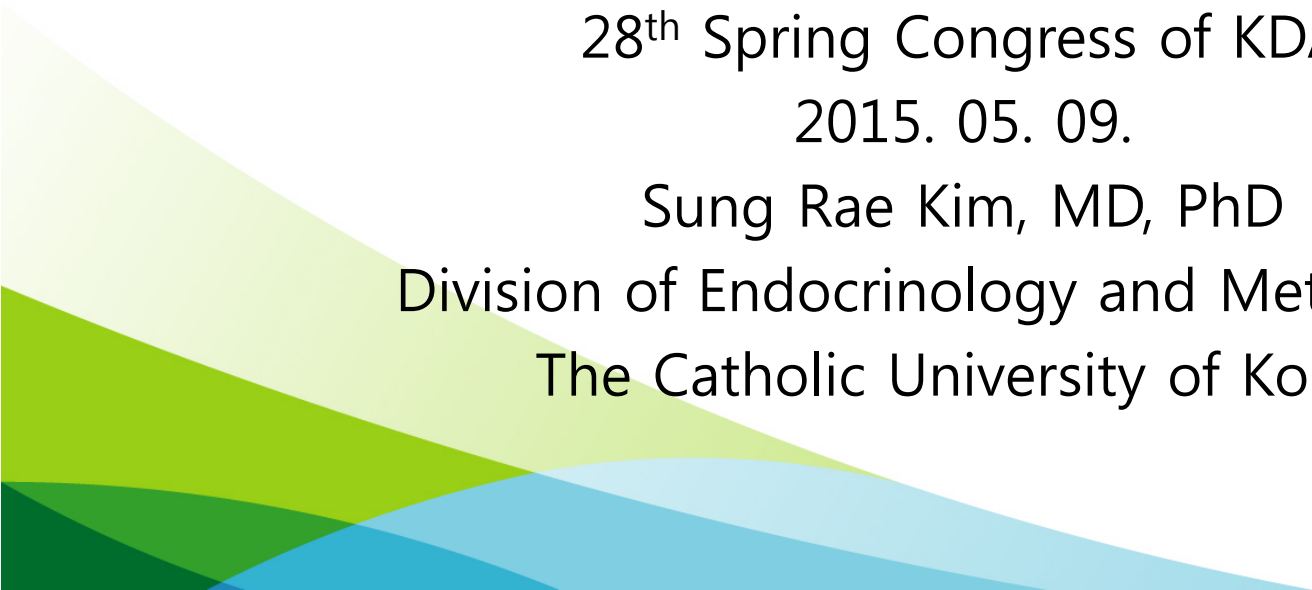


Metabolic syndrome, dyslipidemia, and cardiovascular disease

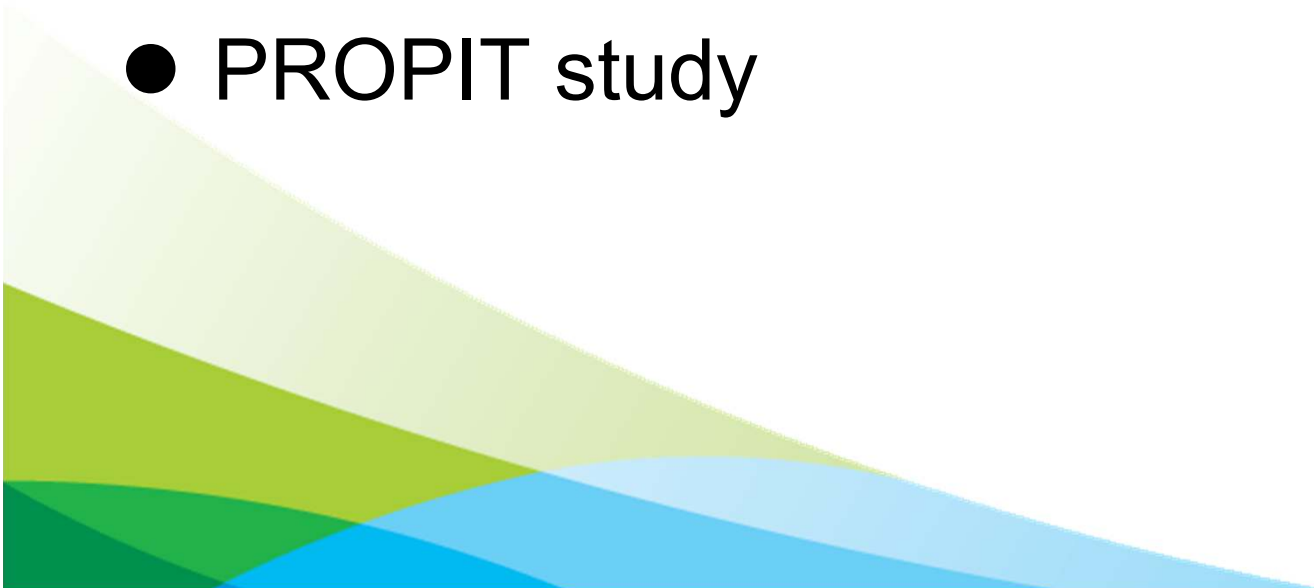
28th Spring Congress of KDA
2015. 05. 09.

Sung Rae Kim, MD, PhD
Division of Endocrinology and Metabolism
The Catholic University of Korea



Today's Talk

- History of Metabolic Syndrome
- Dyslipidemia and Metabolic Syndrome
- PROPIT study



Today's Talk

- History of Metabolic Syndrome



1970

1977
German research group also describes a clustering of cardiovascular risk factors

1960

1960
Yalow and Berson establish the concept that obesity, whether associated with diabetes or not, is a cause of insulin resistance

1950

1940

1930

1938
British physician Harold Percival Hinselwood coins the term insulin sensitivity

1967
Italian research group first describes a clustering of cardiovascular risk factors (hypertension, diabetes, dyslipidemia, and obesity)

2000

2001
National Cholesterol Education Program suggests that behavioral interventions promoting weight loss and increased physical activity are basis of treatment for patients who have metabolic syndrome

2000

1990

1980

1988
Gerald M. Reaven, MD, from Stanford University School of Medicine, first describes syndrome X in a Banting Lecture at annual meeting of American Diabetes Association

2001
Adult Treatment Panel III of the National Cholesterol Education Program proposes diagnostic criteria for metabolic syndrome that establish cutoff points for five risk factors: abdominal girth, blood pressure, serum cholesterol, triglycerides, and fasting glucose. Patients with results showing three or more of these risk factors are considered to have metabolic syndrome







Fig. 1 Eleven blind Buddhist monks examine an elephant but fail to agree upon a definition. An illustration of the old fable by the Japanese artist Hokusai Katsushika (1760–1849)

Syndrome X

Reaven(1988) – cardiovascular dis.의 요인들 ;

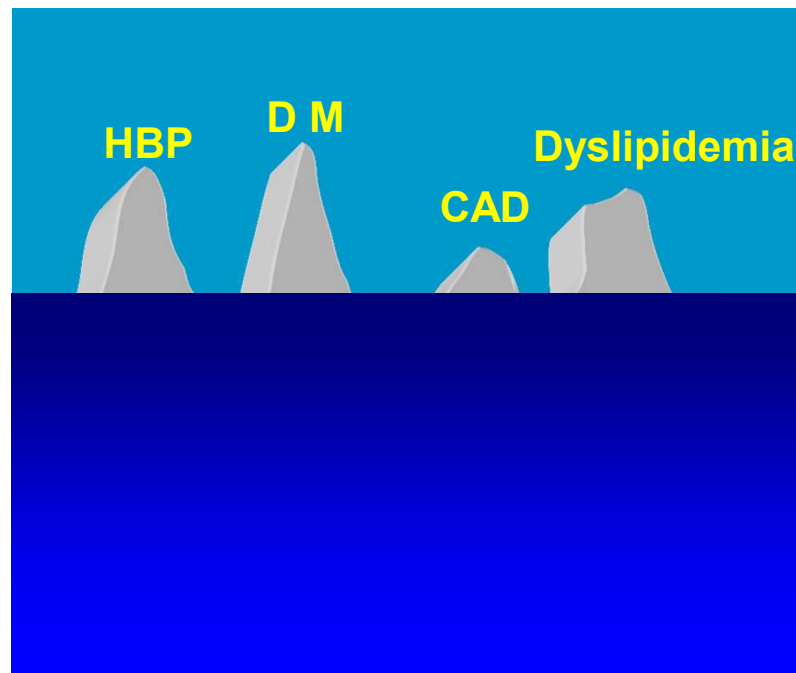
인슐린에 의한 **조직에서의 당 섭취량 감소**

내당능 이상

고 인슐린혈증

고VLDL 혈증, 저HDL 혈증

고혈압



Metabolic Syndrome – WHO 1999

At least 1 of

+

at least 2 of



**Metabolic
Syndrome**

- Type 2 diabetes
- IGT
- Insulin resistance

- Hypertension
- Obesity
- Raised TG or low HDL
- Microalbuminuria

- Hyperuricemia
- Hypercoagulability
- Hyperleptinemia

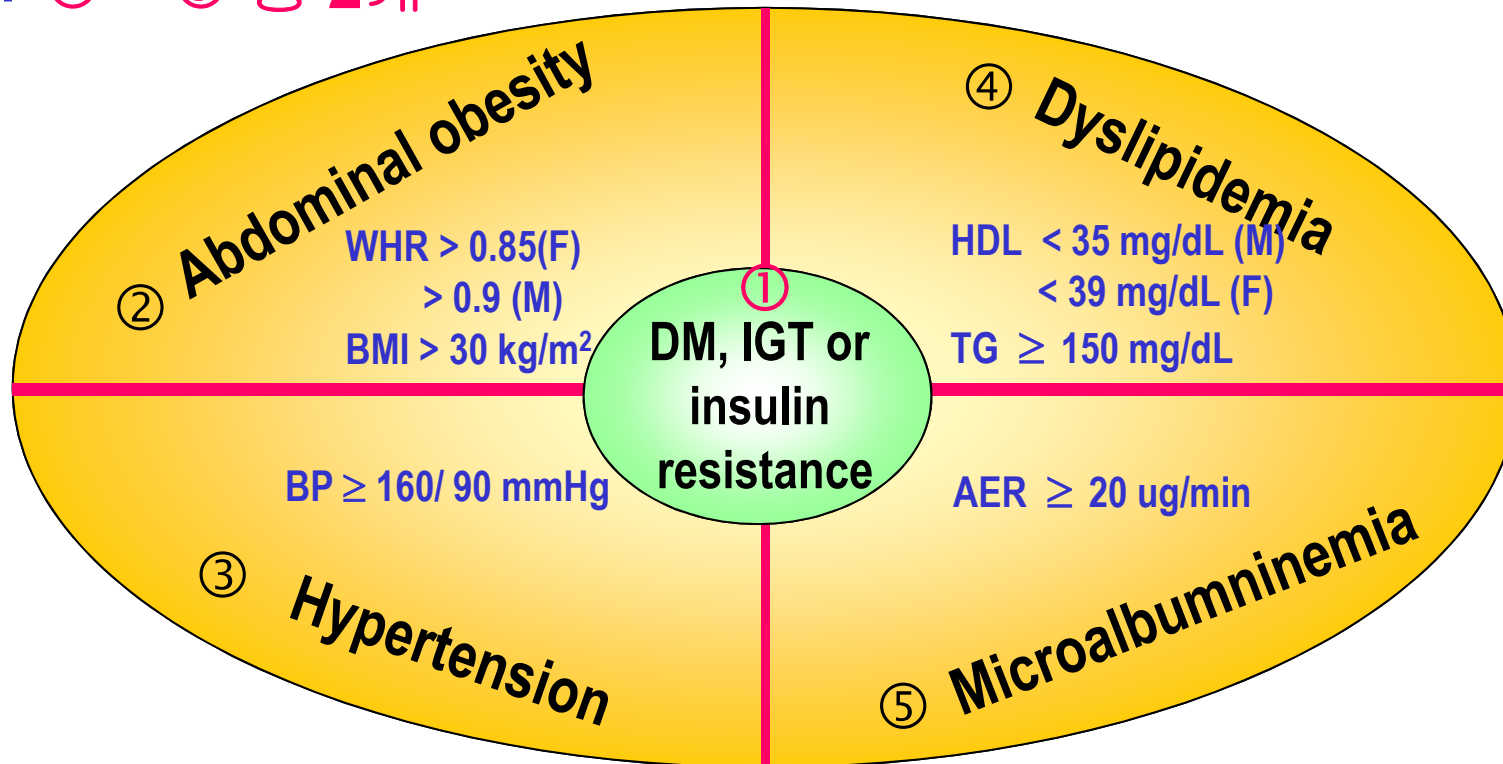
Not required for definition

But may be part of the syndrome



대사증후군의 기준 (WHO,1999)

① + ② ~ ⑤ 중 2개



- Other components: hyperuricemia, coagulation disorders, raised PAI-1
Not necessary for the recognition of the conditions.

대사증후군의 기준 (NCEP-ATP III, 2001)

Clinical identification (≥ 3 risk determinants)

Risk Factor	Definition Level
Waist circumference	
Men (cm)	> 102 (90)
Women (cm)	> 88 (80)
Triglyceride (mg/dL)	≥ 150
HDL-C	
Men (mg/dL)	< 40
Women (mg/dL)	< 50
Blood pressure (mmHg)	≥ 130 / ≥ 85
Fasting glucose (mg/dL)	≥ 110

EGIR Criteria

(European Group for the Study of Insulin Resistance)

- ◆ **Non-diabetic subjects** 대상
- ◆ **Hyperinsulinemia + 나머지 4개중 2개 이상**

Risk Factor	Definition Level
Hyperinsulinemia	Fasting insulin concentration above the upper quartile for the non-diabetic subjects
Hyperglycemia	FPG \geq 110 (mg/dL)
Hypertension	\geq 140 and/or \geq 90 (mmHg)
Dyslipidemia	Triglyceride (mg/dL) \geq 180 and/or HDL-C (mg/dL) $<$ 40 and/or Treatment for dyslipidemia
Central obesity	WC \geq 94 cm(M), 80 cm(F)

AACE Criteria

(American Association of Clinical Endocrinologists)

- ◆ **Non-diabetic subjects** 대상
- ◆ **Insulin resistance + 나머지 4개중 2개 이상**

Risk Factor	Definition Level
Plasma glucose (mg/dL) <ul style="list-style-type: none">▪ Fasting glucose▪ 120 min post-glucose challenge(75g)	110 - 125 ≥ 140
Triglyceride *(mg/dL)	≥ 150
HDL-C * Men (mg/dL) Women (mg/dL)	< 40 < 50
Blood pressure *(mmHg)	≥ 130 / ≥85 or current Medication
Obesity (BMI, WC)	Physiological variables Not a criteria for Dx.

대사증후군의 기준

	WHO	NCEP	EGIS	AACE
기준	Insulin resistance & at least 2 of the following	At least 3 of the following	Hyperinsulinemia	IR
Glucose	Insulin resistance	FBS \geq 110 mg/dL	FBS \geq 110	PP2H \geq 140
Abdominal obesity	WHR $>$ 0.9(M) / 0.85(F) or BMI \geq 30	WC(cm) $>$ 102 (M) $>$ 88 (F)	$>$ 94 (M) $>$ 80 (F)	-
BP	\geq 160/90	\geq 130/85	\geq 140/90	\geq 130/85
TG	\geq 150	\geq 150	\geq 180	\geq 150
HDL-C	$<$ 35 (M) / $<$ 39 (F)	$<$ 40 (M) / $<$ 50 (F)	$<$ 40	$<$ 40 (M) $<$ 50 (F)
기타	Microalbuminuria Hyperuricemia Hypercoagulability			



Metabolic Syndrome

Key components

- Glucose intolerance
- Hypertriglyceridaemia
- ↑Apolipoprotein B
- ↓HDL-cholesterol
- Central Obesity
- Hypertension
- ↓Fibrinolysis
- ↑Small dense LDL

Insulin Resistance

Endothelial dysfunction



1st International Congress on
"PREDIABETES"
and the
METABOLIC SYNDROME

Epidemiology, Management and Prevention of Diabetes
and Cardiovascular Disease

BERLIN, GERMANY
APRIL 12-16, 2005

1st International Congress on
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METABOLIC SYNDROME

Epidemiology, Management and Prevention of Diabetes
and Cardiovascular Disease

BERLIN, GERMANY
APRIL 12-16, 2005

IDF Consensus

- And what of ***INSULIN RESISTANCE*** ?
 - Not measured - too difficult
 - But – **central obesity plus TG** likely to have **IR**
 - What of insulin resistant non-obese ?

IDF Consensus

- Central Obesity

	M	(cm)	F
Europids	94		80
South Asians	90		80
Chinese	90		80
Japanese	85		90

Sub-Saharan Africans, Middle East – use Europid figures

South/Central Americans – use South Asian figures

IDF Consensus

- Definition

Central Obesity

Plus any two of :

- Raised Triglycerides
- Low HDL-cholesterol
- Raised blood pressure
- Raised fasting plasma glucose
(or pre-existing DM)

IDF Consensus

Cutpoints

- **Triglycerides** : ≥ 1.7 mM (150 mg/dl)
- **HDL-cholesterol** : < 0.9 mM (40 mg/dl) M
 < 1.1 mM (50 mg/dl) F
- **Blood Pressure** : ≥ 130 mm Systolic
or ≥ 85 mm Diastolic
or treatment
- **Fasting plasma glucose** : ≥ 5.6 mM(100mg/dl)

Joint Scientific Statement

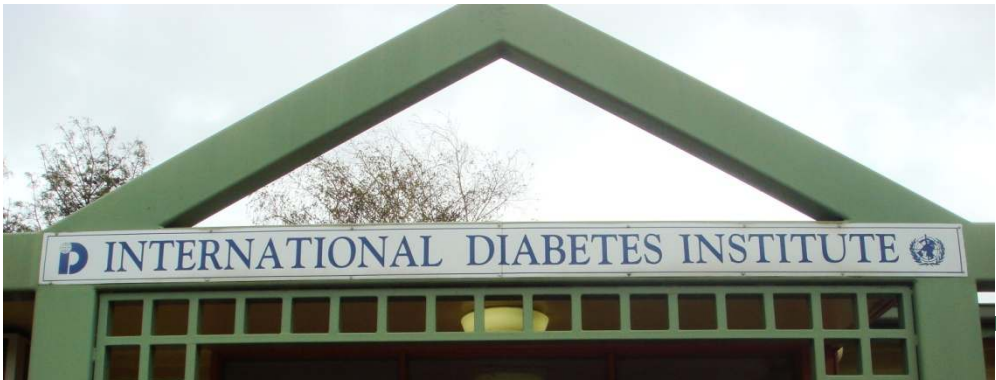
Harmonizing the Metabolic Syndrome

A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity

K.G.M.M. Alberti, FRCP; Robert H. Eckel, MD, FAHA; Scott M. Grundy, MD, PhD, FAHA;
Paul Z. Zimmet, MD, PhD, FRACP; James I. Cleeman, MD; Karen A. Donato, SM;
Jean-Charles Fruchart, PharmD, PhD; W. Philip T. James, MD;
Catherine M. Loria, PhD, MS, MA, FAHA; Sidney C. Smith, Jr, MD, FAHA

Abstract—A cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus, which occur together more often than by chance alone, have become known as the metabolic syndrome. The risk factors include raised blood pressure, dyslipidemia (raised triglycerides and lowered high-density lipoprotein cholesterol), raised fasting glucose, and central obesity. Various diagnostic criteria have been proposed by different organizations over the past decade. Most recently, these have come from the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute. The main difference concerns the measure for central obesity, with this being an obligatory component in the International Diabetes Federation definition, lower than in the American Heart Association/National Heart, Lung, and Blood Institute criteria, and ethnic specific. The present article represents the outcome of a meeting between several major organizations in an attempt to unify criteria. It was agreed that there should not be an obligatory component, but that waist measurement would continue to be a useful preliminary screening tool. Three abnormal findings out of 5 would qualify a person for the metabolic syndrome. A single set of cut points would be used for all components except waist circumference, for which further work is required. In the interim, national or regional cut points for waist circumference can be used. (*Circulation*. 2009;120:1640-1645.)

Key Words: AHA Scientific Statements ■ metabolic syndrome ■ risk factors ■ diabetes mellitus



<http://www.diabetes.com.au/>



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The International Diabetes Institute is a research based organisation helping people live with diabetes

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AusDiab 2005

The Australian Diabetes, Obesity and Lifestyle Study

Tracking the Accelerating Epidemic: Its Causes and Outcomes



Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



Baseline data from AusDiab 2000

- The AusDiab survey carried out in 1999–2000 provides benchmark Australian prevalence data
- 2000 findings, Australians ≥ 25 years old:
 - 7.4% had diabetes (doubled since 1981)
 - 16.3% had pre-diabetes (IFG/IGT*)
 - 59.6% were mildly overweight or obese
 - 28.8% had hypertension
 - 51.2% had total cholesterol ≥ 5.5 mmol/L, and 20.5% had elevated triglycerides (≥ 2.0 mmol/L)
 - 2.5% had proteinuria, 6.4% had haematuria and 1.1% had elevated serum creatinine



* IFG — impaired fasting glucose; IGT — impaired glucose tolerance.

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Aims of the five-year follow-up

- Describe the natural history of:
 - Type 2 diabetes
 - Pre-diabetes (IFG/IGT*)
 - Associated cardiovascular disease, risk factors and complications
- Identify risk factors associated with worsening glucose tolerance status and diabetic complications
- Measure the progression of renal disease in diabetic and non-diabetic populations



* IFG – impaired fasting glucose; IGT – impaired glucose tolerance.

