How do DPP4is Matter the Early Stages of the T2D Journey ?

2024.03.28　12：30—13：30 嘉義市醫師公會

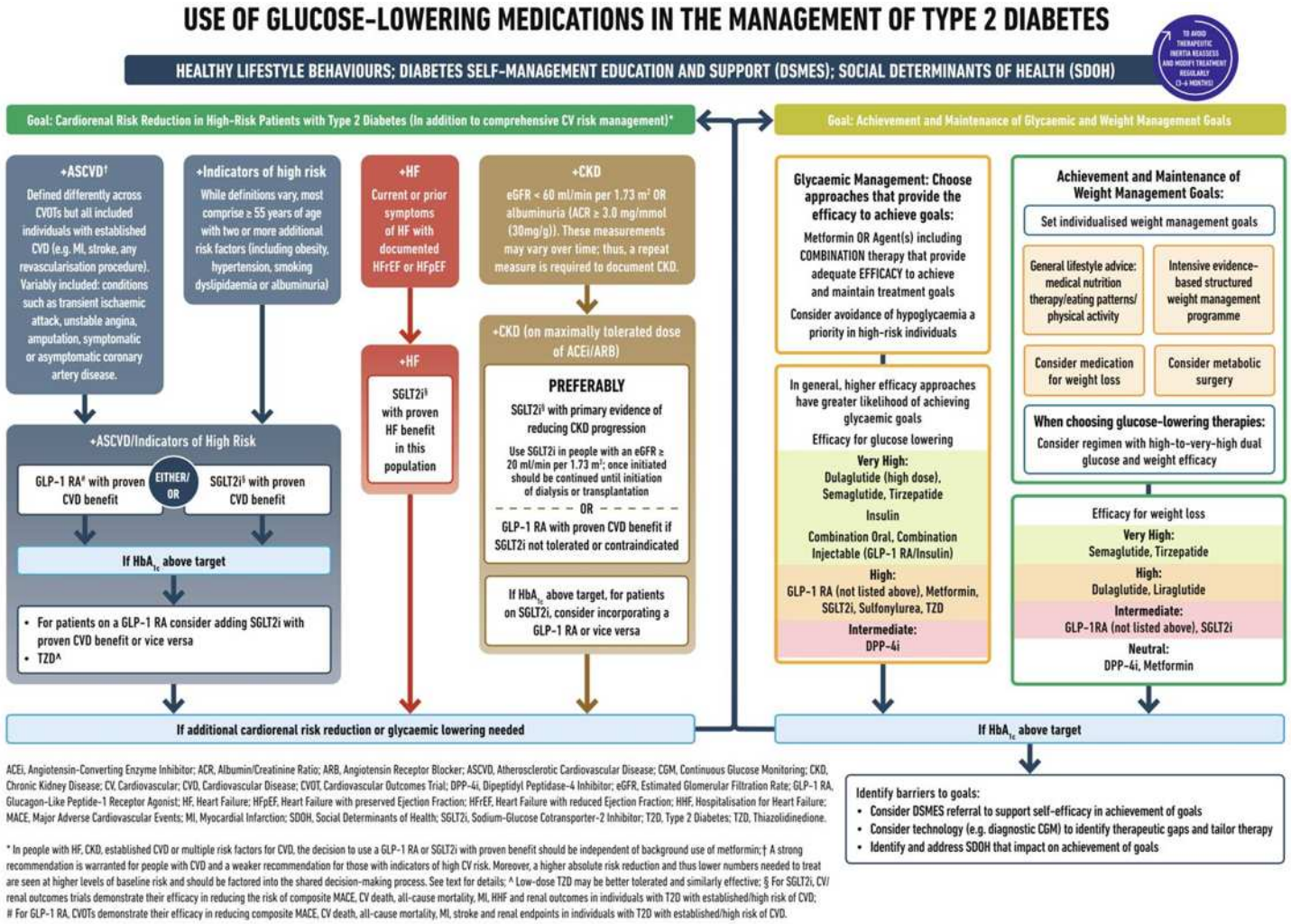
游智宏醫師　台中榮民總醫院嘉義分院 腎臟內科

Speaker Disclosure

- I hereby disclose that I am an invited speaker Boehringer-Ingelheim Taiwan.
- I have no any conflicts of interest with BI.

Person-centered treatment: Comorbidities and treatment goals

Cardiorenal Risk Reduction



Glycemic Control

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Diabetes Care. 2023;46(Suppl 1):S140-S157.

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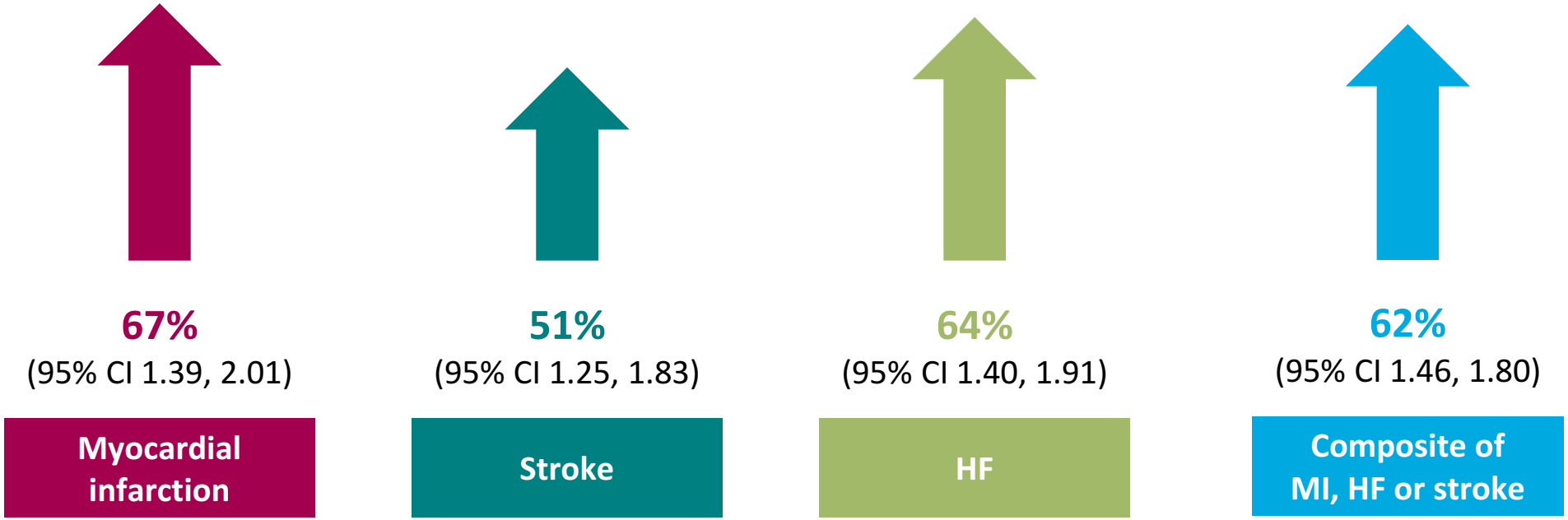
Delayed intervention is associated with an increased risk of complications

