GLYCEMIC AND NON-GLYCEMIC EFFECTS OF GLP-1 RECEPTOR AGONIST (INCRETIN)
(舉例 LIRAGLUTIDE; VICTOZA 胰妥善)

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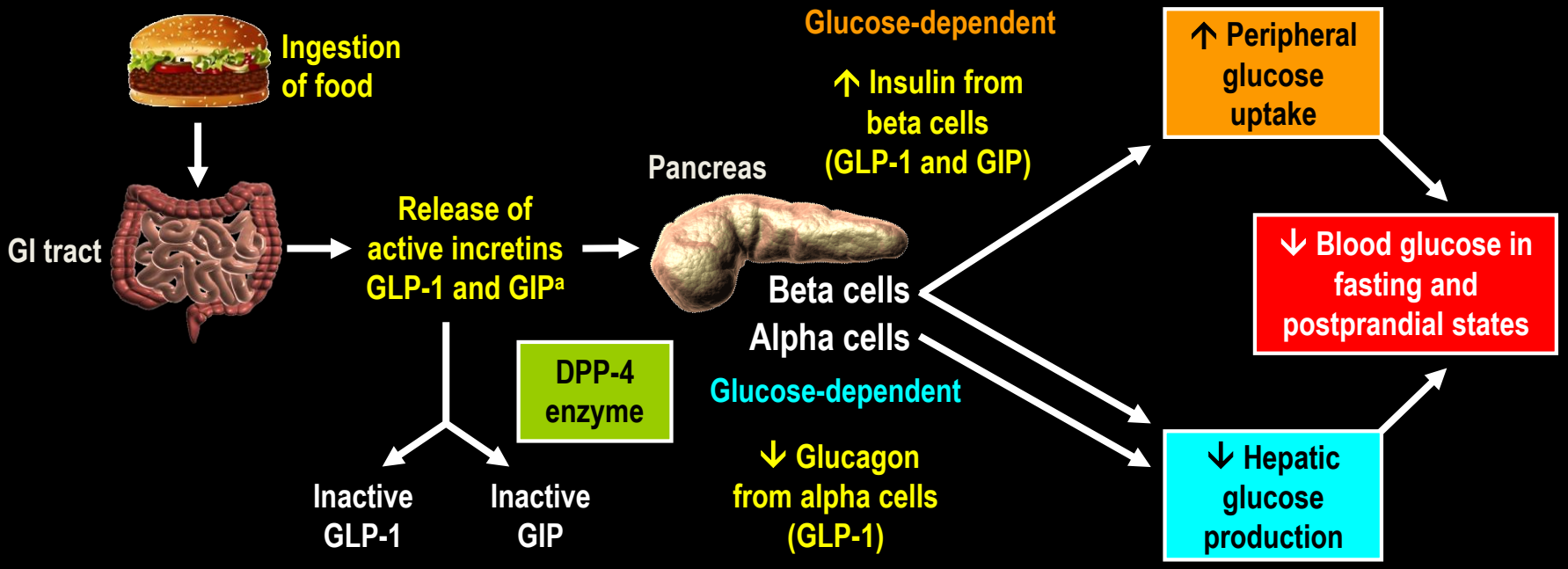
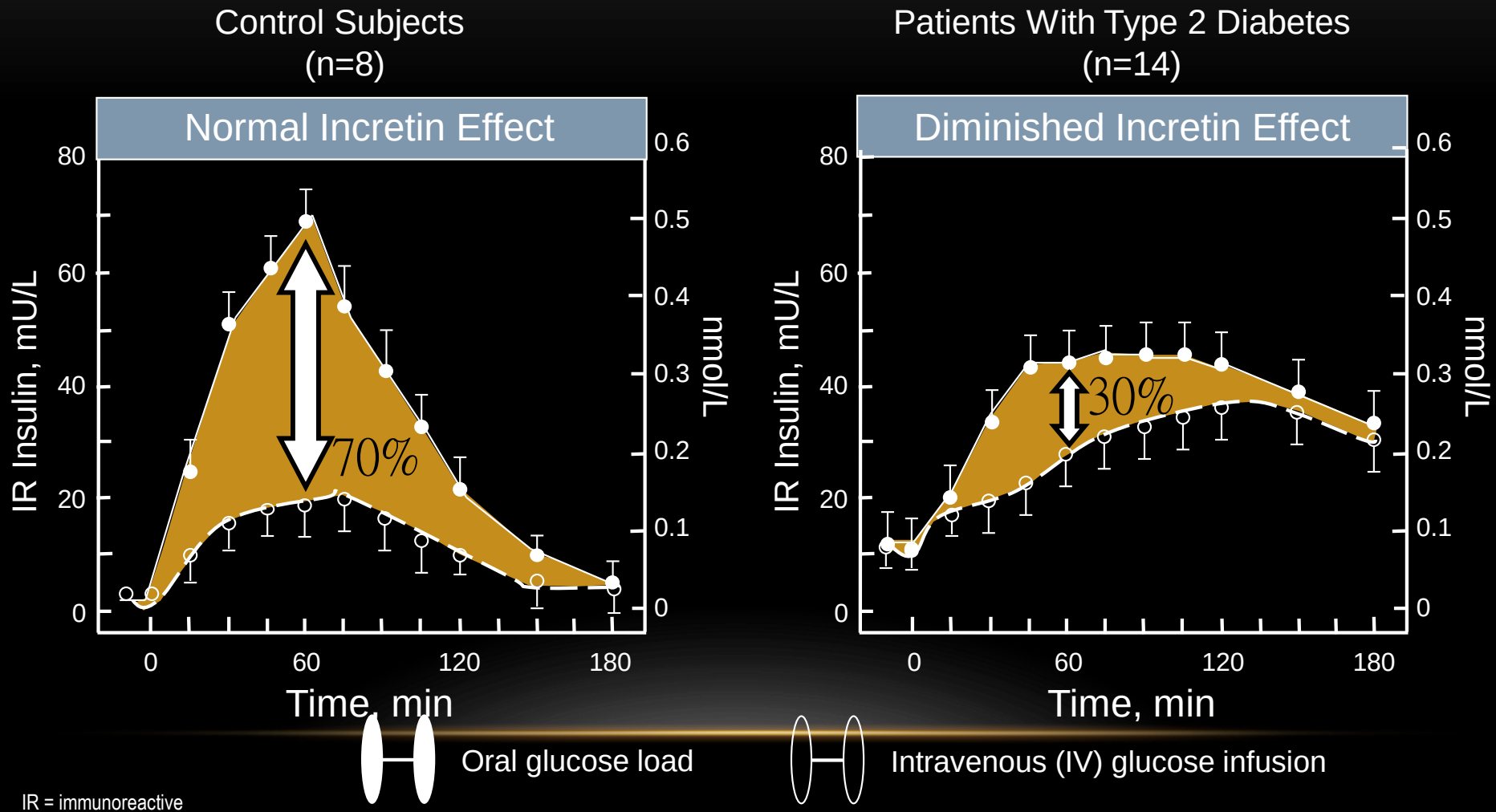
Incretin (GLP-1, GIP) and Type 2 DM



DPP-4=dipeptidyl peptidase-4; GI=gastrointestinal; GIP=glucose-dependent insulinotropic peptide; GLP-1=glucagon-like peptide-1.
[a]Incretin hormones GLP-1 and GIP are released by the intestine throughout the day, and their levels increase in response to a meal.

1. Kieffer TJ et al. *Endocr Rev*. 1999;20(6):876–913. 2. Ahrén B. *Curr Diab Rep*. 2003;3(5):365–372. 3. Drucker DJ. *Diabetes Care*. 2003;26(10):2929–2940. 4. Holst JJ. *Diabetes Metab Res Rev*. 2002;18(6):430–441.

INCRETIN EFFECT(腸促胰素作用)是重要生理血糖調控機制，而T2DM的 INCRETIN 作用較差



IR = immunoreactive

Vilsbøll T, Holst JJ. *Diabetologia* 2004;47:357–366.

Clinical Application of Incretin-Based Therapy: Therapeutic Potential, Patient Selection and Clinical Use

缺乏腸促胰素(Incretin)是造成糖尿病前期,及第二型糖尿病病患的胰島素阻抗性增加,體重增加及血糖升高的主要因素之一！

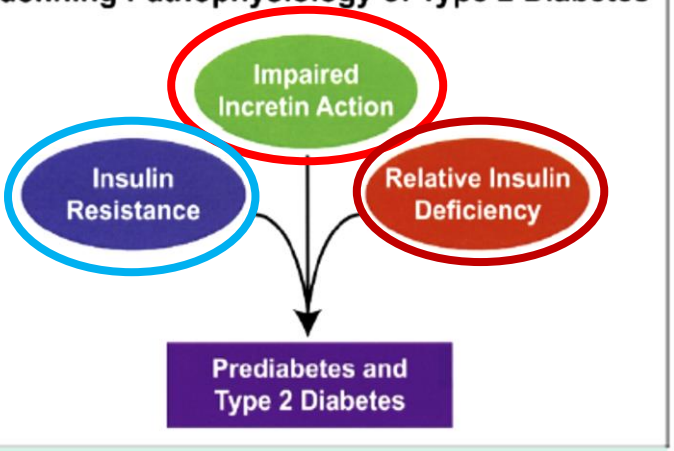


Figure 1 Postulated role of insulin resistance, β-cell dysfunction, and an impaired incretin effect in the pathogenesis of type 2 diabetes mellitus. (Adapted from *J Clin Endocrinol Metab*,[23] *Diabetes*,[24,27] *Eur J Clin Endocrinol*,[25] and *J Clin Invest*.[26])

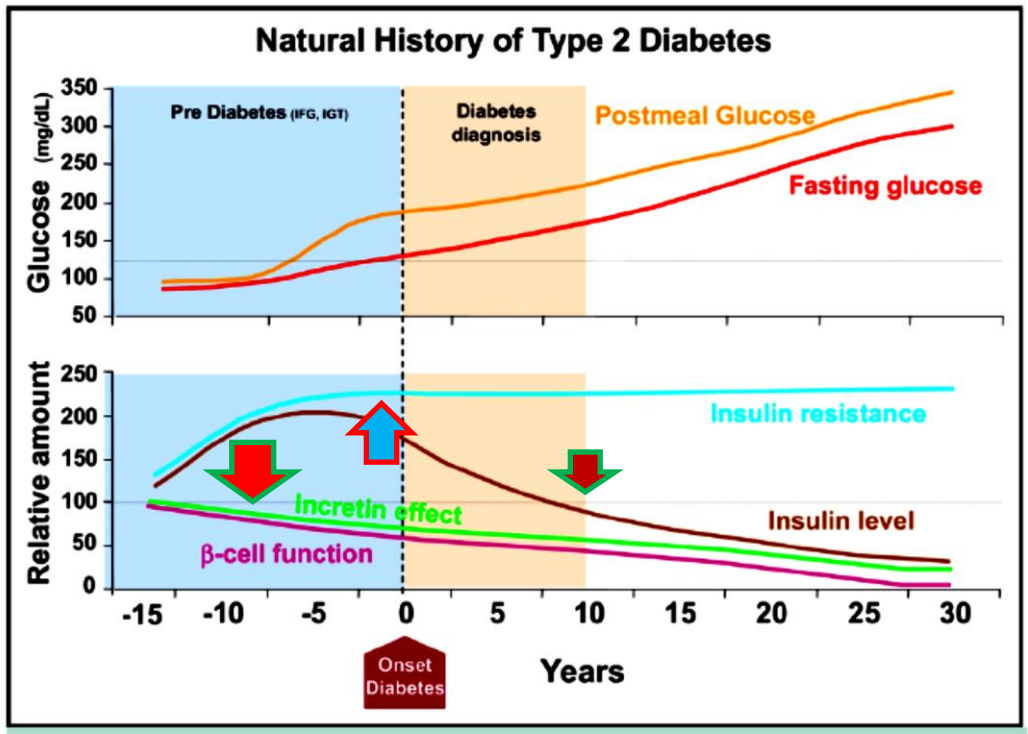
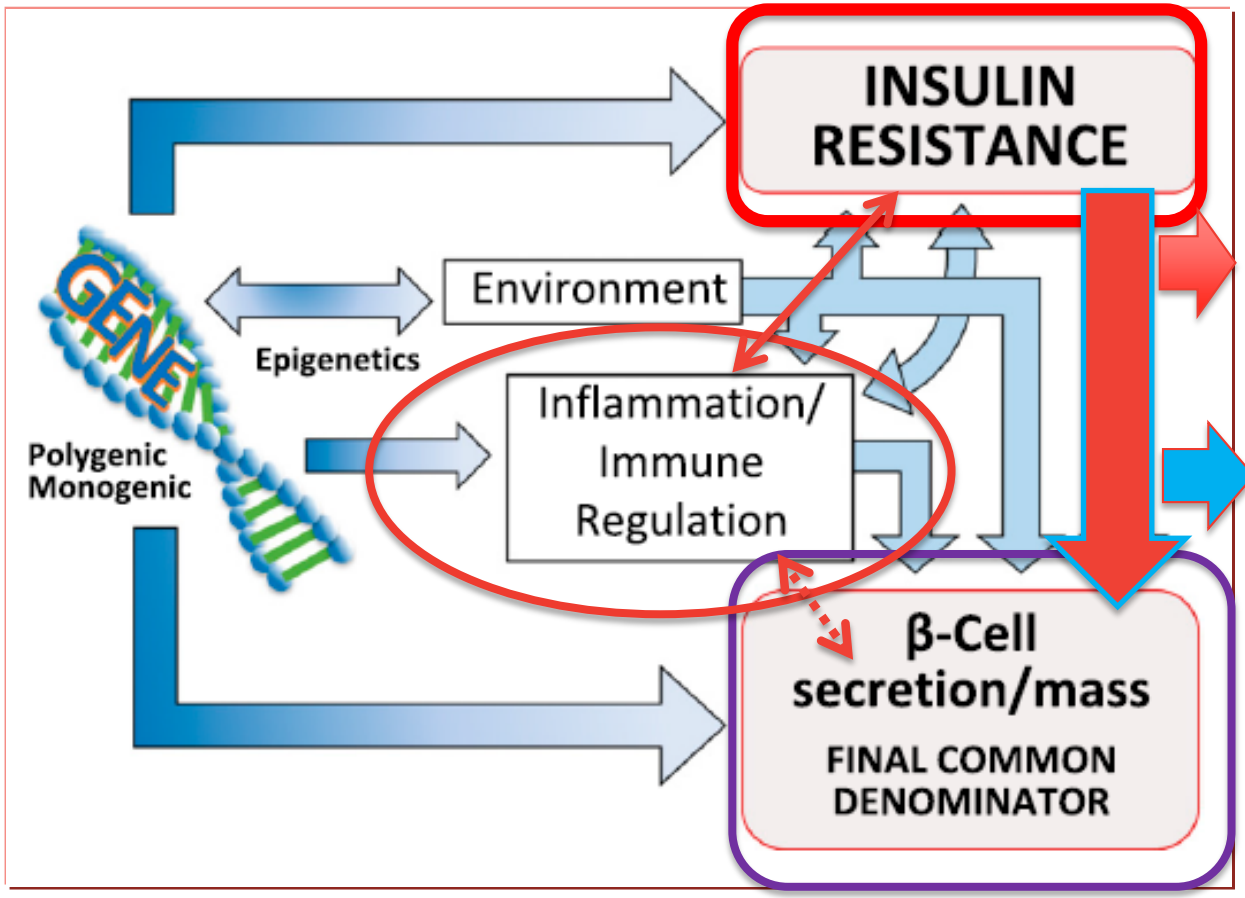


Figure 2 Representative depiction of the natural history of type 2 diabetes mellitus highlighting the role of insulin resistance, insulin deficiency, and impaired incretin effect. Both the time course and relative function are descriptive. These 3 core pathophysiologic defects likely combine to contribute to the progressive nature of the disease, and may account for much of the deterioration in glucose control observed clinical in patients with type 2 diabetes. IFG = impaired fasting glucose; IGT = impaired glucose tolerance. For glucose, 1 mg/dL = 0.5551 mmol/L. (Courtesy of the International Diabetes Center © 2008.)

