SG4 KDA research group on exercise:
Current issues on exercise

Debate session: benefits of exercise with or without weight loss

Weight plays a more dominant role in diabetes risk

김 대 중

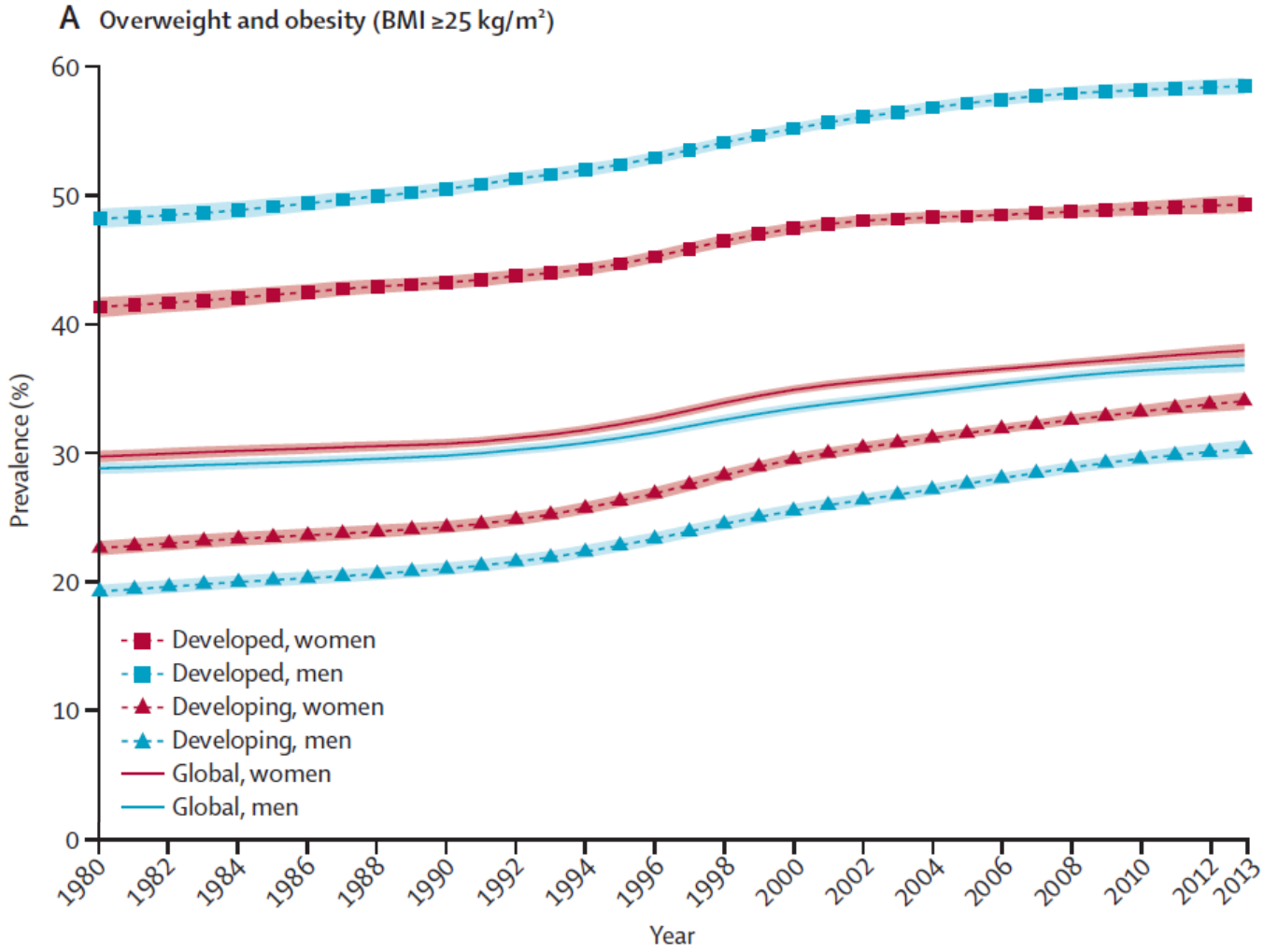
아주의대 내분비대사내과

Debate Topic

- **Exercise vs. Weight = Unfit vs. Fat**

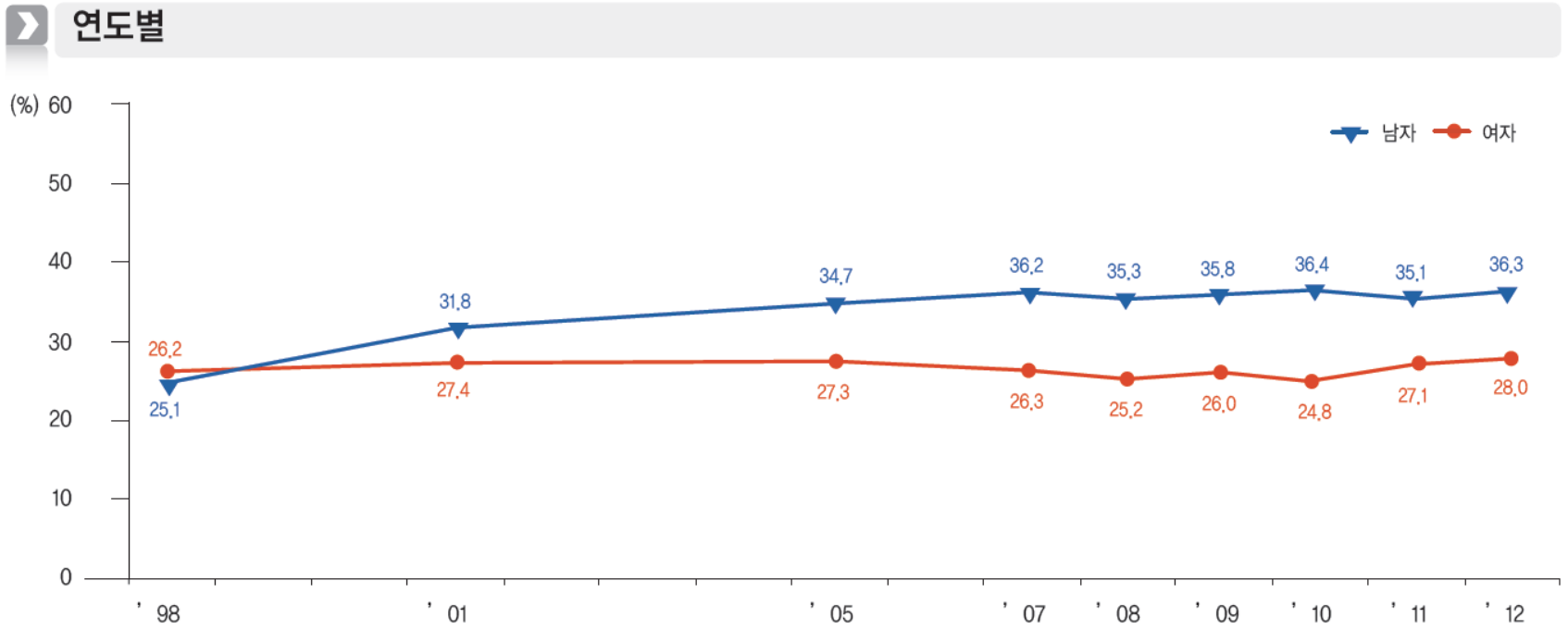
- Which is associated with increased risk of diabetes?
- Which is associated with worse cardiometabolic risk biomarker profiles?

Age-standardised prevalence of overweight and obesity and obesity alone, ages ≥20 years, by sex, 1980–2013



Lancet 2014; 384: 766–81

우리나라 성인비만 유병률



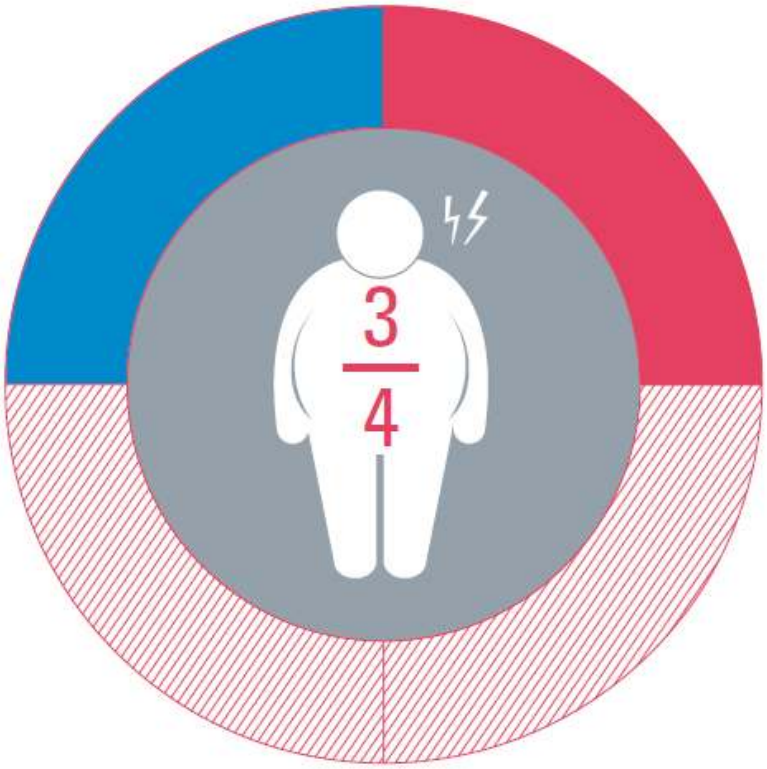
성인 비만 유병률 : 체질량지수 25 kg/m^2 이상인 분율, 만19세 이상
2005년 추계인구로 연령 표준화
자료원 : 국민건강영양조사

PREVALENCE OF OBESITY IN DIABETES

74.7%

› Approximately, three-fourths of Korean patients with diabetes are overweight or obese.

› The mean body mass index (BMI) was found to be 25.2 kg/m^2.