Percent increase in CV events in patients with a 1-year delay in receiving intensive therapy and HbA_{1c} ≥7% vs <7%*: retrospective UK study (N=105,477)



*Following adjustments for various confounding factors, $p<0.01$ for all HR

HbA_{1c}, glycated haemoglobin; HF, heart failure; MI, myocardial infarction

Paul SK et al. *Cardiovasc Diabetol* 2015;14:100

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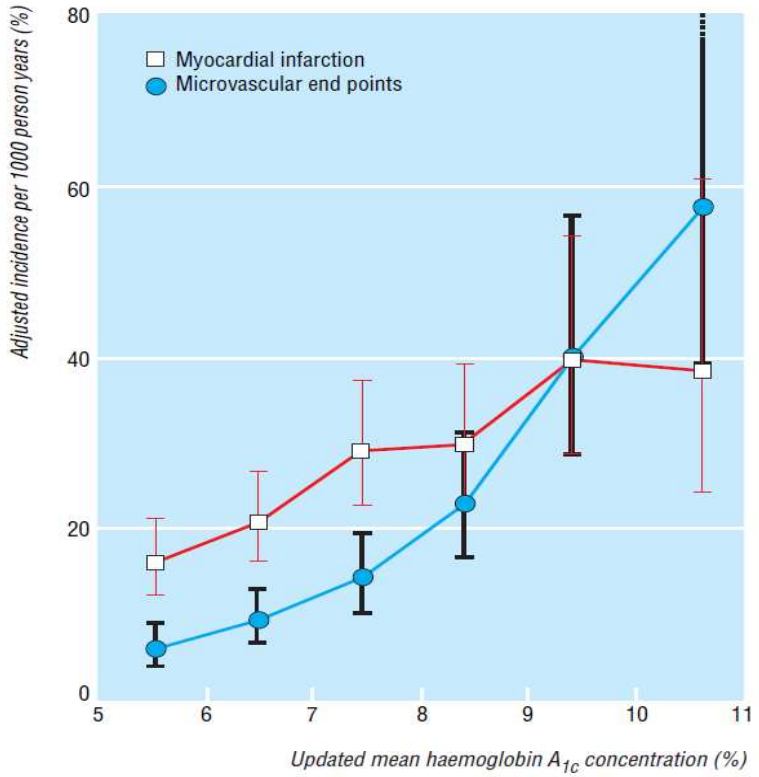
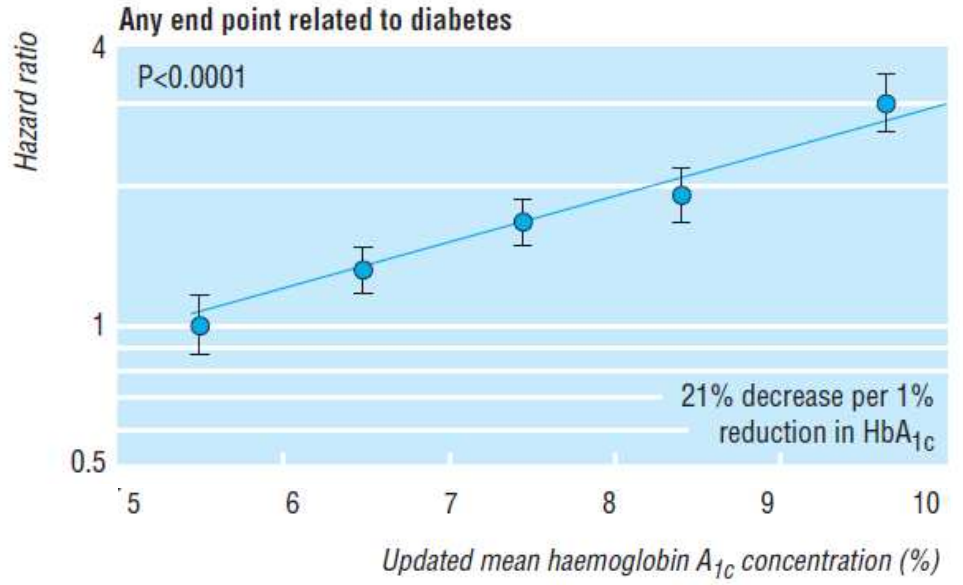
UKPDS 35 demonstrated that elevated HbA1c level is strongly associated with an increased risk of complications

A prospective observational study evaluating the relation between glycemic level and the risk of macrovascular or microvascular complications with T2D patients

Incidence rate of myocardial infarction and microvascular endpoints



Each 1% reduction in HbA1c was associated with reductions in risk of 21% for any end point related



Reference category (hazard ratio 1.0) is HbA1c <6% with log linear scales.

*End points included deaths related to diabetes, all cause mortality, MI, stroke, peripheral vascular disease, microvascular disease, HF and cataract extraction

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Stratton IM et al. BMJ 2000;321:405-12

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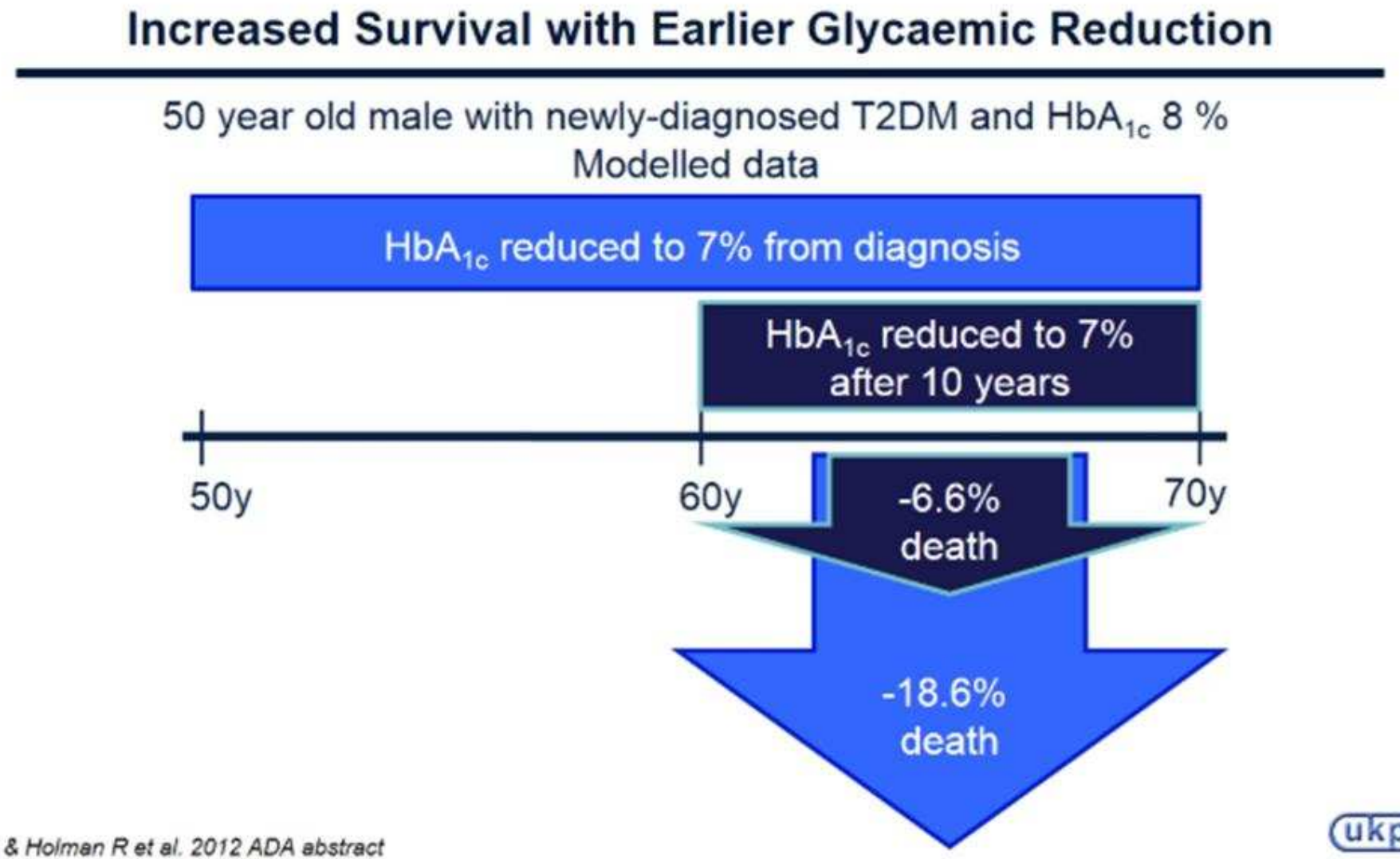
The Earlier, the Longer

