

Non-Pharmacological & Pharmacological Interventions for Prevention of Type 2 Diabetes

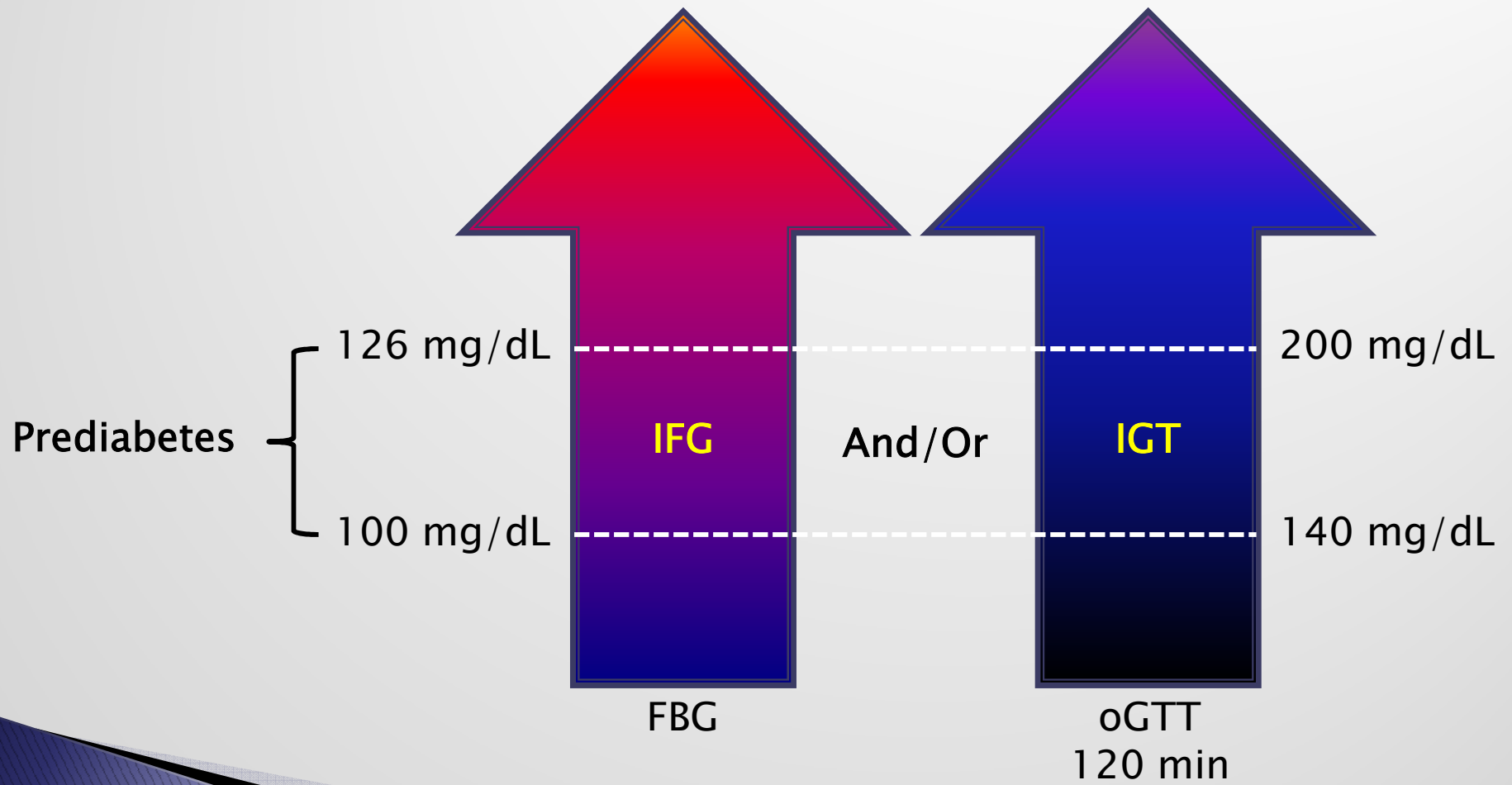
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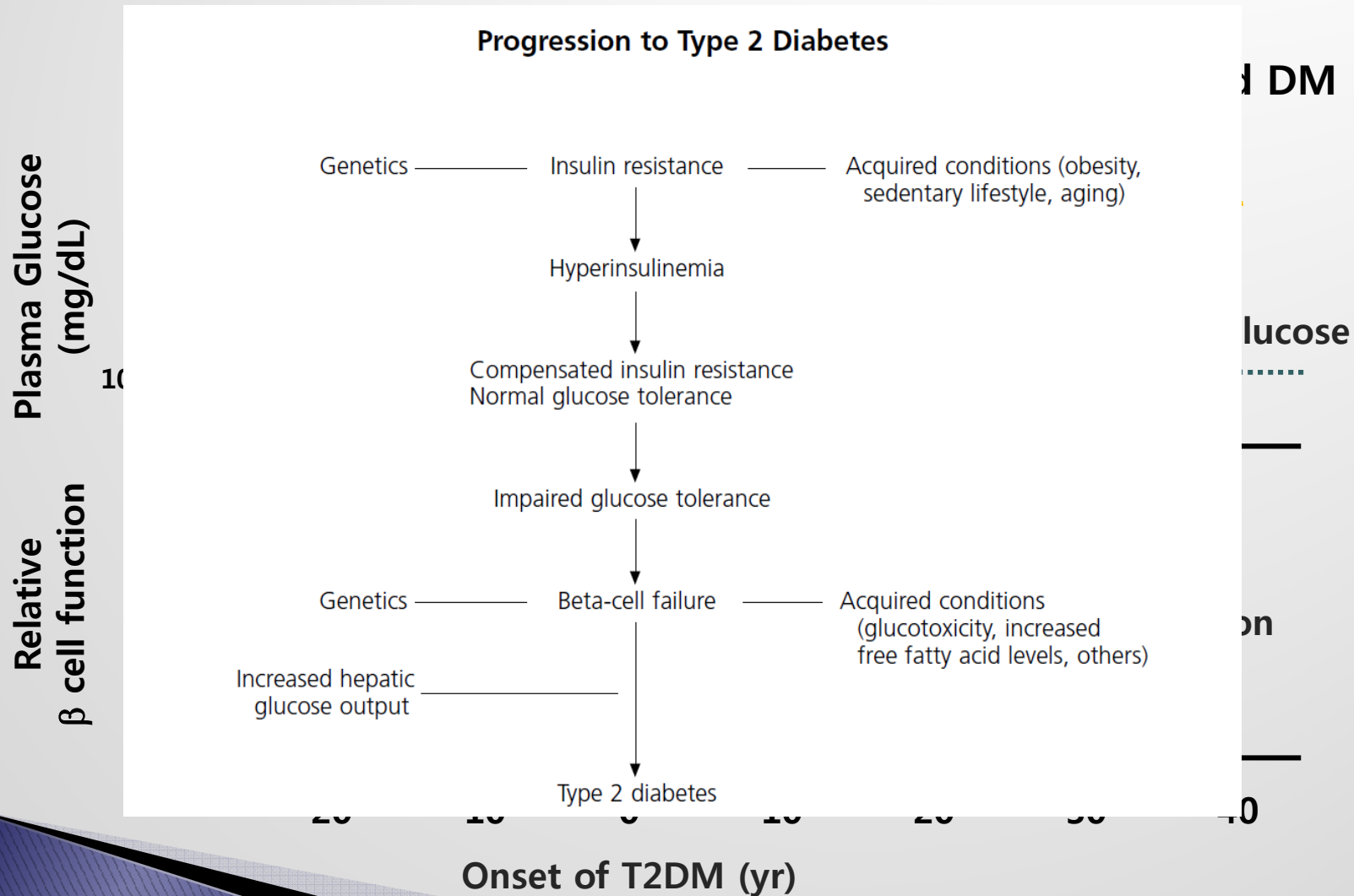
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Prediabetes



