Meet the Professor Session

Clinical implications of insulin resistance in Pre-diabetic stage

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46th Annual Conference of Endocrine Society of India

Moderator: Dr. Sudip Chatterjee

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23rd October 2016 1.50 - 2.40 pm

Department of Endocrinology and Diabetes,
Saitama Medical Center, Saitama Medical University

Matsuda, Masafumi

Endocrine Society of India

CV

Masafumi Matsuda, MD, PhD

Research Field:

Metabolism, Endocrinology, Insulin action, Regulation in hypothalamus

Professional Experience

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Resident: University of Tokyo Hospital Branch (Meziro, Tokyo, Japan, 1/10/1983)
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Clinical Instructor: Diabetes Division, UTHSCSA (San Antonio, Texas, USA, 3/1993)
Instructor: Diabetes Division, UTHSCSA (San Antonio, Texas, USA, 9/1/1994)
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Medical Research Director, Clinical Research Center, Texas Diabetes Institute (1997)
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Lecturer, Endocrine and Diabetes Division, Internal Medicine, Kawasaki Medical School, Kurashiki, Okayama, Japan (4/1/2000)
Director, Diabetes and Endocrine Department, Kameda Medical Center (1/1/2006)
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Degree, Licensure and Certification

Faculty of Medicine, The University of Tokyo, Bachelor of Medicine [M.D.]
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Fellow of the Japanese Society of Internal Medicine
Standard ECFMG Certificate (USA) USMLE Step 1, Step 2 and Step 3 passed (USA)

Works original articles 117 (total citation: 7220, *h*-index: 33 from Scopus)

Matsuda M, DeFronzo RA : Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22:1462-1470, 1999. (citation:>2600)
Matsuda M: Management of glucose levels in the hospital – theory and practice, Kanehara Ltd. Tokyo, Japan

DISCLOSURE

Name of First Author : Masafumi Matsuda, MD PhD

The authors have no financial conflicts of interest to disclose concerning the presentation.

Case A

- **56-year-old women, 151 cm, 51.6 kg: BMI 22.6 kg/m^2**

She visited the clinic with her daughter, because her result of health check revealed increased HbA1c and fasting PG.

BP 106/72mmHg, PR 81/min, waist 76cm
HbA1c 6.3%, PG 111mg/dL, Cr 0.53mg/dL, UA 4.6mg/dL
LDL-C 169mg/dL, TG 149mg/dL, HDL-C 69mg/dL
Urine: Protein(-), Glucose(-), Ketone(-)

<Diagnostic procedure>

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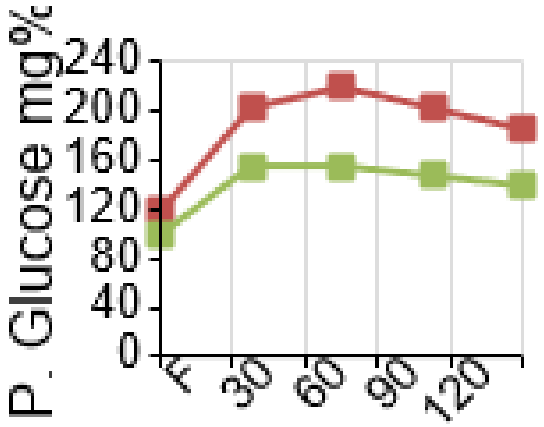
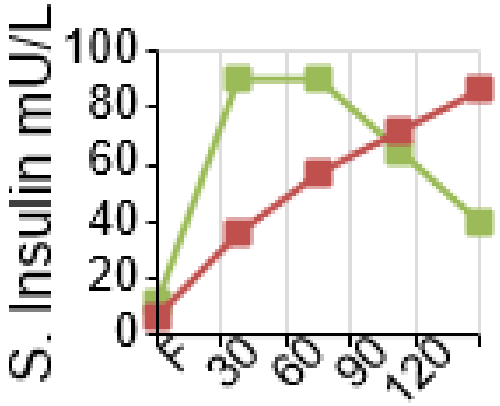
<Diagnostic procedure>
OGTT (75g oral glucose tolerance test)

Case A



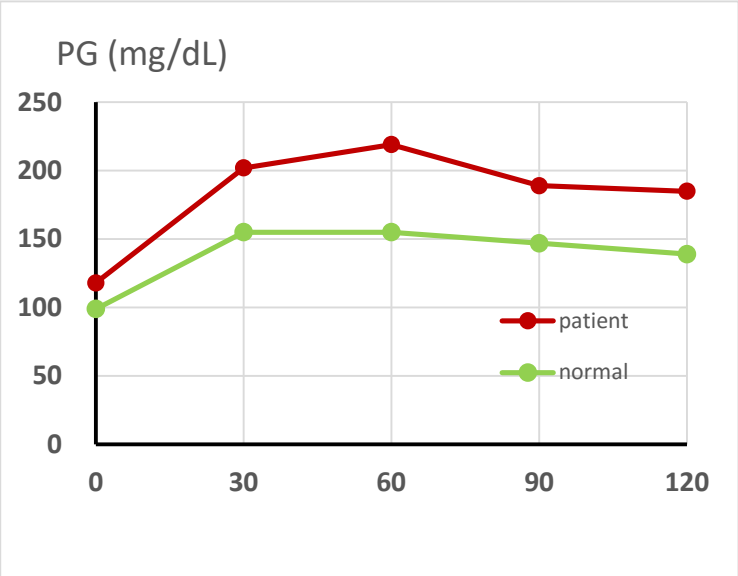


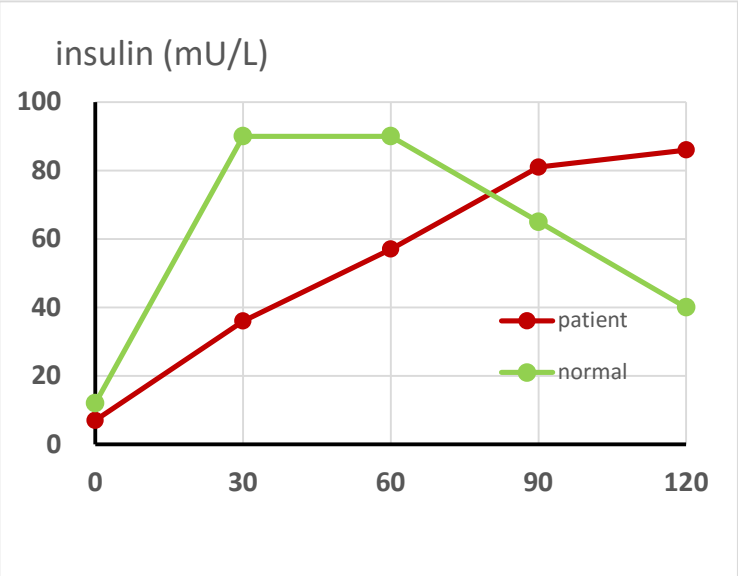
Green-Normal
Red-Patient

(powered by http://www.ogttplus.com ©2016 Dr.Suresh Shinde,MD.)

	PG (mg/dL)	Insulin (mU/L)
0 min	118	7
30 min	202	36
60 min	219	57
90 min	189	81
120 min	185	86

Case A





	PG (mg/dL)	Insulin (mU/L)
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Matsuda Index	3.40	>2.5
HOMA-IR	2.04	<2.5
Insulinogenic Index	0.35	>0.4
Disposition Index (IGI*ISI)	1.17	>1.0
SigmaI /SigmaG	0.290	>0.10

Diagnosis: impaired glucose tolerance
(increased FPG
and postprandial hyperglycemia)

Pathophysiology: decreased insulin secretion
(beta-cell damages)

What should we do to prevent further damage to pancreatic beta-cells?

Case A

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<Therapeutic procedure>

1400 kcal/day diet, moderate exercise

?