34



Lind M & Holman R et al. 2012 ADA abstract

ukpds

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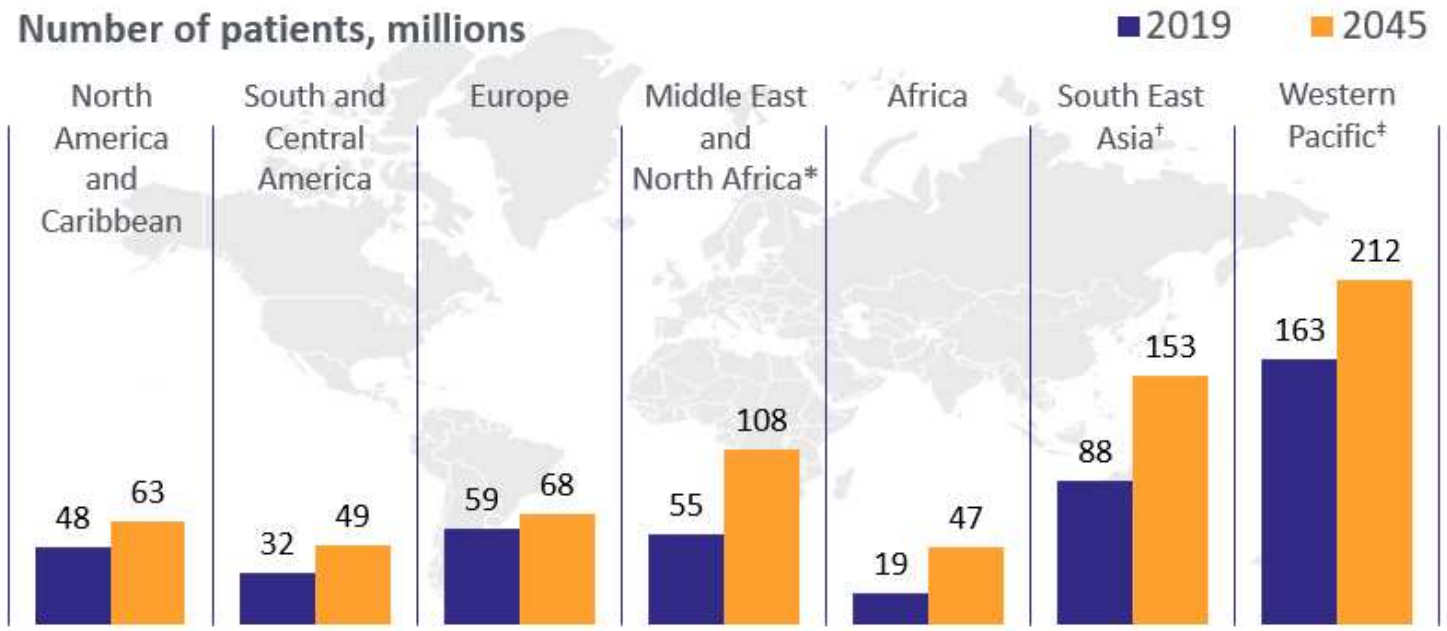
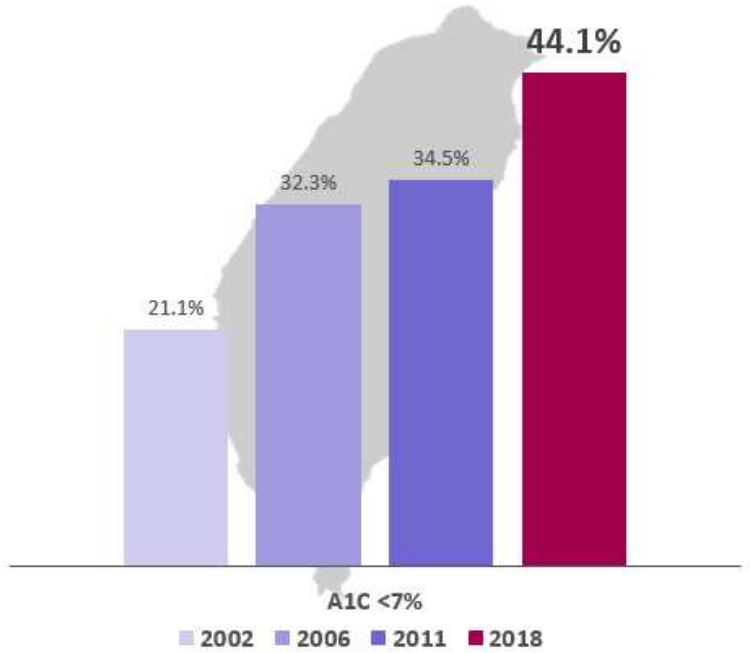
Prevalence of diabetes is increasing worldwide

Patients with diabetes in each region between 2019 and 2045 (aged 20–79 years)



55.9 %

Uncontrolled in Taiwan in 2018[2]



*Comprising 21 countries; †Comprising Bangladesh, Bhutan, India, Maldives, Mauritius, Nepal and Sri Lanka; ‡Comprising 36 countries, including Japan, South Korea, Brunei Darussalam, Indonesia and Malaysia

International Diabetes Federation. IDF Diabetes Atlas. 9th edn. 2019. https://www.diabetesatlas.org/ (accessed Apr 2022)