DEFINITION OF OBESITY

Overweight : BMI 23.0~24.9 kg/m^2

Obese : BMI ≥ 25.0 kg/m^2

Diabetes Metab J 2014;38:35-43

우리나라 에너지 섭취량 추이

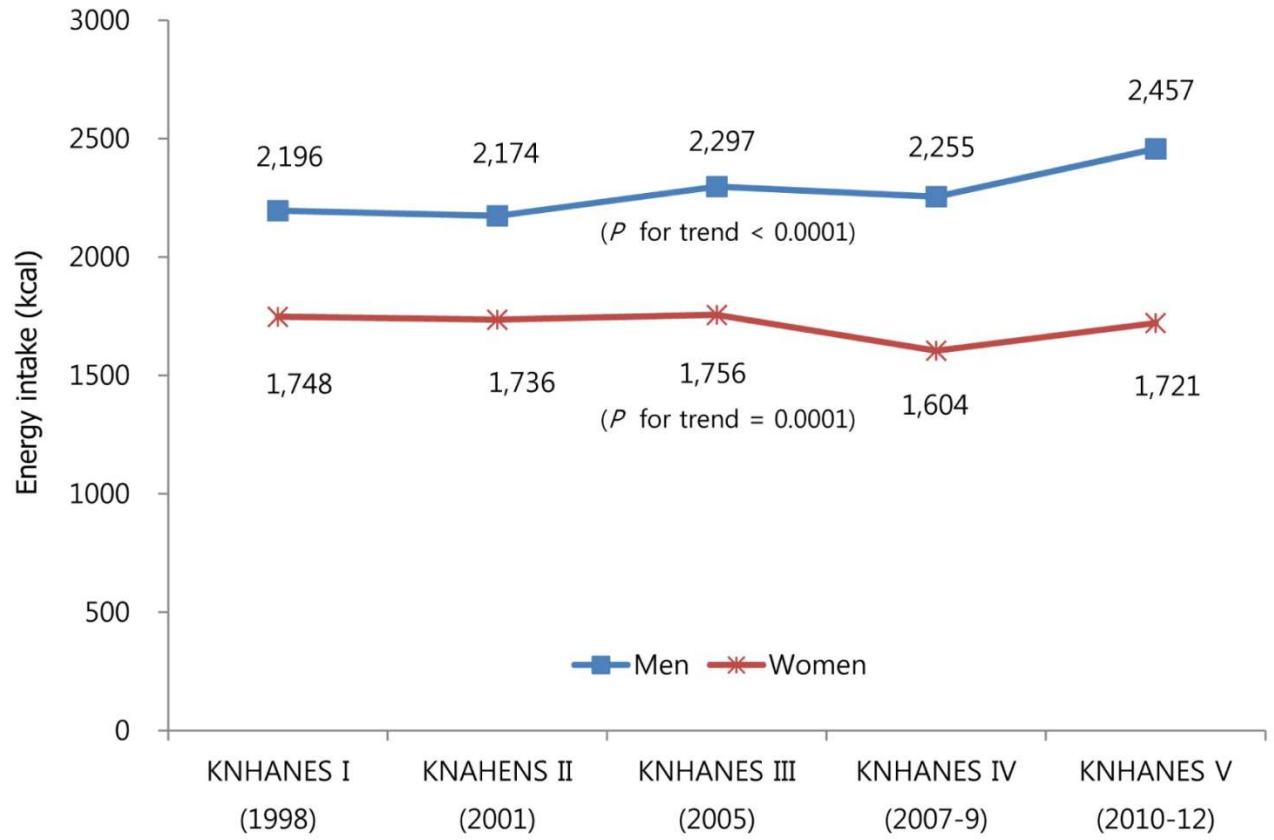


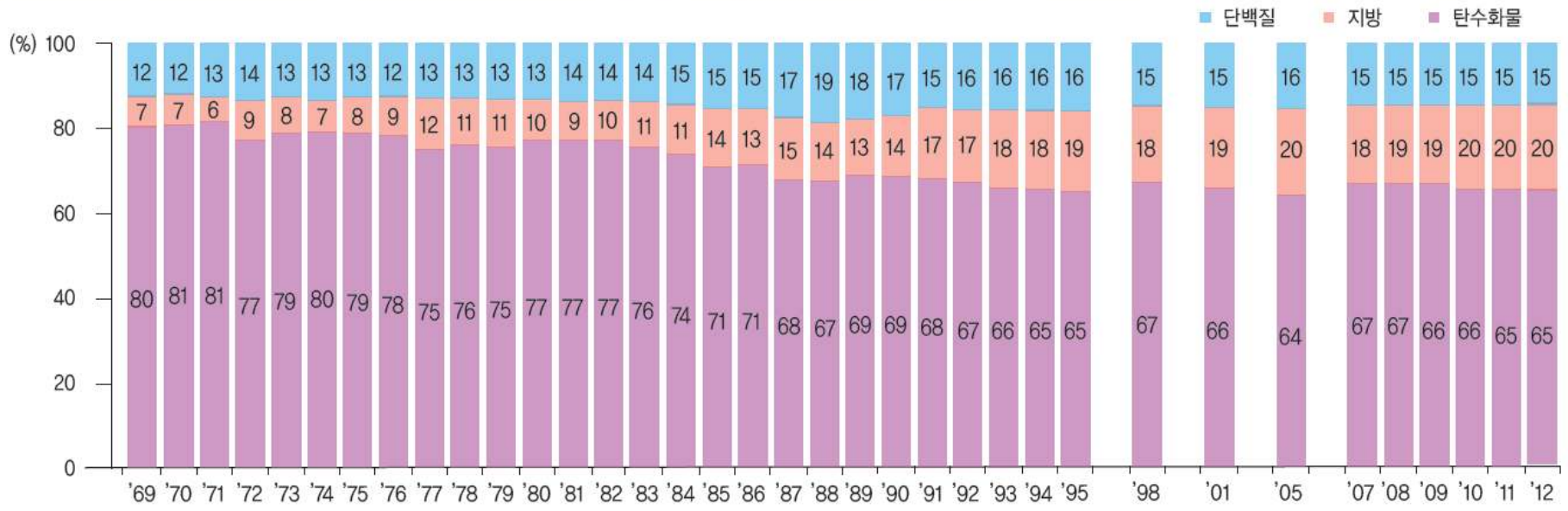
Figure 1. Trends in energy intake among Korean adults above 19 years old in KNHANES I–V

*Age-standardized mean was calculated using the age and sex specific structures of estimated population based on the 2005 Korea Census

*Abbreviations: KNHANES= Korea National Health and Nutrition Examination Survey

우리나라 에너지 섭취 분율

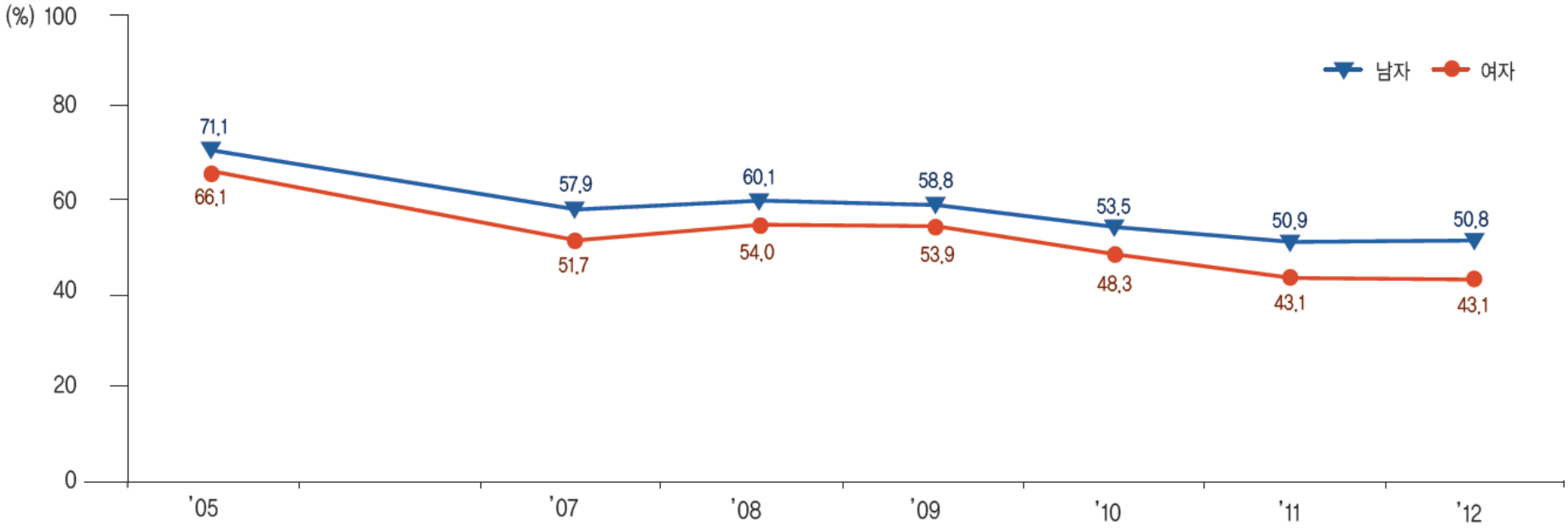
에너지 섭취



- 단백질급원 에너지섭취분율 : {(단백질 섭취량)×4}의 {(단백질 섭취량)×4+(지방 섭취량)×9+(탄수화물 섭취량)×4}에 대한 분율, 만1세이상
- 지방 및 탄수화물급원 에너지섭취분율 : 단백질급원 에너지섭취분율과 같은 정의에 의해 산출
- 1969년~1995년 : 원시자료 확보가 불가하여 각 영양소 섭취량의 평균값을 이용하여 계산
- 1998년~2012년 : 2005년 추계인구로 연령 표준화
- 자료원 : 국민건강영양조사

우리나라 신체활동 실천율

연도별



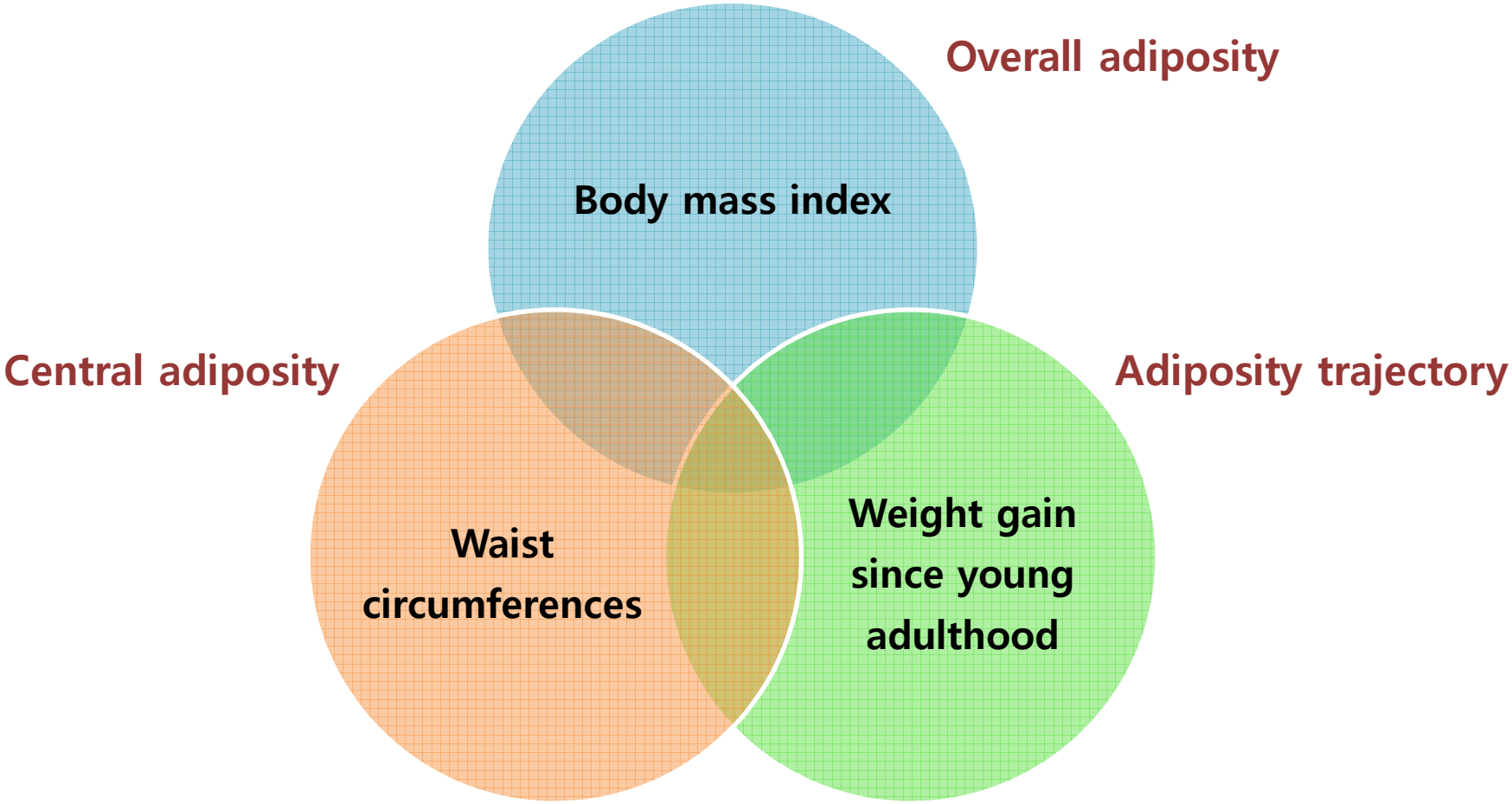
중등도이상 신체활동실천율(걷기포함) : 최근 1주일 동안 격렬한 신체활동을 1회 10분 이상, 1일 총 20분 이상, 주 3일 이상 실천 또는 중등도 신체활동을 1회 10분 이상, 1일 총 30분 이상, 주 5일 이상 실천 또는 걷기를 1회 10분 이상, 1일 총 30분 이상, 주 5일 이상 실천한 분율, 만19세이상

2005년 추계인구로 연령 표준화
자료원 : 국민건강영양조사

Fitness vs. Fatness debate

- Both increased body weight and physical inactivity are powerful predictors of diabetes, cardiovascular diseases and death.
- Both are associated with cardiometabolic risk factors and they often occur together.
- This has led to some controversy over the relative contributions of each to cardiovascular risk.

