

2013 ICDM & 5th AASD, Seoul, Korea
CD7. Measurement of insulin resistance
and secretion in diabetes clinic



Insulin resistance: anthropometric measurement

Dae-Jung Kim, M.D.

Department of Endocrinology and Metabolism, Aju(亞洲)
University, Korea
djkim@ajou.ac.kr

WHO: obesity epidemic

- Overweight and obesity are defined as abnormal or **excessive fat accumulation** that presents a risk to health.
- Globally, around 35% of adults aged 20 and over were overweight in 2008.
- More than 1.4 billion adults, 20 and older, were overweight. Of these overweight adults, over 200 million men and nearly 300 million women were obese.

Obesity and insulin resistance

- Insulin resistance is a fundamental aspect of the etiology of type 2 diabetes, and other diseases including hypertension, dyslipidemia, metabolic syndrome and atherosclerosis.
- Obese individuals develop resistance to the cellular actions of insulin, characterized by an impaired ability of insulin to inhibit glucose output from the liver and to promote glucose uptake in fat and muscle.

Methods of estimating body fat and its distribution

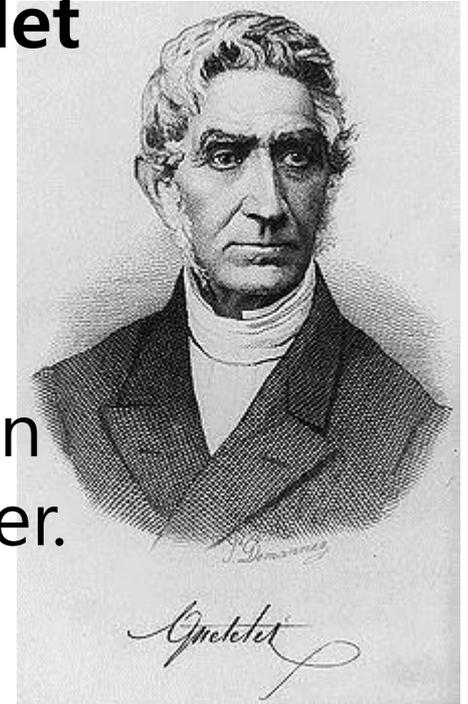
Method	Cost	Ease of use	Accuracy	Measures regional fat
Height and weight	\$	Easy	High	No
Skin folds	\$	Easy	Low	Yes
Circumferences	\$	Easy	Moderate	Yes
Ultrasound	\$\$	Moderate	Moderate	Yes
Density				
Immersion	\$	Moderate	High	No
Plethysmograph	\$\$\$	Difficult	High	No
Heavy water				
Tritiated	\$\$	Moderate	High	No
Deuterium oxide, or heavy oxygen	\$\$\$	Moderate	High	No
Potassium isotope (40K)	\$\$\$\$	Difficult	High	No
Total body electrical conductivity (TOBEC)	\$\$\$	Moderate	High	No
Bioelectric impedance (BIA)	\$\$	Easy	High	No
Fat-soluble gas	\$\$	Difficult	High	No
Absorptiometry (dual energy x-ray absorptiometry (DEXA); dual photon absorptiometry (DPA)	\$\$\$	Easy	High	No
Computed tomography (CT)	\$\$\$\$	Difficult	High	Yes
Magnetic resonance imaging (MRI)	\$\$\$\$	Difficult	High	Yes
Neutron activation	\$\$\$\$	Difficult	High	No

\$ = low cost; \$\$ = moderate cost; \$\$\$ = high cost; \$\$\$\$ = very high cost.

BODY MASS INDEX

History of Body mass index

- **Lambert-Adolphe-Jacques Quetelet**
 - Belgian mathematician
 - In 1832, **Quetelet Index**
 - Among adults, **weight** in kgs seemed to increase in proportion to the **square of stature** in meter.
 - **W/S^b** (historically)
 - Based on age, gender, race, diseases
 - **W/S^2** ; Kg/m², lb/in²*703



History of Body mass index

- **Ansel Keys**, American scientist
 - “Indices of relative weight and obesity” (Journal of Chronic Diseases, 1972)
 - 7,424 healthy men in 12 cohorts
 - New term “**body mass index**”
 - Useful index for grading adiposity in population studies; **kg/m²**



What is a healthy weight?

- Minimal **mortality** rates and lowest **risks** for developing diseases associated with obesity
 - BMI of 22 kg/m²
 - 20-25 kg/m²; healthy weight range
 - Committee on Dietary Guidelines;
 - 19-25 as normal

BMI definition for obesity

- In 1980, dietary guidelines
 - normal weight; <25-26 kg/m²(M) 24-25(F)
- In 1985, NIH consensus Development Panel
 - Overweight, obesity; ≥27.8 kg/m²(M), 27.3kg/m²(F)
- **In 1995, WHO, In 1998, NHLBI Expert panel**
 - Overweight; from BMI 27.8 to 25 kg/m²(M/F)
 - Obese; ≥30.0 kg/m²(M/F)
- **In 2002, WHO, for Asians**
 - Overweight; BMI of 23, Obese; ≥25.0 kg/m²(M/F)

Definition of obesity in adults

Classification	BMI (kg/m ²) ¹	Risk of comorbidities ²
Underweight	<18.5	Low (but risk of other clinical problems increased)
Normal range	18.5–24.9	Average
Overweight	25.0–29.9	Mildly increased
Obese	≥30.0	
Class I	30.0–34.9	Moderate
Class II	35.0–39.9	Severe
Class III	≥40.0	Very severe

Note: Obesity is classified as body mass index (BMI) ≥ 30 kg/m².

¹BMI = Body Mass Index (kg/m²).

²Comorbidities = diabetes; hypertension; sleep apnea; heart disease; gall bladder disease.