2018 台灣糖尿病健康促進機構之品管調查研究

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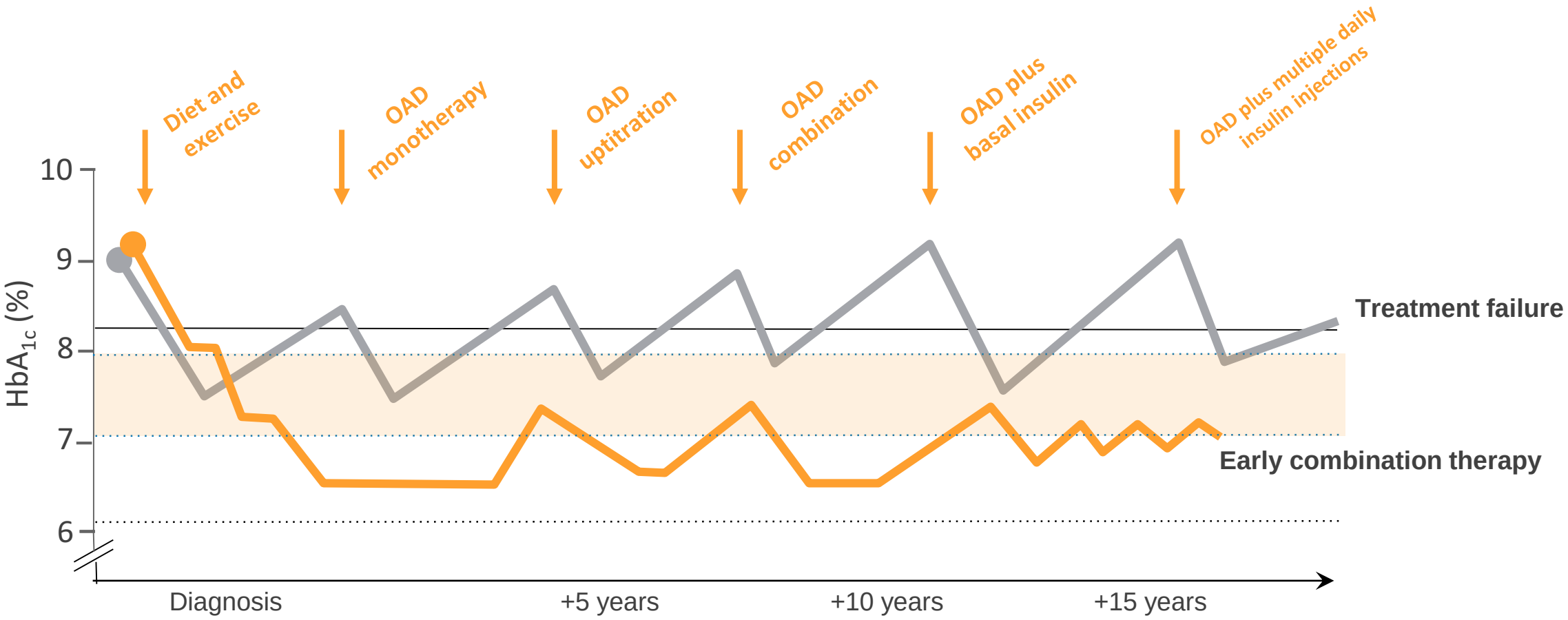
Earlier combination therapy may improve achieving to treatment target

A retrospective analysis from the UK CPRD Database (2004–2006; Follow-up to 2011) highlighting median time to intensification and mean HbA_{1c} at intensification in patients with T2DM treated with 1 or 2 OADs with intensification to 2 OADs or insulin, respectively



Del Prato S, et al. Int J Clin Pract 2005;59:1345-55.

