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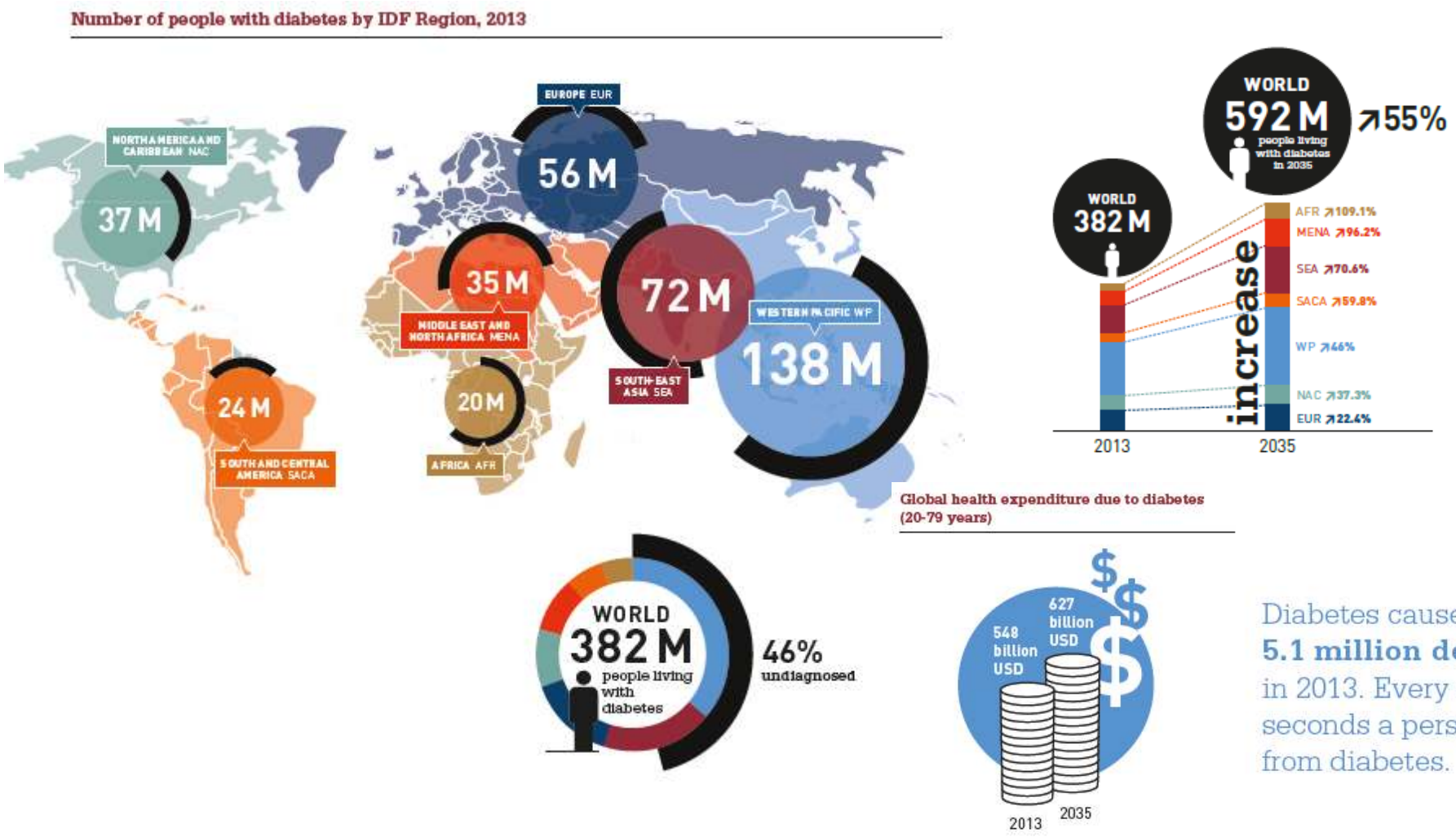
Serum adiponectin and type 2 diabetes : a 6-year follow-up cohort study

Ji Sun Nam, M.D., Ph.D.

Division of Endocrinology, Department of Internal Medicine,
College of Medicine, Yonsei University
Gangnam Severance Hospital

BACKGROUND

Diabetes in the World
: IDF 2013



Diabetes caused **5.1 million deaths** in 2013. Every six seconds a person dies from diabetes.