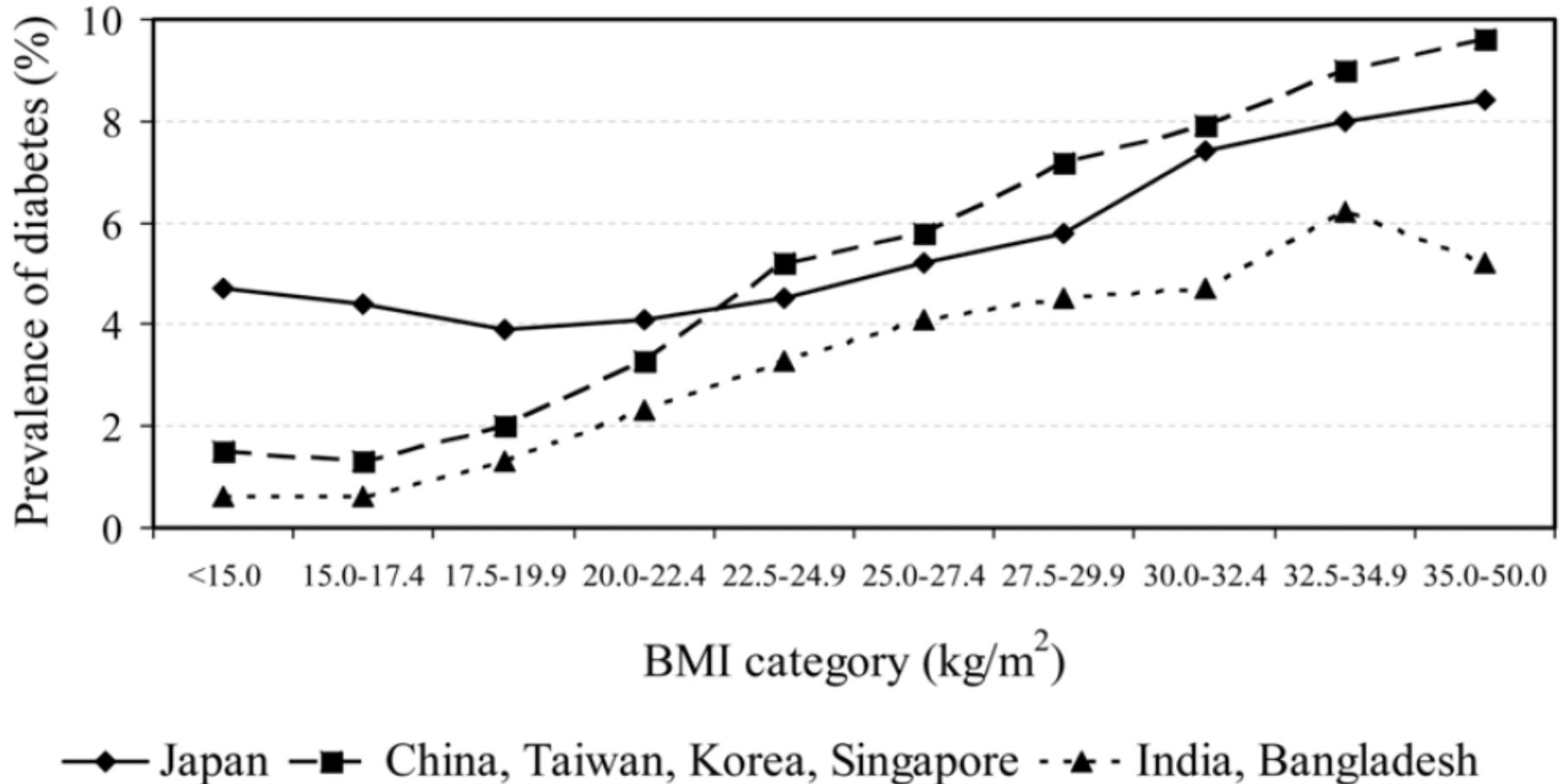
Definition of obesity in Asians

Classification	BMI (kg/m ²)	Risk of co-morbidities
Underweight	< 18.5	Low (but increased risk of other clinical problems)
Normal range	18.5 – 22.9	Average
Overweight	≥ 23	
At risk	23 – 24.9	Increased
Obese I	25 – 29.9	Moderate
Obese II	≥ 30	Severe

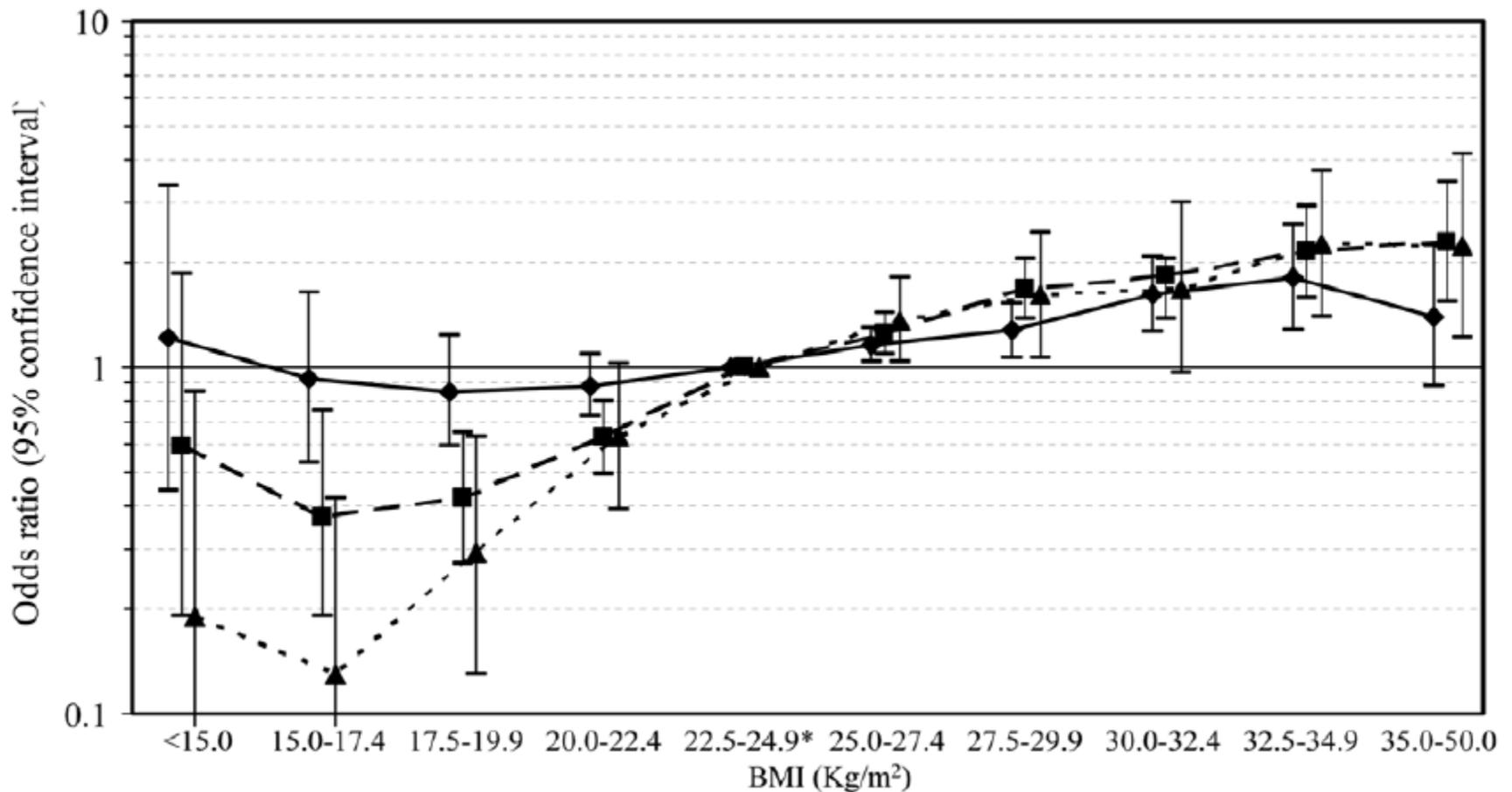
BMI and diabetes in Asia

- Pooled cross-sectional analysis
- Self-reported diabetes status
- N=900,000, 18 cohorts
- Korea Multi-center Cancer (KMCC) data in Korea (n=15,058)
- Referent BMI; 22.5-24.9 kg/m²

