated hemoglobin levels.[113] In a prospective survey of Japanese Americans, visceral fat area and reduced incremental insulin response were independent predictors for diabetes.[114] Taken together, in some Asian populations, inadequate beta cell response to increasing insulin resistance results in loss of glycemic control and increased risk of diabetes, even with relatively little weight gain.

Developmental Origins of Diabetes. Many Asian adults who experienced great hardship during wartime or civil unrest in early life are now experiencing marked changes in lifestyle. In addition, low birth weight and exposure to undernutrition in utero are common in some Asian populations, especially in India, where 30% of infants are underweight.[115] Insults or stresses during the intrauterine period can lead to permanent changes in structure, metabolism, and physiology through altered expression of the genome without changes in the DNA codes, a process called epigenetics.[116] These early life events may influence later susceptibility to diabetes, the metabolic syndrome, and cardiorenal diseases. Prospective studies from India have shown the impact of fetal undernutrition (often manifested as low birth weight) as well as overnutrition (eg, the infant of a mother with diabetes) on future risk of diabetes.[115] In India, thinness in infancy and overweight at age 12 years was associated with increased risk of developing IGT or diabetes in young adulthood.[117]

A recent meta-analysis of 30 studies found a significant graded association between low birth weight and increased risk of type 2 diabetes.[118] Low birth weight has also been found to predict diabetes and the metabolic syndrome in Asian adults and children,[119-121] thus lending support to the notion that fetal programming with exposure to poor nutrition in utero or during early childhood can promote a fat-preserving or thrifty phenotype. These metabolic changes predispose individuals to insulin resistance and reduced beta cell function. Positive energy balance in later life, caused by rapid westernization of diet and lifestyle, may then exaggerate accumulation of adiposity, particularly in the central depots.[122]

The 2- to 3-fold higher risk of gestational diabetes in Asian women than in their white counterparts also may contribute to the increasing epidemic of young-onset diabetes in Asia.[123] Asian women with a history of gestational diabetes have a substantially increased risk of diabetes, while their offspring exhibit early features of the metabolic syndrome, thus setting up a vicious cycle of "diabetes begetting diabetes." This combination of gestational diabetes, in utero nutritional imbalance, childhood obesity, and overnutrition in adulthood will continue to fuel the epidemic in Asian countries undergoing rapid nutritional transitions.[115]

Genetic Susceptibility. Among lean, healthy individuals matched for age, BMI, waist circumference, birth weight, and current diet, Asians (especially those of Southeast Asian descent) had higher levels of postprandial glycemia and lower insulin sensitivity than whites in response to a 75-g carbohydrate load.[124] These findings raise the possibility that Asians are more genetically susceptible to insulin resistance and diabetes than whites.

Several diabetes genes recently discovered through genome-wide association studies in white populations have been confirmed in Asians as well.[125-129] However, there were significant interethnic differences in risk allele frequency and location. Using the transcription factor 7-like 2 gene *TCF7L2* (rs7901349) as an example, the minor allele frequency was 0.03 in Asian and 0.27 in European populations.[125,126,130] For the potassium voltage-gated channel, subfamily Q, member 1 gene *KCNQ1*, the minor allele frequency of rs2237892 was 0.28 to 0.41 and 0.05 to 0.07 in East Asian and European populations, respectively.[131] Most diabetes genetic variants identified so far, including those in *TCF7L2* and *KCNQ1*, appear to be associated with decreased insulin secretion in whites as well as Asians. In addition, among Asian adults diagnosed with diabetes before age 40 years, approximately 40% had a lean, nonautoimmune phenotype with rapid oral drug failure.[132-135] Approximately 10% of these patients carried genetic variants encoding pancreatic beta cell pathways, including transcription factors and amylin, or mitochondrial polymorphisms. These findings provide further evidence that beta cell dysfunction plays a critical role in the development of diabetes in Asians.

Other Risk Factors. Emerging evidence suggests that exposure to environmental irritants, such as persistent organic pollutants, is associated with increased insulin resistance, the metabolic syndrome, and diabetes.[136,137] Studies from Taiwan and Bangladesh have found a strong association between chronic arsenic exposure and risk of diabetes.[138]

Consistent with studies in whites,[139] Sun et al[140] found that moderate iron overload predicted diabetes in Chinese individuals. Hemoglobinopathies, such as α and β thalassemia traits and hemoglobin H disease, which are associated with increased iron turnover, are present in 8% to 10% of Chinese individuals.[141,142] Asian individuals with thalassemia traits were reported to have a several-fold increased risk of gestational diabetes,[143] insulin resistance,[144] and glucose intolerance.[145]

Approximately 8% to 10% of Asian populations, including Chinese individuals, are chronic hepatitis B viral carriers.[146] Compared with noncarriers, Chinese women who were hepatitis B carriers had a 30% increased risk of gestational diabetes, independent of other well-known diabetes risk factors.[147] Chronic hepatitis B carriers affected by type 2 diabetes also had an earlier age of diagnosis and 4-fold higher risk of end stage renal disease (ESRD) than noncarriers.[148] Similar risk associations with diabetes and diabetic kidney disease have been reported in chronic hepatitis C carriers.[149] Other infections endemic in Asia, such as tuberculosis,[150] have also been associated with increased risk of diabetes and severe clinical course of the disease.

Complications and Comorbid Conditions of Diabetes in Asia

In the World Health Organization Multinational Study of Vascular Diseases in Diabetes, conducted in the early 1970s, stroke and kidney failure were leading causes of death in Chinese, Japanese, and Pima Indian patients with diabetes, compared with coronary heart disease (CHD) in white patients.[151]

In the Asia-Pacific Collaborative Study, among patients with diabetes, the leading cardiovascular cause of death was stroke (42%) in Asia and CHD (59%) in Australia and New Zealand. However, within Asia, there were marked differences in these complications, with China and Japan having higher rates of stroke than CHD, while in Hong Kong and Singapore, the rate of stroke was similar to or even lower than that of CHD.[152]

Asian patients with diabetes continue to exhibit high risk for renal complications, even after accounting for socioeconomic status.[153] In an international survey, 55% of Asian and 40% of white patients with type 2 diabetes had increased albuminuria.[154] Chinese individuals with IGT were found to have a high prevalence of albuminuria, with 2-hour plasma glucose level as an independent predictor.[155] In observational studies as well as clinical trials, Asian patients with diabetes were more likely to develop ESRD than their white counterparts. However, only a small fraction of these patients can afford renal replacement therapy in developing countries such as China.[156] Importantly, albuminuria and renal function are powerful predictors of CHD in Asian as well as white populations, with or without diabetes.[157,158]

In a 25-year prospective survey, 60% of young Japanese patients with type 2 diabetes diagnosed before age 35 years became blind or had developed ESRD at a mean age of 50 years.[159] In a multiethnic study in Singapore, Indians had the highest risk of diabetes. Among the individuals with diabetes, Indians had the highest risk for CHD,[160] while Malays had the highest risk for ESRD[56] and mortality due to heart failure.[161] In a Malaysian dialysis registry, diabetic nephropathy contributed 55% of all new cases of dialysis, with a mean age of 50 years and a preponderance of women.[162] In this multiethnic registry, Malays had the highest incidence of ESRD, followed by Indians and Chinese.