David M. Kendall et al. The American Journal of Medicine 2009 (122): S37–S50.

The Time Is Right for a New Classification System for Diabetes: Rationale and Implications of the β-Cell–Centric Classification Schema (Egregious Eleven)



Stanley S. Schwartz et al . Diabetes Care 2016;39(2):179–186

Clinical Application of Incretin-Based Therapy: Therapeutic Potential, Patient Selection and Clinical Use

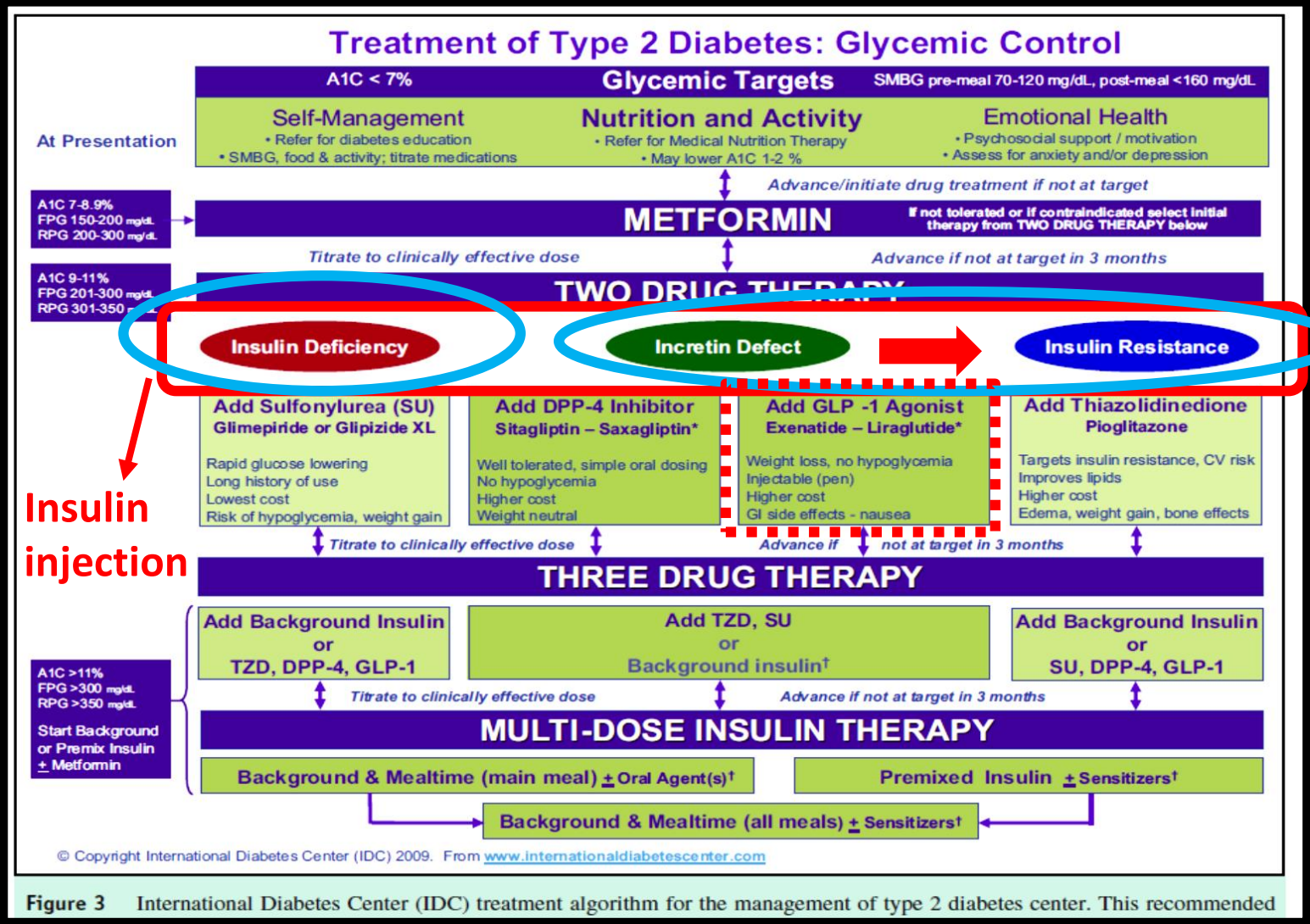
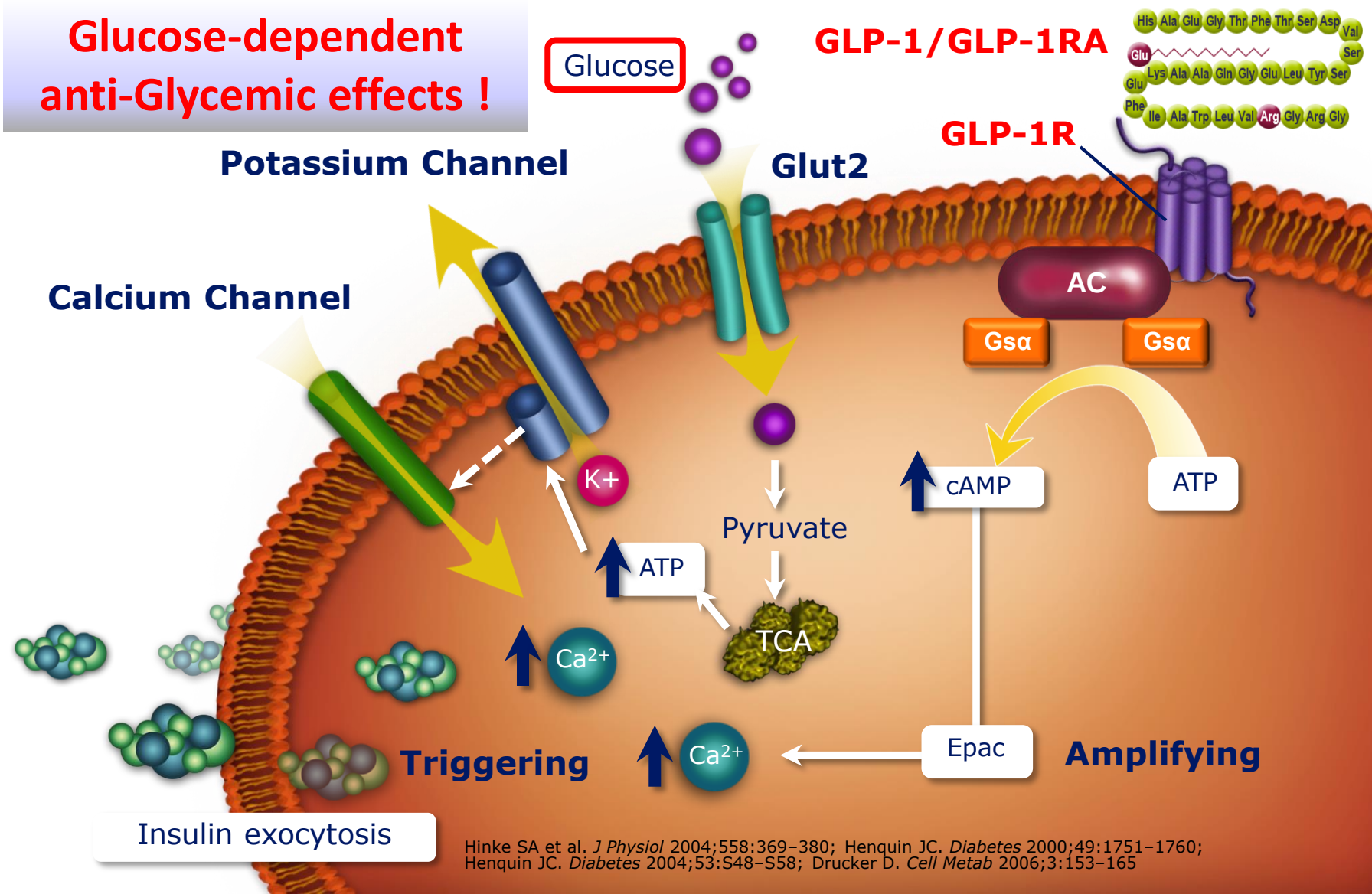


Figure 3 International Diabetes Center (IDC) treatment algorithm for the management of type 2 diabetes center. This recommended

David M. Kendall et al. The American Journal of Medicine 2009 (122): S37–S50.

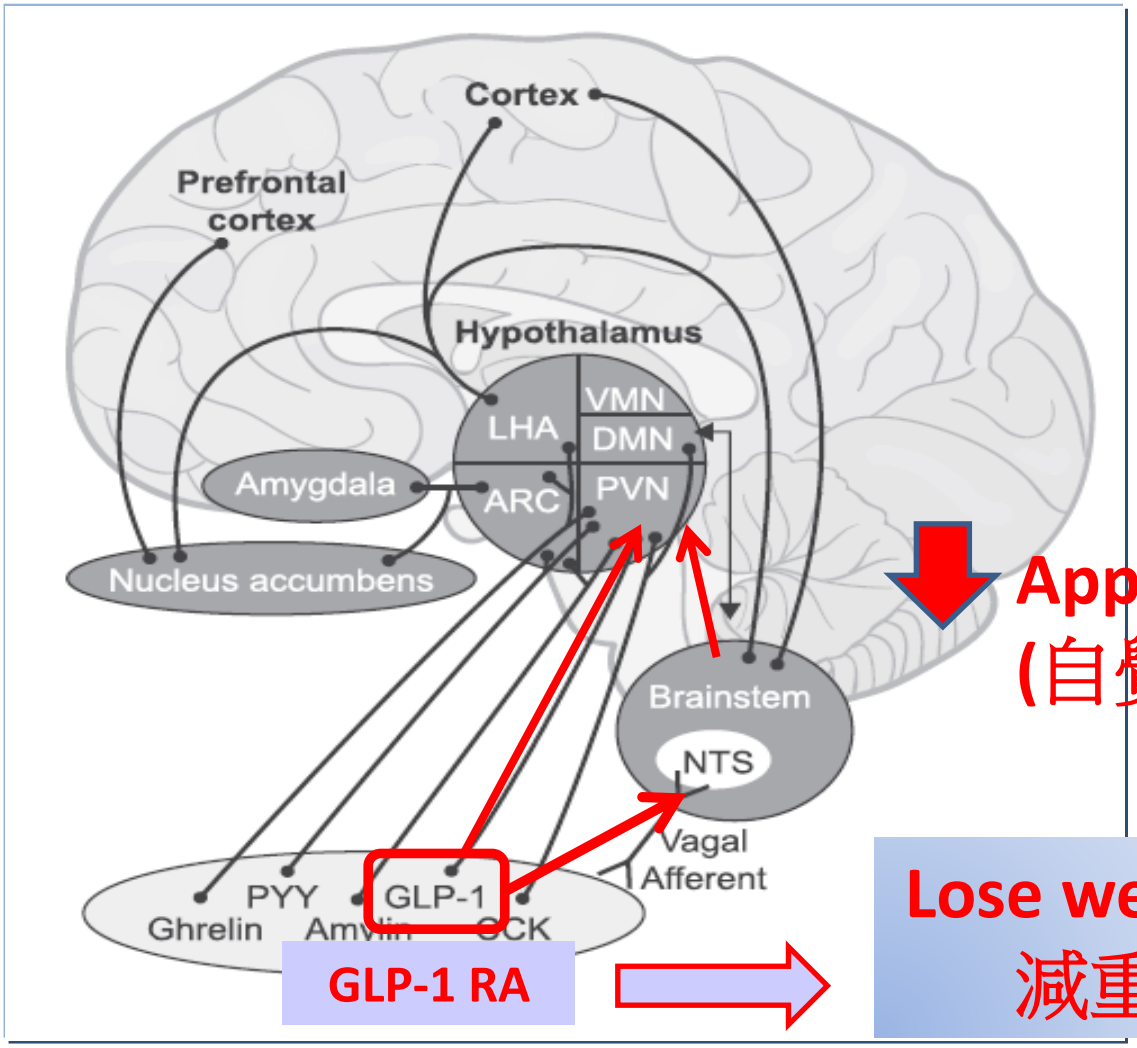
Anti-Glycemic Effects of GLP-1 RA in Type 2 DM