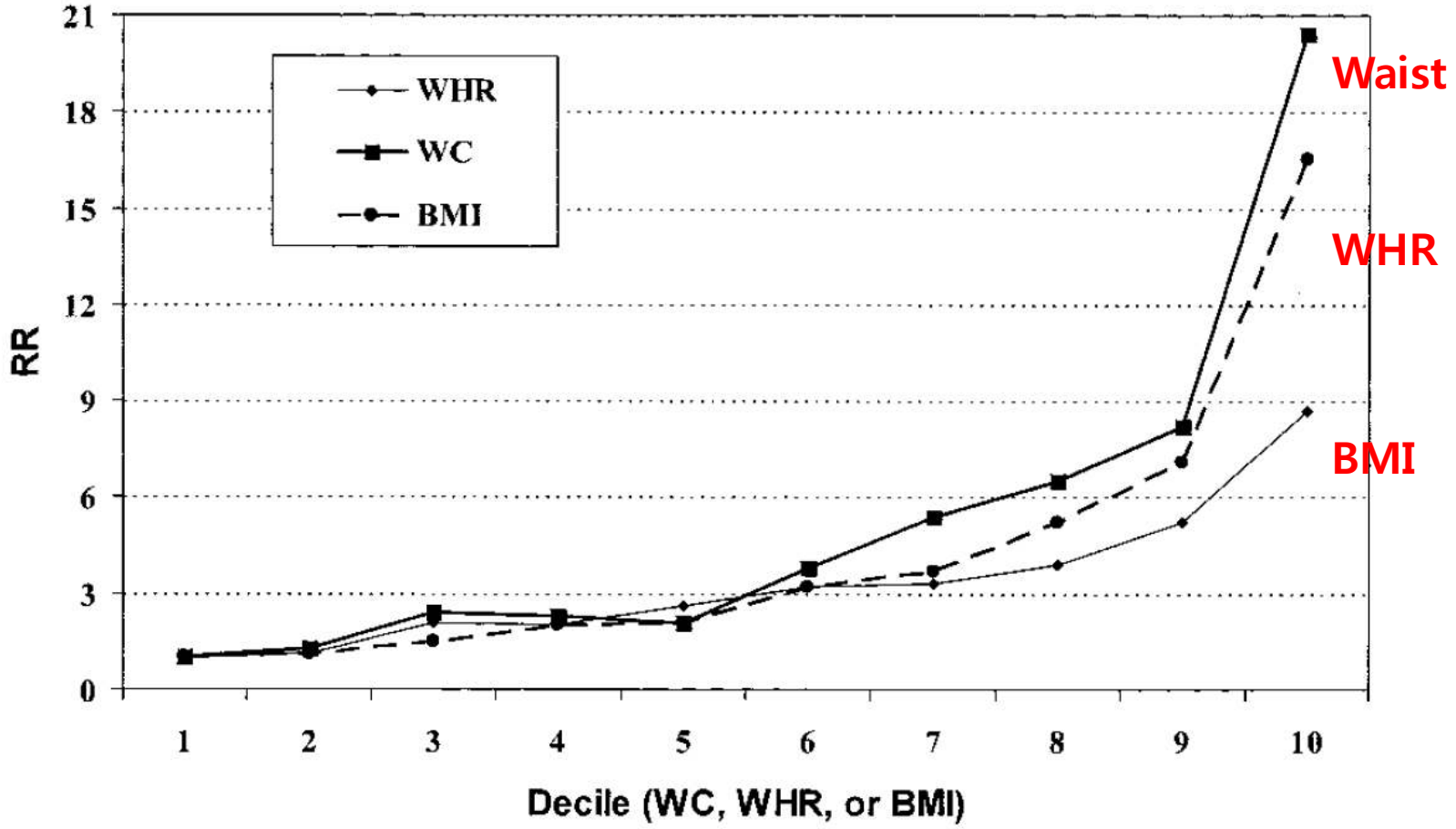
Adiposity Triad



Frank B. Hu. Obesity Epidemiology

Adiposity and diabetes risk

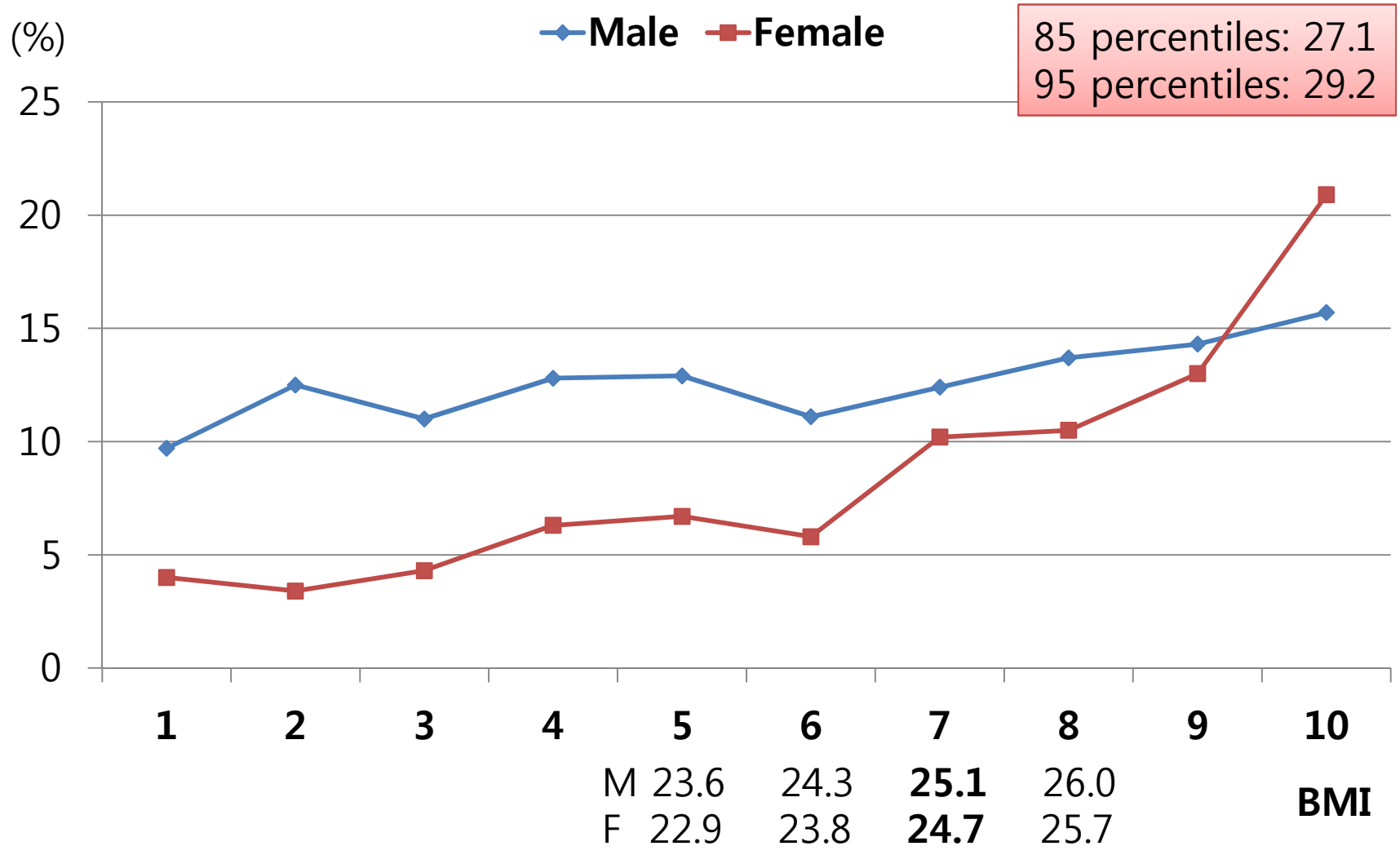
Health Professionals Follow-up Study; 13y, N=27,270



Am J Clin Nutr 2005;81:555– 63

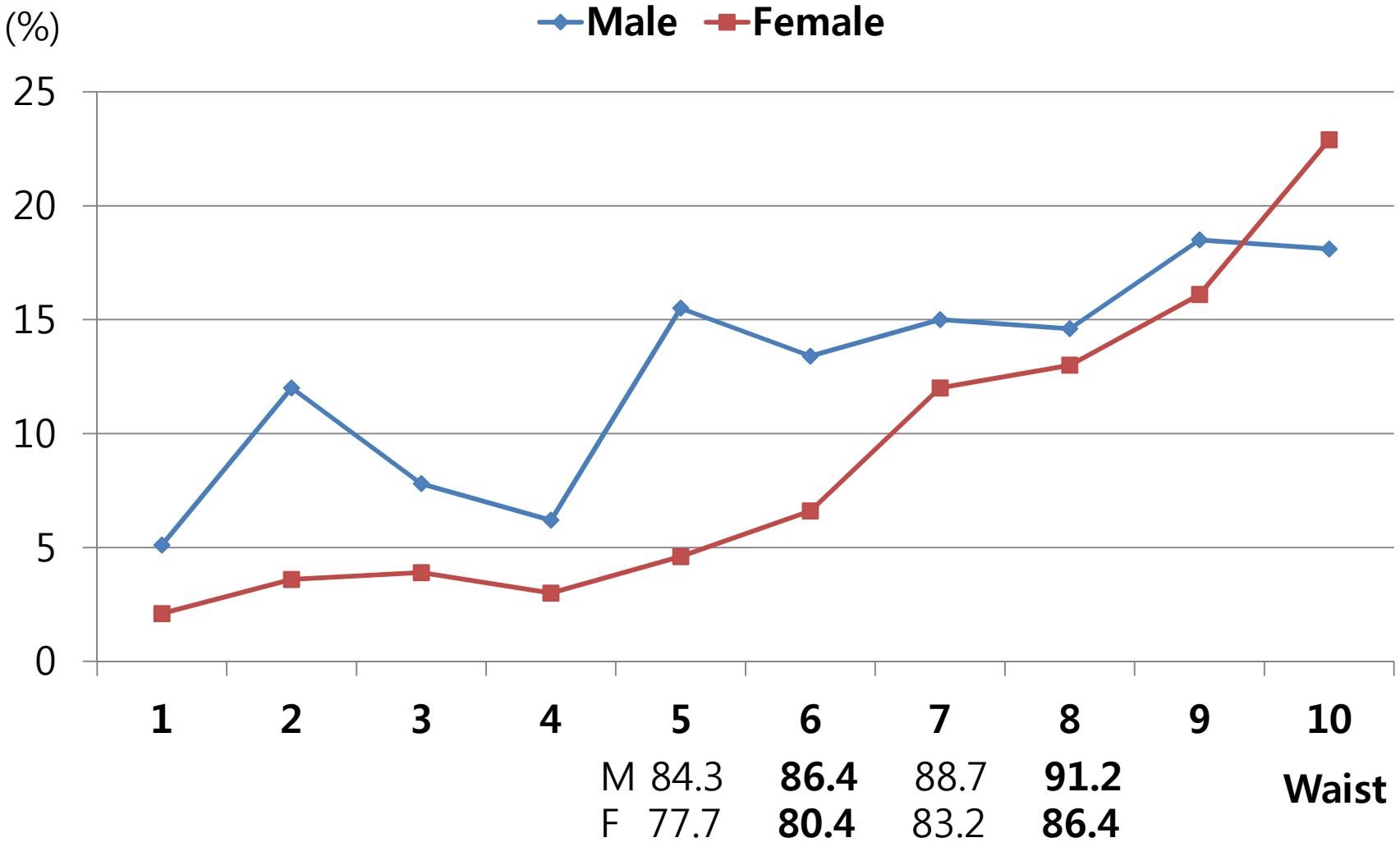
BMI and diabetes in Korea

-2011 KNHANES

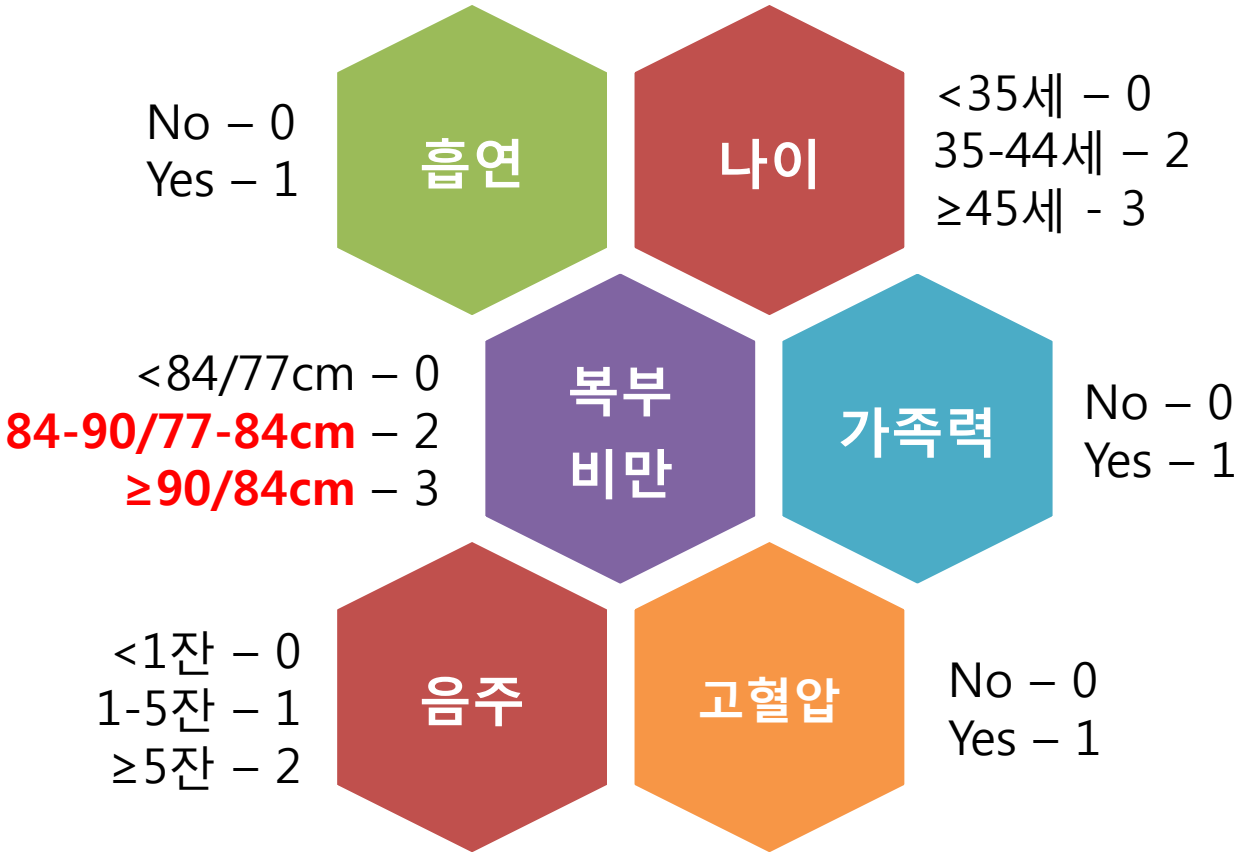


Waist and diabetes in Korea

-2011 KNHANES



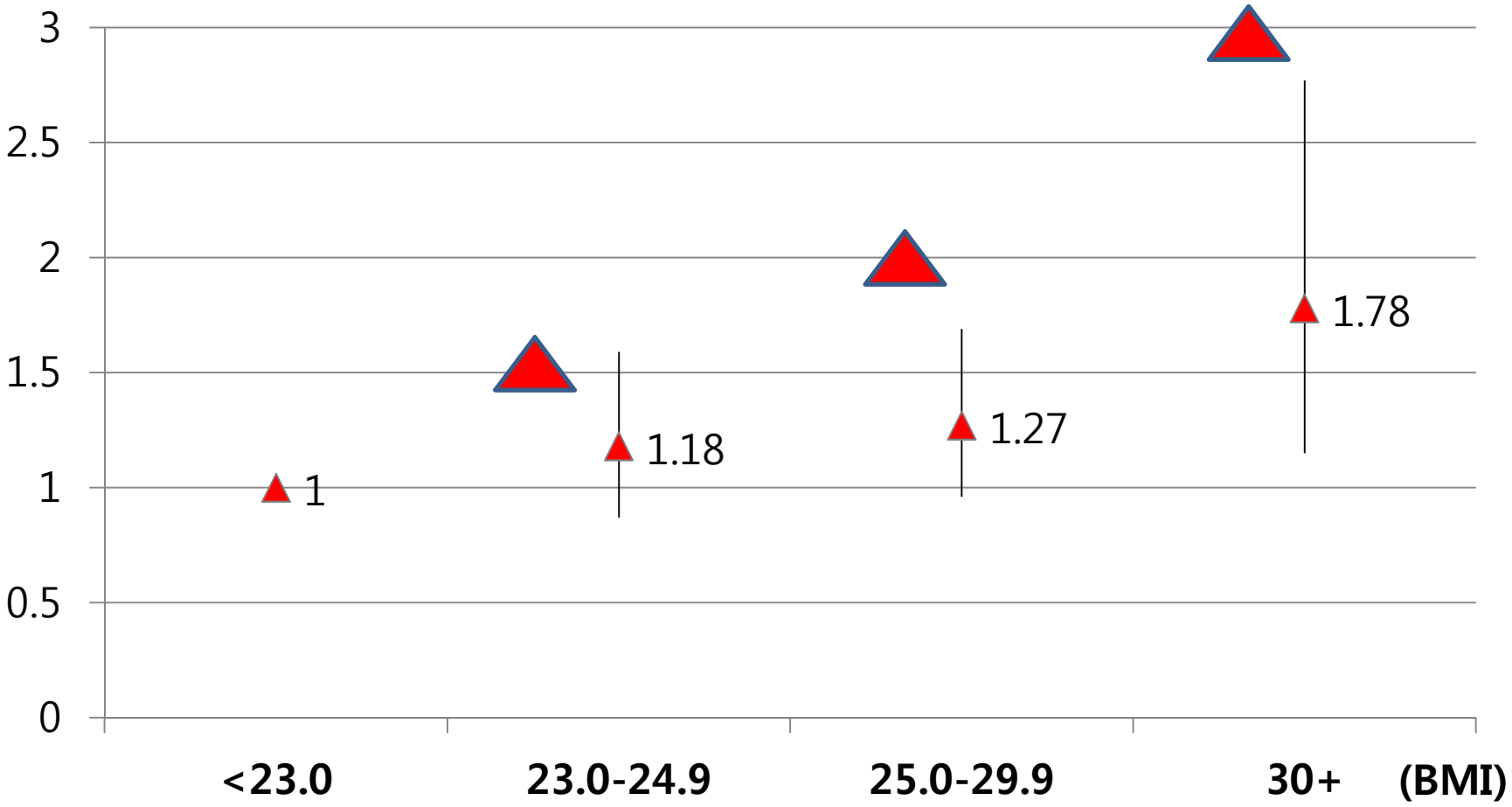
한국인 당뇨병 위험지수



총점이 **5점** 이상이면 혈당 검사를 해봐야 한다.

