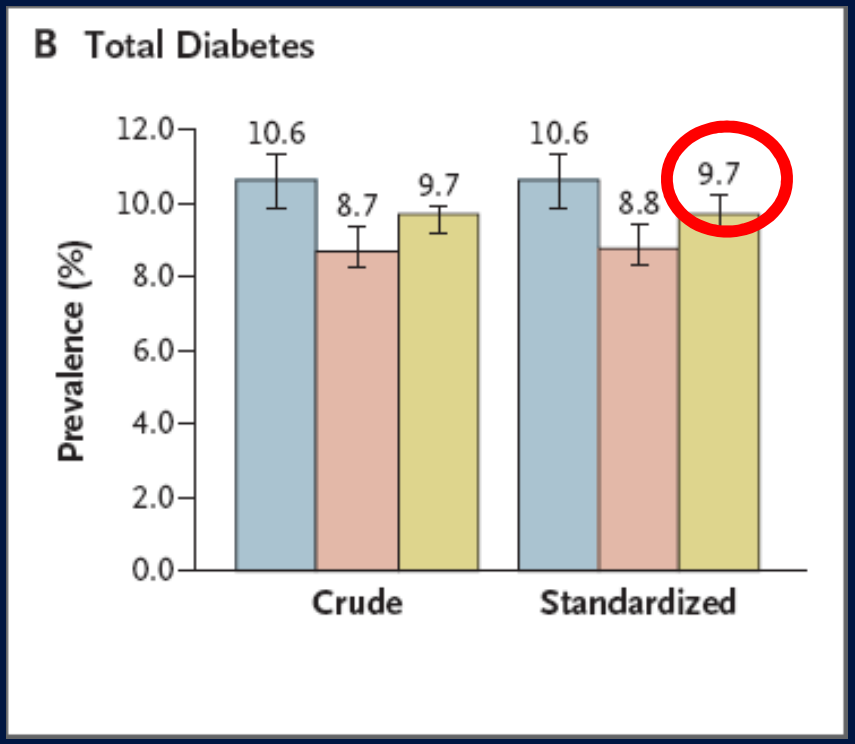
Characteristics of Glucose Disposal Index in General Population in China

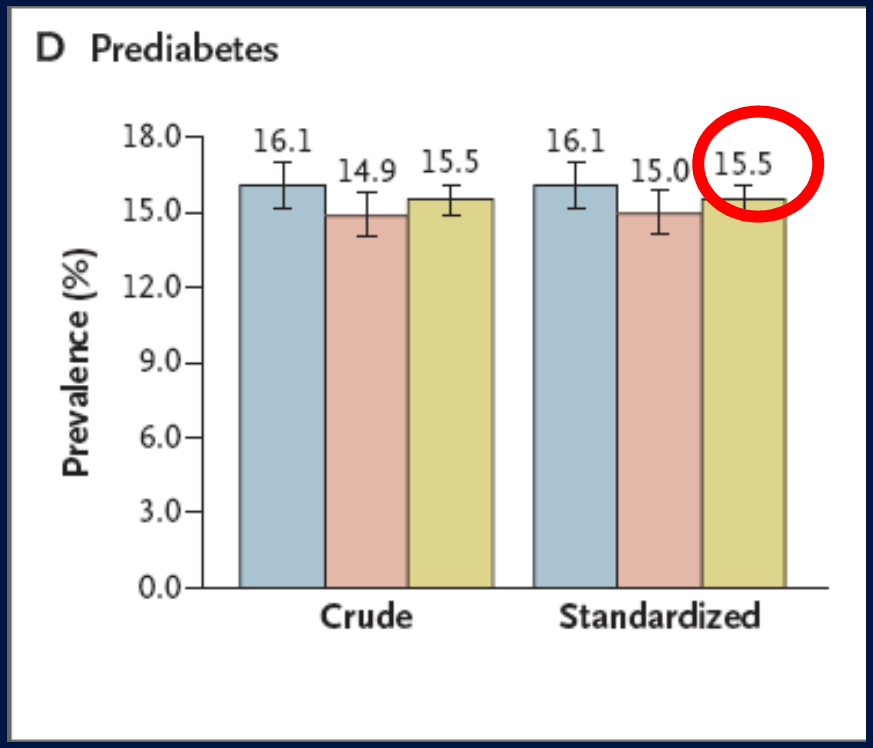
Qian Ren M.D

Department of Endocrinology and Metabolism,

Peking University, People's Hospital

Background





- We need to further characterize the pathophysiology of prediabetic status in order to guide the basic research and personalized diabetes prevention and treatment.

N Engl J Med 2010;362:1090-101.

Background

- β-cell function is an important factor to predict diabetes.
- However, only use HOMA-β to evaluate β-cell function may lead to wrong conclusion

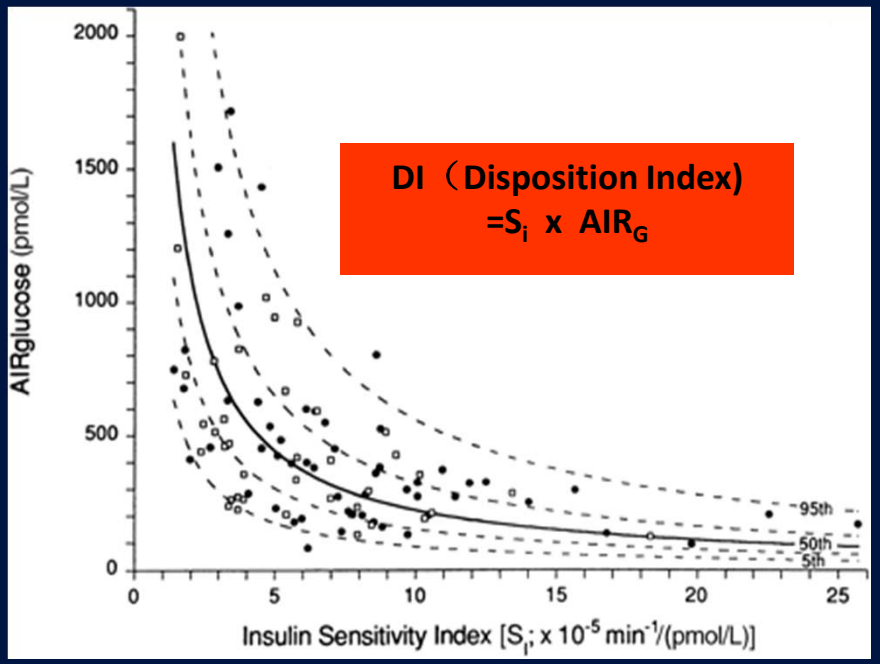
Table 1—*Baseline characteristics by diabetes status in 2008*

	NFG			IFG-100			IFG-110		
	Nondiabetic	Diabetic	*P**	Nondiabetic	Diabetic	*P**	Nondiabetic	Diabetic	*P**
n	10,097	35		2,419	127		174	72	
Clinical variables									
Age (years)	41 ± 6	40 ± 6	0.83	42 ± 6	43 ± 6	0.02	44 ± 7	43 ± 5	0.18
BMI (kg/m^2)	23.6 ± 2.8	26.0 ± 3.2	<0.001	24.7 ± 2.7	26.9 ± 3.4	<0.001	25.6 ± 2.7	26.3 ± 3.1	0.09
Male (%)	6,918 (69)	32 (91)	0.001	1,964 (81)	114 (90)	0.007	154 (89)	62 (86)	0.37
Laboratory variables									
Glucose (mmol/l)									
Unadjusted	5.0 (5.0–5.0)	5.1 (5.0–5.3)	0.003	5.8 (5.8–5.8)	5.9 (5.9–5.9)	<0.001	6.5 (6.5–6.5)	6.6 (6.6–6.7)	<0.001
Adjusted*	5.0 (5.0–5.0)	5.1 (5.0–5.2)	0.04	5.8 (5.8–5.8)	5.9 (5.9–5.9)	<0.001	6.5 (6.5–6.5)	6.6 (6.6–6.7)	<0.001
Insulin (pmol/l)									
Unadjusted	49 (49–49)	68 (61–74)	<0.001	54 (54–55)	67 (64–71)	<0.001	60 (56–64)	67 (62–73)	0.04
Adjusted*	49 (49–49)	62 (56–68)	<0.001	55 (54–56)	61 (58–65)	<0.001	61 (58–64)	65 (60–71)	0.19
HOMA2-IR									
Unadjusted	1.1 (1.0–1.1)	1.4 (1.3–1.6)	<0.001	1.2 (1.2–1.2)	1.5 (1.4–1.6)	<0.001	1.4 (1.3–1.5)	1.6 (1.4–1.7)	0.03
Adjusted*	1.1 (1.0–1.1)	1.3 (1.2–1.5)	<0.001	1.2 (1.2–1.2)	1.4 (1.3–1.4)	<0.001	1.4 (1.3–1.5)	1.5 (1.4–1.6)	0.17
HOMA2-B									
Unadjusted	99 (98–99)	115 (106–123)	<0.001	80 (79–80)	87 (84–91)	<0.001	68 (65–71)	71 (66–75)	0.28
Adjusted*	99 (98–99)	110 (102–118)	0.009	80 (79–81)	82 (78–85)	0.26	68 (66–71)	69 (65–73)	0.82

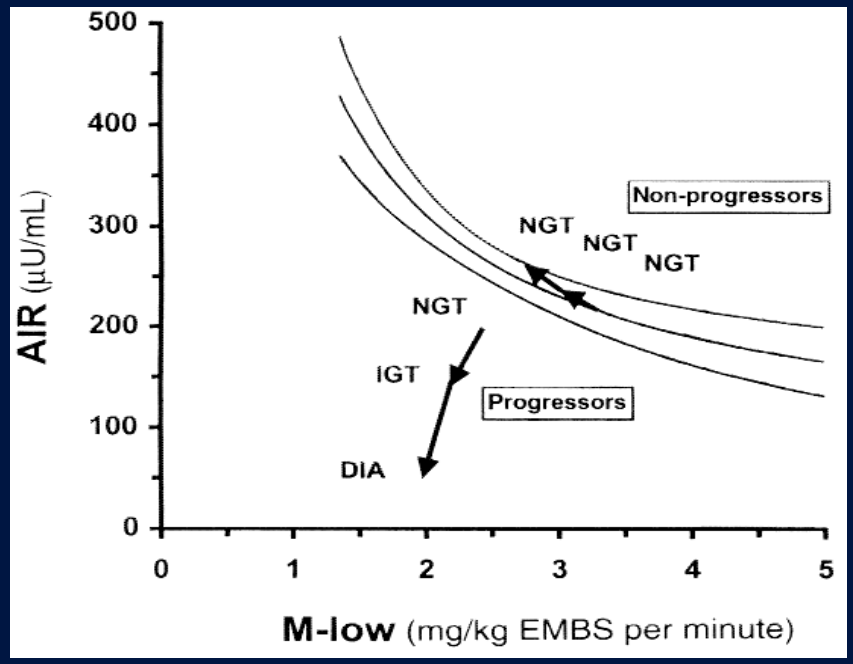
Data are means ± SD or means (95% CI). *Data are adjusted for age, sex, and BMI.