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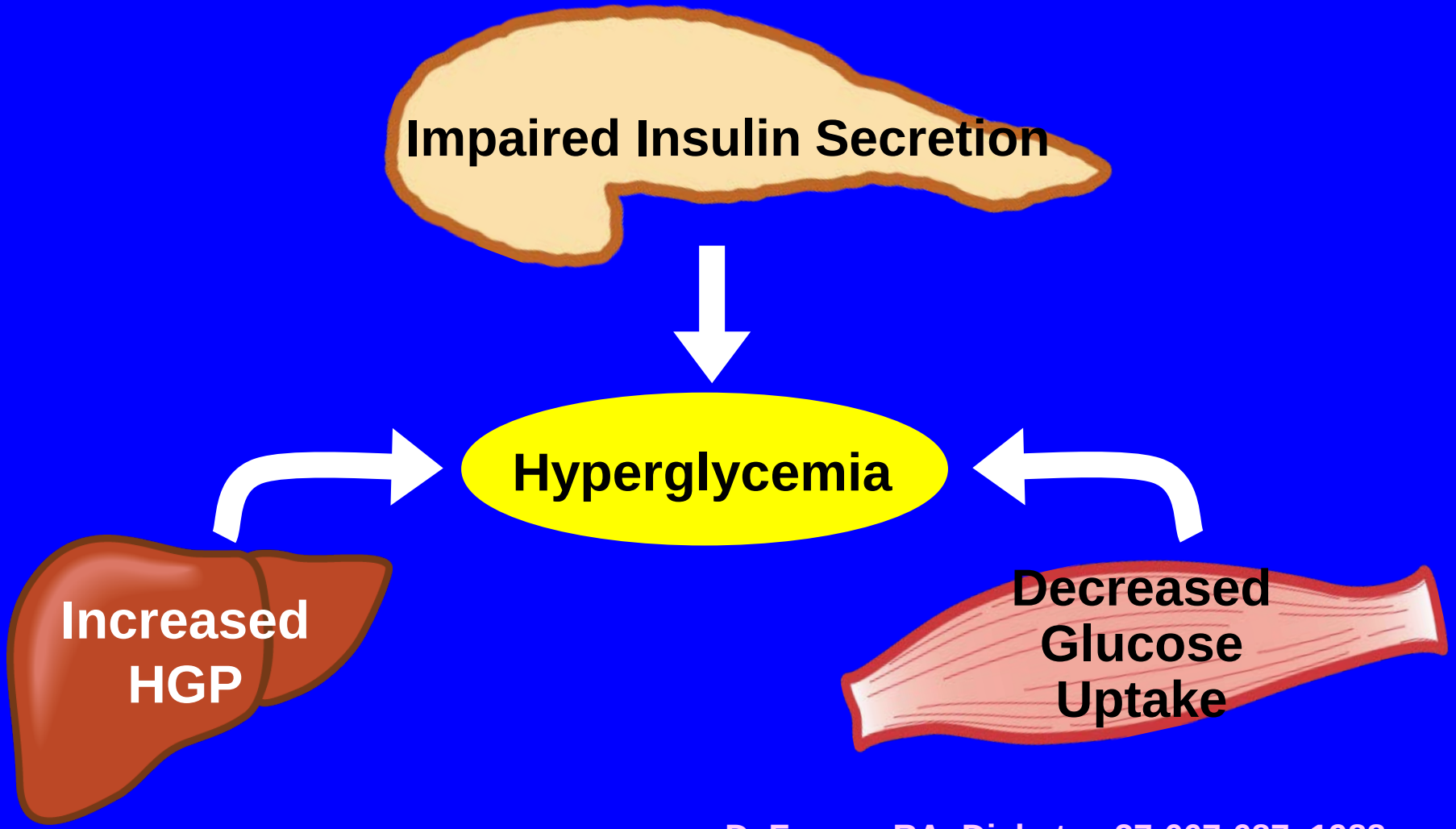
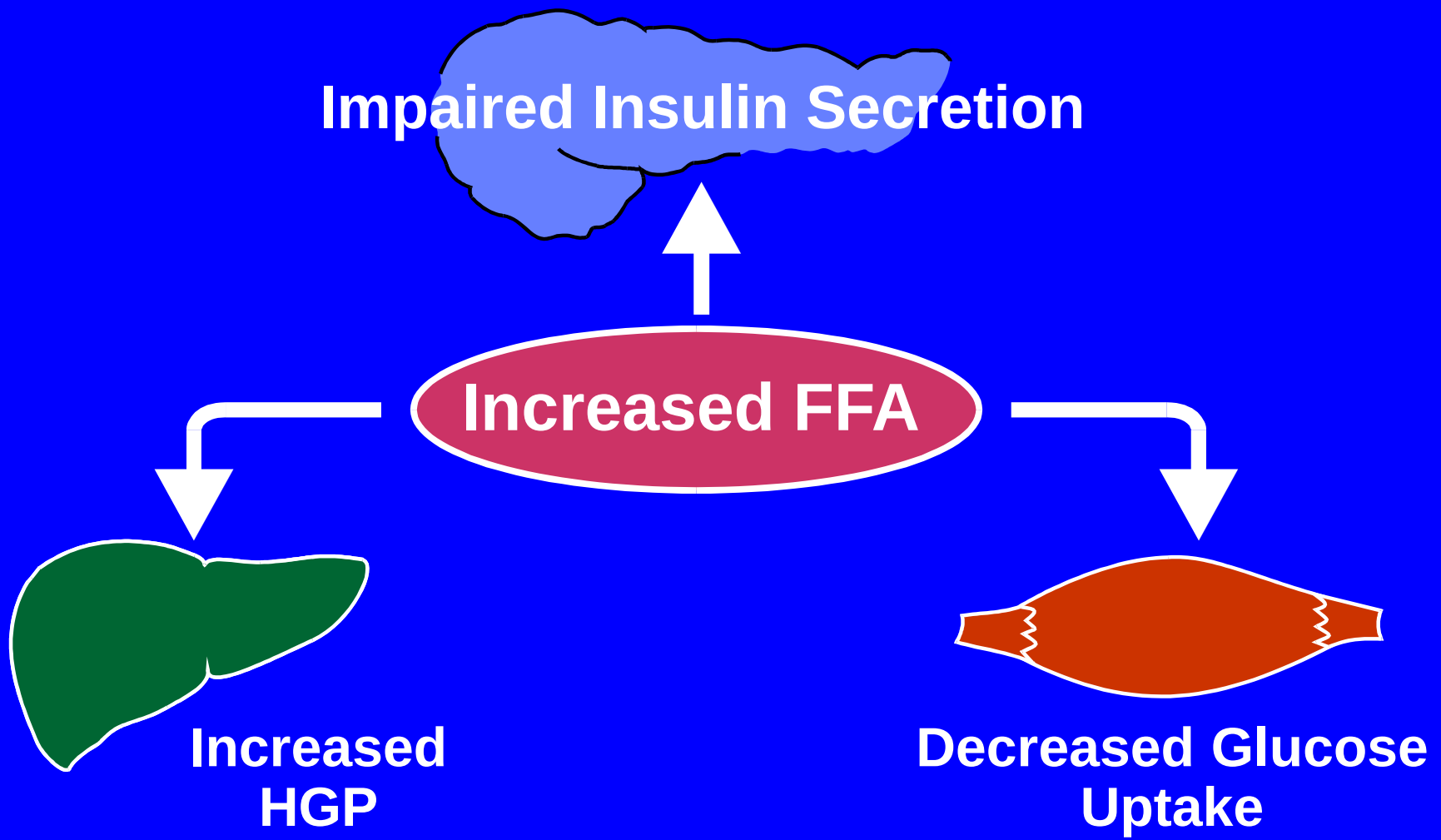
1400 kcal/day diet, moderate exercise
<u>voglibose 0.2mg tid</u>

THE TRIUMVIRATE

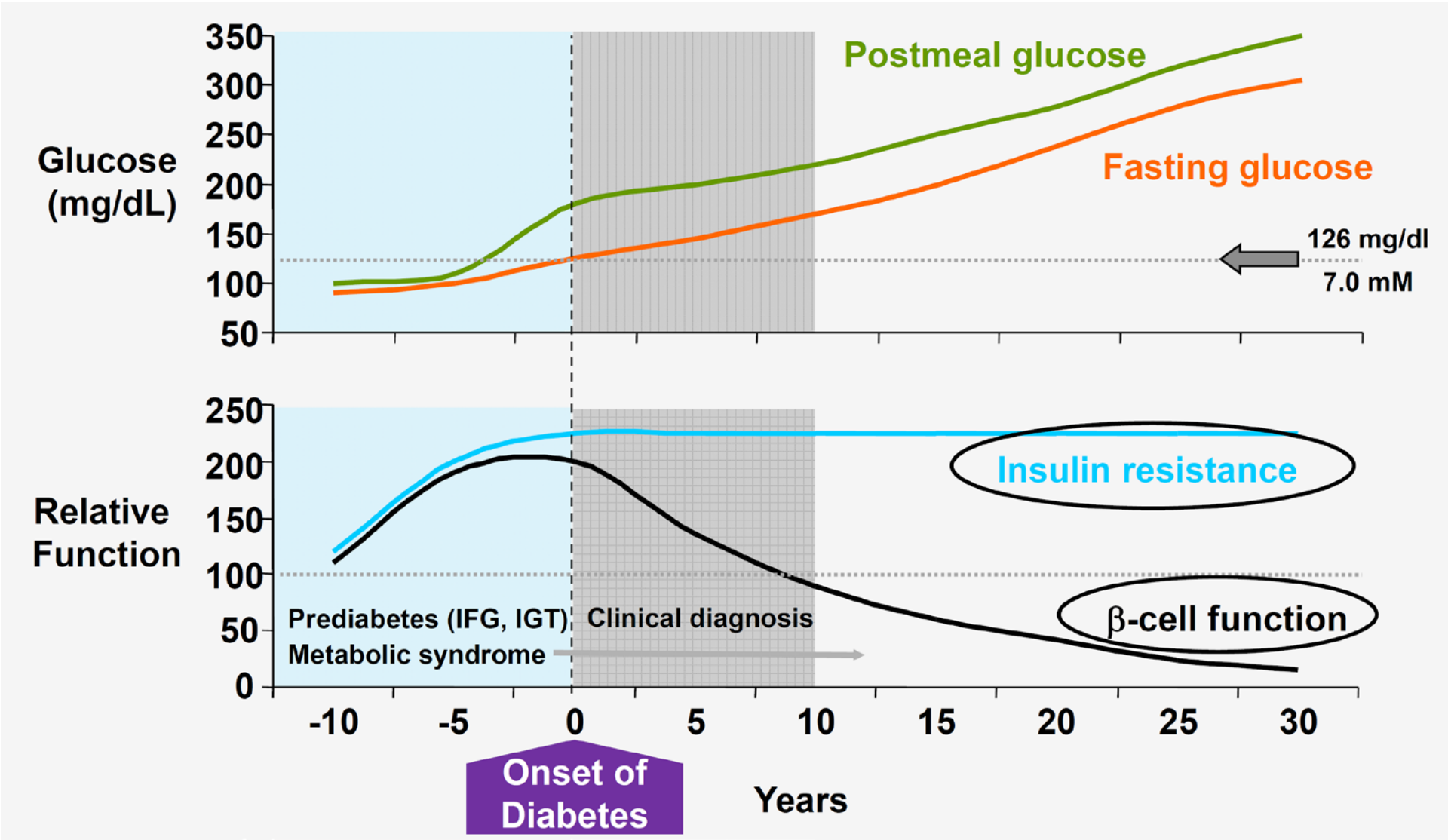


DeFronzo RA, Diabetes 37:667-687, 1988

ETIOLOGY OF T2DM



Natural History of Type 2 Diabetes Mellitus



Lifestyle Modification Intervention

- **Lifestyle intervention continues to have an effect, even after 20 years**

Study		N	Intervention	Treatment	Risk Reduction
Da Qing[1,2]	IGT	577	Lifestyle	6 years 20 years	34% - 69%
Finnish DPS[3,4]	IGT	523	Lifestyle	3+ years 7 years	58%
Diabetes Prevention Program (DPP)[5,6]	IGT	3324	Lifestyle	3 years 10 years	58% 34%

1. *Diabetes Care*. 1997;20:537-544.
2. *Lancet*. 2008;371:1783-1789.
3. *N Engl J Med*. 2001;344:1343-1350.
4. *Lancet*. 2006;368:1673-1679.
5. *N Engl J Med*. 2002;346:393-403.
6. *Lancet*. 2009;374:1677-1686.

Intervention Studies to Prevent T2D

Trial	publication	follow-up, year	drug	No. of new on-set of DM	No.(total)	event per 1000 person-years	control	No. of new on-set of DM	No.(total)	event per 1000 person-years
Thiazolidine										
*DPP	2005	0.9	Troglitazone	10	387	28.7	Placebo Metformin ILS	37 21 16	391 397 393	105.1 58.8 45.2
TRIPOD	2002	2.5	Troglitazone	17	114	59.6	Placebo	37	122	121.3
PIPOD	2006	3.0	Pioglitazone	11	86	42.6	-			
*DREAM	2006	3.0	Rosiglitazone	306	2365	43.1	Placebo	686	2634	86.8
*ACTNOW	2008	4.0	Pioglitazone	10	303	8.3	Placebo	45	299	37.6
*CANOE	2010	3.9	Met+Rosi	14	103	34.9	Placebo	41	104	101.1
Other (α-GI, statin, fibrate, glinide)										
WOSCOP	2001	5.0	Pravastation	57	2999	3.8	Placebo	82	3975	5.5
*STOP- NIDDM	2002	3.3	Acarbose	221	682	98.2	Placebo	285	686	125.9
BIP	2004	6.2	Bezafibrate	66	156	68.2	Placebo	80	147	87.8
*VICTORY	2009	4.0	Voglibose	50	897	13.9	Placebo	106	881	30.0
*NAVIGATOR	2010	6.5	Nateglinide	1674	3726	69.1	Placebo	1580	3747	64.9

*: pre-specfied outcome

Matsuda M.;GEKKAN TOUNYOUBYOU;2,16-22,2010 2:16-22, 2010.