이용호, 김대중, 박석원 등. Diabetes Care 2012

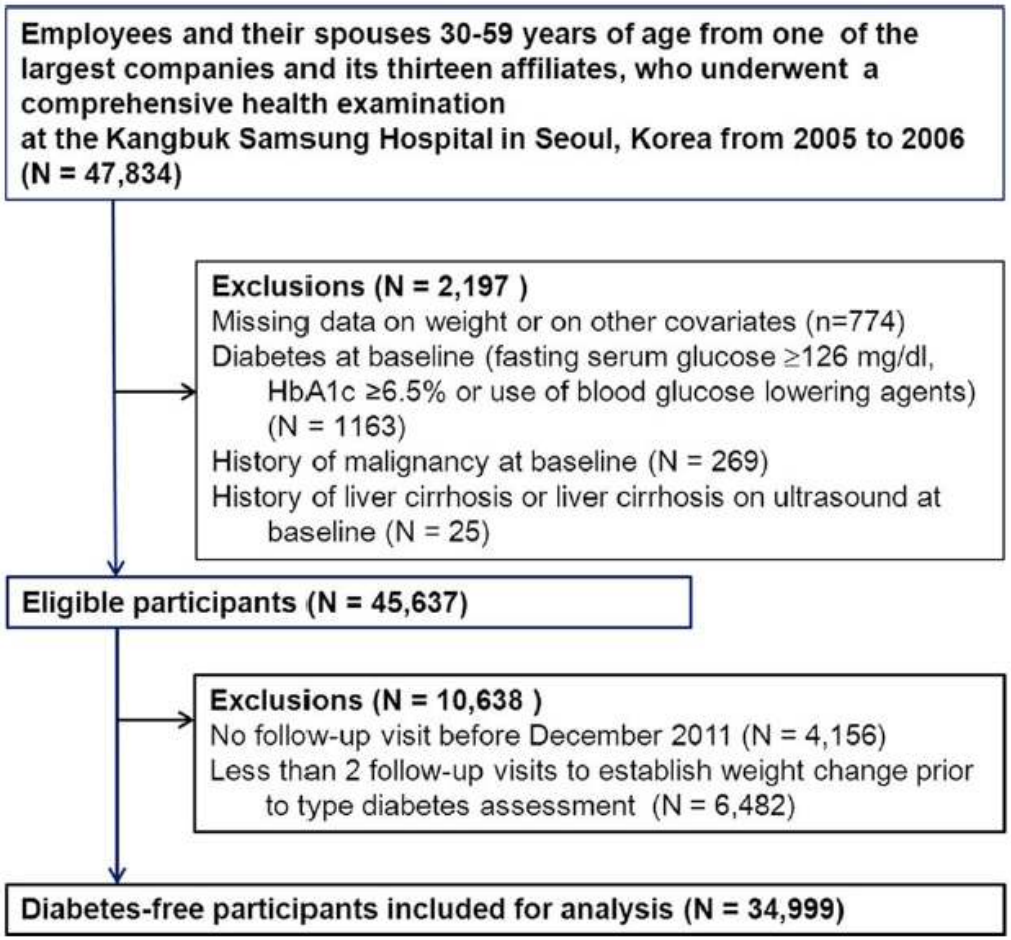
Risk for diabetes in middle-aged Korean: KoGES, n=6,342



Clinical model 2. AROC 0.77

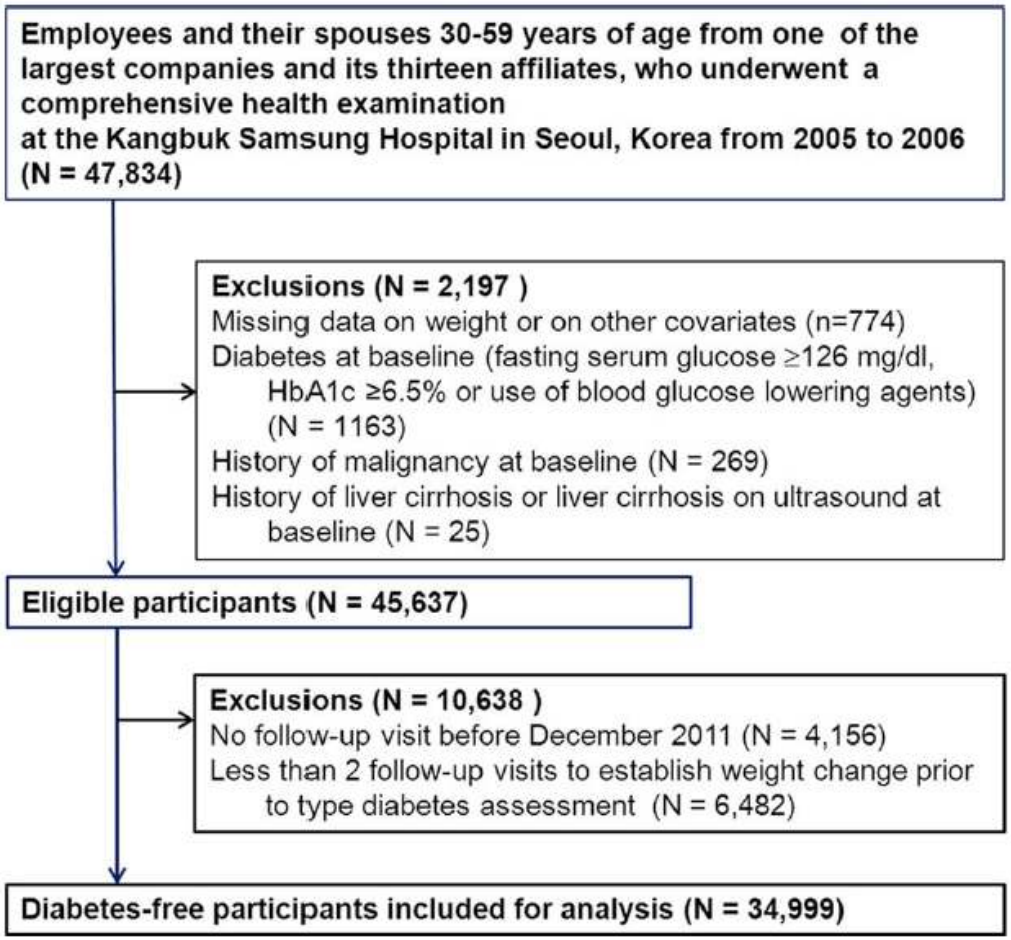
Lim NK, et al. Circulation J 2012

BMI, Metabolic Health and Weight Change on Incident Diabetes in a Korean Population



Obesity (2014) 22, 1880–1887

BMI, Metabolic Health and Weight Change on Incident Diabetes in a Korean Population



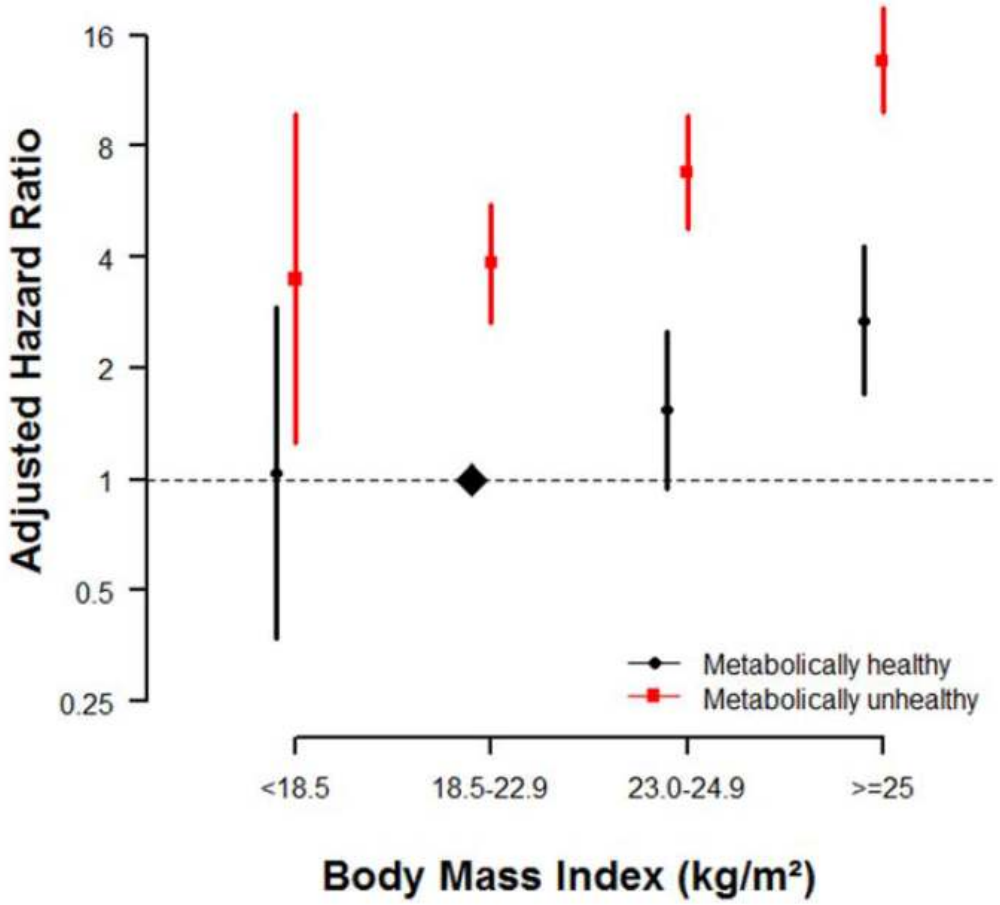
Obesity (2014) 22, 1880–1887

BMI, Metabolic Health and Weight Change on Incident Diabetes in a Korean Population

BMI (kg m^{-2}) category	Person-years	Incident case	Incidence Density (per 1000 person-years)	Age- and sex-adjusted HR (95% CI)	Multivariate HR[a] (95% CI)
Total (*N* = 34,999)					
<18.5	6534.2	8	1.2	0.82 (0.40-1.67)	0.81 (0.40-1.66)
18.5-22.9	74539.3	136	1.8	1.00 (reference)	1.00 (reference)
23.0-24.9	44133.4	198	4.5	2.15 (1.72-2.69)	2.16 (1.72-2.70)
≥25.0	51671.6	547	10.6	5.06 (4.15-6.17)	5.01 (4.10-6.12)
P for trend				<0.001	<0.001
Metabolically healthy persons (*N* = 17,097)					
<18.5	5148.8	4	0.8	0.98 (0.35-2.75)	1.02 (0.36-2.87)
18.5-22.9	48317.6	41	0.8	1.00 (reference)	1.00 (reference)
23.0-24.9	19075.7	26	1.4	1.71 (1.03-2.83)	1.66 (1.00-2.76)
≥25.0	13521.9	32	2.4	3.10 (1.90-5.06)	2.98 (1.82-4.89)
P for trend				<0.001	<0.001
Metabolically unhealthy persons (*N* = 17,897)					
<18.5	1385.3	4	2.9	0.93 (0.34-2.53)	0.92 (0.34-2.51)
18.5-22.9	26205.2	95	3.6	1.00 (reference)	1.00 (reference)
23.0-24.9	25057.7	172	6.9	1.72 (1.34-2.23)	1.74 (1.34-2.24)
≥25.0	38137.5	515	13.5	3.49 (2.78-4.38)	3.48 (2.77-4.38)
P for trend				<0.001	<0.001

Obesity (2014) 22, 1880–1887

BMI, Metabolic Health and Weight Change on Incident Diabetes in a Korean Population



Obesity (2014) 22, 1880–1887

BMI, Metabolic Health and Weight Change on Incident Diabetes in a Korean Population