Disposition index (DI)

- DI is the product of insulin secretion and insulin sensitivity.
- DI is the gold standard for measuring β-cell function.

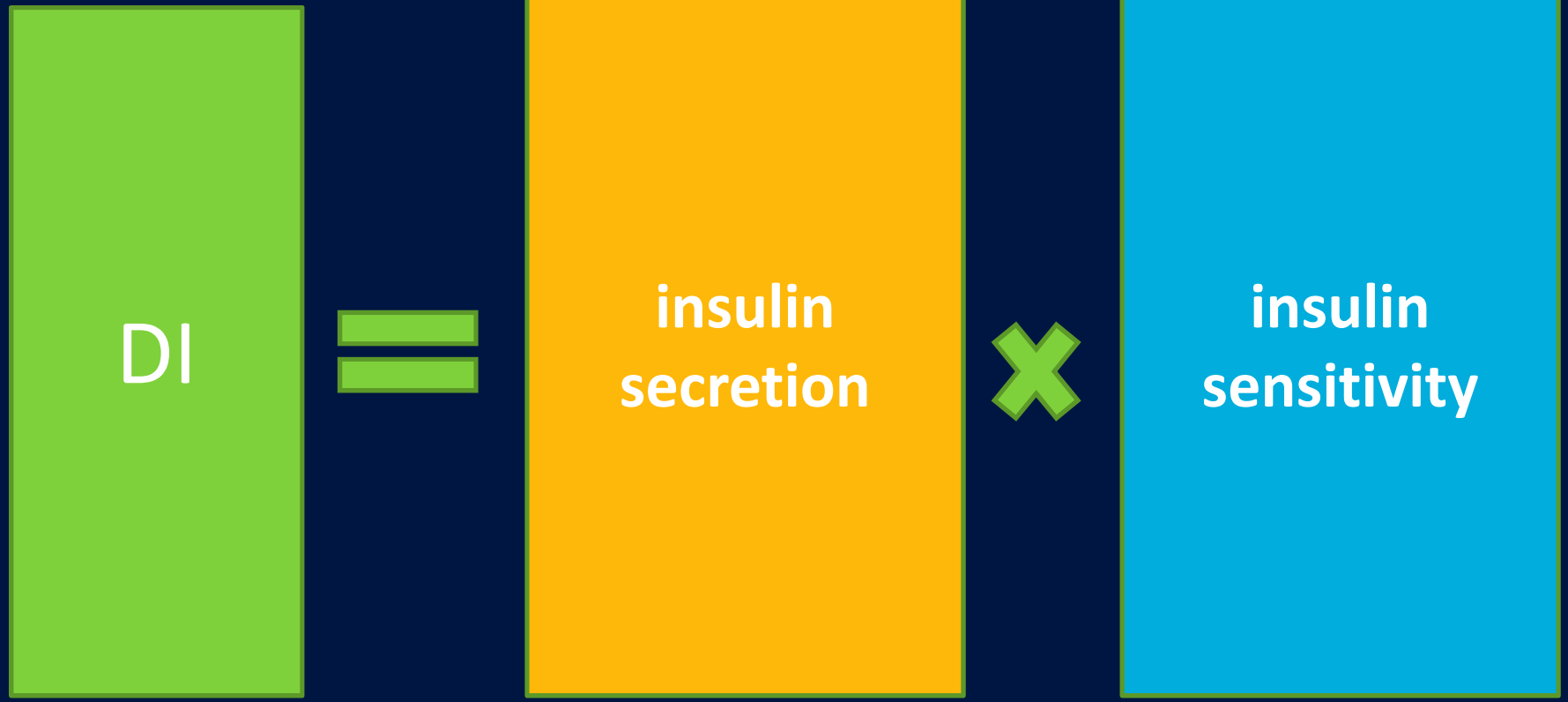


Kahn S et al diabetes,1995



Weyer JCI, 1999

Calculation of DI



Calculation of DI

	Name	Formula	Ref.
insulin secretion	**HOMA-B**	20×FI/(FPG-3.5)	1
	IGI	(I30- FI) /(PG30- FPG)	2
	EPIR	2032+(4.681×FI×6.965)-(135.0×PG120)+(0.995×I120×6.965)+（27.99×BMI）-（269.1× FPG）	3
	LPIR	277 +(0.8000 ×FI×6.965)-（42.79×PG120）+（0.321×I120×6.965）+ (5.338 ×BMI)	3
	AUCIns/Gluci-j and ΔAUCIns/Gluci-j		4

1. Diabetologia 28, 412-419 (1985),
2. 2. Diabetes 53, 1549-1555 (2004).
3. Diabetes Care 24, 796-797 (2001).
4. Diabetic Medicine 26, 1198-1203 (2009).

Calculation of DI

	Name	Formula	Site	Ref.
insulin sensitivity	**HOMA-IR**	FPG × FI/22.5	**Hepatic**	1
	QUICKI	1/(Log(FI)+Log(FPG × 18))	Hepatic	2
	HIR	$1/16 \times (I_{30}+FI) \times (PG_{30}+ FPG)$	Hepatic	6
	MSI	$10000/(FPG \times 18 \times FI \times MPG \times 18 \times MI)^{0.5}$	**Whole body**	3
	$ISI_{0,120}$	(75000+(FPG–PG120) × 18 × 0.19 × BW)/120/(MPG × 18)/LogMI	**peripheral**	4
	$OGIS_{180}$	$(637 \times 10^6 \times (18 \times PG120–90)+1 \times Cl_{OGTT}$	Whole body	5
	SMIS	dG/dt ÷ MI	Skeletal Muscle	6

1. Diabetologia ***28, 412-419*** (1985). 2. Journal of Clinical Endocrinology & Metabolism 85, 2402-2410 (2000). 3. Diabetes Care 22, 1462-1470 (1999). 4. Diabetes research and clinical practice 47, 177-184 (2000). 5. Diabetes Care 24, 539-548 (2001). 6. Diabetes Care 30, 89-94 (2007).

Calculation of DI

DI=insulin secretion × insulin sensitivity

DI	Abr.	insulin secretion	insulin sensitivity	Ref.
Baseline	DI_b	HOMA-B	1/HOMA-IR	1
Early phase	DI_1	EPIR	$ISI_{0,120}$	2
	DI_{30}	$AUCIns/Gluc_{0-30}$	MSI	3
Late phase	DI_2	LPIR	$ISI_{0,120}$	4
	DI_{30-120}	$AUCIns/Gluc_{30-120}$	MSI	5
OGTT total	**DI_{120} (ISSI-2)**	**$AUCIns/Gluc_{0-120}$**	**MSI**	**3**

(1) American Journal of Physiology-Endocrinology and Metabolism .293,E1-E15, 2007; (2) Diabetes Care 33, 200-202, 2010;; (3) Diabetes Care 30, 773-795, 2009; (4) Diabetes Care 32, 439-444 2009 ;(5) Diabetes Care 30 1544-1548,2007

ISSI-2

- **ISSI-2=AUCIns/Gluc$_{0\text{-}120}$ × MSI**

  =AUCIns/Gluc$_{0\text{-}120}$ × （10000/（FPG × 18 × FI × **MPG** × 18 × **MI**）$^{0.5}$）

- Derived from more than **three measures** of blood glucose and insulin levels
- A best predictor of future diabetes

DI in epidemiological studies in China

- Few studies
- Less than three measurements of blood glucose and insulin levels during OGTT are obtained
- little information about the effects of clinical characteristics of diabetes on DI in different glucose tolerance subjects

Aim of this study

- To assess the disposition indices (DIs) in Chinese subjects in different glucose tolerance categories.
- To evaluate the applicability of using DIs derived from less than **three measures** of blood glucose and insulin levels to assess β-cell function in large-scale epidemiological studies.
- To investigate **the impacts of clinical characteristics of diabetes on DI** in different glucose tolerance groups.

Research Design and Methods

- **Database**

  China National Diabetes and Metabolic Disorders Study

Yang W, et al. N Engl J Med. 2010

Research Design and Methods

- 54,240 people were selected and invited to participate in the study.
- 47,325 persons completed the National study.
- 33,324 persons were included in our study after excluding diabetic patients receiving drug therapy and persons with incomplete data

Yang W, et al. N Engl J Med. 2010

Research Design and Methods

- Groups:

Group	Sub-Group	Definition	No.
NGT	NGT	FPG＜6.1mmol/l and 2h-PG＜7.8mmol/l	25,848
FH	IFG	6.1≤FPG＜7.0 mmol/l and 2h-PG＜7.8mmol/l	1.046
	DFG	FPG≥7.0 mmol/l and 2h-PG＜7.8mmol/l	203
PH	IGT	FPG＜6.1mmol/l and 7.8≤2h-PG＜11.1 mmol/l	3,532
	DGT	FPG ＜ 6.1mmol/l and2h-PG≥11.1 mmol/l	531
FH/PH	IFG/IGT	6.1≤FPG＜7.0 mmol/l and 7.8≤2h-PG＜ 11.1mmol/l	735
	DFG/DGT	FPG≥7.0mmol/l and 2h-PG≥7.8mmol/l or FPG≥6.1mmol/l and 2h-PG≥11.1mmol/l	1,405
DM	DM	FPG≥7.0mmol/l and 2h-PG≥11.1mmol/l	1,069

RESULTS

Baseline characteristics

		FH		PH		FH/PH	
	NGT	IFG	DFG	IGT	DGT	IFG/IGT	DFG/DGT
No	25848	1046	203	3532	531	735	1450
Male (%)	9985 (38.6)	480 (45.9)	94 (46.3)	1297 (36.7)	238 (44.8)	287 (39.0)	646 (44.6)
Age	42±13*	46±13†	44±13*†	50±13‡	54±12§	50±13‡	53±12§
SBP	119±18*	126±21†	122±18*†	129±21‡	132±21§	132±21§	135±21§
DBP	77±11 *	80±12 †	78±10 *†	82±12 ‡	83±12 ‡§	83±12§	84±12§
Waist	80±10 *	85±11 †	83±11 †	85±10 †	87±10 ‡	88±10 ‡§	89±10§
BMI	23.6±3.5 *	24.9±3.7 †	24.6±4.0 †	25.3±3.8 †	25.4±3.8 †	26.2±3.8 ‡	26.2±3.8 ‡
Family history（%）	2899 (11.2)	126 (12.0)	27 (13.3)	514 (14.6)	76 (14.3)	127 (17.3)	329 (22.7)
Metabolic syndrome（%）	4262 (16.5)	468 (44.7)	77 (37.9)	1353 (38.3)	240 (45.2)	466 (63.4)	946 (65.2)