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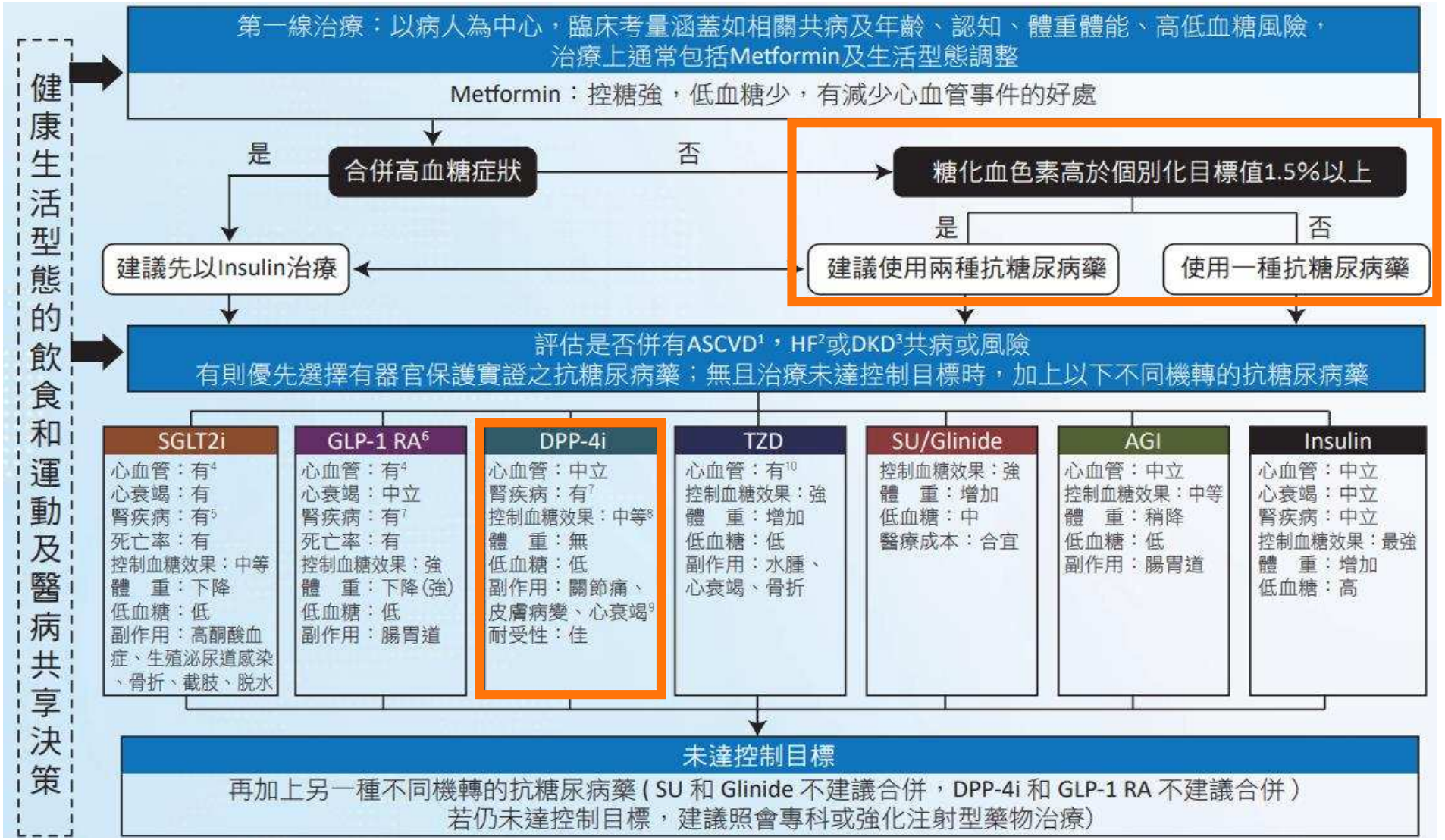
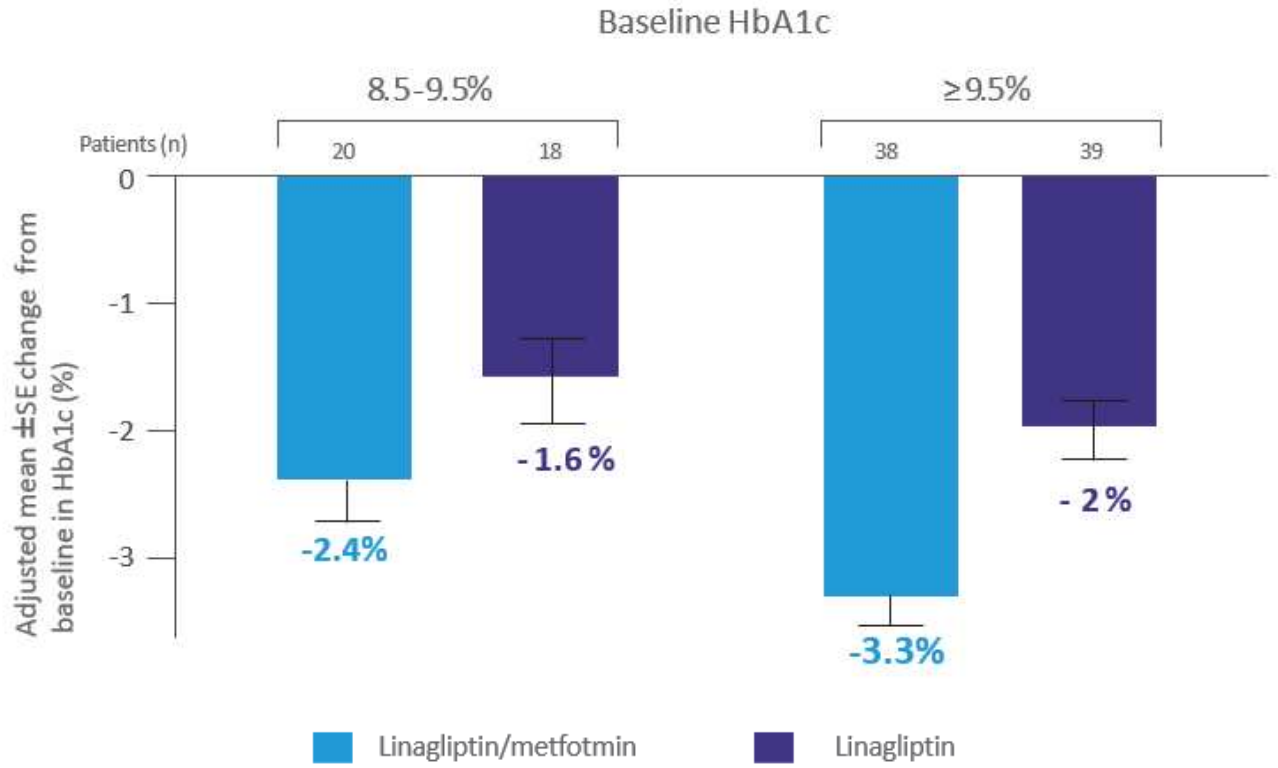
台灣糖尿病學會建議第 2 型糖尿病人高血糖的處理流程圖

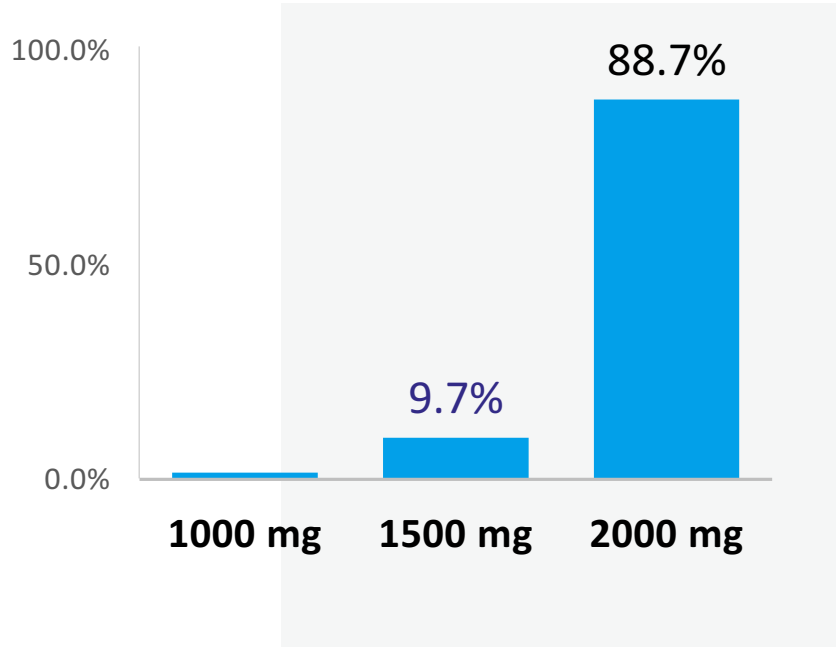


1. ASCVD:動脈硬化心血管疾病
2. HF:心衰竭
3. DKD:糖尿病腎疾病
4. 選擇具有實證能減少心血管事件之藥物
5. 指腎絲球過濾率，透析及腎因性或心因性死亡終點
6. 包含口服及注射GLP-1 RA
7. 指蛋白尿之改善
8. 初診斷即合併metformin+vildagliptin比metformin能更長期控制血糖
9. Saxagliptin 潛在性心衰竭風險
10. 對減少心血管事件有潛在性的好處

Asians newly diagnosed with T2D, the initial combination of linagliptin and metformin substantially improved glycemic control



98% *metformin titrate to 1500-2000mg /day*



Combined metformin titration dose

J Diabetes Investig. 2017 Sep 16;9(3):579-586.

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Trajneta Duo was well tolerated in Asians newly diagnosed with T2D who had marked hyperglycemia

Patients (%)	Linagliptin/ metformin (n = 62)	Linagliptin (n = 63)
Any adverse event	71.0	63.5
Drug-related adverse event	9.7	4.8
Serious adverse event	1.6	1.6
Death	0.0	0.0
Requiring hospitalization	1.6	1.6
Adverse event leading to discontinuation	0.0	1.6
Adverse events of special interest[†]		
Hepatic adverse events	3.2	4.8
Hypersensitivity reactions	1.6	3.2
Gastrointestinal disorders[‡]	12.9	12.7
Adverse events with an incidence >5.0% in either group[§]		
Dyslipidemia	17.7	30.2
Urinary tract infection	9.7	12.7
Headache	6.5	4.8
Hypoglycemia[¶]	6.5	4.8
Back pain	6.5	3.2
Hypertension	6.5	0.0
Upper respiratory tract infection	4.8	7.9
Hyperglycemia	3.2	12.7

J Diabetes Investig. 2017 Sep 16;9(3):579-586.