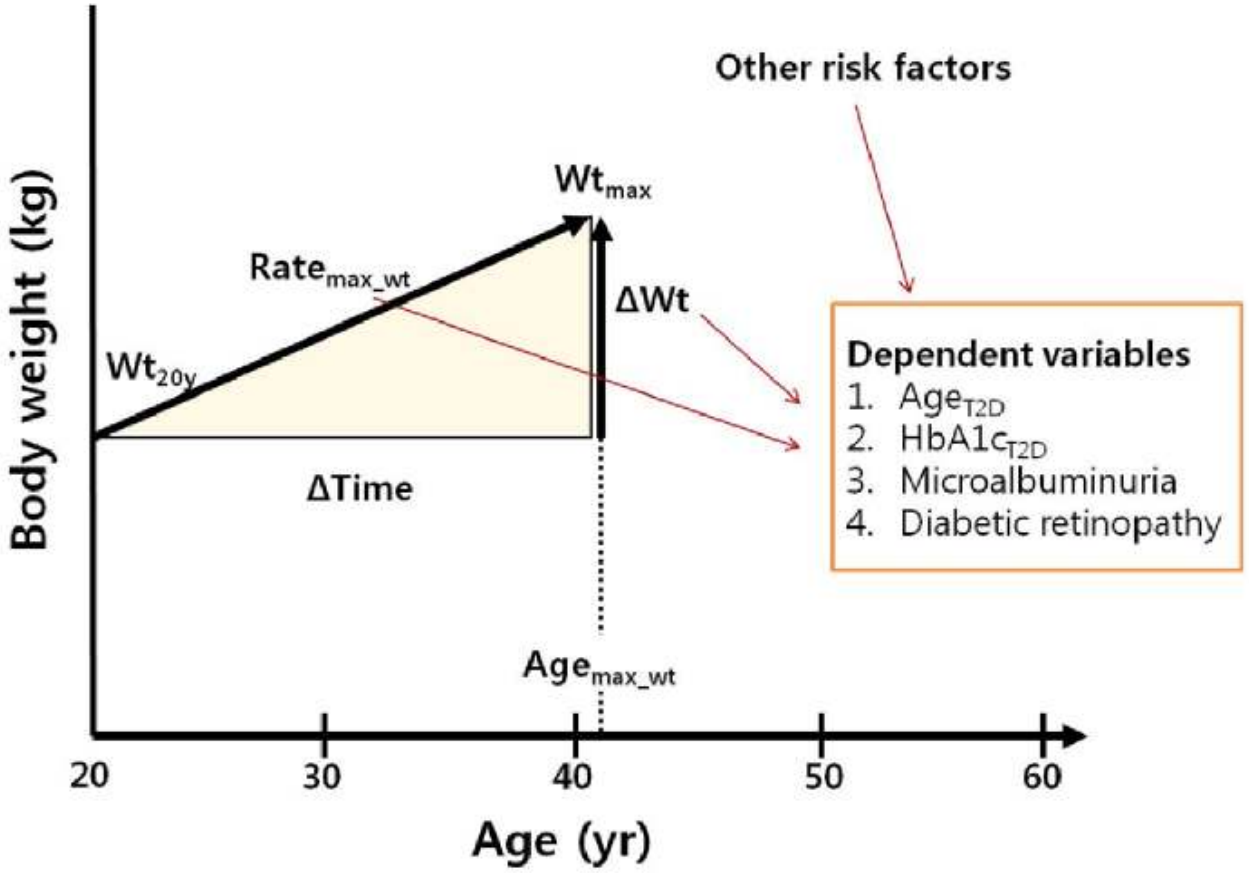
TABLE 3 Development of diabetes by weight change categories

Weight change (kg) over 1.9 years	Person-years	Incident case	Incidence Density (1000 person-year)	Age·sex-adjusted HR (95% CI)	Multivariate HR[a] (95% CI)	HR (95% CI)[b] in the model using time-dependent variables
Quartiles						
Q1 (<−0.9)	46,475.2	226	4.9	0.99 (0.82-1.20)	0.80 (0.66-0.97)	0.71 (0.58-0.89)
Q2 (−0.9 to 0.4)	42,332.0	216	5.1	1.00 (reference)	1.00 (reference)	1.00 (reference)
Q3 (0.5 to 2.0)	46,063.7	221	4.8	0.96 (0.79-1.15)	0.99 (0.82-1.20)	1.21 (0.98-1.50)
Q4 (≥2.1)	42,007.5	226	5.4	1.27 (1.06-1.54)	1.24 (1.02-1.49)	1.53 (1.25-1.87)
P for trend				0.03	<0.001	<0.001
Per 1 SD increase in weight change				1.07 (1.00-1.16)	1.17 (1.10-1.25)	1.28 (1.21-1.35)

[a]Estimated from parametric Cox models adjusted for age, sex, smoking status, alcohol intake, regular exercise, and BMI at baseline.
[b]Estimated from pooled logistic regression models with weight change as a time-dependent categorical variable adjusted for age, sex, and BMI at baseline; and adjusted for current smoker, current alcohol use, and regular exercise over time as time-dependent variables.
Weight change was categorized into quartiles. The category containing 0 kg of weight change was used as the reference group.
Abbreviations: BMI, body mass index; CI, confidence intervals; HR, hazard ratios.
1 SD of weight change: 2.80 kg.

Obesity (2014) 22, 1880–1887

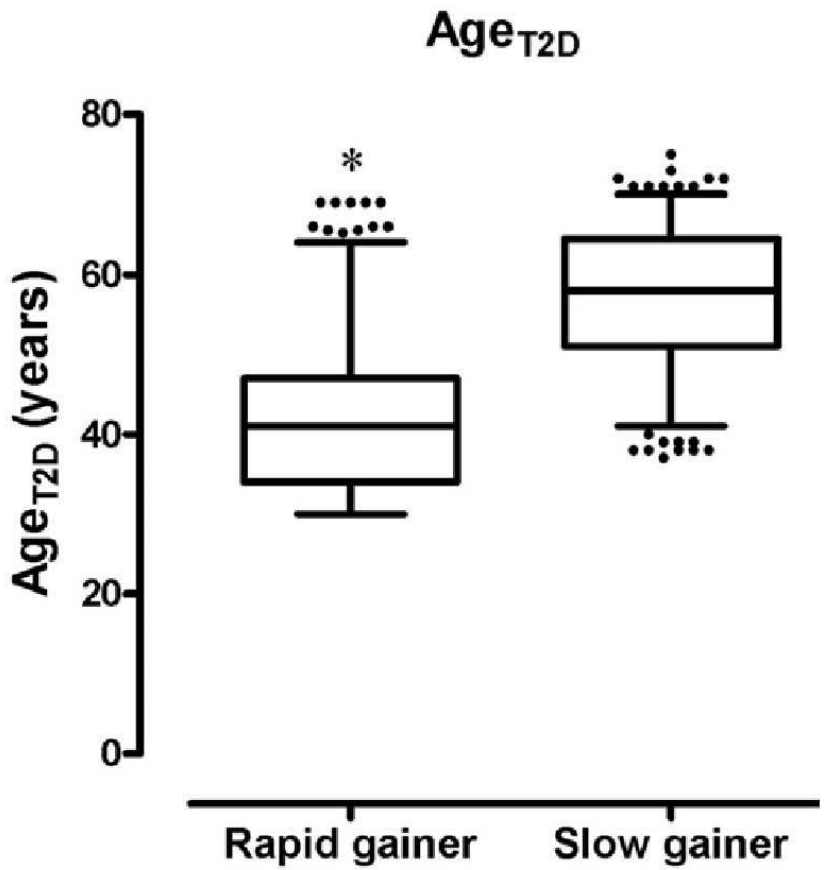
Association of Maximum Body Weight on the Development of Type 2 Diabetes



Lim S & Jang HC. PLoS ONE 2013;8(12): e80525

Association of Maximum Body Weight on the Development of Type 2 Diabetes

- **MAXWEL cohort**
- In 2006, N=2,977
- Weight at age 20 years was 59.9 and maximum lifetime weight was 72.9 kg, resulting in 13.0 kg of change in body weight from age 20 years to maximum weight (DWt)
- **Greater weight gain** and **shorter duration** to maximum weight showed a tendency to be diagnosed with **T2D earlier**



Lim S & Jang HC. PLoS ONE 2013;8(12): e80525

Physical activity, BMI and risk of diabetes Women's Health Study, N=37,878, 6.9y F/U

Table 2. Hazard Ratios of Diabetes Mellitus by Body Mass Index

Variable	Body Mass Index Category			*P* for Trend
	Normal Weight (n = 19 630)	Overweight (n = 11 700)	Obese (n = 6548)	
No. (%) of women with diabetes mellitus	178 (0.9)	421 (3.6)	762 (11.6)	
Hazard ratio (95% CI)				
Age adjusted	1.00	3.99 (3.35-4.76)	14.0 (11.9-16.4)	<.001
Multivariate adjusted*	1.00	3.22 (2.69-3.87)	9.09 (7.62-10.8)	<.001
Multivariate adjusted†	1.00	3.22 (2.69-3.87)	9.06 (7.60-10.8)	<.001

Abbreviation: CI, confidence interval.
*Adjusted for age, family history of diabetes, alcohol use, smoking status, hormone therapy use, hypertension, high cholesterol, dietary factors, and randomized Women's Health Study treatment groups.
†Adjusted for aforementioned covariates and physical activity.

JAMA. 2004;292:1188-1194

Physical activity, BMI and risk of diabetes Women's Health Study, N=37,878, 6.9y F/U

Table 3. Hazard Ratios of Diabetes Mellitus by Physical Activity Category

Variable	Inactive*	Active†
Women, No. (%)		
Total	24 942 (65.8)	12 936 (34.2)
With diabetes mellitus	985 (3.9)	376 (2.9)
Adjusted hazard ratio (95% CI)		
Age	1.00	0.73 (0.65-0.83)
Multivariate‡	1.00	0.85 (0.75-0.97)
Multivariate§	1.00	0.91 (0.80-1.03)

Abbreviation: CI, confidence interval.
*Energy expenditure was less than 1000 kcal/wk.
†Energy expenditure was at least 1000 kcal/wk.
‡Adjusted for age, family history of diabetes, alcohol use, smoking status, hormone therapy use, hypertension, high cholesterol, dietary factors, and randomized Women's Health Study treatment groups.
§Adjusted for aforementioned covariates and body mass index.

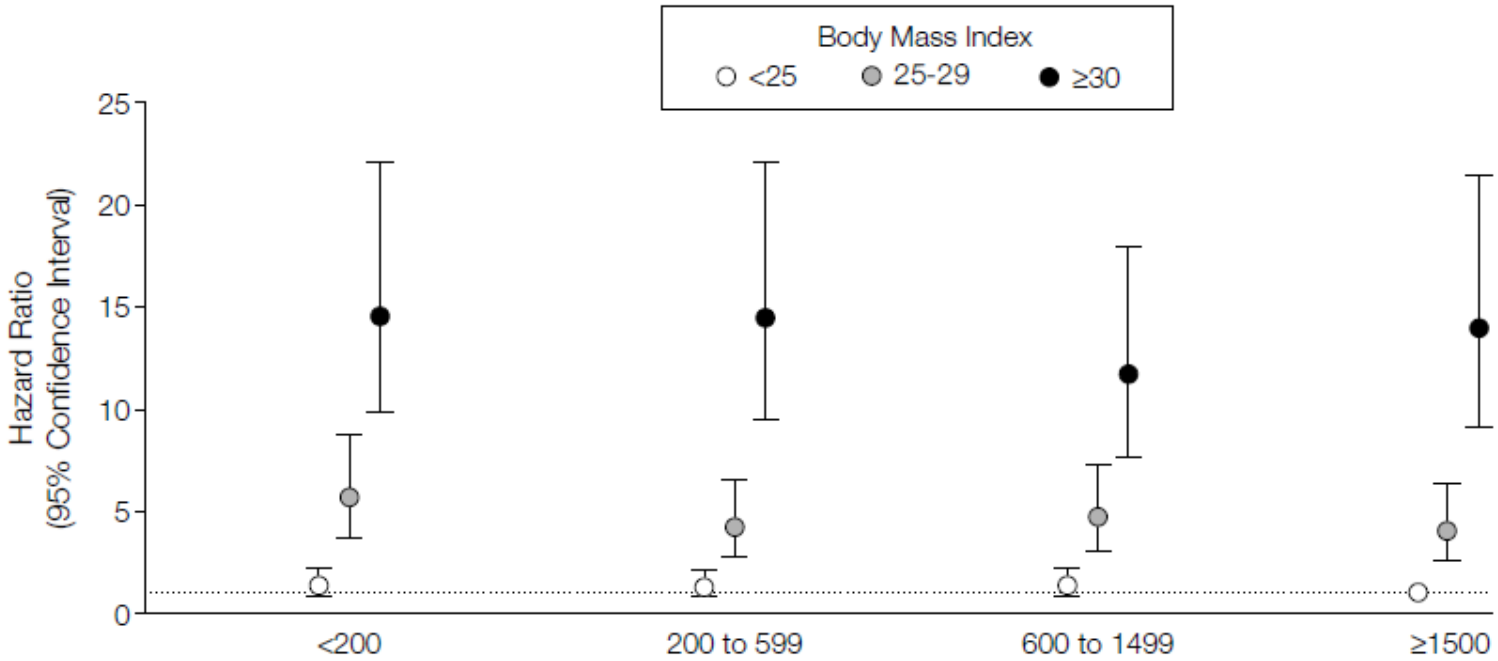
Table 4. Hazard Ratios of Diabetes Mellitus by Expediture of Energy

Variable	Energy Expenditure, kcal/wk				*P* for Trend
	0-199	200-599	600-1499	≥1500	
Women, No. (%)					
Total	9735 (25.7)	9541 (25.2)	10 517 (27.8)	8085 (21.3)	
With diabetes mellitus	478 (4.9)	337 (3.5)	306 (2.9)	240 (3.0)	
Adjusted hazard ratio (95% CI)					
Age	1.00	0.72 (0.62-0.82)	0.58 (0.50-0.67)	0.60 (0.52-0.70)	<.001
Multivariate*	1.00	0.78 (0.68-0.90)	0.69 (0.59-0.80)	0.74 (0.63-0.88)	<.001
Multivariate†	1.00	0.91 (0.79-1.06)	0.86 (0.74-1.01)	0.82 (0.70-0.97)	.01

Abbreviation: CI, confidence interval.
*Adjusted for age, family history of diabetes, alcohol use, smoking status, hormone therapy use, hypertension, high cholesterol, dietary factors, and randomized Women's Health Study treatment groups.
†Adjusted for aforementioned covariates and body mass index.