Baseline characteristics

		FH		PH		FH/PH	
	NGT	IFG	DFG	IGT	DGT	IFG/IGT	DFG/DGT
No	25848	1046	203	3532	531	735	1450
Male (%)	9985 (38.6)	480 (45.9)	94 (46.3)	1297 (36.7)	238 (44.8)	287 (39.0)	646 (44.6)
Age	42±13*	46±13†	44±13*†	50±13‡	54±12§	13‡	53±12§
SBP	119±18*	126±21†	122±18*†	129±21‡	1	132±21§	135±21§
DBP	77±11 *	80±12 †	78±10 *†	82±1	±12 ‡§	83±12§	84±12§
Waist	80±10 *	85±11 †	83±11 †	†	87±10 ‡	88±10 ‡§	89±10§
BMI	23.6±3.5 *	24.9±3.7 †	24	25.3±3.8 †	25.4±3.8 †	26.2±3.8 ‡	26.2±3.8 ‡
Family history（%）	2899 (11.2)		27 (13.3)	514 (14.6)	76 (14.3)	127 (17.3)	329 (22.7)
Metabolic syndrome（%）	4262 (16.5)	468 (44.7)	77 (37.9)	1353 (38.3)	240 (45.2)	466 (63.4)	946 (65.2)

Baseline characteristics

	FH			PH		FH/PH	
	NGT	IFG	DFG	IGT	DGT	IFG/IGT	DFG/DGT
FPG	4.9±0.5 *	6.4±0.2 †	8.0±1.2 ‡	5.3±0.5§	5.4±0.6 $	6.4±0.2 †	8.6±2.6 ¶
2-h PG	5.7±1.1 *	6.2±1.0 †	6.1±1.1 †	8.9±0.9 ‡	12.9±2.1§	9.2±0.9 $	15.0±4.9 ¶
FI	8.1±5.5 *	10.2±7.9 †	15.8±17.8 ‡	8.8±6.0§	9.6±7.4 †§	10.5±7.1 † $	11.5±8.6 $
2-h insulin	32.3±30.8 *	35.2±36.1 *	37.3±41.9 *	66.3±60.4 †	75.2±68.5 †	63.2±52.6 †	48.9±48.6 ‡
T-CHOL	4.59±0.96*	4.95±1.01†	4.87±1.14†	4.95±0.99†	5.05±1.03†‡	5.11±1.01‡ §	5.21±1.02§
LDL-c	2.68±0.84*	2.90±0.79†	2.82±0.90*†	2.94±0.90†	2.90±0.90†	3.00±0.82† ‡	3.08±0.95‡
TG	1.2(0.8,1.7) *	1.5(1.0,2.1) †	1.4(1.0,2.0) †	1.5(1.1,2.2) †	1.5（1.1,2.2) † ‡	1.7(1.2,2.3) ‡	1.8(1.3,2.7) §
HDL-c	1.34±0.34 *	1.30±0.35 †	1.30±0.31 †	1.32±0.35* †	1.33±0.37 *†	1.31±0.36 *†	1.31±0.33 *†

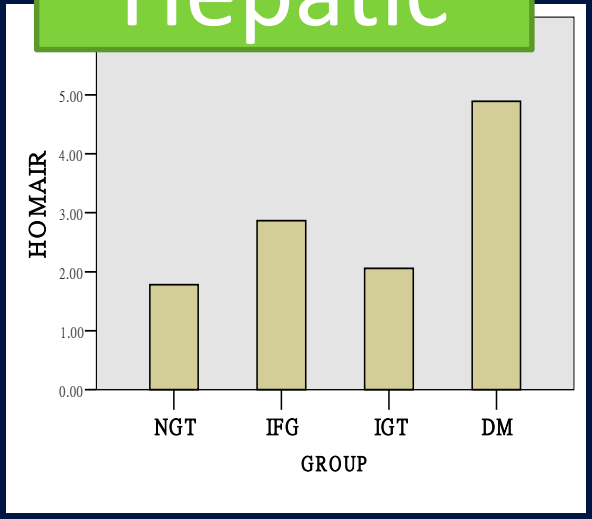
Baseline characteristics

		FH		PH		FH/PH	
	NGT	IFG	DFG	IGT	DGT	IFG/IGT	DFG/DGT
FPG	4.9±0.5 *	6.4±0.2 †	8.0±1.2 ‡	5.3±0.5§	5.4±0.6 $	6.4±0.2 †	8.6±2.6 ¶
2-h PG	5.7±1.1 *	6.2±1.0 †	6.1±1.1 †	8.9±0.9 ‡	12.[illegible]	[illegible]±0.9 $	15.0±4.9 ¶
FI	8.1±5.5 *	10.2±7.9 †	15.8±17.8 ‡	8.8±6.0§	[illegible]	10.5±7.1 † $	11.5±8.6 $
2-h insulin	32.3±30.8 *	35.2±36.1 *	37.3±41.9 *	[illegible]	75.2±68.5 †	63.2±52.6 †	48.9±48.6 ‡
T-CHOL	4.59±0.96*	4.95±1.01†	4.[illegible]	4.95±0.99†	5.05±1.03†‡	5.11±1.01‡ §	5.21±1.02§
LDL-c	2.68±0.84*	2.9[illegible]	[illegible]82±0.90*†	2.94±0.90†	2.90±0.90†	3.00±0.82† ‡	3.08±0.95‡
TG	1.2(0.8,1.7) *	[illegible].0,2.1) †	1.4(1.0,2.0) †	1.5(1.1,2.2) †	1.5（1.1,2.2) †‡	1.7(1.2,2.3) ‡	1.8(1.3,2.7) §
HDL-c	1.34±0.34 *	1.30±0.35 †	1.30±0.31 †	1.32±0.35* †	1.33±0.37 *†	1.31±0.36 *†	1.31±0.33 *†

IFG, IGT, DM

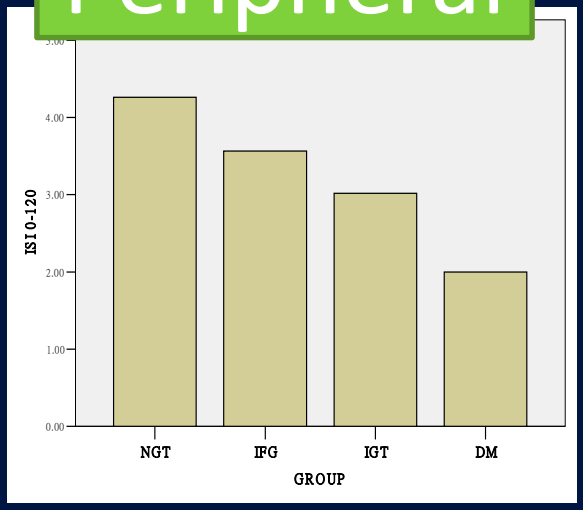
Insulin sensitivity between IFG, IGT and DM

Hepatic



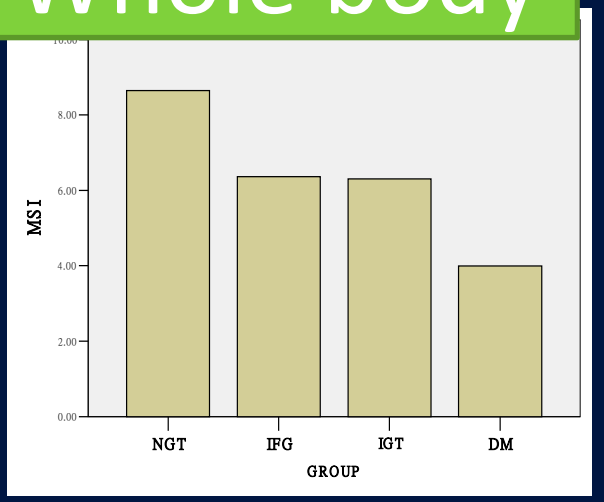
Hepatic IR: IFG>IGT

Peripheral



Peripheral IR: IGT>IGT

Whole body

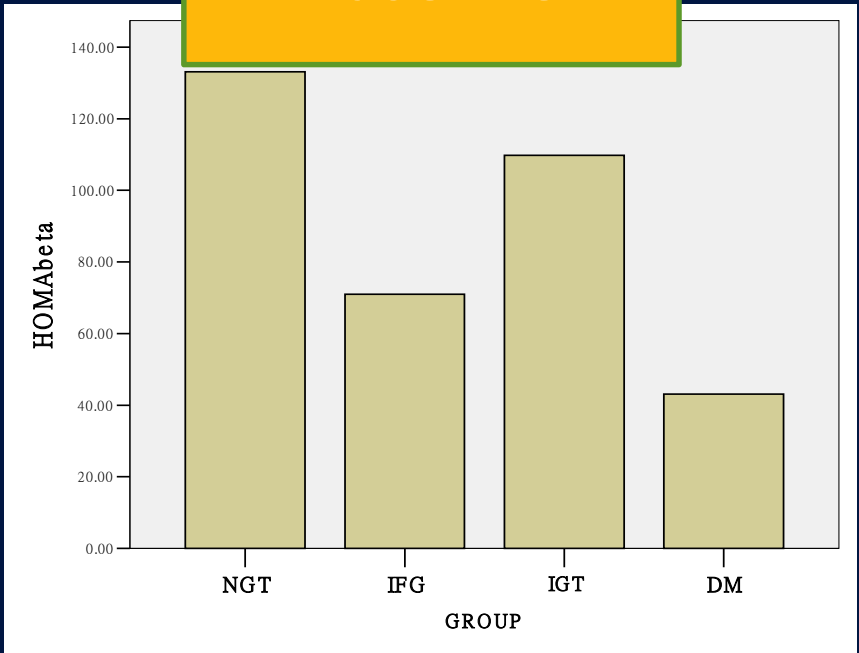


Whole body IR: IFG=IGT

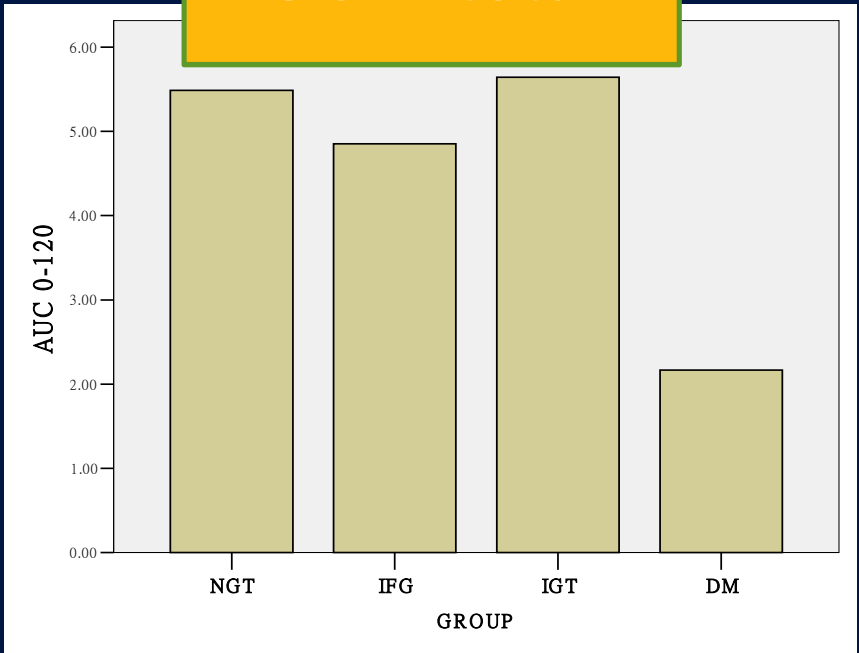
NGT has the lowest IR, while DM is the highest