In Chinese patients with diabetes, risk factors for chronic kidney disease included smoking; long disease duration; high calcium phosphate product; albuminuria; increased blood pressure, waist circumference, and levels of triglycerides, low-density lipoprotein cholesterol, and glycated hemoglobin; and decreased glomerular filtration rate and levels of high-density lipoprotein cholesterol.[163] Genetic factors, including aldose reductase and angiotensin-converting enzyme deletion/insertion polymorphisms, were associated with risk of chronic kidney disease in patients with diabetes. In addition, low hematocrit values were found to be an independent predictor of ESRD and cardiovascular complications in Chinese individuals.[164] Furthermore, low blood hemoglobin level was associated with decreased levels of insulin growth factor 1 and testosterone in Asian and white men with diabetes, the metabolic syndrome, or diabetic kidney disease.[165-169] Given the possible epigenetic regulation of the hypothalamic-pituitary-adrenal axis and the growth hormone–insulin growth factor 1 axis, neurohormonal dysregulation is likely to be implicated in diabetic kidney disease.[116,170]

Several meta-analyses have shown that except for prostate cancer,[171] diabetes was associated with a 30% to 40% increased risk of breast,[172] endometrial,[173] pancreatic,[174] liver,[175] and colorectal cancers.[176] Patients with cancer as well as diabetes also had a 40% to 80% higher risk of death than those without diabetes.[177] Community-based prospective surveys, including those conducted in Asia, reported independent associations of fasting[178,179] and 2-hour plasma glucose levels[180,181] with cancer risk. Given the high rates of IGT, which predicts all-cause mortality in Asian populations,[182] there is a need to understand the potential role of glucose metabolism and insulin resistance in carcinogenesis.[183,184]

Changing patterns of disease and medical care are accompanied by secular changes in causes of death in Asian patients with diabetes. In Hong Kong, for example, the majority of Chinese patients with type 2 diabetes died from stroke and ESRD until the early 1990s.[185] In the mid-1990s, heart disease emerged as the leading cause of death.[186] In 1995, a prospective diabetes registry was established in Hong Kong. It recruited 7000 patients with type 2 diabetes, half of whom were middle-aged at diagnosis. Ten years after diagnosis, 30% had died or had sustained a major clinical event, with cancer (20%), CHD (20%), ESRD (10%), and stroke (10%) as major causes of death.[187]

COMMENT

The diabetes epidemic in Asia is characterized by rapid rates of increase over short periods and onset at a relatively young age and low BMI. The epidemic is heterogeneous, varying according to different ethnic and cultural subgroups, degree of urbanization, and socioeconomic conditions in different Asian populations. In parallel with economic development and nutrition transition, the rates of overweight and obesity have been increasing rapidly in Asian countries. Abdominal or central adiposity, particularly detrimental to type 2 diabetes and other metabolic diseases, is highly prevalent in Asians. The high rates of gestational diabetes, in combination with in utero exposure to poor nutrition, childhood obesity, and overnutrition in later life, may contribute substantially to the increasing diabetes epidemic in Asia.

While further research is needed to systematically monitor secular trends of diabetes in Asian populations, characterize risk factors, and understand interactions between genetic and environmental risk factors, ample evidence from Asia has shown that diabetes and its complications is preventable and highly treatable. In the early 1990s, a randomized trial in China demonstrated that dietary and exercise intervention reduced diabetes risk by 31% to 46% in individuals with IGT.[188] These results have since been confirmed in Europe,[189] the United States,[190] India,[191] and Japan.[192] In observational studies and randomized trials conducted in Asia and Europe, control of multiple risk factors reduced cardiorenal complications and all-cause death by 50% to 70% in individuals with type 2 diabetes.[193-195]

Type 2 diabetes mellitus has become an epidemic in Asia. To curb this epidemic, an integrated strategy combining population-wide preventive policies (eg, changing food and the built environment), early detection, and multidisciplinary care programs may reduce the risk of diabetes and associated complications in the general population and in high-risk individuals.

Author Contributions: Drs Chan and Hu had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Chan, Malik, Hu.
Acquisition of data: Chan, Malik, Hu.
Analysis and interpretation of data: Jia, Kadowaki, Yajnik, Yoon
Drafting of the manuscript: Chan, Malik, Hu.
Critical revision of the manuscript for important intellectual content: Chan, Malik, Jia, Kadowaki, Yajnik, Yoon, Hu.
Administrative, technical, or material support: Chan, Hu.
Study supervision: Chan, Hu.

Financial Disclosures: Dr Chan reported receiving research funding or speakers' honoraria from AstraZeneca, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, GlaxoSmithKline, Lilly, Merck Serono, Merck Sharp & Dohme, Novo Nordisk, Pfizer, Roche, and sanofi-aventis; serving as a member of the advisory boards, and/or speaker forums, and/or steering committees of international projects sponsored by AstraZeneca, Bayer, Lilly, and Merck Sharp & Dohme; with her group and on behalf of the Chinese University of Hong Kong, filing a patent application to use genetic markers to predict risk of diabetes and diabetic kidney disease in Chinese populations; and, in a technology transfer project, establishing a university-affiliated diabetes center (Qualigenics) to deliver a multidisciplinary chronic care program in the community (all related revenues and proceeds go to the Chinese University of Hong Kong to support ongoing research and development in diabetes). Dr Kadowaki reported receiving research funding or speakers' honoraria from Takeda, Daiichi-Sankyo, Astellas, Ono, Dainippon Sumitomo, sanofi-aventis, Novo Nordisk, Novartis, and Lilly and serving as a member of the advisory board of Daiichi-Sankyo, Ono, Merck, Lilly, sanofi-aventis, Novo Nordisk, and Novartis (all funds go to the University of Tokyo to support ongoing research and development in diabetes). Dr Yoon reported serving as a member of the steering committees, and/or advisory boards, and/or speaker forums of Merck Sharp & Dohme, GlaxoSmithKline, Lilly, Merck Serono, Novartis, and Choongwae Korea on diabetes-related subjects; serving as an investigator on clinical trials supported by AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Merck Sharp & Dohme, Lilly, sanofi-aventis, GlaxoSmithKline, Roche, CJ Pharmaceutical, and CW Korea; with his team and on behalf of the Catholic University of Korea, filing a patent application to use various Web-based diabetes management programs and intracellular miRNA targets to improve beta cell function in patients with diabetes; and, in a technology project, working with his team to establish a university-affiliated institute for ubiquitous health care and a joint venture company called C & I Healthcare to use protocol-driven care delivered through Internet and mobile communications to improve diabetes care in the community. Dr Hu reported receiving research funding from Merck, Unilever, and the California Walnut Commission and receiving payment or honoraria for presentations at academic conferences supported by Novartis and Novo Nordisk. Mr Malik, Dr Jia, and Dr Yajnik reported no financial disclosures.
Additional Contributions: We thank Louisa Lam, MLib, MAIS, librarian, Li Ping Medical Library, Faculty of Medicine, The Chinese University of Hong Kong, The Prince of Wales Hospital, for her assistance and advice on search strategy. Ms Lam received no extra compensation for her contributions. We regret that limited space allows us to cite only a fraction of the work conducted in Asian countries.