NGT - IFG/IGF - T2DM

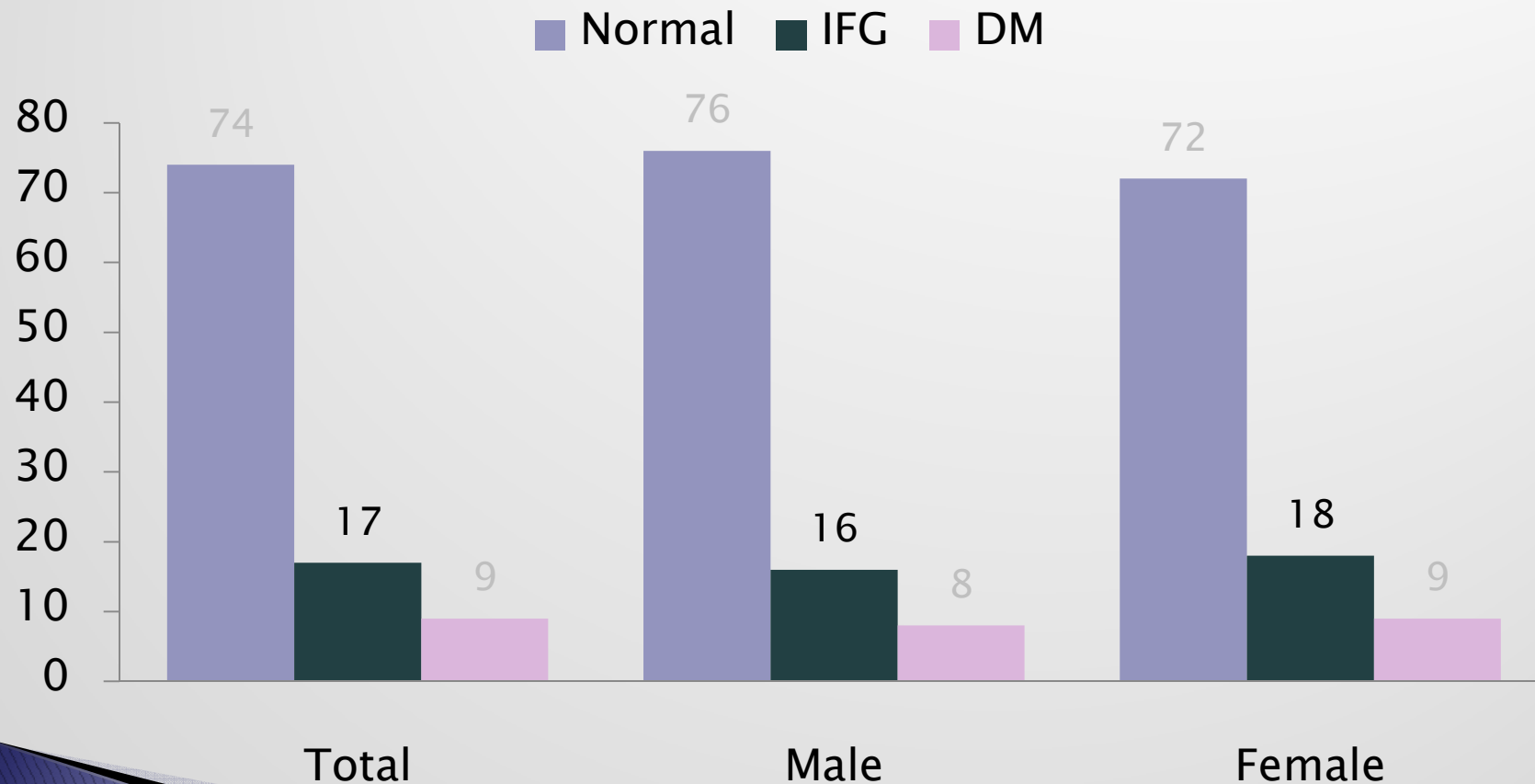


Pathophysiology of prediabetes

Pathophysiology	i-IFG	i-IGT	IFG/IGT
Muscle			
Insulin sensitivity	Unaltered	Reduced	Reduced
Liver			
Insulin sensitivity	Reduced	Unaltered	Reduced
Hepatic glucose production	Elevated	Unaltered	Elevated
Pancreas			
First-phase insulin response	Reduced	Reduced or unaltered	Reduced
Disposition index ^a	Reduced	Reduced	Reduced
Glucagon secretion	Elevated	Elevated	Elevated
Gut			
GLP-1 secretion	Reduced or elevated	Reduced or unaltered	?
GIP secretion	Unaltered	Reduced or unaltered	?
Adipose tissue			
Insulin sensitivity	Reduced	Reduced	?
NEFA release	Unaltered	Elevated	?
Adipocytokine release	?	?	?
Brain	?	?	?
Kidney	?	?	?

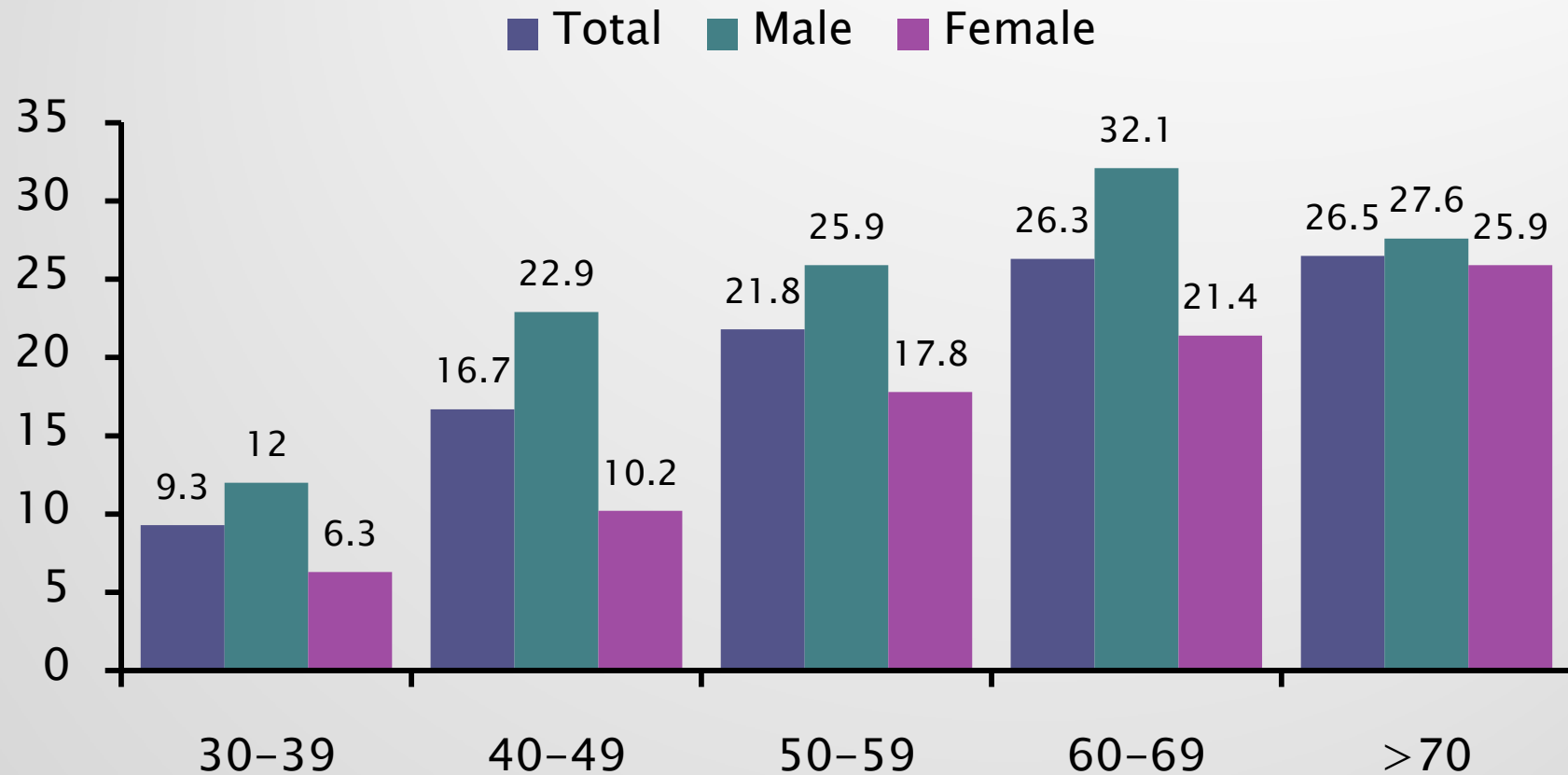
DM Prevalence; by sex

Korean Multi Center Cancer Cohort
1993~2004, 충주, 함안, 울진 포항
Use Fasting Blood Sugar (FBS)