JAMA. 2004;292:1188-1194

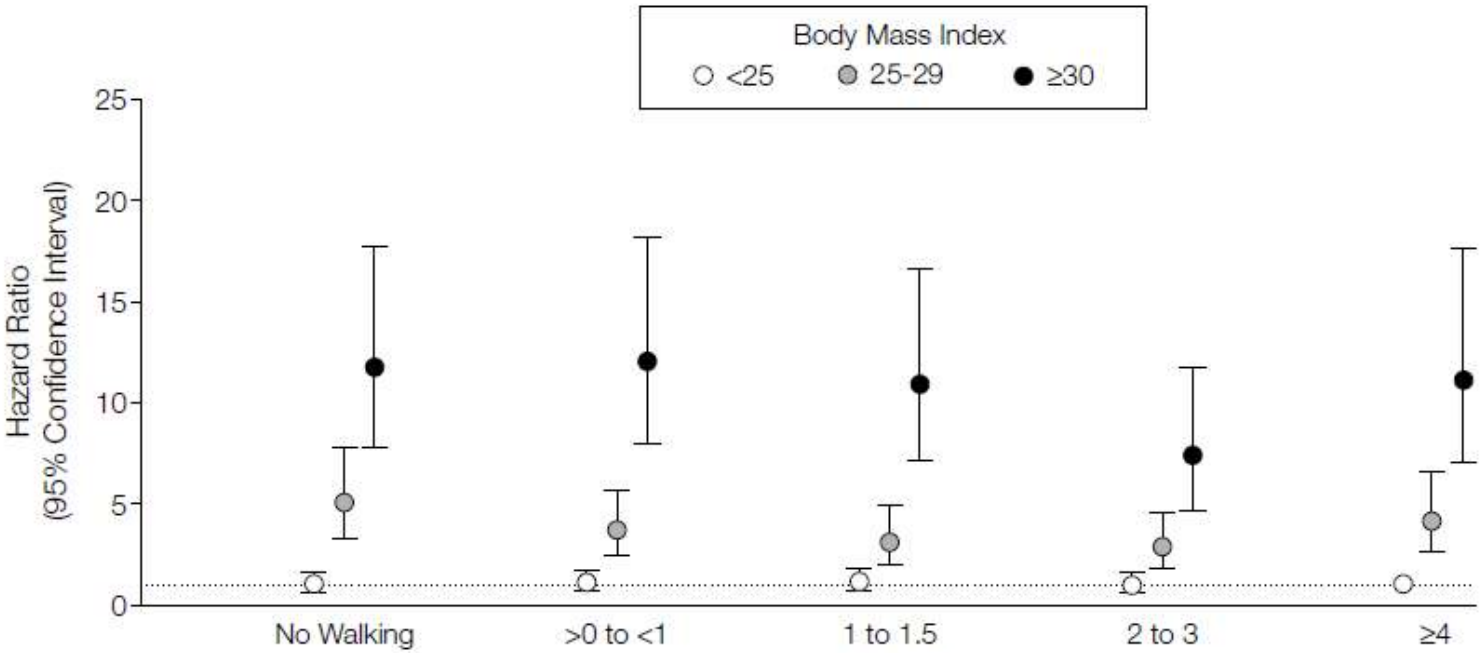
Physical activity, BMI and risk of diabetes Women's Health Study, N=37,878, 6.9y F/U



No. of Patients				
BMI <25	4285	4727	5713	4220
BMI 25-29	2841	2944	3021	2397
BMI ≥30	2165	1530	1411	1109

JAMA. 2004;292:1188-1194

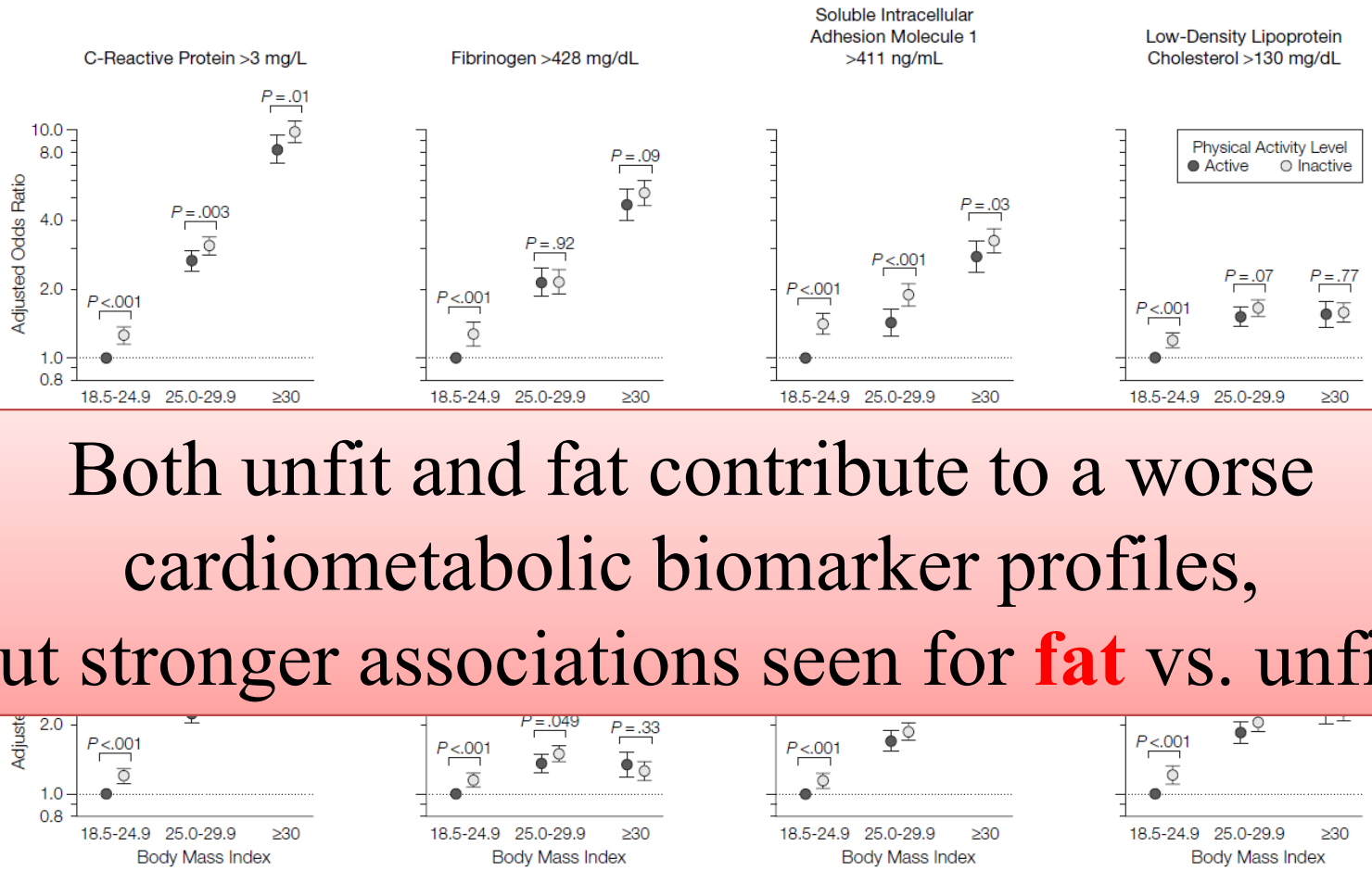
Physical activity, BMI and risk of diabetes Women's Health Study, N=37,878, 6.9y F/U



No. of Patients					
BMI <25	3254	4767	4228	3503	3161
BMI 25-29	2216	3016	2482	1867	1612
BMI ≥30	1816	1846	1190	776	583

JAMA. 2004;292:1188-1194

Physical activity, BMI and cardiovascular biomarkers
Women's Health study, N=27,158, cross-sectional



Both unfit and fat contribute to a worse cardiometabolic biomarker profiles, but stronger associations seen for **fat** vs. unfit.

JAMA. 2006;295:1412-1419

DIABETES PREVENTION TRIAL

Diabetes Prevention Program (DPP)

- Primary goal
  - **Reduction** of at least **7%** of initial body weight and an enhanced level of **physical activity** in overweight or obese people at high risk of diabetes
- A total of **1,079** participants were aged 25–84 years (mean 50.6 years, BMI 33.9kg/m^2)

N Engl J Med 2002; 346: 393-403

Weight loss, physical activity and diabetes risk; DPP trial

Variables (unit change)	Model	Models assessing one characteristic at a time* HR (95% CI)‡	*P*	R^2 (%)§	Multivariate model† HR (95% CI)‡	*P*	R^2 (%)§
Baseline variables							
Lower weight (10 kg)	1	0.81 (0.75–0.86)	<0.0001	3.46	0.88 (0.81–0.96)	0.003	0.82
Higher leisure physical activity (MAQ) (5 MET hours/week)	2	1.00 (0.96–1.05)	0.89	0.00	1.00 (0.96–1.04)	0.98	0.00
Higher recreational activity (LoPAR) (20 MET hours/week)	3	1.12 (1.01–1.23)	0.03	0.42	1.08 (0.97–1.20)	0.16	0.19
Lower percent of calories from fat (5%)	4	0.96 (0.84–1.10)	0.57	0.03	0.91 (0.79–1.05)	0.19	0.16
Follow-up variables							
Weight loss (5 kg)	1	0.49 (0.43–0.57)	<0.0001	7.55	0.42 (0.35–0.50)	<0.0001	8.09
Higher leisure physical activity (MAQ) (5 MET hours/week)	2	0.95 (0.88–1.02)	0.17	0.17	0.97 (0.90–1.05)	0.50	0.04
Higher recreational activity (LoPAR) (5 MET hours/week)	3	0.99 (0.97–1.02)	0.66	0.01	0.99 (0.96–1.02)	0.45	0.05
Lower percent of calories from fat (5%)	4	0.75 (0.63–0.88)	0.0007	1.06	0.93 (0.77–1.12)	0.42	0.06

Diabetes Care 29:2102–2107, 2006

DPP: weight change and diabetes incidence

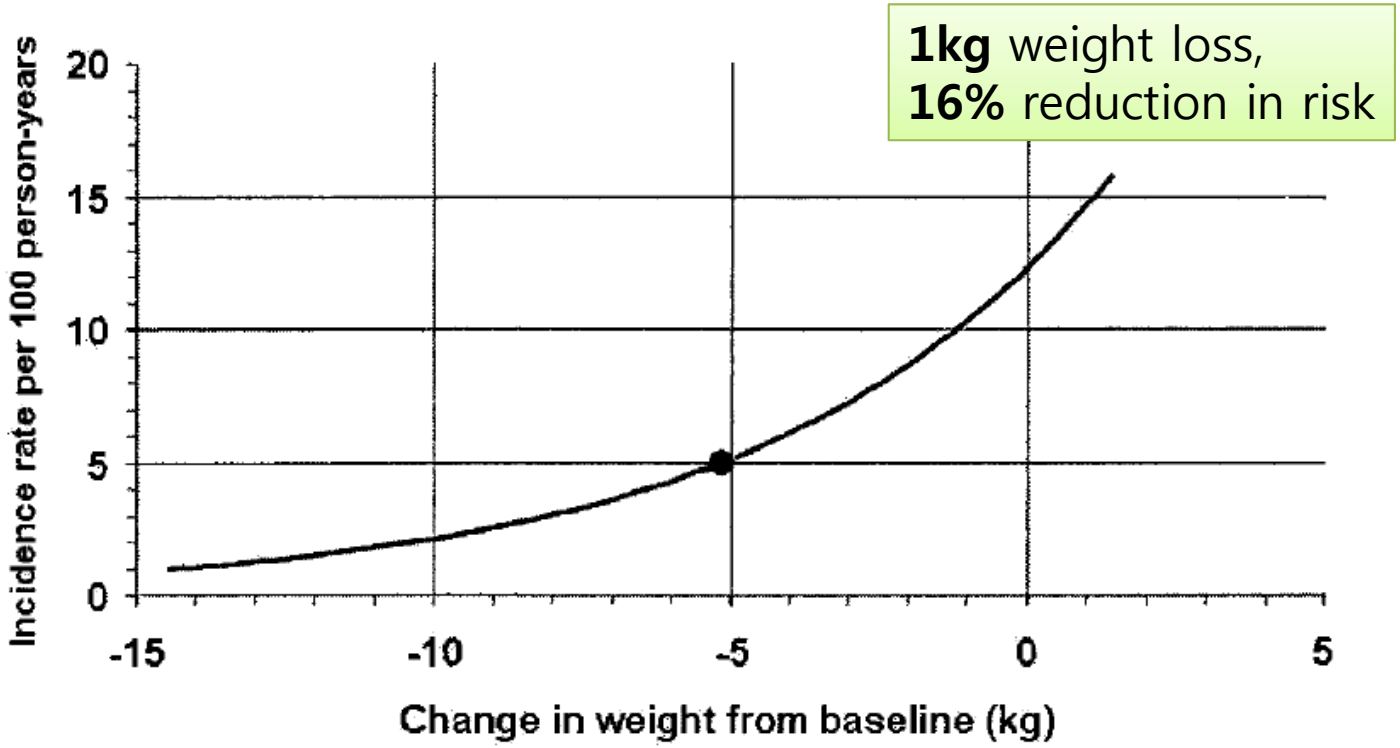
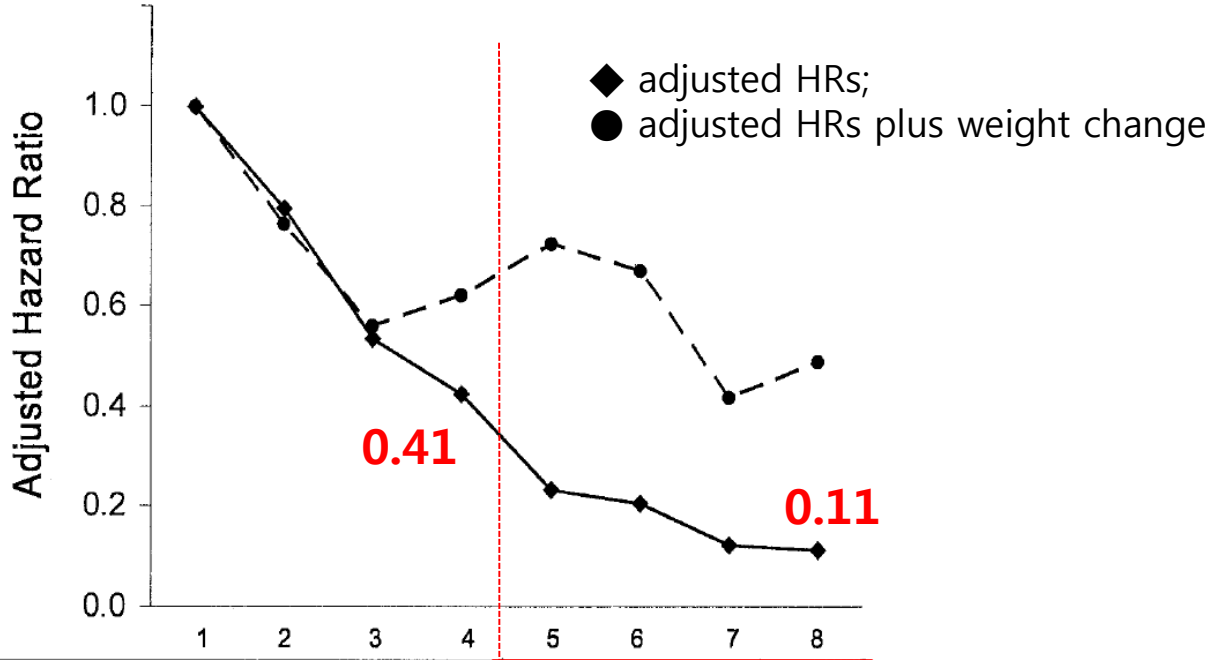