REFERENCES

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-1053.
2. International Diabetes Federation. *Diabetes Atlas.* 3rd ed. Brussels, Belgium: International Diabetes Federation; 2006.
3. World Economics Forum. *Global Risks 2009. A Global Risk Network Report.* Geneva, Switzerland: World Economics Forum; 2009.
4. Gregg EW, Cadwell BL, Cheng YJ, et al. Trends in the prevalence and ratio of diagnosed to undiagnosed diabetes according to obesity levels in the U.S. *Diabetes Care*. 2004;27(12):2806-2812.
5. Cowie CC, Rust KF, Ford ES, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. *Diabetes Care*. 2009;32(2):287-294.
6. National Center for Health Statistics. National Health and Nutrition Examination Survey 2005-2006. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/nchs/about/major/nhanes2005-2006/nhanes05_06.htm. Accessed March 31, 2008.
7. Gu D, Reynolds K, Duan X, et al; InterASIA Collaborative Group. Prevalence of diabetes and impaired fasting glucose in the Chinese adult population: International Collaborative Study of Cardiovascular Disease in Asia (InterASIA). *Diabetologia*. 2003;46(9):1190-1198.
8. Zhong XL. Diabetes mellitus survey in China. *Chin Med J (Engl)*. 1982;95(6):423-430.
9. Pan XR, Yang WY, Li GW, Liu J; National Diabetes Prevention and Control Cooperative Group. Prevalence of diabetes and its risk factors in China, 1994. *Diabetes Care*. 1997;20(11):1664-1669.
10. Cockram CS, Woo J, Lau E, et al. The prevalence of diabetes mellitus and impaired glucose tolerance among Hong Kong Chinese adults of working age. *Diabetes Res Clin Pract*. 1993;21(1):67-73.
11. Janus ED, Watt NMS, Lam KSL, et al; Hong Kong Cardiovascular Risk Factor Steering Committee, American Diabetes Association. The prevalence of diabetes, association with cardiovascular risk factors and implications of diagnostic criteria (ADA 1997 and WHO 1998) in a 1996 community based population study in Hong Kong Chinese. *Diabet Med*. 2000;17(10):741-745.
12. Chou P, Chen HH, Hsiao KJ. Community-based epidemiological study on diabetes in Pu-Li, Taiwan. *Diabetes Care*. 1992;15(1):81-89.
13. Lu FH, Yang YC, Wu JS, Wu CH, Chang CJ. A population-based study of the prevalence and associated factors of diabetes mellitus in southern Taiwan. *Diabet Med*. 1998;15(7):564-572.
14. Kitazawa Y, Murakami K, Goto Y, Hamazaki S. Prevalence of diabetes mellitus detected by 75 g GTT in Tokyo. *Tohoku J Exp Med*. 1983;141(suppl):229-234.
15. Ohmura T, Ueda K, Kiyohara Y, et al. Prevalence of type 2 (non-insulin-dependent) diabetes mellitus and impaired glucose tolerance in the Japanese general population: the Hisayama Study. *Diabetologia*. 1993;36(11):1198-1203.
16. Sekikawa A, Eguchi H, Tominaga M, et al. Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in a rural area of Japan: the Funagata diabetes study. *J Diabetes Complications*. 2000;14(2):78-83.
17. Park Y, Lee H, Koh CS, et al. Prevalence of diabetes and IGT in Yonchon County, South Korea. *Diabetes Care*. 1995;18(4):545-548.
18. Song KH, Nam-Goomg IS, Han SM, et al. Change in prevalence and 6-year incidence of diabetes and impaired fasting glucose in Korean subjects living in a rural area. *Diabetes Res Clin Pract*. 2007;78(3):378-384.
19. Kim SM, Lee JS, Lee J, et al. Prevalence of diabetes and impaired fasting glucose in Korea: Korean National Health and Nutrition Survey 2001. *Diabetes Care*. 2006;29(2):226-231.
20. Ramachandran A. Epidemiology of diabetes in India—three decades of research. *J Assoc Physicians India*. 2005;53:34-38.
21. Sadikot SM, Nigam A, Das S, et al; DiabetesIndia. The burden of diabetes and impaired fasting glucose in India using the ADA 1997 criteria: prevalence of diabetes in India study (PODIS). *Diabetes Res Clin Pract*. 2004;66(3):293-300.
22. Mohan V, Mathur P, Deepa R, et al. Urban rural differences in prevalence of self-reported diabetes in India—the WHO-ICMR Indian NCD risk factor surveillance. *Diabetes Res Clin Pract*. 2008;80(1):159-168.
23. Shera AS, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan. *Diabetes Res Clin Pract*. 2007;76(2):219-222.
24. Sayeed MA, Hussain MZ, Banu A, Rumi MA, Azad Khan AK. Prevalence of diabetes in a suburban population of Bangladesh. *Diabetes Res Clin Pract*. 1997;34(3):149-155.
25. Rahim MA, Hussain A, Azad Khan AK, Sayeed MA, Keramat Ali SM, Vaaler S. Rising prevalence of type 2 diabetes in rural Bangladesh: a population based study. *Diabetes Res Clin Pract*. 2007;77(2):300-305.
26. Hussain A, Rahim MA, Azad Khan AK, Ali SM, Vaaler S. Type 2 diabetes in rural and urban population: diverse prevalence and associated risk factors in Bangladesh. *Diabet Med*. 2005;22(7):931-936.
27. Sasaki H, Kawasaki T, Ogaki T, et al. The prevalence of diabetes mellitus and impaired fasting glucose/glycaemia (IFG) in suburban and rural Nepal—the communities-based cross-sectional study during the democratic movements in 1990. *Diabetes Res Clin Pract*. 2005;67(2):167-174.
28. Singh DL, Bhattarai MD. High prevalence of diabetes and impaired fasting glycaemia in urban Nepal. *Diabet Med*. 2003;20(2):170-171.