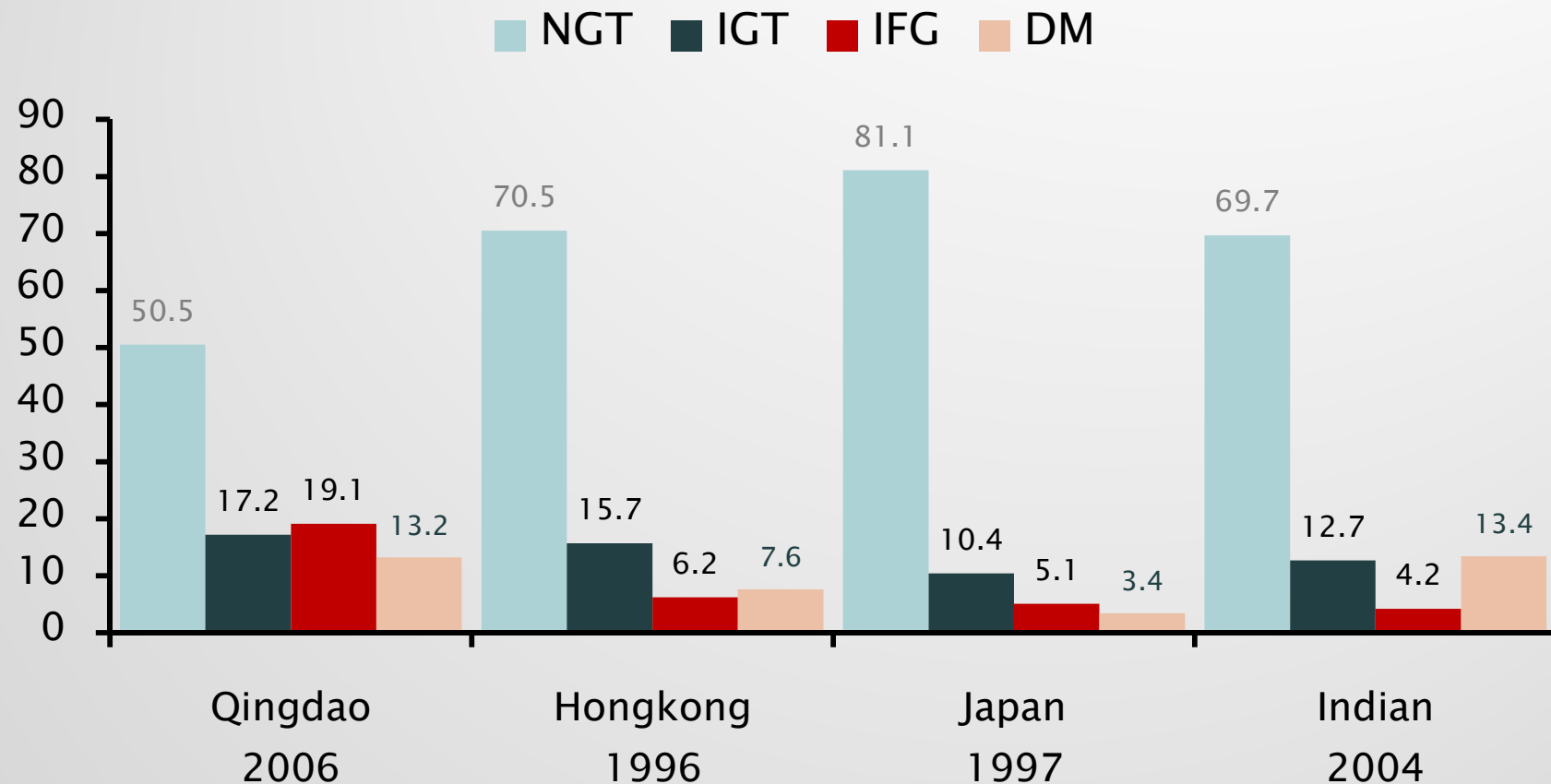


IFG Prevalence in Korean

The Korea National Health and Nutrition Examination Survey (KNHANES), 2005

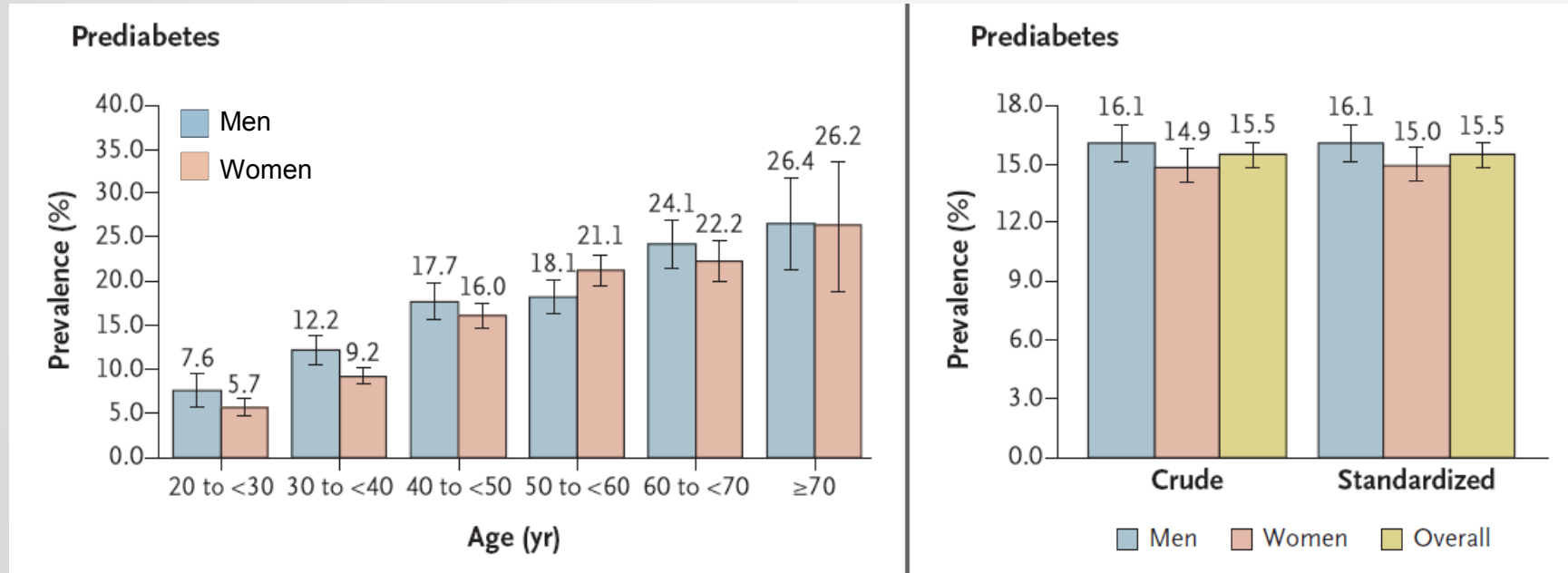


DM and Prediabetes in Asian



In China Report, 2010

China National Diabetes and Metabolic Disorders Study
June/2007~May/2008
46,239 명 (남: 18,419명, 여: 27,820)



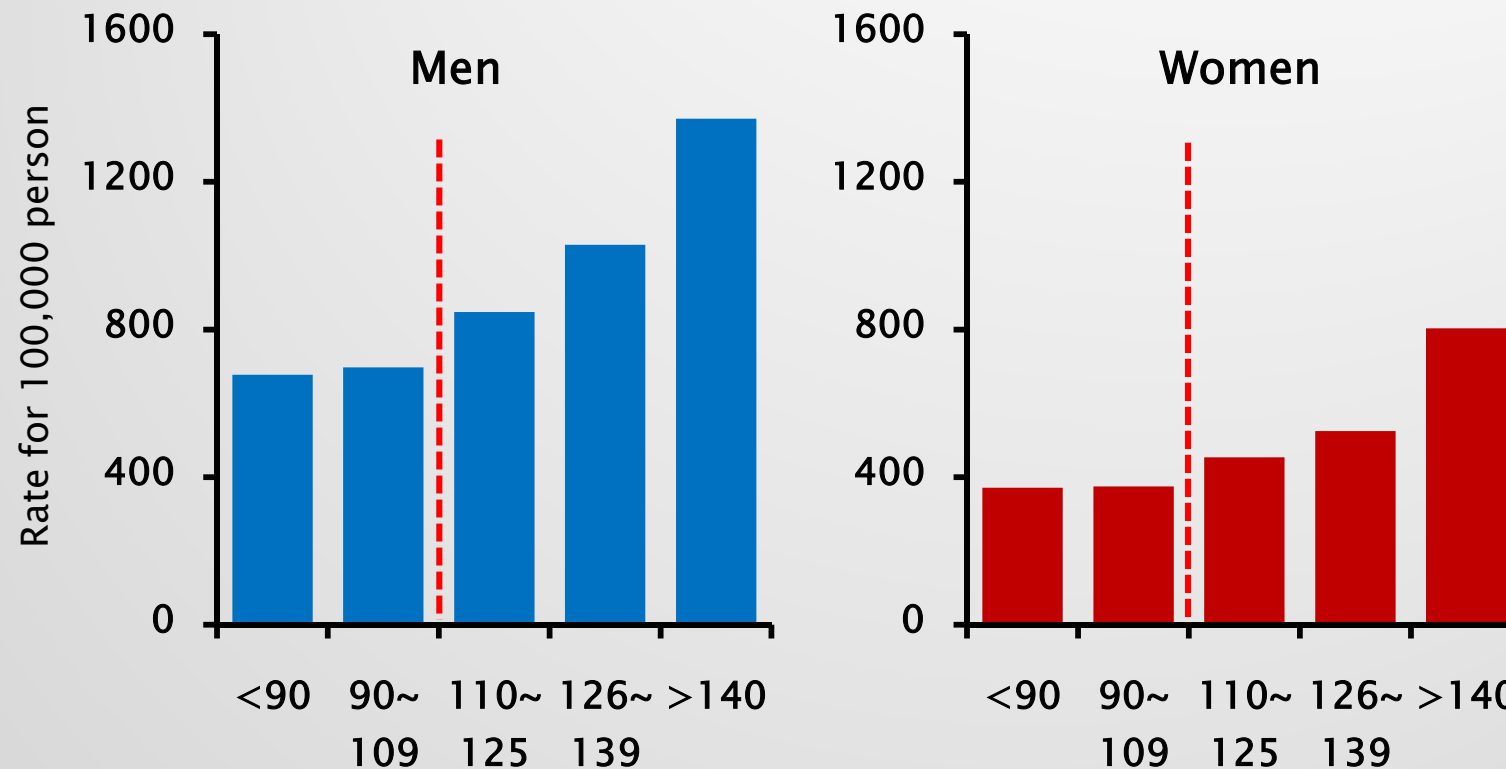
FBS and All Cause Mortality

The National Health Insurance Corp (NHIC)

Biennial medical evaluation in 1992-1995 (with follow-up for up to 10 years)

1,329,525 Koreans (846,907 men and 482,618 women)

Age: 30 ~ 95 years



Prediabetes

- Transition to T2DM.
- Increased Mortality and Morbidity itself.

Normal

IFG/IGT

T2DM

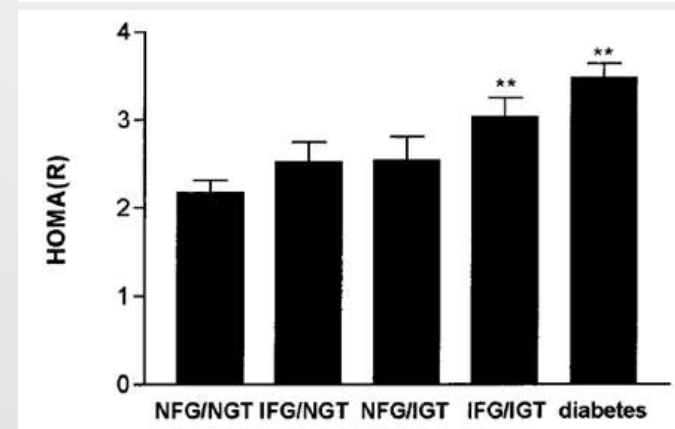
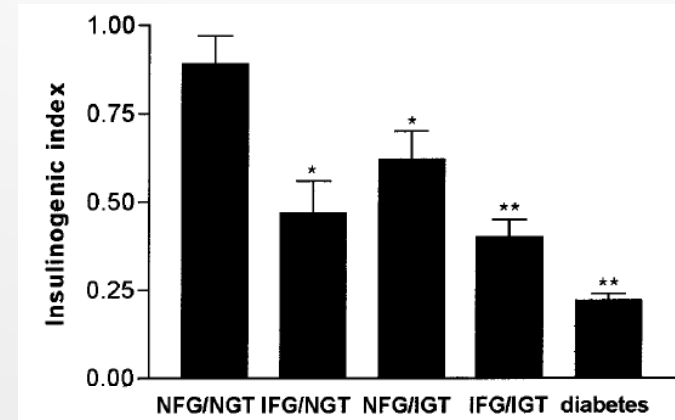
- Preservation of beta cell function
- Reduction of Insulin resistance

In Korean T2DM



In KOREAN T2DM

- Less Obese
- Earlier **Insulin secretion defect**
- Milder **insulin resistance**



Non Pharmacologic Intervention

- Da Qing Diabetes Prevention Study
- Japanese Trial in IGT males
- Finnish Diabetes Prevention Study