Insulin secretion between IFG, IGT and DM

Baseline



OGTT total



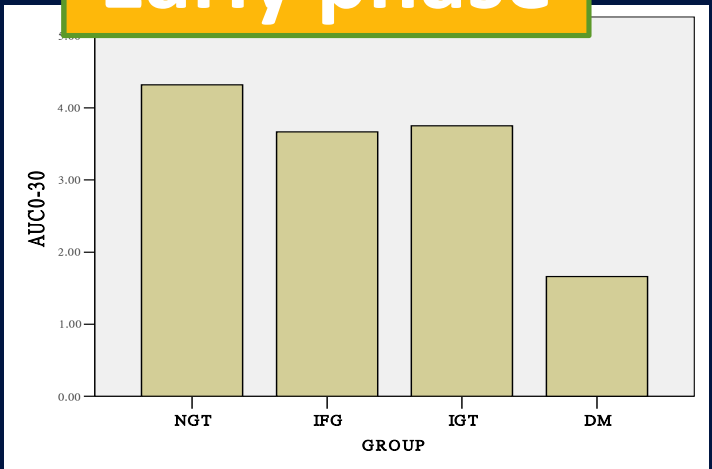
Baseline: IFG<IGT

Total: IFG<IGT

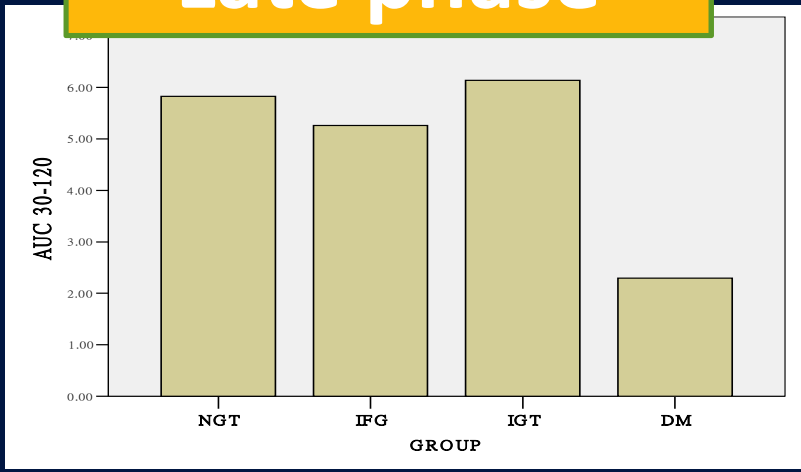
NGT: highest in both baseline and total

Insulin secretion between IFG, IGT and DM

Early phase



Late phase



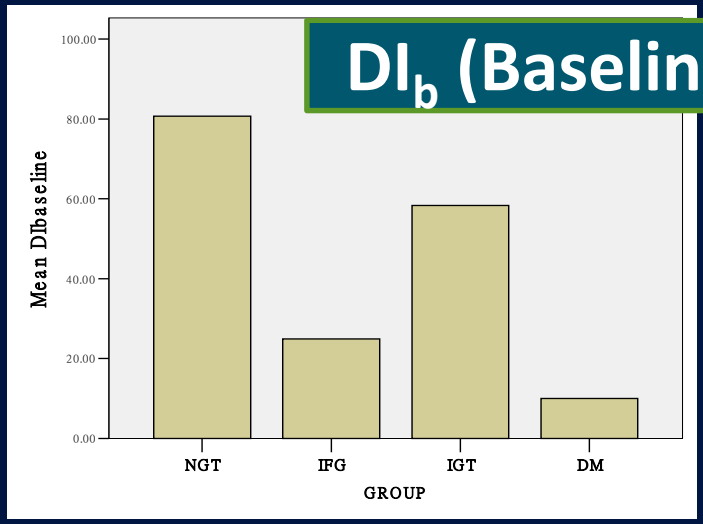
Early phase: IFG=IGT

Late phase: IFG<IGT

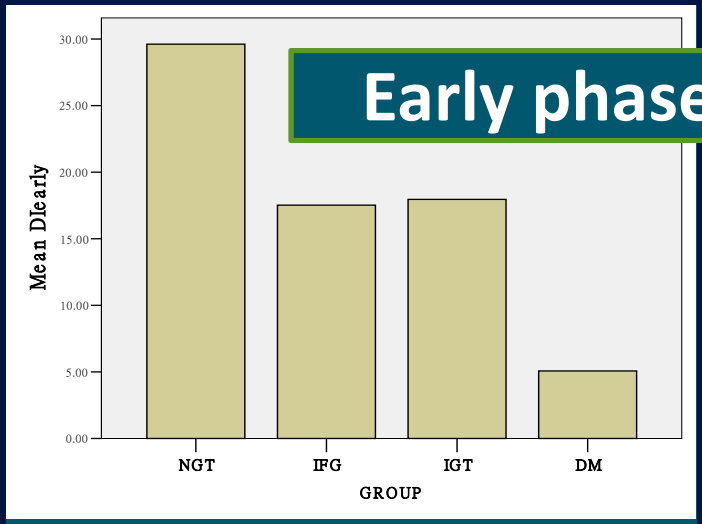
DM: lowest in both early phase and late phase

DI between IFG, IGT and DM

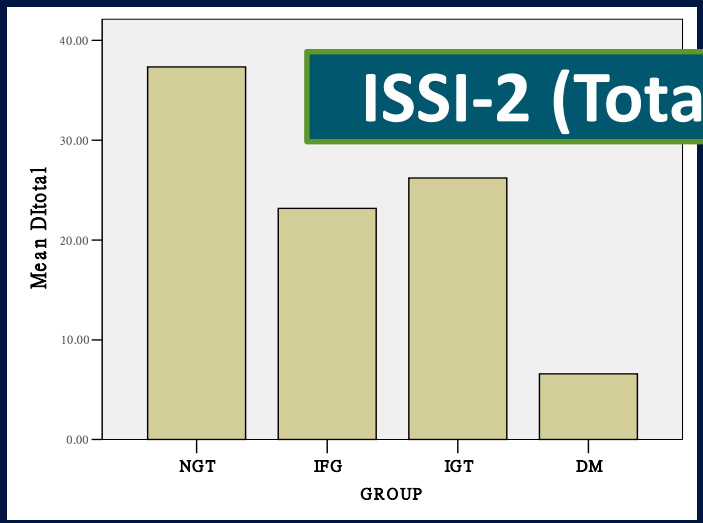
DI_b (Baseline)



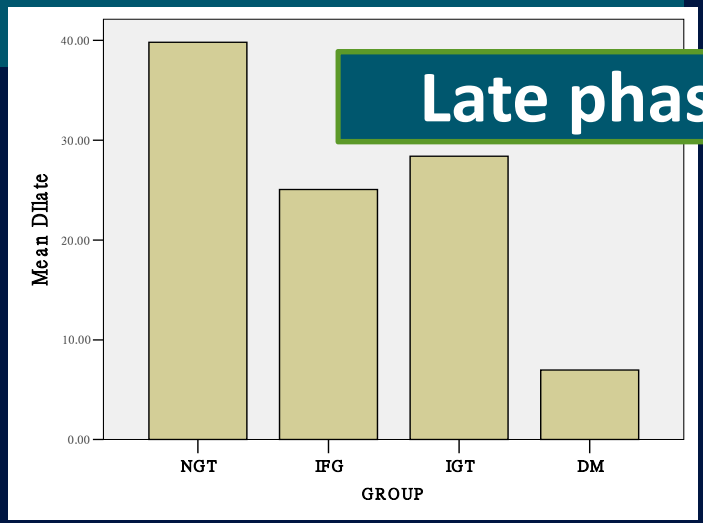
Early phase



ISSI-2 (Total)