Figure 1—*Diabetes incidence (per 100 person-years) by change in weight after baseline among DPP ILS participants based on the multivariate model in Table 2.* ●, *overall risk in the group at the mean weight loss over an average of 3.2 years of follow-up.*

Diabetes Care 29:2102–2107, 2006

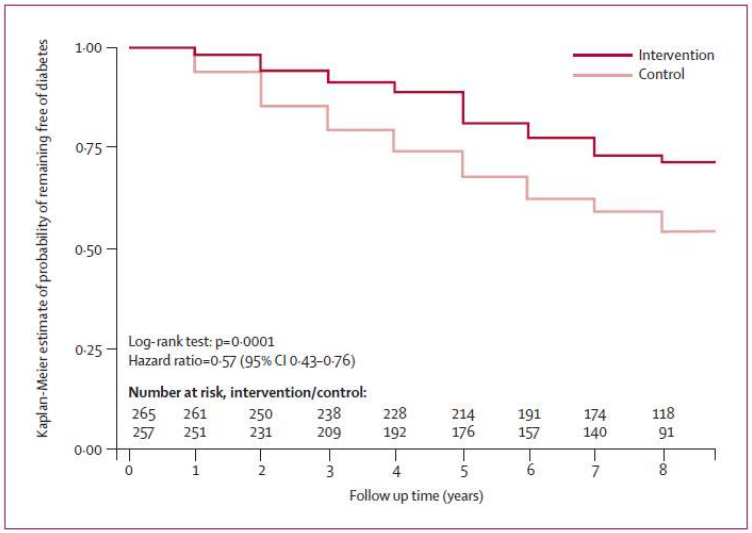
DPP: diabetes incidence, y1



At weight goal	No	No	No	No	Yes	Yes	Yes	Yes
At exercise goal	No	No	Yes	Yes	No	No	Yes	Yes
At fat goal	No	Yes	No	Yes	No	Yes	No	Yes
Mean weight loss (Kg)	-1.5	-2.5	-2.2	-3.5	-11.5	-11.5	-11.8	-13.4
Sample size	134	32	226	103	51	34	208	187

Diabetes Care 29:2102–2107, 2006

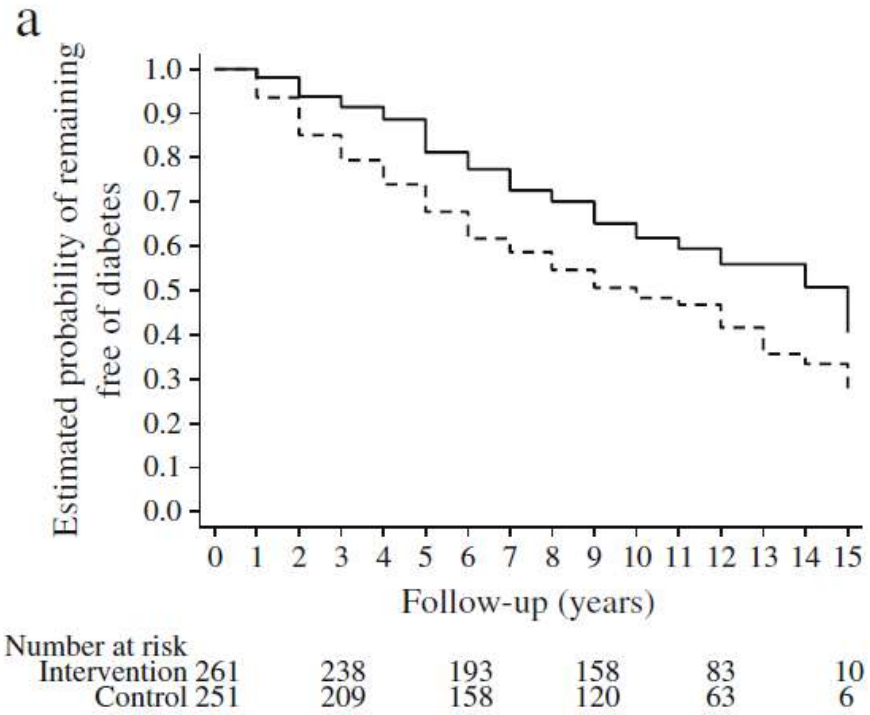
Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study



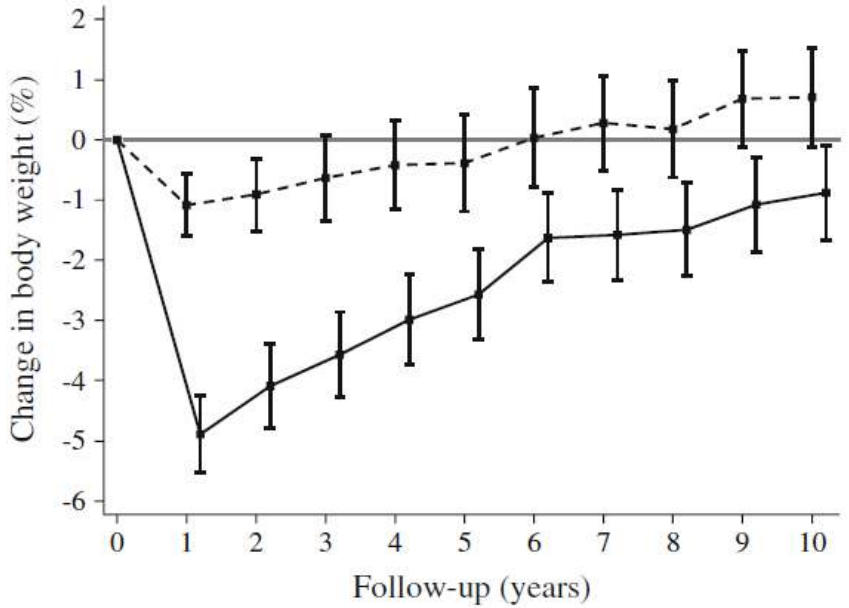
- To assess the independent effects of achieving the success score components at the 3-year examination on diabetes incidence during the total follow-up,
- the multivariate-adjusted hazard ratios for diabetes (95% CI) were **0·43 (0·30–0·61) for weight reduction**, 0·80 (0·48–1·34) for intake of fat, 0·55 (0·26–1·16) for intake of saturated fat, 0·97 (0·63–1·51) for intake of fibre, and **0·80 (0·57–1·12) for physical activity**.

Lancet 2006; 368: 1673–79

Improved lifestyle and decreased diabetes risk over 13 years: Finnish Diabetes Prevention Study



Incidence rates per 100 person-years were 4.5 (95% CI 3.8, 5.5) in the intervention group and 7.2 (95% CI 6.1, 8.5) in the control group; **HR was 0.614 (95% CI 0.478, 0.789; p<0.001).**



Lifestyle intervention in people at high risk of type 2 diabetes induces sustaining lifestyle change and results in long-term prevention of progression to type 2 diabetes.

Diabetologia (2013) 56:284–293

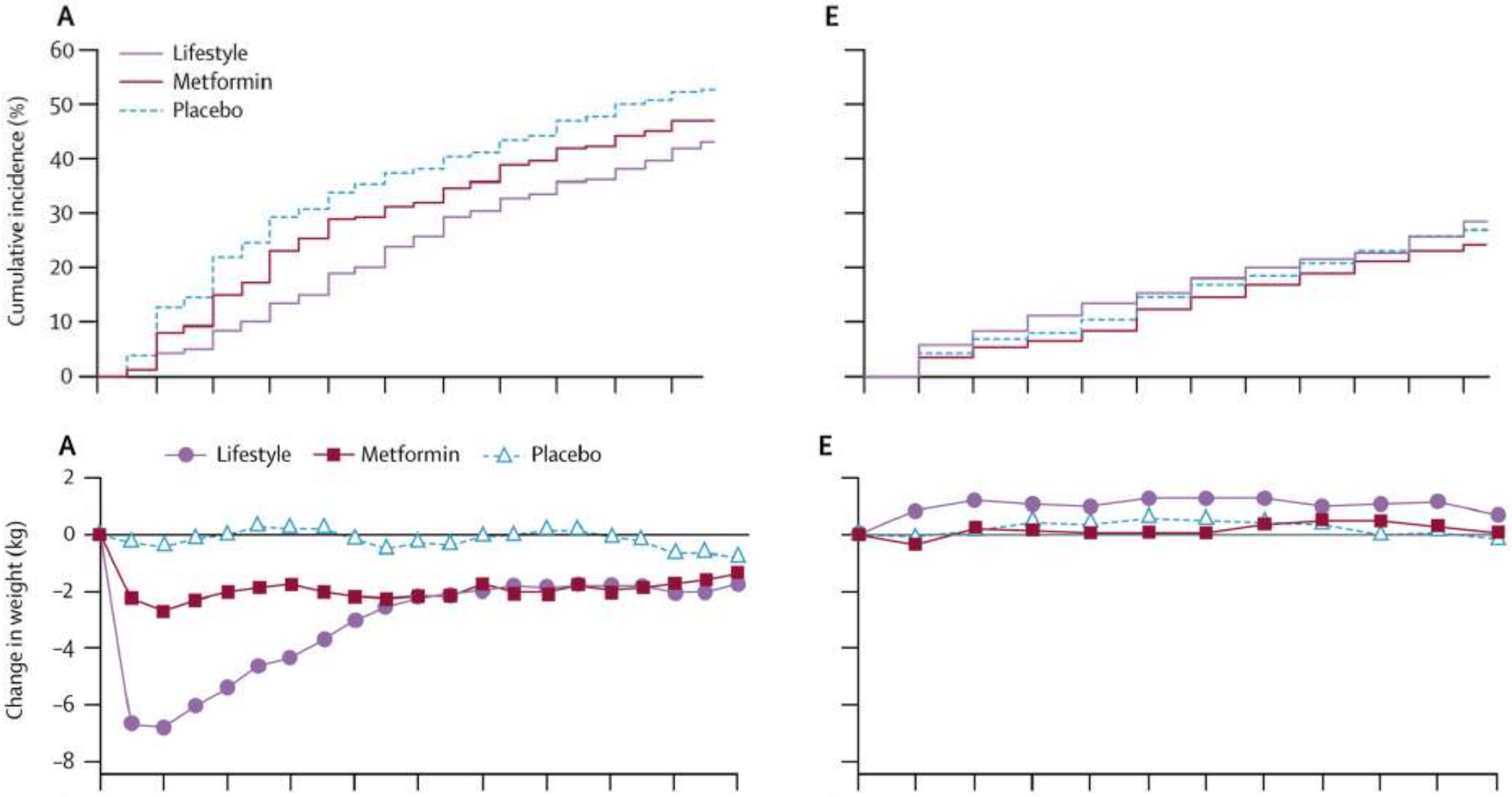
How much weight loss protects against diabetes?

- **Every kilogram** of weight loss in the DPP resulted in a **16% reduction** in risk, but their results were based entirely on data from the initial 3 years of the study.
- As **weight regain** occurred in DPS (and DPP too); the cumulative incidence data over the initial years mask a **much lower difference** between groups in the annual incidence of diabetes in subsequent years.

- Weight loss of **at least 3–4%** over an extended period of time is necessary to achieve appreciable diabetes prevention.