Diabetes in Korea

: Diabetes Fact Sheet in Korea 2013

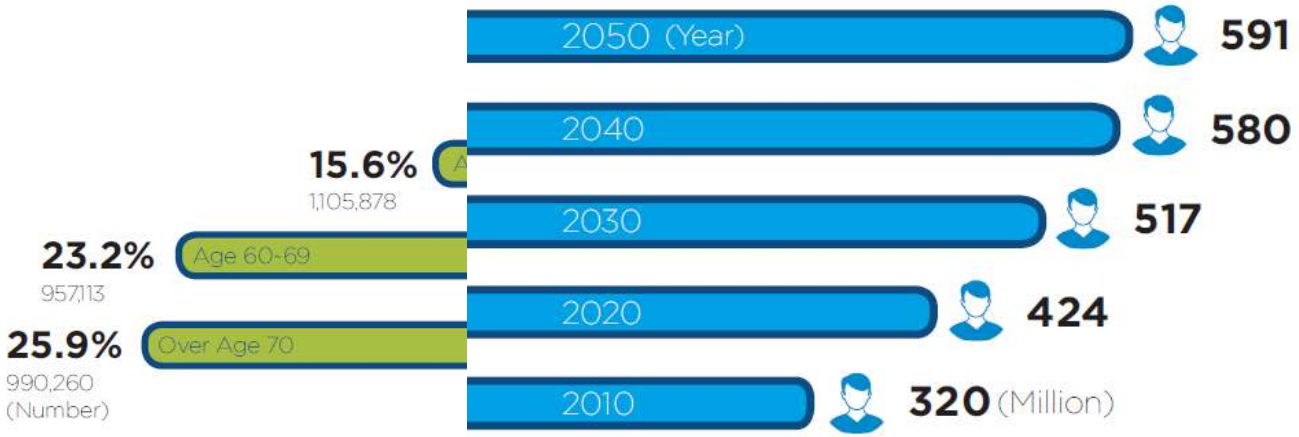
PREVALENCE OF DIABETES 2011 (≥3

› The prevalence of diabetes in adults 30 years and older is 12.4%.
› As of 2011, an estimated 4.0 million people (about 1 every 8 adults) had diabetes.

FUTURE DIABETES POPULATION

190%

› Diabetic population expected to reach about 6 million in 2050.
› 183% increase compared to 2010 : two-fold growth expected for the next 40 years.



STATISTICAL ANALYSIS
CURRENT (2010)

Diabetes prevalence by age (in decades) and gender, multiplied by estimated future population.

Figure 2.3 Number of people with IGT by age (20-79 years), 2013 and 2035

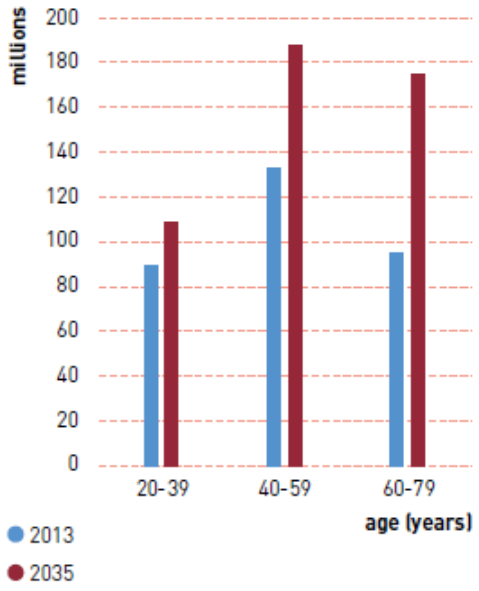
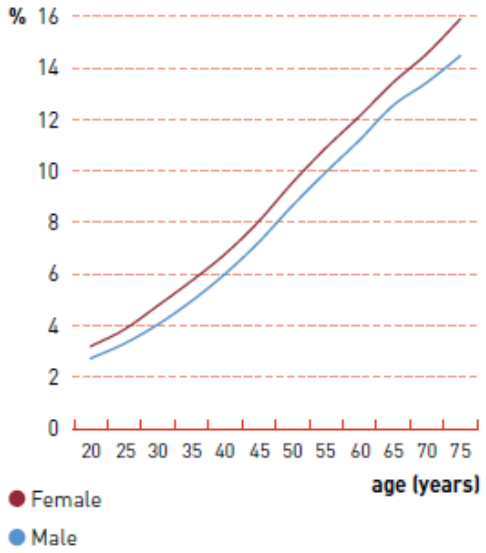


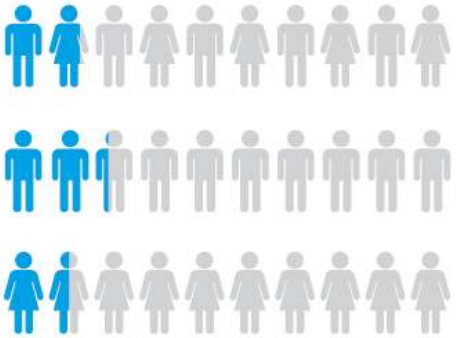
Figure 2.4 Prevalence (%) of IGT (20-79 years) by age and sex, 2013



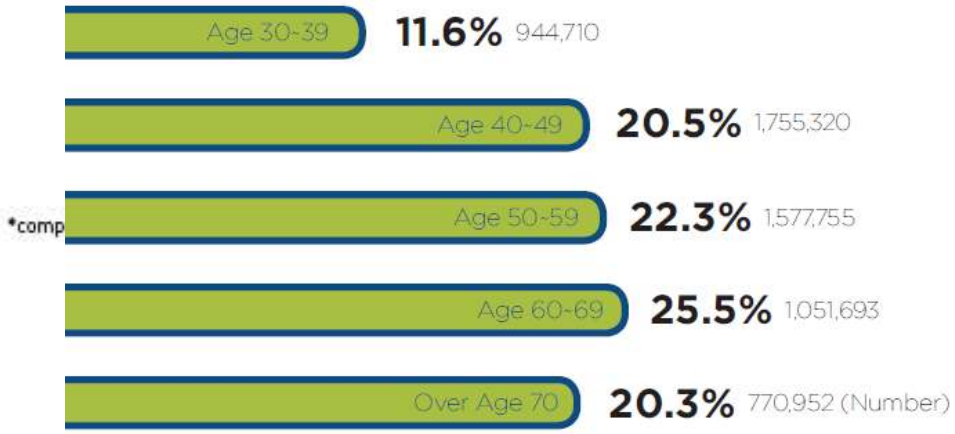
Prediabetes

IMPAIRED FASTING GLUCOSE

Map



› Approximately 20% of adults 30 years and older(6.1 million people) have impaired fasting glucose.
› Therefore, about 1 in 3 adults was diabetes or had potential risk for diabetes.