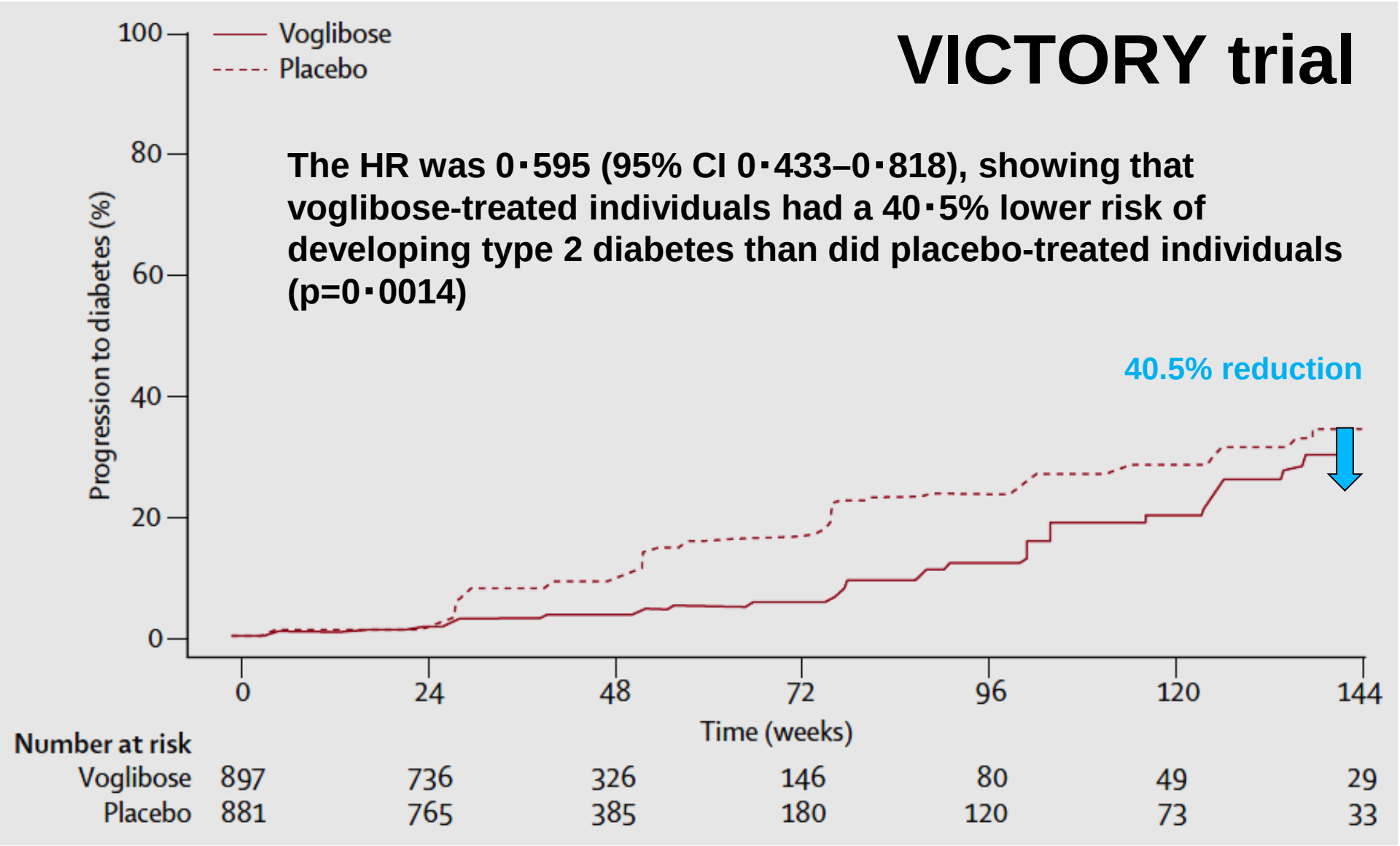
Prevention of Diabetes Mellitus

Trial	publication	follow-up, year	drug	No. of new on-set of DM	No.(total)	event per 1000 person-years	control	No. of new on-set of DM	No.(total)	event per 1000 person-years
antihypertensive drug										
CAPPP	1999	6.1	ACEI	337	5183	10.7	β blocker	380	5230	11.9
STOP-2	1999	4.0	ACEI	93	1970	11.8	β blocker Diuretic CCB	97 95	1960 1935	12.4 12.1
HOPE	2001	4.5	ACEI	102	2837	8.0	Placebo	155	2883	11.9
ALLHAT	2002	4.0	ACE	119	4096	7.3	CCB Diuretic	154 302	3954 6766	9.7 11.2
PEACE	2004	4.8	ACEI	335	3432	20.3	Placebo	399	3472	23.9
ANBP-2	2005	4.1	ACEI	138	2800	12.0	Diuretic	200	2826	17.3
AASK	2006	3.8	ACEI	45	410	28.9	β blocker CCB	70 32	405 202	45.5 41.7
*DREAM	2006	3.0	ACEI	449	2623	57.1	Placebo	489	2646	61.6
LIFE	2002	4.8	ARB	242	4020	12.5	β blocker	320	3979	16.8
*ALPINE	2003	1.0	ARB	1	196	5.1	Diuretic	8	196	40.8
CHARM	2003	3.1	ARB	163	2715	19.4	Placebo	202	2721	23.9
SCOPE	2003	3.7	ARB	93	2167	11.6	Placebo	115	2175	14.3
VALUE	2004	4.2	ARB	690	5087	32.3	CCB	845	5074	39.7
CASE-J	2007	3.2	ARB	38	1343	8.8	CCB	59	1342	13.7
*ProFESS	2008	2.5	ARB	125	7306	6.8	Placebo	151	7283	8.3
*ONTARGET	2008	4.7	ARB	399	8542	10.0	ACEI	366	8576	9.2
*ONTARGET	2008	4.7	ARB +ACEI	323	8502	8.1	ACEI	366	8576	9.2
*TRANSCEND	2008	4.7	ARB	319	2954	26.4	Placebo	395	2972	28.8
*HIJ-CREATE	2009	4.2	ARB	7	645	2.6	Placebo	18	624	6.9
*Kyoto Heart	2009	3.27	ARB+X	58	1116	51.6	X	86	998	76.7
*NAVIGATOR	2010	6.5	ARB	1532	3748	62.9	Placebo	1722	3725	71.1

Matsuda M.; Endocrinology＆Diabetology;26,1,35-41,2008.

VICTORY trial

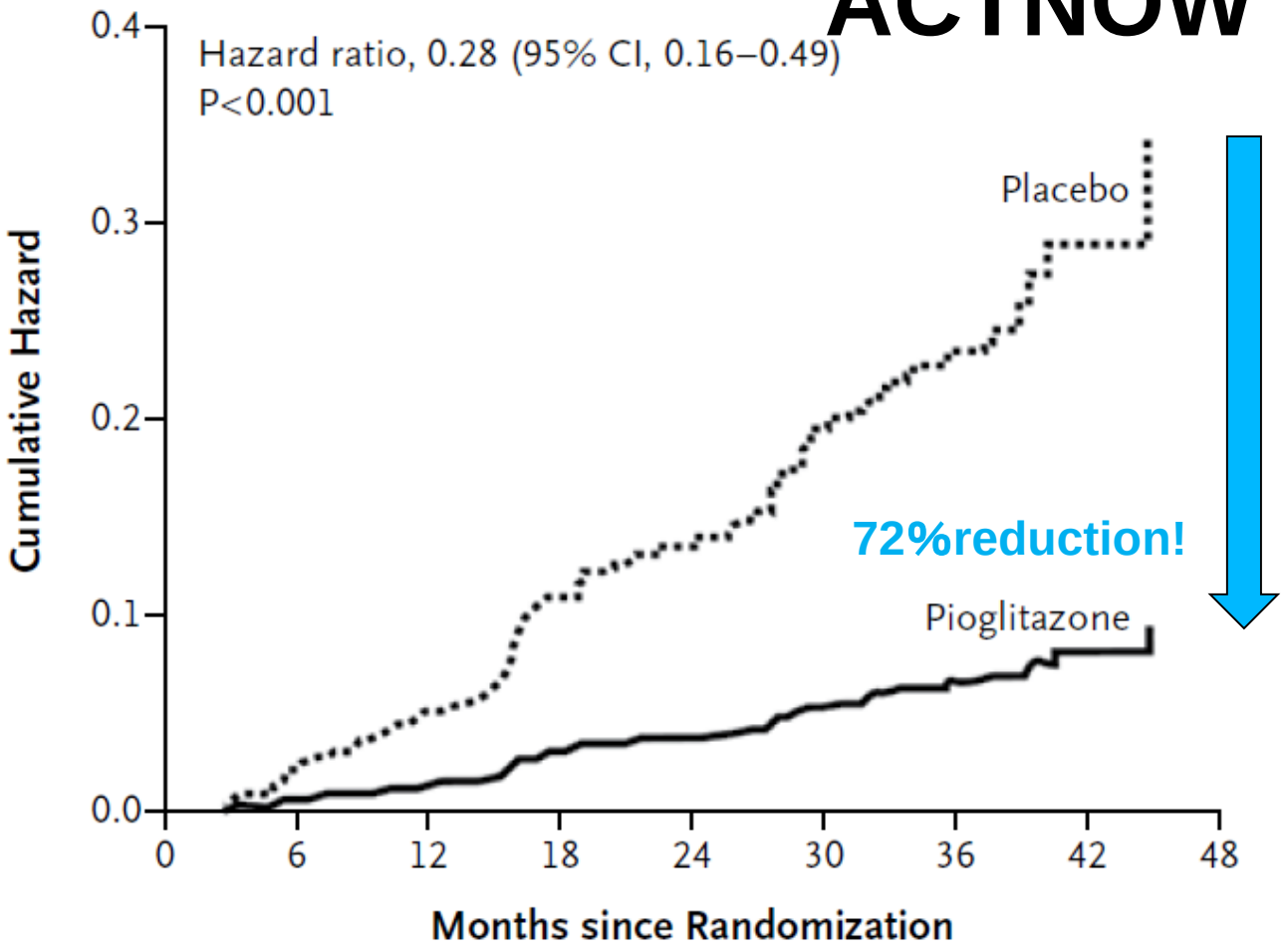
The HR was 0·595 (95% CI 0·433–0·818), showing that voglibose-treated individuals had a 40·5% lower risk of developing type 2 diabetes than did placebo-treated individuals (p=0·0014)



Effect of voglibose and placebo on the cumulative probability of individuals developing type 2 diabetes (Kaplan–Meier method)

Kawamori R, Tajima N, Iwamoto Y, Kashiwagi A, Shimamoto K, Kaku K; Voglibose Ph-3 Study Group.: Voglibose for prevention of type 2 diabetes mellitus: a randomised, double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet. 2009 May 9;373(9675):1607-14.