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Definitions for 'prevalence' and 'incidence'

- **1999–2000 data:**

Prevalence – the proportion of people within a population who have a certain disease or condition at a particular time

- **2004–05 data:**

Incidence – number of new cases of a disease or condition arising in a population over a period of time

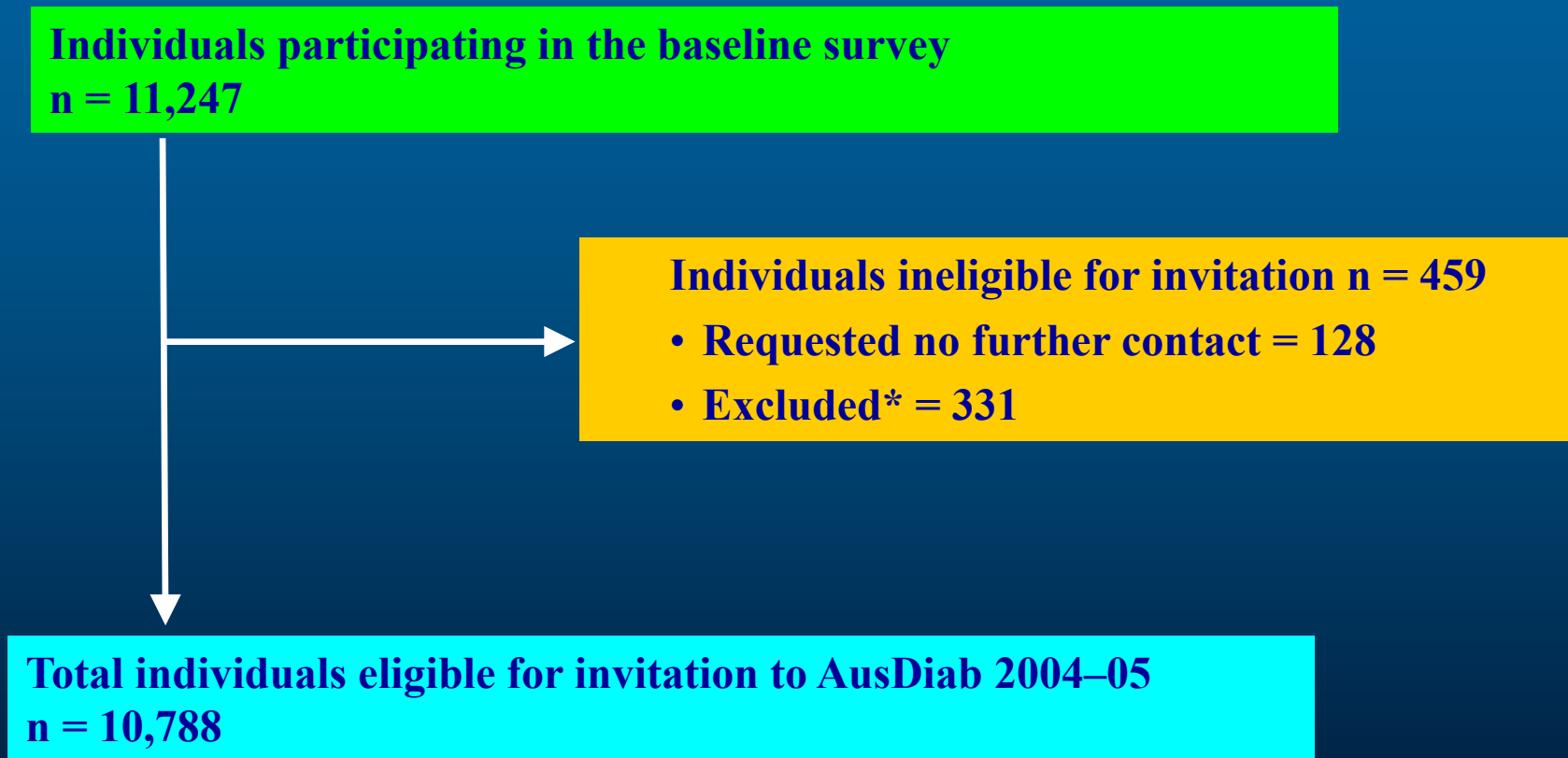
Survey methods and response rates



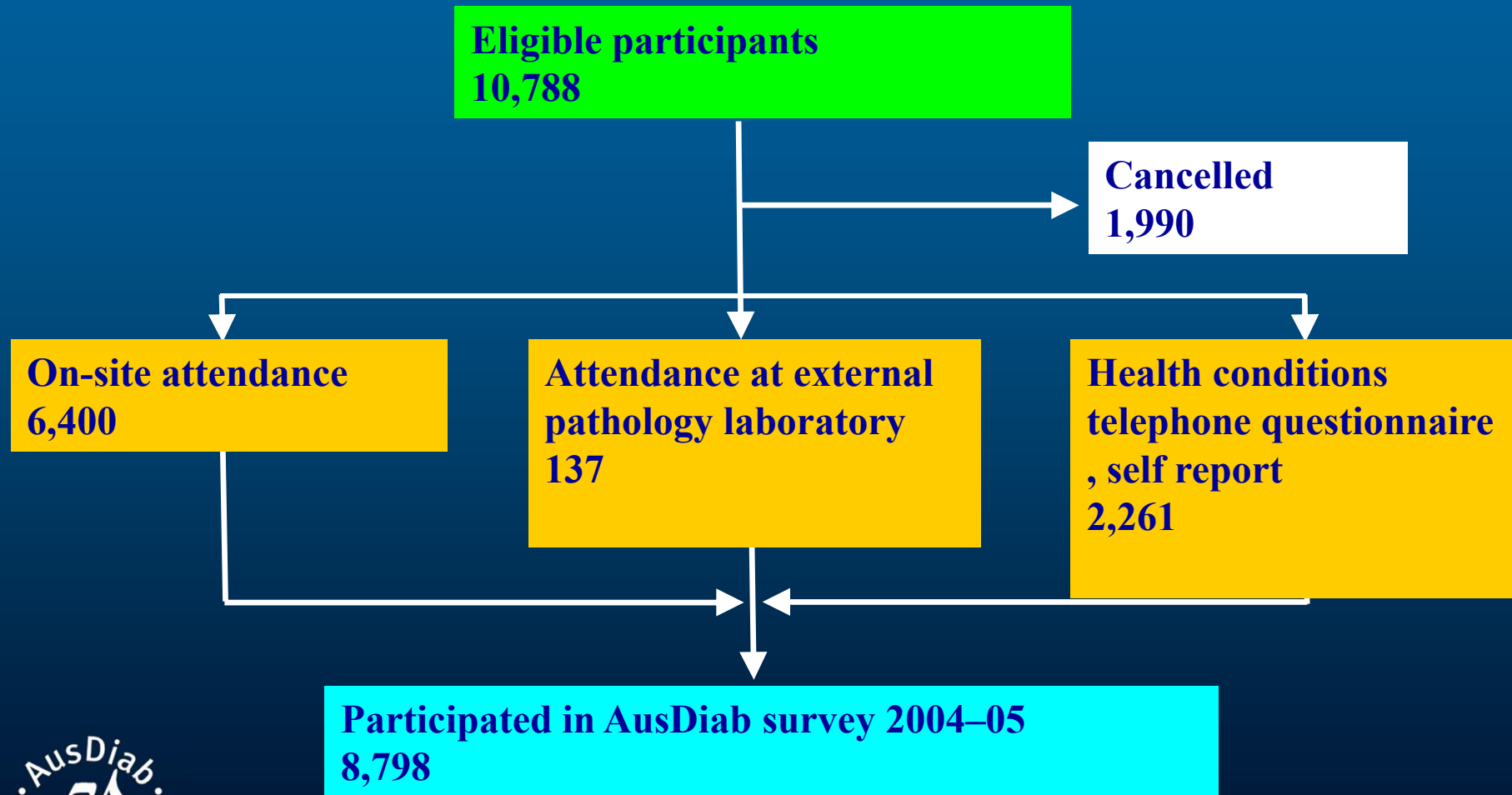
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Sampling frame for the AusDiab follow-up 2004–05



Response rates to the AusDiab survey 2004–5





Australian Report Map
 © copyright Commonwealth of Australia
 (Geoscience Australia) 1996



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Response rates by state or territory

State	Number eligible n	On-site testing n (%)	Pathology laboratory attendance* n (%)	Self-reported medical conditions only n (%)	Overall responders n (%)
VIC	1,429	821 (57.5)	52 (3.6)	337 (23.6)	1,210 (84.7)
WA	1,526	990 (64.9)	28 (1.8)	210 (13.8)	1,228 (80.5)
NSW	1,458	871 (59.7)	14 (1.0)	323 (22.1)	1,209 (82.9)
TAS	1,700	1,102 (64.8)	2 (0.1)	296 (17.4)	1,400 (82.4)
SA	1,700	945 (55.6)	29 (1.7)	467 (27.5)	1,441 (84.8)
NT	1,202	702 (58.4)	5 (0.4)	189 (15.7)	895 (74.5)
QLD	1,748	954 (54.6)	7 (0.4)	433 (24.8)	1,394 (79.7)
ACT	25	15 (60.0)	0 (0)	6 (24.0)	21 (84.0)
Total	10,788	6,400 (59.3)	137 (1.3)	2,261 (21.0)	8,798 (81.6)

* External pathology laboratory facilities were either not available or were limited in TAS, SA, NT and QLD



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Name

.....



Office use only

Please fill out the following questionnaires on Birth Weight, Medication Use and General Health and Wellbeing (SF36) and bring them with you to the testing site. Each of the following 3 pages has questions on both sides of the paper.

Birth Weight

The following questions are about your weight at birth. We are trying to find out if there is any relationship between birth weight and chronic diseases, such as diabetes (high blood sugar), high blood pressure, and kidney disease.

In order for us to achieve our goal we would like you to record your birth weight, or an estimate that is as accurate as possible, in the space provided below. You may need to ask a family member, or trace the information through your hospital or medical records.

1) What was your birth weight?

..... lb/ oz **OR** Kg/grams **OR** Don't Know

2) How accurate do you think this estimate is?

() Very accurate () Fairly accurate () A guess

3) Please indicate how you obtained this birth weight?

- () Family member
- () Medical records
- () Local Doctor
- () Other - please specify

4) Do you know if you were born:

- () Full Term (9 months)?
- () Two or more weeks before the due date?
- () Don't know?
- () Other - please specify

5) Any other comments you wish to

make?.....





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Observer ID

AusDiab: Diabetes Complications Survey Form

SIGNS AND SYMPTOMS IN FEET & LEGS

1. Have you ever had a foot ulcer (defined as - full thickness skin break below the malleoli for more than 1 week)?

- Yes
- No
- Don't Know

2. If yes, What was the cause? (eg shoes)

Site

3. How long ago did you have the ulcer?

- In the last month
- In the last year
- In the last 3 years
- More than 3 years ago

4. Do you get any pain or discomfort in your legs or feet?

- Yes
- No
- Don't Know

If no, go on to foot examination Q15

5. How would you describe the pain or discomfort? (Mark all types of pain)

- Burning / numb / tingling
- Aching / cramp-like / tired
- Other



31714

6. When is the pain the worst?

- During the night
- Day and night the same
- During the day

7. Does the pain ever wake you at night?

- Yes
- No

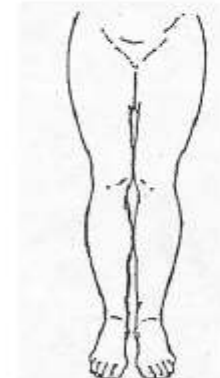
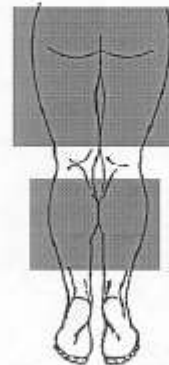
8. Do any of the following help or reduce the pain?

- Walking
- Standing
- Sitting down or lying down
- Other (including medication)

Multiple responses allowed

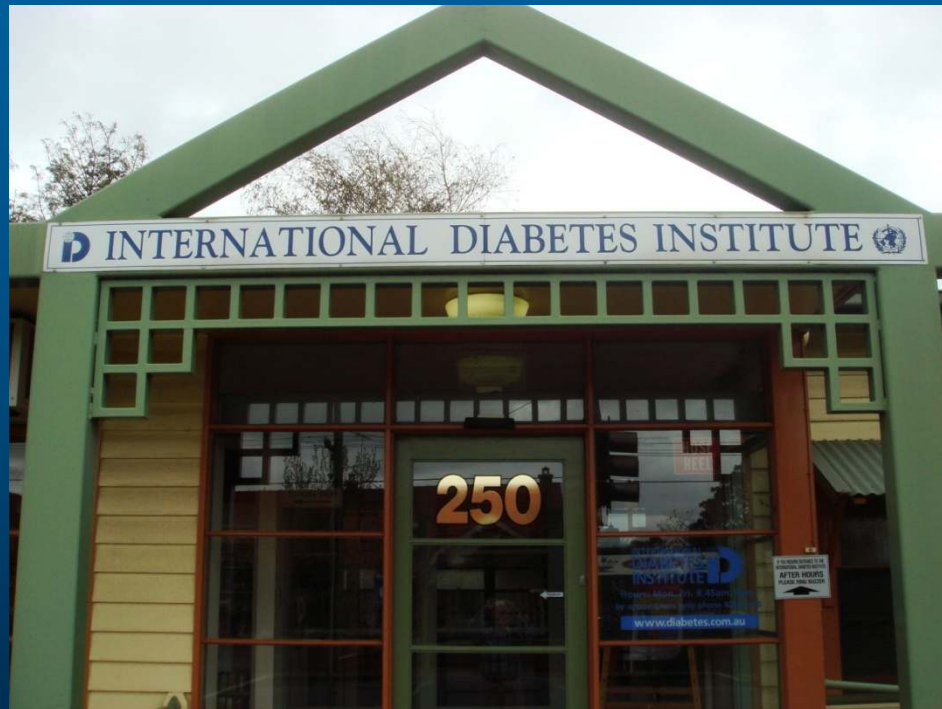
9. Where do you get this pain or discomfort?

Mark in the place(s) with an "x" on the diagram



(Score only the highest scoring site)

- 2. Feet
- 1. Knee to ankle
- 0. Anywhere else



Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006





Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



AusDiab Follow-up 2007: "Every Person Counts"

F:77 23/08/07 990970167

These are your details we have on file. Please update your details if you have any additions or changes in the spaces provided.

Name
Mr Robert Loucks *OK* →

Residential Address
15/7 Charlotte Cl
Woree *OK* →
QLD 4868

Phone Numbers
(AH): (07) 4054 7274
(BH):
(Mobile): *0437412492* →
EMAIL: KANGAROOHOP@HOTMAIL.COM
Email: kangaroohop@hotmail.com & robertal *OK*
ALSO: ROBERTALERE@LOUCKS@YAHOO.COM

Mailing Address (if different to residential)
P O Box 409e
Earlville →
QLD 4870

Survey Questions

The date this questionnaire is being completed: *8/9/07*

Have you seen your GP in the last 6 months? Yes No

In the last 12 months, have you been diagnosed by your doctor as having any of the following new health problems?

(Please tick a box for all questions)

Diabetes Yes No

High blood pressure Yes No

Angina Yes No

Heart disease Yes No

Stroke or transient ischaemic attack (TIA) Yes No

Other illness (please specify) Yes No

DIFFERENT SKIN CONDITIONS, REELUXE WITH ONE POST BLE FOOT INFECTION HAD SERIES OF 5 OR 6 WALKING FLUS OVER 6 MONTHS

Have you been hospitalised in the last 12 months? (If Yes, please specify) Yes No *OK NOW*

Almost one quarter of Australians move house every year. In case we lose contact with you, you have provided us with the following contact details of your next of kin / close friends. Please update if there are any changes in the spaces provided

First next of kin/close friend contact details *DAUGHTER*

Name: Mrs Erica Rose Mellado *MOVED!* *MRS ERICA ROSE MELLADO*
Address: *257 TURTON STREET*
Suburb: Kuraby *NEW!* *SUNNYBANK, BRISBANE*
Postcode: 4112 *4109, QUEENSLAND*
Phone: *PHONE: 32196266*
MOBILE: 0433941987
ERICA @LOUCKS EMAIL: ERILOUCKS@GMAIL.COM
ERICA'S HUSBAND OCTAVIO MOBILE: 0433941986

Second next of kin/close friend contact details *SON*

Name: *STANLEY LOUCKS*
Address: *SAME* → *UNIT 15, CHARLOTTE*
Suburb: *AS* *WOREE, QLD 4868*
Postcode: *MINE* *QUEENSLAND 4868*
Phone: *STANLEY LOUCKS@HOTMAIL.COM*
CAIRNS



http://www.bakeridi.edu.au/ausdiab/

Baker IDI - AusDiab - Microsoft Internet Explorer

파일(F) 편집(E) 보기(V) 즐겨찾기(A) 도구(T) 도움말(H)



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AusDiab

The Australian Diabetes, Obesity and Lifestyle (AusDiab) study is the largest Australian longitudinal population-based study examining the natural history of diabetes, pre-diabetes (in which glucose metabolism is impaired but not to the level to cause diabetes), heart disease and kidney disease.

The baseline study conducted in 1999-2000 provided benchmark national data on the prevalence (or number of people) with diabetes, obesity, hypertension and kidney disease in Australia. The second phase of AusDiab, completed in December 2005, is a five year follow-up of the people who participated in the baseline survey. The results of the follow-up provide a unique picture of the incidence (or number of new cases) of diabetes, cardiovascular disease and kidney disease over five years, and allows us to improve our understanding of the factors that increase the risk of these conditions.

Field survey



Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006





Features:

- Who is the average AusDiab participant?
- The latest AusDiab research results
- The AusDiab Cardiovascular Disease sub-study
- AusDiab attracts top international researchers

Newsletter of the AusDiab Study: 2007

AusDiab: wins Research Excellence award

Confirming that AusDiab is a high quality research study of great importance to improving the health of all Australians, the AusDiab study was awarded the 2006 Victorian Department of Human Services Public Health Research Award for Excellence.

Presented by the Minister for Health, The Hon. Bronwyn Pike, MP, the award was accepted by Professor Jonathan Shaw (who co-directs the AusDiab study with Professor Paul Zimmet AO), together with members of the AusDiab team.

"This award acknowledges not only our dedicated team of skilled researchers but also the thousands of volunteers who have participated in the study so far." - Professor Paul Zimmet

Currently, preparations have begun for the third stage of AusDiab. This will involve the researchers re-visiting all the study's participants, and recruiting another 20,000 people, so that we can again benchmark the nation's health and conduct comparisons with the first stage on the rate of diabetes and related conditions, such as obesity and kidney disease.



From Left: Liz Barr, Jonathan Shaw, The Hon. Bronwyn Pike MP, Shirley Murray, Adrian Cameron

A Global Sharing of Knowledge - Meet our Visiting Researchers

The AusDiab team is fortunate to have visiting researchers from all over the world who come to work on analysing data from the project, encouraging a constant exchange of information and knowledge, adding to our understanding of diabetes and increasing the international reputation of the AusDiab study.

Over the past 12 months, we have had four visiting researchers working with the AusDiab team:

Dr Beverly Balkov

Recently awarded the 2007 Kelly West Award for Outstanding Achievement in Epidemiology, Beverly has been based in Paris for the last 20 years, working for INSERM (the French Medical Research Council) as a Director of Research in the epidemiology department. Interested now in being based part-time in both France and Melbourne, Beverly is hoping to form collaborations with French and Australian researchers - 'to encourage a flow of people, and the development of new skills, in both directions.' Beverly greatly enjoys working with the AusDiab team, which she says has a lively research base and a strong collegial atmosphere.



Assistant Professor Sang-Rae Kim

Sang-Rae Kim recently commenced a 12 month period working at the International Diabetes Institute where he hopes to learn as much as he can about the epidemiology of diabetes. He is the first diabetes physician from Korea to visit the Institute, and his ultimate aim is to return to Seoul, and establish a diabetes research institute like ours. While in Australia, Sang-Rae will work with the AusDiab team on analysing data with a specific focus on diabetes complications.

Associate Professor Stefan Söderberg

Based at Umea University, Sweden, Stefan is a cardiologist, and comes annually to work with our research team, concentrating specifically on the development of diabetes and cardiovascular disease in relation to obesity and adipokines (hormones produced by fat tissue). 'I am so grateful for this opportunity to be part of two countries and cultures,' says Stefan, who works with both AusDiab data and data from a series of similar surveys conducted in Mauritius since 1987.

Stefan brings a wealth of experience to the team, and his research is making excellent progress, with Stefan presenting his work at numerous international conferences.



Professor Ed Boyko

One of the world's leading epidemiologists in the diabetes field - Ed Boyko from the University of Washington is spending 12 months at the International Diabetes Institute. In conjunction with the AusDiab team, Ed is principally looking at the predictors of diabetes and hypertension. Ed won the University of Washington Medicine Award for Outstanding Mentorship in 2004, so this is also a valuable opportunity for our young researchers to receive his mentoring. 'I enjoy collaborating with researchers who have particular issues and problems to work out, as I very much enjoy problem solving'. Ed spent his last sabbatical period working at the International Diabetes Institute in the late 1990s and consequently has seen how our research team has evolved over the last eight years. 'Overall, the Institute has a more developed and assured research team now, with more investigators and a greater focus on Australian studies'.



Annual AusDiab Partnership Meeting

This year the AusDiab partnership scientific meeting will be held on the 6th and 7th December and will draw together AusDiab collaborators from around the country. It will provide researchers with the opportunity to present recent analyses stemming from the AusDiab study, as well as pro-

viding a forum for collaborators to discuss future plans and initiatives. Adrian, Dianna, and Liz will present findings on the outcomes of obesity and mortality, baseline predictors of diabetes, lifetime risk of diabetes and life expectancy in those with diabetes, the role that weight

change plays in the incidence of diabetes, and the association between blood glucose and the development of hypertension.



Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006





Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
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KEY FINDINGS

THE TWELVE YEAR FOLLOW-UP SURVEY IN 2011/2012 REVEALED THE FOLLOWING...

[Click here to hear AusDiab Co-Chief Investigator, Professor Jonathan Shaw talk about the study, the latest findings and the implications for individuals, communities and policy makers.](#)

- Every year, 0.7% of adults developed diabetes, 3% developed high blood pressure, 0.4-0.7% developed signs of kidney damage.
- Living in the most socially-disadvantaged areas of Australia doubled the risk of developing diabetes.
- Over 12 years, the average gain in waist circumference was 5.3 cm, and was greater in women than in men, and in younger people than in older people.
- People with previously known diabetes have a similar risk of mortality to smokers.
- Self-report physical activity time was approximately 50% greater than objectively measured physical activity time, whilst self-report sitting time was approximately half that measured by objective means.