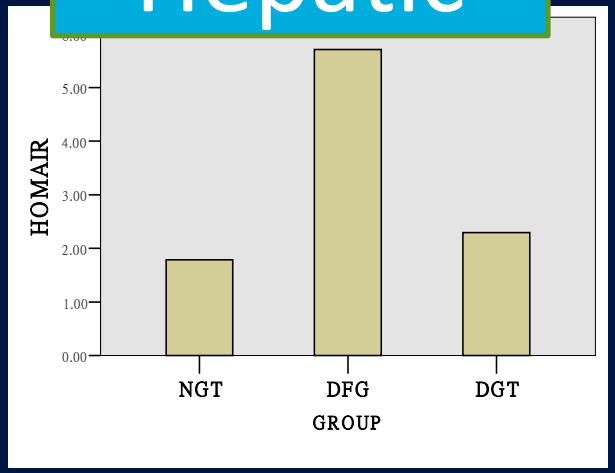
Late phase



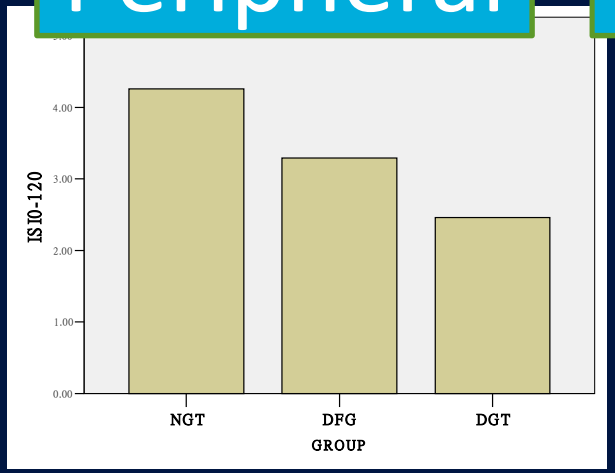
DFG, DGT

Insulin sensitivity between DFG and DGT

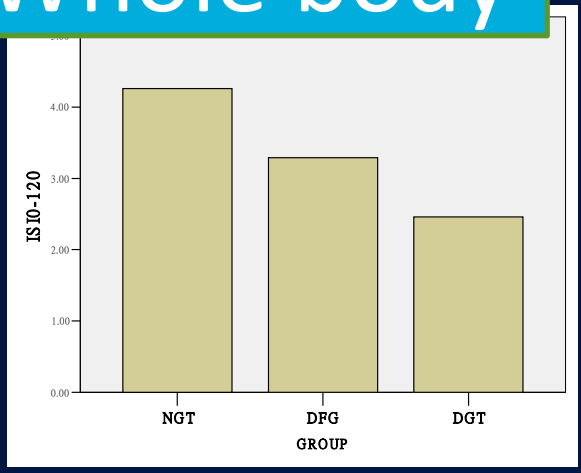
Hepatic



Peripheral



Whole body



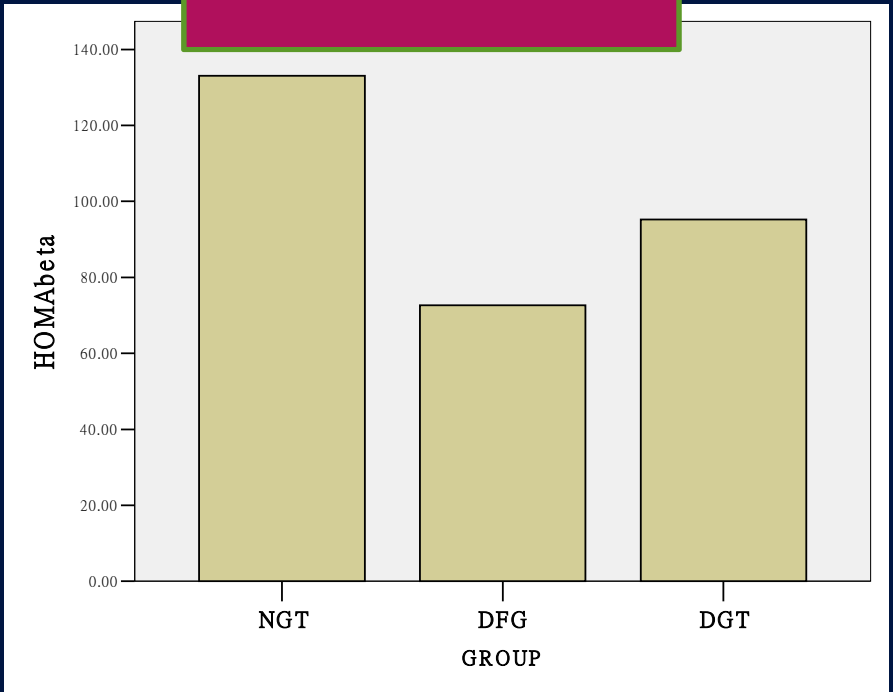
Hepatic IR: DFG>DGT

Peripheral IR: DGT>DFG

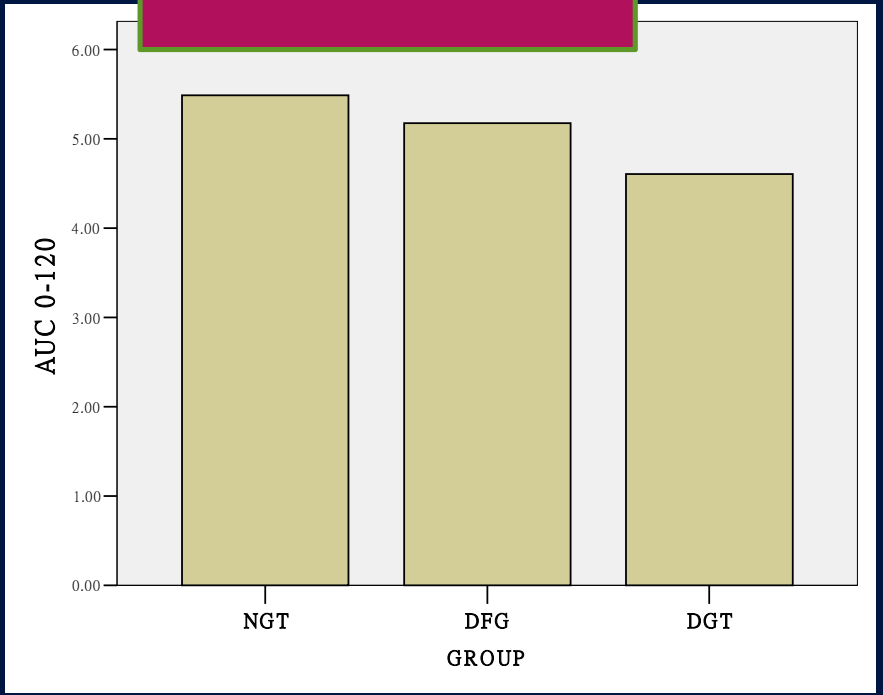
DFG and DGT resemble the pathophysiologic characteristics of individuals with IFG and IGT.

Insulin secretion between DFG and DGT

Baseline



OGTT total

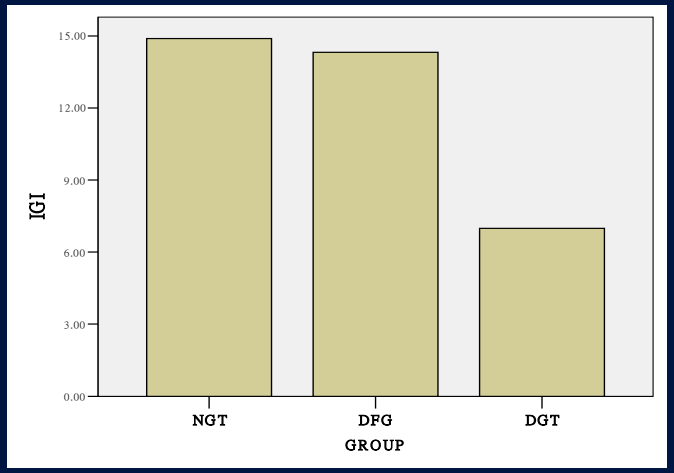


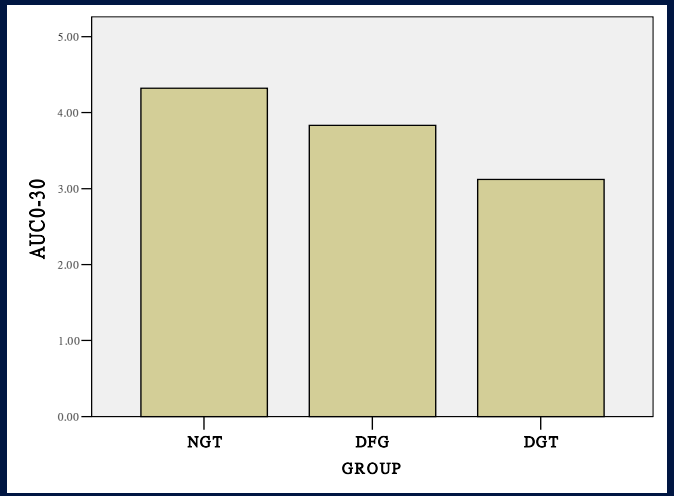
Baseline: DFG<DGT, Total: DFG>DGT

Subjects with DFG and DGT have distinct pathophysiological disturbances.