GLP-1/GLP-1 RA action in the β cell via GLP-1R



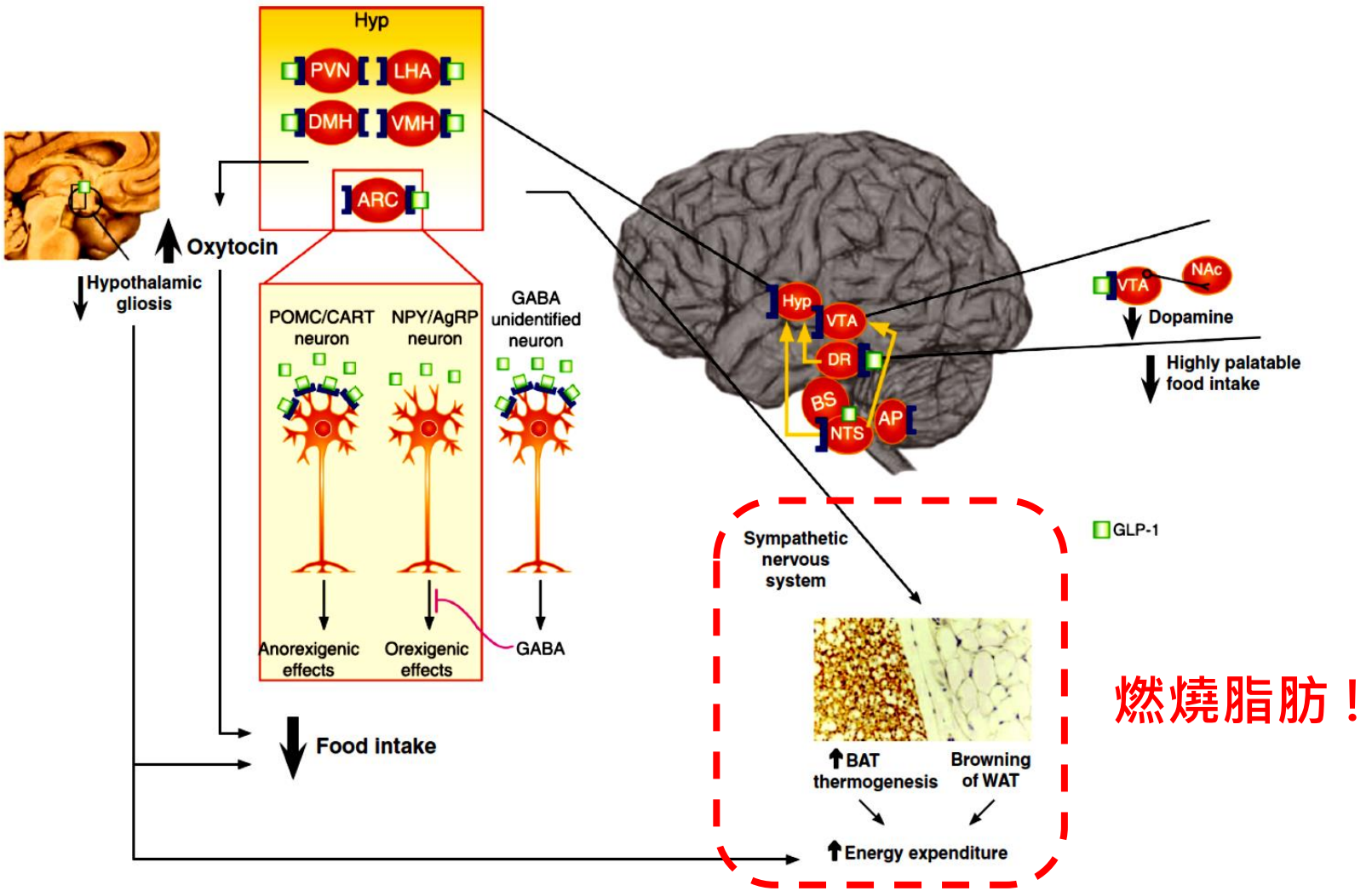
Hinke SA et al. *J Physiol* 2004;558:369–380; Henquin JC. *Diabetes* 2000;49:1751–1760; Henquin JC. *Diabetes* 2004;53:S48–S58; Drucker D. *Cell Metab* 2006;3:153–165

Harnessing glucagon-like peptide-1 receptor agonists for the pharmacological treatment of overweight and obesity



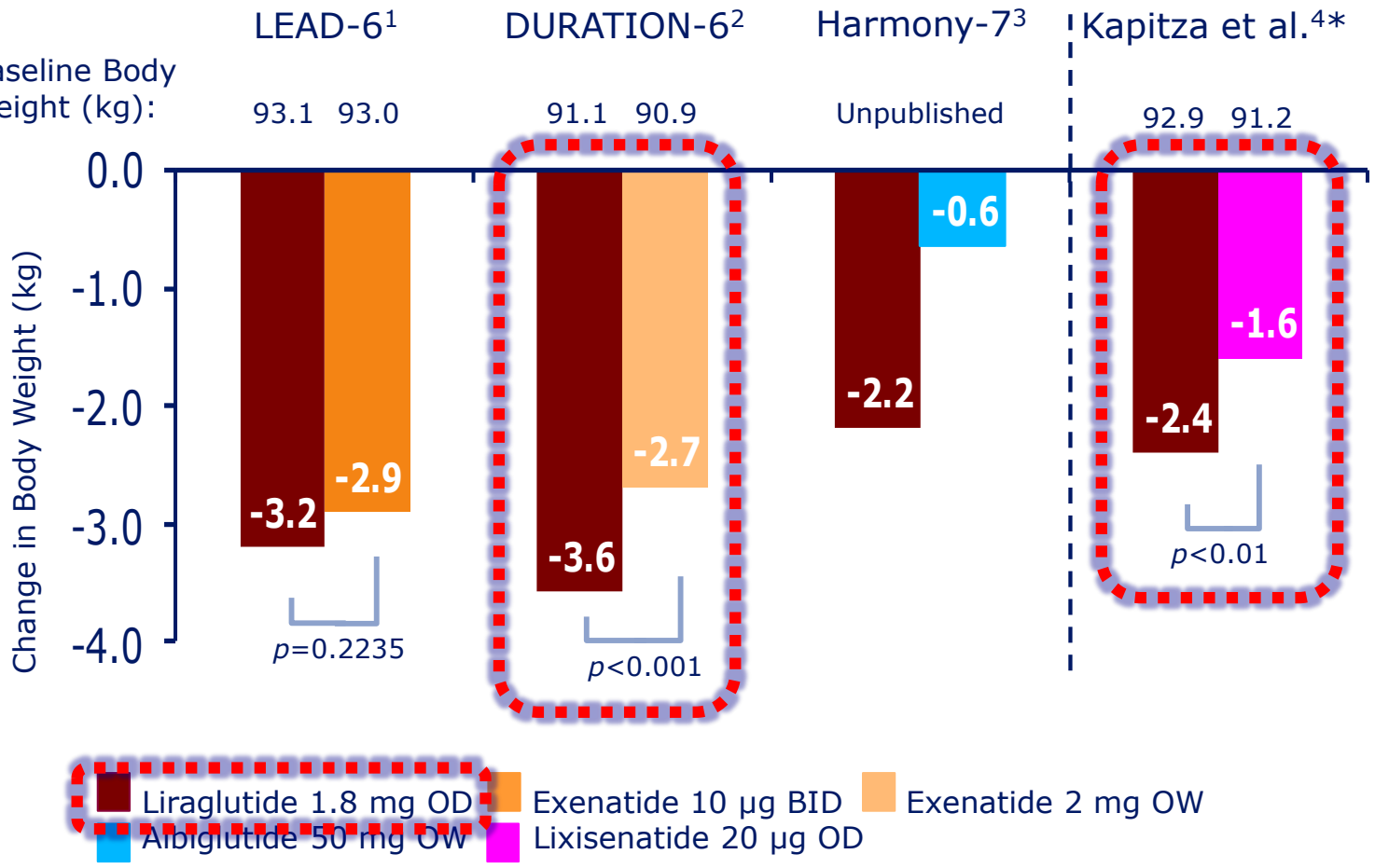
R. Burcelin and P. Gourdy. Obesity Reviews 2017;18, 86–98.

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs) in the Brain–Adipocyte Axis



Bruno Geloneze et al. Drugs (2017) 77:493–503.

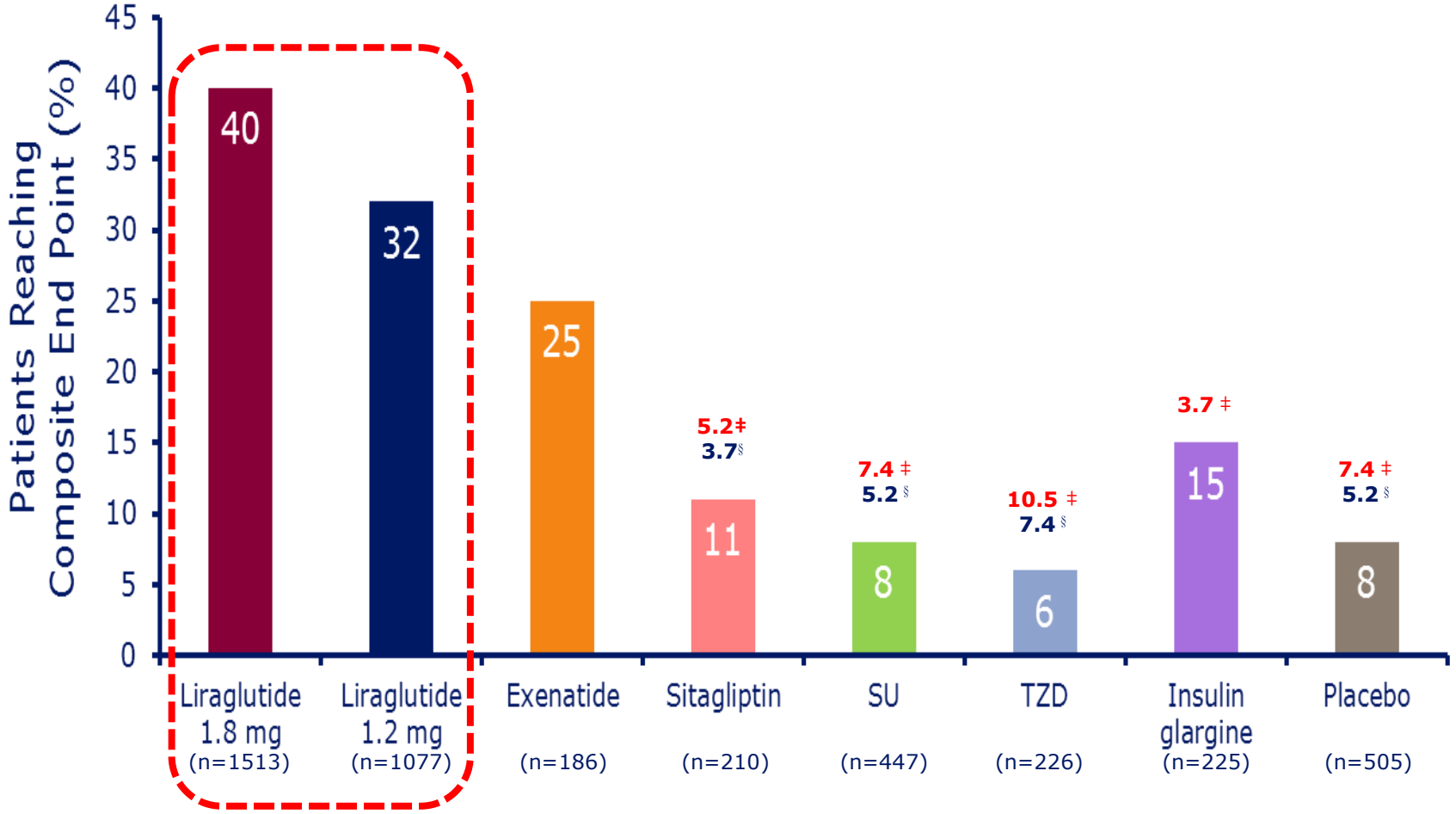
GLP-1RA comparative studies:
Change in body weight



*4-week data
BID, twice daily; GLP-1RA, glucagon-like peptide 1 receptor agonist; HbA_{1c}, glycosylated haemoglobin; OD, once daily; OW, once weekly

1. Buse JB et al. *Lancet* 2009;374:39–47; 2. Buse JB et al. *Lancet* 2013;381:117–124; 3. Pratley R et al. ADA 2012 poster presentation 945-P; 4. Kapitza C et al. *Diabetes Obes Metab* 2013;15:642–649

Composite end point:
HbA_{1c} <7.0%, No weight gain, No hypoglycaemia



Odds ratio of achieving composite end point with liraglutide 1.8 mg is superior, with *p<0.001; †p<0.01; ‡p<0.0001
Odds ratio of achieving composite end point with liraglutide 1.2 mg is superior, with §p<0.0001
HbA_{1c}, glycosylated haemoglobin; SU, sulphonylurea; TZD, thiazolidinedione

Zinman B et al. *Diabetes Obes Metab* 2012;14:77–82

SUMMARY OF LIRAGLUTIDE EFFICACY IN PREVIOUS 6 LEAD STUDY (MAX 1.8 MG QD)

(MONOTHERAPY OR IN COMBINATION WITH OTHER OADS OR INSULIN)

- Lower HbA1C by 1.1~ 1.6%
- Reduce Weight by 2.2~3.6 kg
- 30~40% Patients reached the goal A1C <7% without hypoglycemia and no weight gain
- Lower systolic BP by 3~ 4 mmhg
- Reduce LDL-C by 0.1% and reduce TG by 0.3%
- Proven Cost-effectiveness

EFFECTIVE LIRAGLUTIDE DOSAGE

0.9 mg qd ~ 1.8 mg qd for HbA1C reduction !

1.2 mg qd ~ 3.0 mg qd for weight reduction !

Effect of renal impairment on the pharmacokinetics of the GLP-1 analogue liraglutide