Diabetes and pre-diabetes



Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



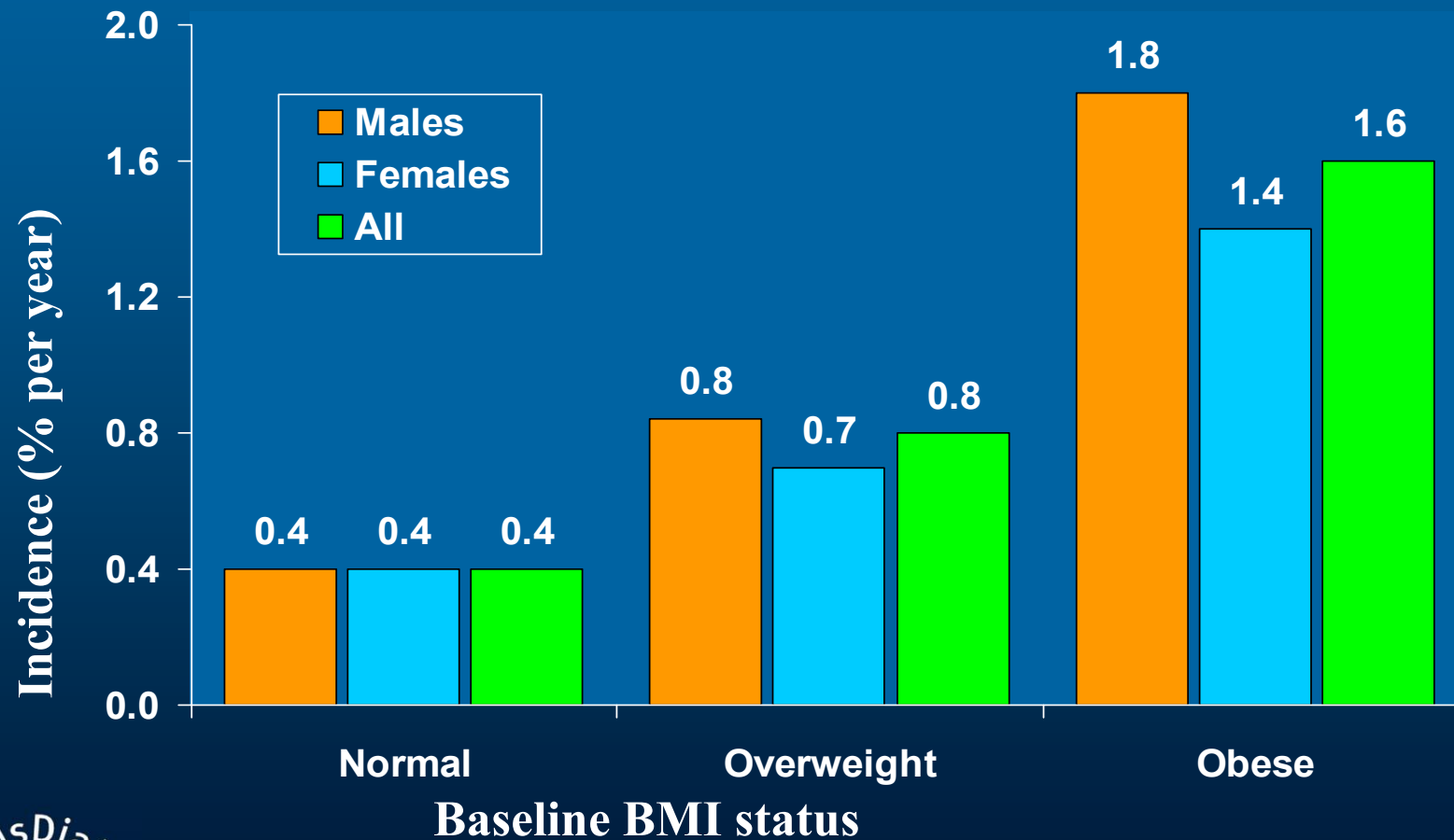
Weighted prevalence (%) of associated conditions stratified by glucose tolerance status

Associated condition	Glucose tolerance status			
	Diabetes	IFG	IGT	Normal
Hypertension*	69.3	43.5	50.1	21.1
Obesity (BMI ≥ 30 kg/m ²)	44.4	30.1	31.5	15.9
LDL (≥ 3.5 mmol/L)	45.9	59.6	53.0	44.1
HDL (< 1.0 mmol/L)	23.1	16.8	11.6	10.6
Triglycerides (≥ 2.0 mmol/L)	42.9	31.4	31.1	16.0

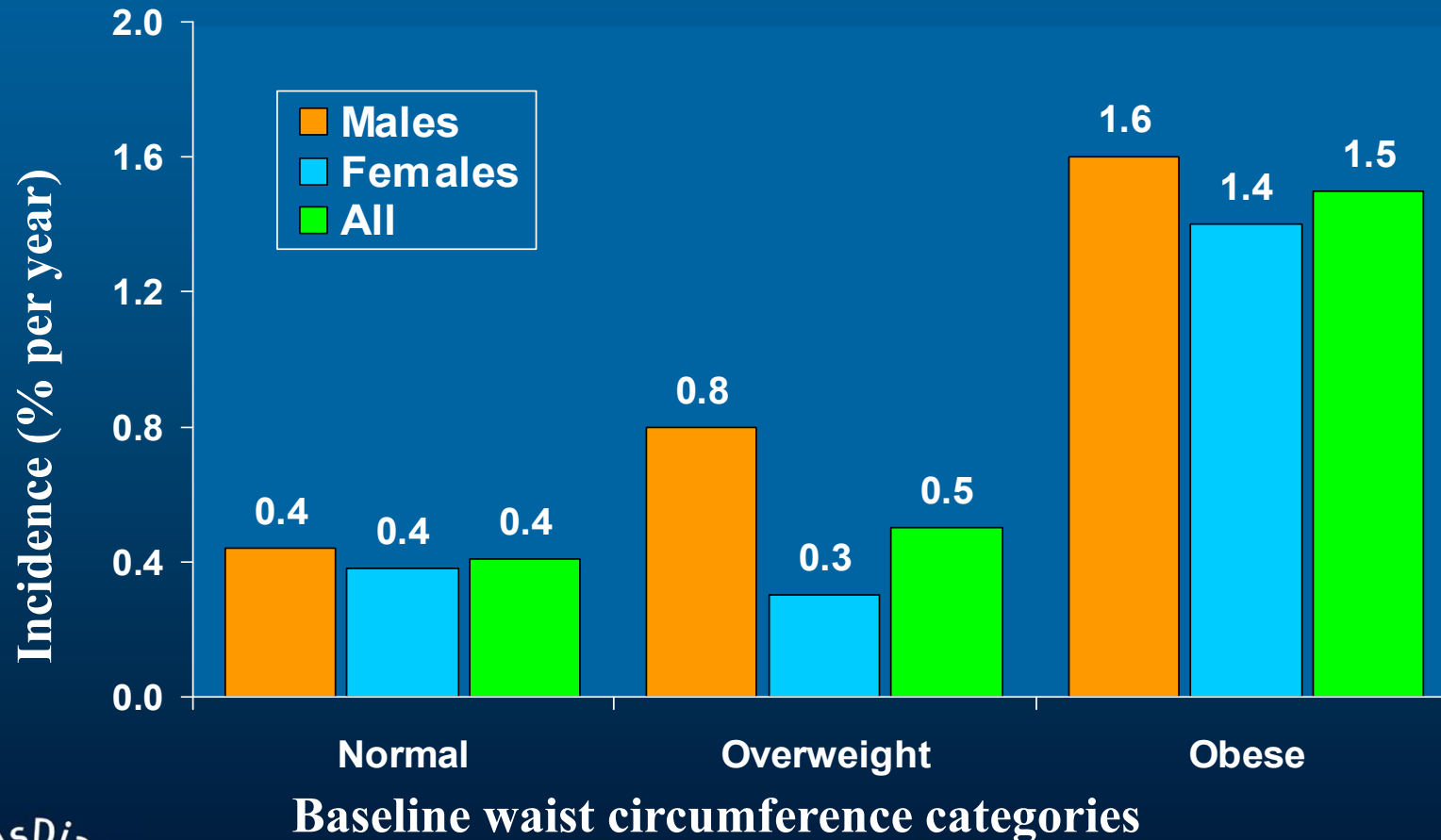
* On treatment, or systolic pressure ≥ 140 mmHg,
or diastolic pressure ≥ 90 mmHg

IGT — impaired glucose tolerance; IFG — impaired fasting glucose.

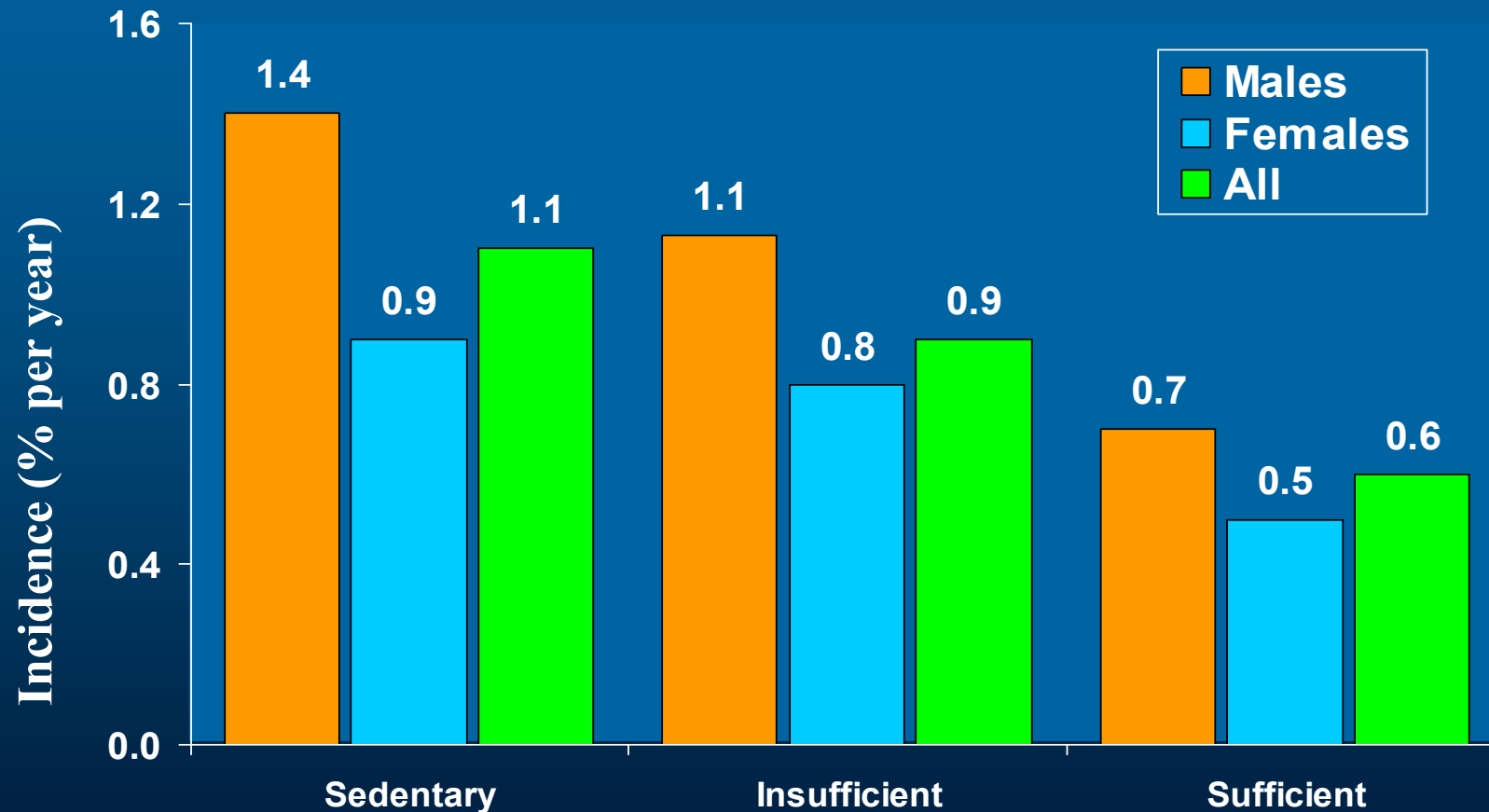
Incidence of diabetes according to baseline body mass index



Incidence of diabetes according to baseline waist circumference categories

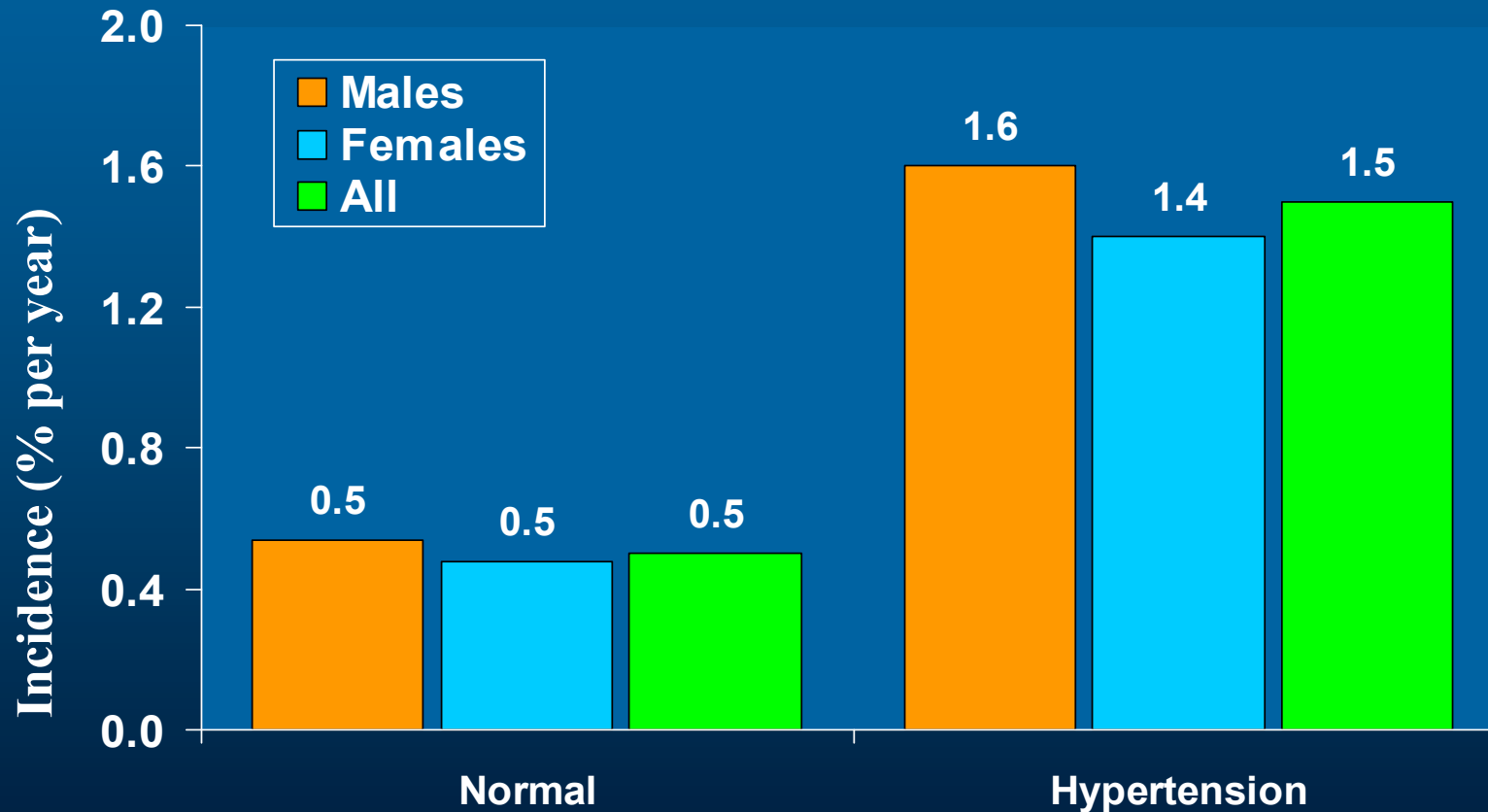


Incidence of diabetes according to baseline physical activity



Baseline physical activities categories

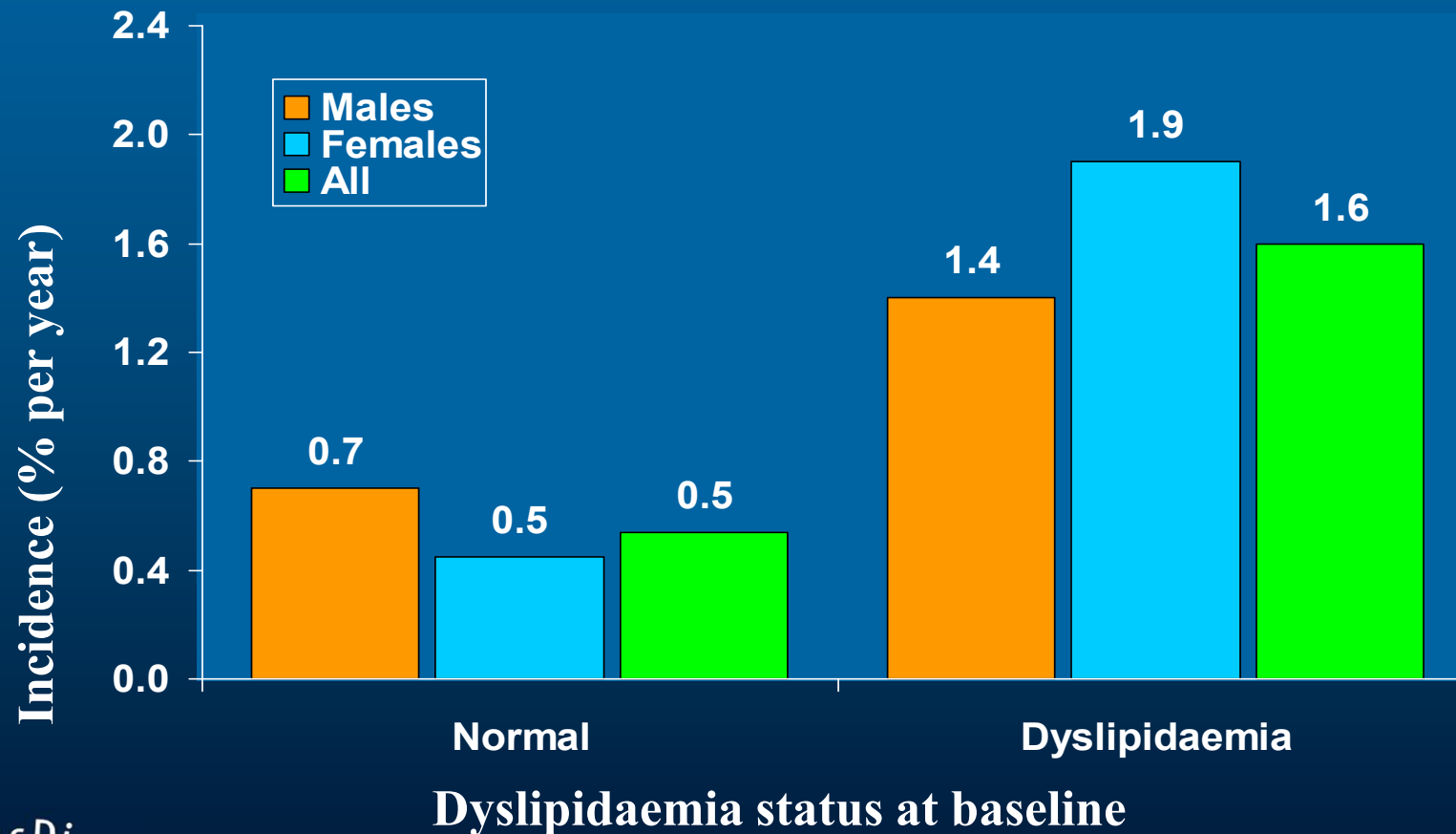
Incidence of diabetes according to baseline hypertension status



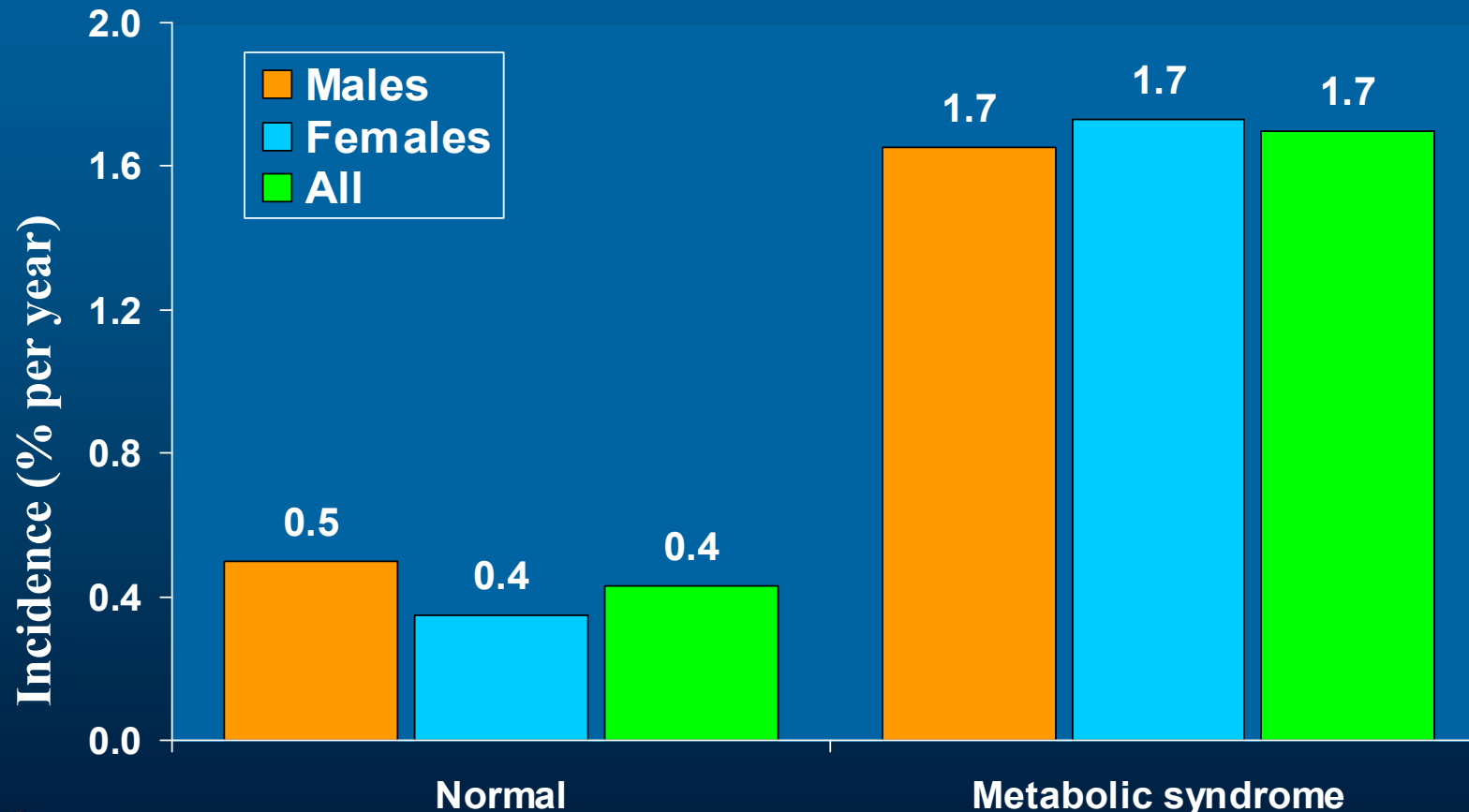
Baseline hypertension status

Hypertension (high blood pressure) was defined as having a blood pressure $\geq 140/90$ mmHg and/or taking blood-pressure lowering medication.