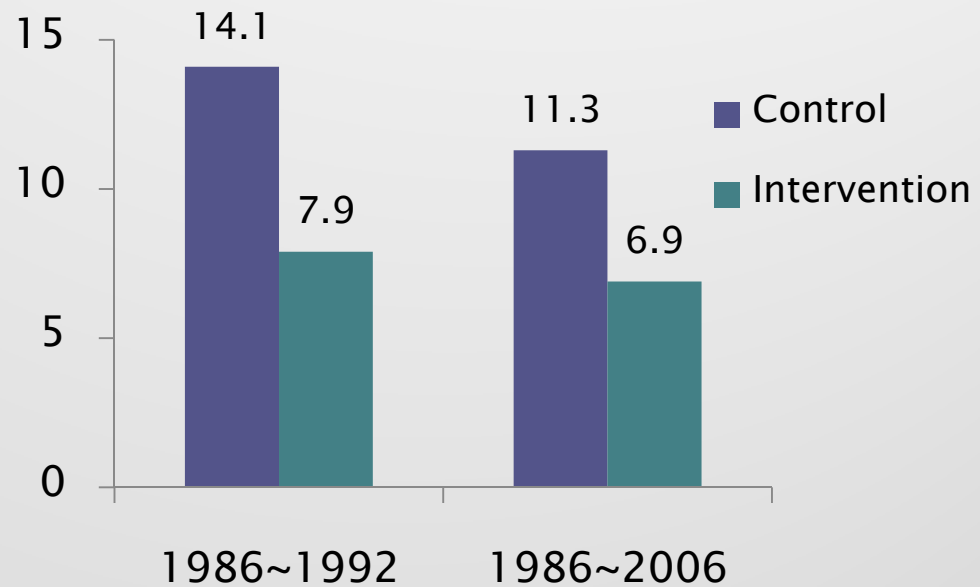
China Da Qing Diabetes Prevention Study

a 20-year follow-up study

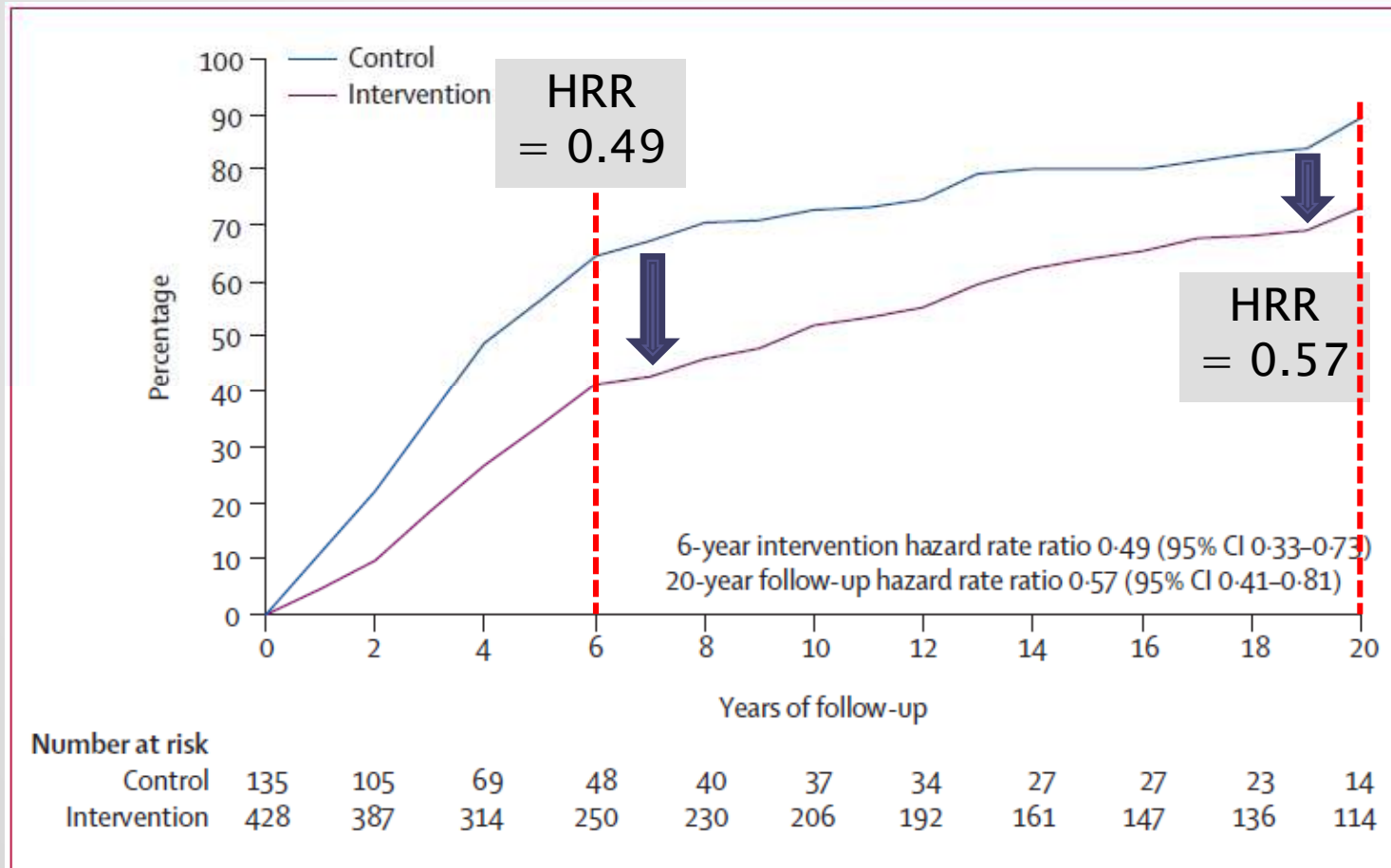


Diabetes Risk reduction

Diet: 31%
Exercise: 46%
Diet+Exercise: 42%



Cumulated Incidence of T2DM

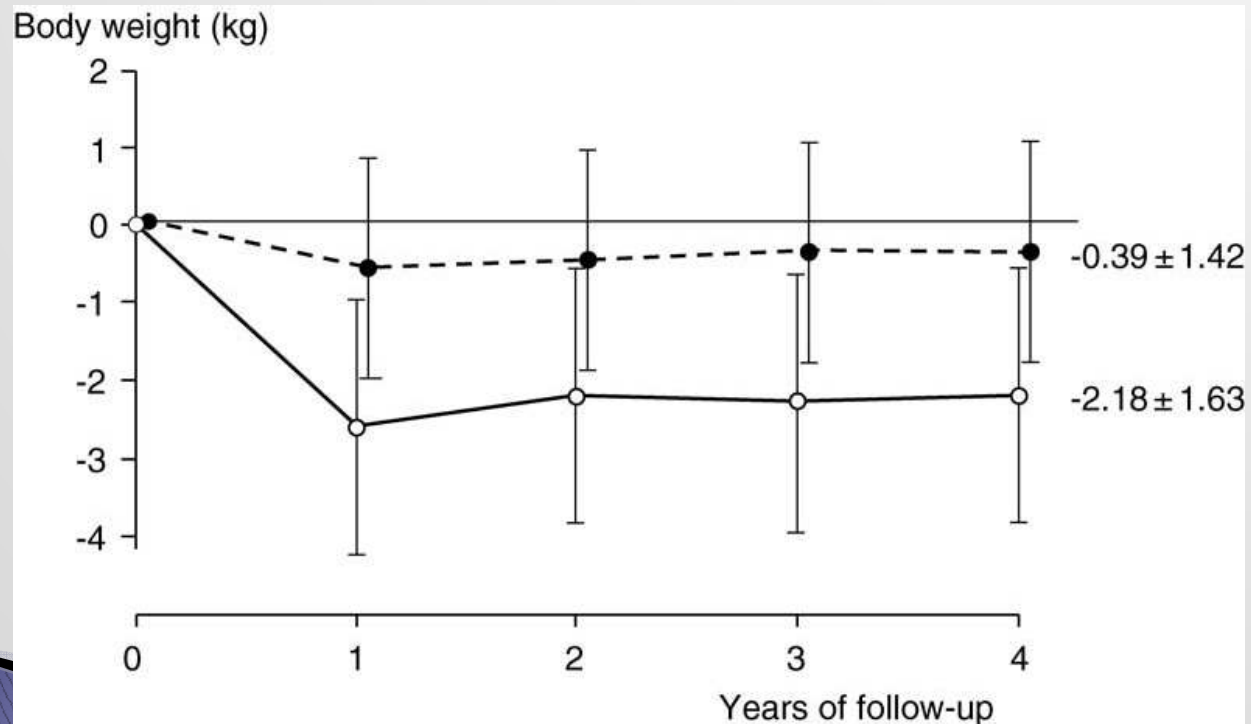


Japanese Trial in IGT males

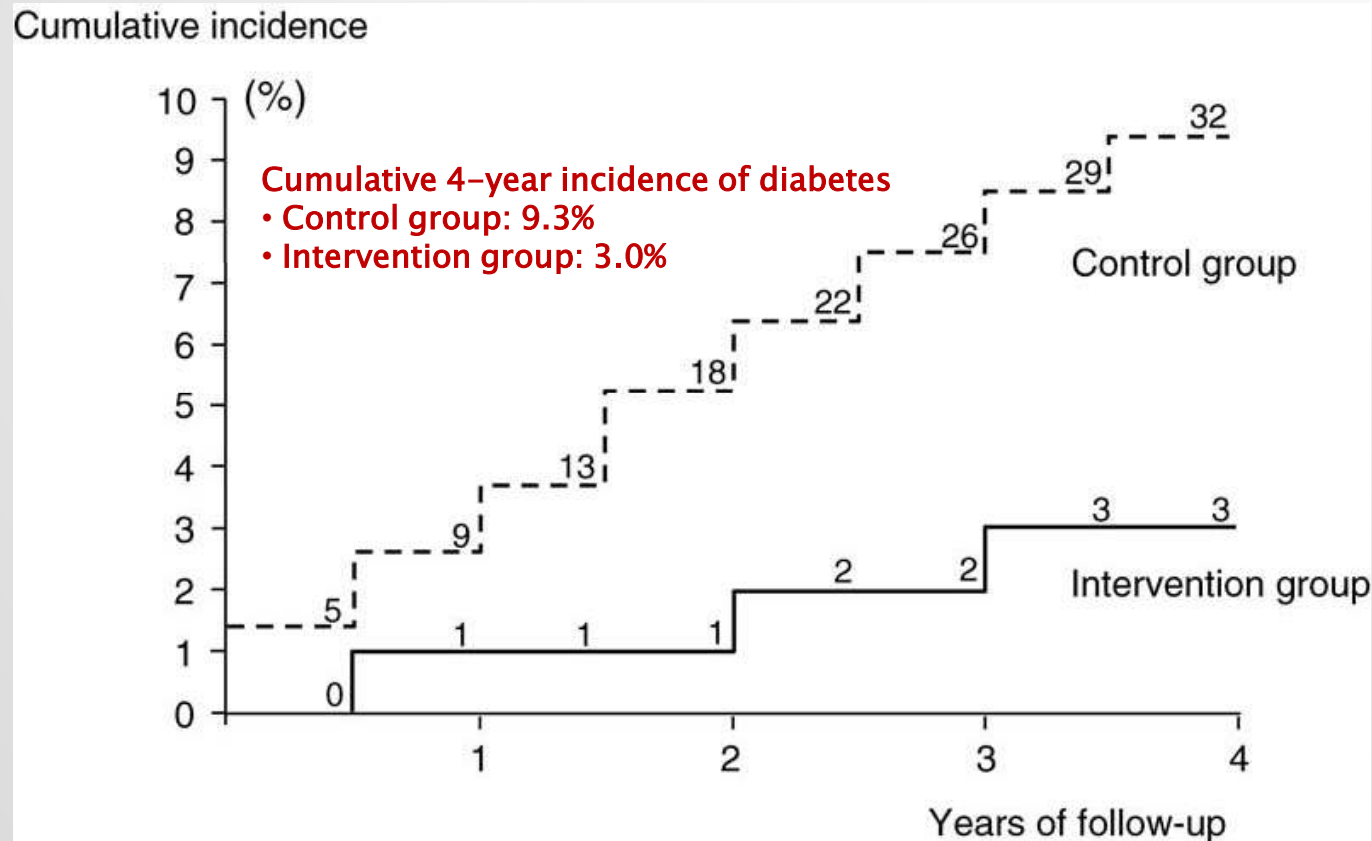
Health Medical Center in Toranomon Hospital

458 men with IGT Baseline BMI=24 kg/m²

- Standard intervention group (control group; 356)
 - to BMI 24 kg/m²
- Intensive intervention group (intervention group; 102)
 - to BMI 22 kg/m²



Cumulated Incidence of T2DM



Incidence by Variable

Variable	Incidence of DM	
Body Weight change		Δ weight
Control: increased weight	14.7	1.58 kg
neutral	10.6	- 0.20 kg
decreased weight	4.3	- 1.77 kg
Intervention	3.0	- 2.18 kg
FPG		
Up to 109	5.4	
110 ~ 139	11.8	
Insulinogenic index		
< 0.5		Δ weight
Control	12.3	- 0.38 kg
Intervention	4.1	- 2.16 kg
\geq 0.5		Δ weight
Control	1.9	- 0.41 kg
Intervention	0	- 2.21 kg