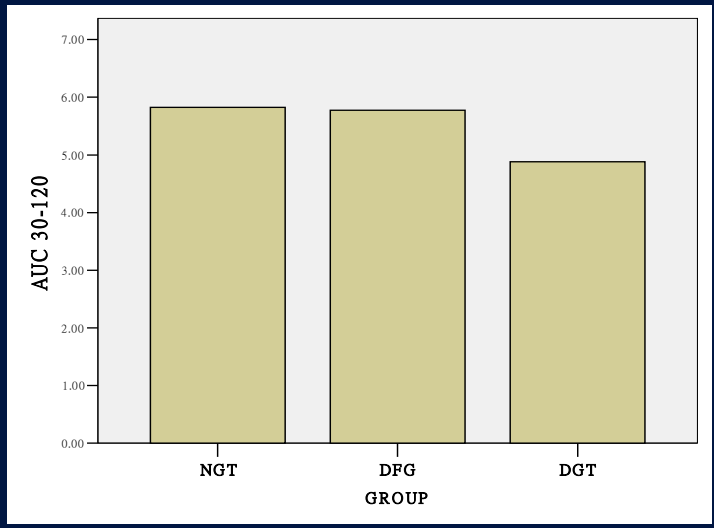
Insulin secretion between DFG and DGT

Early phase





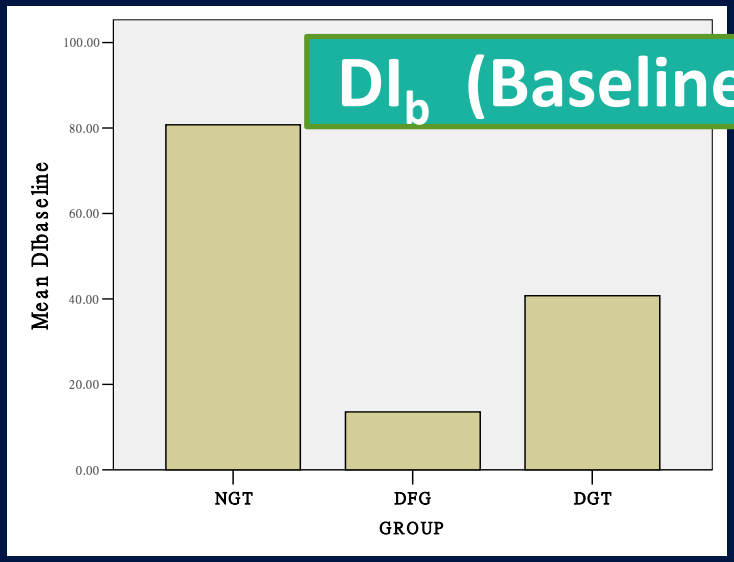
Late phase

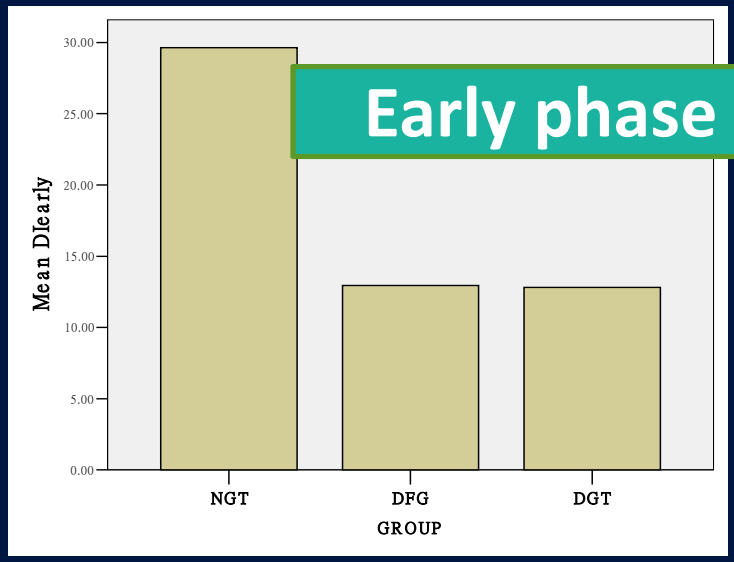


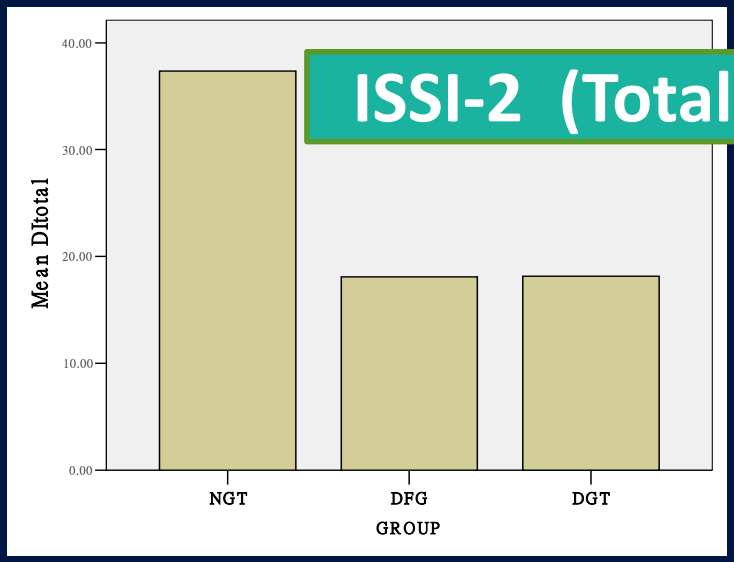
Early phase: DFG>DGT

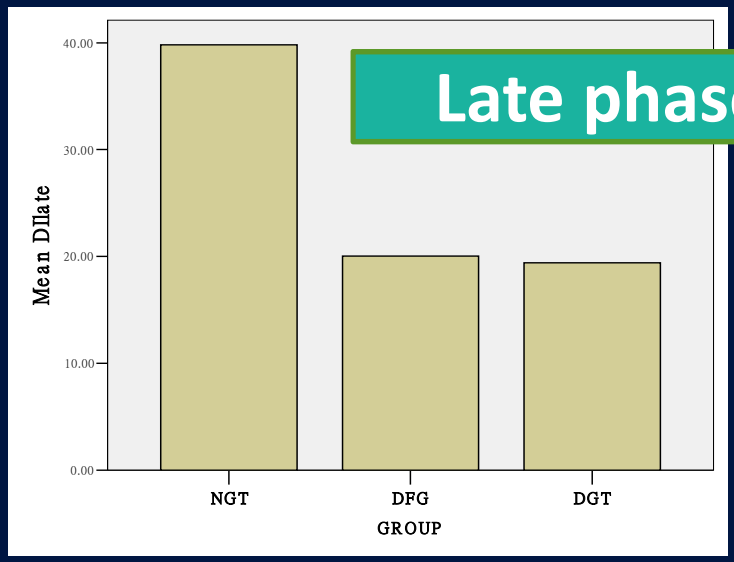
Late phase: DFG>DGT

DI between DFG, DGT









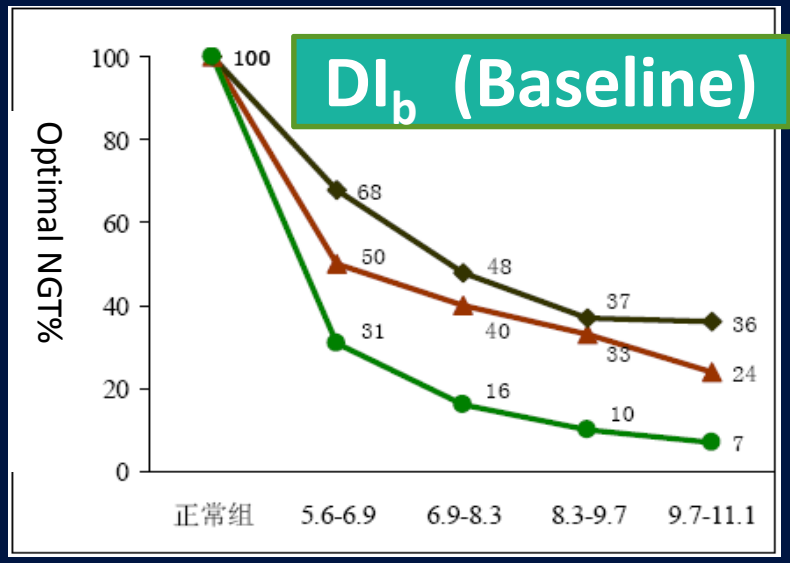
Conclusion 1

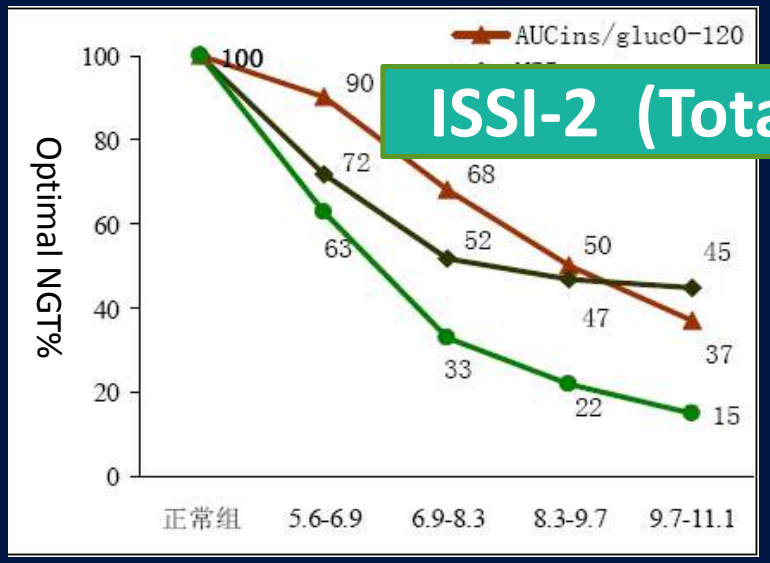
- Insulin resistances (hepatic and peripheral) were lowest in subjects with NGT and highest in those with DFG/DGT.
- All-phase insulin secretions and DIs were highest in those with NGT and lowest in those with DFG/DGT.

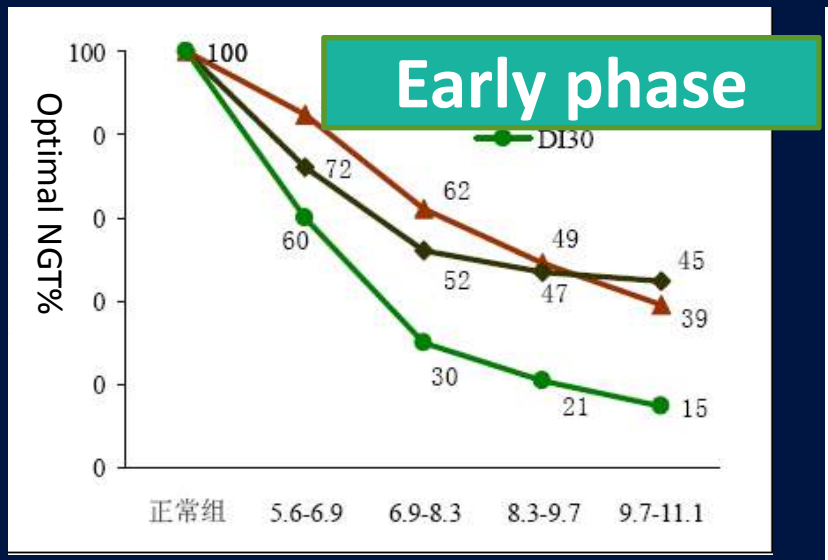
Conclusion 1

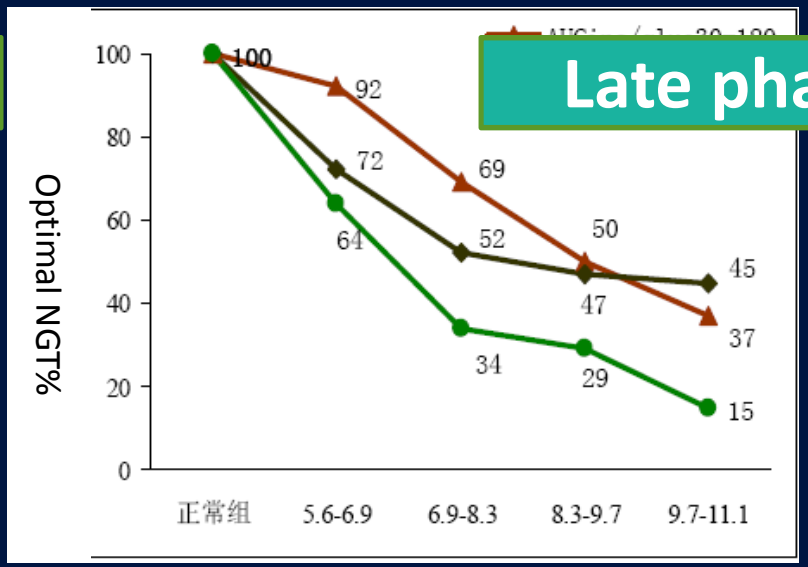
- Subjects with IFG and IGT have distinct pathophysiological disturbances.
- Subjects with DFG resembles the pathophysiologic characteristics of individuals with IFG. (The highest hepatic insulin resistance and the lowest DIb)
- DGT is similar to the pathophysiologic characteristics of those with IGT. (A lower peripheral insulin sensitivity， a higher DIb and a lower DI2 than DFG which)