Incidence of diabetes according to baseline dyslipidaemia status

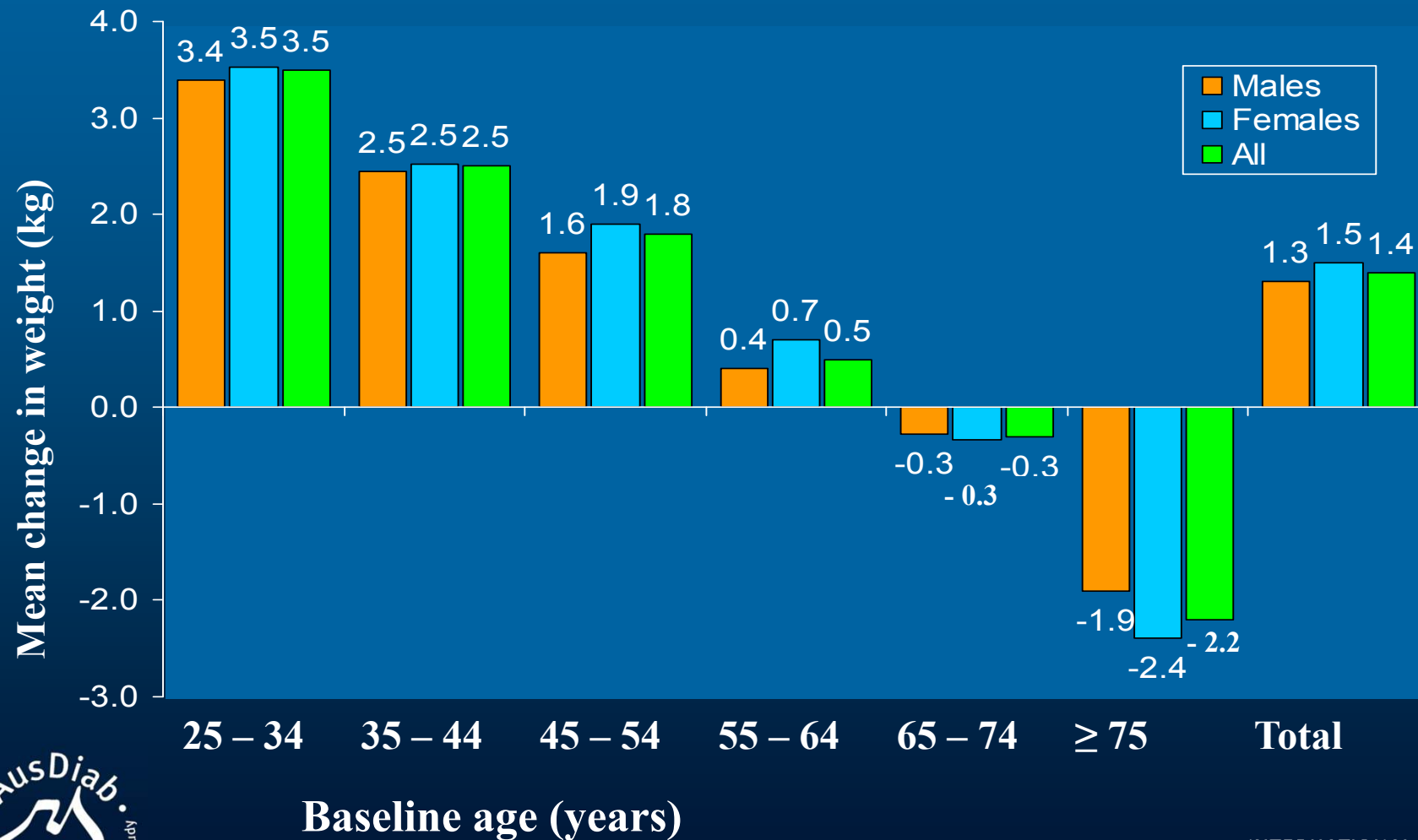


Incidence of diabetes according to baseline metabolic syndrome status



Baseline metabolic syndrome status

Mean weight change over five years according to baseline age



Proportion of individuals classified by body mass index in 2004–05 according to baseline body mass index status

BMI status at baseline	n	BMI in 2004–05		
		Normal n (%)	Overweight n (%)	Obese n (%)
Normal	2,369	1,831 (77.3)	530 (22.4)	8 (0.34)
Overweight	2,560	194 (7.6)	1,917 (74.9)	449 (17.5)
Obese	1,356	6 (0.4)	120 (8.9)	1,230 (90.7)
Total	6,285	2,031	2,567	1,687

Proportion of individuals classified by waist circumference in 2004–05 according to baseline waist circumference categories

Waist circumference categories at baseline	n	Waist circumference categories in 2004–05		
		Normal n (%)	Overweight n (%)	Obese n (%)
Normal	2,496	1,752 (70.2)	628 (25.2)	116 (4.7)
Overweight	1,637	301 (18.4)	771 (47.1)	565 (34.5)
Obese	2,163	44 (2.0)	238 (11.0)	1,881 (87.0)
Total	6,296	2,097	1,637	2,562

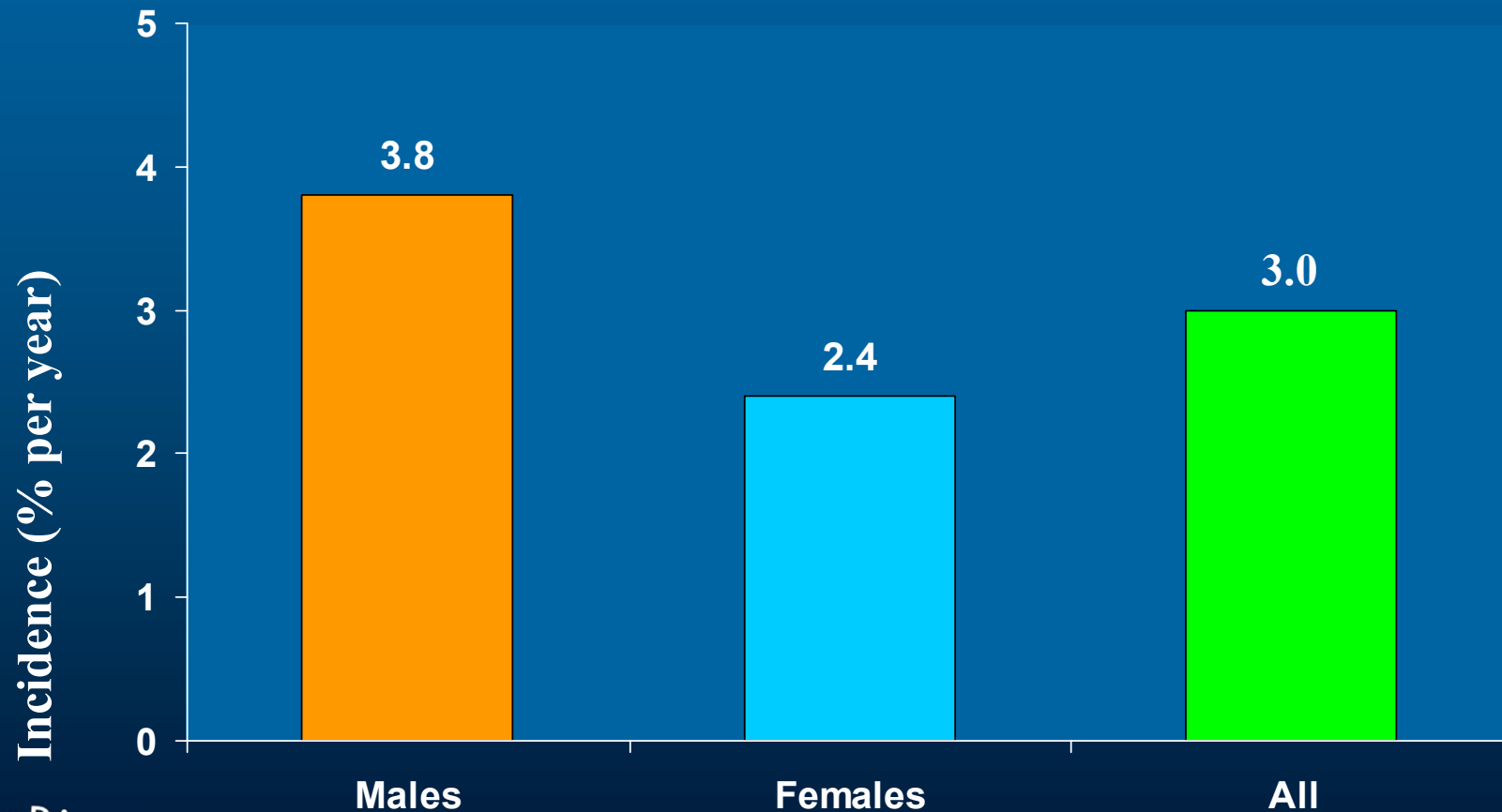
Metabolic syndrome



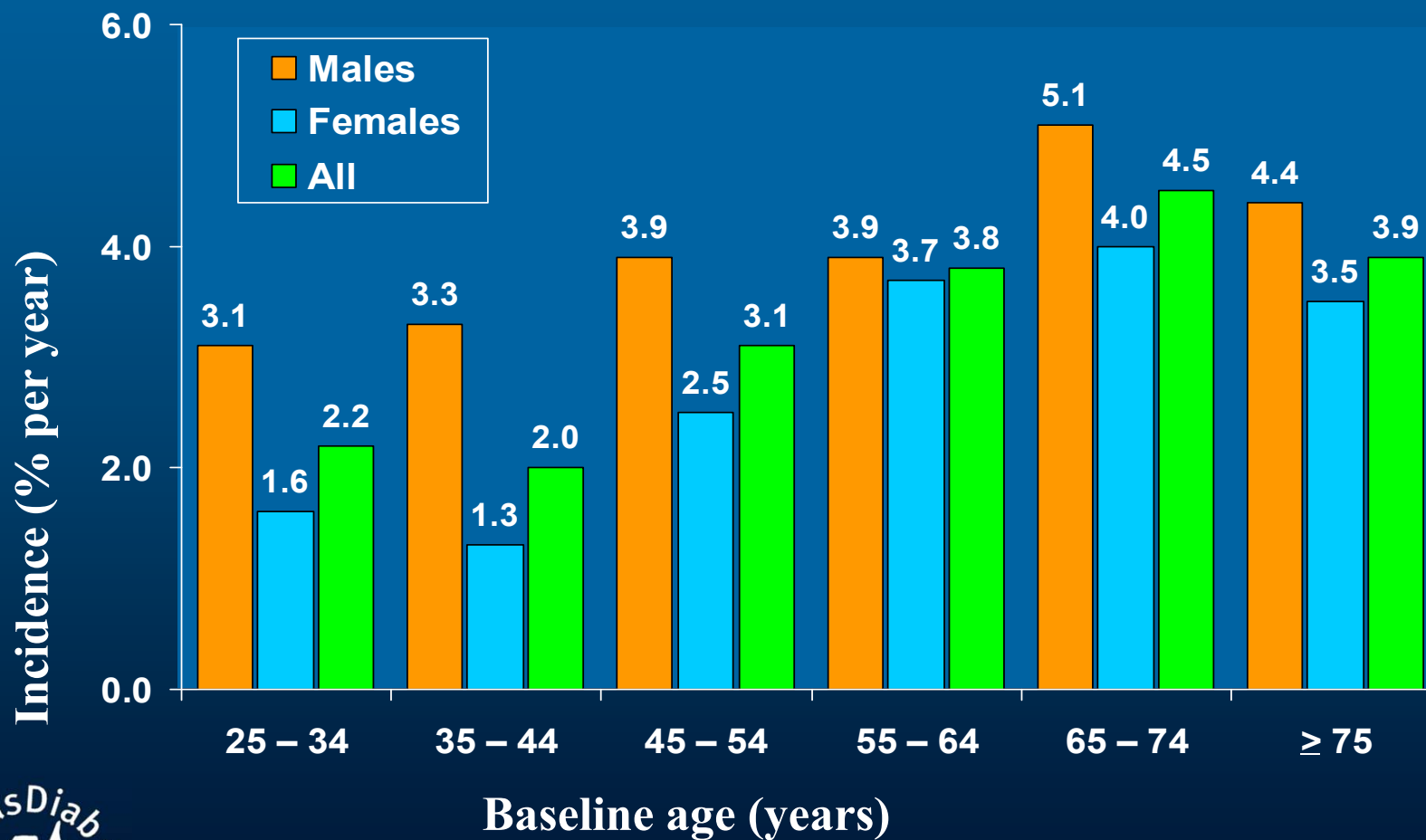
Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



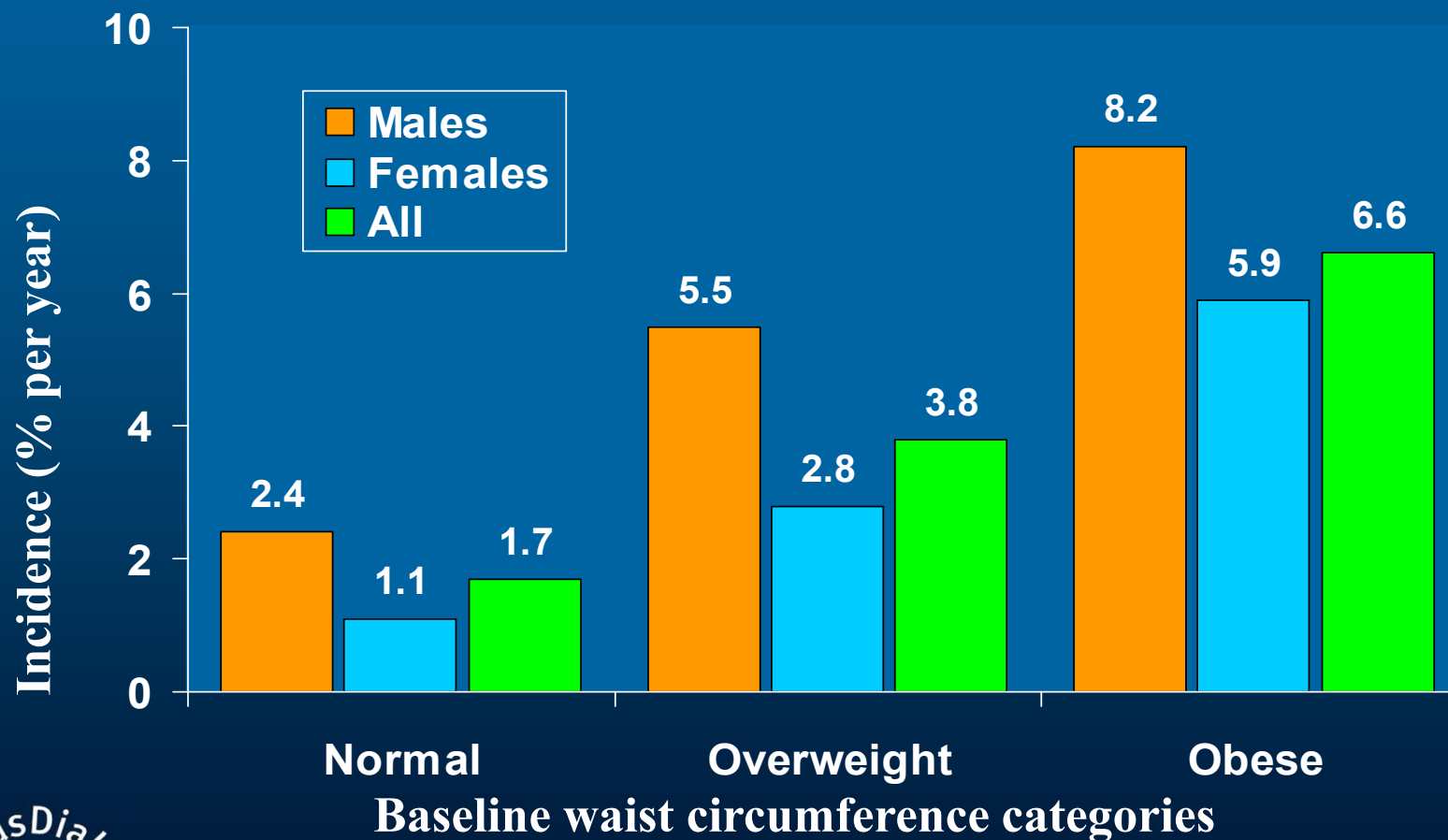
Incidence of the metabolic syndrome according to gender



Incidence of the metabolic syndrome according to baseline age



Incidence of the metabolic syndrome according to baseline waist circumference categories

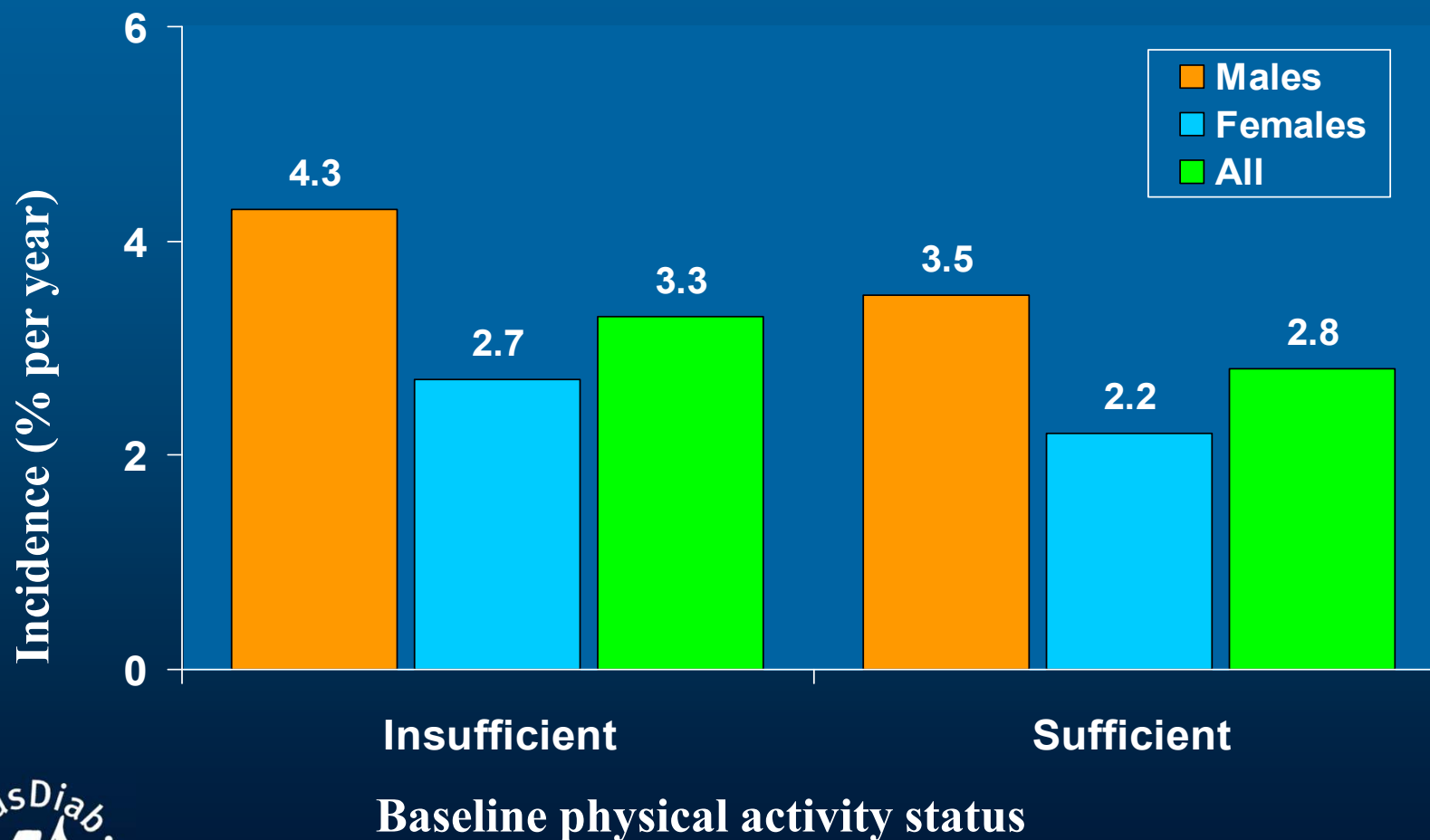


Waist circumference: (i) normal: < 94.0 cm for males, < 80.0 cm for females; (ii) overweight: 94.0–101.9 cm for males, 80.0–87.9 cm females; (iii) obese: ≥ 102.0 cm for males, ≥ 88.0 cm for females.

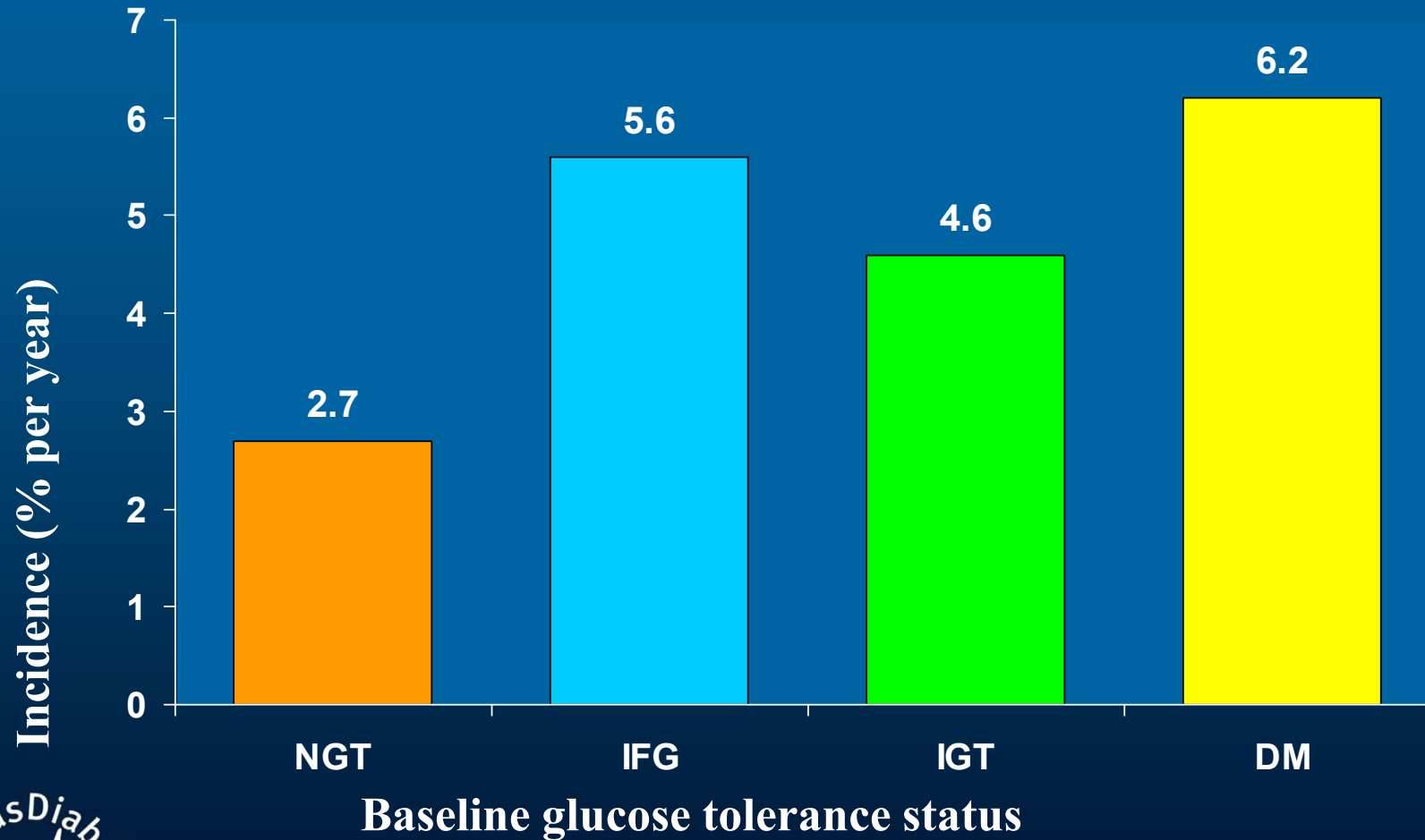
Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



Incidence of the metabolic syndrome according to baseline physical activity



Incidence of the metabolic syndrome according to baseline glucose tolerance status