BMI and diabetes in Asia



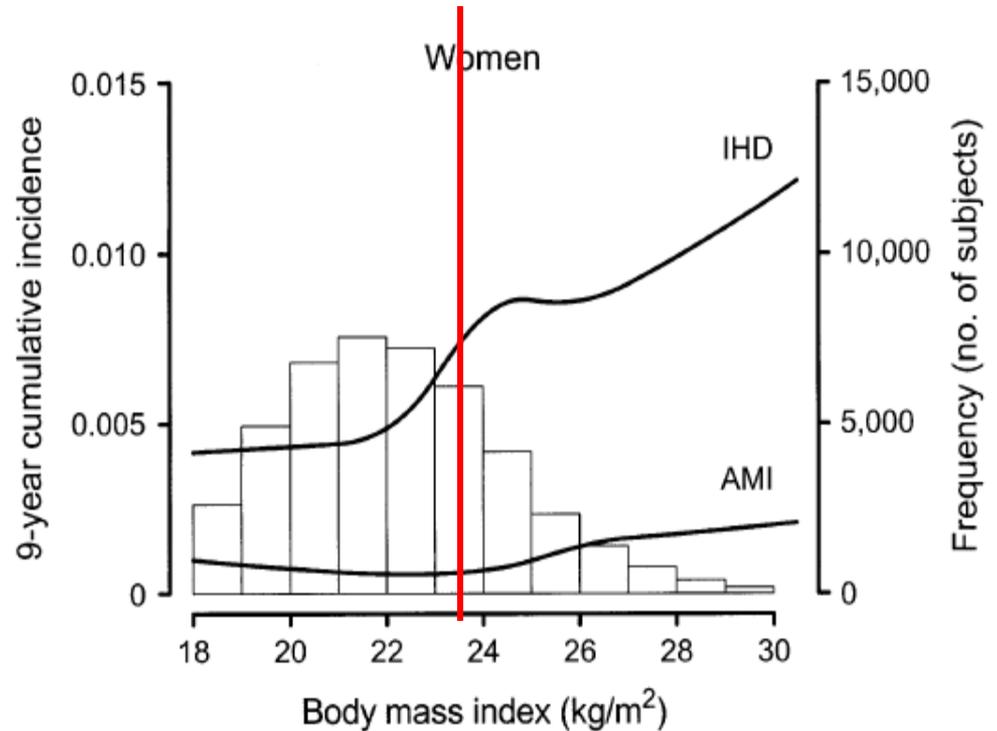
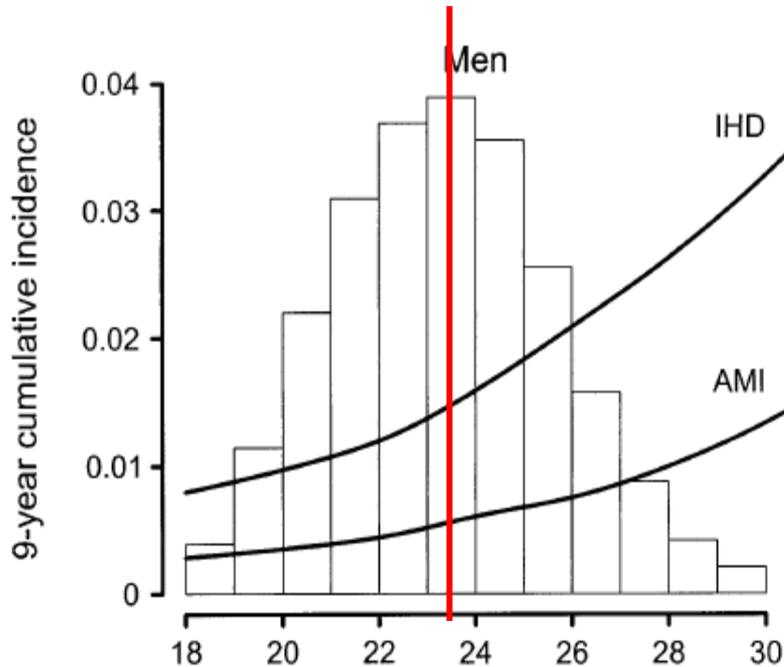
BMI and diabetes in Asia



Diamonds: Japan (N=180,405); squares: China, Taiwan, Singapore, Korea (N=198,471); triangles: India, Bangladesh (N=73,909)

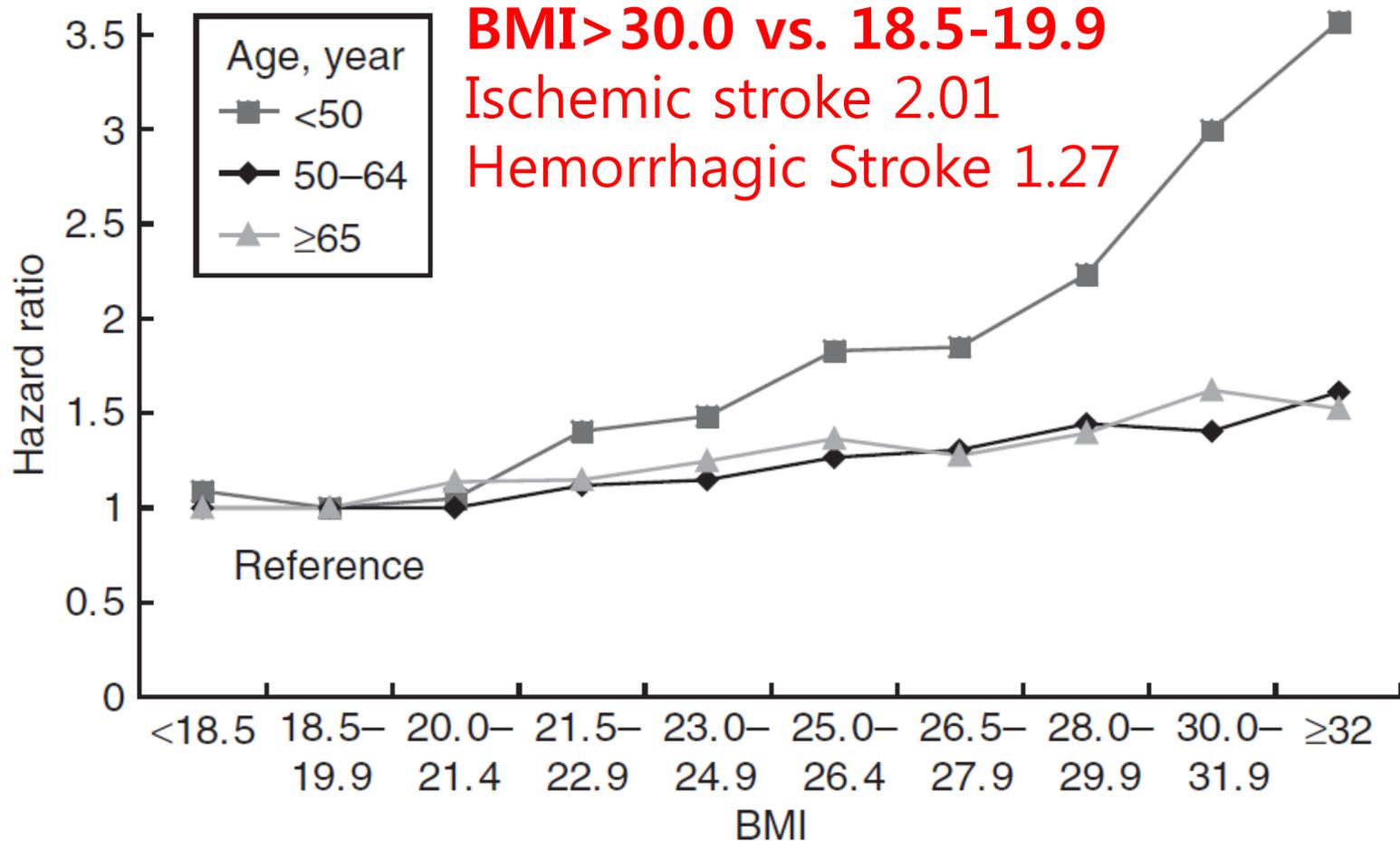
BMI and incident IHD

HR: 2.01 (1.32-3.05)