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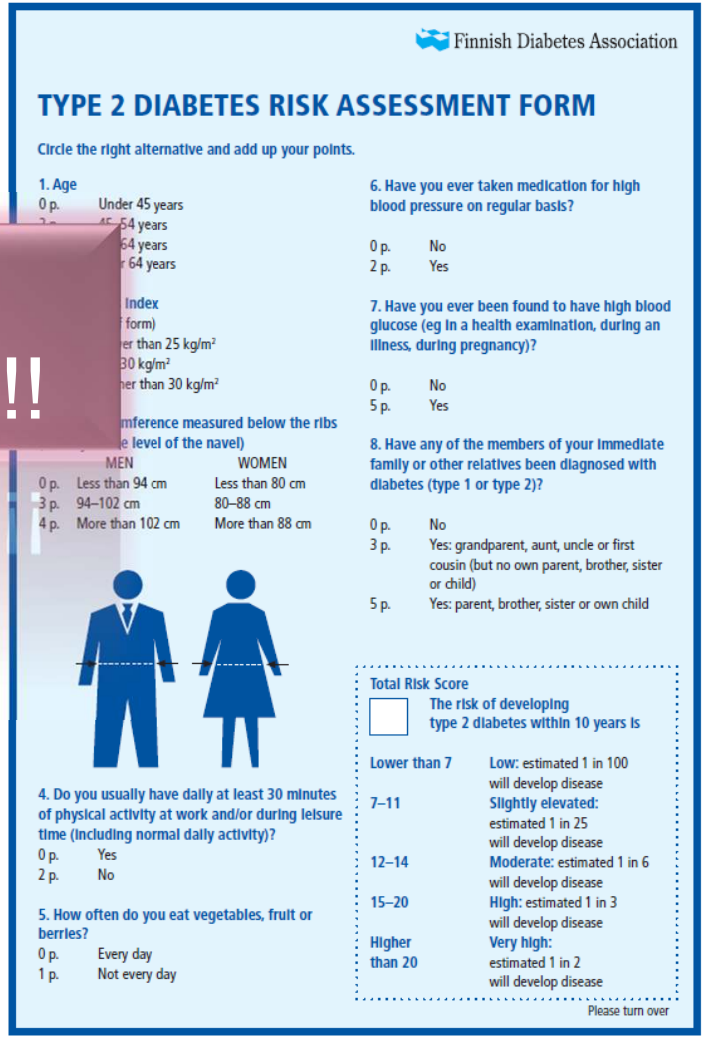
2014 ICDM

Risk factors for developing type 2 diabetes

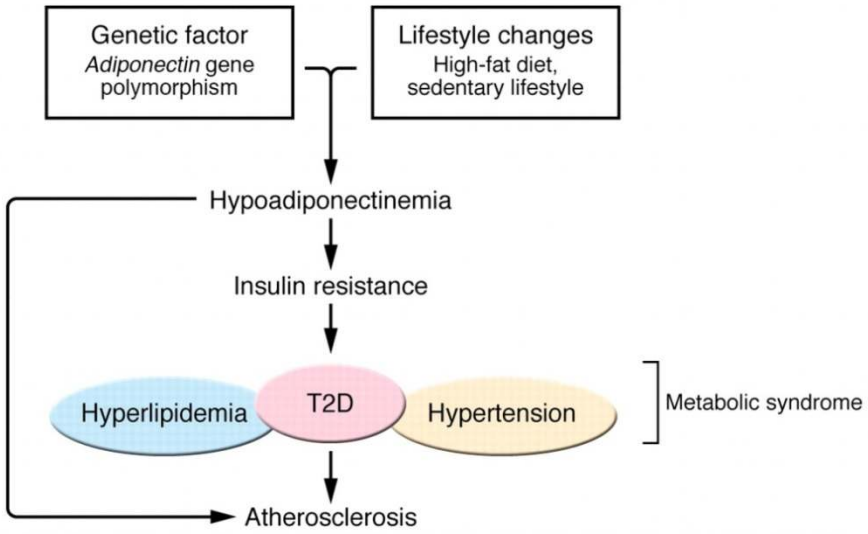
- Weight
- Waist circumference
- Inactivity
- Family history, race
- Age
- Prediabetes
- Gestational DM
- PCOS

NEW BIOMARKER!!!