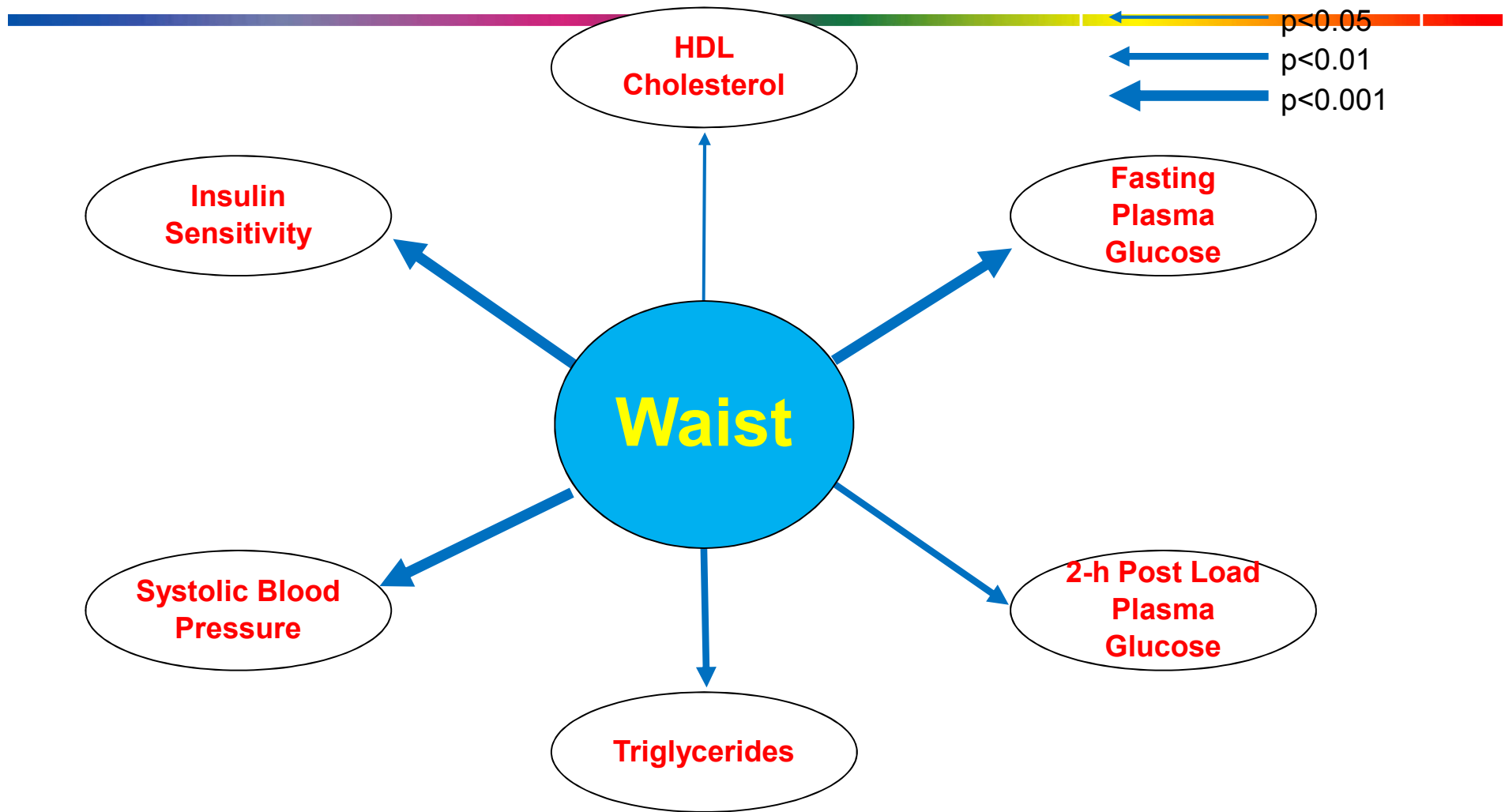
2005

NGT – normal glucose tolerance; IFG – impaired fasting glucose;
IGT – impaired glucose tolerance; DM – diabetes mellitus

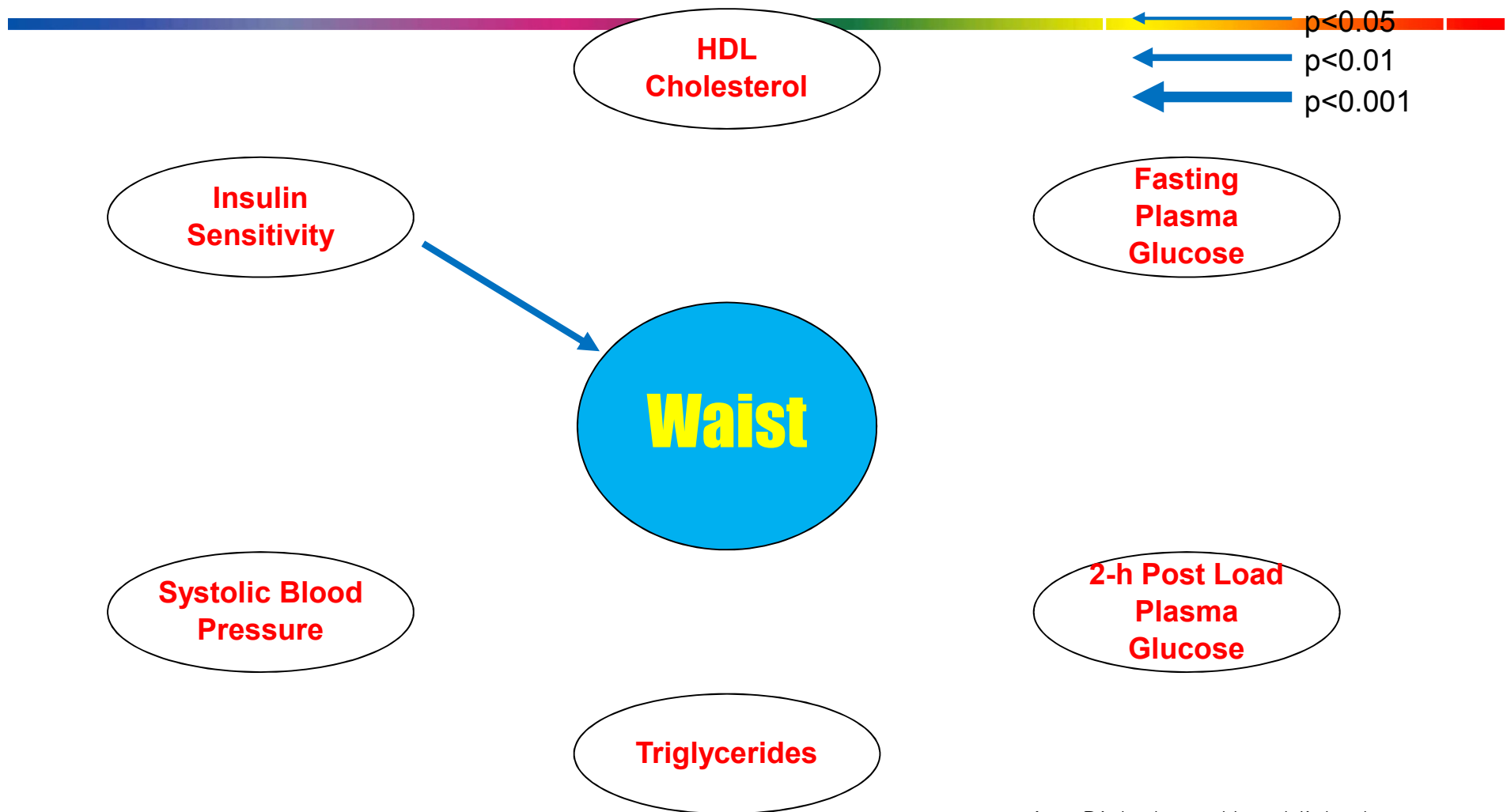
Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
International Diabetes Institute Melbourne 2006



Obesity as a predictor of deterioration in all components of the Metabolic Syndrome



Do components of the Metabolic Syndrome predict an increase in obesity?



Aus Diab data. Unpublished

Today's Talk

- History of Metabolic Syndrome
- **Dyslipidemia and Metabolic Syndrome**

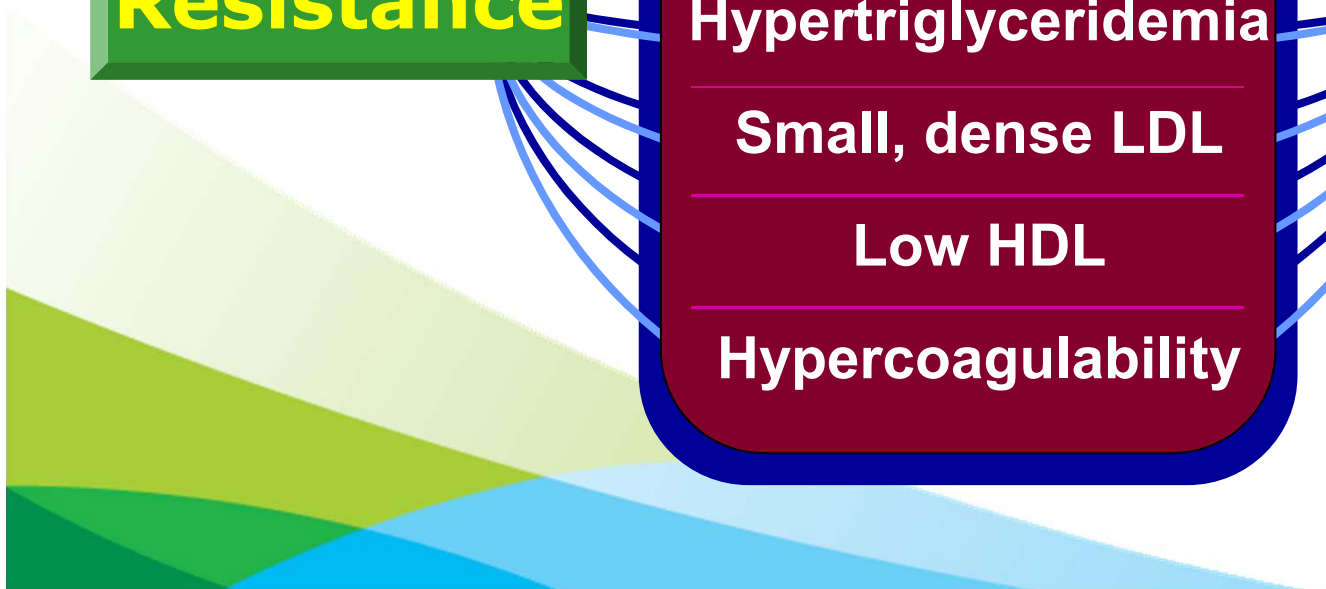


Interrelation Between Atherosclerosis and Insulin Resistance

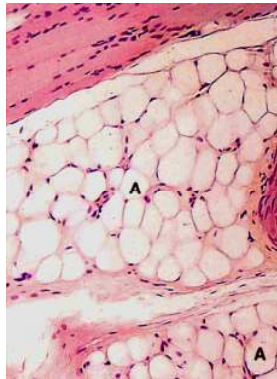
**Insulin
Resistance**

Hypertension
Obesity
Hyperinsulinemia
Diabetes
Hypertriglyceridemia
Small, dense LDL
Low HDL
Hypercoagulability

Atherosclerosis



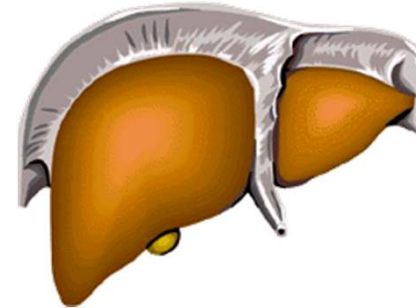
Role of FFA in Insulin Resistance



Adipocytes

- Increase in adipocyte number and size increases FFA output
- High FFA concentration decreases glucose uptake and utilization in muscle and liver

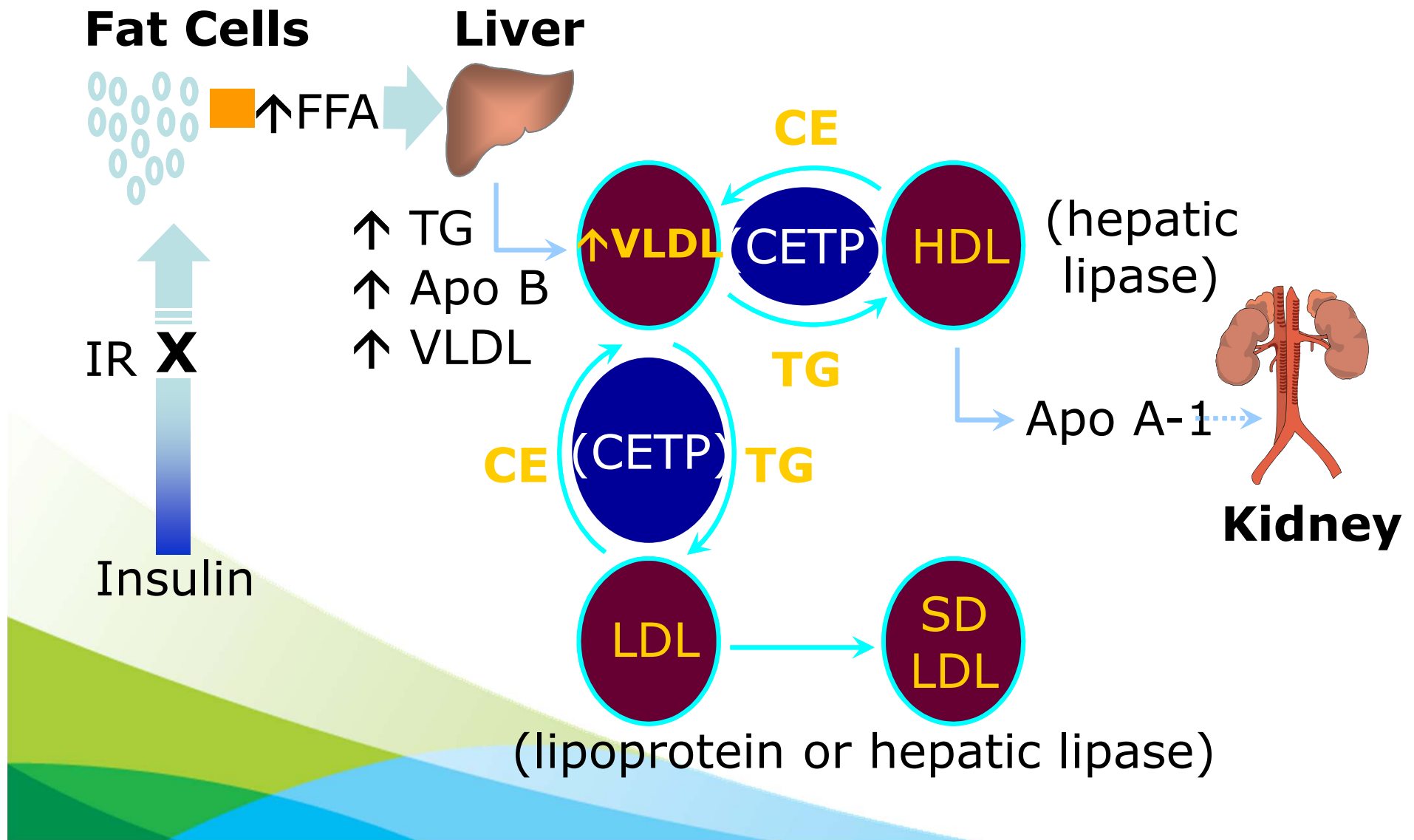
FFA



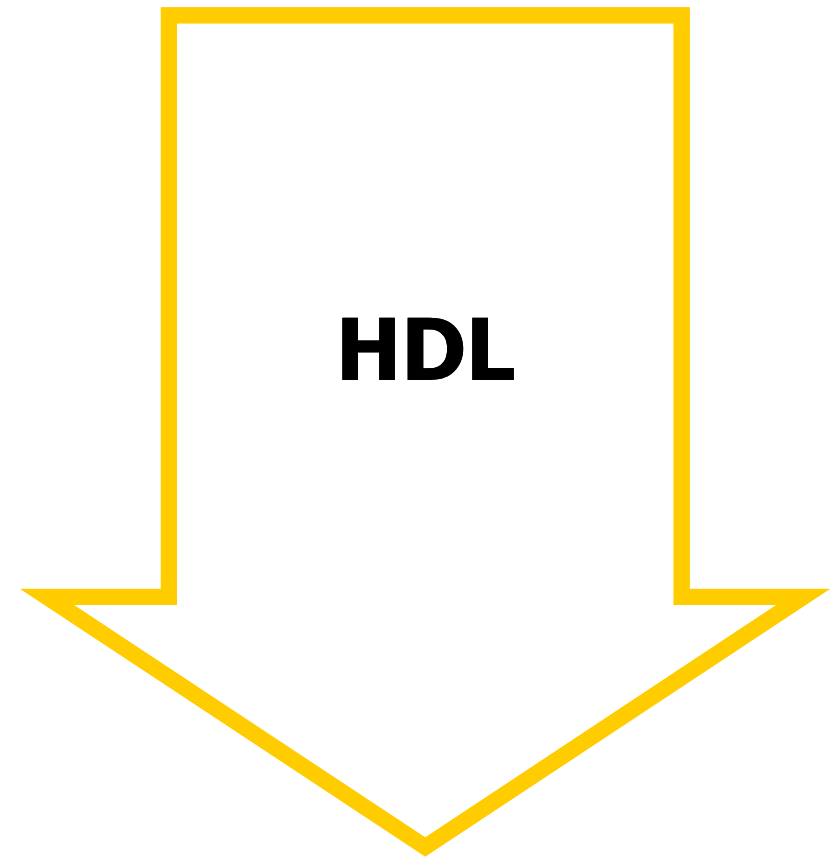
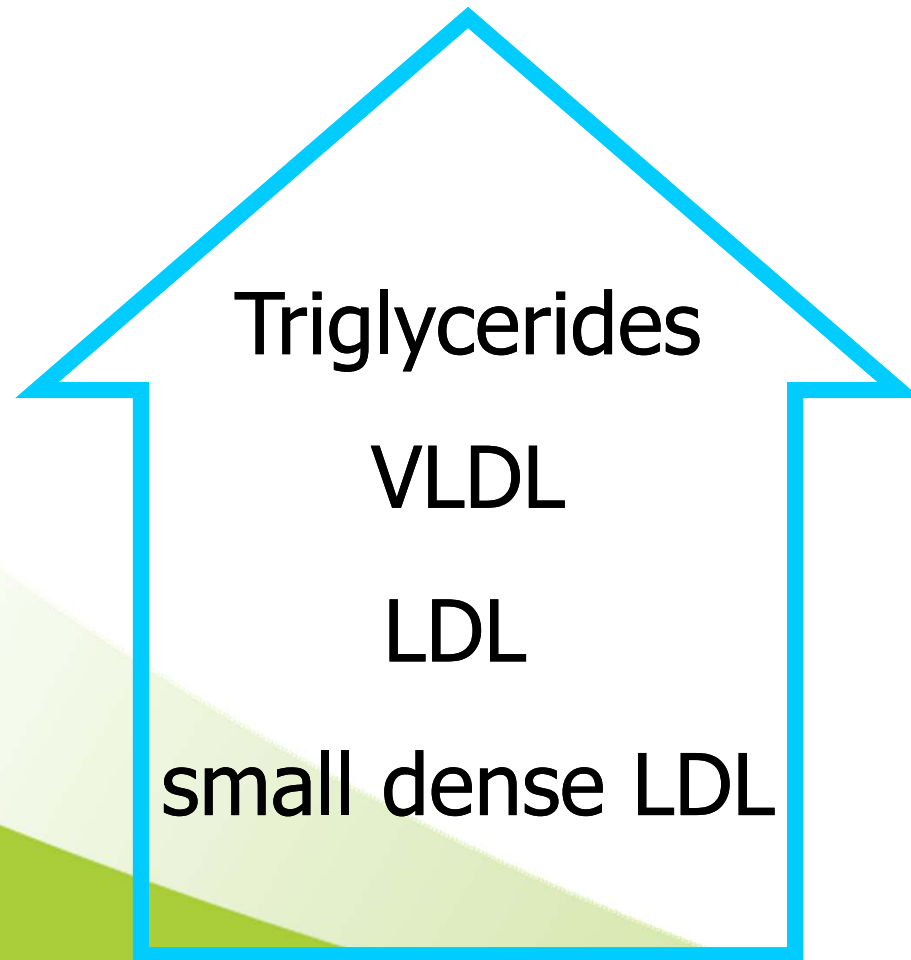
Liver

- Increased accumulation of triglyceride in liver
- Hepatic glucose output ↑
- Overproduction of TG rich VLDL → small dense lipoprotein

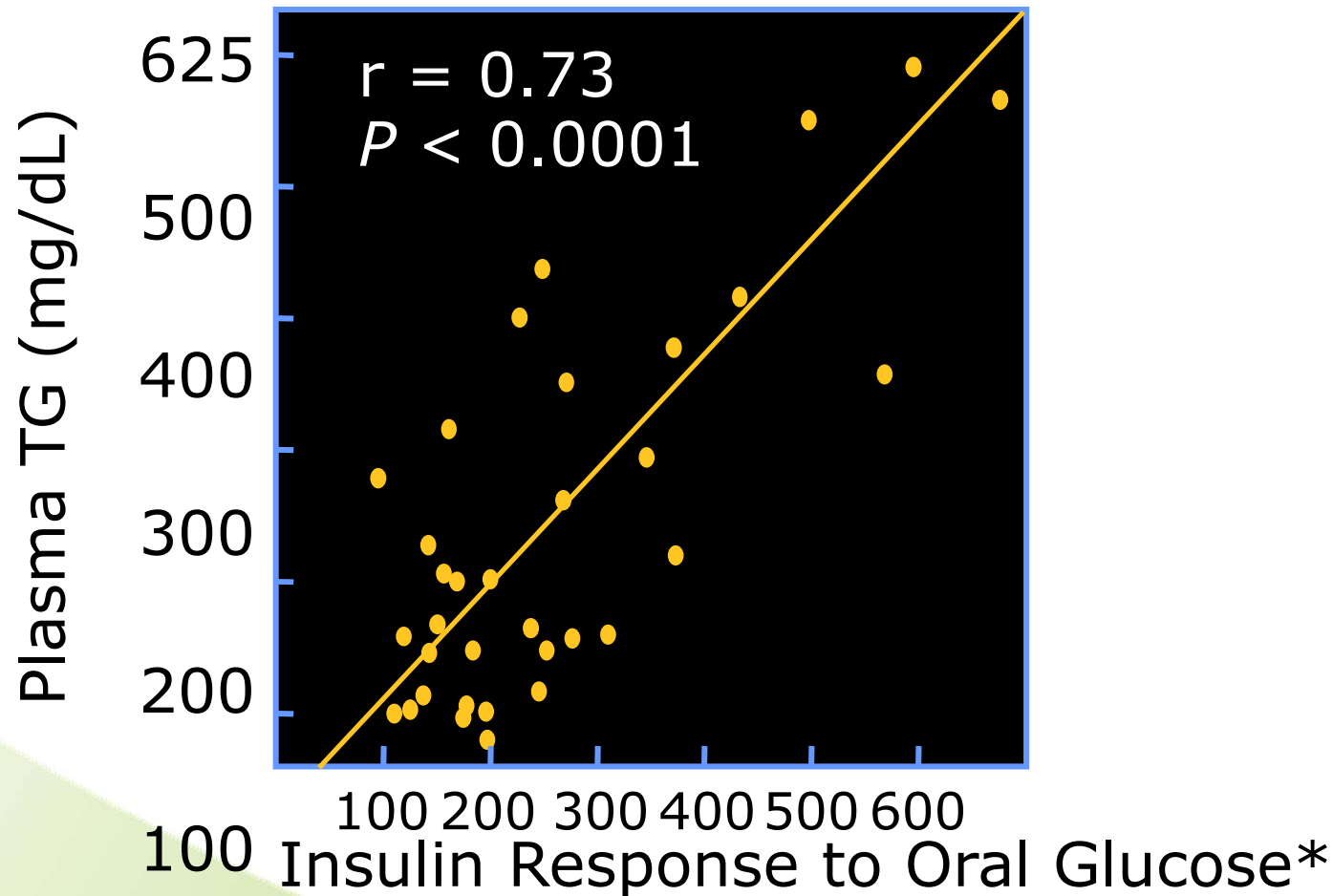
Mechanisms Relating Insulin Resistance and Dyslipidemia