29. Ono K, Limbu YR, Rai SK, et al. The prevalence of type 2 diabetes mellitus and impaired fasting glucose in semi-urban population of Nepal. *Nepal Med Coll J*. 2007;9(3):154-156.

30. Fernando DJ, Siribaddana S, de Silva D. Impaired glucose tolerance and diabetes mellitus in a suburban Sri Lankan community. *Postgrad Med J*. 1994; 70(823):347-349.

31. Katulanda P, Constantine GR, Mahesh JG, et al. Prevalence and projections of diabetes and prediabetes in adults in Sri Lanka—Sri Lanka Diabetes, Cardiovascular Study (SLDCS). *Diabet Med*. 2008; 25(9):1062-1069.

32. Waspadji S, Ranakusuma AB, Suyono S, Supartondo S, Sukaton U. Diabetes mellitus in an urban population in Jakarta, Indonesia. *Tohoku J Exp Med*. 1983; 141(suppl):219-228.

33. Sutanegara D, Budhiarta AA. The epidemiology and management of diabetes mellitus in Indonesia. *Diabetes Res Clin Pract*. 2000;50(suppl 2):S9-S19.

34. Zaini A. Where is Malaysia in the midst of the Asian epidemic of diabetes mellitus? *Diabetes Res Clin Pract*. 2000;50(suppl 2):S23-S28.

35. Mafauzy M, Mokhtar N, Mohamad WB, Musalmah M. Diabetes mellitus and associated cardiovascular risk factors in north-east Malaysia. *Asia Pac J Public Health*. 1999;11(1):16-19.

36. Disease Control Division, Ministry of Health Malaysia. NCD risk factors in Malaysia. World Health Organization Web site. http://www.who.int/chp/steps/MalaysiaSTEPSReport.pdf#. Accessibility verified April 23, 2009.

37. Tatsanavivat P, Klungboonkrong V, Chirawatkul A, et al. Prevalence of coronary heart disease and major cardiovascular risk factors in Thailand. *Int J Epidemiol*. 1998;27(3):405-409.

38. Aekplakorn W, Abbott-Klafter J, Premgamone A, et al. Prevalence and management of diabetes and associated risk factors by regions of Thailand: Third National Health Examination Survey 2004. *Diabetes Care*. 2007;30(8):2007-2012.

39. Aekplakorn W, Stolk RP, Neal P, et al; INTERASIA Collaborative Group. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. *Diabetes Care*. 2003;26(10):2758-2763.

40. Duc Son LN, Kusama K, Hung NT, et al. Prevalence and risk factors for diabetes in Ho Chi Minh City, Vietnam. *Diabet Med*. 2004;21(4):371-376.

41. Quoc PS, Charles MA, Cuong NH, et al. Blood glucose distribution and prevalence of diabetes in Hanoi (Vietnam). *Am J Epidemiol*. 1994;139(7):713-722.

42. King H, Keuky L, Seng S, Khun T, Roglic G, Pinget M. Diabetes and associated disorders in Cambodia: two epidemiological surveys. *Lancet*. 2005;366 (9497):1633-1639.

43. Baltazar JC, Ancheta CA, Aban IB, Fernando RE, Baquilod MM. Prevalence and correlates of diabetes mellitus and impaired glucose tolerance among adults in Luzon, Philippines. *Diabetes Res Clin Pract*. 2004; 64(2):107-115.

44. Thai AC, Yeo PP, Lun KC, et al. Diabetes mellitus and its chronic complications in Singapore: an increasing healthcare problem. *Ann Acad Med Singapore*. 1990;19(4):517-523.

45. Tan CE, Emmanuel SC, Tan B, Jacob E. Prevalence of diabetes and ethnic differences in cardiovascular risk factors: the 1992 Singapore National Health Survey. *Diabetes Care*. 1999;22(2):241-247.

46. Ministry of Health. WHO Global Infobase: National Health Survey 2004, Singapore. World Health Organization Web site. http://www.who.int/infobase/. 2005. Accessed March 31, 2009.

47. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 1997;20(7):1183-1197.

48. World Health Organization Expert Committee on Diabetes Mellitus. *Second Report of Diabetes Mellitus.* Geneva, Switzerland: World Health Organization; 1980. Technical reports series 646.

49. World Health Organization. *Diabetes Mellitus: Report of a WHO Study Group.* Geneva, Switzerland: World Health Organization; 1985:11. Technical reports series 727.

50. Alberti K, Aschner P, Assal J. *Definition, Diagnosis and Classification of Diabetes Mellitus.* Geneva, Switzerland: World Health Organization; 1999.

51. Jia WP, Pang C, Chen L, et al. Epidemiological characteristics of diabetes mellitus and impaired glucose regulation in a Chinese adult population: the Shanghai Diabetes Studies, a cross-sectional 3-year follow-up study in Shanghai urban communities. *Diabetologia*. 2007;50(2):286-292.

52. Wong KC, Wang Z. Prevalence of type 2 diabetes mellitus of Chinese populations in Mainland China, Hong Kong, and Taiwan. *Diabetes Res Clin Pract*. 2006;73(2):126-134.

53. Ramachandran A, Mary S, Yamuna A, Murugesan N, Snehalatha C. High prevalence of diabetes and cardiovascular risk factors associated with urbanization in India. *Diabetes Care*. 2008;31(5):893-898.

54. Lee WR. The changing demography of diabetes mellitus in Singapore. *Diabetes Res Clin Pract*. 2000; 50(suppl 2):S35-S39.

55. Western Pacific Declaration on Diabetes Steering Committee. Plan of Action for the Western Pacific Declaration on Diabetes 2006-2010. Western Pacific Declaration on Diabetes Web site. http://www.wpdd.org. 2008. Accessibility verified April 23, 2009.

56. Yoon KH, Lee JH, Kim JW, et al. Epidemic obesity and type 2 diabetes in Asia. *Lancet*. 2006; 368(9548):1681-1688.

57. Huxley R, James WP, Barzi F, et al; Obesity in Asia Collaboration. Ethnic comparisons of the cross-sectional relationships between measures of body size with diabetes and hypertension. *Obes Rev*. 2008; 9(suppl 1):53-61.