Adiponectin

- Adipose tissue-derived insulin sensitizer
- Modifies glucose homeostasis by stimulating peripheral glucose utilization and fatty acid oxidation.
- Anti-inflammatory, anti-atherogenic effects
- Cross sectional and longitudinal studies
  - Lower adiponectin level in type 2 diabetes, metabolic syndrome, HTN, cardiovascular disease
  - Studies with patients with IFG are lacking



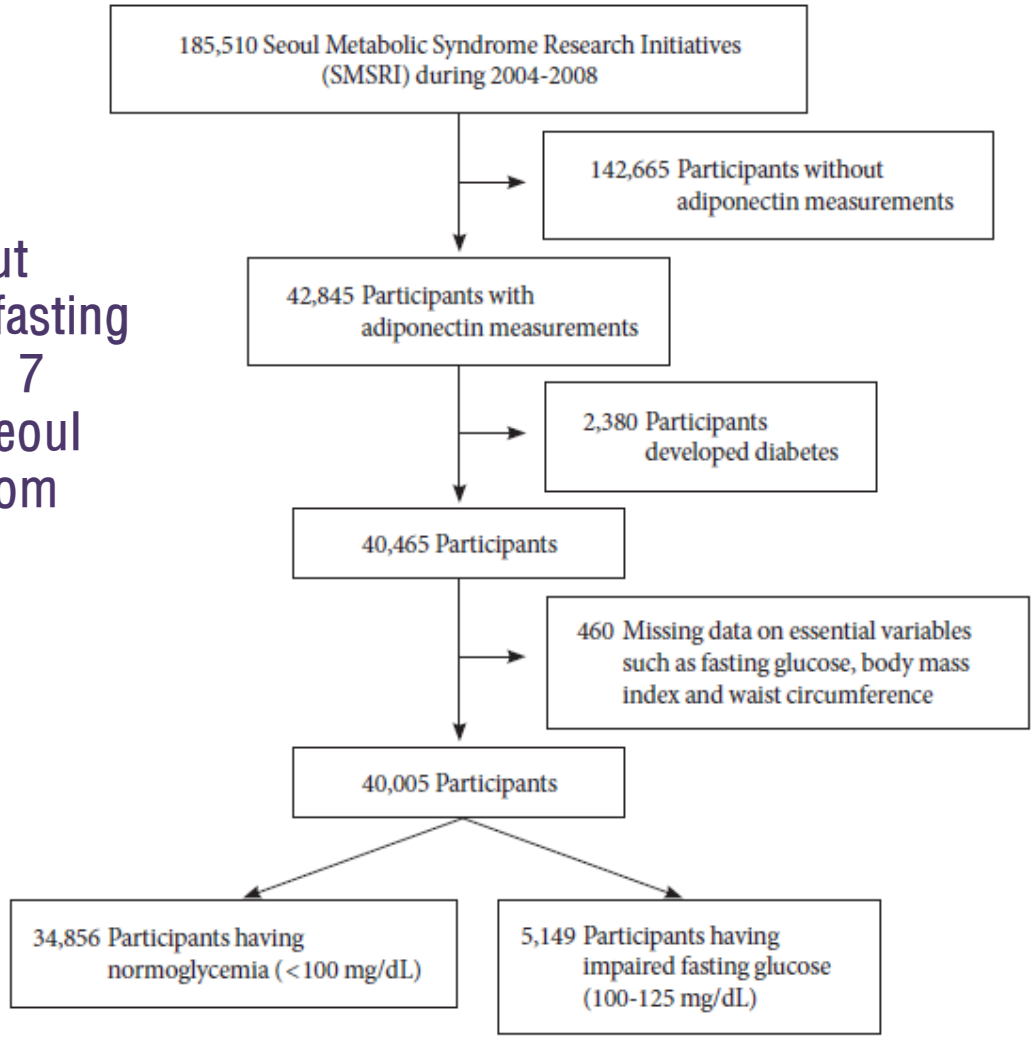
Study objective

- To evaluate the predictive role of adiponectin in the development of diabetes among subjects with normoglycemia and impaired fasting glucose

STUDY DESIGN AND METHODS

Study population

- Study population
  - 40,005 participants without diabetes (34,856 normal fasting glucose, 5,149 IFG) from 7 health exam centers in Seoul and Gyeonggi province from 2004 to 2008



- **Data collection and measurement of biomarkers**
  - Age, gender
  - Structured questionnaire: smoking, alcohol history, exercise
  - Anthropometric measurements: waist circumference, weight, height
  - Blood pressure
  - Fasting venous sample: glucose, adiponectin, lipid profiles

- **Primary outcome : Incidence of diabetes**
  - Fasting glucose $\geq$ 126mg/dL in subsequent health exams until 2010
  - Outpatient treatment for diabetes(at least 3 visits for diabetes care within 365 days) (based on ICD-10 codes from National Health Insurance Service)
  - Hospitalization due to diabetes up to 2010 (at least one hospitalization for diabetes during the study period) (based on ICD-10 codes from National Health Insurance Service)
  - Prescription of diabetes medication between 2004 and 2010 (Health Insurance Review & Assessment Service)

- **Anaylsis**
  - Incidence and age-adjusted incidences of diabetes per 100 person-years (PY)
  - Adiponectin levels were also divided into tertiles as a categorical variable. the highest tertile of adiponectin was a referent which was used to compare the effects of the other two groups in the association with diabetes
  - In multivariable models, age, BMI, and waist circumference were adjusted in model 1, whereas fasting serum glucose was additionally adjusted in model 2. Hypertension, smoking status, alcohol intake, total cholesterol, and a family history of diabetes were additionally adjusted in model 3
  - Cox proportional hazard models were used to evaluate the association between adiponectin and the risk for type 2 diabetes