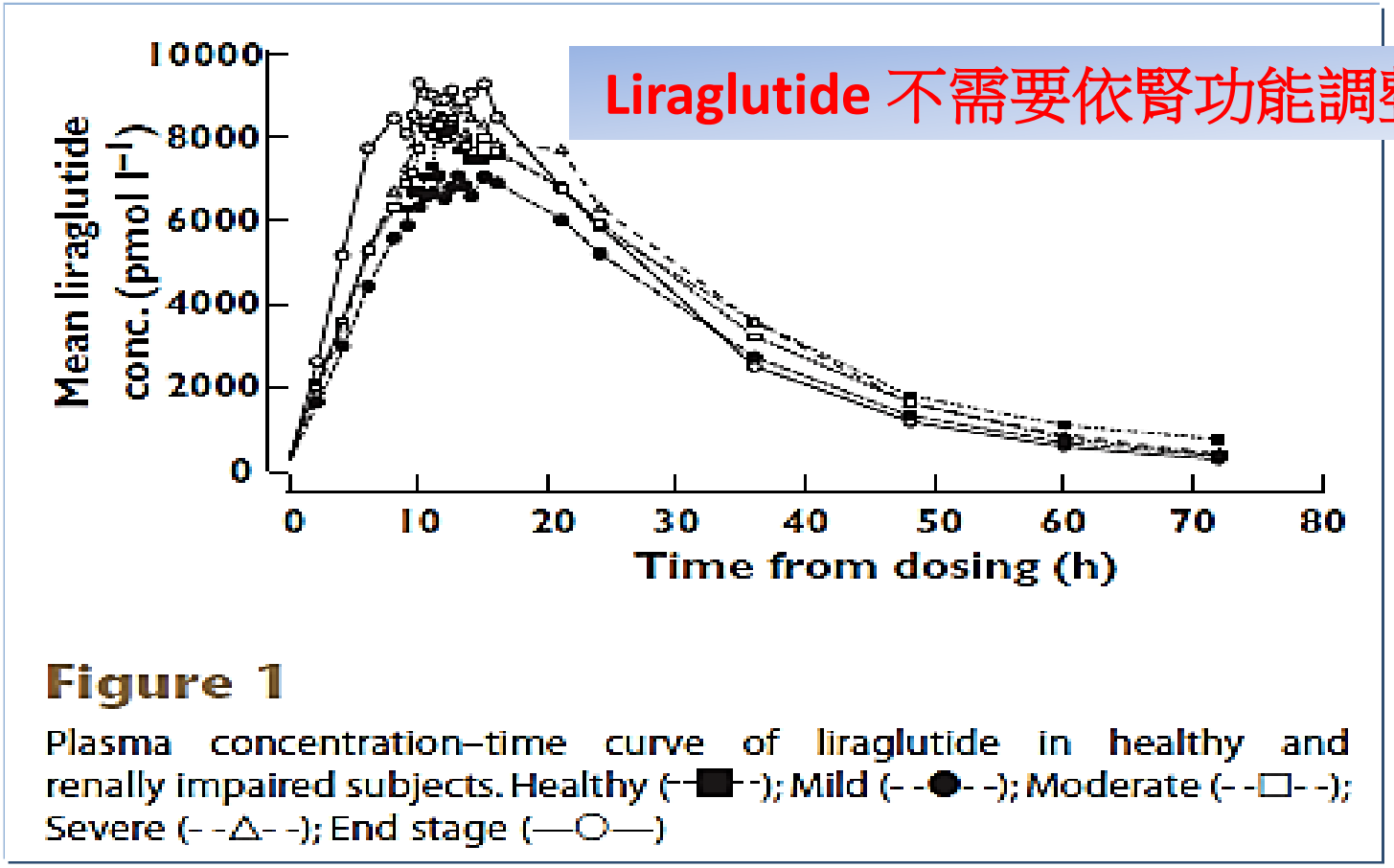


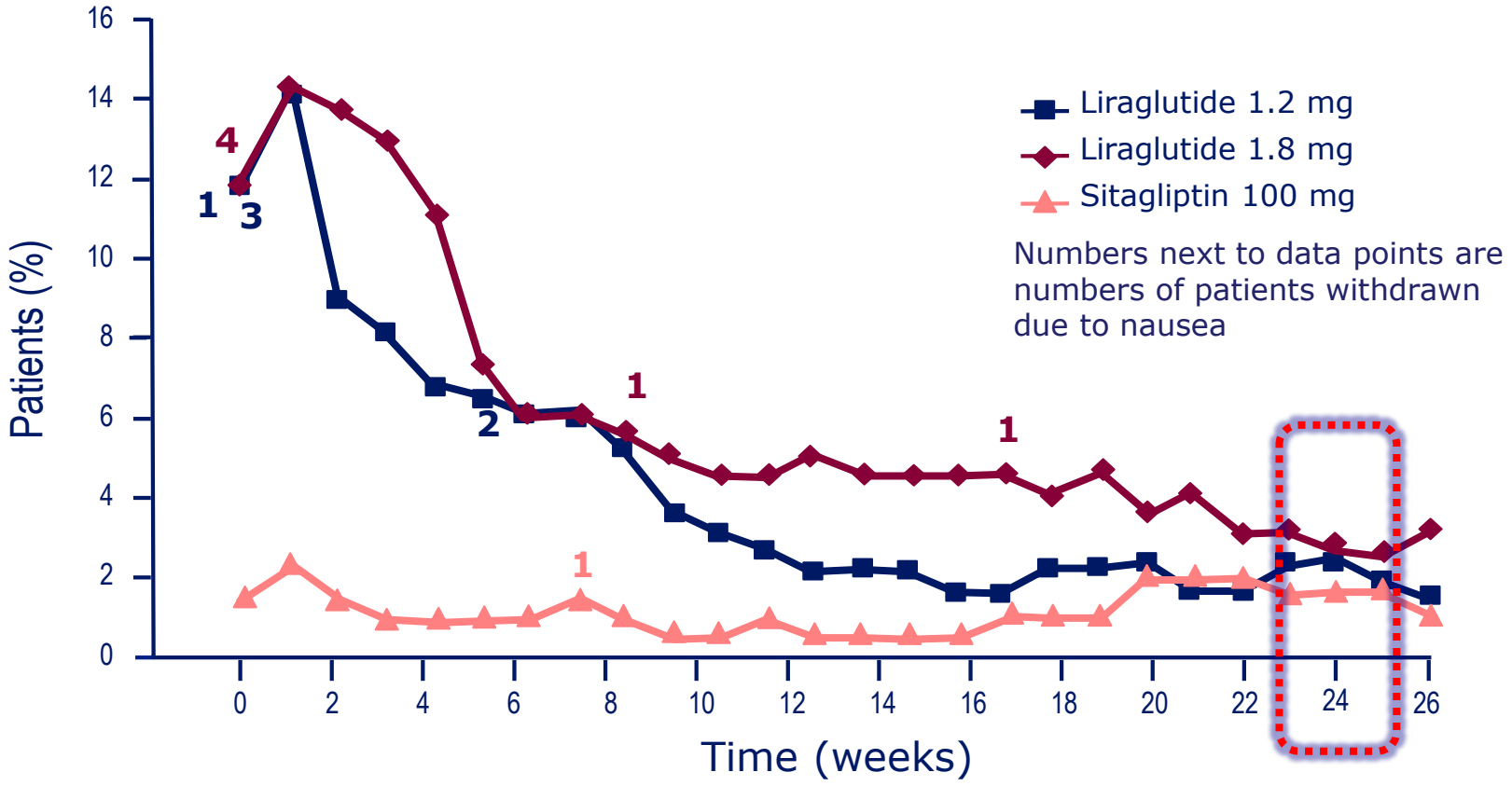
Figure 1

Plasma concentration–time curve of liraglutide in healthy and renally impaired subjects. Healthy (–■–); Mild (– –●– –); Moderate (– –□– –); Severe (– –△– –); End stage (—○—)

A single dose of 0.75-mg Liraglutide

Lisbeth V. Jacobsen et al. Br J Clin Pharmacol 2009; 68(6): 898–905

Nausea/vomit with liraglutide is transient



Liraglutide was generally well-tolerated with transient GI side effects the most common.

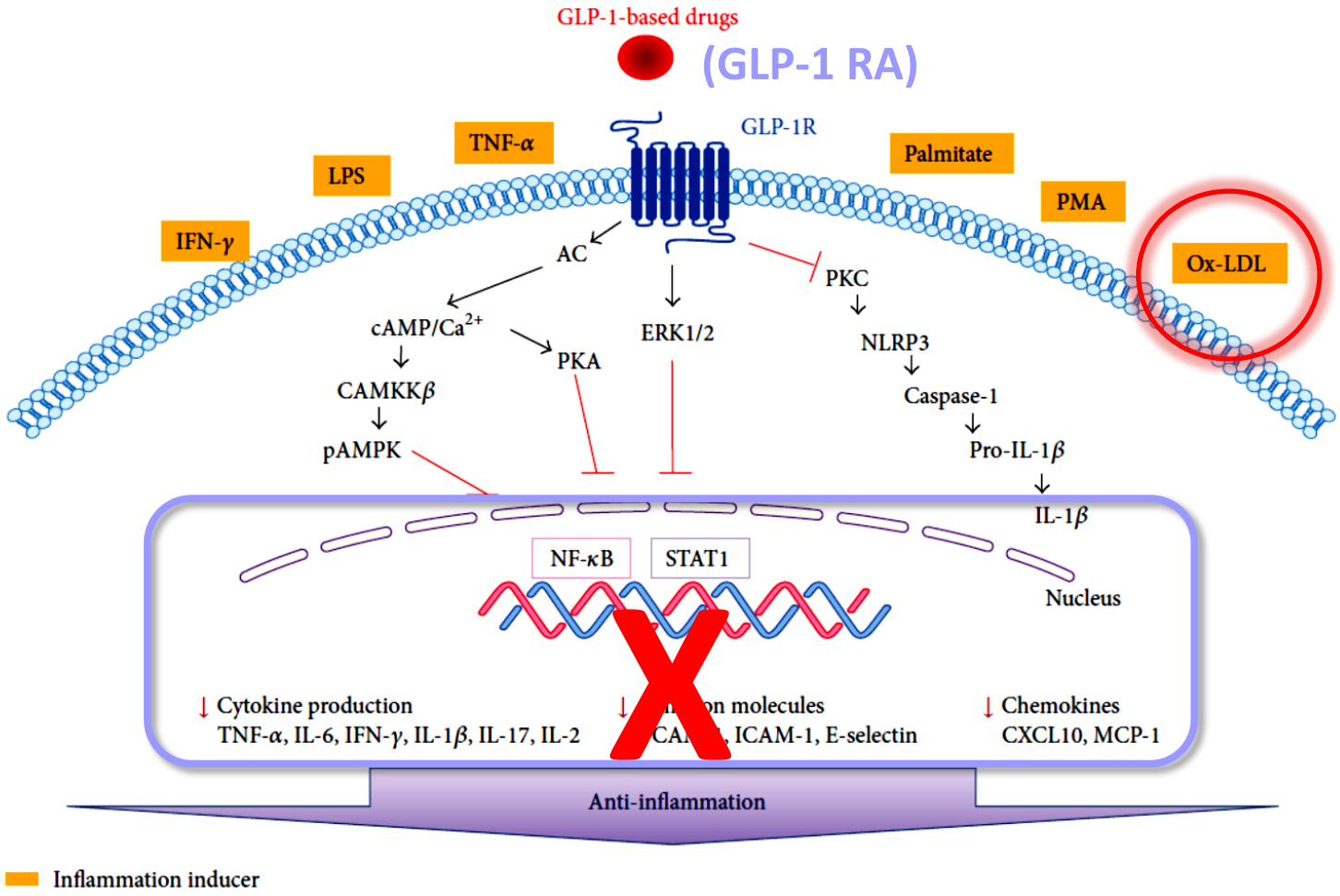
Data are from the safety analysis set

Pratley R et al. *Lancet* 2010;375:1447–1456

Non-Glycemic Effects of

GLP-1 RA

Anti-Inflammatory Effects of GLP-1-Based Therapies beyond Glucose Control



Young-Sun Lee et al. Mediators of Inflammation 2016, Article ID 3094642, 11 pages
http://dx.doi.org/10.1155/2016/3094642

Treatment with GLP1 receptor agonists reduce serum CRP concentrations in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
A. Faurschou	-0.006	0.449	0.202	-0.887	0.875	-0.013	0.99
Aaron S Kelly	0.000	0.283	0.080	-0.554	0.554	0.000	1.000
G. Derosa	-3.333	0.287	0.082	-3.896	-2.771	-11.613	0.000
Hui Fan	-0.499	0.190	0.036	-0.872	-0.126	-2.622	0.009
Jin-dan Wu	-2.837	0.591	0.349	-3.995	-1.678	-4.800	0.000
MATHIJS C. BUNCK	-2.000	0.319	0.102	-2.625	-1.375	-6.27	0.000
Ziwen Liang	-6.743	0.618	0.382	-7.954	-5.531	-10.910	0.000
	-2.148	0.696	0.484	-3.512	-0.784	-3.086	0.002

Statistics for each study

Std diff in means and 95% CI

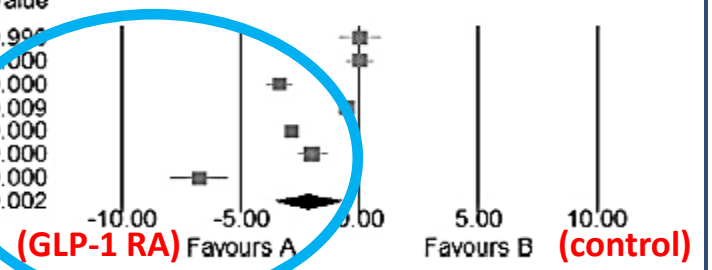


Fig. 1. Plot to display weighted mean difference and 95% confidence intervals for the impact of glucagon-like peptide-1 therapy on C-reactive protein.

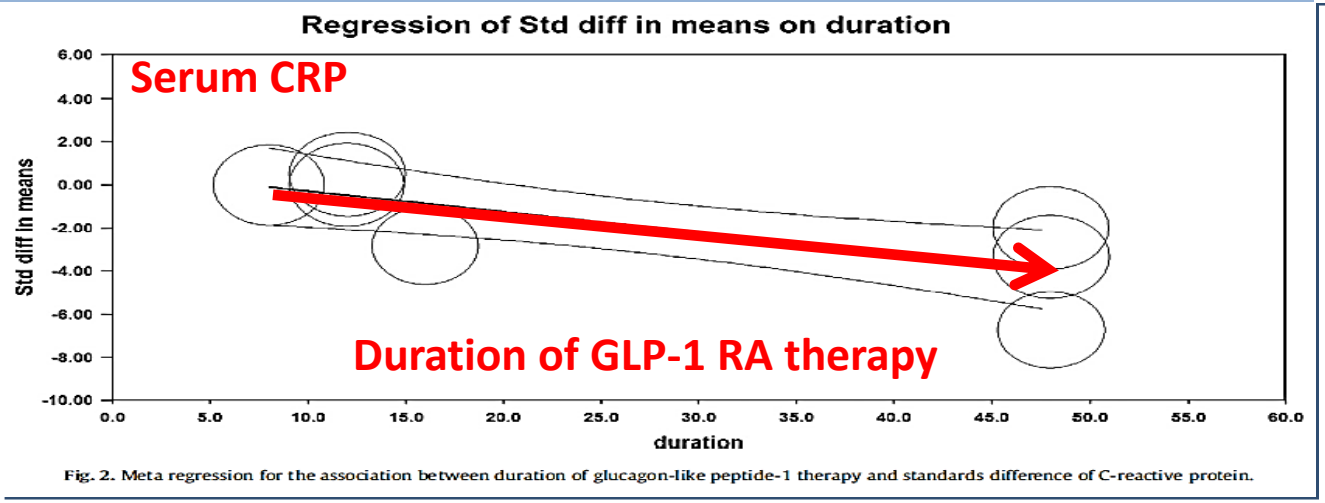
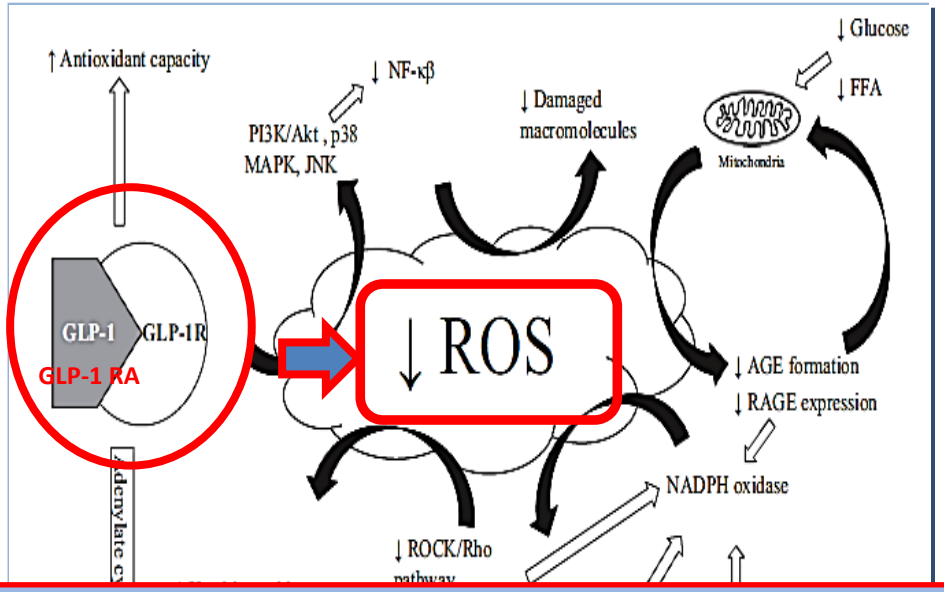


Fig. 2. Meta regression for the association between duration of glucagon-like peptide-1 therapy and standards difference of C-reactive protein.

Mohsen Mazidi et al. . Journal of Diabetes And Its Complications 2017;31(7):1237-1242.