58. Wang Y, Mi J, Shan XY, Wang QJ, Ge KY. Is China facing an obesity epidemic and the consequences? the trends in obesity and chronic disease in China. *Int J Obes (Lond)*. 2007;31(1):177-188.

59. Gu D, Reynolds K, Wu X, et al; InterASIA Collaborative Group. Prevalence of the metabolic syndrome and overweight among adults in China. *Lancet*. 2005;365(9468):1398-1405.

60. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. *J Clin Endocrinol Metab*. 2008;93(11)(suppl 1):S9-S30.

61. Scharoun-Lee M, Kaufman JS, Popkin BM, Gordon-Larsen P. Obesity, race/ethnicity and life course socioeconomic status across the transition from adolescence to adulthood. *J Epidemiol Community Health*. 2009;63(2):133-139.

62. Zhou H, Yamauchi T, Natsuhara K, et al. Overweight in urban schoolchildren assessed by body mass index and body fat mass in Dalian, China. *J Physiol Anthropol*. 2006;25(1):41-48.

63. Kim HM, Park J, Kim HS, Kim DH, Park SH. Obesity and cardiovascular risk factors in Korean children and adolescents aged 10-18 years from the Korean National Health and Nutrition Examination Survey, 1998 and 2001. *Am J Epidemiol*. 2006;164(8): 787-793.

64. Kim DM, Ahn CW, Nam SY. Prevalence of obesity in Korea. *Obes Rev*. 2005;6(2):117-121.

65. Likitmaskul S, Kiattisathavee P, Chaichanwatanakul K, Punnakanta L, Angsusingha K, Tuchinda C. Increasing prevalence of type 2 diabetes mellitus in Thai children and adolescents associated with increasing prevalence of obesity. *J Pediatr Endocrinol Metab*. 2003;16(1):71-77.

66. Ozaki R, Qiao Q, Wong GW, et al. Overweight, family history of diabetes and attending schools of lower academic grading are independent predictors for metabolic syndrome in Hong Kong Chinese adolescents. *Arch Dis Child*. 2007;92(3):224-228.

67. Aekplakorn W, Bunnag P, Woodward M, et al. A risk score for predicting incident diabetes in the Thai population. *Diabetes Care*. 2006;29(8):1872-1877.

68. Ma RCW, Ko GT, Chan JC. Health hazards of obesity—an overview. In: Williams G, Frubeck G, eds. *Obesity: Science to Practice.* Hoboken, NJ: John Wiley & Sons; 2009:215-236.

69. Nakagami T, Qiao Q, Carstensen B, et al; The DECODE-DECODA Study Group. Age, body mass index and type 2 diabetes—associations modified by ethnicity. *Diabetologia*. 2003;46(8):1063-1070.

70. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obes Rev*. 2002;3(3):141-146.

71. Reynolds K, Gu D, Whelton PK, et al; InterASIA Collaborative Group. Prevalence and risk factors of overweight and obesity in China. *Obesity (Silver Spring)*. 2007;15(1):10-18.

72. Le DS, Kusama K, Yamamoto S. A community-based picture of type 2 diabetes mellitus in Vietnam. *J Atheroscler Thromb*. 2006;13(1):16-20.

73. Stolk RP, Suriyawongpaisal P, Aekplakorn W, Woodward M, Neal B; InterASIA Collaborative Group. Fat distribution is strongly associated with plasma glucose levels and diabetes in Thai adults—the InterASIA study. *Diabetologia*. 2005;48(4):657-660.

74. Balkau B, Deanfield JE, Despres JP, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. *Circulation*. 2007; 116(17):1942-1951.

75. Lear SA, Humphries KH, Kohli S, Chockalingam A, Frohlich JJ, Birmingham CL. Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT). *Am J Clin Nutr*. 2007; 86(2):353-359.

76. Yajnik CS, Lubree HG, Rege SS, et al. Adiposity and hyperinsulinemia in Indians are present at birth. *J Clin Endocrinol Metab*. 2002;87(12):5575-5580.

77. Ruderman N, Chisholm D, Pi-Sunyer X, Schneider S. The metabolically obese, normal-weight individual revisited. *Diabetes*. 1998;47(5):699-713.

78. Liu KH, Chan Y, Chan W, Chan J, Chu W. Mesenteric fat thickness is an independent determinant of metabolic syndrome and identifies subjects with increased carotid intima-media thickness. *Diabetes Care*. 2006;29(2):379-384.

79. Cheung BM, Wat NM, Man YB, et al. Development of diabetes in Chinese with the metabolic syndrome: a 6-year prospective study. *Diabetes Care*. 2007;30(6):1430-1436.

80. Cho NH, Jang HC, Choi SH, et al. Abnormal liver function test predicts type 2 diabetes: a community-based prospective study. *Diabetes Care*. 2007; 30(10):2566-2568.

81. Mak KH, Ma S, Heng D, et al. Impact of sex, metabolic syndrome, and diabetes mellitus on cardiovascular events. *Am J Cardiol*. 2007;100(2):227-233.

82. Thomas GN, Schooling CM, McGhee SM, et al; Hong Kong Cardiovascular Risk Factor Prevalence Study Steering Committee. Metabolic syndrome increases all-cause and vascular mortality: the Hong Kong Cardiovascular Risk Factor Study. *Clin Endocrinol (Oxf)*. 2007;66(5):666-671.

83. Zhang X, Shu XO, Yang G, et al. Abdominal adiposity and mortality in Chinese women. *Arch Intern Med*. 2007;167(9):886-892.

84. Wang C, Hou X, Bao Y, et al. The metabolic syndrome increased risk of cardiovascular events in Chinese—a community based study [published online ahead of print November 27, 2008]. *Int J Cardiol*. doi:10.1016/j.ijcard.2008.10.012.