ACTNOW trial

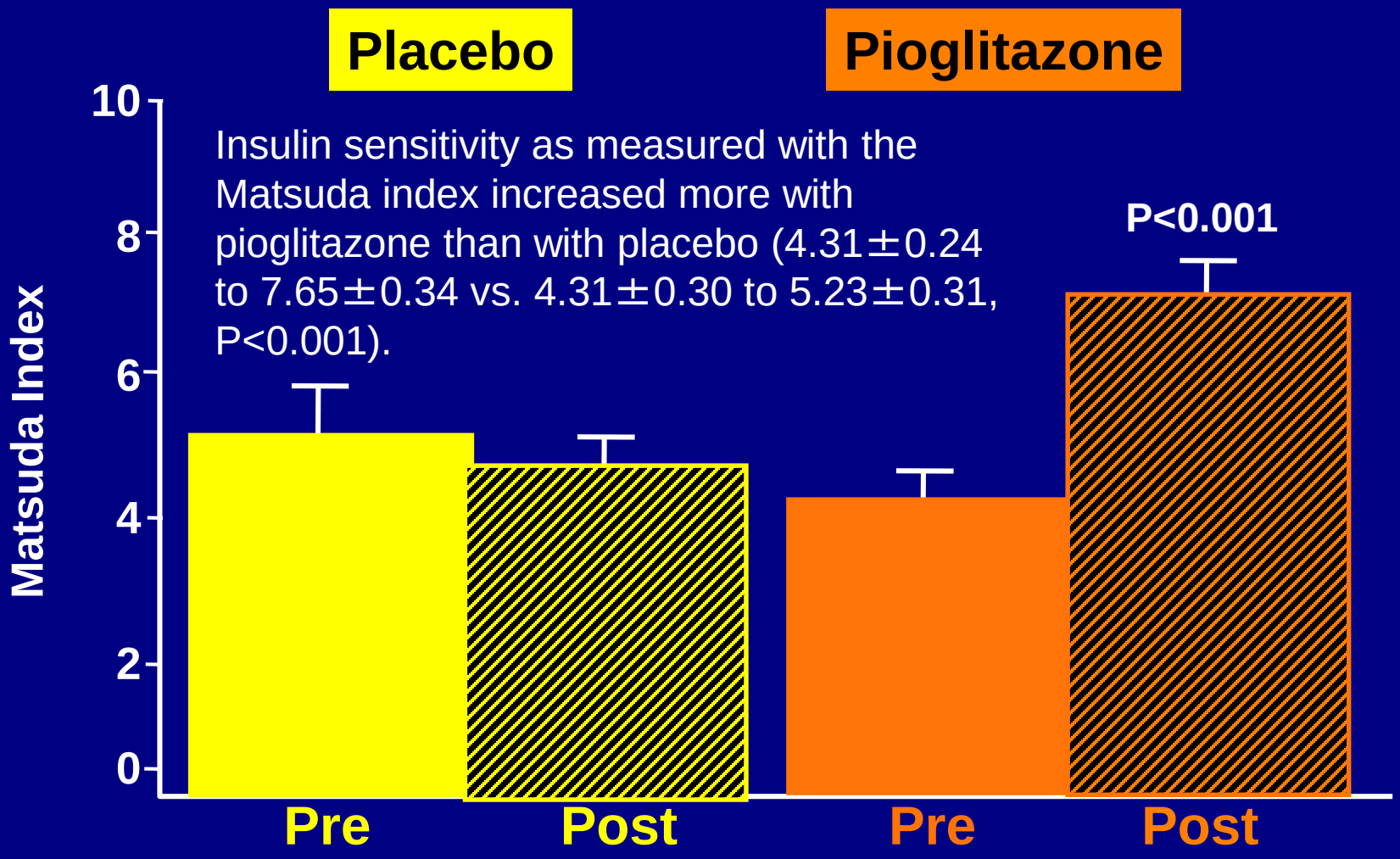


No. at Risk								
Placebo	299	259	228	204	191	134	83	17
Pioglitazone	303	262	244	228	218	140	87	24

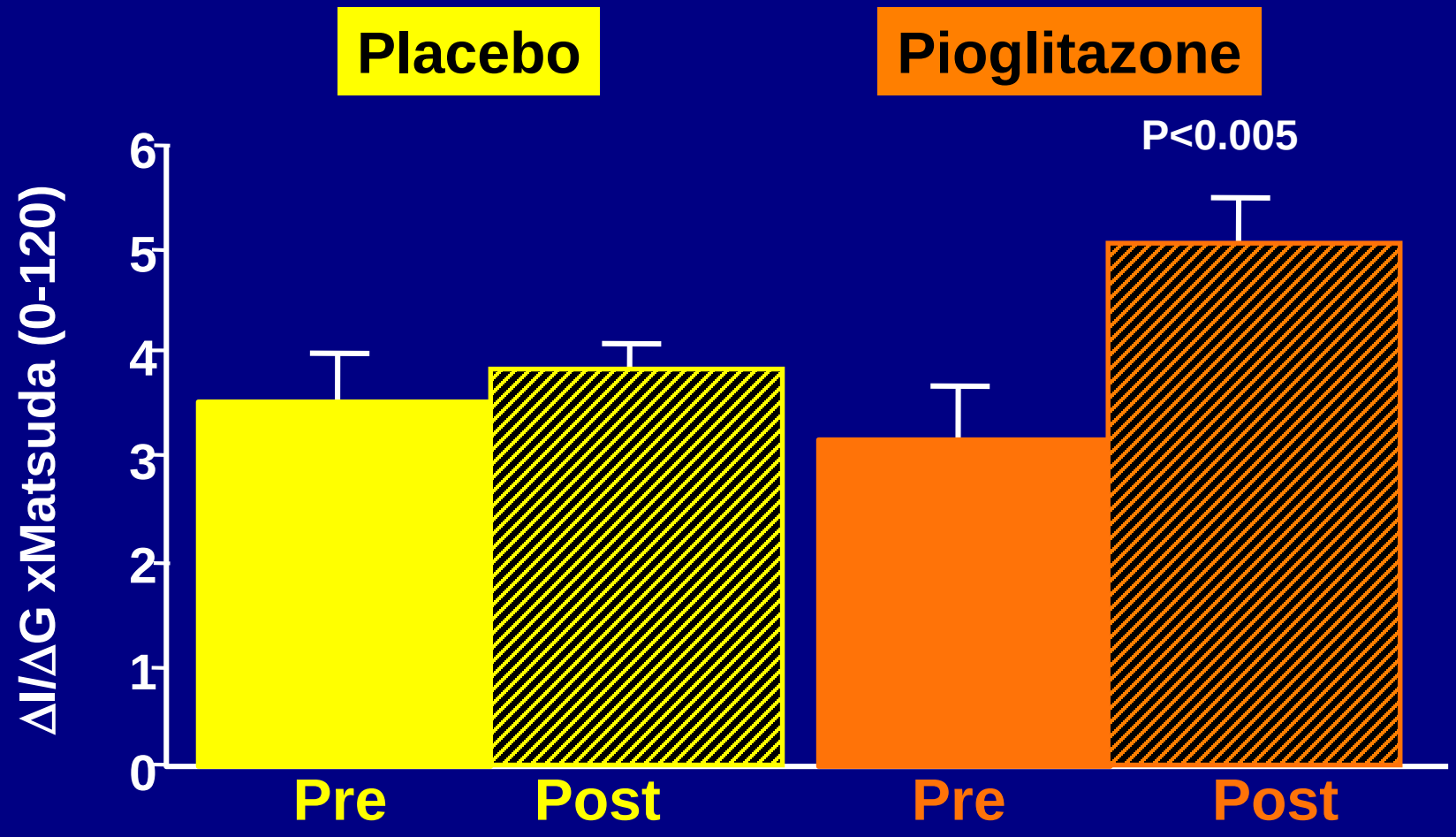
Figure 2. Kaplan–Meier Plot of Hazard Ratios for Time to Development of Diabetes.

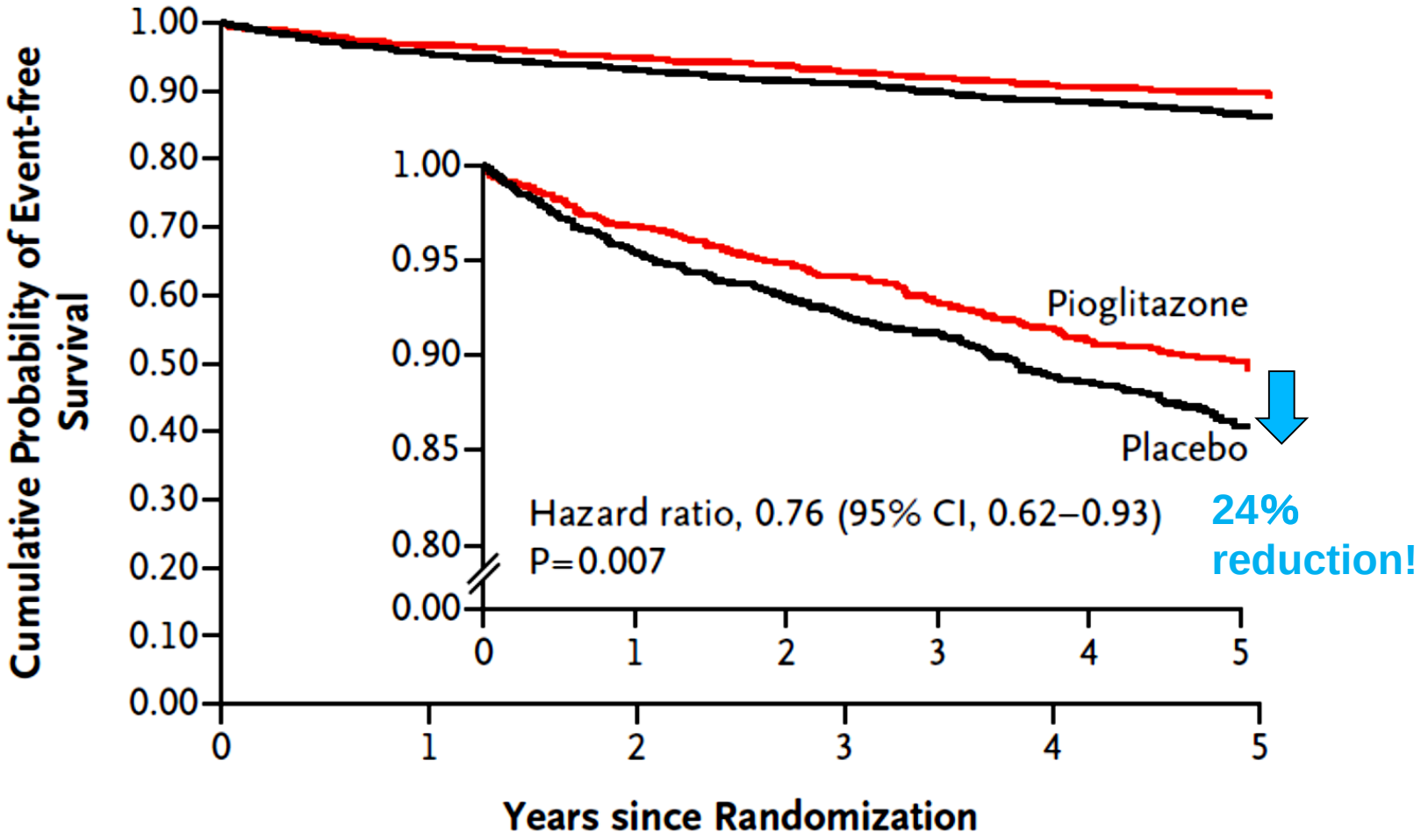
N Engl J Med 2011;364:1104-15.