Dyslipidemia in Diabetes and Metabolic syndrome

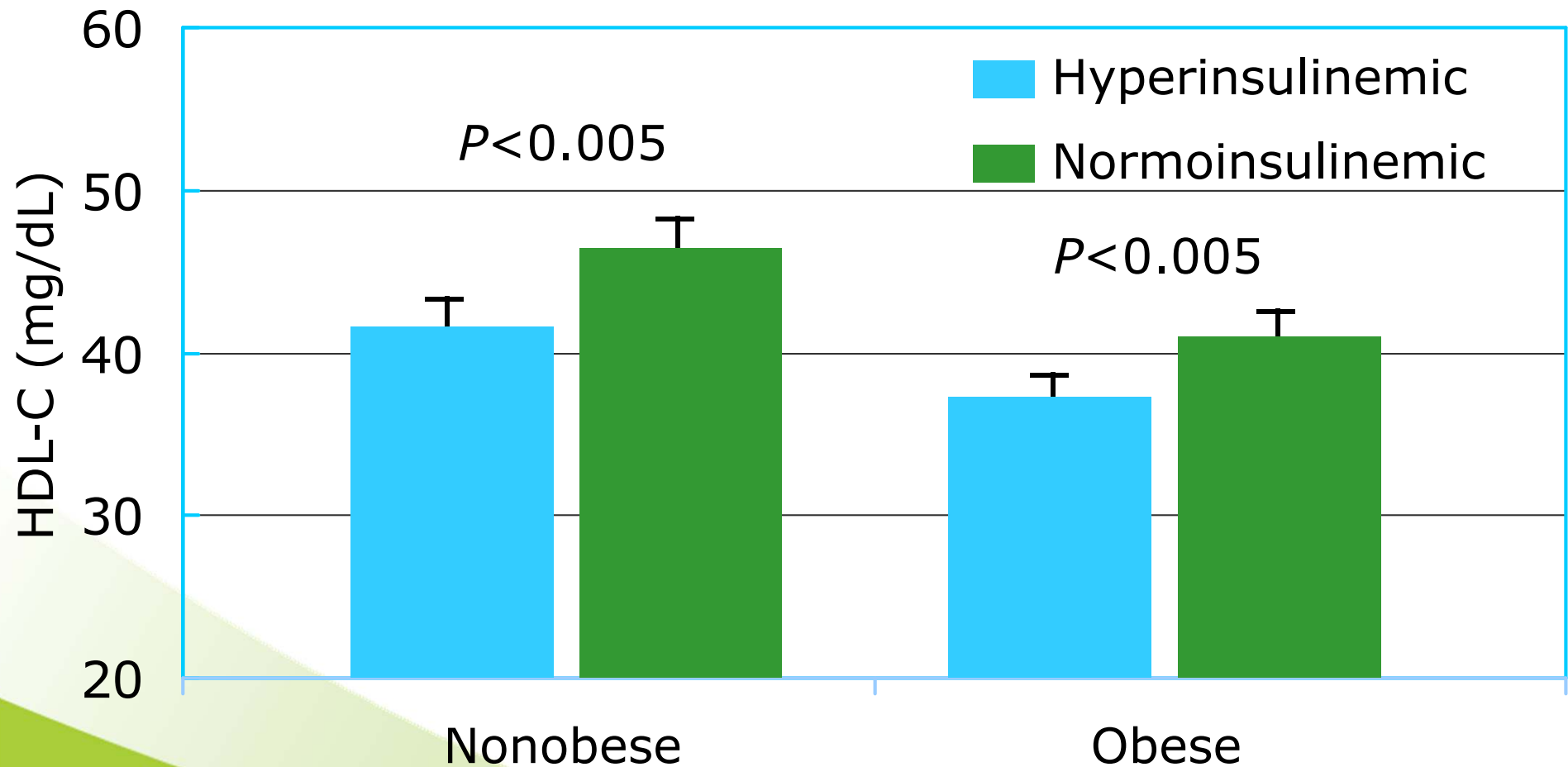


Relation Between Insulin Resistance and Hypertriglyceridemia



* Total area under 3-hour response curve (mean of 2 tests).
Olefsky JM et al. *Am J Med.* 1974;57:551-560.

Association Between Hyperinsulinemia and Low HDL-C



Reaven GM. In: LeRoith D et al., eds. *Diabetes Mellitus*. Philadelphia: Lippincott-Raven, 1996:509-519.

Increased Small LDL Particle Number

A Prominent Feature of the Metabolic Syndrome in the Framingham Heart Study

TABLE 3. Correlations Among Small LDL Particle Number and Components of the MetSyn

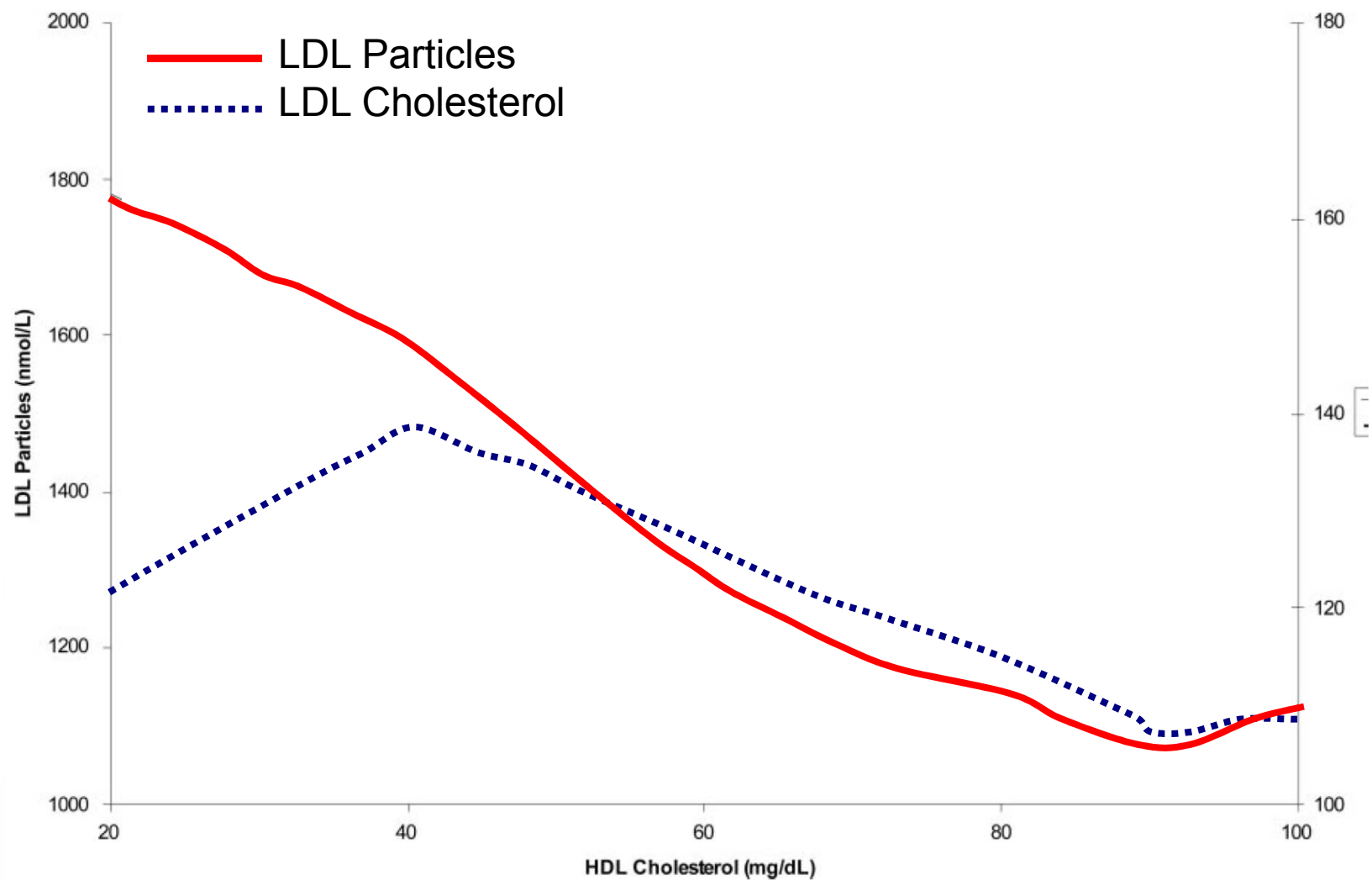
	ApoB	SBP	DBP	Waist Circumference	Fasting Glucose	HDL-C	Triglycerides
Small LDL particle No.	0.61	0.19	0.20	0.30	0.20	-0.55	0.61
ApoB	...	0.18	0.20	0.28	0.16	-0.34	0.55
SBP	0.73	0.29	0.23	-0.06	0.23
DBP	0.32	0.17	-0.07	0.25
Waist circumference	0.28	-0.35	0.41
Fasting glucose	-0.14	0.18
HDL-C	-0.52
Triglycerides

See the footnote to Table 1 and text for explanation of abbreviations.

Data are Pearson partial correlations adjusted for age and sex.

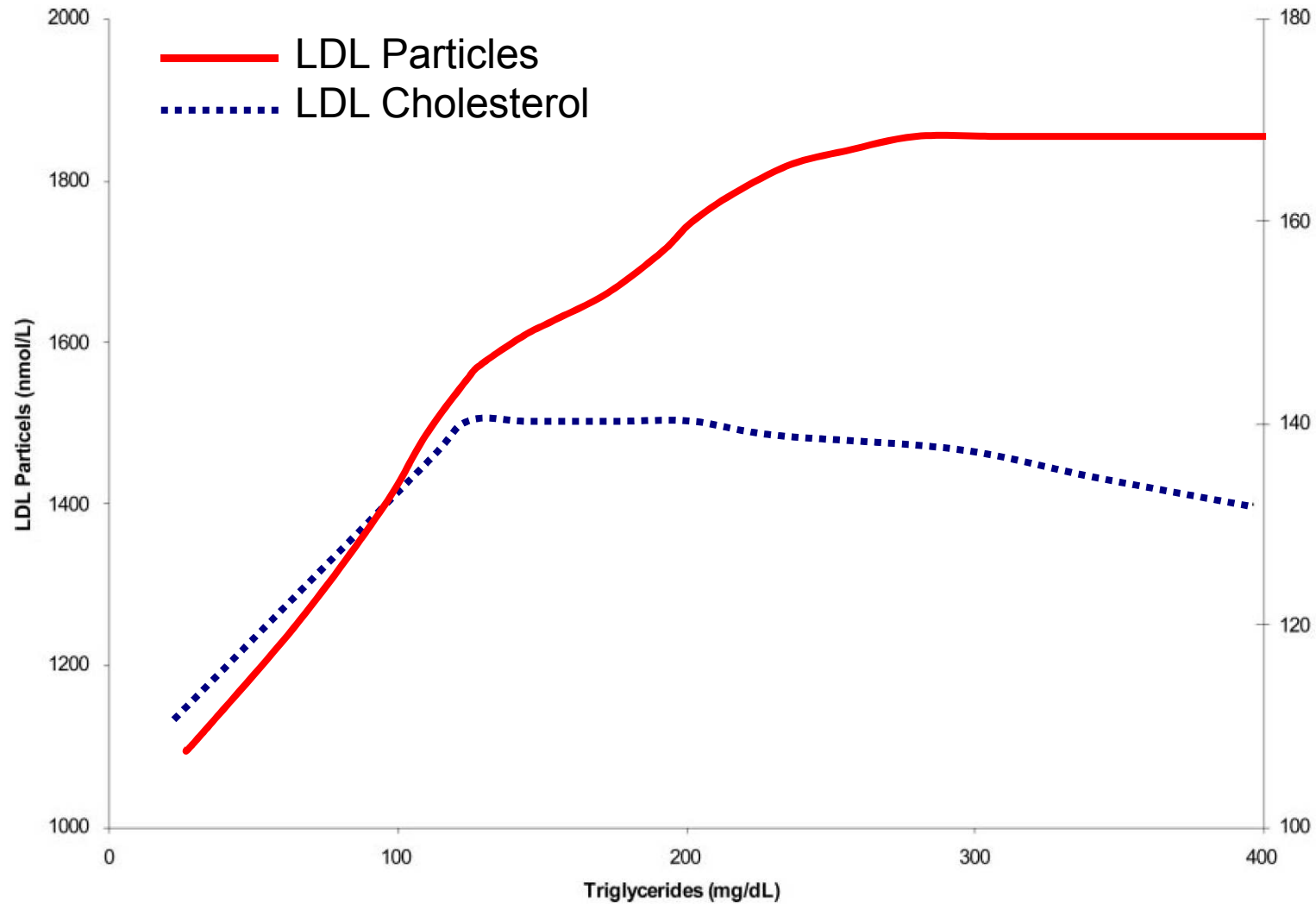
Circulation. 113:20-29, 2006

Relations of total LDL particle number and LDL cholesterol value to the level of HDL cholesterol



Increased Small LDL Particle Number

A Prominent Feature of the Metabolic Syndrome in the Framingham Heart Study



Increased Small LDL Particle Number

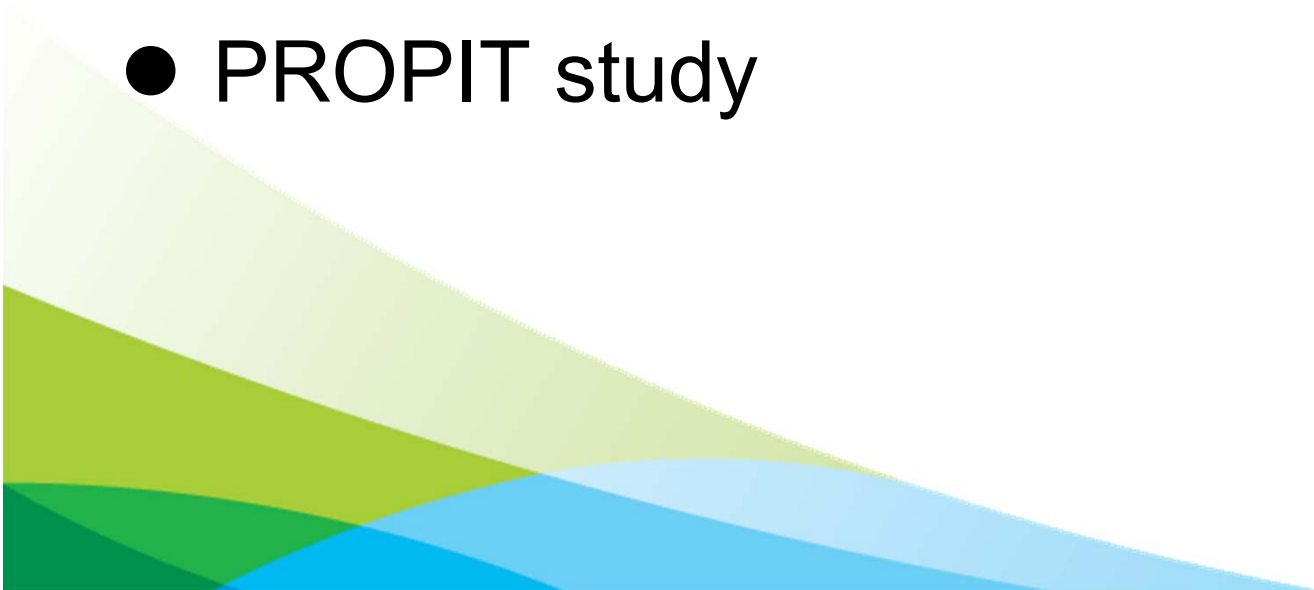
A Prominent Feature of the Metabolic Syndrome in the Framingham Heart Study

TABLE 4. Plasma Levels of NMR-Determined Lipoprotein Measures and Biochemical Lipid Measures With Increasing Number of MetSyn Features*

	No. of Components of MetSyn						<i>P</i> for Trend
	0	1	2	3	4	5	
Women	n=562	n=464	n=298	n=134	n=102	n=29	
NMR-derived lipoprotein measures							
Total LDL particle No., nmol/L	1169±16	1344±17	1496±22	1600±32	1678±37	1663±69	<0.0001
Small LDL particles, nmol/L	428±15	591±16	756±20	918±30	1090±34	1187±64	<0.0001
Large LDL particles, nmol/L	714±12	716±13	697±17	618±25	529±28	419±53	<0.0001
Biochemical lipid measures							
LDL-C, mg/dL	117±1	128±2	135±2	137±3	138±3	133±6	<0.0001
ApoB, mg/dL	84±1	92±1	101±1	110±2	111±2	113±4	<0.0001
Triglycerides, mg/dL	71±2	84±2	121±2	154±4	188±4	211±8	<0.0001
HDL-C, mg/dL	66±1	57±1	51±1	45±1	40±1	36±2	<0.0001
Men	n=286	n=407	n=335	n=233	n=113	n=30	
NMR-derived lipoprotein measures							
Total LDL particle No., nmol/L	1290±23	1485±19	1554±21	1690±25	1783±36	1767±69	<0.0001
Small LDL particles, nmol/L	574±26	813±21	991±24	1232±29	1396±41	1361±79	<0.0001
Large LDL particles, nmol/L	684±17	630±14	520±16	411±19	336±27	362±52	<0.0001
Biochemical lipid measures							
LDL-C, mg/dL	127±2	137±2	135±2	137±2	135±3	136±6	0.01
ApoB, mg/dL	90±1	99±1	103±1	111±1	115±2	115±4	<0.0001
Triglycerides, mg/dL	71±3	96±3	133±3	178±4	214±5	231±10	<0.0001
HDL-C, mg/dL	52±1	48±1	43±1	37±1	33±1	32±2	<0.0001

Today's Talk

- History of Metabolic Syndrome
- Dyslipidemia and Metabolic Syndrome
- **PROPIT study**



ProPit study

PROPIT: A PROspective comparative clinical study evaluating the efficacy and safety of PITavastatin in patients with metabolic syndrome

Short title: efficacy and safety of pitavastatin in metabolic syndrome (PROPIT study)

PROPIT Study Team:

Sung Hee Choi^{1*}, Soo Lim^{1*}, Eun Shil Hong^{1*}, Ji A Seo², Cheol Young Park³, Jung Hyun Noh⁴, Ji Oh Mok⁵, Ki Young Lee⁶, Jong Sook Park⁷, Dae Jung Kim⁸, Chang Beom Lee⁹, Sung Rae Kim¹⁰ †, and Hak Chul Jang¹ †

임상명 : ProPit study

발표 저널: Clinical Endocrinology (Oxford) 2015 May;82(5):670-7

참여병원

PROFIT study team

- 분당서울대학교 병원 장학철*, 최성희, 임수, 홍은실
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- 강북삼성병원 박철영
- 고려대학교 의과대학 안산병원 서지아
- 순천향대학교 부천병원 목지오
- 아주대학교병원 김대중
- 연세대학교 의과대학 강남세브란스병원 박종숙
- 인제대학교 일산백병원 노정현
- 한양대학교 구리병원 이창범
- 가천의과대학교 길병원 김연선

* 임상시험 조정자

Metabolic syndrome(MS) Score

The IDF
consensus
worldwide
definition
of the

**METABOLIC
SYNDROME**



International Diabetes Federation



아래의 조건 해당 개수 = MS score

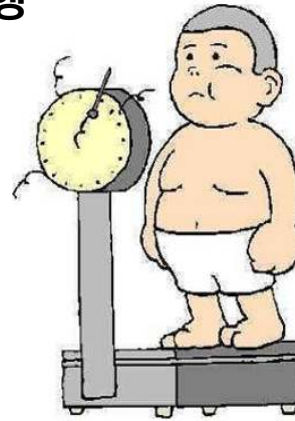
- 1) **허리둘레 (남 90cm이상, 여 85cm이상)**
→IDF가이드라인 기준 필수
- 2) **공복혈당 (100mg/dL 이상)**
- 3) **중성지방 (150mg/dL 이상)**
- 4) **HDL 콜레스테롤 (남 \leq 40mg/dL, 여 \leq 50mg/dL)**
- 5) **혈압 : 수축기 혈압 \geq 130mmHg 또는 이완기
혈압 \geq 85mmHg, 고혈압 치료제 복용**

대사증후군 환자 = MS score \geq 3

대사증후군 치료

- 1) 체중감소 (임상 시작 전의 몸무게의 7-10% 감소)
- 2) 30분-1시간 사이의 신체운동, 일주일에 4~5번

진행



생활습관 개선



약물치료

이상지질혈증 치료를 위해 리바로[®] 투여

ProPit study Design

대상환자	대사증후군 환자 (MS score ≥ 3)
Primary endpoint	대사질환환자의 MS score 개선정도
Secondary endpoints	심혈관 질환 위험성 지표 : LDL-C, 내장지방/피하지방의 비율, Apo B/Apo A1, hs-CRP, Adiponectin, Framingham Risk Score, etc.
총 환자 수	리바로 투여군 (n=80), Control 군(n=84)

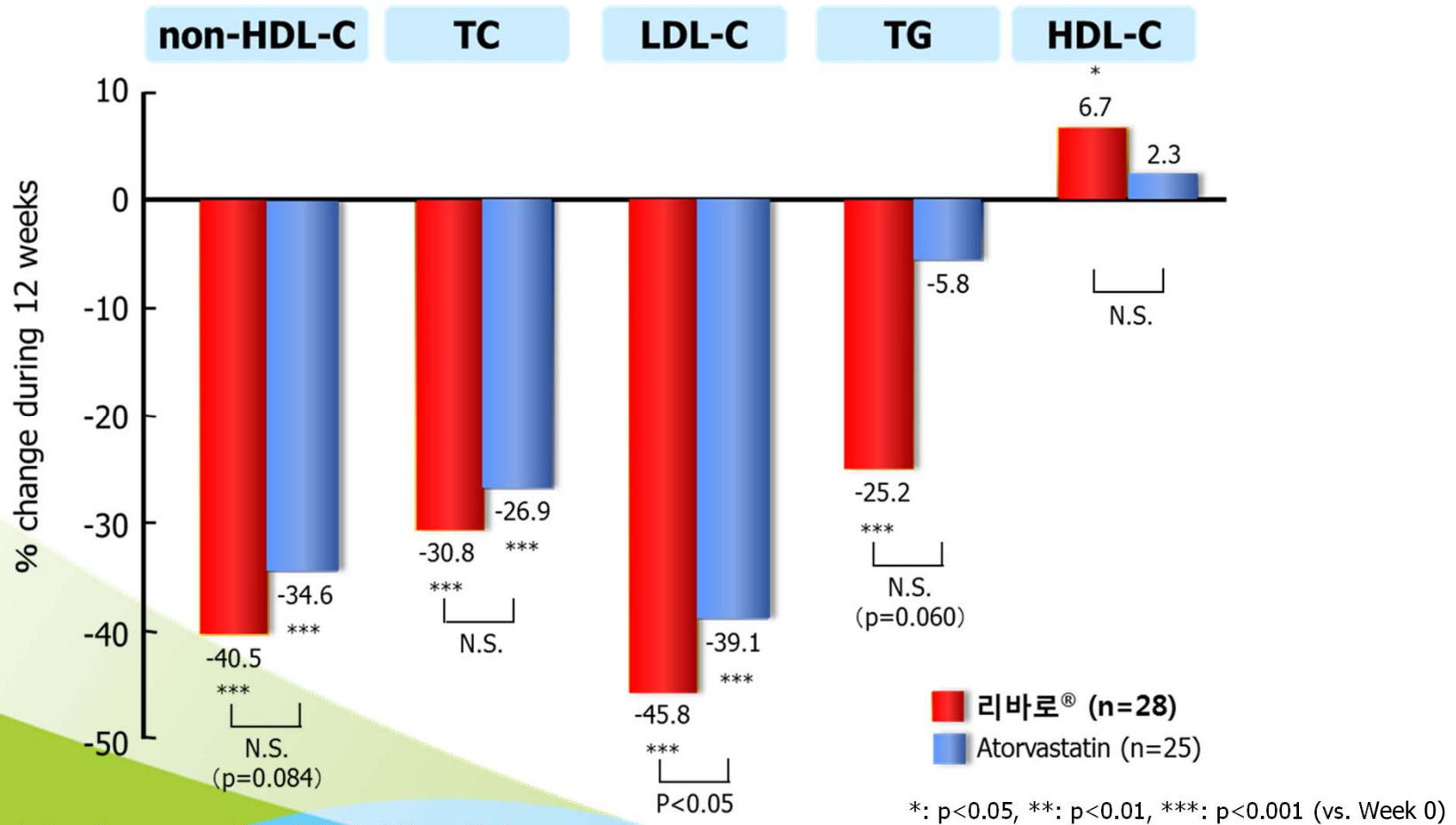
Prospective, randomized, multi-center, open-label study



Clinical Endocrinology (Oxford) 2015 May;82(5):670-7

CHIBA Study - Subgroup analysis of MS pts.