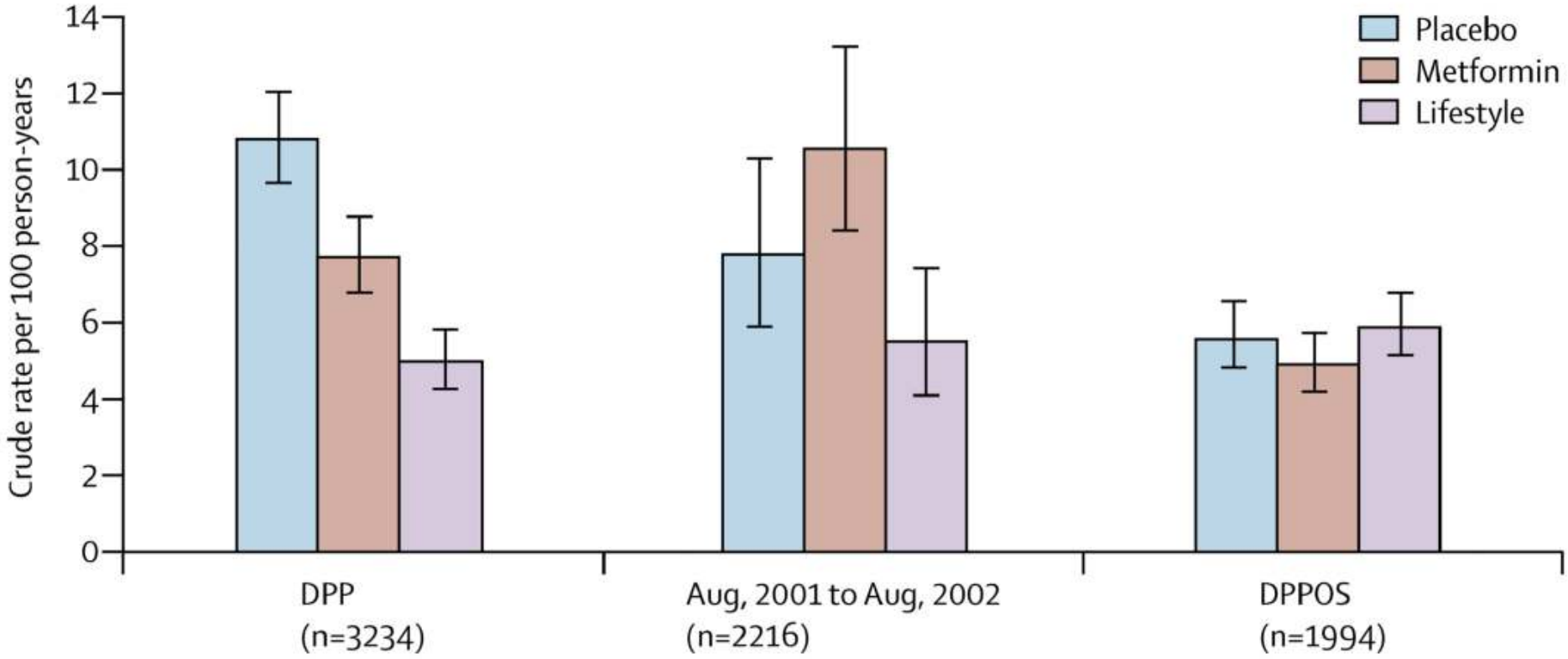
Diabetes Care 2014; 37: 943-949

10-year F/U of diabetes incidence and weight loss in the DPP Outcomes Study



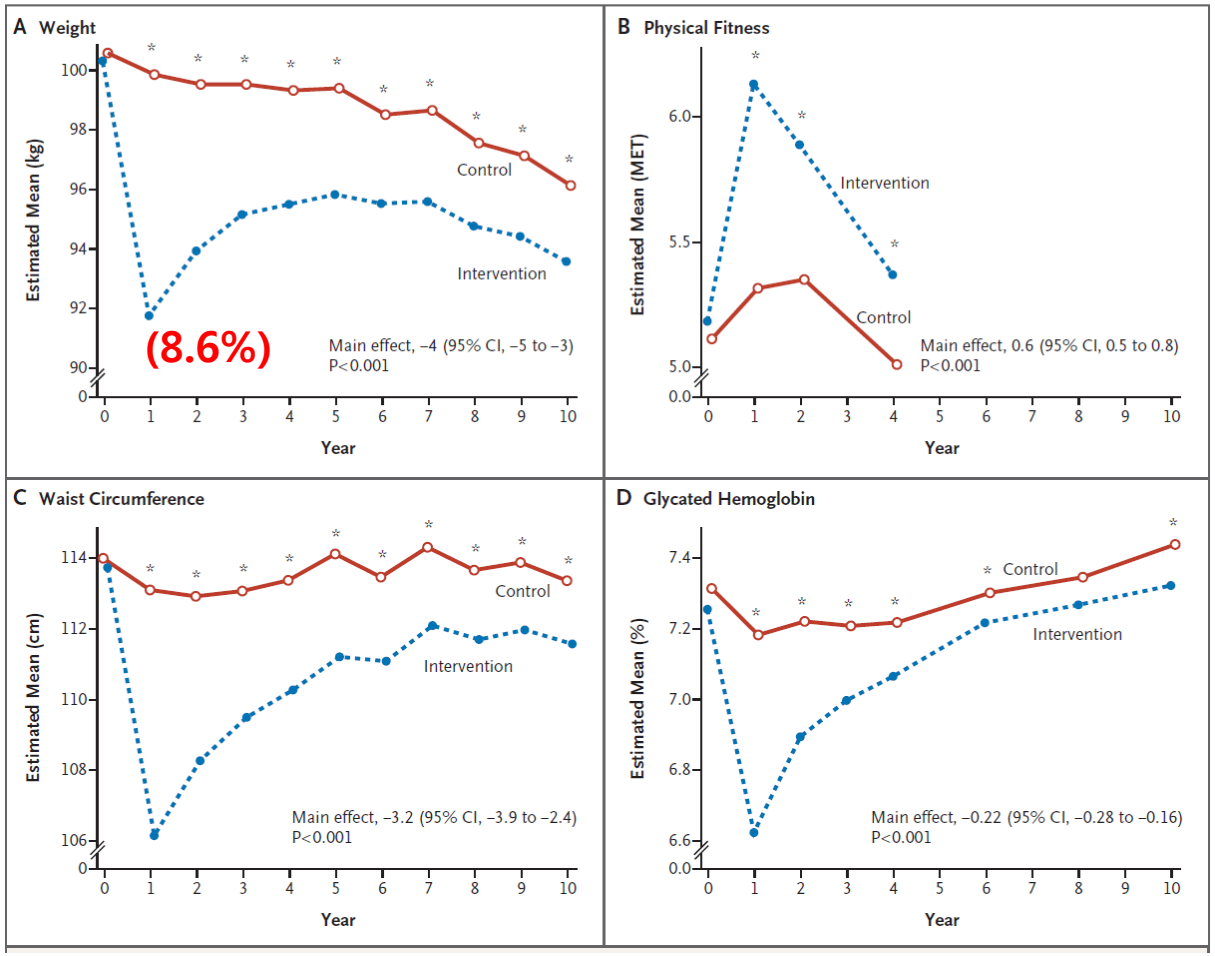
Lancet. 2009; 374(9702): 1677–1686

10-year F/U of diabetes incidence and weight loss in the DPP Outcomes Study



Lancet. 2009; 374(9702): 1677–1686

Look AHEAD trial in diabetes n=5,145, f/u 9.6y



N Engl J Med 2013;369:145-54

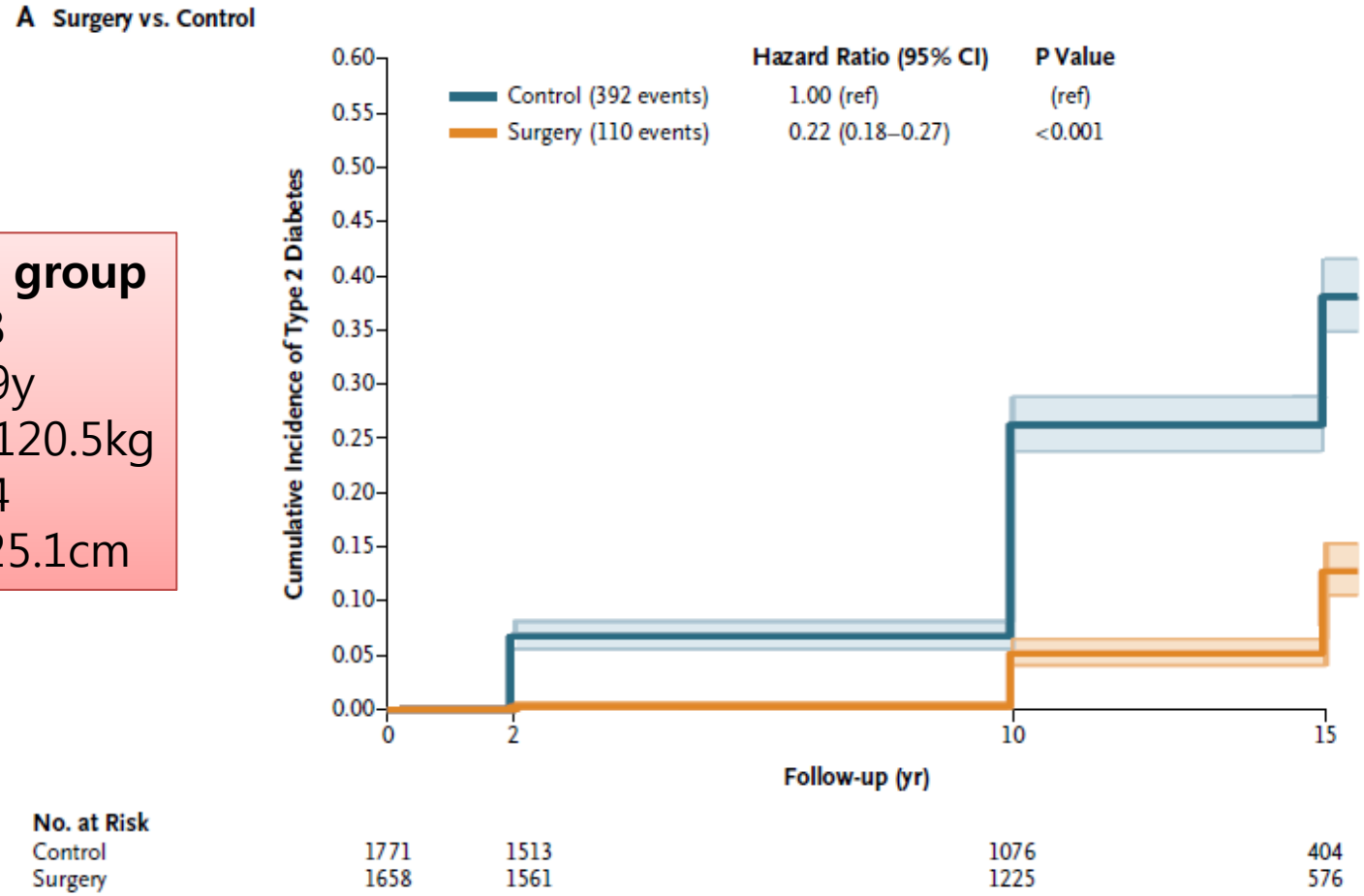
Look AHEAD trial in diabetes Intensive lifestyle intervention

- **Phase I (first year)**
  - **four times per month** (three group sessions and one individualized session) for six months and then **twice per month** for six months
  - Goal; **7-10% weight loss, exercise to 175 minutes per week**
- **Phase II (2-4years)**
  - at least one time **contact** per month (in person or by phone, e-mail, voice-mail, or mail).
  - Goal; to **maintain** a weight loss of 7-10% and an activity level of greater than 175 minutes per week.

N Engl J Med 2013;369:145-54

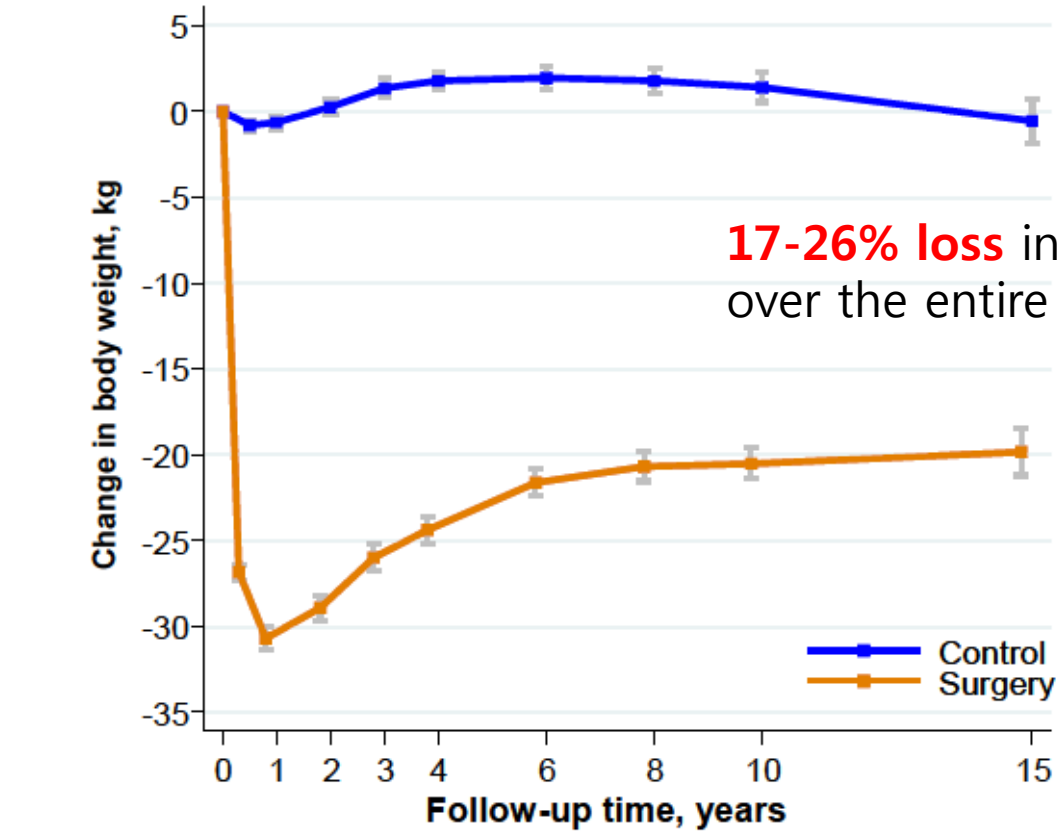
Bariatric Surgery and Prevention of Type 2 Diabetes in Swedish Obese Subjects

Surgery group
N=1,658
Age 46.9y
Weight 120.5kg
BMI 42.4
Waist 125.1cm



N Engl J Med 2012;367:695-704

Bariatric Surgery and Prevention of Type 2 Diabetes in Swedish Obese Subjects



17-26% loss in body weight over the entire f/u period

N Engl J Med 2012;367:695-704

Summary

- Both **obesity (fat)** and **physical activity (unfit)** are associated with higher risk of diabetes and cardiometabolic biomarkers.
- **Weight loss** is the most important contributor to prevention of diabetes.
- **Lifestyle intervention** resulted in an overall mean delay in the development of diabetes of about 4-5 years.
- **Sustained weight loss of at least 3-4%** over the time is necessary to achieve appreciable diabetes prevention.