- ***Improve*** *glycemic control without weight gain and hypoglycemia*
- ***Low*** *treatment discontinuation*
- ***Comparable*** *GI tolerance vs Trajenta*

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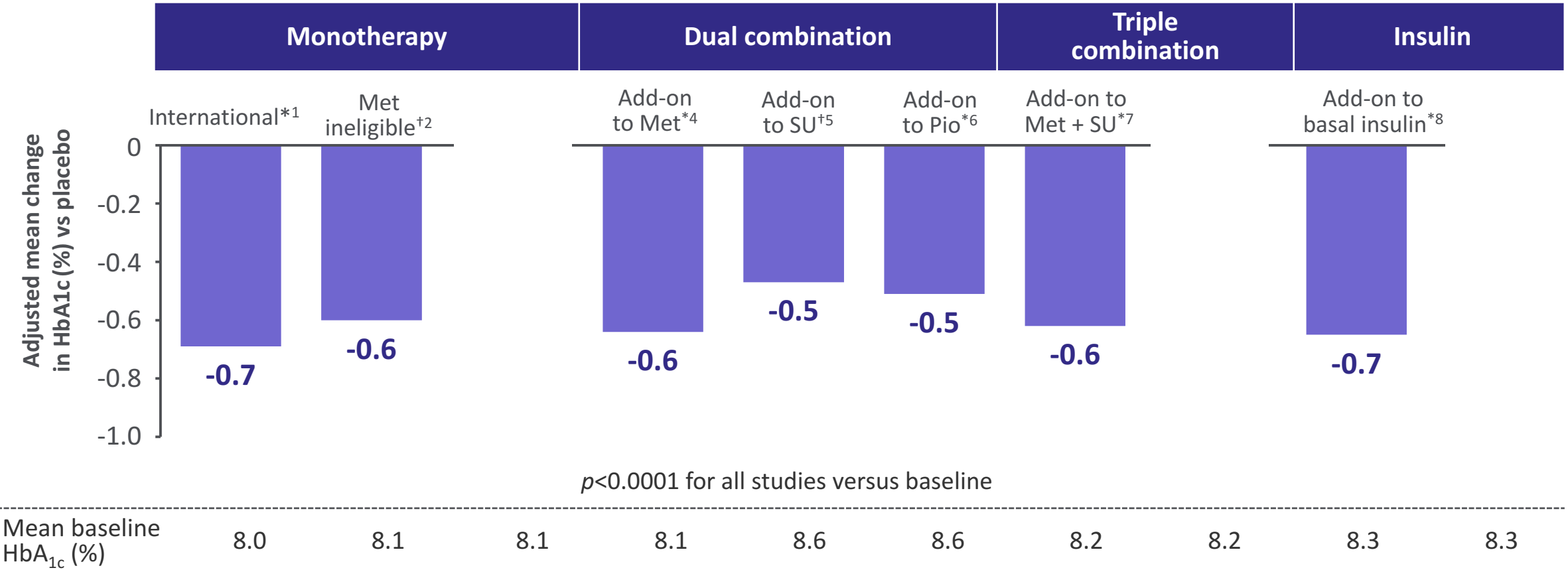
Trajenta demonstrates efficacy independent of background therapy and disease duration



Treatment duration: *24 weeks. †18 weeks. ‡12 weeks

HbA1c, glycated haemoglobin; Met, metformin; Pio, pioglitazone; SU, sulphonylurea

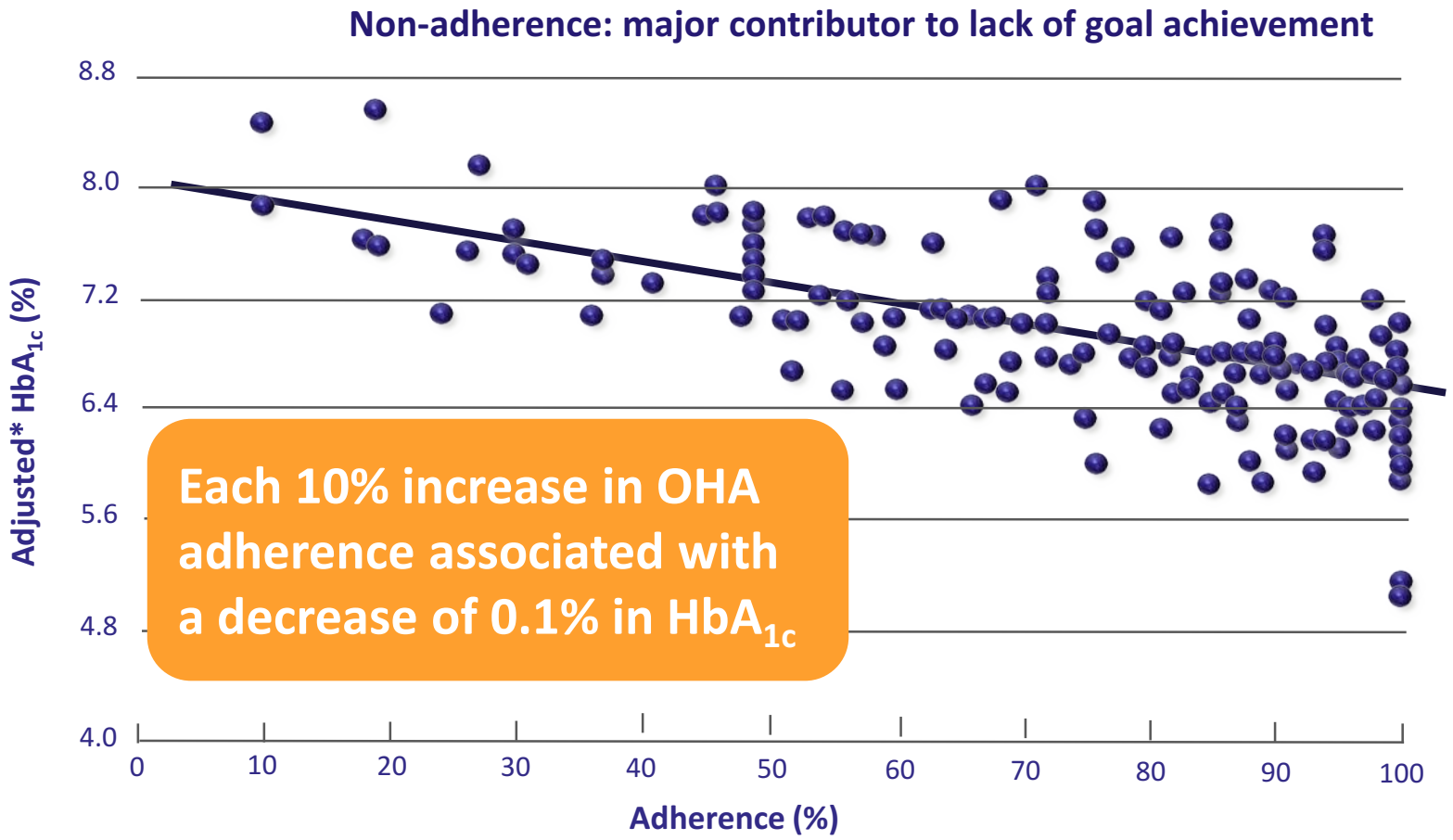
1. Del Prato S *et al. Diabetes Obes Metab* 2011;13:258; 2. Barnett AH *et al. Diabetes Obes Metab* 2012;14:1145; 3. Kawamori R *et al. Diabetes Obes Metab* 2012;14:348; 4. Taskinen MR *et al. Diabetes Obes Metab* 2011;13:65; 5. Lewin AJ *et al. Clin Ther* 2012;34:1909; 6. Gomis R *et al. Diabetes Obes Metab* 2011;13:653; 7. Owens DR *et al. Diabetic Med* 2011;28:1352; 8. Yki-Järvinen H *et al. Diabetes Care* 2013;36:3875; 9. Diabetes Care. 2013 Dec; 36(12): 3875–3881. 10.