리바로는 대사증후군 환자대상 Atorvastatin 대비 유의적인 LDL-C 감소효과가 나타났습니다.



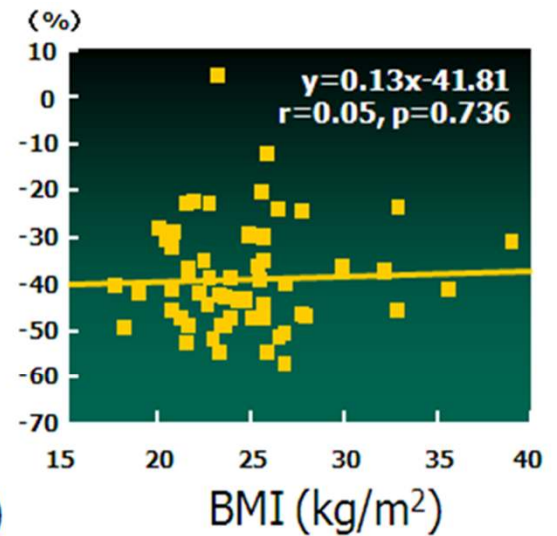
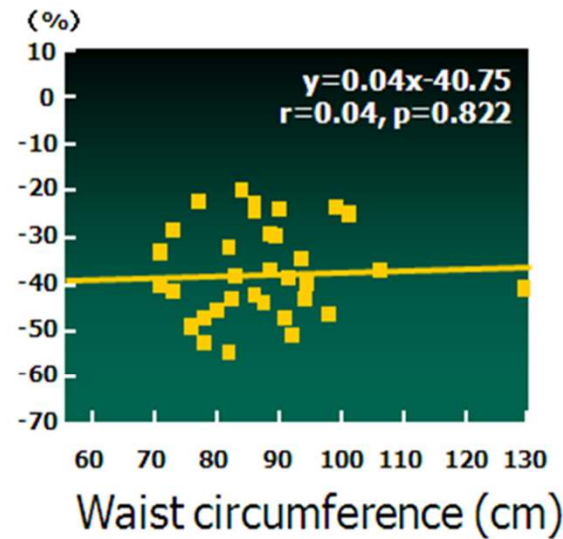
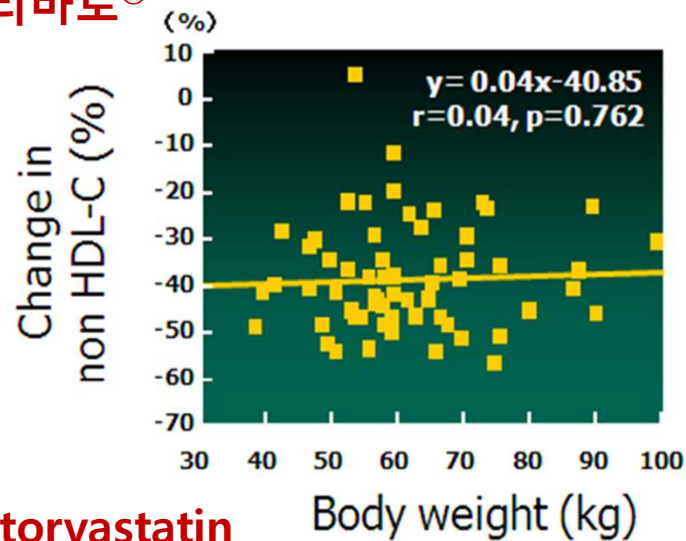
대상증후군: 대사증후군을 동반한 이상지질혈증 환자(n=53)

시험방법: pitavastatin 2mg/day or atorvastatin 10mg/day for 12weeks

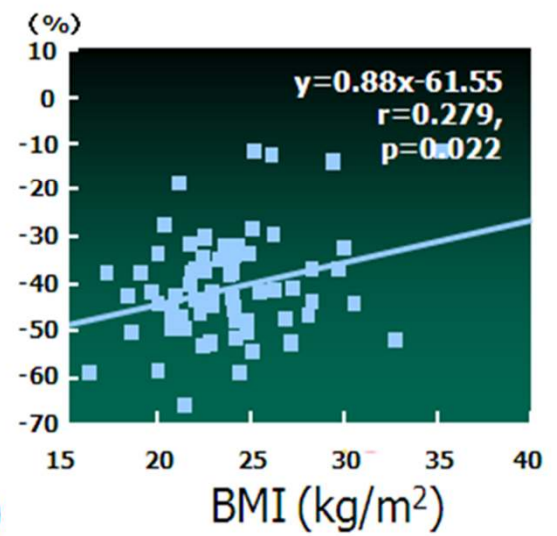
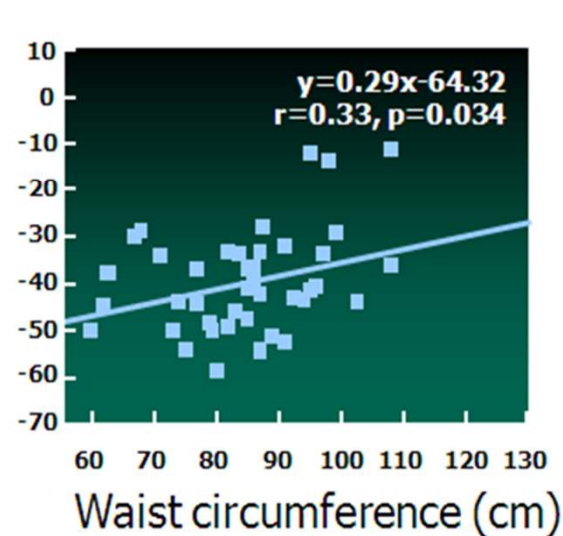
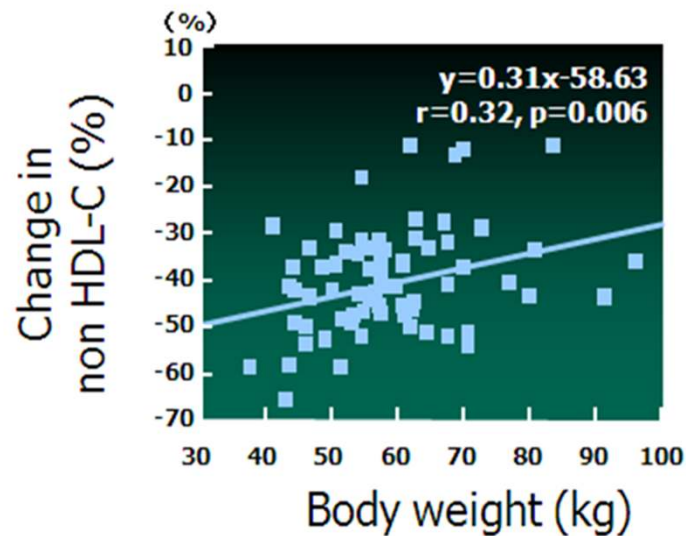
Yokote K Atherosclerosis 2008, 201(2):345-352

CHIBA Study

리바로®

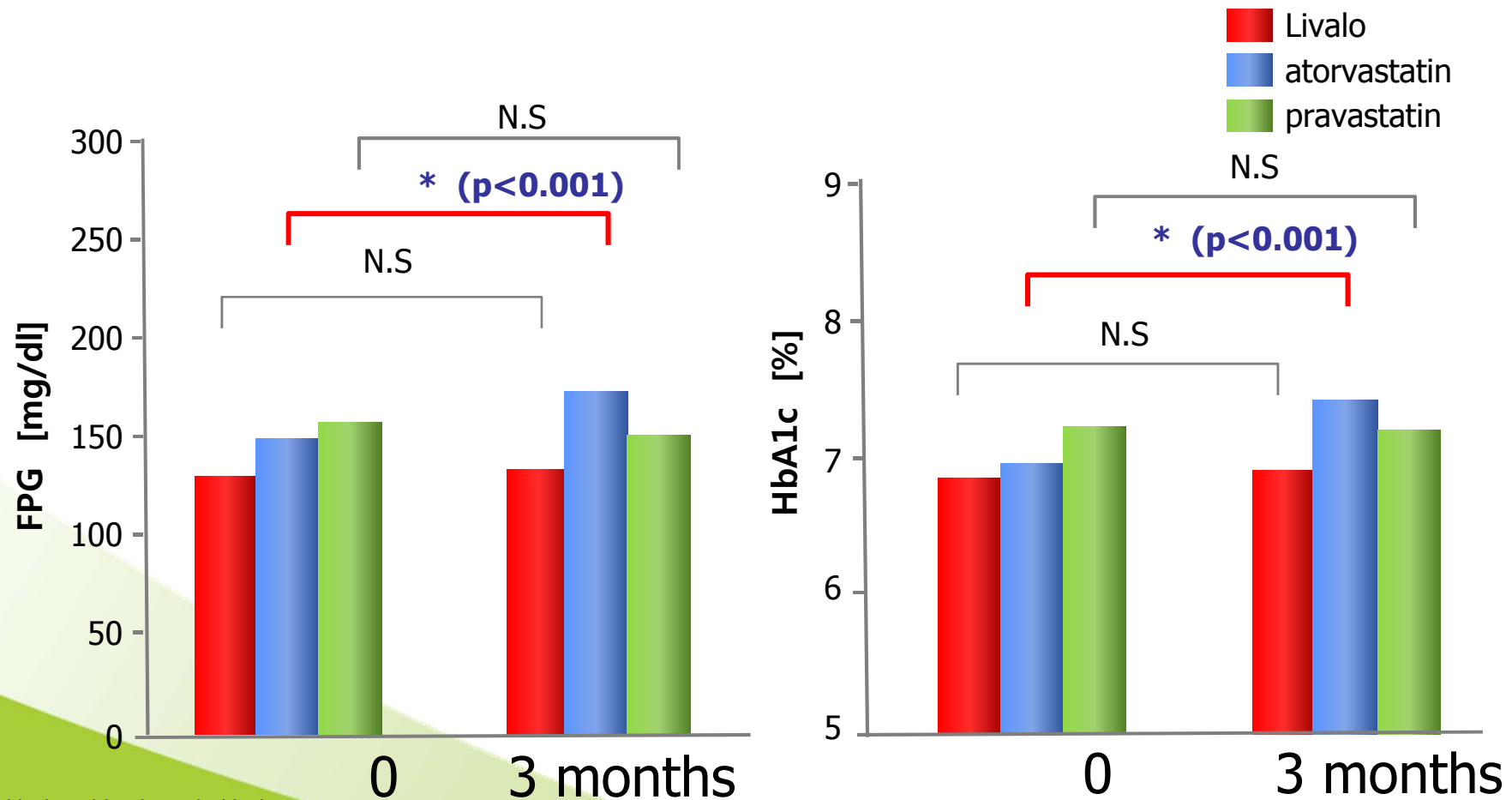


Atorvastatin



Change on Glucose metabolism

리바로는 당뇨병 환자의 혈당 및 당화혈색소에 영향을 주지 않는 제제입니다.



대상환자: 2형 당뇨병 환자(n=279)

시험방법: Pitavastatin(n=95);2mg/day, Atorvastatin(n=99);10mg/day, Pravastatin(n=85);10mg/day for 3month

Exclusion criteria

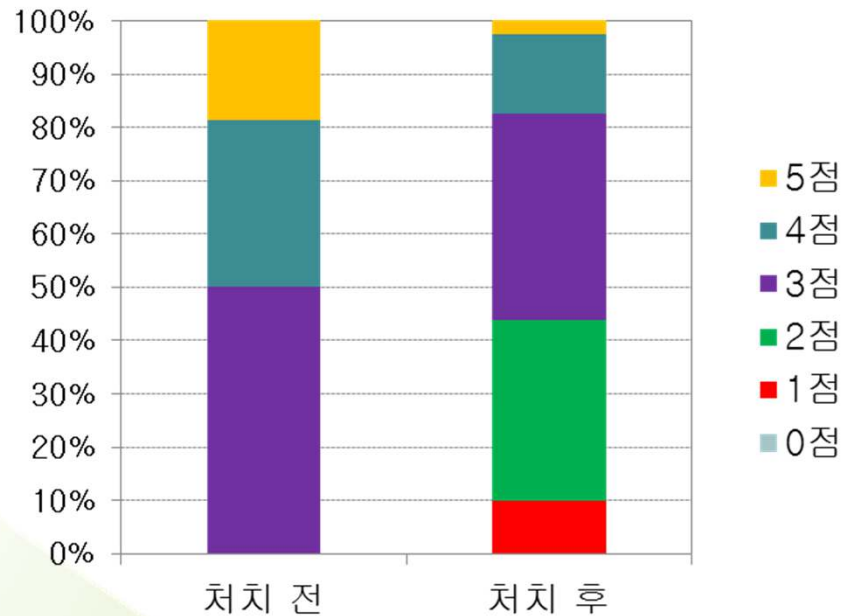
- 다른 임상시험의 시험약을 복용한 지 3개월 미만인 자
- 등록 전 3개월 이내에 statin 제제를 복용한 자
- 조절되지 않는 고혈압 환자(DBP \geq 95mmHg)
- 당뇨 약물을 복용 중이거나 HbA1c > 8% 인 자
- LDL \geq 190mg/dL 또는 TG \geq 400mg/dL 인 자
- 관상동맥질환 또는 다른 동맥경화로 인한 질병이 있는 자
- 6개월 이내 종양학적 병력이 있는 자
- 생명을 위협하는 감염질환과 같이 시험을 수행하기 어려운 심각한 질환이 있는 자
- 신기능 장애가 의심되는 자(serum creatinine \geq 2.0mg/dL)
- 간기능 장애가 의심되는 자(AST 또는 ALT \geq ULN * 2.5)
- CPK가 정상 상한치의 2배 이상인 자
- 조절되지 않는 갑상선기능저하증이 있는 자(TSH \geq ULN * 1.5)
- 수유중, 임신중 또는 임신을 희망하는 여성
- 기타 시험자가 부적합하다고 판단한 자

Baseline patient characteristics

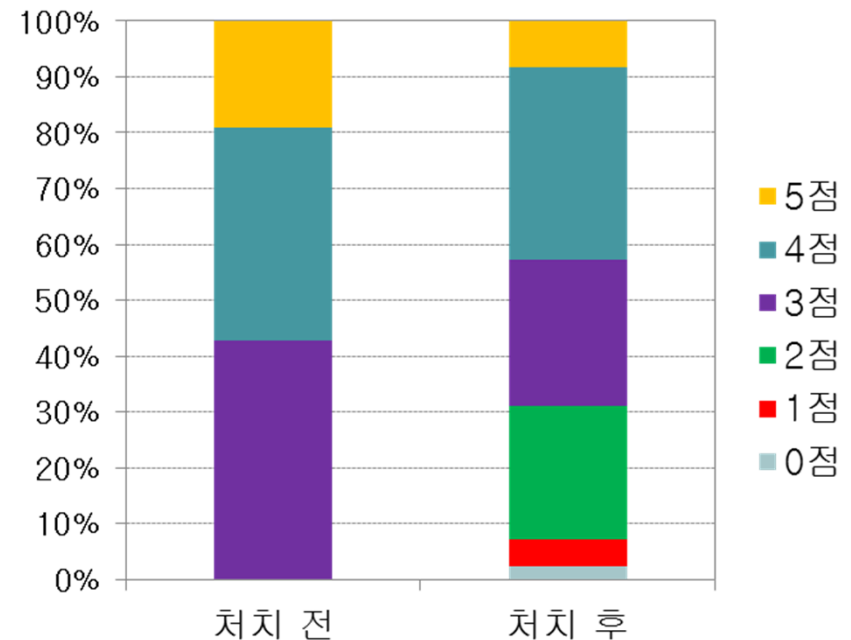
Category	리바로® 투여군	생활습관개선군	p-value
성별: 환자수 (%)			
남성	50(62.50)	51(60.71)	0.8142
여성	30(37.50)	33(39.29)	
나이 평균(SD)	51.68(9.17)	50.79(10.18)	0.5581
신장 (cm)	164.72(8.03)	165.94(9.21)	0.3697
몸무게 (Kg)	73.43(11.82)	75.81(12.50)	0.2119
체질량 지수 (kg/m ²)	26.96(3.14)	27.43(3.18)	0.3362
혈당 (mg/dL)	114.21(12.31)	118.40(15.33)	0.0560
중성지방 (mg/dL)	157.46(56.73)	178.62(72.09)	0.0379
HDL콜레스테롤(mg/dL)	47.72(9.45)	47.01(10.41)	0.6496
허리둘레 (cm)	92.84(5.63)	94.36(6.74)	0.1208
수축기혈압 (mmHg)	129.76(10.62)	127.83(10.97)	0.2544
이완기혈압 (mmHg)	81.06(7.61)	81.14(7.89)	0.9472
맥박 (bpm)	73.15(8.15)	73.35(8.13)	0.1208

Metabolic Syndrome(MS) Score

리바로® 투여군
(N=80)



생활습관 개선군
(N=84)



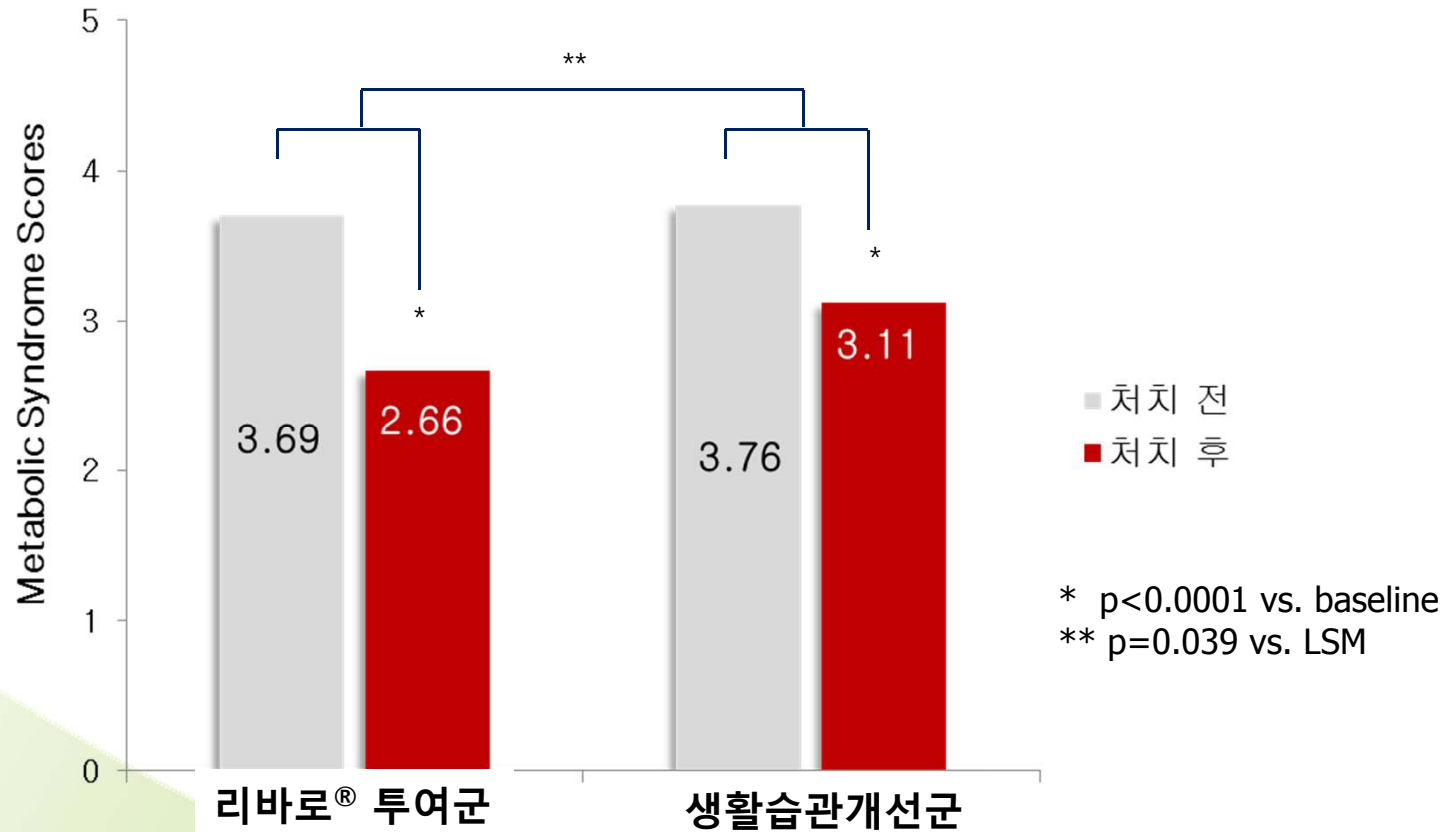
MS score 개선 된 환자 비율 : 52/80 (65%)