Relationship between DI and FBG

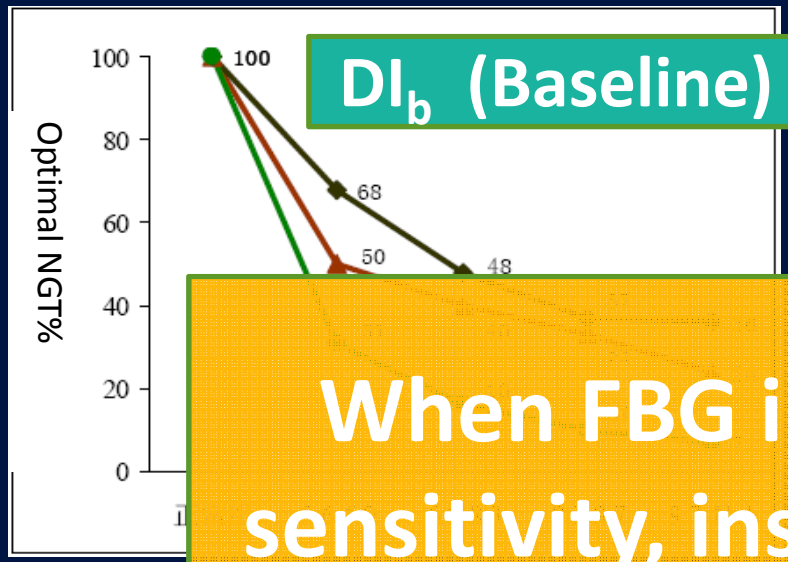




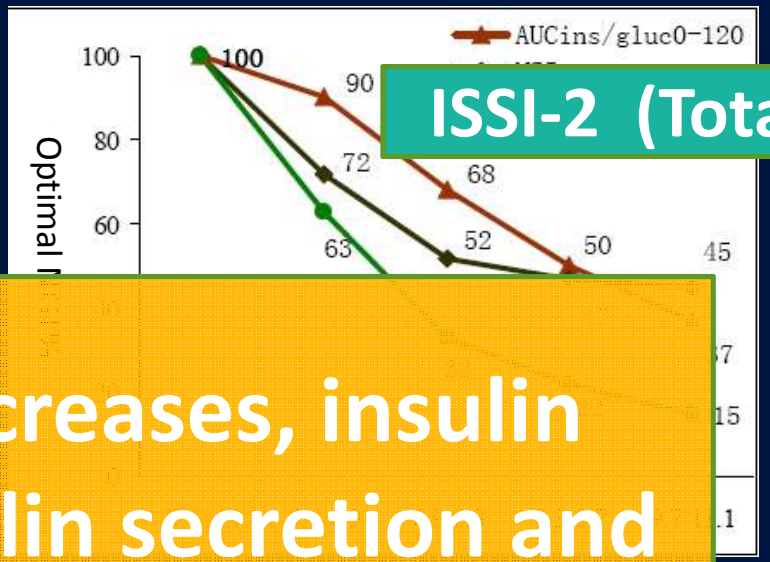




Relationship between DI and FBG

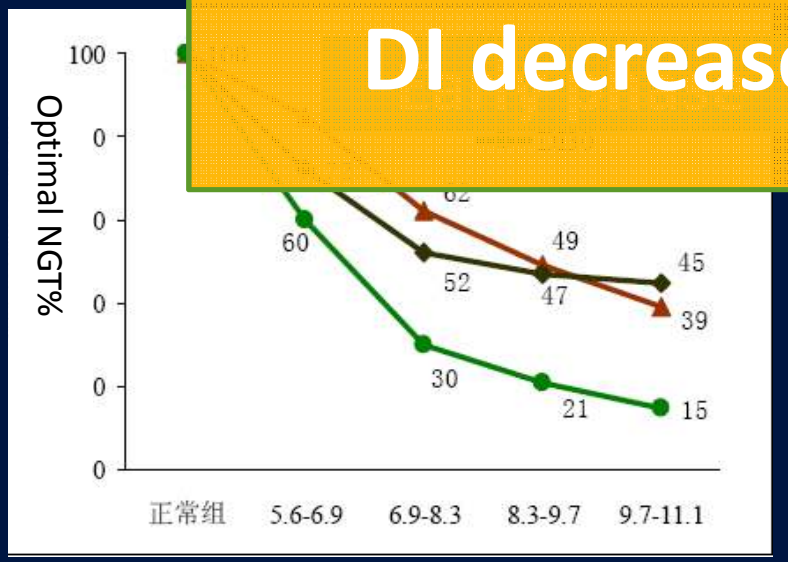


DI_b (Baseline)

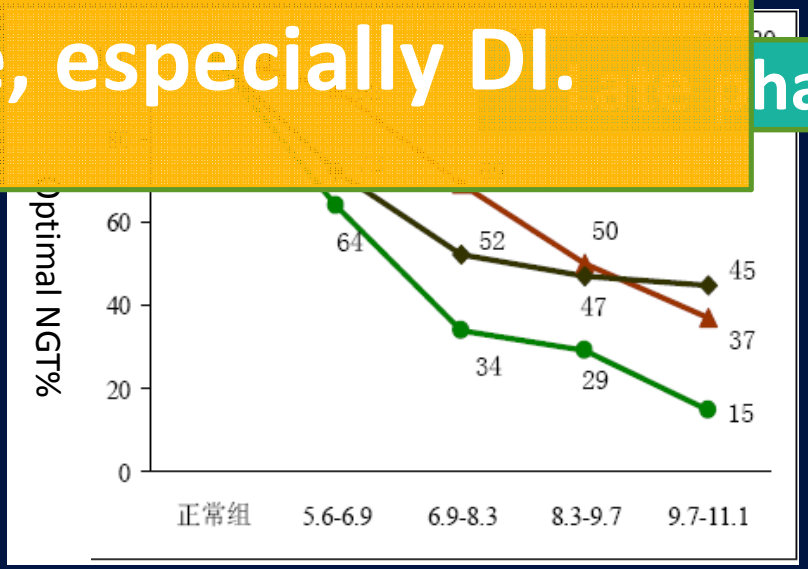


ISSI-2 (Total)

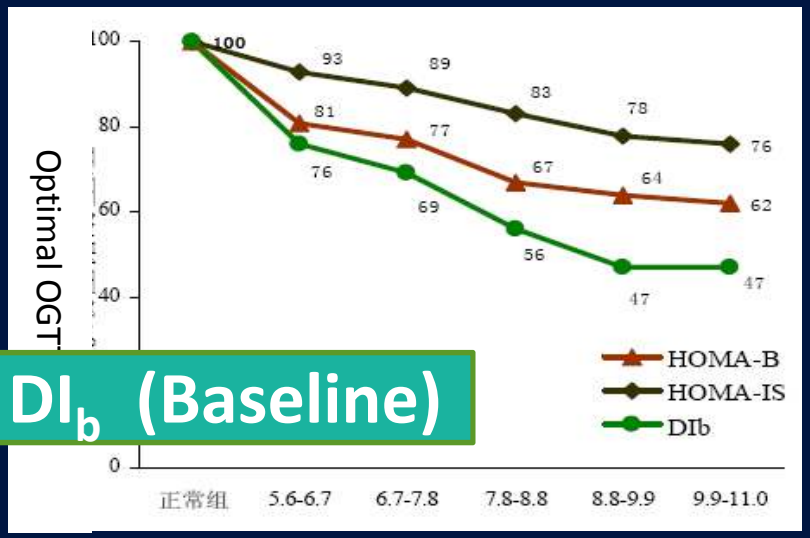
When FBG increases, insulin sensitivity, insulin secretion and DI decrease, especially DI.



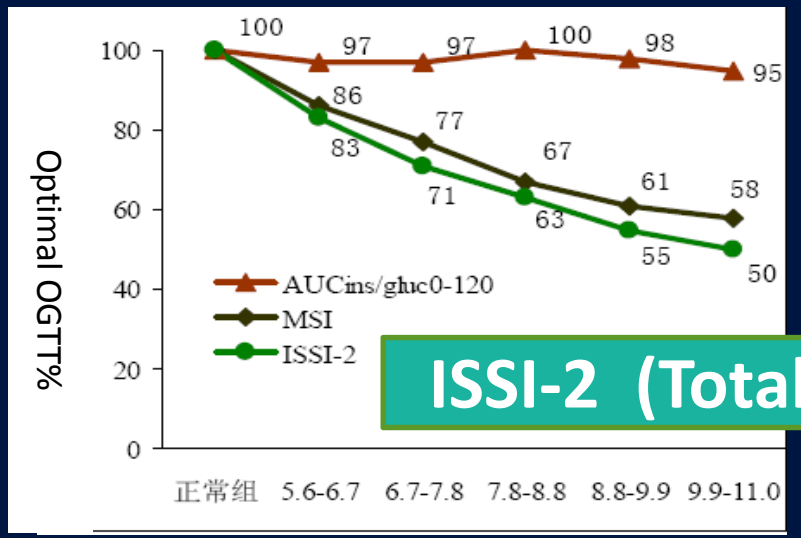
hase



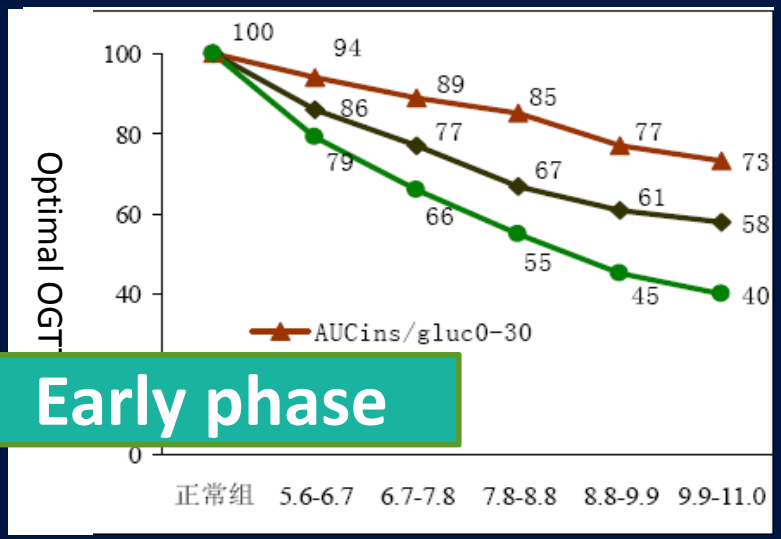
Relationship between DI and PBG



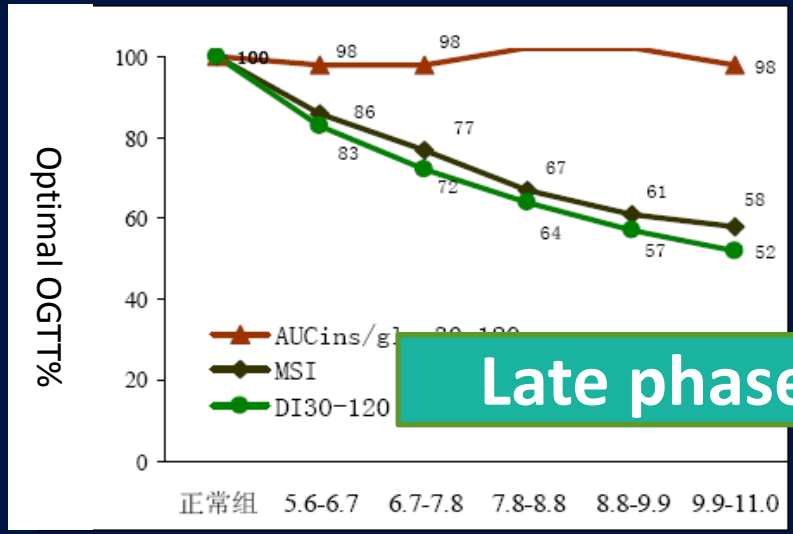
DI_b (Baseline)



ISSI-2 (Total)