Average BMI: 23.4(M) 22.3(F)

BMI and stroke risk in Korean women



Baseline BMI 23.2

BMI and mortality in Korean

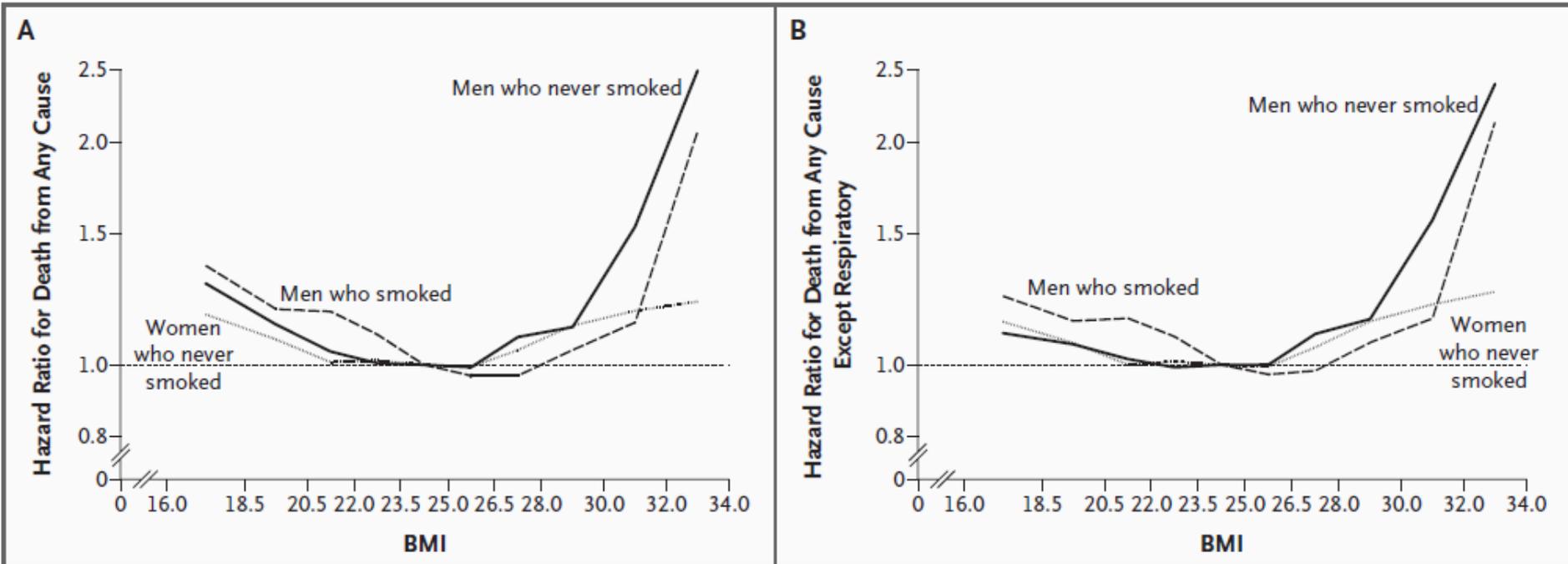


Figure 1. Hazard Ratios for Death from Any Cause and from Any Cause Except Respiratory, According to BMI and Smoking History.

Data are from the KCPS, 1993–2004.^{12,13} The reference category was a BMI of 23.0 to 24.9. Results for men who reported having smoked cigarettes were further adjusted for whether the subject was a former smoker or a current smoker and the number of cigarettes smoked per day (1 to 9, 10 to 19, and 20 or more). All hazard ratios were adjusted for age.

Referent BMI 23-24.9

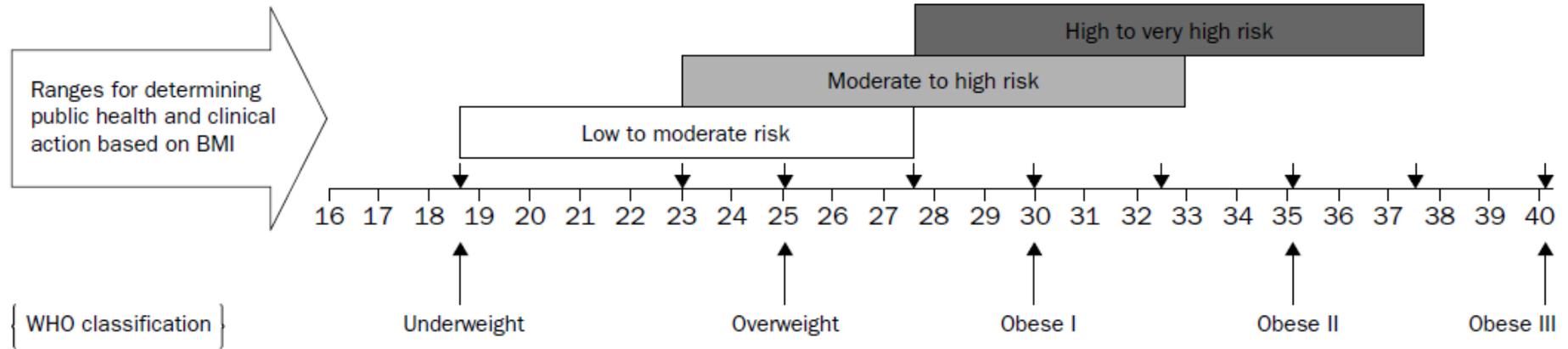
Optimal BMI in Koreans?

- **Risk for diseases and mortality**
 - Diabetes: 23(M/F)
 - IHD: 23-24
 - Stroke: linear, 21.5-22.9 (esp. <50yrs)
 - All-cause mortality: U shape, 30
 - Cardiovascular mortality: 26-28(M) 28-30(F)

Appropriate BMI for Asian populations

- IASO, IOTF and WHO proposed BMI cut-points 23.0 to 24.9 kg/m² for being overweight and ≥ 25.0 kg/m² for obesity in adults Asians
- In 2002, the WHO Expert Consultation concluded that there was **no** universal cut-point for overweight or obese in all Asian populations

BMI cut-off points for Asians



Appropriate BMI for Asian populations

BMI (kg/m ²)		Weight Categories	Health Risk
WHO	Asian		
30 & above	27.5 & above	Obese	High risk of developing heart disease, high blood pressure, stroke and diabetes
25 to 29.9	23 to 27.4	Overweight	Moderate risk of developing the above diseases
18.5 to 24.9	18.5 to 22.9	Healthy Range	Low risk of developing the above diseases
Below 18.5	Below 18.5	Underweight	At risk of developing nutritional deficiency diseases and osteoporosis