RESULTS

Baseline characteristics of the study participants

Characteristic	Men			Women		
	Normoglycemia[a] (*n*=21,766)	IFG[b] (*n*=4,101)	Diabetes[c] (*n*=1,895)	Normoglycemia[a] (*n*=13,090)	IFG[b] (*n*=1,048)	Diabetes[c] (*n*=485)
Age, yr	41.5±9.1	45.2±9.3	50.4±9.6	40.9±10.0	47.7±11.2	54.4±11.0
BMI, kg/m^2	24.2±2.9	25.2±2.8	25.3±3.0	22.1±2.9	24.1±3.5	24.8±3.3
Waist circumference, cm	83.7±8.9	86.9±7.4	87.6±7.8	73.1±7.8	78.8±8.9	81.9±8.8
SBP, mm Hg	120.7±12.7	126.4±13.7	127.2±14.3	112.1±13.9	121.8±15.7	125.4±16.1
DBP, mm Hg	76.3±9.9	79.6±10.6	80.1±19.9	70.6±9.7	75.3±11.0	76.6±11.3
Fasting serum glucose, mg/dL	85.8±7.6	106.5±6.1	141.3±44.5	84.4±7.4	105.5±5.4	128.2±43.9
Total cholesterol, mg/dL	189.6±31.7	197.8±33.5	194.0±36.9	181.3±31.7	198.2±34.6	196.8±39.3
HDL-C, mg/dL	48.7±8.6	48.3±10.0	47.3±9.3	57.2±10.9	55.0±11.5	51.7±11.0
Triglyceride, mg/dL	150.4±91.2	177.4±113.4	196.2±135.2	94.7±53.6	122.5±70.6	160.3±103.4
Adiponectin, μg/mL	6.6±3.7	5.7±3.3	5.7±3.8	10.5±5.5	8.6±5.0	8.9±6.0
HMW adiponectin, μg/mL	2.3±1.9	2.0±1.5	2.1±1.9	4.1±2.6	3.3±2.2	3.8±3.2
Smoking status, nonsmoker/ ex-smoker/current smoker (%)	27.7/28.3/44.0	25.1/35.3/39.6	20.9/37.7/41.4	93.0/3.0/4.0	95.0/2.1/2.9	96.7/1.8/1.5
Alcohol intake, no/yes (%)	29.0/71.0	30.3/69.7	37.3/62.7	58.3/41.7	64.1/35.9	79.2/20.8
Exercise, yes/no (%)	67.0/33.0	69.2/30.8	76.5/23.5	50.2/49.8	59.0/41.0	61.6/38.4

Values are presented as mean±standard deviation or percentage.
IFG, impaired fasting glucose; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; HMW, high molecular weight.
[a]Normoglycemia (fasting serum glucose <100 mg/dL), [b]IFG (fasting serum glucose, 100 to 125 mg/dL), [c]Diabetes (fasting serum glucose ≥126 mg/dL or medication).

Overall incidence rate of type 2 diabetes

- **Among 40,005 participants, 959 developed type 2 diabetes during 6 year follow-up**
  - Normoglycemia: 360 of the 34,856 (1.03%) participants (21,766 men and 13,090 women) developed type 2 diabetes
  - IFG: 599 out of 5,149 (11.63%) participants (4,101 men and 1,048 women) developed type 2 diabetes

Incidence rate per 100 person years of type 2 diabetes among Korean men

	Normoglycemia (n=21,766)			Impaired fasting glucose 100-125 (n=4,101)		
	PY	Incident diabetes	Incidence rate/100 PY	PY	Incident diabetes	Incidence rate/100 PY
20-29 yr	5,690	2	0.04 (0.03-0.04)[a]	390	3	0.77 (0.73-0.81)[a]
30-39 yr	40,733	43	0.11 (0.11-0.11)[a]	4,934	86	1.74 (1.73-1.75)[a]
40-49 yr	34,684	84	0.24 (0.24-0.24)[a]	7,393	191	2.58 (2.58-2.58)[a]
50-59 yr	14,245	69	0.48 (0.48-0.49)[a]	3,854	150	3.89 (3.88-3.99)[a]
60+ yr	4,257	34	0.80 (0.79-0.80)[a]	1,385	55	3.97 (3.94-4.00)[a]
Total	99,609	232		17,956	485	
Incidence						
Cumulative method[b]		1.07	-		11.83	-
Incidence density[c]		-	0.23		-	2.70
Age-adjusted incidence density[d]		-	0.29		-	2.39

PY, person years.
[a]95% confidence interval, [b]Cumulative method per 100 persons: 1.07=(232/21,766)×100; 11.83=(485/4,101)×100, [c]Incidence density per 100 PY: 0.23=(232/99,609)×100; 2.70=(485/17,956)×100, [d]Age-adjusted incidence density using the national population in 2005 as a standard population.