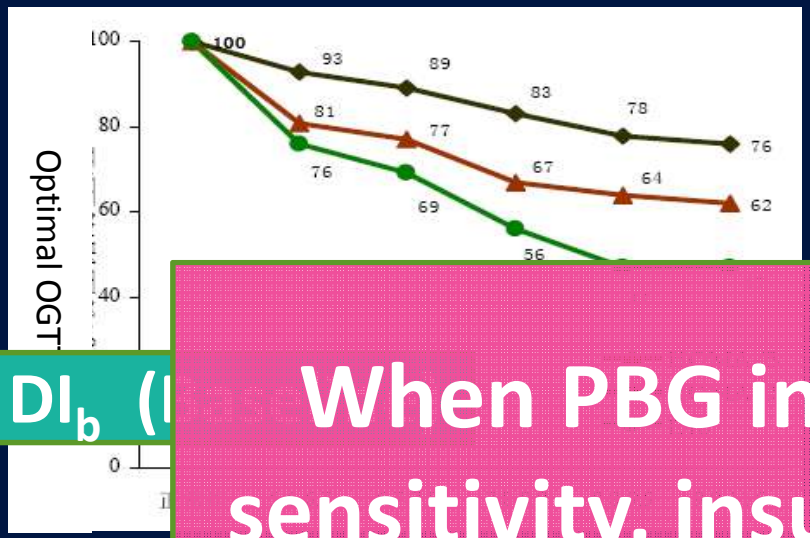


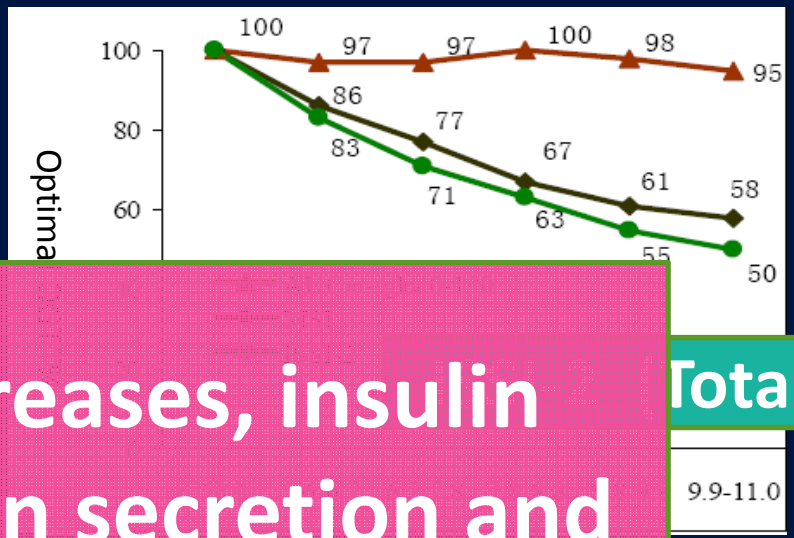
Early phase



Late phase

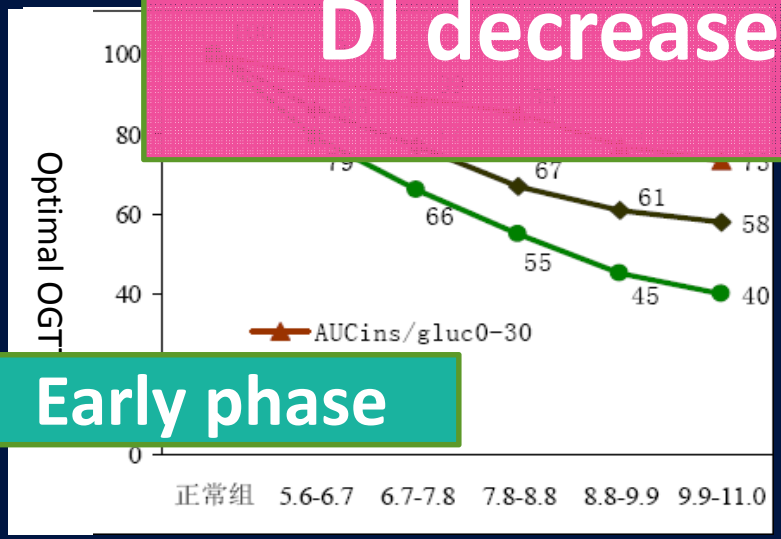
Relationship between DI and PBG



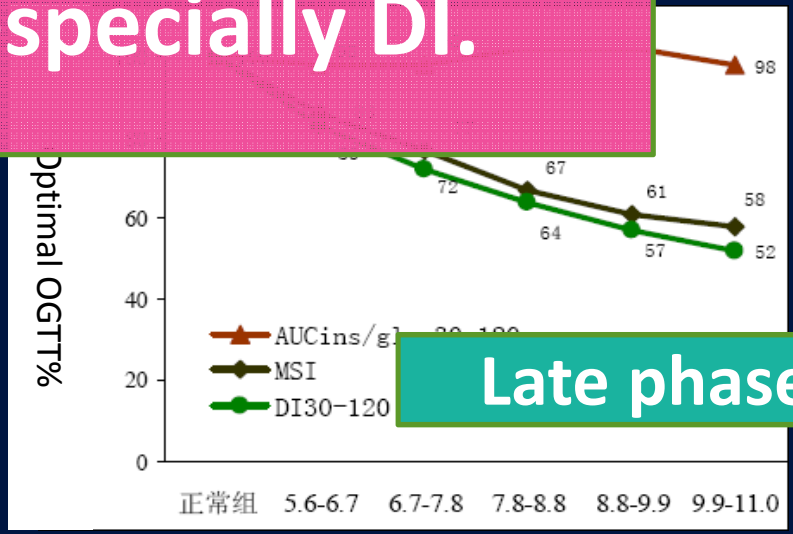


DI_b (I Total)

When PBG increases, insulin sensitivity, insulin secretion and DI decrease, especially DI.



Early phase



Late phase

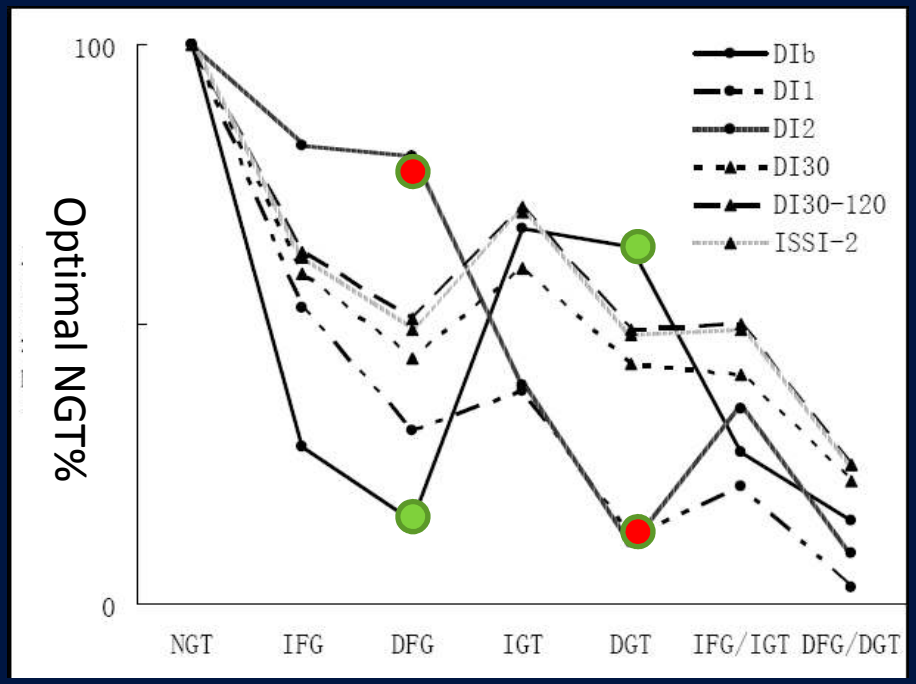
Comparison of DI

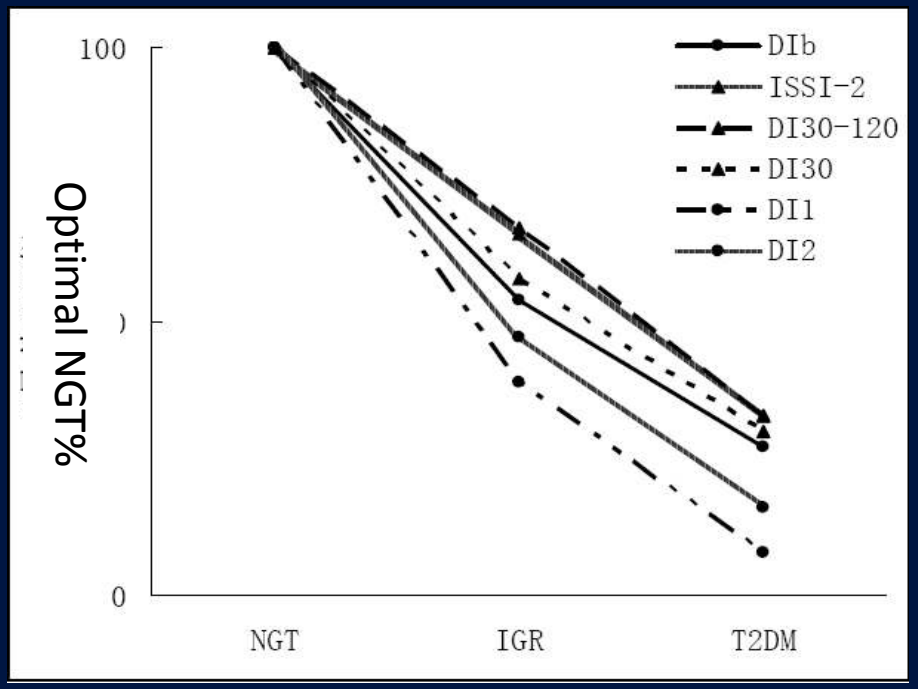
DI	Abr.	insulin secretion	insulin sensitivity	Time points
Baseline	DI_b	HOMA-B	1/HOMA-IR	One
Early phase	DI_1	EPIR	$ISI_{0,120}$	Two
Late phase	DI_2	LPIR	$ISI_{0,120}$	Two
OGTT total	**ISSI-2**	**AUCIns/Gluc$_{0\text{-}120}$**	**MSI**	**Three**

Golden standard

Can we use DIs derived from less than **three measures** of blood glucose and insulin levels to assess β-cell function ?

Comparison of DI





Mirror image-DI_b and DI2

Glu increase, DI decrease

Comparison of DI

		Total		NGT		IGR		DM	
		r	p	r	p	r	p	r	p
DIb	ISSI-2	0.54	0.000	0.39	0.000	0.39	0.000	0.60	0.000
DI1	ISSI-2	0.36	0.000	0.64	0.000	0.30	0.000	0.61	0.000
DI2	ISSI-2	0.50	0.000	0.32	0.000	0.18	0.000	0.54	0.000

General linear regression showed DIb could explain more than 90% change of FPG and DI2 could explain more than 50% change of 2h-PG.

It is possible to evaluate β-cell function by DIs derived from less than three measures of OGTT.

Conclusion 2

- DIs (DI1， DI2 and DIb) derived from less than three measures of blood glucose and insulin levels correlated well with the one from three measures (ISSI-2)

Take home message

Take home message

- Subjects with IFG and IGT in China have different pathophysiologic characteristics.
- Subjects with DFG and DGT share the pathophysiologic characteristics of individuals with IFG and IGT respectively.
- It is possible to evaluate β-cell function by DIs derived from less than three measures of OGTT in epidemiological studies.

Acknowledgement

- Thank you for all the participants in the survey
- Designed Research: Linong Ji
- Performed Research: Xianghai Zhou, Yong Tang, Qian Ren, Xiuying Zhang, Yingying Luo, Linong Ji
- Analyzed Data: Huaiqing Wang, Xianghai Zhou, Qian Ren, Xueyao Han, Linong Ji