WAIST CIRCUMFERENCES

Waist circumference cutoff points for Korean adults

- In 2005, the International Diabetes Federation (IDF) in a global consensus statement formulated a new, clinically accessible, worldwide definition of metabolic syndrome.
- A prominent feature of the IDF definition is that central obesity is an essential, not an optional, component of metabolic syndrome, with central obesity defined according to ethnically specific values of waist circumference (WC)

Waist circumference cutoff points for Korean adults

- The cutoff point for central obesity in the United States was defined as 102 cm for men and 88 cm for women, whereas, for Europeans, the cutoff was 94 cm for men and 80 cm for women.
- Asians are more prone to obesity-related comorbidities than Caucasians, even at lower BMI and/or smaller WC values. Therefore, cutoff values of 90 cm for men and 80 cm for women were adopted for South Asians and Chinese, and the Japanese used cutoff points of 85 cm for men and 90 cm for women

To develop new WC cutoff in Korea

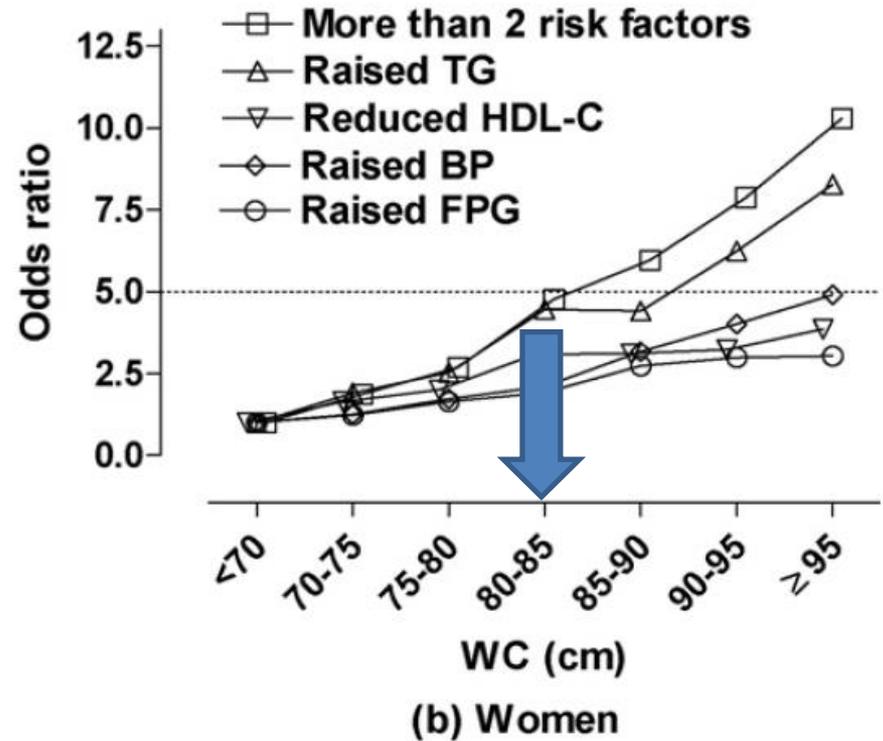
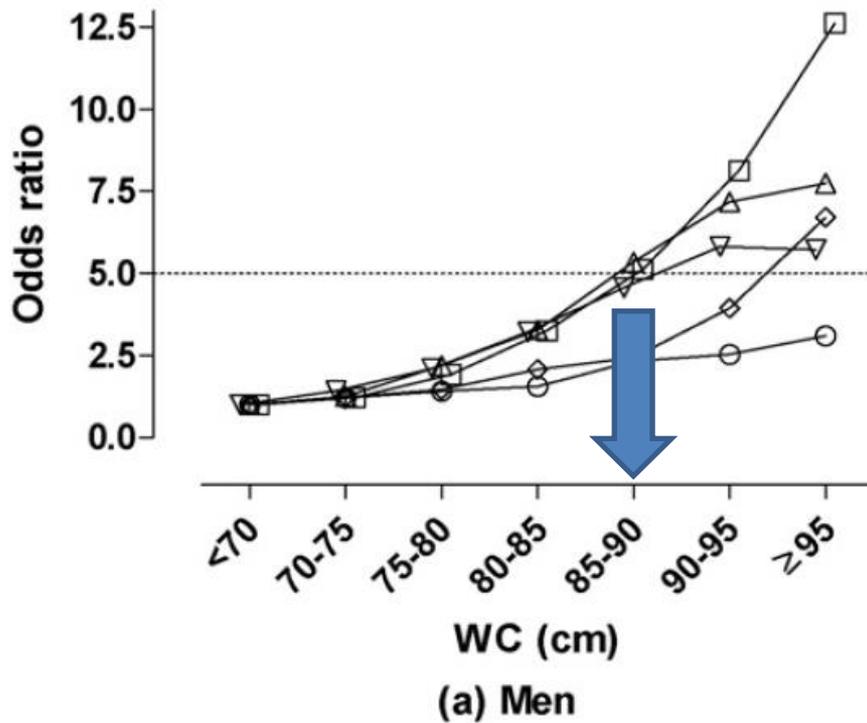
- Korean Society for the Study of Obesity (KSSO)
- **Korea Health and Nutritional Examination Survey** of 1998
 - a cross-sectional health survey of a nationally representative sample of Koreans
 - 6561 adults, aged 20–80 years
- **ROC curve analysis**; WC value for predicting metabolic risk factors in Koreans
- **Odds ratio** for the risk of two or more metabolic risk factors

Waist; ROC analysis

WC cutoff (cm)	Percentile	Elevated triacylglycerol			Reduced HDL cholesterol			Elevated blood pressure			Elevated fasting glucose			Two or more risk factors		
		Sensitivity	Specificity	Yuden index	Sensitivity	Specificity	Yuden index	Sensitivity	Specificity	Yuden index	Sensitivity	Specificity	Yuden index	Sensitivity	Specificity	Yuden index
Men																
60	0.1	100.0	0.1	0.1	100.0	0.1	0.1	99.9	0.1	0.0	99.8	0.0	-0.2	99.9	0.1	0.0
65	1.1	99.5	1.4	0.9	99.7	1.3	1.0	99.4	1.4	0.8	99.2	1.2	0.4	99.5	1.5	1.0
70	5.6	97.7	7.5	5.2	97.6	6.6	4.2	96.6	7.2	3.8	96.4	7.0	3.4	97.5	8.2	5.7
75	18.8	91.7	24.8	16.5	90.3	21.9	12.2	87.7	23.6	11.3	86.1	22.3	8.4	90.8	27.2	18.0
80	38.1	77.4	47.0	24.4	75.6	42.8	18.4	72.9	46.3	19.2	68.6	42.9	11.5	76.8	51.1	27.9
85	61.2	54.6	70.3	24.9	51.7	65.6	17.3	49.8	69.4	19.2	47.0	67.1	14.1	53.6	74.1	27.7
90	80.2	30.4	86.2	16.6	28.0	82.9	10.9	29.3	87.2	16.5	25.3	84.1	9.4	30.5	89.5	20.0
95	92.8	11.0	94.9	5.9	9.8	93.6	3.4	11.8	96.2	8.0	9.5	94.4	3.9	11.8	96.7	8.5
100	97.6	4.3	98.7	3.0	3.6	98.0	1.6	4.6	99.2	3.8	3.0	98.0	1.0	4.2	99.2	3.4
Women																
60	0.6	99.9	0.8	0.7	99.7	0.9	0.6	99.7	0.7	0.4	99.3	0.6	-0.1	99.7	0.9	0.6
65	6.1	98.7	7.5	6.2	96.4	8.4	4.7	97.8	7.9	5.7	96.1	7.4	3.5	98.0	9.2	7.2
70	20.4	93.7	24.6	18.3	87.3	27.5	14.8	91.5	26.0	17.5	87.9	25.4	13.3	92.6	30.2	22.8
75	39.8	81.4	46.1	27.5	70.6	49.6	20.2	79.9	49.2	29.1	73.0	47.5	20.5	79.7	54.5	34.2
80	58.5	65.7	65.7	31.4	51.9	68.3	20.2	62.2	68.4	30.6	54.4	66.3	20.7	62.0	74.0	36.0
85	75.5	42.5	80.8	23.3	31.3	81.8	13.1	42.6	84.0	26.6	35.2	81.9	17.1	39.8	87.0	26.8
90	87.9	24.2	91.4	15.6	15.8	91.3	7.1	23.1	93.1	16.2	18.2	91.5	9.7	21.0	94.5	15.5
95	94.5	11.9	96.4	8.3	7.5	96.3	3.8	10.9	97.0	7.9	8.4	96.2	4.6	9.9	97.7	7.6
100	97.7	5.1	98.6	3.7	3.3	98.7	2.0	4.3	98.7	3.0	3.4	98.4	1.8	3.9	99.0	2.9