Does Glucagon-like Peptide-1 Ameliorate Oxidative Stress in Diabetes? Evidence Based on Experimental and Clinical Studies



Duration of treatment	Study Design: Subjects (S), Intervention (I) and Treatment Duration (TD)	End point: Effect of GLP-1 Intervention on Oxidative Stress Markers (Compared to control Unless Otherwise Stated)	Comments
	S: T2D (n=23) on metformin and/or sulfonylurea. I: Exenatide (5 μg for 4 weeks then 10 μg twice daily). TD: 5 months.	Plasma: ↓ 8-iso-$PGF_{2\alpha}$ ($p<0.05$).	Covariance analysis indicated glucose independent effect on 8-iso-$PGF_{2\alpha}$ levels that was independent of HbA1c, mean SD, body weight, and BMI. [75]
> 6 months	S: T2D (n=65) (58.7±10.2 years) no more than 15 years of disease duration. n=32 on sulfonylurea. I: Liraglutide (started at 0.3 mg/day then 0.6-0.9 mg/day (mean dose 0.74 mg/day). TD: 8 months.	Blood: ↓ d-ROMs ($p<0.05$) (compared to baseline). No change in MDA.	Decreased HbA1c and blood glucose when compared to baseline ($p<0.01$). No effect on body weight [176].
			Decrease in blood glucose ($p<0.001$) and triglycerides ($p<0.05$) both com-

- **Collectively, the available data demonstrates that GLP-1 can decrease OS but also that this effect is dependent on dose, diabetic status, obesity etc.**
- **This effect of GLP-1 may have therapeutic potential if OS is in fact causally related to the development of late-onset diabetic complications.**

Karen Ekkelund Petersen et al. Current Diabetes Reviews, 2016, 12, 331-358

Efficacy of Liraglutide for Weight Loss Among Patients With Type 2 Diabetes (SCALE)

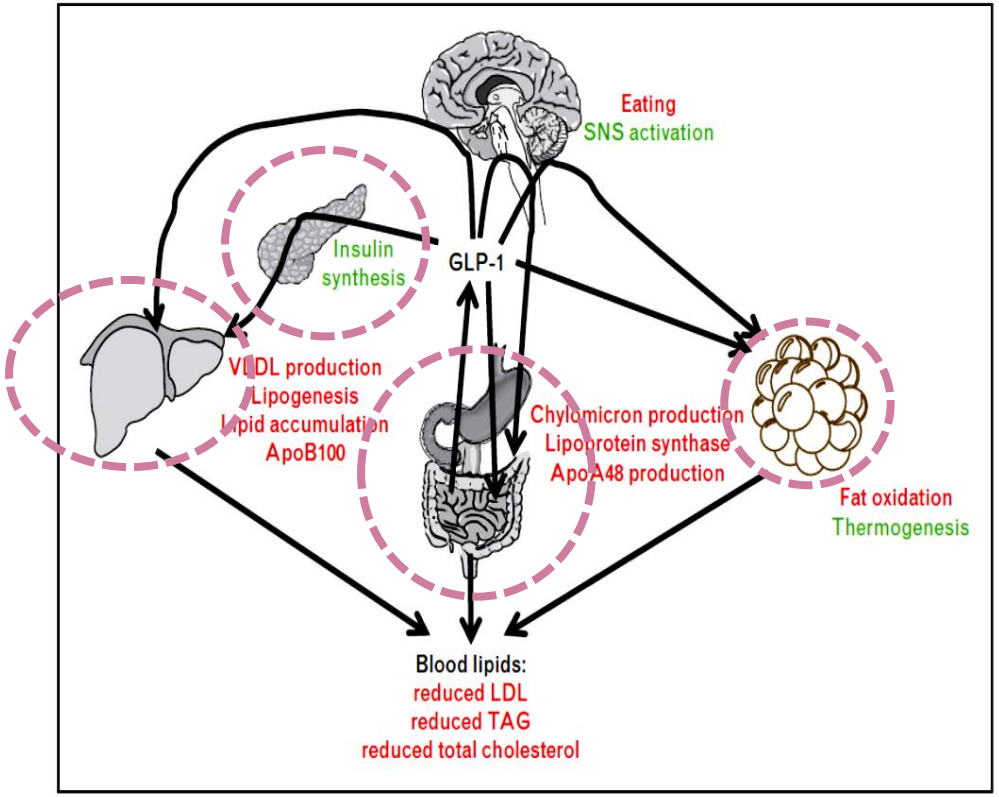
Estimated treatment difference/ratio/odds ratio [95% CI], p - value

	Liraglutide 3.0 mg *vs* Placebo	P value	Liraglutide 1.8 mg *vs* placebo	P value	Liraglutide 3.0 mg *vs* liraglutide 1.8 mg	P value
HOMA-B, % (CV)	1.71 [1.52 to 1.92]	< 0.0001	1.53 [1.34 to 1.74]	< 0.0001	1.12 [1.00 to 1.25]	0.0424
	↑ ß cell function					
HOMA-IR, % (CV)	0.84 [0.75 to 0.94]	0.0031	0.93 [0.82 to 1.07]	0.32	0.90 [0.80 to 1.00]	0.0496
	↓ Insulin resistance					
hsCRP, % (CV)	0.73 [0.64 to 0.83]	<0.0001	0.75 [0.65 to 0.88]	0.0002	0.97 [0.85 to 1.10]	0.64
	↓ Inflammation					

Dose-dependent effects of Liraglutide

Melanie J. Davies et al. JAMA. 2015;314(7):687-699. Supplementary Online Content

Glucagon-like peptide-1, glucagon-like peptide-2, and lipid metabolism



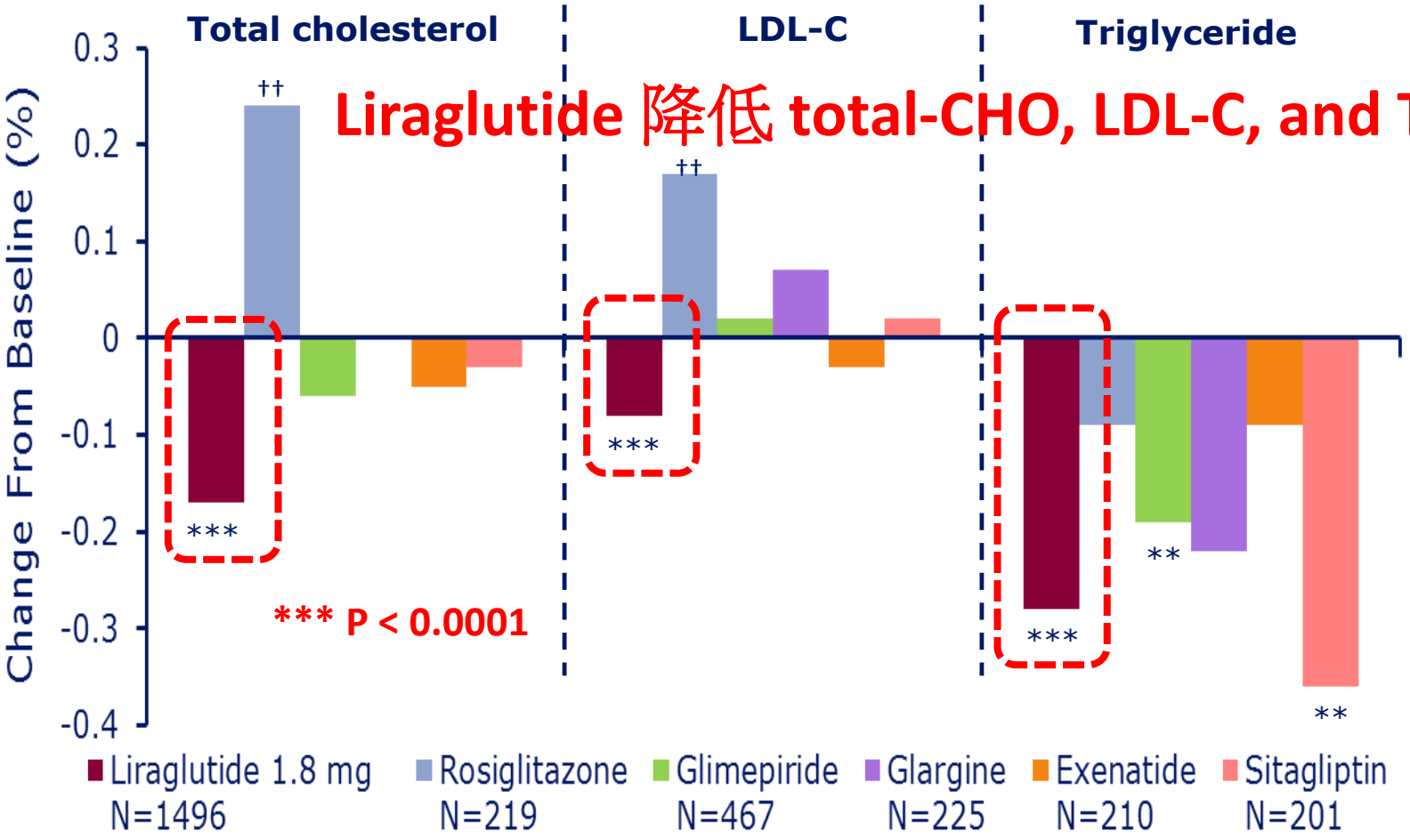
KEY POINTS

- GLP-1 improves dyslipidaemia in obesity.
- GLP-1 directly affects intestinal lipoprotein metabolism.
- GLP-1's effect on liver lipoprotein metabolism is indirect.
- GLP-2 has opposite effects compared with GLP-1.

FIGURE 1. Summary of glucagon-like peptide-1 (GLP-1)-mediated effects on lipid metabolism. GLP-1, which is released from intestinal L cells acts directly on the intestine, the brown adipose tissue, the brain, and the pancreas. The latter effects contribute to GLP-1's effects on hepatic lipid metabolism and eventually on blood lipid levels. For details, please see text. Red: inhibitory effect; green: stimulatory effect.

Lutz, Thomas A; Osto, Elena. Current Opinion in Lipidology, 2016; 27(3):257-263.

Liraglutide effect on fasting lipid levels



Lead 1–6: meta-analysis

*p<0.05; **p<0.01; ***p<0.0001; all vs baseline; † is used instead of * to indicate a significant increase from baseline
LDL-C, low-density lipoprotein cholesterol; T2DM, type 2 diabetes

Fonseca V et al. International Diabetes Federation 21st World Diabetes Congress, 4–8 December 2011, Dubai, UAE. P-1355

As GLP-1 has been implicated as a mediator in the putative gut–renal axis (a rapid-acting feed-forward loop that regulates

Oral sodium load -> Induces Gut GLP-1 secretion -> GLP-1 acts on renal GLP-1 receptor and induces more renal sodium excretion (via inhibiting NaH exchanger 3) than direct intravenous sodium load !

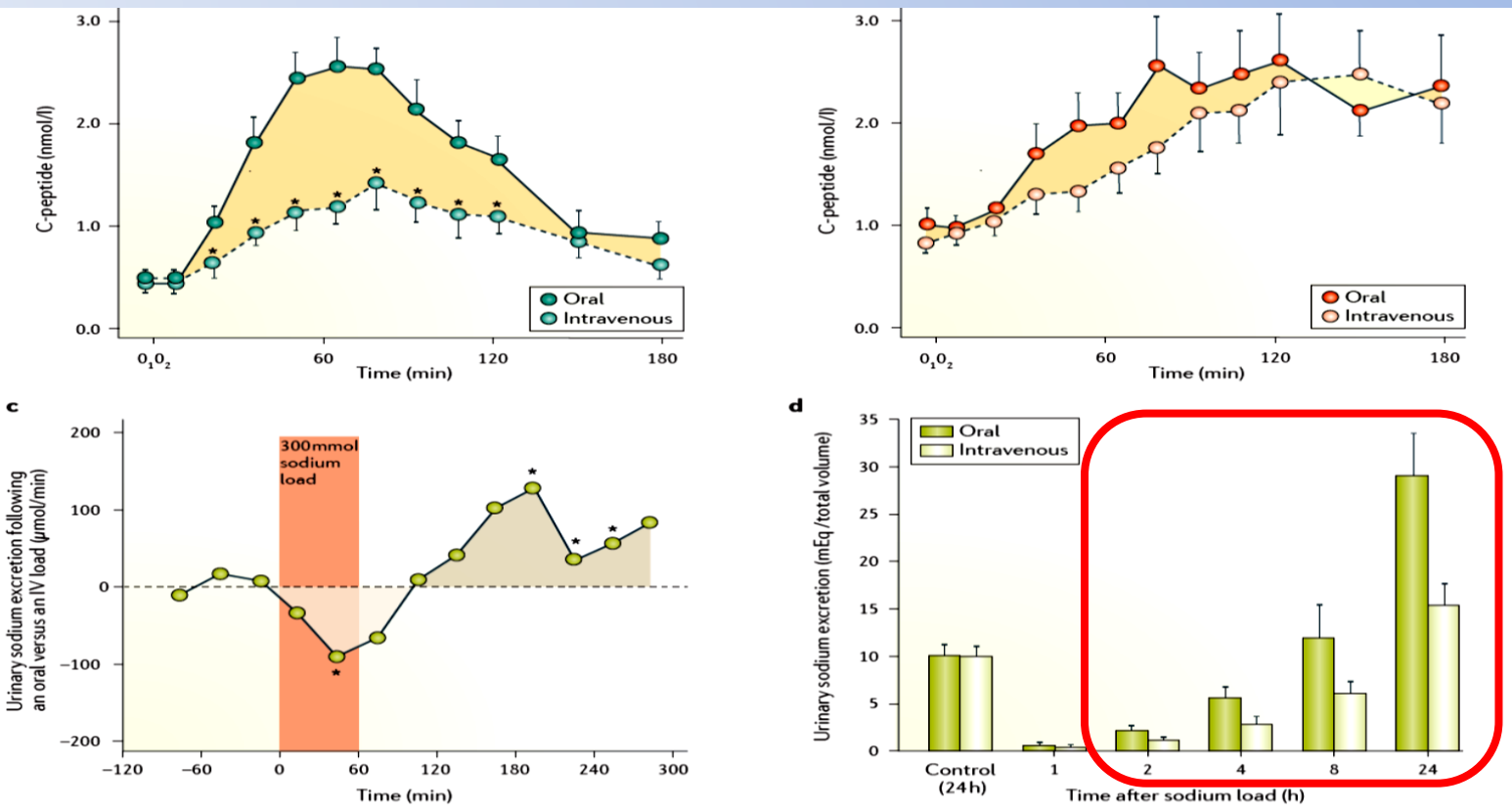
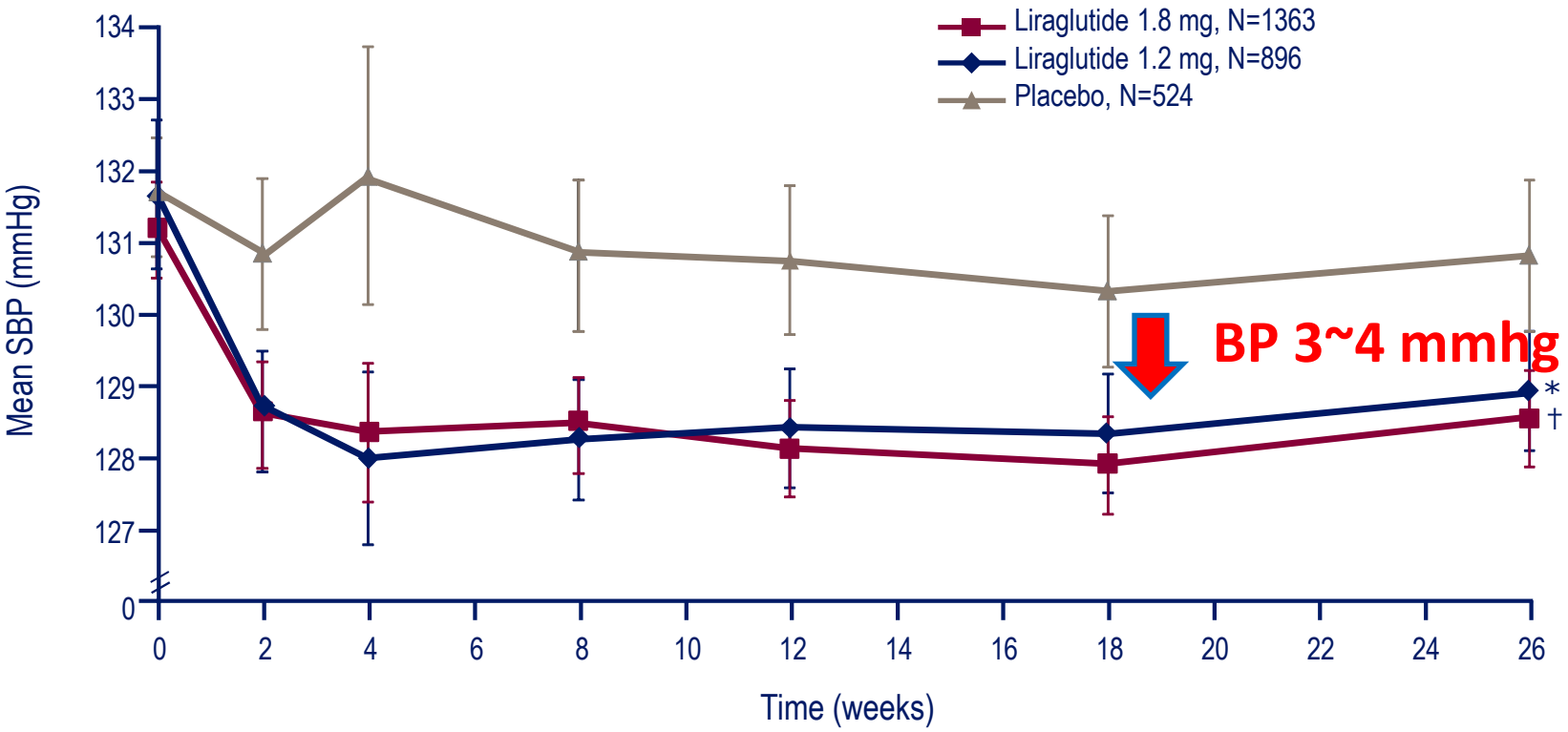