Finnish Diabetes Prevention Study

522 middle-aged, overweight subjects with IGT

- Control (265)
- Intervention group (257)

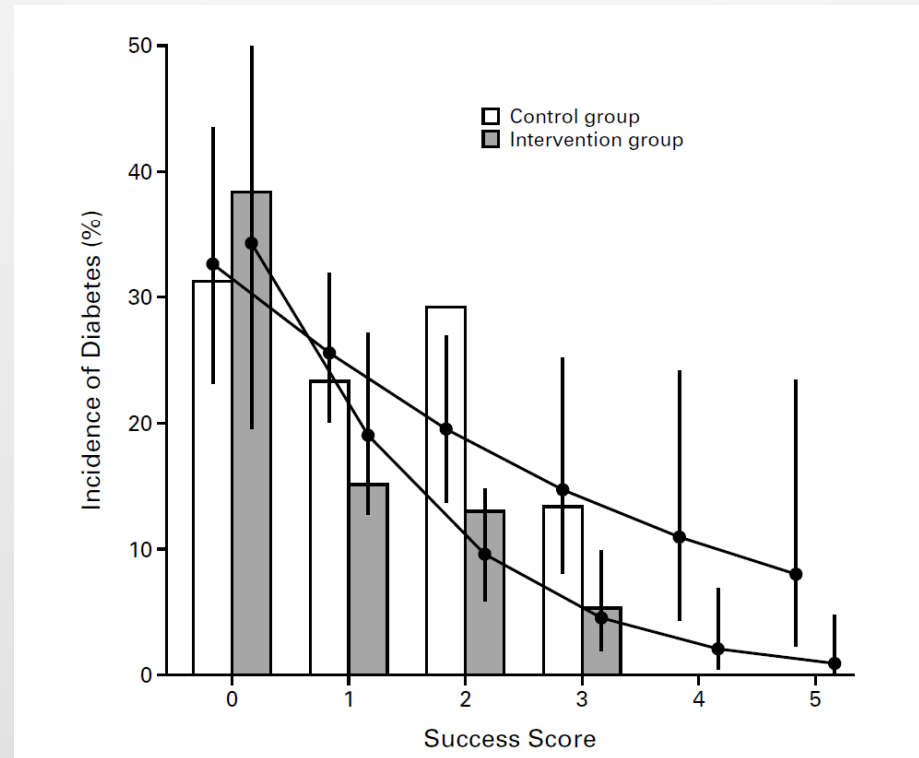
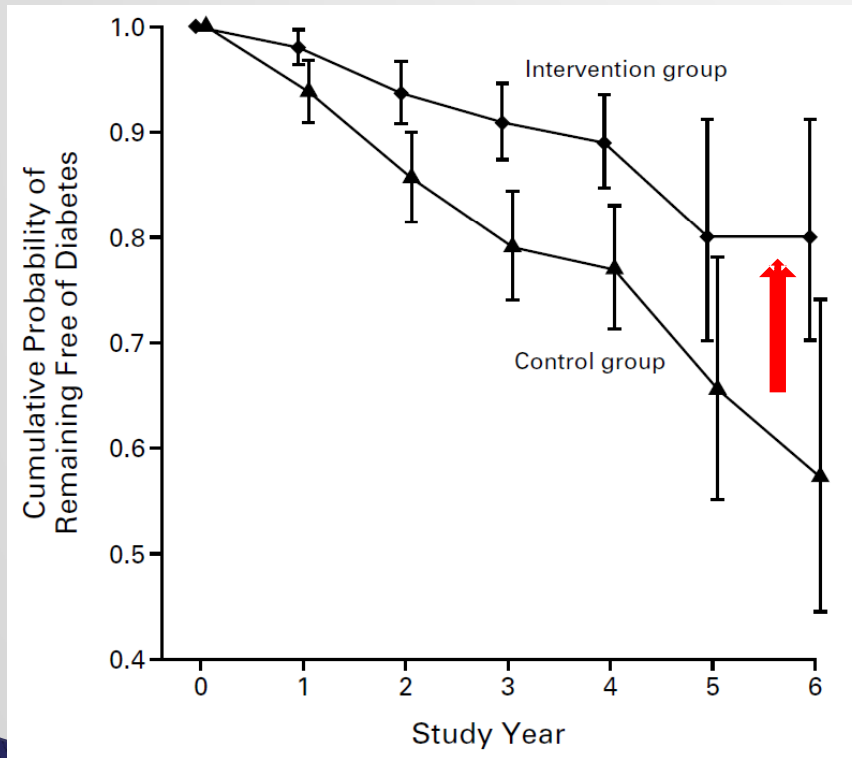
Reducing weight, Total intake of fat, Intake of saturated fat
Increasing intake of fiber, Physical activity

TABLE 4. SUCCESS IN ACHIEVING THE GOALS OF THE INTERVENTION BY ONE YEAR, ACCORDING TO TREATMENT GROUP.*

GOAL	INTERVENTION GROUP	CONTROL GROUP	P VALUE†
	% of subjects		
Weight reduction >5%	43	13	0.001
Fat intake <30% of energy intake	47	26	0.001
Saturated-fat intake <10% of energy intake	26	11	0.001
Fiber intake \geq 15 g/1000 kcal	25	12	0.001
Exercise >4 hr/wk‡	86	71	0.001

Cumulative incidence of diabetes after four years

- Intervention group: 11 percent
- Control group: 23 percent



Exercise and T2DM

국민건강보험공단, 23,737명 (남: 19,440명, 여자: 4,297명)
 2000'에 FBS: 100 ~ 125 mg/dL, 30~69세 수진자
 4년 후 T2DM 여부와 운동여부를 조사

		Subject	Person-year	No. of cases	Incidence rate*
Male	Total	19,440	81,570.2	3,239	39.7
	Regular : over 3/week	4,400	18,620.8	670	36
	Irregular : 1-2/week	8,120	34,225.8	1,337	39.1
	None	6,920	28,725	1,232	42.9
Female	Total	4,297	18,399.8	283	15.4
	Regular : over 3/week	331	1,396.2	24	17.2
	Irregular : 1-2/week	412	1,733.3	50	28.9
	None	3,554	15,271.5	209	13.7

* Unit : per 1,000 person-year † p<0.001, ‡ p<0.05, §p<0.0001

Recommended Lifestyle Changes

- ▶ Daily Calories
 - Fat: < 25 to 30 percent
 - Saturated fat: < 10 percent
 - Carbohydrates: 50 to 60 percent
 - Protein: 15 to 20 percent
- ▶ Daily fiber intake: > 15 g for every 1,000 calories consumed
- ▶ Foods: salad, vegetables, fruits, whole grains, fish high in omega-3 fatty acids, legumes, lean meat; minimal intake of refined sugars
- ▶ Exercise: moderate-intensity physical activity, such as brisk walking or biking, for 150 minutes per week
- ▶ Weight loss goal: 5 to 7 percent of body weight

Pharmacologic Intervention

- STOP-NIDDM
- Diabetes Prevention Program
- The DREAM Trial
- Swedish Obese Subjects Study

Assess Point for Pharmacologic Intervention

1. Impact of the study drug upon the **incidence of diabetes**.
2. Impact of the study drug upon diagnosis of diabetes after the **post-treatment washout phase**.
3. Assessment of **insulin sensitivity/ β -cell function/insulin secretion and blood glucose**.
4. Assessment of confounding factors (e.g., exercise or weight loss and medication compliance).
5. Impact of the study drug on the **occurrence of cardiovascular disease**.

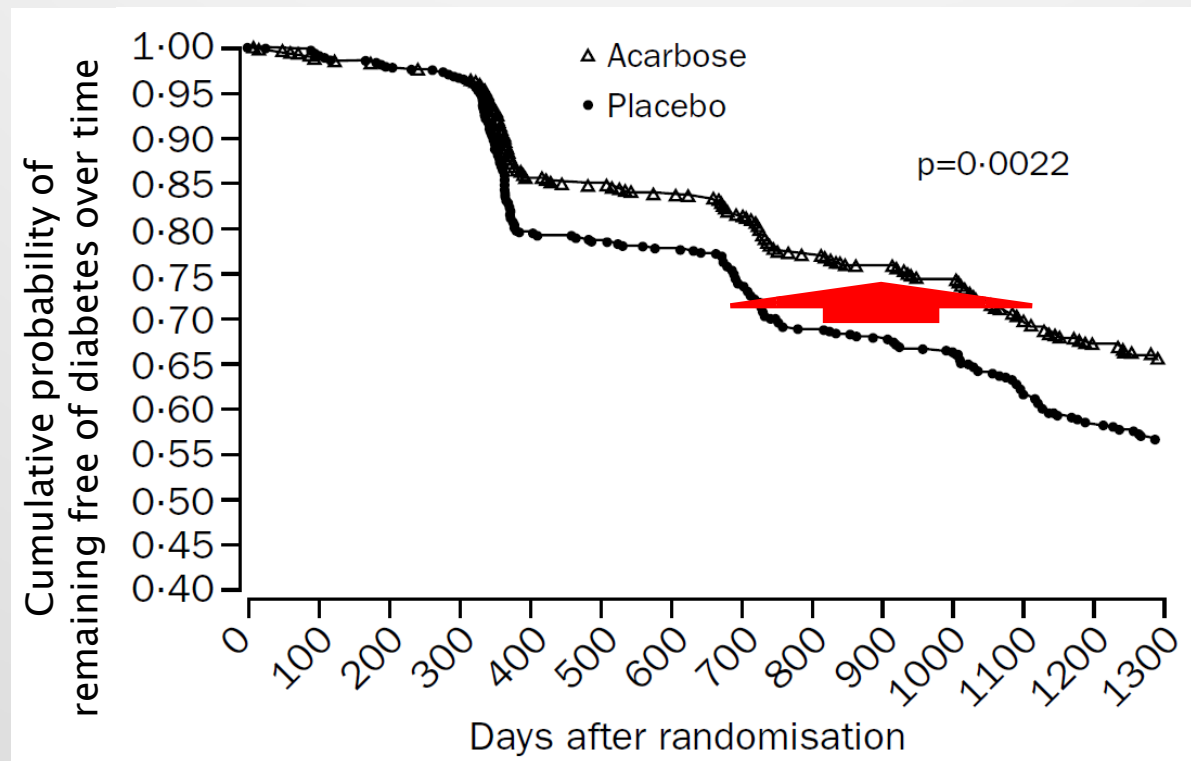
STOP-NIDDM

Multicentre, placebo-controlled randomized Trial
1,468 patients with impaired glucose tolerance