- WC values of about 80–85 cm in men and about 75–80 cm in women

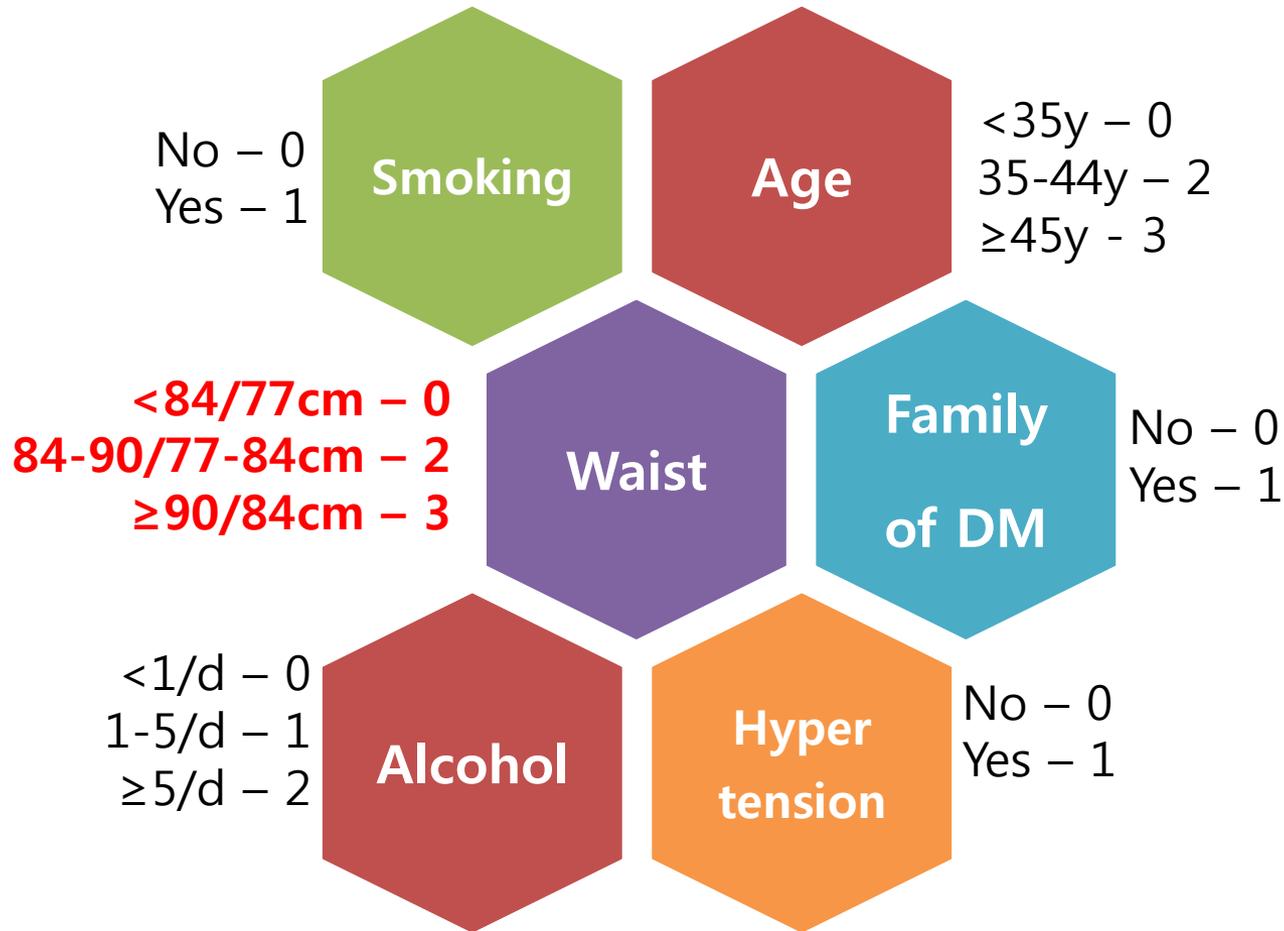
Waist and metabolic risks



Waist cutoff; KSSO

- Korean Society for the Study of Obesity (KSSO) suggests that WC values of **90 cm** for **men** and **85 cm** for **women** are appropriate cutoff points for the designation of central obesity in Koreans.

Korean Diabetes Risk Score



Blood glucose should be tested if the score is more than 5

Risk associated with central fat

	Risk		
	Low (0)	Moderate (+2)	High (+4)
Men			
Waist circumference			
in	<37	37–40	>40
cm	<94	94–102	>102
WHR	<0.90	0.90–1.00	>1.00
Women			
Waist circumference			
in	<32	32–35	>35
cm	<80	80–88	>88
WHR	<0.75	0.75–0.85	>0.85

This evaluation and adjustment of body mass index (BMI) for the added risk of central fat is done for individuals with a BMI below 30 kg/m².

Cut-off points for central obesity in Asia

Authors	Nation	Cut-off point (Men)	Cut-off point (Women)
Lee et al. [20]	Korea	90	85
Hyun et al. [21]	Korea		88 (Premeno)
Seo et al. [22]	Korea	86.5	86.5
Park et al. [23]	Korea	85	80
Koh et al. [24]			82-83
Hara et al. [25]			80
Oka et al. [26]			82.3
Kashihara et al. [27]	Japan	90	85
Yang et al. [28]	China	78.9 (20-30 yr) 82.4 (31-45 yr)	65.8 (20-30 yr) 71.4 (31-45 yr)
Li et al. [29]	China	85	80
Wang et al. [30]	China	86.95	79.95
Lin et al. [31]	Taiwan	86.5	82.1

Low risk: 85 (M) 80 (F)
High risk: 90 (M) 85 (F)

VISCERAL FAT AREA

Visceral Fat

- Central (abdominal) obesity, independent of overall obesity, has been associated with coronary heart disease and Type 2 diabetes, as well as with cardiovascular risk factors.
- Using sophisticated imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), fat depots can be distinguished at a given waist circumference, with visceral fat particularly associated with increased risk of cardiovascular diseases.