85. Siegel K, Narayan KM, Kinra S. Finding a policy solution to India's diabetes epidemic. *Health Aff (Millwood)*. 2008;27(4):1077-1090.
86. Shetty PS. Nutrition transition in India. *Public Health Nutr*. 2002;5(1A):175-182.
87. Matsumura Y. Nutrition trends in Japan. *Asia Pac J Clin Nutr*. 2001;10(suppl):S40-S47.
88. Choi YJ, Cho YM, Park CK, et al. Rapidly increasing diabetes-related mortality with socio-environmental changes in South Korea during the last two decades. *Diabetes Res Clin Pract*. 2006;74(3):295-300.
89. Kosulwat V. The nutrition and health transition in Thailand. *Public Health Nutr*. 2002;5(1A):183-189.
90. Popkin BM, Horton S, Kim S, Mahal A, Shuigao J. Trends in diet, nutritional status, and diet-related noncommunicable diseases in China and India: the economic costs of the nutrition transition. *Nutr Rev*. 2001;59(12):379-390.
91. Haag M, Dippenaar NG. Dietary fats, fatty acids and insulin resistance: short review of a multifaceted connection. *Med Sci Monit*. 2005;11(12):RA359-RA367.
92. Oh K, Hu FB, Manson JE, Stampfer MJ, Willett WC. Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the Nurses' Health Study. *Am J Epidemiol*. 2005;161(7):672-679.
93. Lopez-Garcia E, Schulze MB, Meigs JB, et al. Consumption of *trans* fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr*. 2005;135(3):562-566.
94. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA*. 2002;287(18):2414-2423.
95. Villegas R, Liu S, Gao YT, et al. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. *Arch Intern Med*. 2007;167(21):2310-2316.
96. Murakami K, Sasaki S, Takahashi Y, et al. Dietary glycemic index and load in relation to metabolic risk factors in Japanese female farmers with traditional dietary habits. *Am J Clin Nutr*. 2006;83(5):1161-1169.
97. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr*. 2006;84(2):274-288.
98. Ko GT, Chan JC, Chow CC, Tsang LW, Cockram CS. A low socioeconomic status is an additional risk factor for glucose intolerance in high risk Hong Kong Chinese. *Eur J Epidemiol*. 2001;17(3):289-295.
99. Kleinman A. Culture and depression. *N Engl J Med*. 2004;351(10):951-953.
100. Ko GT, Chan JC, Chan AW, et al. Association between sleeping hours, working hours and obesity in Hong Kong Chinese: the "better health for better Hong Kong" health promotion campaign. *Int J Obes (Lond)*. 2007;31(2):254-260.
101. Takeuchi T, Nakao M, Nomura K, Yano E. Association of metabolic syndrome with depression and anxiety in Japanese men. *Diabetes Metab*. 2009;35(1):32-36.
102. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. *Diabetes Care*. 2008;31(12):2383-2390.
103. Katon WJ, Rutter C, Simon G, et al. The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care*. 2005;28(11):2668-2672.
104. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2007;298(22):2654-2664.
105. Hur NW, Kim HC, Nam CM, Jee SH, Lee HC, Suh I. Smoking cessation and risk of type 2 diabetes mellitus: Korea Medical Insurance Corporation Study. *Eur J Cardiovasc Prev Rehabil*. 2007;14(2):244-249.
106. Chen CC, Li TC, Chang PC, et al. Association among cigarette smoking, metabolic syndrome, and its individual components: the metabolic syndrome study in Taiwan. *Metabolism*. 2008;57(4):544-548.
107. Ko GT, Chan JC, Tsang LW, Critchley JA, Cockram CS. Smoking and diabetes in Chinese men. *Postgrad Med J*. 2001;77(906):240-243.
108. Cheng TO. Smoking in China. *BMJ*. 1995;310(6971):61.
109. Kabir Z, Clancy L, Connolly GN. Tobacco control efforts: where is India now? *Lancet*. 2007;370(9582):134.
110. Kadowaki T, Miyake Y, Hagura R, et al. Risk factors for worsening to diabetes in subjects with impaired glucose tolerance. *Diabetologia*. 1984;26(1):44-49.
111. Fukushima M, Usami M, Ikeda M, et al. Insulin secretion and insulin sensitivity at different stages of glucose tolerance: a cross-sectional study of Japanese type 2 diabetes. *Metabolism*. 2004;53(7):831-835.
112. Kuroe A, Fukushima M, Usami M, et al. Impaired beta-cell function and insulin sensitivity in Japanese subjects with normal glucose tolerance. *Diabetes Res Clin Pract*. 2003;59(1):71-77.
113. Chan WB, Tong PCY, Chow CC, et al. The associations of body mass index, C peptide and metabolic status in Chinese type 2 diabetic patients. *Diabet Med*. 2004;21(4):349-353.
114. Boyko EJ, Fujimoto WY, Leonetti DL, Newell-Morris L. Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. *Diabetes Care*. 2000;23(4):465-471.
115. Yajnik CS. Nutrient-mediated teratogenesis and fuel-mediated teratogenesis: two pathways of intrauterine programming of diabetes. *Int J Gynaecol Obstet*. 2009;104(suppl 1):S27-S31.
116. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med*. 2008;359(1):61-73.
117. Bhargava SK, Sachdev HS, Fall CH, et al. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. *N Engl J Med*. 2004;350(9):865-875.