EFFECT OF PIOGLITAZONE AND PLACEBO ON MATSUDA INDEX OF INSULIN SENSITIVITY



EFFECT OF PIOGLITAZONE AND PLACEBO ON INSULIN SECRETION / INSULIN RESISTANCE INDEX



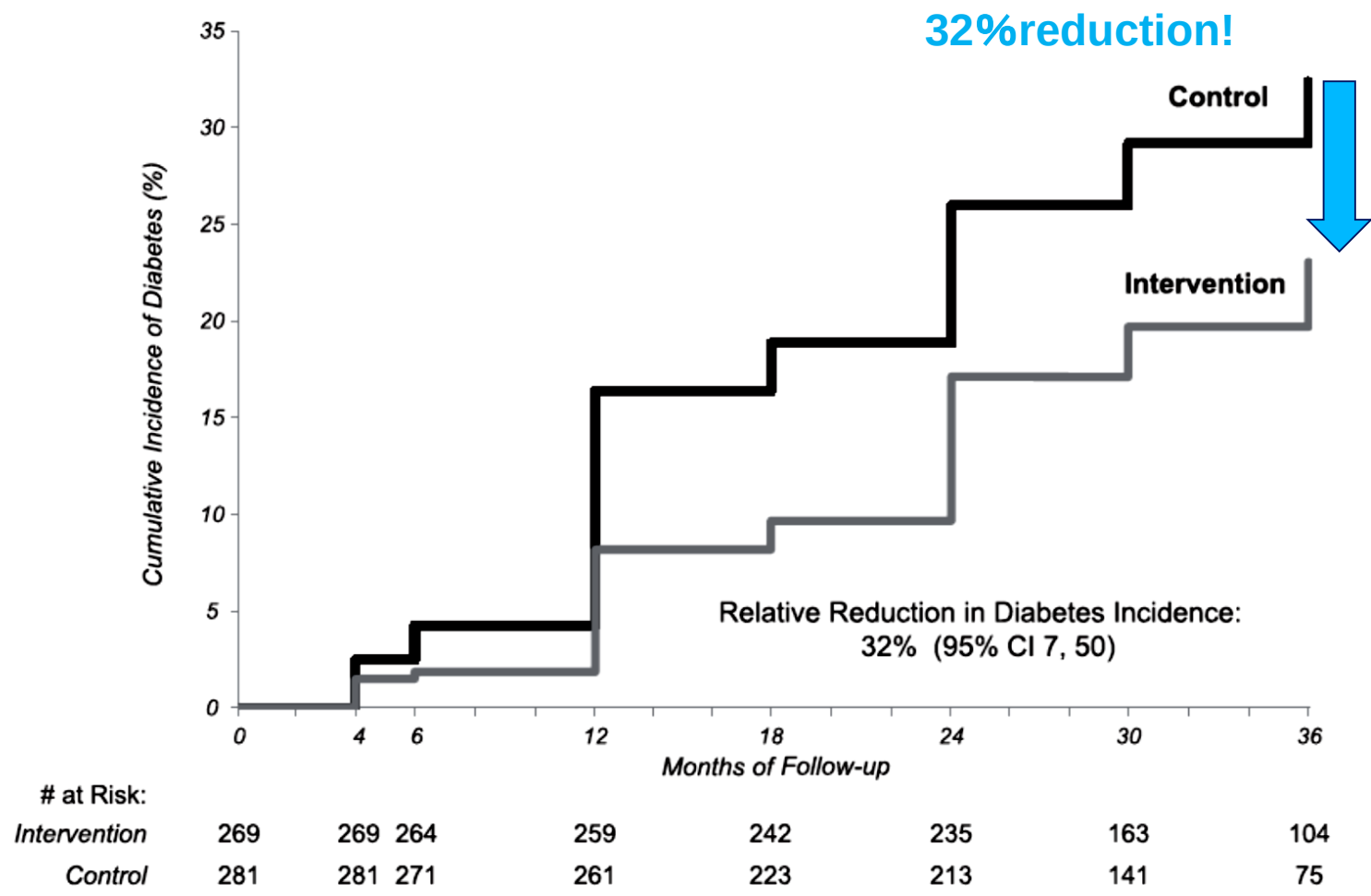


No. at Risk

Pioglitazone	1939	1793	1701	1491	1196	481
Placebo	1937	1778	1690	1476	1182	459

Figure 1. Primary Outcome. By 5 years, the primary outcome (fatal or nonfatal stroke or fatal or nonfatal myocardial infarction) had occurred in 175 of 1939 patients (9.0%) in the pioglitazone group and in 228 of 1937 (11.8%) in the placebo group. The inset shows the same data on an enlarged y axis. The numbers at risk were the numbers of patients who were alive without an event and still being followed at the beginning of each time point. **N Engl J Med. 2016 Apr 7;374(14):1378-9.**

At 4 months or later (after the core lifestyle curriculum was completed), intervention participants were prescribed metformin at a dose of 500 mg twice daily if they were considered at high risk of converting to diabetes, defined as having IFG+IGT or IFG+ HbA1c$5.7% (39mmol/mol).



Cumulative incidence of diabetes by study arm in the D-CLIP trial from baseline to year 3.

Weber MB, Ranjani H, Staimez LR, Anjana RM, Ali MK, Narayan KM, Mohan V.: The Stepwise Approach to Diabetes Prevention: Results From the D-CLIP Randomized Controlled Trial. Diabetes Care. 2016 Oct;39(10):1760-7.

Message

It may be reasonable to use drugs that reduce insulin resistance or beta-cell hyper function to prevent beta-cell damages even to subjects who may not have apparent insulin resistance.

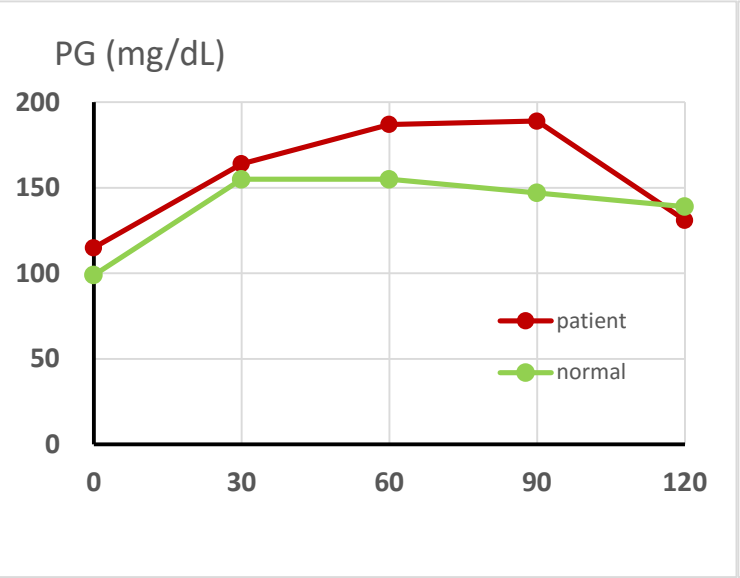
Case A
one year later

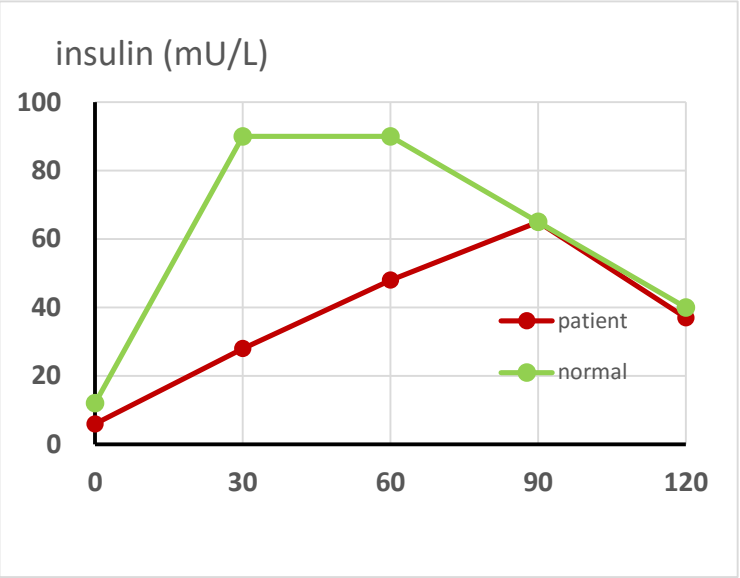
- **57-year-old women, 151 cm, 53.1 kg: BMI 23.3 kg/m^2**
  She visited the clinic for a routine check-up.

  BP 100/68mmHg, PR 79/min
  HbA1c 6.5%, PG 115mg/dL, Cr 0.59mg/dL, UA 4.4mg/dL
  LDL-C 163mg/dL, TG 205mg/dL, HDL-C 69mg/dL
  Urine: Protein(-), Glucose(-), Ketone(-)

  <Diagnostic procedure>
  OGTT (75g oral glucose tolerance test)

Case A
one year later





	PG (mg/dL)	Insulin (mU/L)
0 min	115	6
30 min	164	28
60 min	187	48
90 min	189	65
120 min	131	37

			A year before
Matsuda Index	4.64	>2.5	3.40
HOMA-IR	1.70	<2.5	2.04
Insulinogenic Index	0.45	>0.4	0.35
Disposition Index (IGI*ISI)	2.08	>1.0	1.17
SigmaI /SigmaG	0.245	>0.10	0.290

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  <Therapeutic procedure>
  1400 kcal/day diet, moderate exercise
  voglibose 0.2mg tid
  ?

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  Urine: Protein(-), Glucose(-), Ketone(-)

  <Therapeutic procedure>
  1400 kcal/day diet, moderate exercise
  voglibose 0.2mg tid
  atorvastatin 10mg qd

Case A
two years later

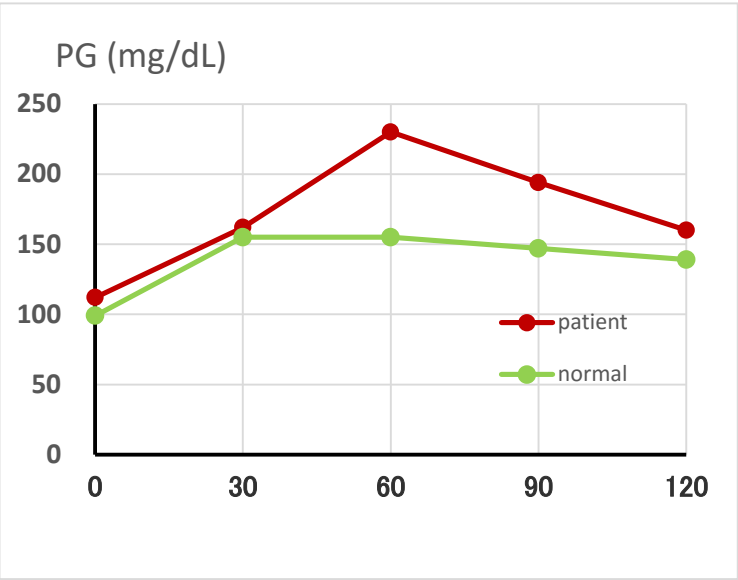
- **58-year-old women, 151 cm, 53.0 kg: BMI 23.3 kg/m^2**

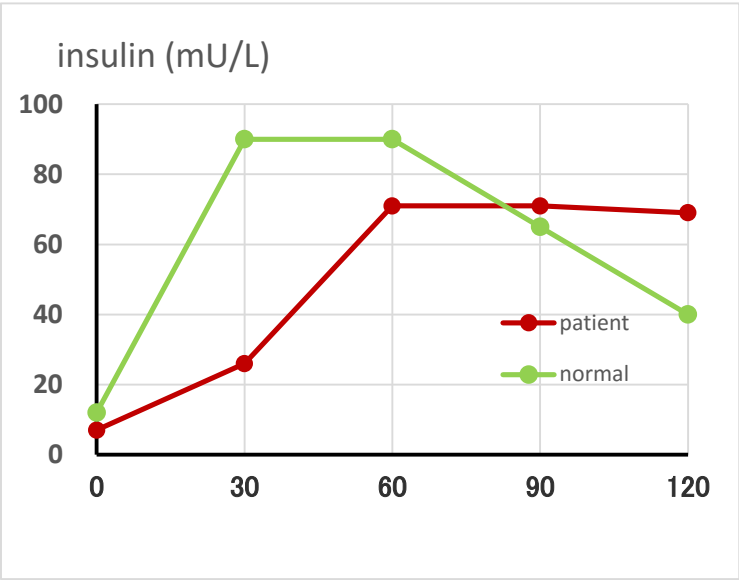
  She visited the clinic for a routine check-up.