Placebo (686)

Acarbose (682): 100 mg tid for 3 years

Mean body weight change
Acarbose: 87.6 kg -> 87.1 kg
Placebo: 87.0 kg -> 87.3 kg



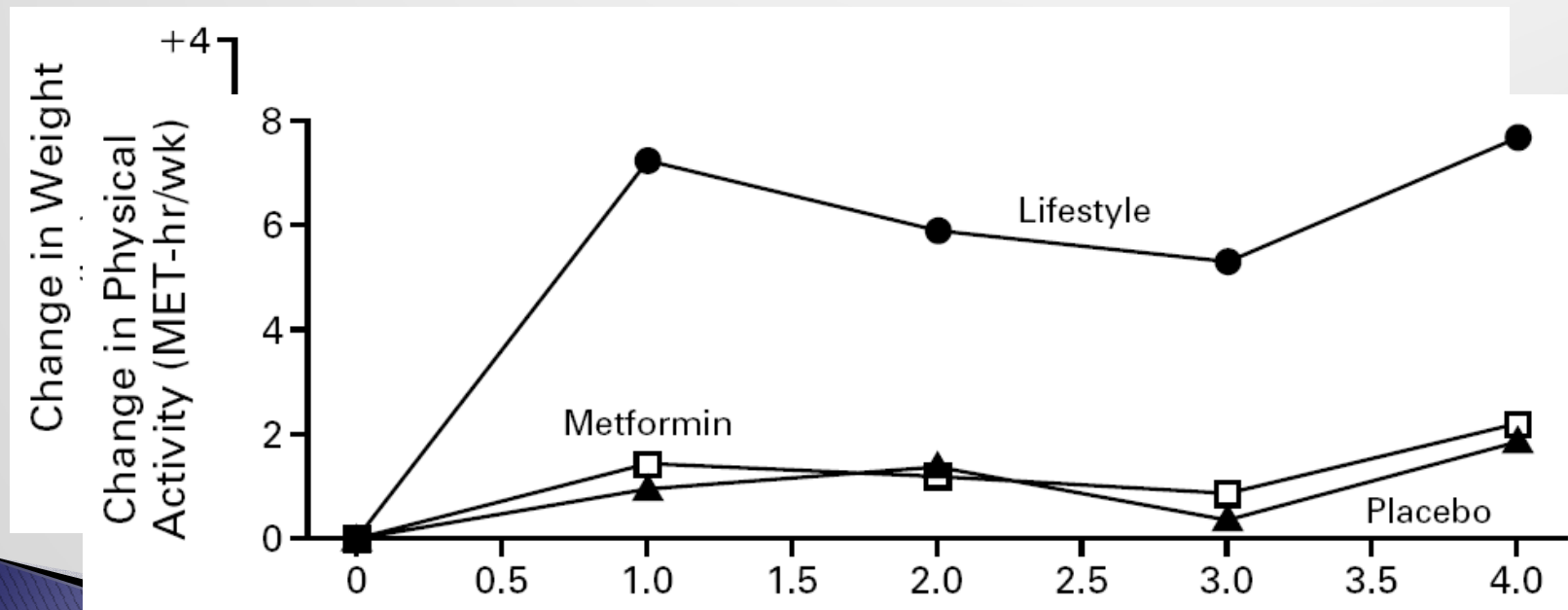
	Glucose tolerance at end of treatment (%)		
	NGT	IGT	T2D
* $p < 0.001$			
Acarbose (n=682)	35.3*	28.4	32.4*
Placebo (n=686)	30.9	24.9	41.5

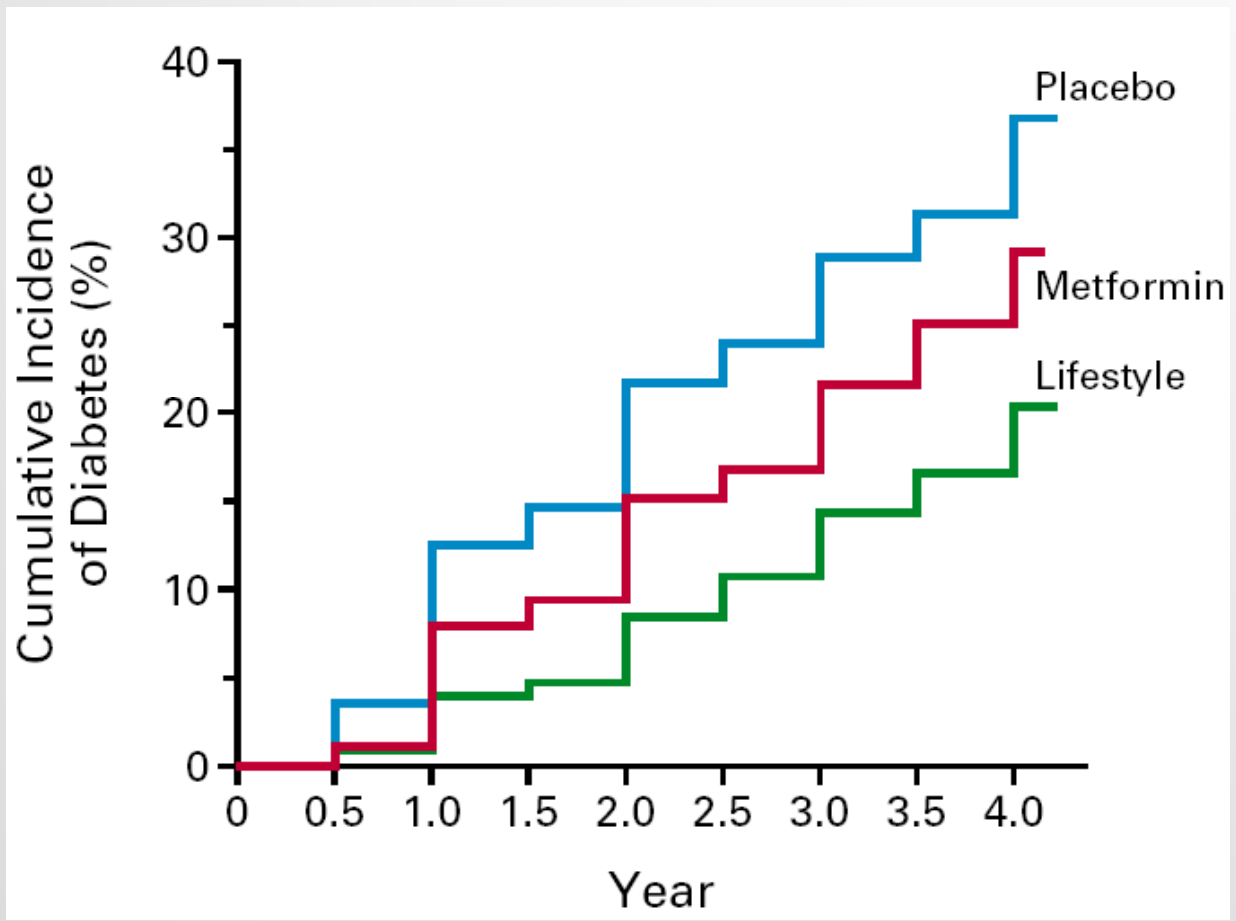
Diabetes Prevention Program

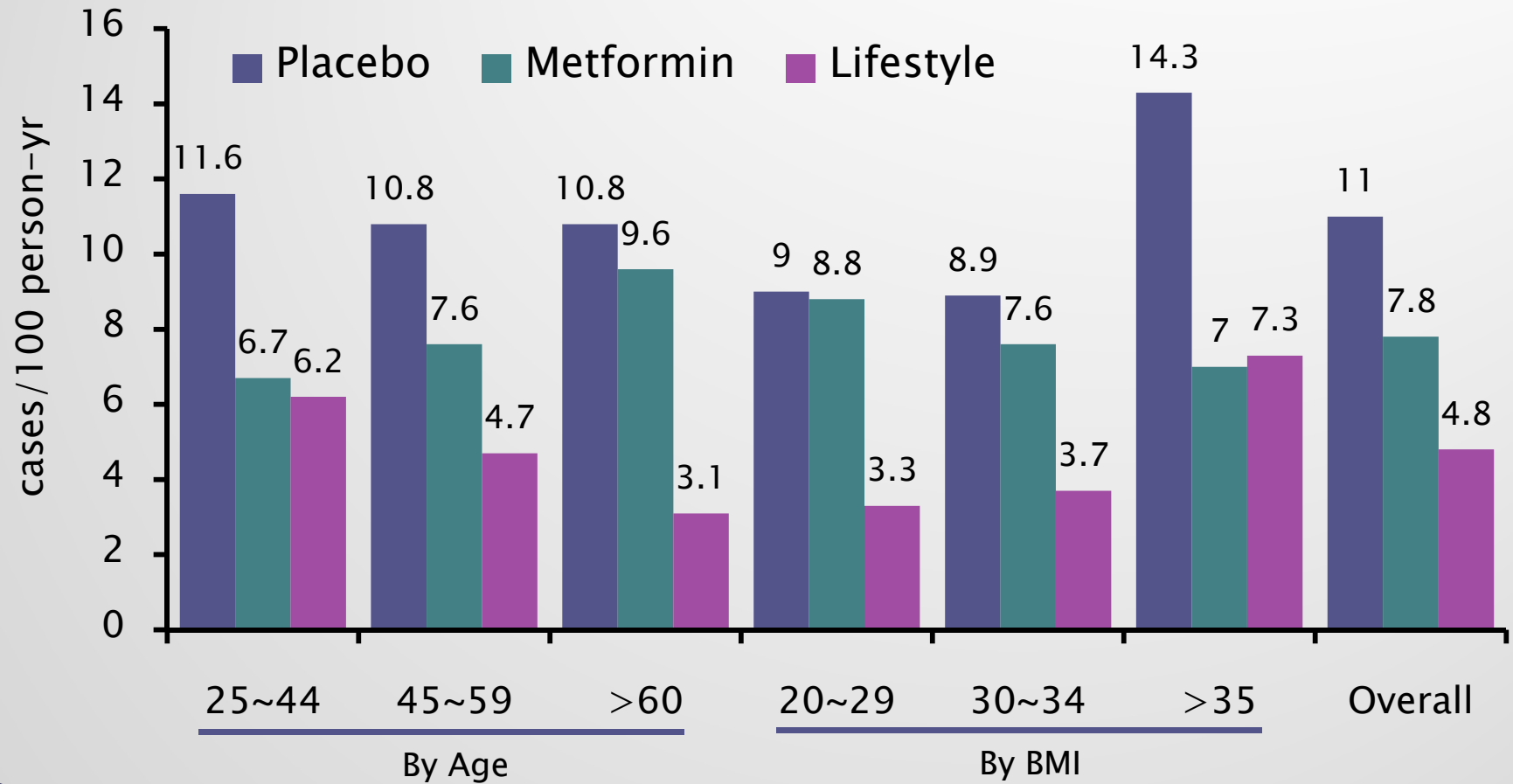
3234 nondiabetic persons with IFG and IGT with 2.8 Yr F/U