Figure 2 | **Evidence for the incretin effect and the putative gastrointestinal regulation of urinary sodium excretion.** **a,b** | Incremental pancreatic β-cell secretory responses (assessed using C-peptide, which is a marker of endogenous insulin secretion) to an oral glucose load (50 g in 400 ml) or isoglycaemic intravenous (IV) glucose infusion in (part **a**) healthy individuals ($n = 8$) and (part **b**) patients with type 2 diabetes mellitus (T2DM; $n = 14$). In both groups, the

Marcel H. A. Muskiet et al. NATURE REVIEWS NEPHROLOGY 2017;13, 605–628.

Liraglutide effect on systolic blood pressure

排尿鈉, 舒張血管 (NOS-dependent cGMP formation);
減體重, 降血脂, 抗發炎, 阻止動脈硬化, 減輕血管阻力 !



Lead 1–6: meta-analysis

Data shown for systolic blood pressure (SBP) expressed as least squares (LS) means±95% confidence interval (CI); *p=0.0030; †p=0.0001
SBP, systolic blood pressure; T2DM, type 2 diabetes

Fonseca V et al. *Diabetes* 2010;59(suppl 1):A79 (Abst 296-OR)

Inflammation and Oxidative Stress: The Molecular Connectivity between Insulin Resistance, Obesity, and Alzheimer's Disease (Type 3 DM)

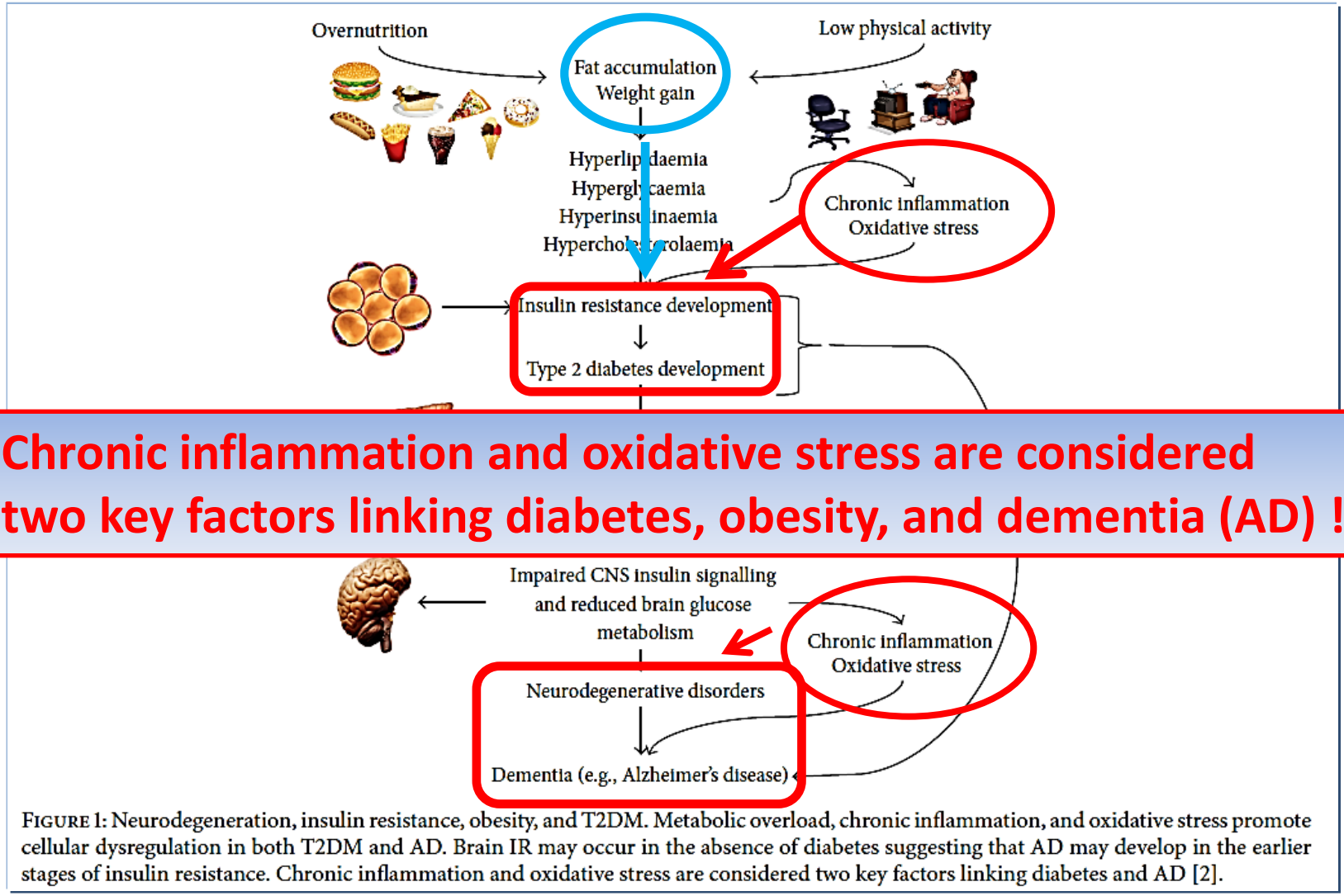


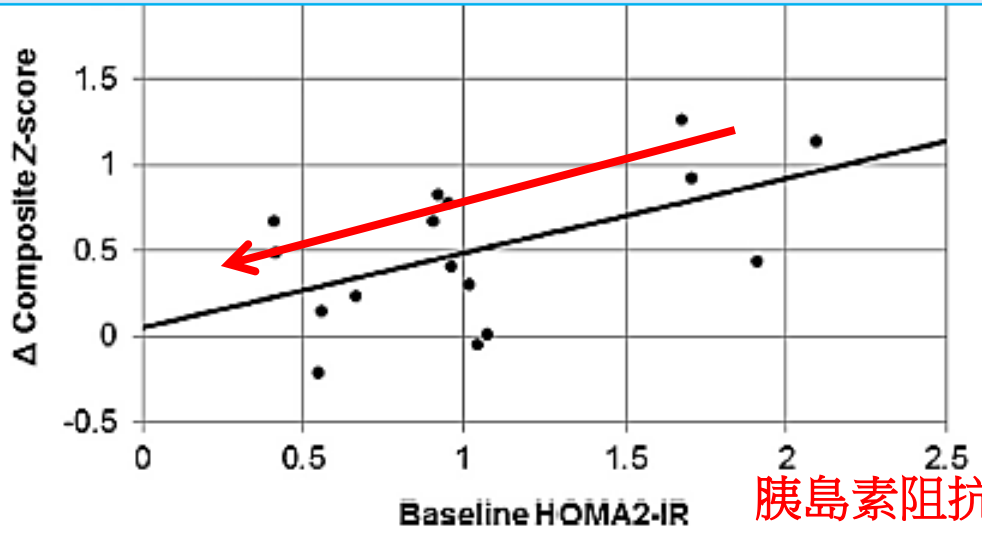
FIGURE 1: Neurodegeneration, insulin resistance, obesity, and T2DM. Metabolic overload, chronic inflammation, and oxidative stress promote cellular dysregulation in both T2DM and AD. Brain IR may occur in the absence of diabetes suggesting that AD may develop in the earlier stages of insulin resistance. Chronic inflammation and oxidative stress are considered two key factors linking diabetes and AD [2].

Giuseppe Verdile et al. Mediators of Inflammation 2015, Article ID 105828, 17 pages

Liraglutide promotes improvements in objective measures of cognitive dysfunction in individuals with mood disorders: A pilot, open-label study

Liraglutide (GLP-1 RA) 改善腦部的胰島素阻抗性，因而改善認知能力及記憶！

認知障礙的嚴重度



胰島素阻抗性嚴重度

Fig. 2. Correlation between percentage change in the composite Z-score and baseline HOMA2-IR. HOMA2-IR: homeostasis model assessment - insulin resistance.

After adjustment for age and gender, there were positive associations between percent- change between baseline and endpoint in the composite z-score and baseline HOMA2-IR (β=0.409, 95% CI 0.090; 0.727, p=0.012) (Fig. 2)

Rodrigo B. Mansur et al. Journal of Affective Disorders 207 (2017) 114-120.

Hepatology Research

Hepatology Research 2016; 46: 933–943 doi: 10.1111/hepr.12634

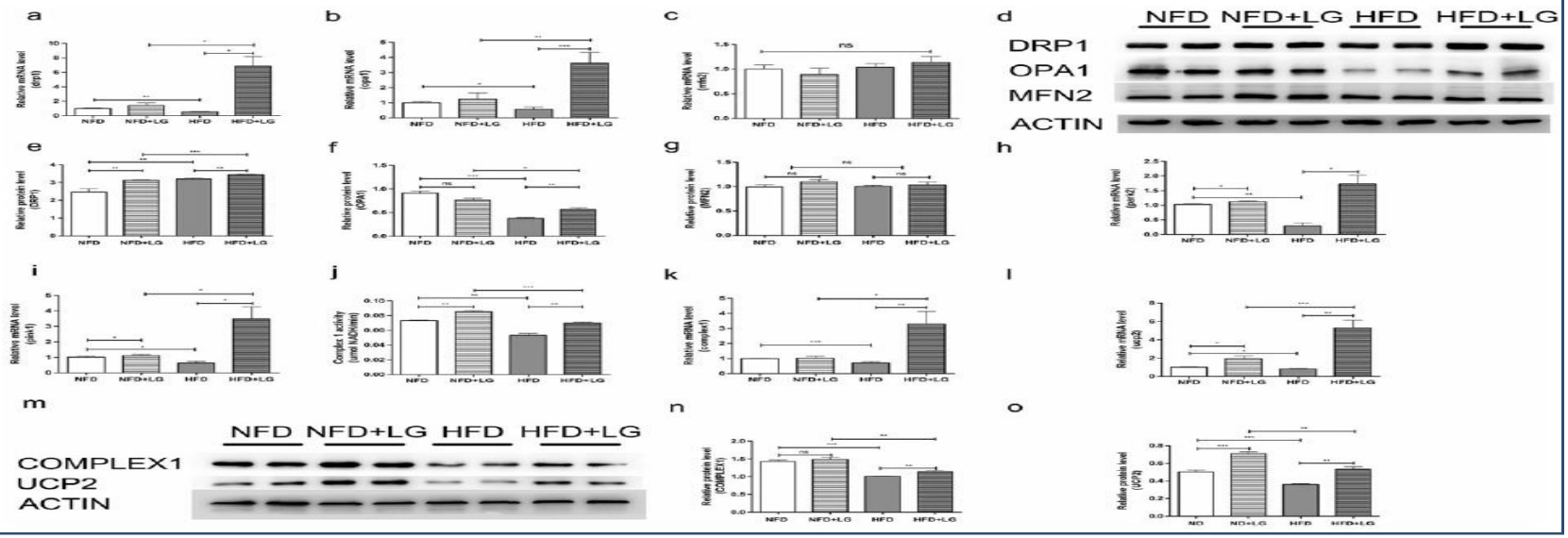
Original Article

Liraglutide ameliorates non-alcoholic fatty liver disease by enhancing mitochondrial architecture and promoting autophagy through the SIRT1/SIRT3–FOXO3a pathway

Insulin Resistance

Wenxin Tong,[1] Liping Ju,[1] Miaoyan Qiu,[1] Qihai Xie,[2] Ying Chen,[1] Weili Shen,[2] Weihong Sun,[3] Weiqing Wang[1] and Jingyan Tian[1]

[1]*Shanghai Clinical Center for Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Department of Endocrinology and Metabolism,* [2]*Shanghai Institute of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine and* [3]*Institute of Health Sciences, Shanghai Institutes for Biological Sciences (SIBS), Chinese Academy of Sciences (CAS) and Shanghai Jiao Tong University School of Medicine, Shanghai, China*



Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study

	Liraglutide	Placebo	Relative risks or mean changes (95% CI) from baseline to 48 weeks (liraglutide vs placebo)	p value*
Primary outcome				
Number of patients with paired liver biopsies	23	22	..	..
Patients with resolution of non-alcoholic steatohepatitis	9 (39%)	2 (9%)	4·3 (1·0 to 17·7)	0·019

Matthew James Armstrong et al. Lancet 2016; 387: 679–90.

Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study

	Mean (SD) change from baseline to 48 weeks		Mean (95% CI) changes from baseline (liraglutide *vs* placebo)	p value*
	Liraglutide (n=23)	Placebo (n=22)		
Metabolic factors				
Glucose (mmol/L)	−1·0 (1·5)	0·72 (2·3)	−1·67 (−2·81 to −0·53)	0·005
Insulin (pmol/L)	−15·9 (54·7)	−34·7 (164·1)	−4·0 (−75·0 to 67·0)	0·91
HOMA-IR (glucose [mmol/L] × insulin [mmol × U/L])	−1·8 (3·7)	0·70 (9·49)	−2·74 (7·24 to 1·76)	0·23
Glycated haemoglobin A_{1c}				
[mmol/L] × insulin [mmol × U/L])				
Weight				
Absolute weight (kg)	−5·3 (4·7)	−0·6 (4·4)	−4·39 (−7·19 to −1·59)	0·003
Percentage (%)	−5·5 (4·9)	−0·7 (4·0)	−4·24 (−6·9 to −1·53)	0·003
Body-mass index (kg/m^2)	−1·8 (1·67)	−0·3 (1·7)	−1·59 (−2·66 to −0·51)	0·005

Liraglutide (GLP-1 RA)改善肝細胞的胰島素阻抗性，因而能有效減少脂肪肝的發生！

Matthew James Armstrong et al. Lancet 2016; 387: 679–90.

A Physiologic and Pharmacological Basis for Implementation of Incretin Hormones in the Treatment of Type 2 Diabetes Mellitus

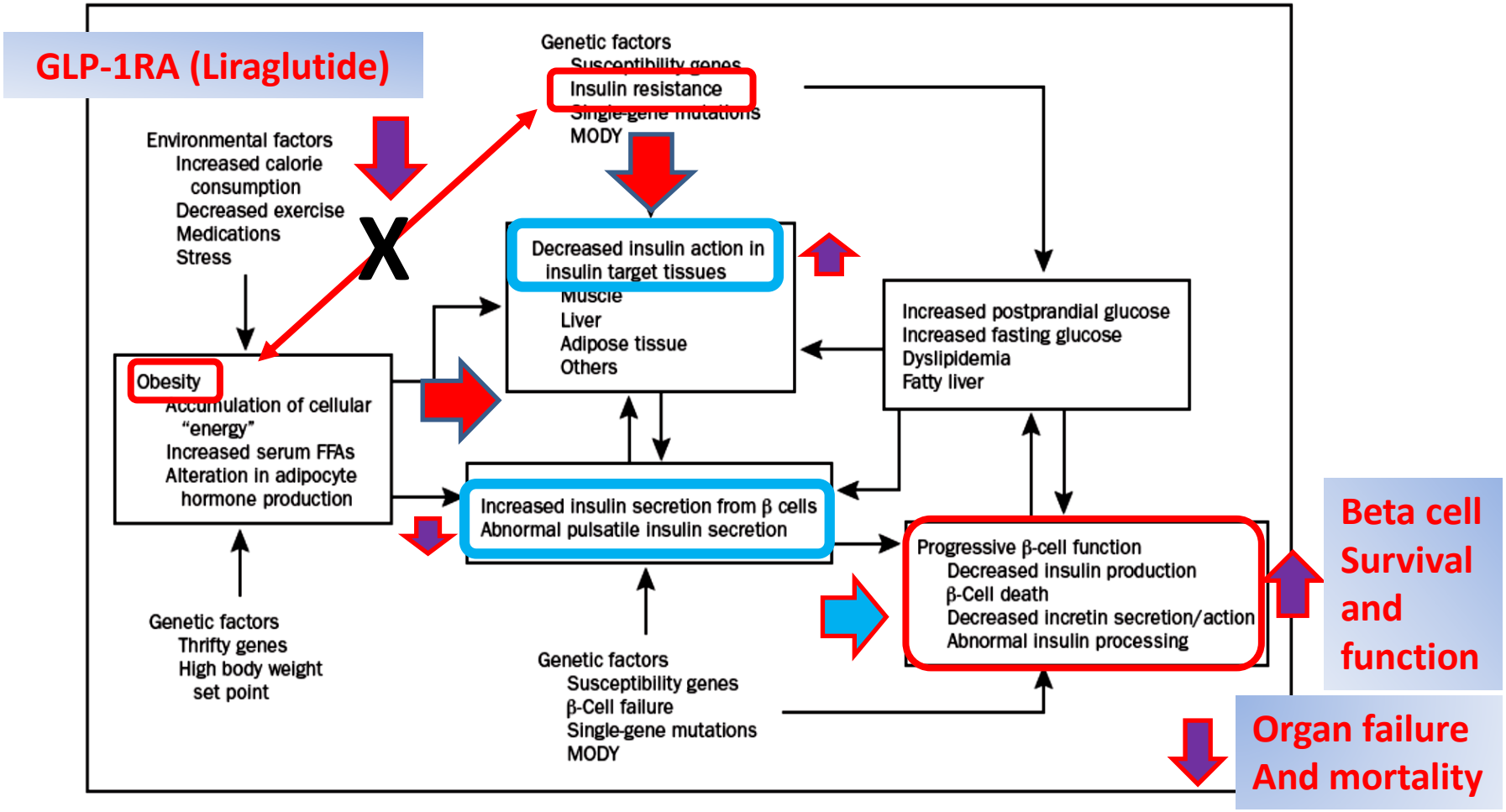


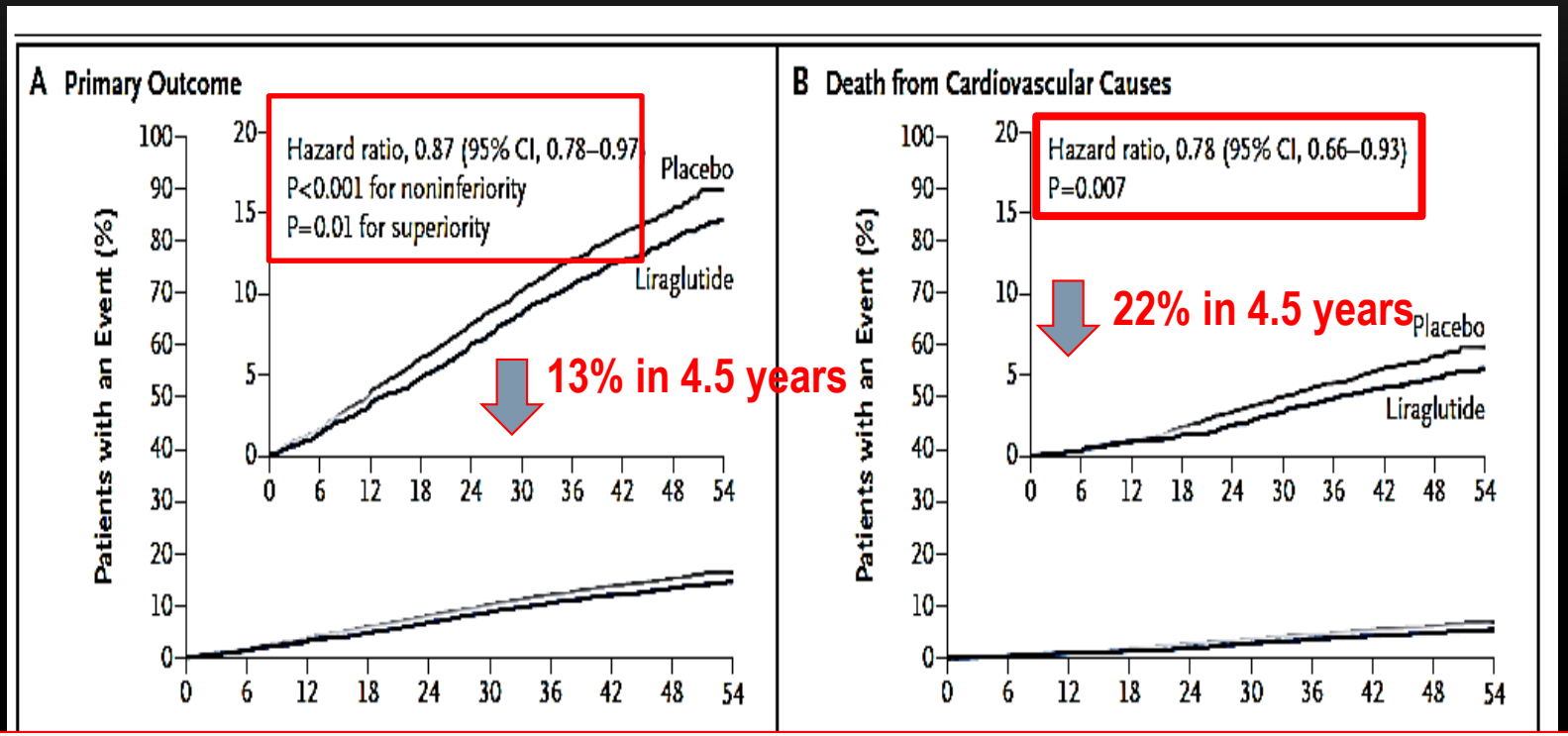
FIGURE 2. Pathogenesis of type 2 diabetes mellitus. The role of environmental and genetic factors on insulin secretion and insulin resistance.

Jeffrey S. Freeman, DO. Mayo Clin Proc. December 2010;85(12)(suppl):S5-S14.

(a GLP-1 Receptor Agonist)

Outcome Studies of Liraglutide Therapy for Type 2 DM

CARDIOVASCULAR OUTCOMES OF LIRAGLUTIDE
2016 LEADER



Liraglutide (GLP-1 RA) 作用在第二型糖尿病最根本的病源
(減少胰島素阻抗性及貝它細胞凋亡),
所以在較短時間內就能減少死亡率,
並產生心血管及腎臟的保護效果！

Steven P. Marso et al. N Eng J Med 2016 (June 13) DOI: 10.1056/NEJMoa1603827

LIRAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES (2016 LEADER)

Table 1. Primary and Secondary Outcomes.*

Outcome	Liraglutide (N=4668)	Incidence Rate	Placebo (N=4672)	Incidence Rate	Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*no. of events/ 100 patient-yr*	*no. of patients (%)*	*no. of events/ 100 patient-yr*		
Primary composite outcome†	608 (13.0)	3.4	694 (14.9)	3.9	0.87 (0.78–0.97)	0.01
Expanded composite outcome‡	948 (20.3)	5.3	1062 (22.7)	6.0	0.88 (0.81–0.96)	0.005
Death from any cause	381 (8.2)	2.1	447 (9.6)	2.5	0.85 (0.74–0.97)	0.02
Death from cardiovascular causes	219 (4.7)	1.2	278 (6.0)	1.6	0.78 (0.66–0.93)	0.007
Death from noncardiovascular causes	162 (3.5)	0.9	169 (3.6)	1.0	0.95 (0.77–1.18)	0.66
Myocardial infarction§	292 (6.3)	1.6	339 (7.3)	1.9	0.86 (0.73–1.00)	0.046
Fatal§	17 (0.4)	0.1	28 (0.6)	0.2	0.60 (0.33–1.10)	0.10
Nonfatal	281 (6.0)	1.6	317 (6.8)	1.8	0.88 (0.75–1.03)	0.11
Silent§	62 (1.3)	0.3	76 (1.6)	0.4	0.86 (0.61–1.20)	0.37
Hospitalization for heart failure	218 (4.7)	1.2	248 (5.3)	1.4	0.87 (0.73–1.05)	0.14
Microvascular event	355 (7.6)	2.0	416 (8.9)	2.3	0.84 (0.73–0.97)	0.02
Retinopathy	106 (2.3)	0.6	92 (2.0)	0.5	1.15 (0.87–1.52)	0.33
Nephropathy	268 (5.7)	1.5	337 (7.2)	1.9	0.78 (0.67–0.92)	0.003

Liraglutide 減少細胞過氧化及發炎傷害, 改善貝它細胞功能及降低胰島素阻抗性; 對心, 腎都確實有保護效果！

nephropathy [defined as the new onset of macroalbuminuria or a doubling of the serum creatinine level and an eGFR of ≤45 ml per minute per 1.73 m2, the need for continuous renal-replacement therapy, or death from renal disease]

§ This analysis was not prespecified.

Steven P. Marso et al. N Eng J Med 2016 (June 13) DOI: 10.1056/NEJMoa1603827

Anti-Inflammatory Effects of GLP-1-Based Therapies beyond Glucose Control

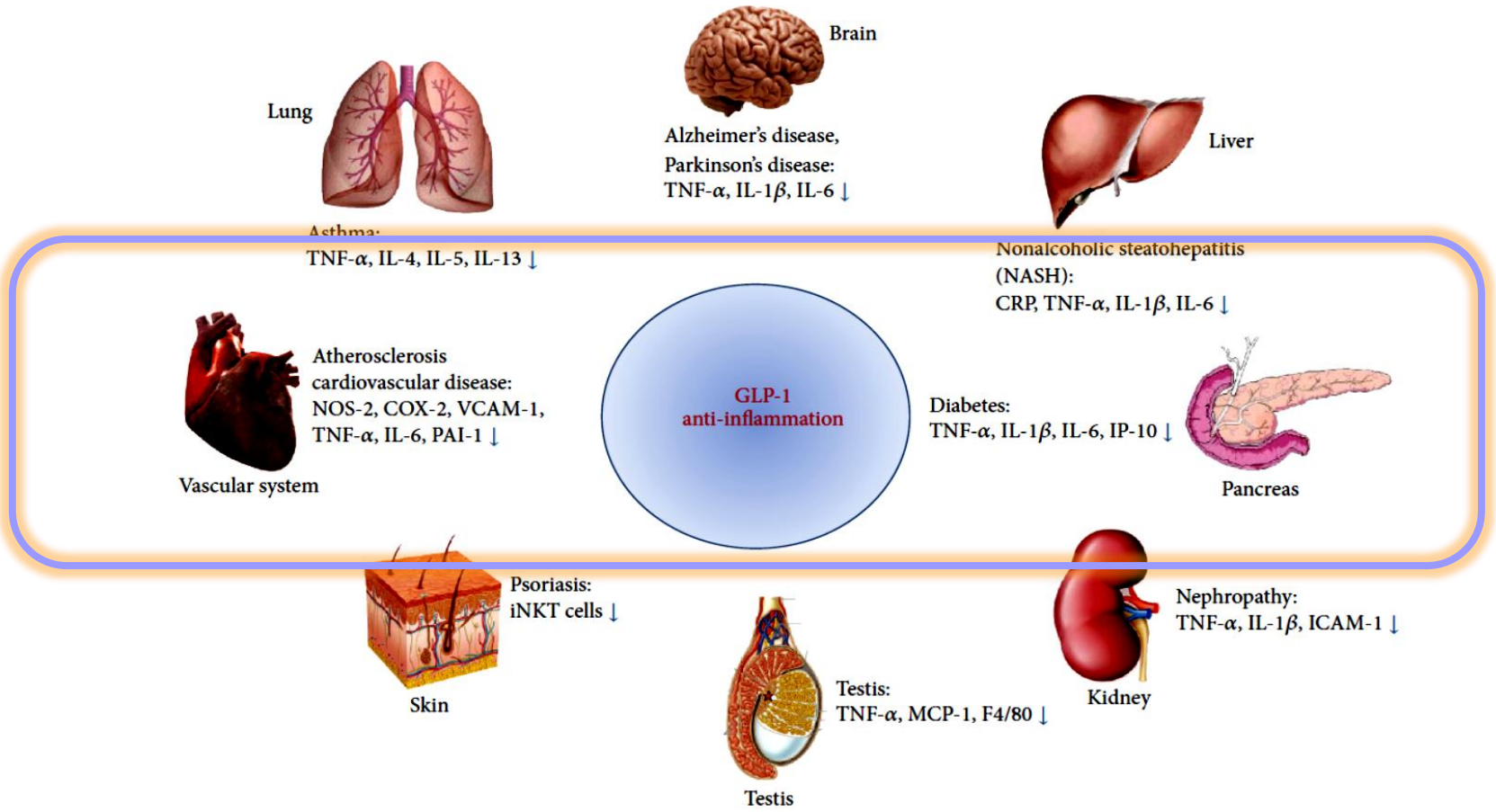


FIGURE 2: GLP-1-based therapies, including GLP-1, GLP-1R agonists and DPP-4 inhibitors, have anti-inflammatory functions in several organs.