118. Whincup PH, Kaye SJ, Owen CG, et al. Birth weight and risk of type 2 diabetes: a systematic review. *JAMA*. 2008;300(24):2886-2897.
119. Mi J, Law C, Zhang KL, Osmond C, Stein C, Barker D. Effects of infant birthweight and maternal body mass index in pregnancy on components of the insulin resistance syndrome in China. *Ann Intern Med*. 2000;132(4):253-260.
120. Veena SR, Geetha S, Leary SD, et al. Relationships of maternal and paternal birthweights to features of the metabolic syndrome in adult offspring: an inter-generational study in South India. *Diabetologia*. 2007;50(1):43-54.
121. Wei JN, Sung F, Li C, et al. Low birth weight and high birth weight infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan. *Diabetes Care*. 2003;26(2):343-348.
122. Yajnik CS, Deshmukh US. Maternal nutrition, intrauterine programming and consequential risks in the offspring. *Rev Endocr Metab Disord*. 2008;9(3):203-211.
123. Ma RC, Chan JC. Pregnancy and diabetes scenario around the world: China. *Int J Gynaecol Obstet*. 2009;104(suppl 1):S42-S45.
124. Dickinson S, Colagiuri S, Faramus E, Petocz P, Brand-Miller JC. Postprandial hyperglycemia and insulin sensitivity differ among lean young adults of different ethnicities. *J Nutr*. 2002;132(9):2574-2579.
125. Wu Y, Li H, Loos RJ, et al. Common variants in *CDKAL1*, *CDKN2A/B*, *IGF2BP2*, *SLC30A8*, and *HHEX/IDE* genes are associated with type 2 diabetes and impaired fasting glucose in a Chinese Han population. *Diabetes*. 2008;57(10):2834-2842.
126. Ng MC, Park KS, Oh B, et al. Implication of genetic variants near *TCF7L2*, *SLC30A8*, *HHEX*, *CDKAL1*, *CDKN2A/B*, *IGF2BP2*, and *FTO* in type 2 diabetes and obesity in 6,719 Asians. *Diabetes*. 2008;57(8):2226-2233.
127. Chang YC, Chang TJ, Jiang YD, et al. Association study of the genetic polymorphisms of the transcription factor 7-like 2 (*TCF7L2*) gene and type 2 diabetes in the Chinese population. *Diabetes*. 2007;56(10):2631-2637.
128. Ren Q, Han XY, Wang F, et al. Exon sequencing and association analysis of polymorphisms in *TCF7L2* with type 2 diabetes in a Chinese population. *Diabetologia*. 2008;51(7):1146-1152.
129. Miyake K, Horikawa Y, Hara K, et al. Association of *TCF7L2* polymorphisms with susceptibility to type 2 diabetes in 4,087 Japanese subjects. *J Hum Genet*. 2008;53(2):174-180.
130. Ng MCY, Wang Y, So WY, et al. Ethnic differences in the linkage disequilibrium and distribution of single nucleotide polymorphisms in 35 candidate genes for cardiovascular diseases. *Genomics*. 2004;83(4):559-565.
131. Yasuda K, Miyake K, Horikawa Y, et al. Variants in *KCNQ1* are associated with susceptibility to type 2 diabetes mellitus. *Nat Genet*. 2008;40(9):1092-1097.
132. Yokoi N, Kanamori M, Horikawa Y, et al. Association studies of variants in the genes involved in pancreatic beta-cell function in type 2 diabetes in Japanese subjects. *Diabetes*. 2006;55(8):2379-2386.
133. Ng MC, Lee SC, Ko GT, et al. Familial early-onset type 2 diabetes in Chinese patients: obesity and genetics have more significant roles than autoimmunity. *Diabetes Care*. 2001;24(4):663-671.
134. Chan JC, Ng MC. Lessons learned from young-onset diabetes in China. *Curr Diab Rep*. 2003;3(2):101-107.
135. Mohan V, Jaydip R, Deepa R. Type 2 diabetes in Asian Indian youth. *Pediatr Diabetes*. 2007;8(suppl 9):28-34.
136. Fujiyoshi PT, Michalek JE, Matsumura F. Molecular epidemiologic evidence for diabetogenic effects of dioxin exposure in U.S. Air force veterans of the Vietnam war. *Environ Health Perspect*. 2006;114(11):1677-1683.
137. Lee DH, Steffes MW, Jacobs DR Jr. Can persistent organic pollutants explain the association between serum gamma-glutamyltransferase and type 2 diabetes? *Diabetologia*. 2008;51(3):402-407.
138. Chen CJ, Wang SL, Chiou JM, et al. Arsenic and diabetes and hypertension in human populations: a review. *Toxicol Appl Pharmacol*. 2007;222(3):298-304.
139. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. *JAMA*. 2004;291(6):711-717.
140. Sun L, Franco OH, Hu FB, et al. Ferritin concentrations, metabolic syndrome, and type 2 diabetes in middle-aged and elderly chinese. *J Clin Endocrinol Metab*. 2008;93(12):4690-4696.
141. Lau YL, Chan LC, Chan YY, et al. Prevalence and genotypes of alpha- and beta-thalassemia carriers in Hong Kong—implications for population screening. *N Engl J Med*. 1997;336(18):1298-1301.
142. Chen FE, Ooi C, Ha SY, et al. Genetic and clinical features of hemoglobin H disease in Chinese patients. *N Engl J Med*. 2000;343(8):544-550.
143. Lao TT, Ho LF. Alpha-thalassaemia trait and gestational diabetes mellitus in Hong Kong. *Diabetologia*. 2001;44(8):966-971.
144. Tong PC, Ng MC, Ho CS, et al. C reactive protein and insulin resistance in subjects with thalasse-