Placebo

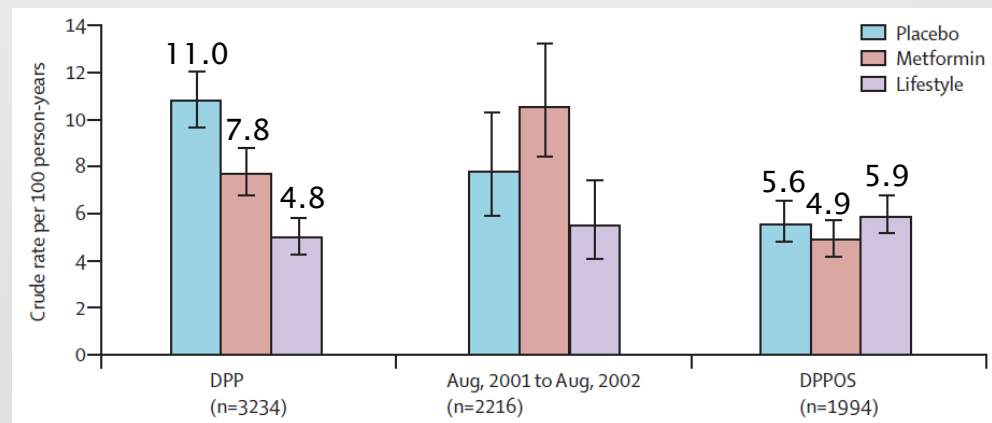
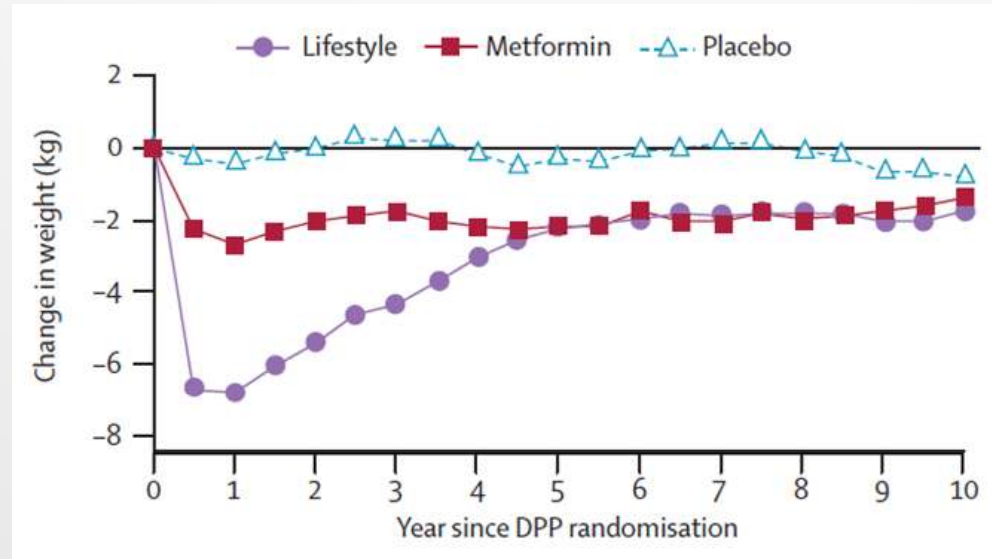
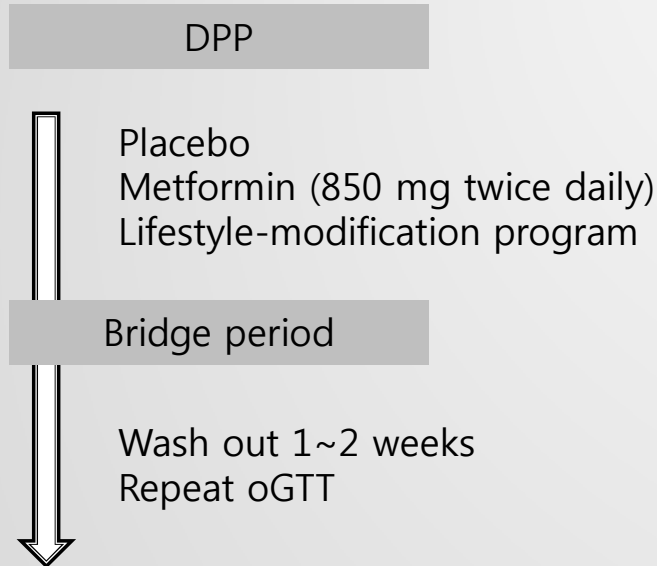
- Metformin (850 mg twice daily)
- Lifestyle-modification program:
 - At least a 7 percent weight loss
 - At least 150 minutes of physical activity per week







10 years after DPP



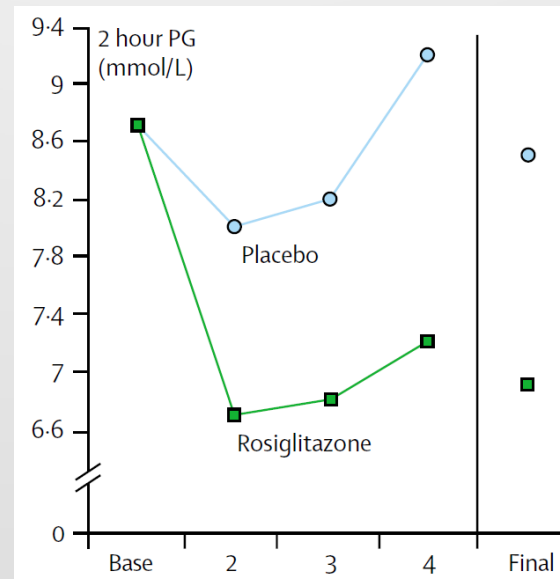
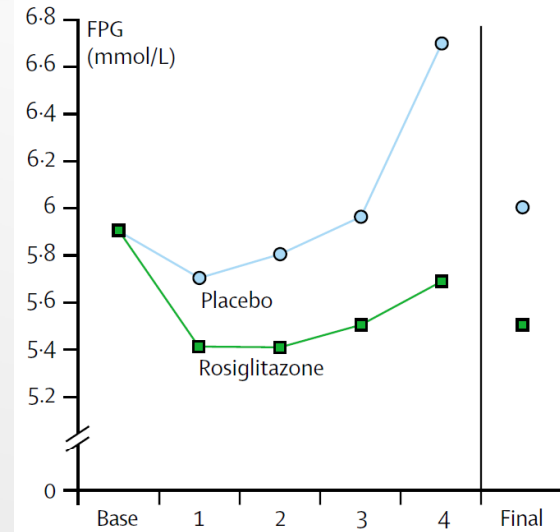
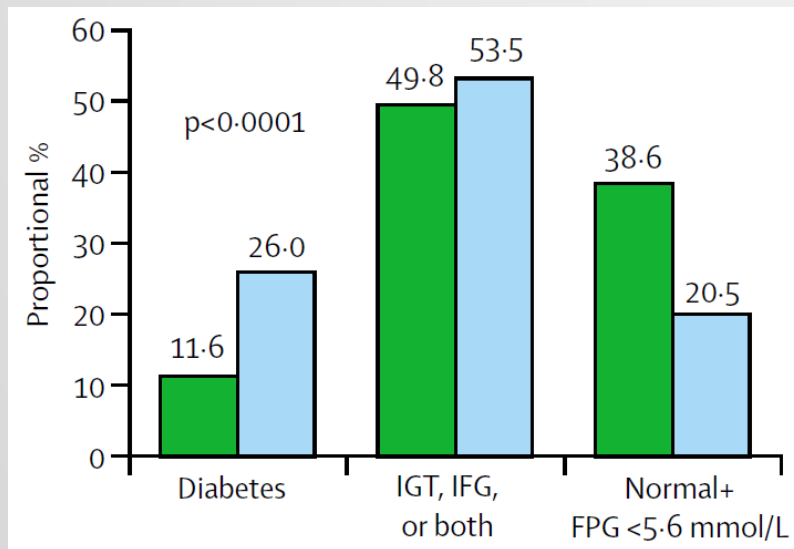
The DREAM Trial

(Diabetes REduction Assessment with ramipril and rosiglitazone Medication)

191 sites in 21 countries
5269 adults with IFG or IGT (No previous CVD)

- Rosiglitazone (8 mg daily; 2365)
- Placebo (2634)

Follow up: 3 years



SOS (Swedish Obese Subjects Study)

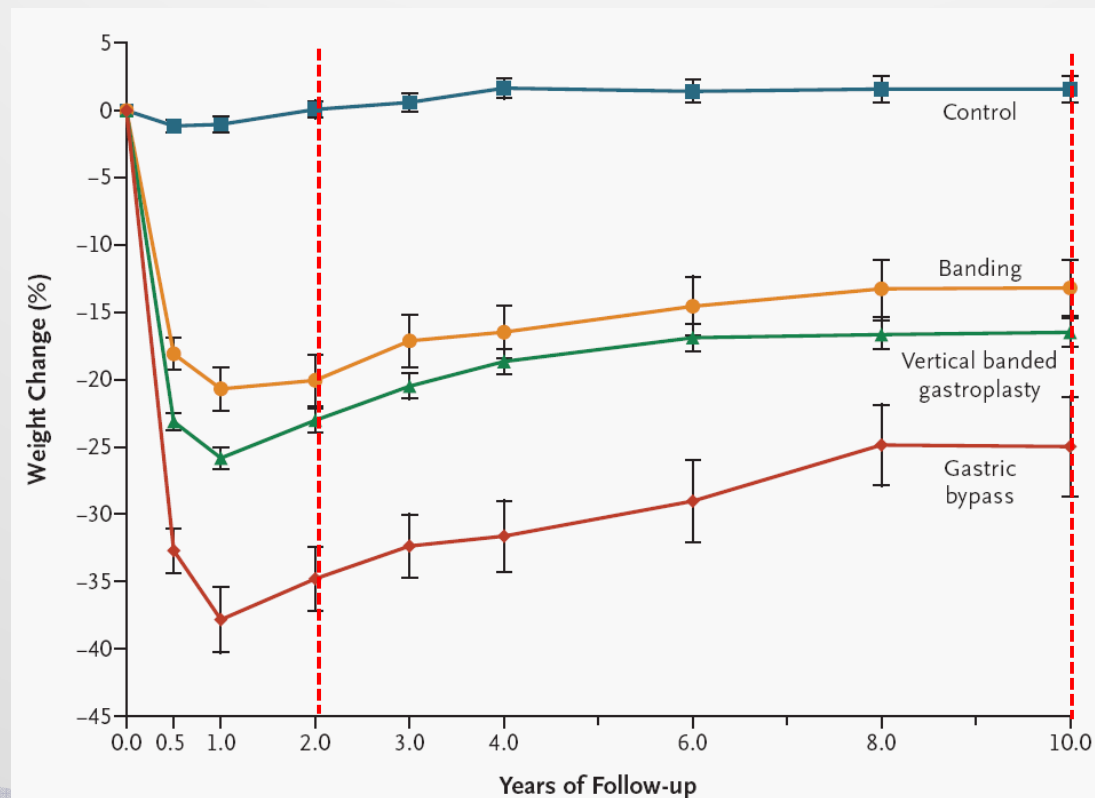
The prospective, controlled Swedish Obese Subjects Study