Visceral adipose tissue by CT scan

- A cross-sectional, hospital-based study
- 276 men and 540 women, aged 17–69 years,
 - health examination check-ups from 2003 to 2005
 - general hospitals in Seoul, Korea.
- Visceral adipose tissue (VAT) was categorized into quintiles for men (≤ 77 , 78–99, 100–122, 123–152 and ≥ 153 cm²) and women (≤ 45 , 46–66, 67–84, 85–109 and ≥ 110 cm²).
- Logistic regression models,
 - odds ratios (ORs) for having two or more metabolic risk factors in each VAT quintile, after adjusting for age and BMI.

VAT and metabolic risk; men

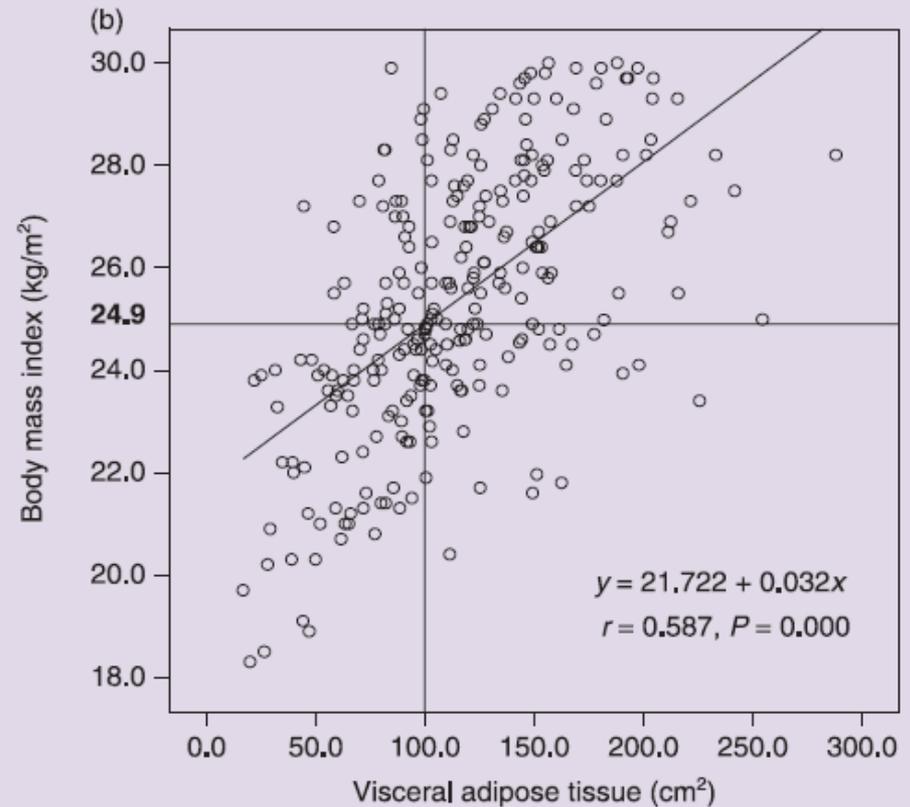
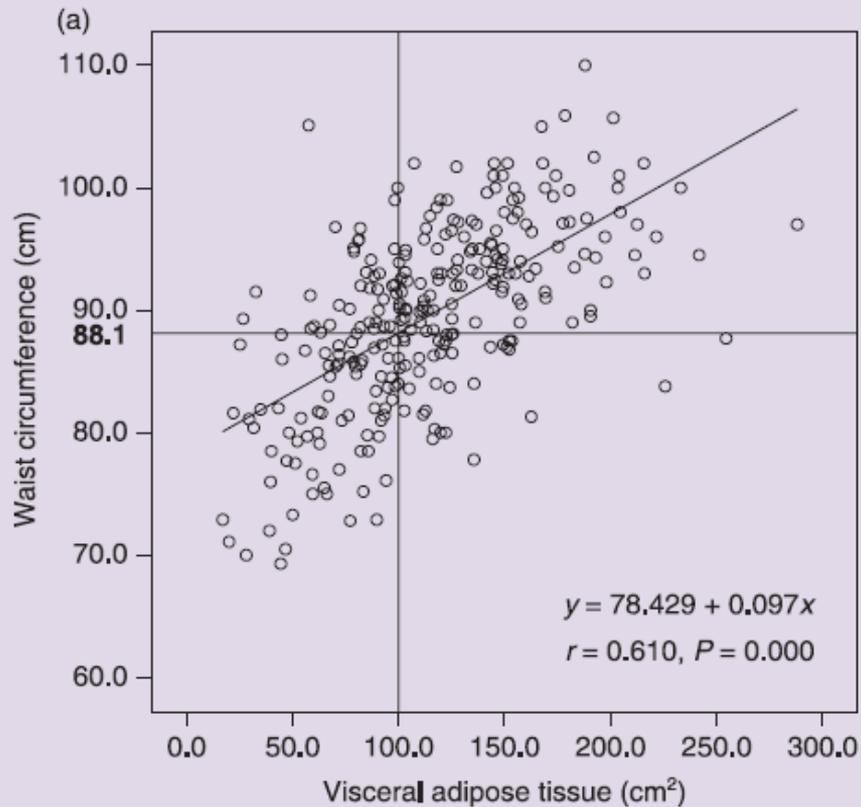
Parameters	Visceral adipose tissue (VAT)					P for trend
	Q1	Q2	Q3	Q4	Q5	
Men (<i>n</i> = 276)	(<i>n</i> = 55)	(<i>n</i> = 55)	(<i>n</i> = 56)	(<i>n</i> = 55)	(<i>n</i> = 55)	
Range of VAT (cm ²)	≤ 77.1	77.2~99.6	99.9~122.2	122.3~152	≥ 152.1	
Median of VAT (cm ²)	58.4	89.4	110.8	136.7	178.5	
Model 1: age	OR	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Blood pressure ≥ 130/80 mmHg	1	1.5 (0.7~3.3)	1.4 (0.6~3.0)	1.7 (0.8~3.6)	3.1 (1.4~6.8)	0.007
Fasting glucose ≥ 5.6 mmol/l	1	1.8 (0.8~3.8)	1.7 (0.8~3.8)	1.3 (0.6~2.8)	2.1 (0.9~4.7)	0.167
Triglycerides ≥ 1.7 mmol/l	1	2.8 (1.3~6.3)	5.2 (2.3~11.9)	3.1 (1.4~7.0)	6.0 (2.6~14.1)	0.000
HDL cholesterol < 1.04 mmol/l	1	3.3 (1.3~8.8)	1.8 (0.6~5.1)	2.3 (0.8~6.3)	2.7 (1.0~7.4)	0.168
Two or more risk factors	1	2.4 (1.1~5.2)	2.6 (1.2~5.8)	2.4 (1.1~5.3)	4.4 (1.9~10.1)	0.001