Incidence rate per 100 person years of type 2 diabetes among Korean women

	Normoglycemia (n=13,090)			Impaired fasting glucose 100-125 (n=1,048)		
	PY	Incident diabetes	Incidence rate/100 PY	PY	Incident diabetes	Incidence rate/100 PY
20-29 yr	6,837	5	0.07 (0.07-0.07)[a]	221	3	1.35 (1.25-1.45)[a]
30-39 yr	23,397	26	0.11 (0.11-0.11)[a]	1,032	10	0.97 (0.95-0.99)[a]
40-49 yr	19,254	30	0.16 (0.16-0.16)[a]	1,475	31	2.10 (2.08-2.12)[a]
50-59 yr	8,775	38	0.43 (0.43-0.43)[a]	1,232	46	3.73 (3.70-3.76)[a]
60+ yr	3,272	29	0.89 (0.88-0.89)[a]	798	24	3.01 (2.97-3.05)[a]
Total	61,535	128		4,758	114	
Incidence						
Cumulative method[b]		0.98	-		10.88	-
Incidence density[c]		-	0.21		-	2.40
Age-adjusted incidence density[d]		-	0.32		-	2.11

PY, person years.
[a]95% confidence interval, [b]Cumulative method per 100 persons: 1.07=(232/21,766)×100; 11.83=(485/4,101)×100, [c]Incidence density per 100 PY: 0.23=(232/99,609)×100; 2.70=(485/17,956)×100, [d]Age-adjusted incidence density using the national population in 2005 as a standard population.

Hazard ratios for diabetes by tertiles of adiponectin among Korean men

	Normoglycemia[a] (FSG <100 mg/dL)			Impaired fasting glucose[b] (FSG 100-125 mg/dL)		
	Model 1[c]	Model 2[d]	Model 3[e]	Model 1[c]	Model 2[d]	Model 3[e]
Serum adiponectin						
(T1) High	1.00	1.00	1.00	1.00	1.00	1.00
(T2) Middle	1.61 (1.15-2.26)	1.51 (1.07-2.12)	1.51 (1.05-2.17)	1.21 (0.96-1.53)	1.14 (0.90-1.44)	1.08 (0.83-1.39)
(T3) Low	1.70 (1.21-2.38)	1.51 (1.07-2.11)	1.54 (1.07-2.20)	1.46 (1.17-1.83)	1.39 (1.11-1.74)	1.27 (1.00-1.63)
Age, yr	1.07 (1.06-1.09)	1.07 (1.05-1.08)	1.06 (1.05-1.08)	1.04 (1.03-1.05)	1.03 (1.02-1.04)	1.03 (1.02-1.04)
BMI, kg/m^2	1.04 (1.03-1.06)	1.05 (1.03-1.06)	1.04 (1.03-1.06)	1.07 (1.00-1.13)	1.04 (0.98-1.11)	1.04 (0.97-1.11)
Waist circumference, cm	1.01 (1.00-1.01)	1.01 (1.00-1.01)	1.01 (1.00-1.01)	1.02 (1.00-1.04)	1.01 (0.99-1.04)	1.02 (0.99-1.04)
Fasting serum glucose, mg/dL		1.06 (1.04-1.08)	1.06 (1.04-1.08)		1.12 (1.11-1.13)	1.11 (1.09-1.12)
Hypertension			1.64 (1.22-2.20)			0.91 (0.73-1.13)
Total cholesterol, per 10 mg/dL			1.05 (1.01-1.10)			1.01 (0.99-1.04)
Smoking status						
Ex-smokers			0.97 (0.67-1.41)			1.03 (0.79-1.36)
Current smokers			1.48 (1.04-2.10)			1.30 (1.00-1.69)
Alcohol intake			0.92 (0.69-1.23)			1.00 (0.81-1.24)
Family history of diabetes			1.31 (0.89-1.95)			1.13 (0.88-1.46)

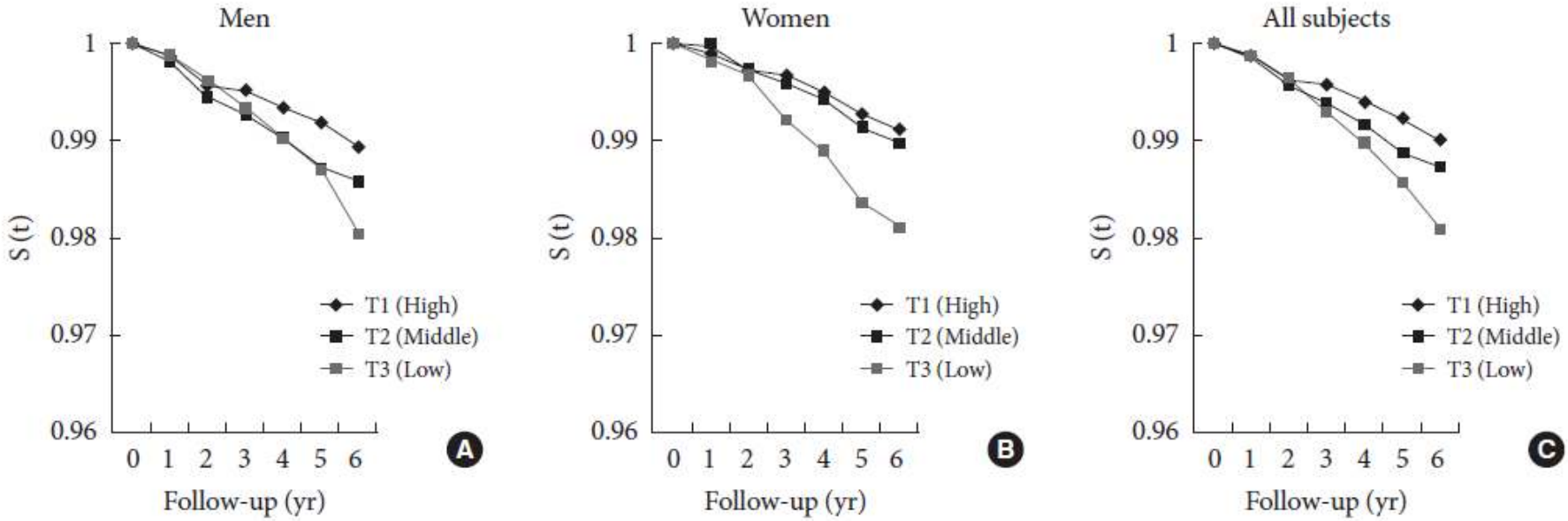
FSG, fasting serum glucose; BMI, body mass index.
[a]Normoglycemia group: high, ≥7.24, middle, 4.61-7.23, low, <4.61 μg/mL, [b]Impaired fasting glucose group: high, ≥6.24, middle, 3.91-6.23, low, <3.91 μg/mL, [c]Model 1, adjusted for age, body mass index, and waist circumference, [d]Model 2, model 1+additional adjustment for fasting glucose, [e]Model 3, model 2+additional adjustment for hypertension, total cholesterol, smoking status, alcohol intake, and family history of diabetes.