Young-Sun Lee et al. Mediators of Inflammation 2016, Article ID 3094642, 11 pages
http://dx.doi.org/10.1155/2016/3094642

Cardiovascular Benefits of Native GLP-1 and its Metabolites

: An Indicator for GLP-1-Therapy Strategies

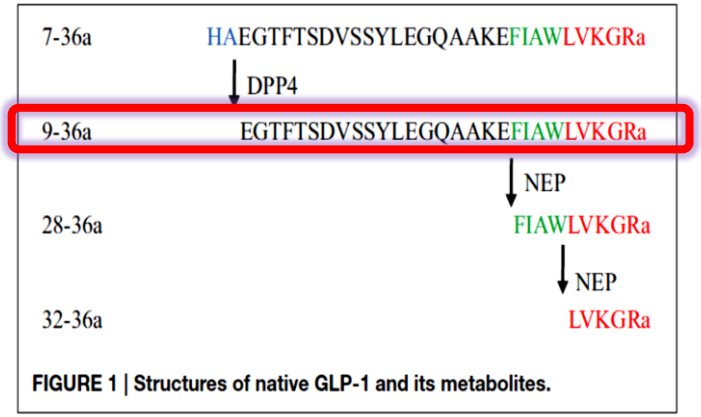


FIGURE 1 | Structures of native GLP-1 and its metabolites.

DPP-4 inhibitors may increase blood level of GLP-1 7-36a, thus have anti-glycemic effects; but loss some of the GLP-1 9-36a cardiovascular protective effects !

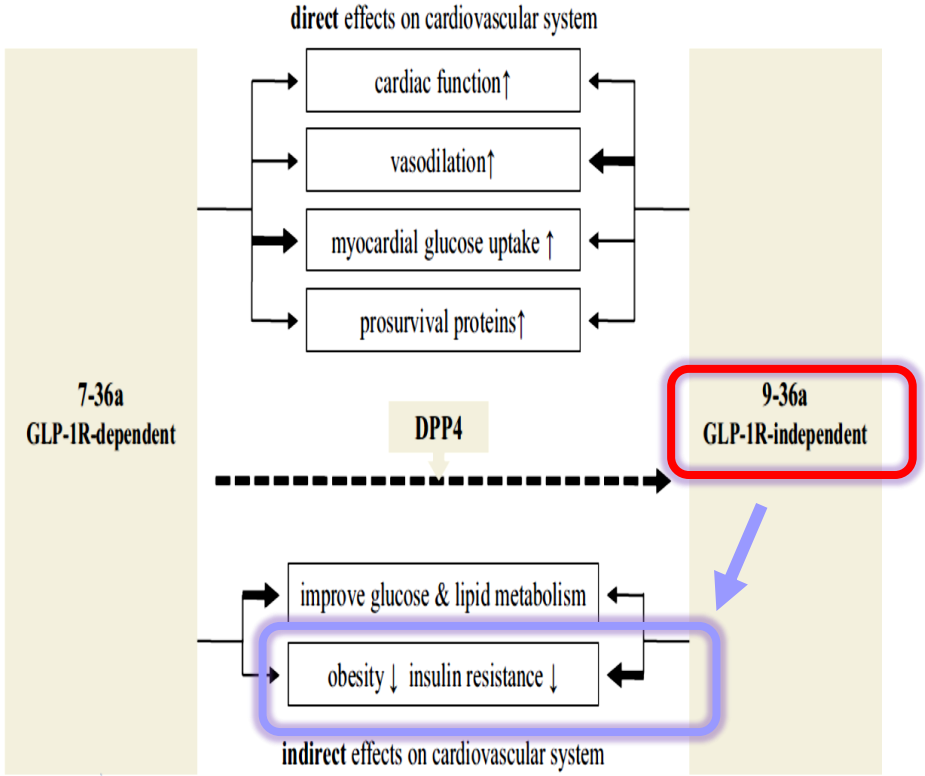
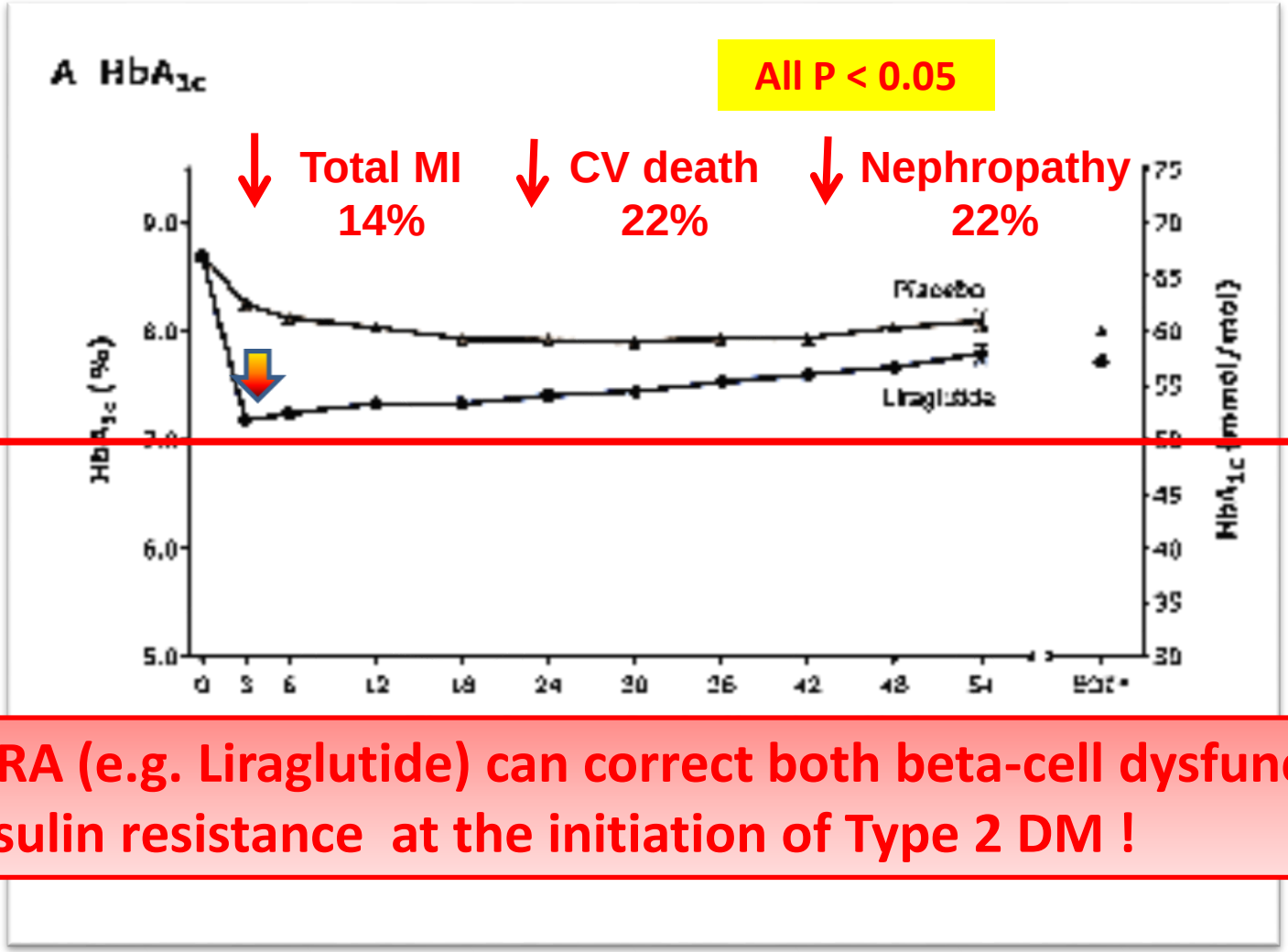


FIGURE 2 | Cardiovascular effects: 7-36a vs. 9-36a. The bold line means stronger effects adapted from available experiments. Related references: cardiac

Junfeng Li et al. Front.Physiol. 2017; 8:15. doi: 10.3389/fphys.2017.00015

2016 LEADER



GLP-1 RA (e.g. Liraglutide) can correct both beta-cell dysfunction and insulin resistance at the initiation of Type 2 DM !

Steven P. Marso et al. N Eng J Med 2016 (June 13) DOI: 10.1056/NEJMoa1603827

GLP-1 and the kidney: from physiology to pharmacology and outcomes in diabetes

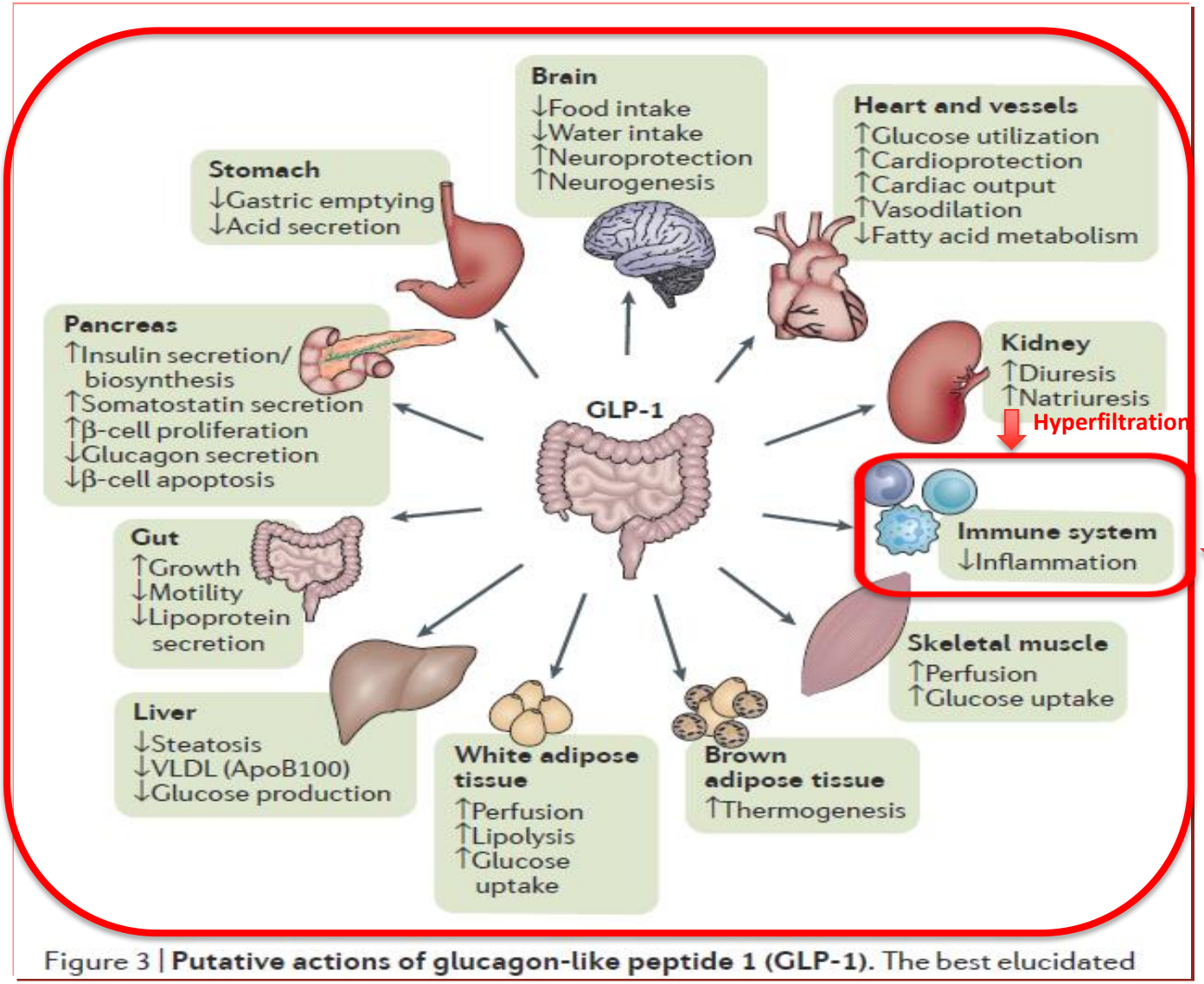


Figure 3 | **Putative actions of glucagon-like peptide 1 (GLP-1).** The best elucidated

Marcel H. A. Muskiet et al . Nature Reviews Nephrology **2017;** 13, 605–628.

Is It Time to Change the Type 2 Diabetes Treatment Paradigm?

Yes! GLP-1 RAs Should Replace Metformin in the Type 2 Diabetes Algorithm

Most relevant results regarding GLP-1 RA were from Liraglutide's trials !

Table 2—Benefits of GLP-1 RAs far outweigh those of metformin

	GLP-1 RAs	Metformin
Pathophysiological defects in T2D (see Fig. 1)	Corrects six of the defects	Corrects only one of the defects
Glucose-lowering efficacy (**Glycemic effects**)	Strong	Strong
Durability of HbA_{1c} reduction (**Glycemic effects**)	Strong	None
Weight loss (**Non-Glycemic effects**)	3–4 kg	1–2 kg
Blood pressure (**Non-Glycemic effects**)	~2–3 mmHg reduction	Neutral
Lipid profile (**Non-Glycemic effects**)	Lowers triglycerides, increases HDL cholesterol	Neutral
Cardiovascular protection (MACE) (**Non-Glycemic effects**)	Reduction by 13–26%	Neutral
Renal protection (**Non-Glycemic effects**)	Reduction by 22%	Neutral
Tolerability (**Non-Glycemic effects**)	~10–15% GI side effects	~10–15% GI side effects
Dosing	Weekly subcutaneous injection	Once to twice daily oral administration
Cost	High	Low

Muhammad Abdul-Ghani and Ralph A. DeFronzo. Diabetes Care 2017;40:1121-1127.

Liraglutide (a GLP-1 RA) can fix
pancreas, heart, Kidney,
adipose tissue, liver, and brain

via anti-glycemic and anti-insulin resistance effects

謝謝聆聽 ！

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