mia minor and a family history of diabetes. *Diabetes Care*. 2002;25(8):1480-1481.
145. Chern JP, Lin KH, Lu MY, et al. Abnormal glucose tolerance in transfusion-dependent beta-thalassemic patients. *Diabetes Care*. 2001;24(5):850-854.
146. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. *Epidemiol Rev*. 2006;28:112-125.
147. Lao TT, Chan BC, Leung WC, Ho LF, Tse KY. Maternal hepatitis B infection and gestational diabetes mellitus. *J Hepatol*. 2007;47(1):46-50.
148. Cheng AY, Kong AP, Wong VW, et al. Chronic hepatitis B viral infection independently predicts renal outcome in type 2 diabetic patients. *Diabetologia*. 2006;49(8):1777-1784.
149. Mehta SH, Brancati F, Strathdee S, et al. Hepatitis C virus infection and incident type 2 diabetes. *Hepatology*. 2003;38(1):50-56.
150. Leung CC, Lam TH, Chan WM, et al. Diabetic control and risk of tuberculosis: a cohort study. *Am J Epidemiol*. 2008;167(12):1486-1494.
151. Morrish NJ, Wang S, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO Multinational Study of Vascular Diseases in Diabetes. *Diabetologia*. 2001;44(suppl 2):S14-S21.
152. Woodward M, Zhang X, Barzi F, et al; Asia Pacific Cohort Studies Collaboration. The effects of diabetes on the risks of major cardiovascular diseases and death in the Asia-Pacific region. *Diabetes Care*. 2003;26(2):360-366.
153. Karter AJ, Ferrara A, Liu J, Moffet H, Ackerson L, Selby J. Ethnic disparities in diabetic complications in an insured population. *JAMA*. 2002;287(19):2519-2527.
154. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG; DEMAND Investigators. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. *Kidney Int*. 2006;69(11):2057-2063.
155. Wang XL, Lu JM, Pan CY, Tian H, Li CL. A comparison of urinary albumin excretion rate and microalbuminuria in various glucose tolerance subjects. *Diabet Med*. 2005;22(3):332-335.
156. Luk A, Chan JC. Diabetic nephropathy—what are the unmet needs? *Diabetes Res Clin Pract*. 2008;82(suppl 1):S15-S20.
157. So WY, Kong AP, Ma RC, et al. Glomerular filtration rate, cardiorenal end points, and all-cause mortality in type 2 diabetic patients. *Diabetes Care*. 2006;29(9):2046-2052.
158. Go AS, Chertow G, Fan D, McCulloch C, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296-1305.
159. Yokoyama H, Okudaira M, Otani T, et al. High incidence of diabetic nephropathy in early onset Japanese NIDDM patients: risk analysis. *Diabetes Care*. 1998;21(7):1080-1085.
160. Yeo KK, Tai BC, Heng D, et al. Ethnicity modifies the association between diabetes mellitus and ischaemic heart disease in Chinese, Malays and Asian Indians living in Singapore. *Diabetologia*. 2006;49(12):2866-2873.
161. Lee R, Chan SP, Chan YH, Wong J, Lau D, Ng K. Impact of race on morbidity and mortality in patients with congestive heart failure: a study of the multiracial population in Singapore [published online ahead of print March 26, 2008]. *Int J Cardiol*. doi:10.1016/j.ijcard.2007.12.107.
162. Liu WJ, Hooi LS. Patients with end stage renal disease: a registry at Sultanah Aminah Hospital, Johor Bahru, Malaysia. *Med J Malaysia*. 2007;62(3):197-200.
163. Luk AO, So WY, Ma RC, et al; Hong Kong Diabetes Registry. Metabolic syndrome predicts new onset of chronic kidney disease in 5,829 patients with type 2 diabetes: a 5-year prospective analysis of the Hong Kong Diabetes Registry. *Diabetes Care*. 2008;31(12):2357-2361.
164. Tong PC, Kong AP, So WY, et al. Hematocrit, independent of chronic kidney disease, predicts adverse cardiovascular outcomes in Chinese patients with type 2 diabetes. *Diabetes Care*. 2006;29(11):2439-2444.
165. Dandona P, Dhindsa S, Chaudhuri A, Bhatia V, Topiwala S, Mohanty P. Hypogonadotrophic hypogonadism in type 2 diabetes, obesity and the metabolic syndrome. *Curr Mol Med*. 2008;8(8):816-828.
166. Kim DH, Kim TY, Kim SM, Yoo SJ, Oh DJ, Yu SH. IGF-1 is an independent risk factor for anemia in diabetic pre-dialysis patients. *Korean J Intern Med*. 2007;22(3):186-191.
167. Grossmann M, Panagiotopolous S, Sharpe K, et al. Low testosterone and anaemia in men with type 2 diabetes. *Clin Endocrinol (Oxf)*. 2009;70(4):547-553.
168. Tong PC, Ho CS, Yeung VT, et al. Association of testosterone, insulin-like growth factor-I, and C-reactive protein with metabolic syndrome in Chinese middle-aged men with a family history of type 2 diabetes. *J Clin Endocrinol Metab*. 2005;90(12):6418-6423.
169. Lee ZS, Chan JC, Yeung VT, et al. Plasma insulin, growth hormone, cortisol and central obesity among young Chinese type 2 diabetic patients. *Diabetes Care*. 1999;22(9):1450-1457.
170. Kong AP, Chan NN, Chan JC. The role of adipocytokines and neurohormonal dysregulation in metabolic syndrome. *Curr Diabetes Rev*. 2006;2(4):397-407.
171. Bonovas S, Filioussi K, Tsantes A. Diabetes mellitus and risk of prostate cancer: a meta-analysis. *Diabetologia*. 2004;47(6):1071-1078.
172. Larsson SC, Mantzoros CS, Wolk A. Diabetes mellitus and risk of breast cancer: a meta-analysis. *Int J Cancer*. 2007;121(4):856-862.
173. Friberg E, Orsini N, Mantzoros CS, Wolk A. Diabetes mellitus and risk of endometrial cancer: a meta-analysis. *Diabetologia*. 2007;50(7):1365-1374.
174. Huxley R, Ansary-Moghaddam A, Berrington de Gonzalez A, Barzi F, Woodward M. Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. *Br J Cancer*. 2005;92(11):2076-2083.
175. El-Serag HB, Hampel H, Javadi F. The association between diabetes and hepatocellular carcinoma: a systematic review of epidemiologic evidence. *Clin Gastroenterol Hepatol*. 2006;4(3):369-380.
176. Larsson SC, Orsini N, Wolk A. Diabetes mellitus and risk of colorectal cancer: a meta-analysis. *J Natl Cancer Inst*. 2005;97(22):1679-1687.
177. Barone BB, Yeh HC, Snyder CF, et al. Long-term all-cause mortality in cancer patients with preexisting diabetes mellitus: a systematic review and meta-analysis. *JAMA*. 2008;300(23):2754-2764.
178. Jee SH, Ohrr H, Sull JW, Yun JE, Ji M, Samet JM. Fasting serum glucose level and cancer risk in Korean men and women. *JAMA*. 2005;293(2):194-202.
179. Seow A, Yuan JM, Koh WP, Lee HP, Yu MC. Diabetes mellitus and risk of colorectal cancer in the Singapore Chinese Health Study. *J Natl Cancer Inst*. 2006;98(2):135-138.
180. Gapstur SM, Gann PH, Lowe W, Liu K, Colangelo L, Dyer A. Abnormal glucose metabolism and pancreatic cancer mortality. *JAMA*. 2000;283(19):2552-2558.
181. Barclay AW, Petocz P, McMillan-Price J, et al. Glycemic index, glycemic load, and chronic disease risk—a meta-analysis of observational studies. *Am J Clin Nutr*. 2008;87(3):627-637.
182. Nakagami T; DECODA Study Group. Hyperglycaemia and mortality from all causes and from cardiovascular disease in five populations of Asian origin. *Diabetologia*. 2004;47(3):385-394.
183. Karin M, Lawrence T, Nizet V. Innate immunity gone awry: linking microbial infections to chronic inflammation and cancer. *Cell*. 2006;124(4):823-835.
184. Ma RC, Chan JC. Metabolic complications of obesity. In: Williams G, Frubeck G, eds. *Obesity: Science to Practice.* Hoboken, NJ: John Wiley & Sons; 2009:237-272.
185. Chan JC, Cheung CK, Cheung MY, Swaminathan R, Critchley JA, Cockram CS. Abnormal albuminuria as a predictor of mortality and renal impairment in Chinese patients with NIDDM. *Diabetes Care*. 1995;18(7):1013-1016.
186. Yang X, So WY, Tong PC, et al; Hong Kong Diabetes Registry. Development and validation of an all-cause mortality risk score in type 2 diabetes. *Arch Intern Med*. 2008;168(5):451-457.
187. Yang X, So WY, Kong AP, et al. Development and validation of a total coronary heart disease risk score in type 2 diabetes mellitus. *Am J Cardiol*. 2008;101(5):596-601.
188. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20(4):537-544.
189. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18):1343-1350.
190. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403.
191. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V; Indian Diabetes Prevention Programme (IDPP). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia*. 2006;49(2):289-297.
192. Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract*. 2005;67(2):152-162.
193. Kong AP, Yang X, Ko GT, et al. Effects of treatment targets on subsequent cardiovascular events in Chinese patients with type 2 diabetes. *Diabetes Care*. 2007;30(4):953-959.
194. Chan JC, So WY, Yeung CY, et al. The SURE study: effects of structured versus usual care on renal endpoint in type 2 diabetes: a randomized multicentre translational study. *Diabetes Care*. In press.
195. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med*. 2008;358(6):580-591.