  BP 122/53mmHg, PR 72/min
  HbA1c 7.1%, PG 112mg/dL, Cr 0.50mg/dL, UA 4.8mg/dL
  LDL-C 100mg/dL, TG 100mg/dL, HDL-C 76mg/dL
  Urine: Protein(-), Glucose(-), Ketone(-)

  <Therapeutic procedure>
  1400 kcal/day diet, moderate exercise
  voglibose 0.2mg tid
  atorvastatin 10mg qd

Case A
two years later





	PG (mg/dL)	Insulin (mU/L)
0 min	112	7
30 min	162	26
60 min	230	71
90 min	194	71
120 min	160	69

			A year before	Two years before
Matsuda Index	3.70	>2.5	4.64	3.40
HOMA-IR	1.94	<2.5	1.70	2.04
Insulinogenic Index	0.38	>0.4	0.45	0.35
Disposition Index (IGI*ISI)	1.41	>1.0	2.08	1.17
SigmaI /SigmaG	0.285	>0.10	0.245	0.290

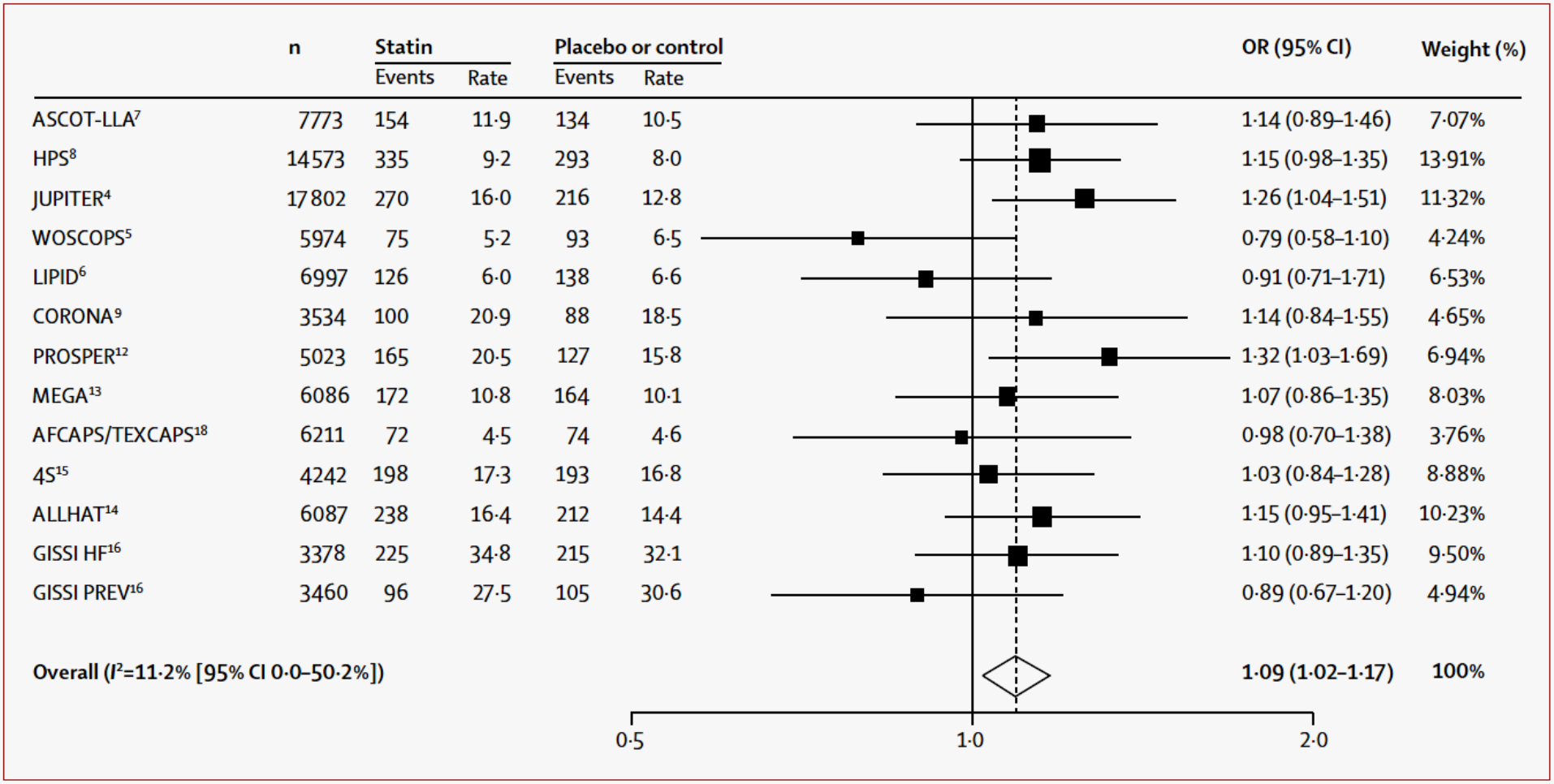
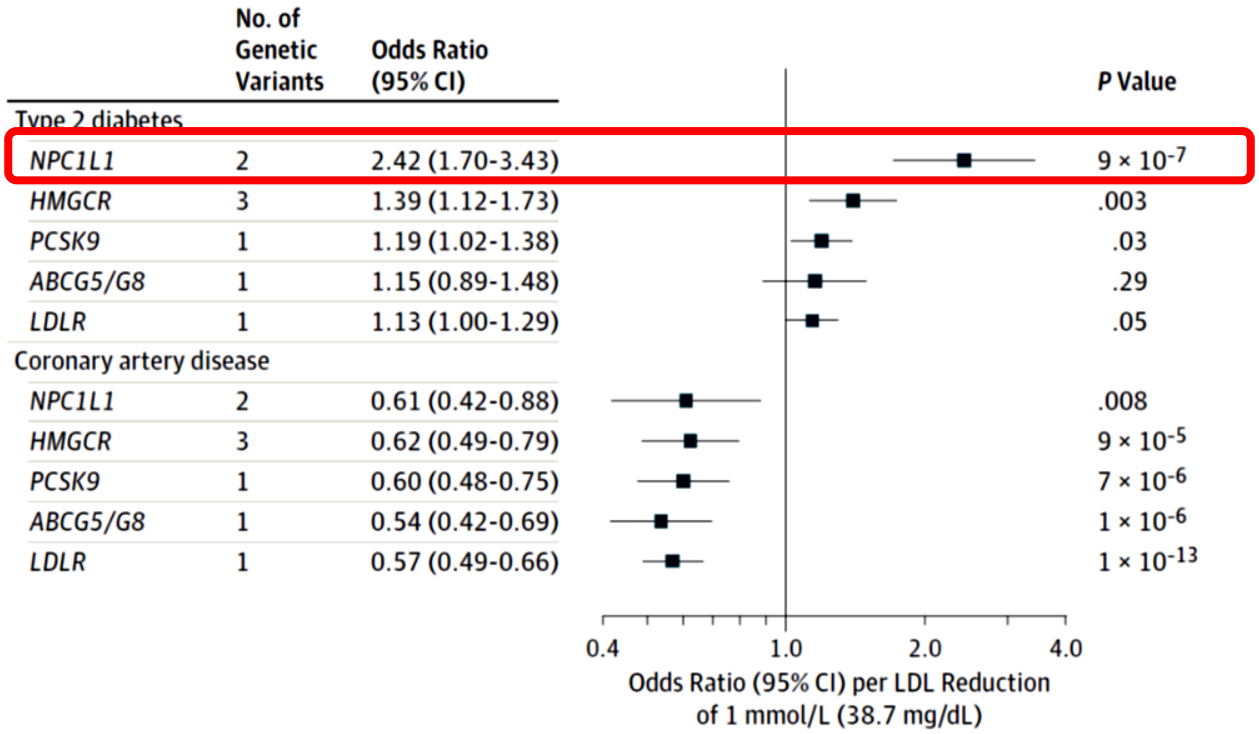


Figure 2: **Association between statin therapy and incident diabetes in 13 major cardiovascular trials†**

*Events per 1000 patient-years. †Weights are from random-effects analysis.

Lancet. 2010 Feb 27;375(9716):735-742.

Figure. Association of Low-Density Lipoprotein Cholesterol (LDL-C)–Lowering Genetic Variants With Coronary Artery Disease and Type 2 Diabetes



Coronary artery disease data are from 60 801 cases with coronary artery disease and 123 504 controls from the Coronary ARtery DIsease Genome wide Replication and Meta-analysis (CARDIoGRAM) plus the Coronary Artery Disease (C4D) Genetics (CARDIoGRAMplusC4D) Consortium.[19] Type 2 diabetes data are from 50 775 cases of type 2 diabetes and 270 269 controls from European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study,[13] the UK Biobank study,[14] and the DIAbetes Genetics Replication And Meta-analysis (DIAGRAM).[15] In addition to the EPIC-InterAct study,[13] the UK Biobank study,[14] and DIAGRAM,[15] type 2 diabetes association analyses of rs12916 at *HMGCR* included 11 studies (4496 cases and 50 677 controls) previously reported by Swerdlow et al.[5] Therefore, the sample size of *HMGCR* genetic variants association with type 2 diabetes was 55 271 cases of type 2 diabetes and 320 946 controls. All results are scaled to represent the odds ratio per 1-mmol/L (38.7-mg/dL) genetically predicted reduction in LDL-C.

Exposure to LDL-C-lowering genetic variants in or near *NPC1L1* and other genes was associated with a higher risk of type 2 diabetes.

JAMA. 2016 Oct 4;316(13):1383-1391.

Case A
two years later

- **58-year-old women, 151 cm, 53.0 kg: BMI 23.3 kg/m^2**

  She visited the clinic for a routine check-up.