Hazard ratios for diabetes by tertiles of adiponectin among Korean women

	Normoglycemia[a] (FSG <100 mg/dL)			Impaired fasting glucose[b] (FSG 100-125 mg/dL)		
	Model 1[c]	Model 2[d]	Model 3[e]	Model 1[c]	Model 2[d]	Model 3[e]
Serum adiponectin						
(T1) High	1.00	1.00	1.00	1.00	1.00	1.00
(T2) Middle	1.11 (0.67-1.83)	1.08 (0.66-1.78)	1.07 (0.63-1.80)	1.06 (0.61-1.85)	1.16 (0.66-2.02)	0.95 (0.52-1.74)
(T3) Low	1.83 (1.17-2.86)	1.75 (1.12-2.74)	1.52 (0.94-2.46)	2.52 (1.57-4.06)	2.35 (1.45-3.79)	2.08 (1.25-3.46)
Age, yr	1.06 (1.04-1.07)	1.05 (1.04-1.07)	1.03 (1.01-1.06)	1.03(1.01-1.05)	1.03 (1.01-1.05)	1.03 (1.00-1.05)
BMI, kg/m^2	1.10 (1.01-1.21)	1.10 (1.00-1.21)	1.08 (0.98-1.19)	1.01 (0.92-1.12)	1.01 (0.91-1.12)	1.02 (0.91-1.14)
Waist circumference, cm	1.03 (0.99-1.07)	1.03 (0.99-1.07)	1.03 (0.99-1.07)	1.03 (0.99-1.08)	1.02 (0.98-1.06)	1.03 (0.98-1.07)
Fasting serum glucose, mg/dL		1.03 (1.00-1.05)	1.03 (1.00-1.06)		1.11 (1.08-1.14)	1.09 (1.06-1.12)
Hypertension			2.00 (1.28-3.12)			1.36 (0.88-2.11)
Total cholesterol, per 10 mg/dL			1.04 (0.98-1.10)			1.00 (0.94-1.05)
Smoking status						
Ex-smokers			1.19 (0.38-3.78)			0.82 (0.20-3.39)
Current smokers			0.62 (0.15-2.54)			1.36 (0.47-3.92)
Alcohol intake			0.91 (0.59-1.42)			1.22 (0.76-1.96)
Family history of diabetes			1.36 (0.84-2.19)			1.75 (1.11-2.76)

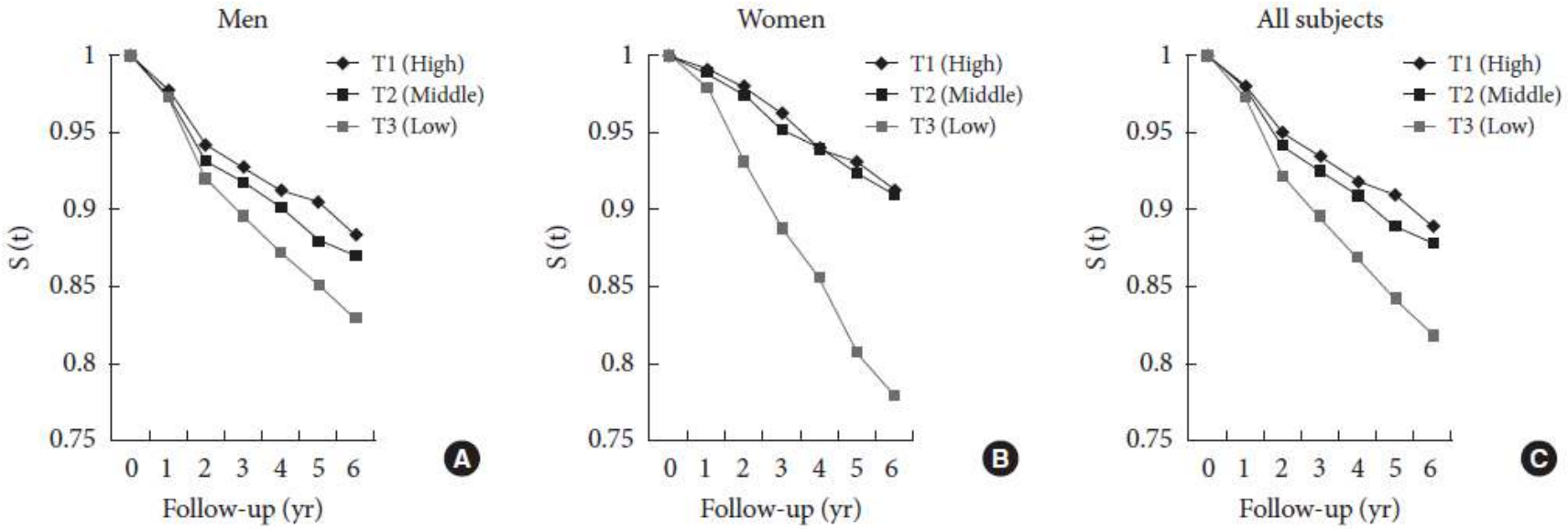
FSG, fasting serum glucose; BMI, body mass index.
[a]Normoglycemia group, high, ≥11.84, middle, 7.44-11.83, low, <7.44 μg/mL, [b]Impaired fasting glucose group, high, ≥9.42, middle, 5.99-9.41, low, <5.99 μg/mL, [c]Model 1, adjusted for age, body mass index, and waist circumference, [d]Model 2, model 1+additional adjustment for fasting glucose, [e]Model 3, model 2+additional adjustment for hypertension, total cholesterol, smoking status, alcohol intake, and family history of diabetes.