Adherence

“Increasing adherence may have a far greater impact than any improvement in specific medical treatments”

(World Health Organization)

And then, the critical point of goal achievement…
The importance of drug adherence in T2DM



Rozenfeld Y, et al. Am J Manag Care. 2008;14:71–75.

*Adjusted for baseline A_{1C} and the oral diabetic medication regimen.
OHA:oral hypoglycaemic agent

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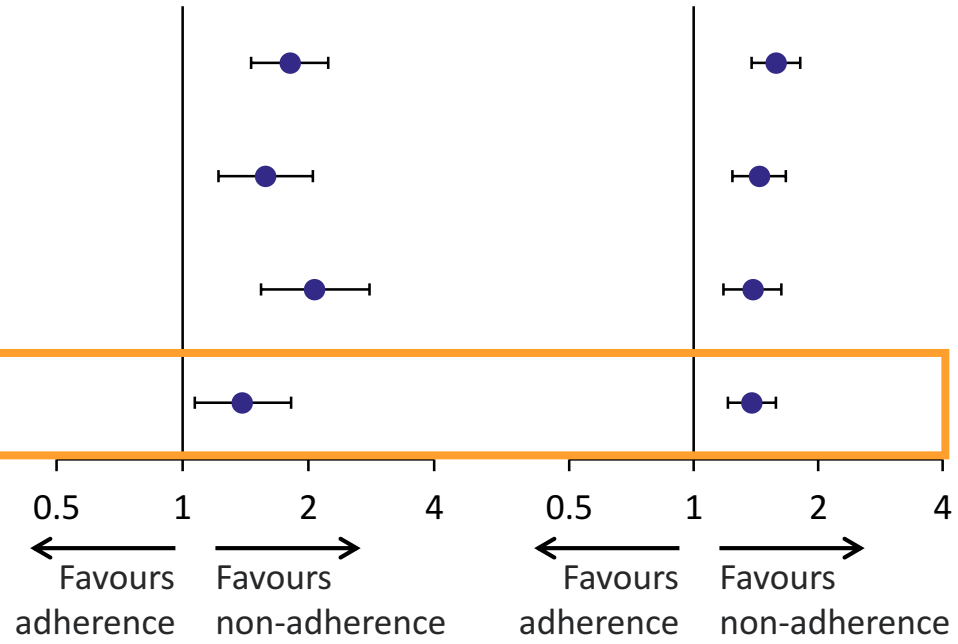
Non-adherence to glucose-lowering therapy may increase risk of mortality and hospitalisation

- In a retrospective cohort study, non-adherent patients tended to be younger and with fewer comorbidities compared with adherent patients

	Patients	
	Non-adherent, %	Total
Overall	21.3	11,532
Antihypertensives	19.1	6217
Statins	24.8	6486
Oral glucose-lowering therapy	20.3	7883



Ho PM et al. Arch Intern Med 2006;166:1836

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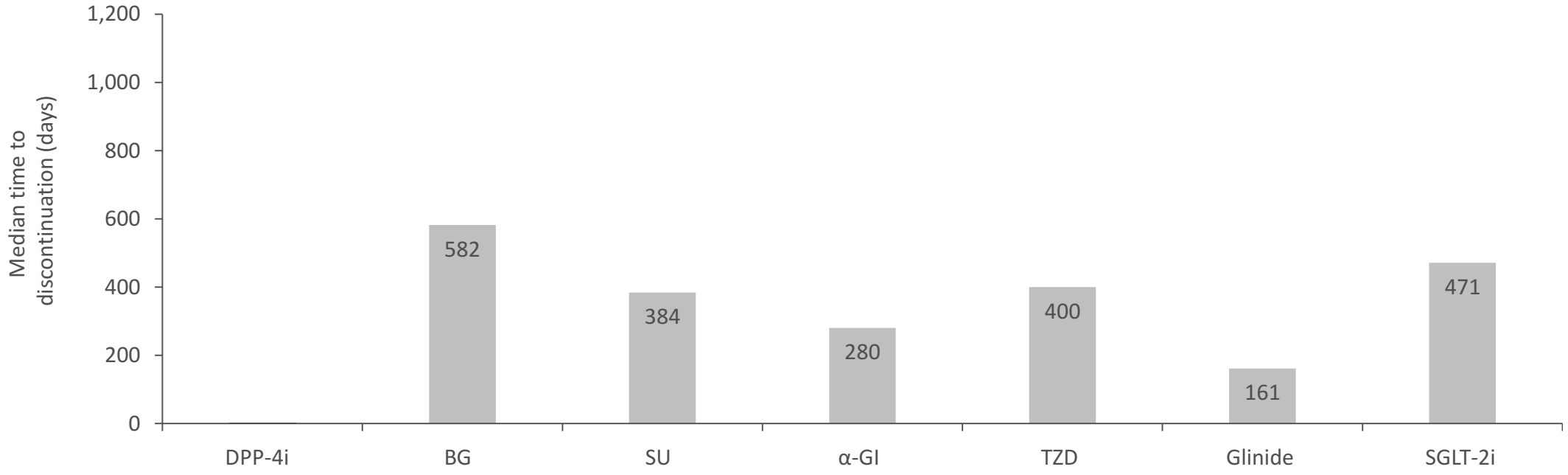
DPP-4 inhibitors demonstrate best persistence and adherence in real-world patients

JMDC database, N= 40908

Persistence with monotherapy schedules of index antidiabetic drug classes



Adapted from table 2. Nishimura R, et al. BMJ Open. 2019;9(3):e025806.