  BP 122/53mmHg, PR 72/min
  HbA1c 7.1%, PG 112mg/dL, Cr 0.50mg/dL, UA 4.8mg/dL
  LDL-C 100mg/dL, TG 100mg/dL, HDL-C 76mg/dL
  Urine: Protein(-), Glucose(-), Ketone(-)

  <Therapeutic procedure>
  1400 kcal/day diet, moderate exercise
  teneligliptin 20mg qd (we started to treat her as T2D)
  atorvastatin 10mg qd

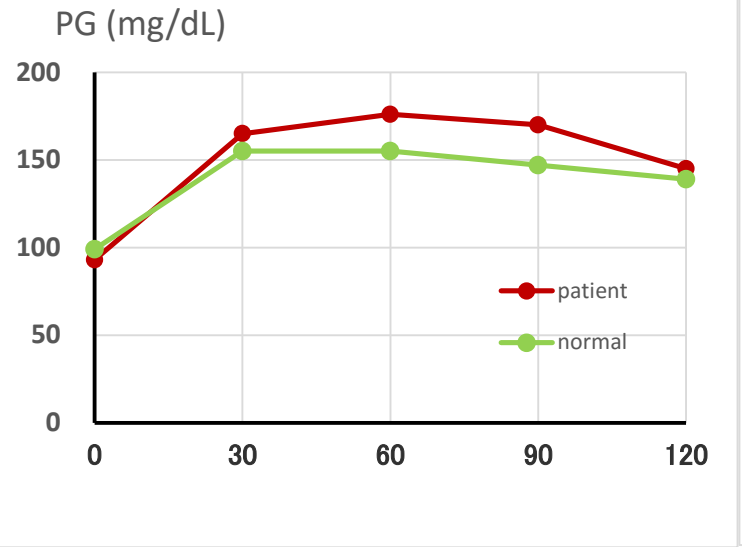
Case B

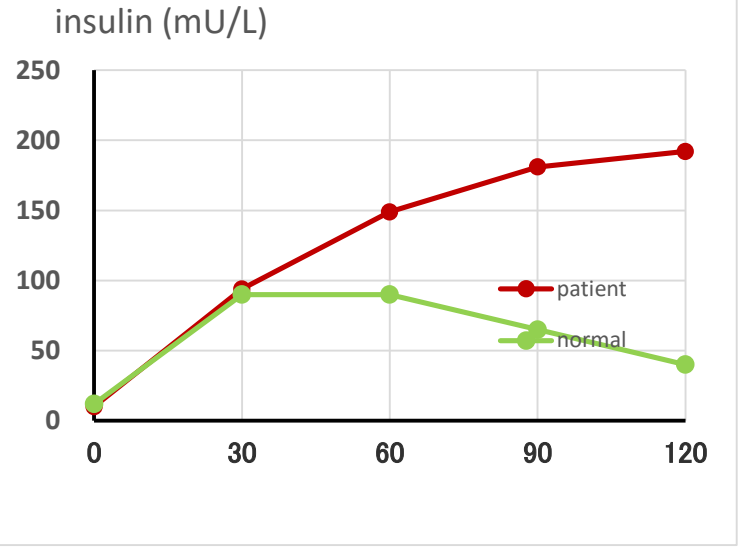
- **65-year-old women, 155 cm, 75 kg: BMI 31.2 kg/m^2**

She was referred from a nephrologist, asking us to exclude secondary obesity from endocrine diseases.

BP 139/79mmHg, PR 54/min, waist 84cm
HbA1c 5.5%, PG 94mg/dL, Cr 1.75mg/dL, UA 4.8mg/dL
LDL-C 105mg/dL, TG 142mg/dL, HDL-C 59mg/dL
Urine: Protein(-), Glucose(-), Ketone(-)
<drugs> lafutidine (10mg) 1T qd, irbesartan (100mg) 1T qd, fenofibrate (53.3mg) 1T 1qd
<Examination>
ACTH 9.2 pg/mL, cortisol 10.0 μg/dL
FT3 2.52 pg/mL, FT4 1.25 ng/mL, TSH 2.50 IU/mL

Case B





	PG (mg/dL)	Insulin (mU/L)
0 min	93	10
30 min	165	94
60 min	176	149
90 min	170	181
120 min	145	192

Matsuda Index	2.28	>2.5
HOMA-IR	2.30	<2.5
Insulinogenic Index	1.17	>0.4
Disposition Index (IGI*ISI)	2.66	>1.0
SigmaI /SigmaG	0.833	>0.10

Diagnosis: impaired glucose tolerance (postprandial hyperglycemia)

Pathophysiology: slightly low insulin sensitivity

Since she had a kidney dysfunction, insulin conc. was kept to be higher.

What should we do to prevent further damage to pancreatic beta-cells?

Case B

- **65-year-old women, 155 cm, 75 kg: BMI 31.2 kg/m^2**

She was referred from a nephrologist, asking us to exclude secondary obesity from endocrine diseases.

BP 139/79mmHg, PR 54/min, waist 84cm
HbA1c 5.5%, PG 94mg/dL, Cr 1.75mg/dL, UA 4.8mg/dL
LDL-C 105mg/dL, TG 142mg/dL, HDL-C 59mg/dL
Urine: Protein(-), Glucose(-), Ketone(-)
<drugs> lafutidine (10mg) 1T qd, irbesartan (100mg) 1T qd, fenofibrate (53.3mg) 1T 1qd
<Therapeutic approach>
1400 kcal/day diet, moderate exercise
?

Case B

- **65-year-old women, 155 cm, 75 kg: BMI 31.2 kg/m^2**

She was referred from a nephrologist, asking us to exclude secondary obesity from endocrine diseases.

BP 139/79mmHg, PR 54/min, waist 84cm
HbA1c 5.5%, PG 94mg/dL, Cr 1.75mg/dL, UA 4.8mg/dL
LDL-C 105mg/dL, TG 142mg/dL, HDL-C 59mg/dL
Urine: Protein(-), Glucose(-), Ketone(-)
<drugs> lafutidine (10mg) 1T qd, irbesartan (100mg) 1T qd, fenofibrate (53.3mg) 1T 1qd
<Therapeutic approach>
1400 kcal/day diet, moderate exercise
colestimide (500mg) 1T bid

Case C

- **40-year-old women, 160 cm, 53 kg: BMI 20.6 kg/m²**

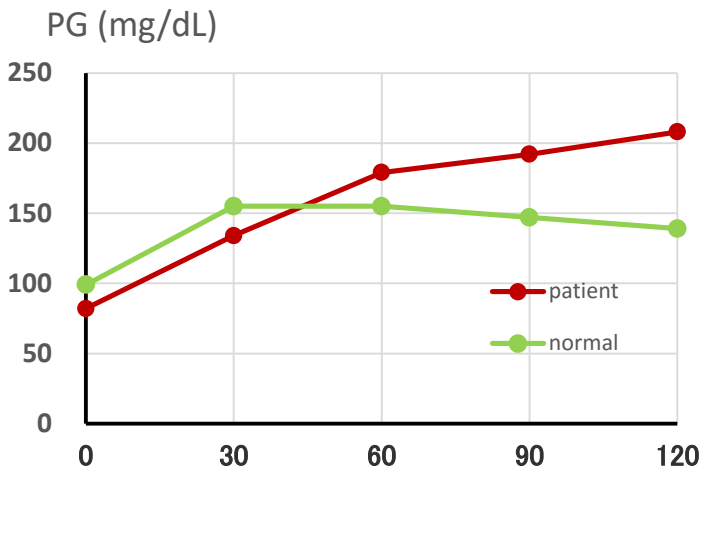
She was referred from an obstetrician for the treatment of hyperglycemia during pregnancy at 14 weeks and 3 days of pregnant, after receiving AIH (artificial insemination by husband).

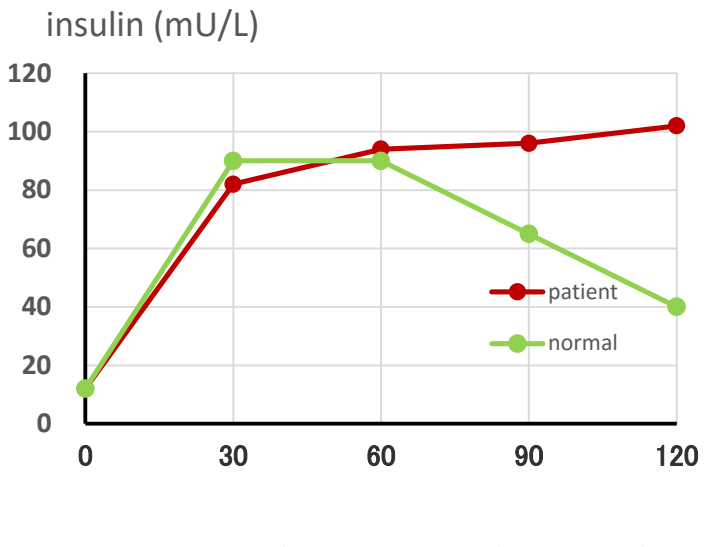
Past history: solid pseudopapillary tumoer in the pancreas, removed partially (30 y.o.), multiple myoma removed (34 y.o.)

Family history: No family history of diabetes

BP 141/61mmHg, PR 91/min, waist 83cm
Glycoalbumin 18.4%, HbA1c 5.8%, PPG 123mg/dL,
Cr 0.46mg/dL, UA 2.8mg/dL
Total-C 157mg/dL, TG 87mg/dL
FT3 2.31 pg/mL, FT4 1.31 ng/mL, TSH 0.10 IU/mL
Urine: Protein(-), Glucose(2+), Ketone(-)

Case C





	PG (mg/dL)	Insulin (mU/L)
0 min	82	12
30 min	134	82
60 min	179	94
90 min	192	96
120 min	208	102

During pregnancy

Matsuda Index	2.76	>2.5
HOMA-IR	2.43	<2.5
Insulinogenic Index	1.35	>0.4
Disposition Index (IGI*ISI)	3.71	>1.0
SigmaI /SigmaG	0.506	>0.10

Diagnosis: gestational diabetes mellitus

What should we do to manage glucose levels during pregnancy?

During pregnancy, the energy requirements of the fetus impose changes in maternal metabolism. Increasing insulin resistance in the mother maintains nutrient flow to the growing fetus, whereas prolactin and placental lactogen counterbalance this resistance and prevent maternal hyperglycemia by driving expansion of the maternal population of insulin-producing beta cells.

Case C

- **40-year-old women, 160 cm, 53 kg: BMI 20.6 kg/m^2**

She was referred from an obstetrician for the treatment of hyperglycemia during pregnancy at 14 weeks and 3 days of pregnant, after receiving AIH (artificial insemination by husband).

<Therapeutic approaches>

1600 kcal/day diet

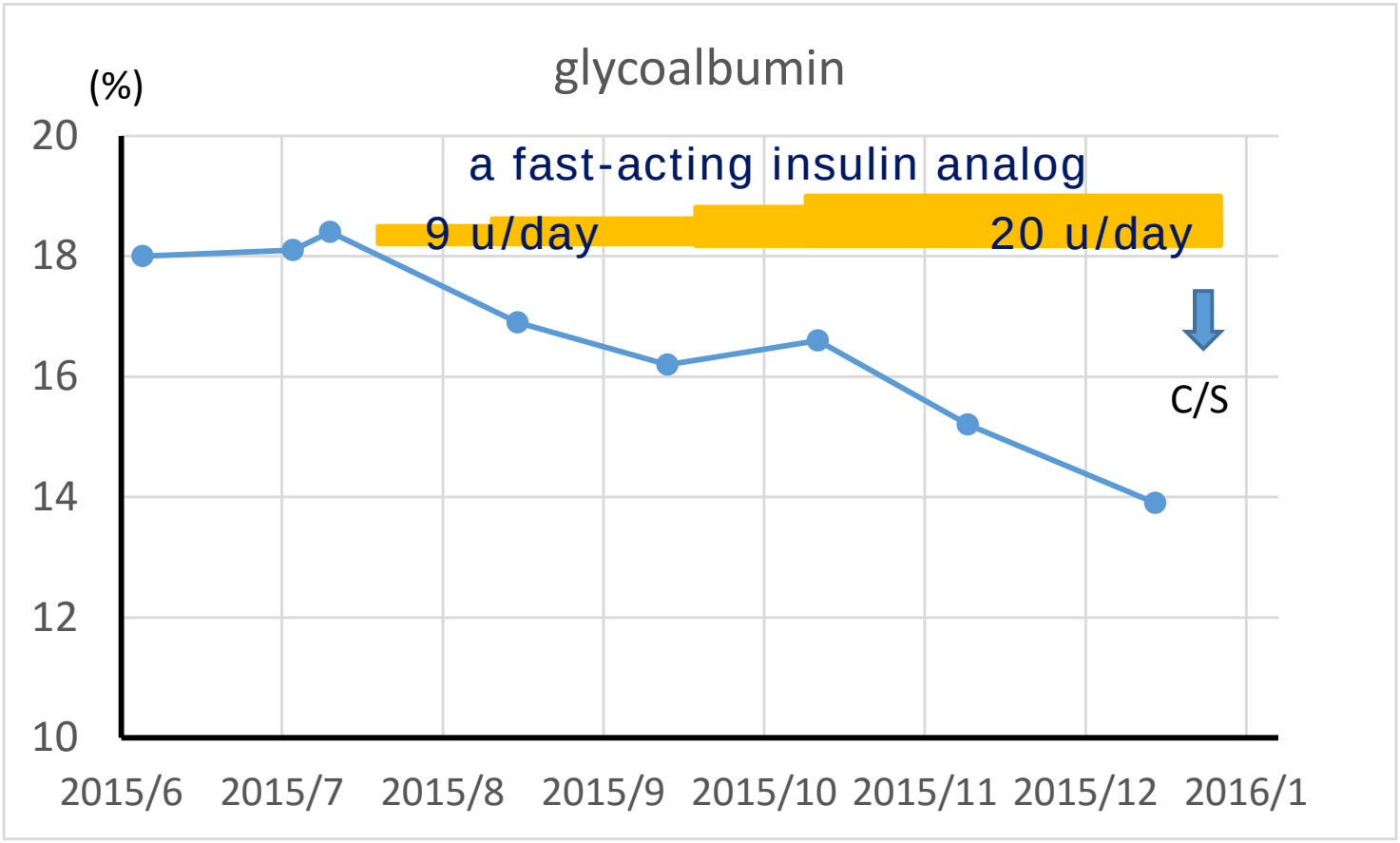
SMBG 6 times a day (before and after 2hr of each meal)