VAT and metabolic risk; women

Parameters	Visceral adipose tissue (VAT)					
	Q1	Q2	Q3	Q4	Q5	
Women (<i>n</i> = 540)	(<i>n</i> = 108)	(<i>n</i> = 108)	(<i>n</i> = 108)	(<i>n</i> = 109)	(<i>n</i> = 107)	
Range of VAT (cm ²)	≤ 45.8	45.9~66.5	66.7~84.5	84.5~109.7	≥ 110.1	
Median of VAT (cm ²)	36	56.3	75.4	94.2	127.7	
Model 1: age	OR	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	<i>P</i> for trend
Blood pressure ≥ 130/80 mmHg	1	1.3 (0.7~2.7)	1.6 (0.8~3.2)	3.0 (1.5~5.9)	3.1 (1.5~6.3)	0.000
Fasting glucose ≥ 5.6 mmol/l	1	1.5 (0.7~3.1)	2.1 (1.1~4.2)	1.5 (0.8~3.1)	2.1 (1.0~4.4)	0.089
Triglycerides ≥ 1.7 mmol/l	1	8.8 (2.0~39.3)	8.3 (1.9~37.3)	16.5 (3.8~72.1)	20.1 (4.5~89.6)	0.000
HDL cholesterol < 1.29 mmol/l	1	3.1 (1.6~6.2)	5.8 (2.9~11.6)	4.3 (2.1~8.8)	7.7 (3.7~16.3)	0.000
Two or more risk factors	1	3.1 (1.3~7.3)	4.9 (2.1~11.4)	6.7 (2.9~15.5)	10.0 (4.2~23.7)	0.000

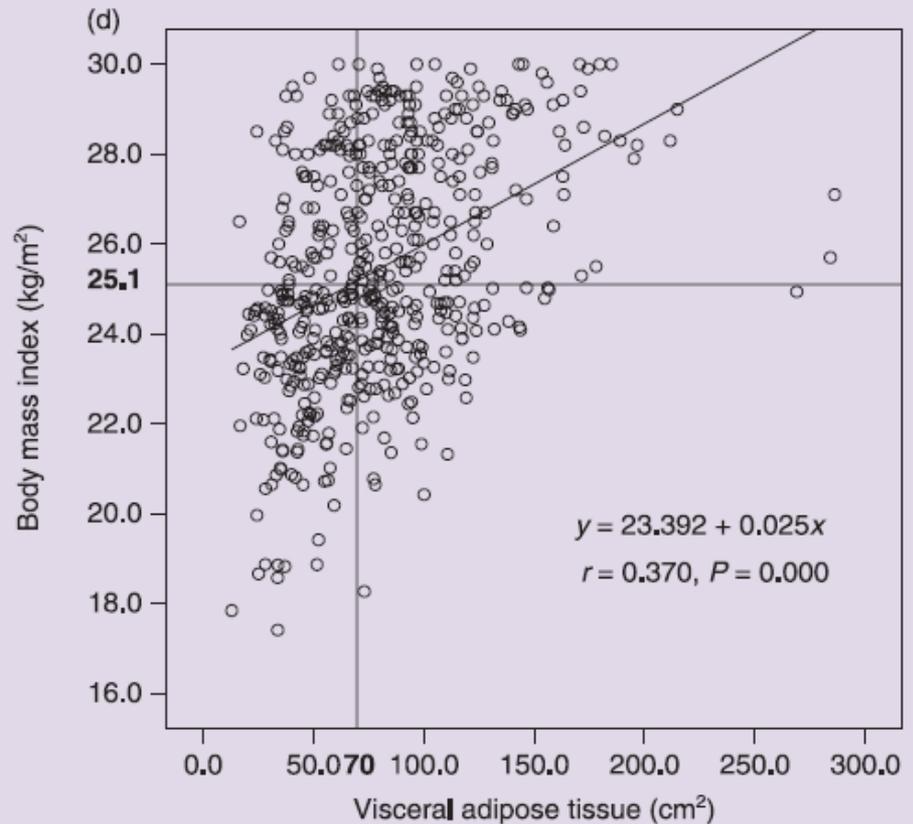
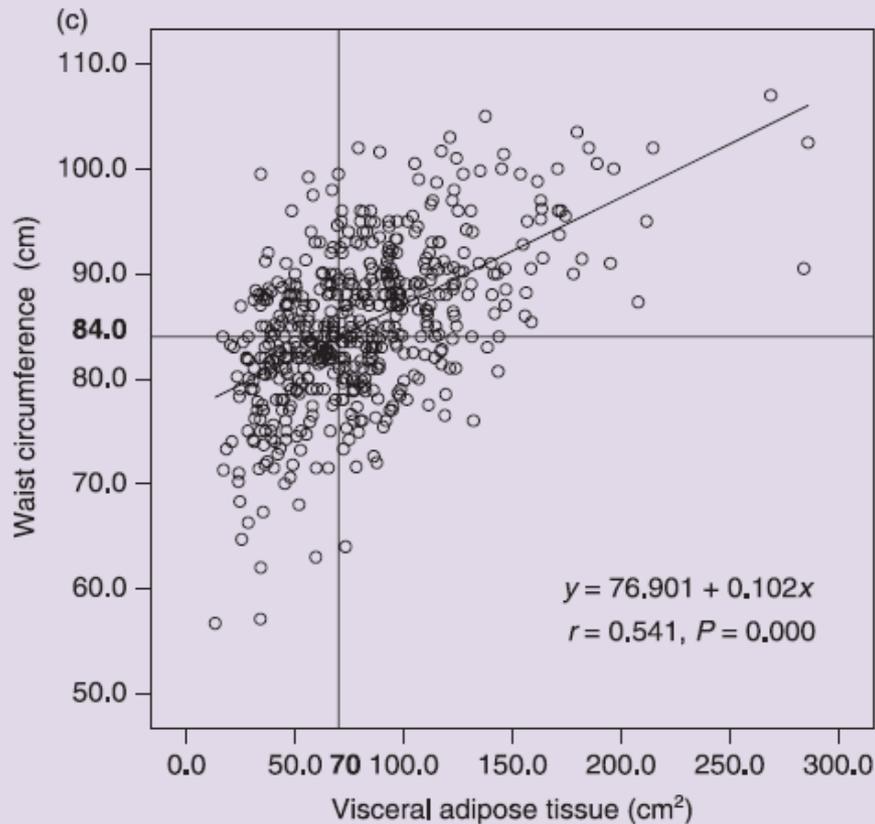
According to the ROC analysis, the **VAT** thresholds of **100 cm² in men** and **70 cm² in women** had the largest sum of sensitivity and specificity in the ROC curves.

VAT and Waist, BMI; men



Men

VAT and Waist, BMI; women



Summary

- Methods of estimating body fat and its distribution in diabetes clinic
 - **Body mass index**; 23 (overweight) 25(27.5) (obese)
 - **Waist circumference**; 85/80 (low risk) 90/85cm (high risk)
 - **Visceral adipose tissue**; 100 (men) 70cm² (women)

Healthy obese people?

- About 30% of obese individuals seem to be protected against obesity-related metabolic diseases.
- The healthy obese phenotype is characterized by preserved insulin sensitivity, relatively low visceral fat mass, and normal adipose tissue function
- If overweight or obese, evaluate the components of metabolic syndrome such as **BP, glucose, insulin (HOMA-IR), HDL-C, and TG** levels