2 years and 10 years follow up

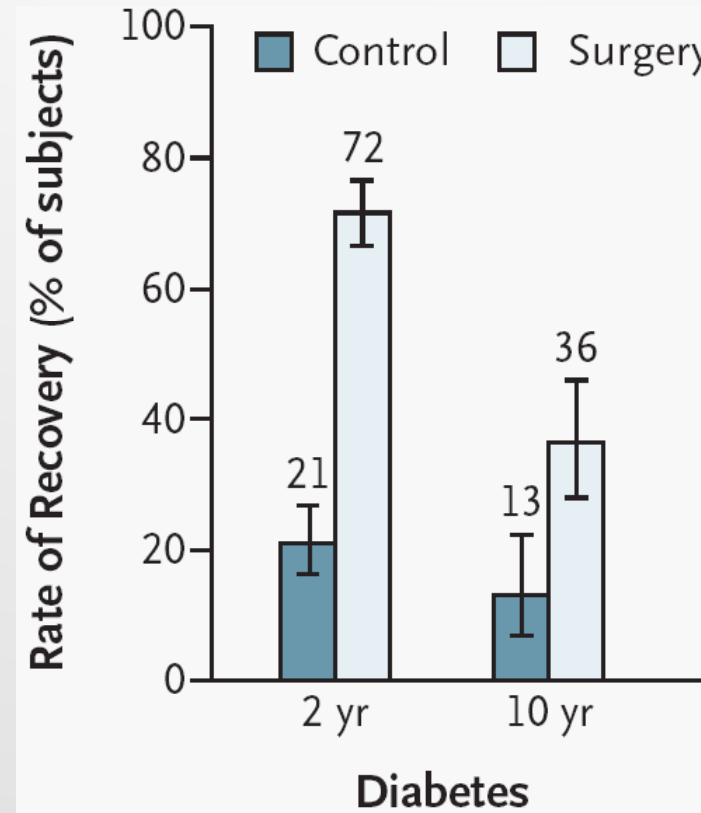
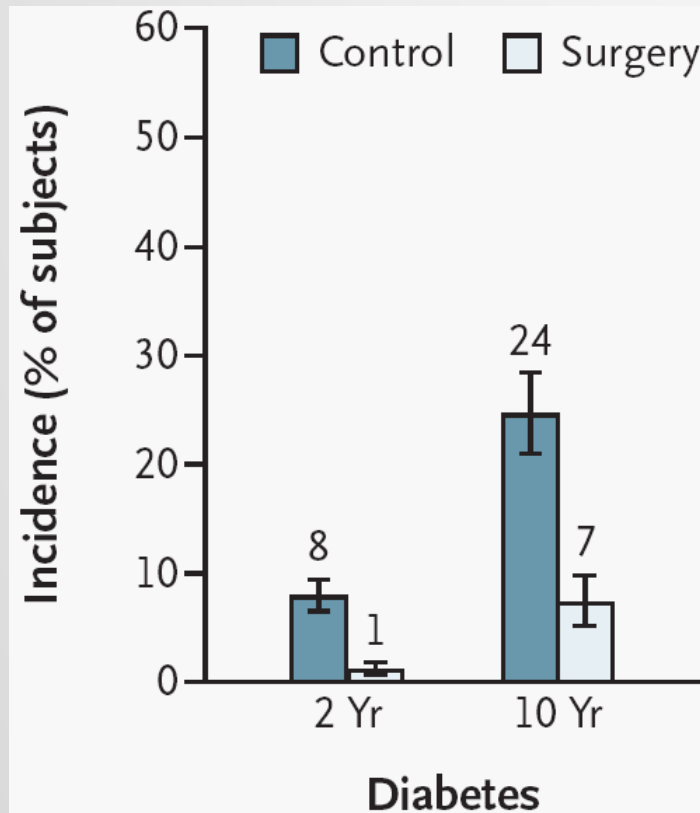
851 surgically treated subjects (BMI>40)

fixed or variable banding, vertical banded gastroplasty, or gastric bypass

852 obese control subjects (BMI>40)



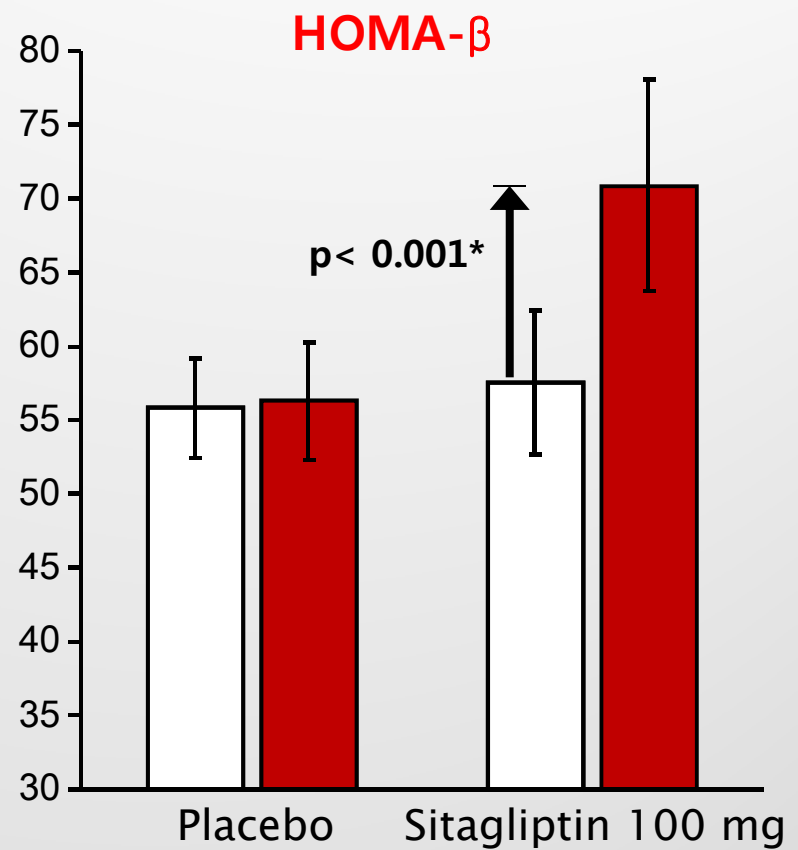
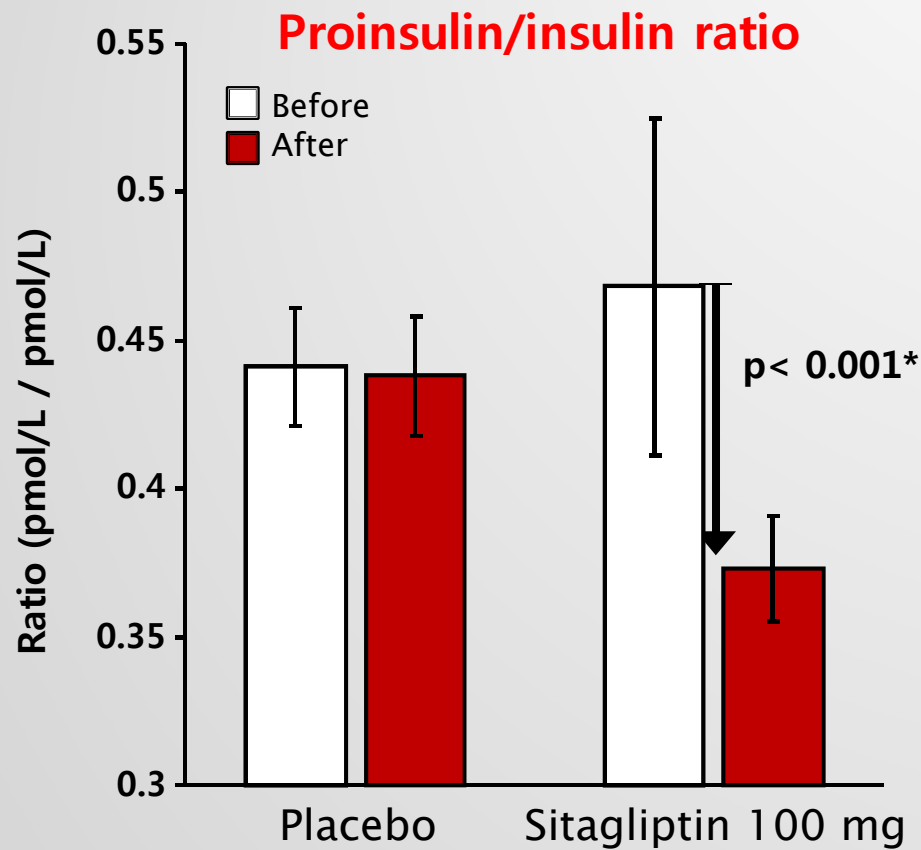
Incidence and Recovery rate



Other Trials

Study and therapy	Population	Length of therapy (yr)	Study parameter	Incidence of diabetes
TRIPOD Troglitazone	266 Hispanic females with history of gestational diabetes	2.5	OGTT and IVGTT	Troglitazone 5.4%, placebo 12.1%
XENDOS Orlistat	3305 obese patients with BMI >30 kg/m ² ; 21% had IGT	4	IGT	Orlistat 6.2%, placebo 9%
DREAM Ramipril	5269 multiethnic; female 58.5%, North America 40.8%	3	IGTT and IFP	Ramipril 17.1%, Placebo 18.5%
IDPP Metformin	531 Asian Indian; female 21%	30 months	IGT	Metformin 40.5%, placebo 55%
Voglibose Ph-3 study	Japanese female 40%; Average BMI 26	45 and 51.3 weeks	IGTT, IFP, A1c	Voglibose 5.6%, placebo 12%

DPPIV inhibitor Improved Markers of β -Cell Function



Summary and Conclusion

- ▶ Prediabetes
 - Progress to T2DM
 - Stop or Delay progression
 - Need to modulation
- ▶ Non-Pharmacologic Intervention
 - Weight reduction
 - Regular exercise
 - Diet Control
- ▶ Pharmacologic Intervention
 - Improve Insulin resistance
 - Preserve islet function

감사합니다.