a fast-acting insulin analog

morning 3- units, lunch 3- units, evening 3- units

Case C

<clinical course>



Case C

- **40-year-old women, 160 cm, 53 kg: BMI 20.6 kg/m²**

She was referred from an obstetrician for the treatment of hyperglycemia during pregnancy at 14 weeks and 3 days of pregnant, after receiving AIH (artificial insemination by husband).

<Delivery>

38 weeks of pregnancy, C/S was performed.

Baby: 2774 g Ap 8/9

After delivery, insulin use was terminated.

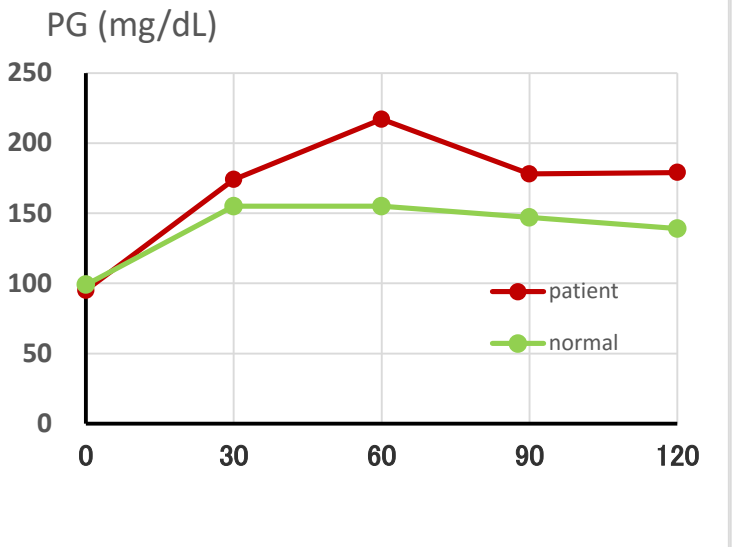
Case C

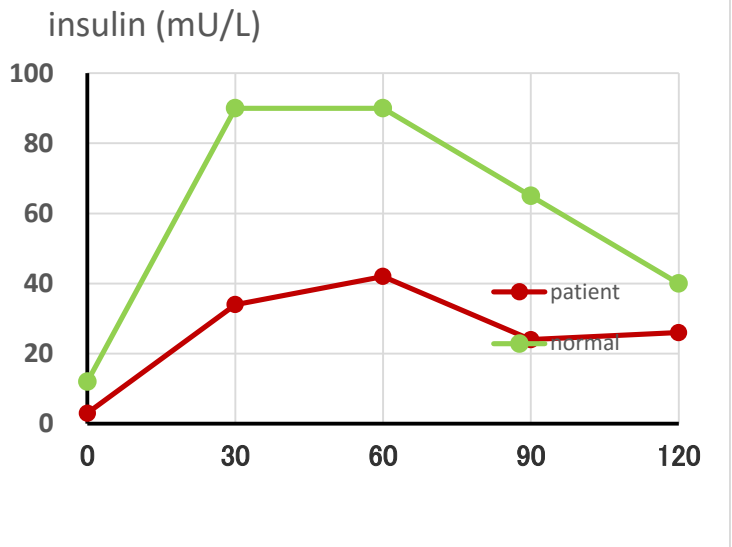
- **40-year-old women, 160 cm, 52.6 kg: BMI 20.6 kg/m^2**

  She returned to the clinic during lactation 6 months after the delivery.

BP 122/54mmHg, PR 72/min
HbA1c 5.9%, PPG 98mg/dL,
Cr 0.50mg/dL, UA 4.3mg/dL
Urine: Protein(-), Glucose(-), Ketone(-)

Case C





	PG (mg/dL)	Insulin (mU/L)
0 min	95	3
30 min	174	34
60 min	217	42
90 min	178	24
120 min	179	26

Six months after delivery

Matsuda Index	8.33	>2.5
HOMA-IR	0.70	<2.5
Insulinogenic Index	0.39	>0.4
Disposition Index (IGI*ISI)	3.27	>1.0
SigmaI /SigmaG	0.162	>0.10

Addendum

A blood pressure monitor to indicate blood vessel condition

Blood vessels lose their elasticity and arteries may harden as people age, or when substances such as cholesterol build up. This can cause a stroke or heart attack. Over the last few years a growing number of homes are using a digital blood pressure monitor, and now you can get a monitor that checks the condition of your blood vessels just about as easily.

A device that does this in about two minutes came on the market in 2011. Wrap the cuff around your upper arm to obtain readings for the artery at that location and the elasticity of your aorta, the largest artery in the body.

The device is useful as a tool to warn about possible hardening of the arteries, and will likely be instrumental in boosting awareness of health issues.

For the detection of vascular stiffness, that indicate advanced atherosclerosis, we have a useful machine in Japan.

Pasesa

Using the same method as the blood pressure monitor, this digital blood pressure monitor for medical use, called Pasesa, displays numbers indicating maximum and minimum blood pressure, pulse, pulse pressure, and the extent of blood vessel elasticity.
(Photo courtesy of Shisei Datum Co., Ltd., with the collaboration of RIKEN and the National Institute of Advanced Industrial Science and Technology)

Conclusion

Insulin resistance is the important feature (or cause) for the development of metabolic syndrome, eventually CVD and T2D.

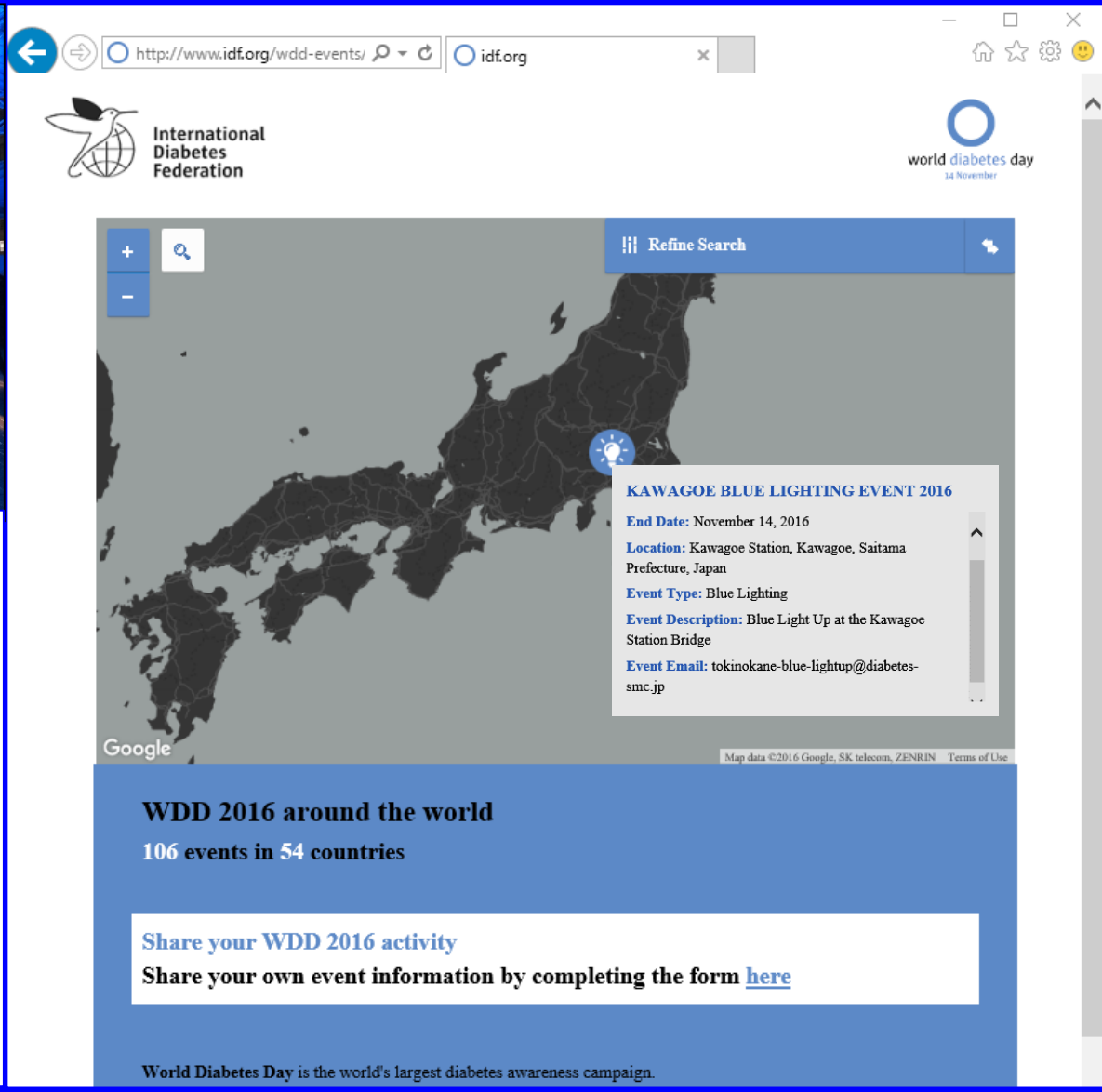
Intervention using medication to reduce insulin resistance has been proven to be effective on both preventing CVD and T2D, and more (dementia, liver adiposity, etc.)!

1 in 11 adults have diabetes (415 million)

46.5% of adults with diabetes are undiagnosed

By 2040, **1 adult in 10** (642 million) will have diabetes

http://www.diabetesatlas.org/key-messages.html



http://tokinokane-blue-lightup.diabetes-smc.jp/forpc.html