Association between adiponectin and type 2 diabetes among participants with normoglycemia during a 6-year follow-up



(A) men, (B) women, (C) all subjects; adiponectin levels: men, (T1) high, ≥7.24, (T2) middle, 4.61-7.23, (T3) low, <4.61 μg/mL; women, (T1) high, ≥11.84, (T2) middle, 7.44-11.83, (T3) low, <7.44 μg/mL.

Association between adiponectin and type 2 diabetes among participants with impaired fasting glucose during a 6-year follow-up



(A) men, (B) women, (C) all subjects; adiponectin levels: men, (T1) high, ≥6.24, (T2) middle, 3.91-6.23, (T3) low, <3.91 μg/mL; women, (T1) high, ≥9.42, (T2) middle, 5.99-9.41, (T3) low, <5.99 μg/mL.

Conclusions

- Adiponectin is the strong predictor of type 2 diabetes independent of various factors including age, BMI, WC, FPG, smoking, HTN, alcohol, and family history.
- The predictive value of adiponectin was stronger in women with IFG, and further studies are needed to explain a such gender difference.
- Serum adiponectin may be used as an ancillary factor with fasting glucose in the prediction of diabetes.
- More vigilance should be paid on normoglycemic as well as IFG subjects with low adiponectin level.

THANK YOU

Original Article

Epidemiology

Diabetes Metab J 2013;37:252-261
http://dx.doi.org/10.4093/dmj.2013.37.4.252
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

Serum Adiponectin and Type 2 Diabetes: A 6-Year Follow-Up Cohort Study

Sun Ha Jee[1], Chul Woo Ahn[2], Jong Suk Park[2], Chang Gyu Park[3], Hyon-Suk Kim[4], Sang-Hak Lee[5], Sungha Park[5], Myoungsook Lee[6], Chang Beom Lee[7], Hye Soon Park[8], Heejin Kimm[1], Sung Hee Choi[9], Jidong Sung[10], Seungjoon Oh[11], Hyojee Joung[12], Sung Rae Kim[13], Ho-Joong Youn[14], Sun Mi Kim[15], Hong Soo Lee[16], Yejin Mok[1], Eunmi Choi[1], Young Duk Yun[17], Soo-Jin Baek[17], Jaeseong Jo[1], Kap Bum Huh[18]

[1]Institute for Health Promotion, Department of Epidemiology and Health Promotion, Yonsei University Graduate School of Public Health, Seoul,
[2]Division of Endocrinology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul,
[3]Cardiovascular Center, Korea University Guro Hospital, Korea University College of Medicine, Seoul,
[4]Department of Laboratory Medicine, [5]Cardiology Division, Department of Internal Medicine, Yonsei University College of Medicine, Seoul,
[6]Department of Food and Nutrition, Sungshin Women's University College of Human Ecology, Seoul,
[7]Department of Endocrinology and Metabolism, Hanyang University College of Medicine, Seoul,
[8]Department of Family Medicine, University of Ulsan College of Medicine, Seoul,
[9]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam,
[10]Division of Cardiology, Department of Medicine, and Cardiac and Vascular Center, Center for Health Promotion, Sungkyunkwan University School of Medicine, Seoul,
[11]Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul,
[12]Division of Public Health Nutrition, Seoul National University School of Public Health and Institute of Health and Environment, Seoul,
[13]Department of Endocrinology and Metabolism, [14]Division of Cardiology, Department of Internal Medicine, The Catholic University of Korea College of Medicine, Seoul,
[15]Department of Family Medicine, Korea University College of Medicine, Seoul,
[16]Department of Family Medicine, Ewha Womans University School of Medicine, Seoul,
[17]National Health Insurance Service, Seoul,
[18]Huh's Diabetes Center and the 21th Century Diabetes and Vascular Research Institute, Seoul, Korea