48주 후 MS 환자가 아닌 자로 분류된 환자 비율
(MS scores ≤2) : 35/80 (44%)

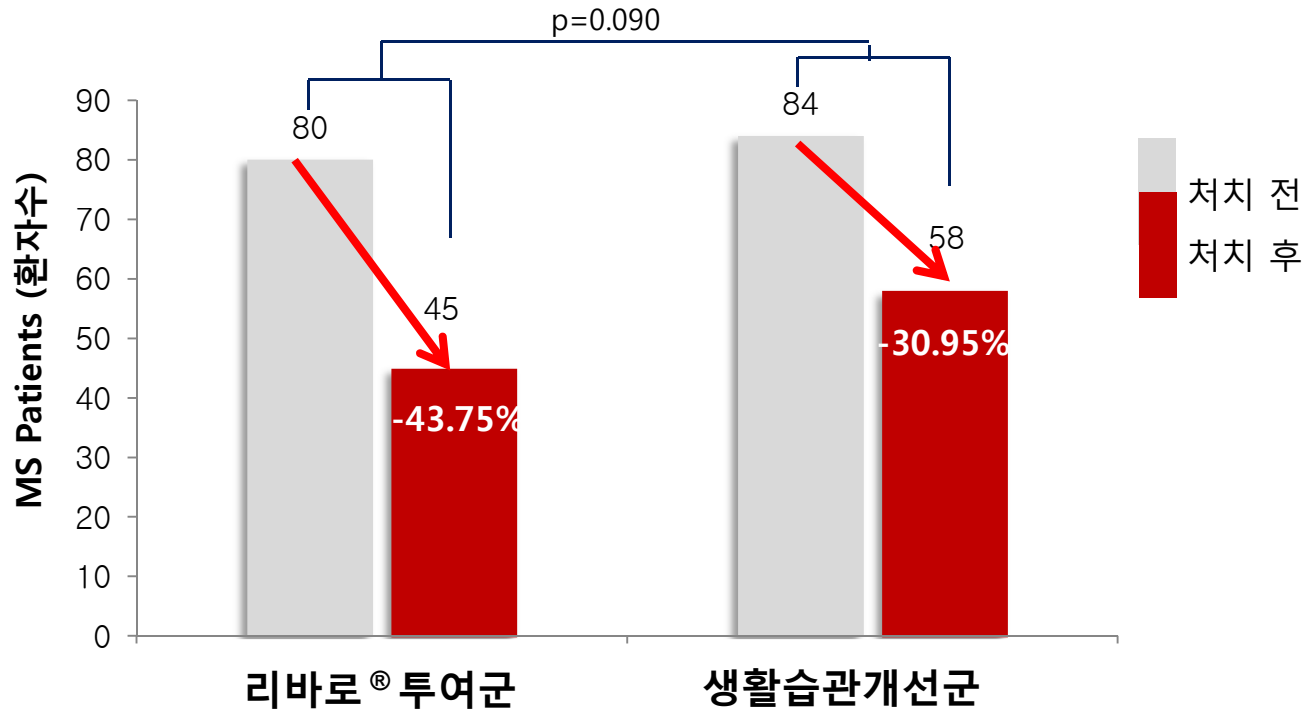
MS score 개선 된 환자 비율 : 41/84 (49%)

48주 후 MS 환자가 아닌 자로 분류된 환자 비율
(MS scores ≤2) : 26/84 (31%)

Metabolic Syndrome(MS) Score

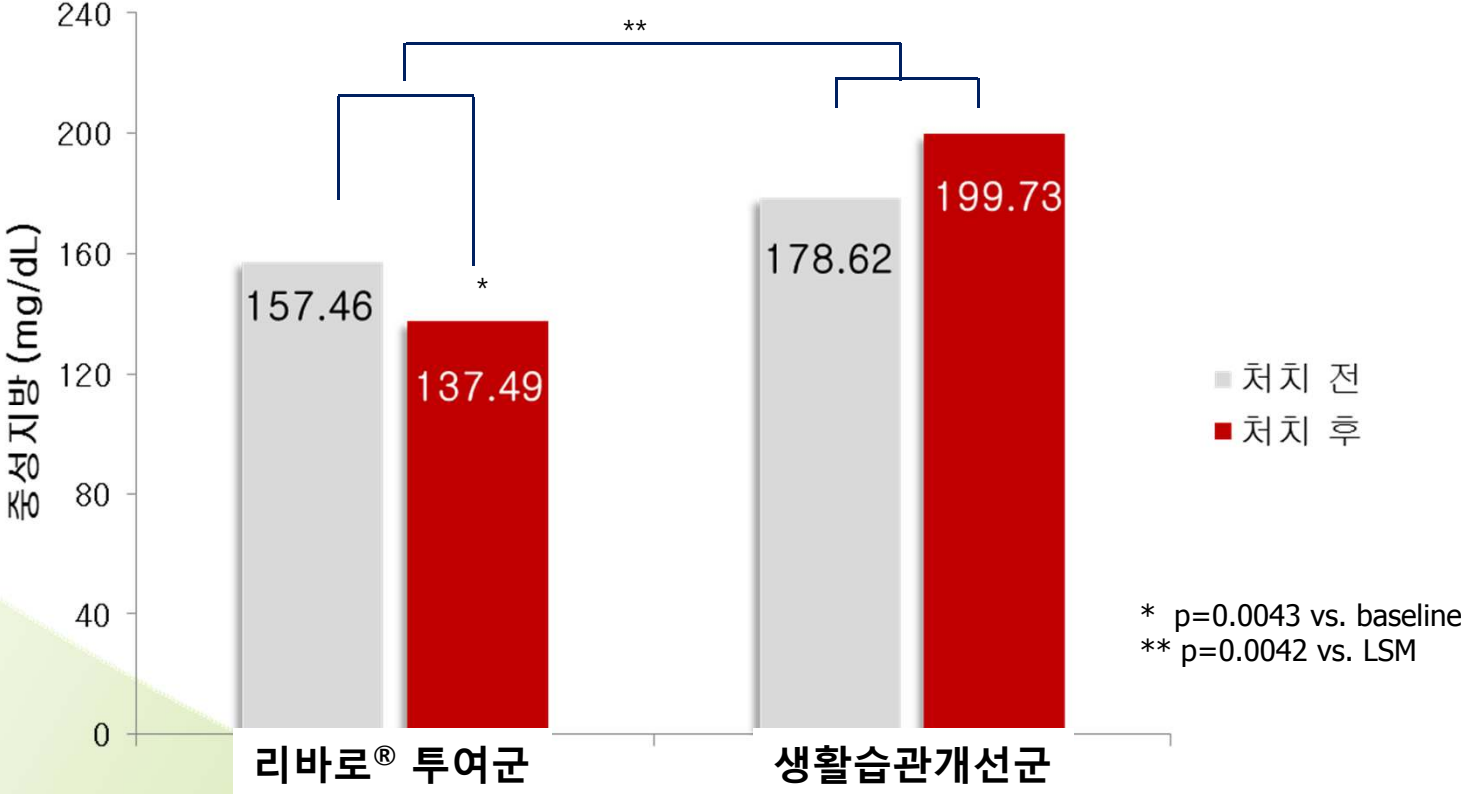


Metabolic Syndrome(MS) Score

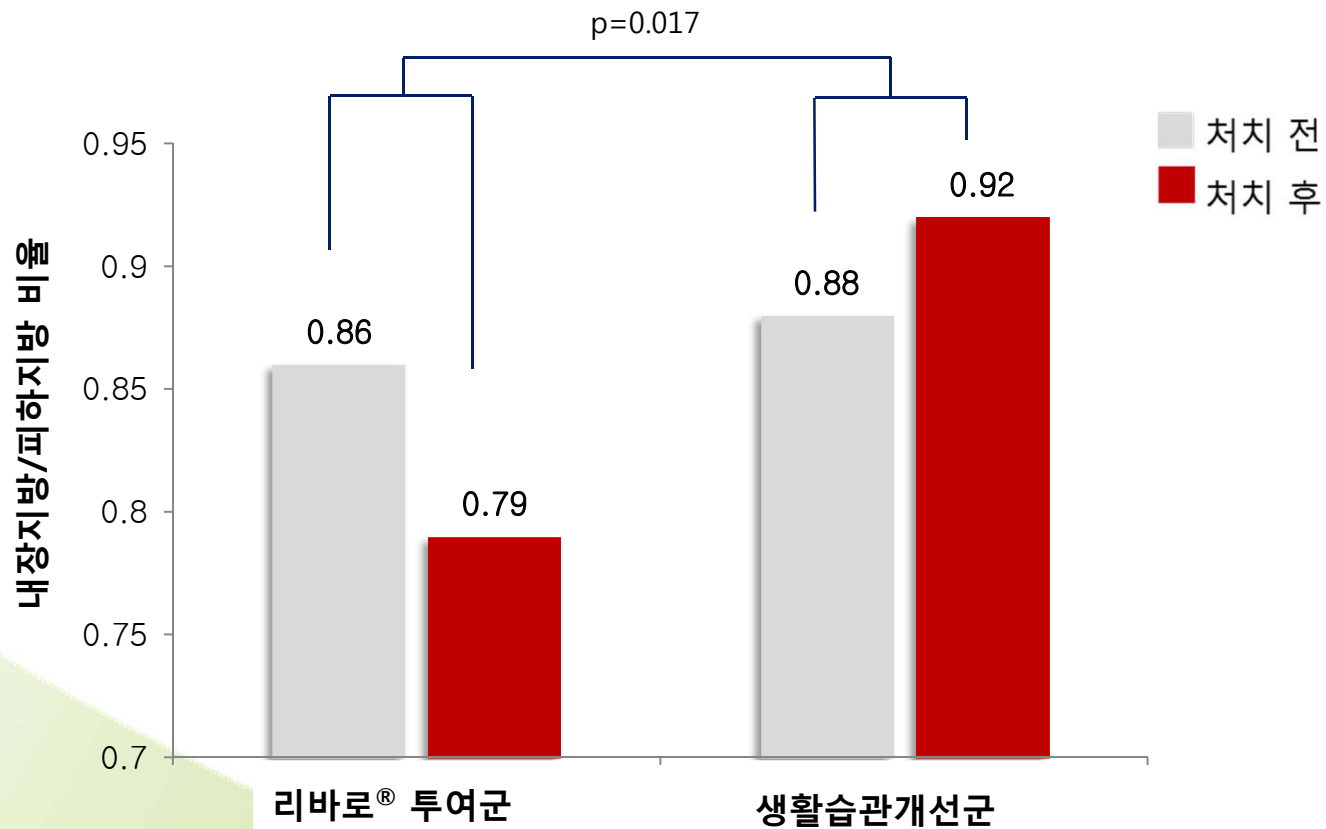


	리바로® 투여군	생활습관개선군	P-value
개선 된 환자	35/80(43.8%)	26/84(31.0%)	0.090
1) 공복혈당	16/80 (20%)	18/80 (22.5%)	0.699
2) 허리둘레	30/80 (37.5%)	22/80 (27.5%)	0.177
3) 중성지방	19/42 (45.2%)	10/50 (20%)	0.009
4) HDL 콜레스테롤	12/30 (40%)	12/37 (32.4%)	0.521
5) 혈압	18/63 (28.6%)	24/61 (39.3%)	0.205

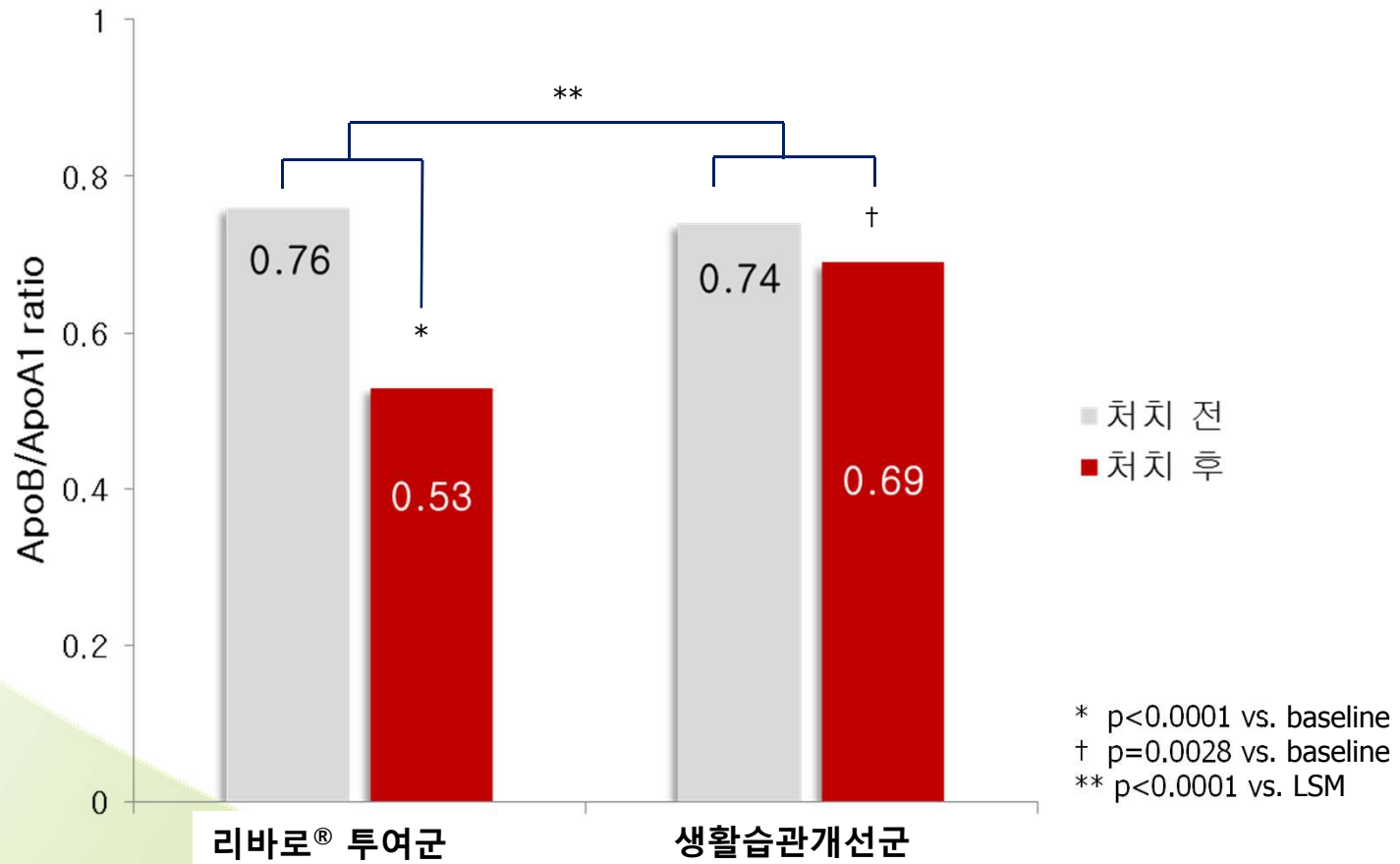
Triglyceride



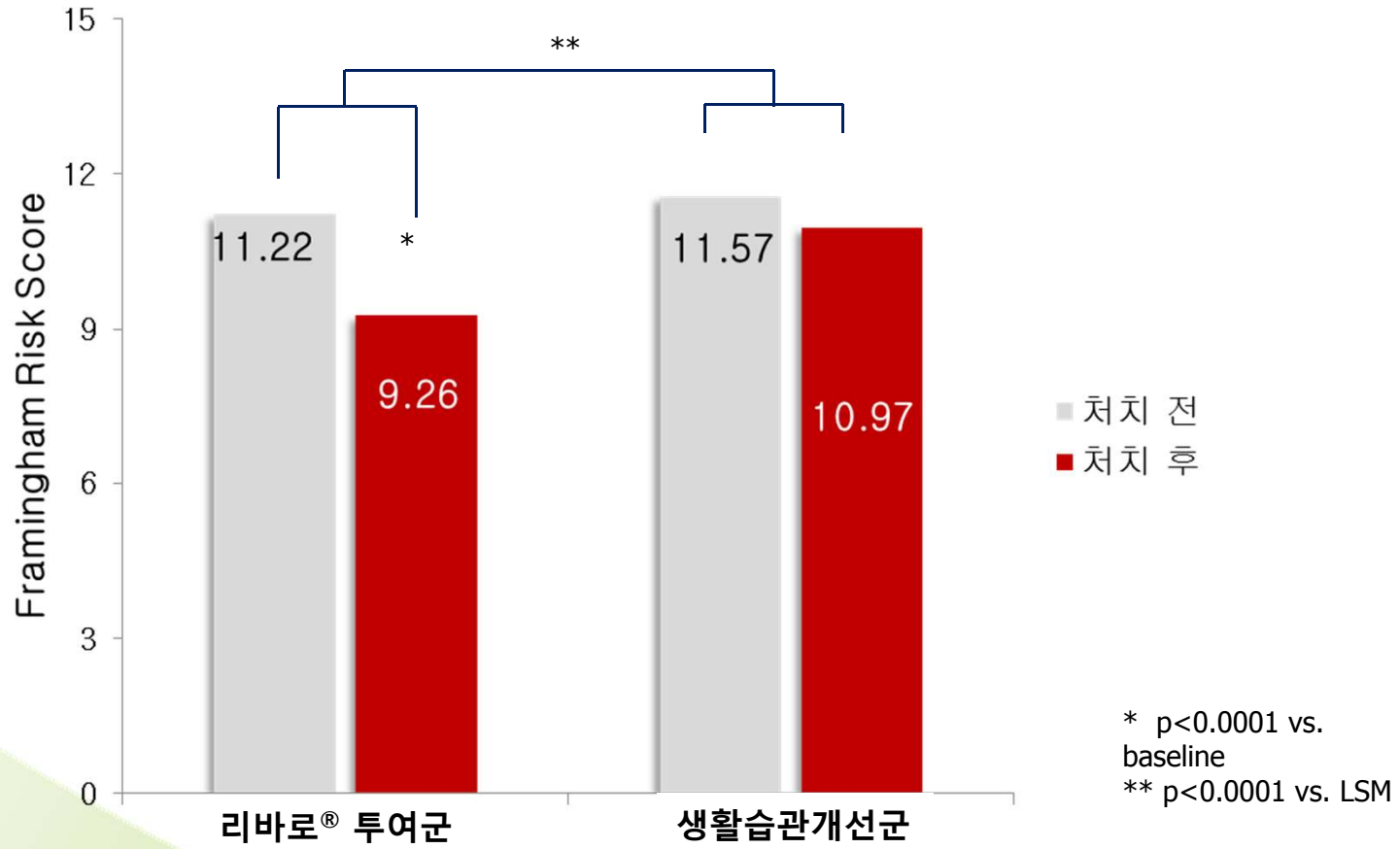
Visceral fat / Subcutaneous fat ratio



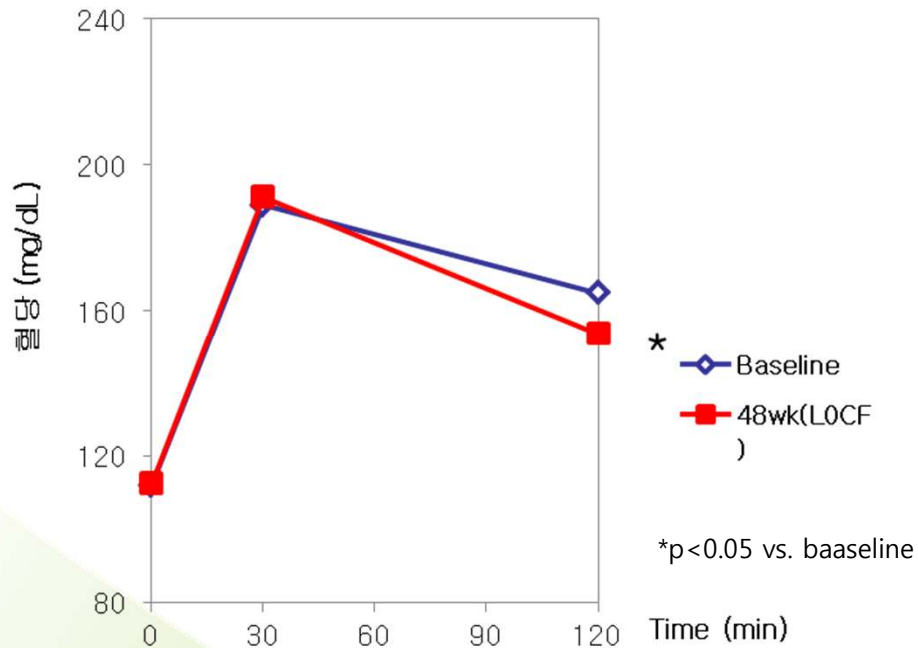
Apo B/A1 ratio



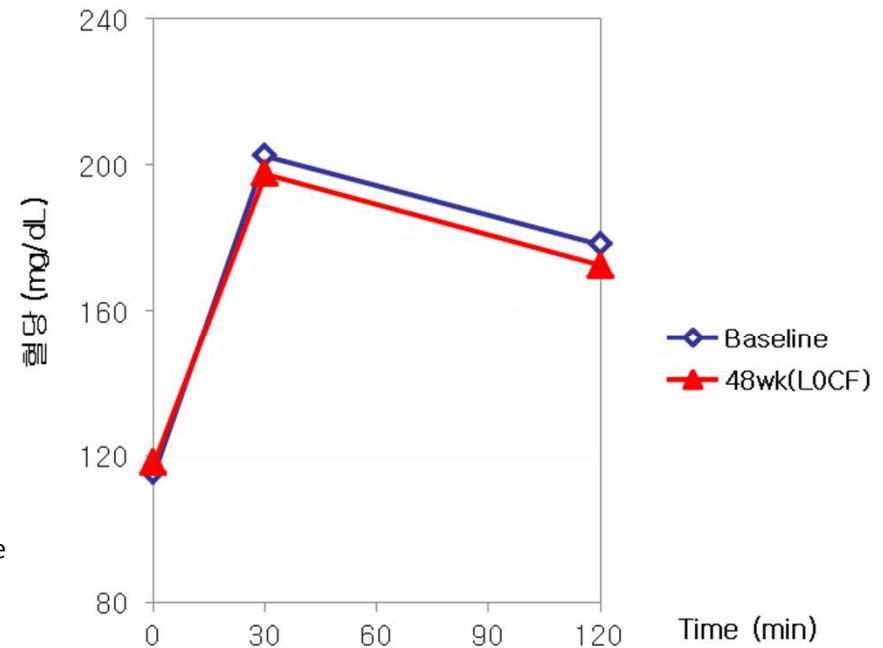
Framingham Risk Score



Changes in glucose tolerance by 75g OGTT



리바로® 투여군



생활습관개선군

경청해주셔서 감사합니다.



Dream4hope