α-GI: α-glucosidase inhibitor; BG: biguanide; DPP-4i: dipeptidyl peptidase-4 inhibitors; JMDC, Japan Medical Data Center; MDV: Medical Data Vision; pts: patients; SGLT-2i: sodium-glucose cotransporter-2 inhibitor; SU: sulfonylurea; TZD: thiazolidinedione; UT: untreated.

Nishimura R, et al. BMJ Open. 2019;9(3):e025806.

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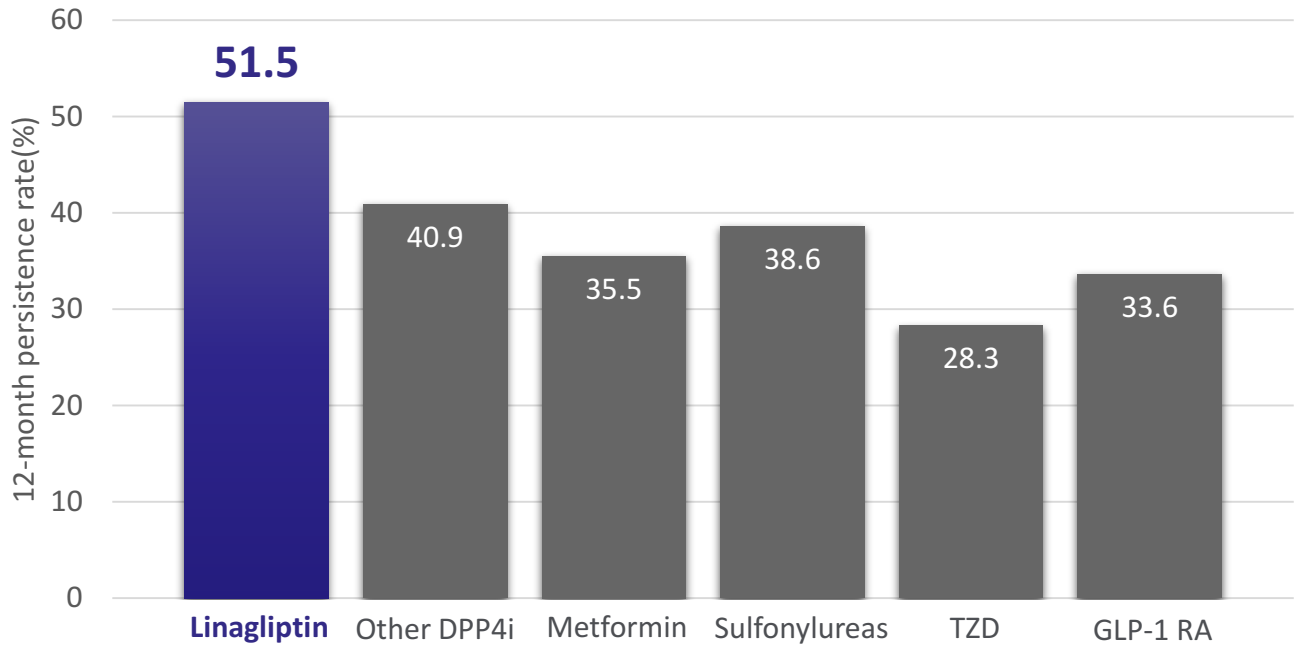
Trajenta has the high persistence rate in 12-month following upUS real world database

US Clinformatics Database,

155,345 T2D patients are selected and enrolled

12-month follow-up



OAD	instruction
Metformin	q.d.-t.i.d. With Meal
SU/Glinide	q.d - t.i.d. Before Meal
α-GI	t.i.d. Before Meal or After Meal
Linagliptin	**q.d. Anytime**
GLP-1 RA	**Injection**

Persistence may be considered as Adherence, Side Effect Tolerance, Glucose Control Efficacy

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Patorno E, et al. ADA 2015, Poster 1707-P.

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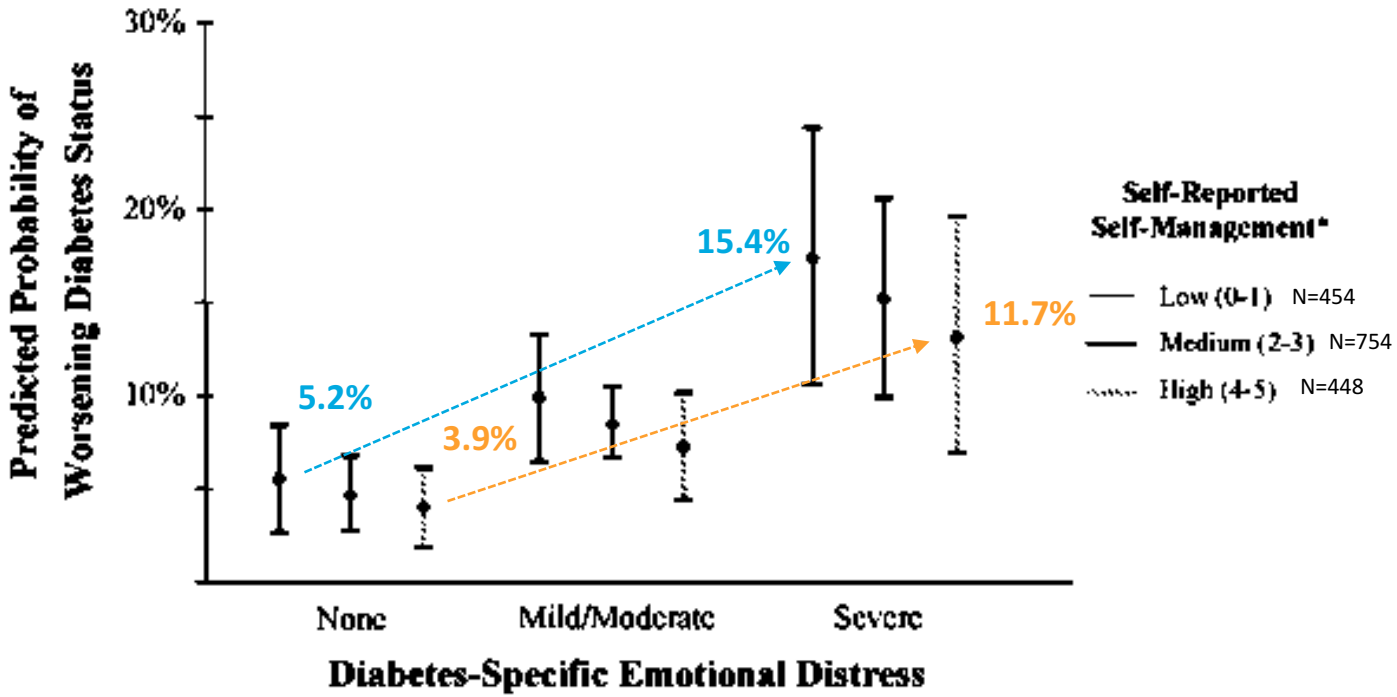
Adherence interventions has strong relationship with psychosocial attributes worsen diabetes status over time

Psychosocial attributes, most notably **diabetes-related emotional distress**, contribute to **difficulty with diabetes self-management, poor glycemic control, and worsening diabetes status over time**

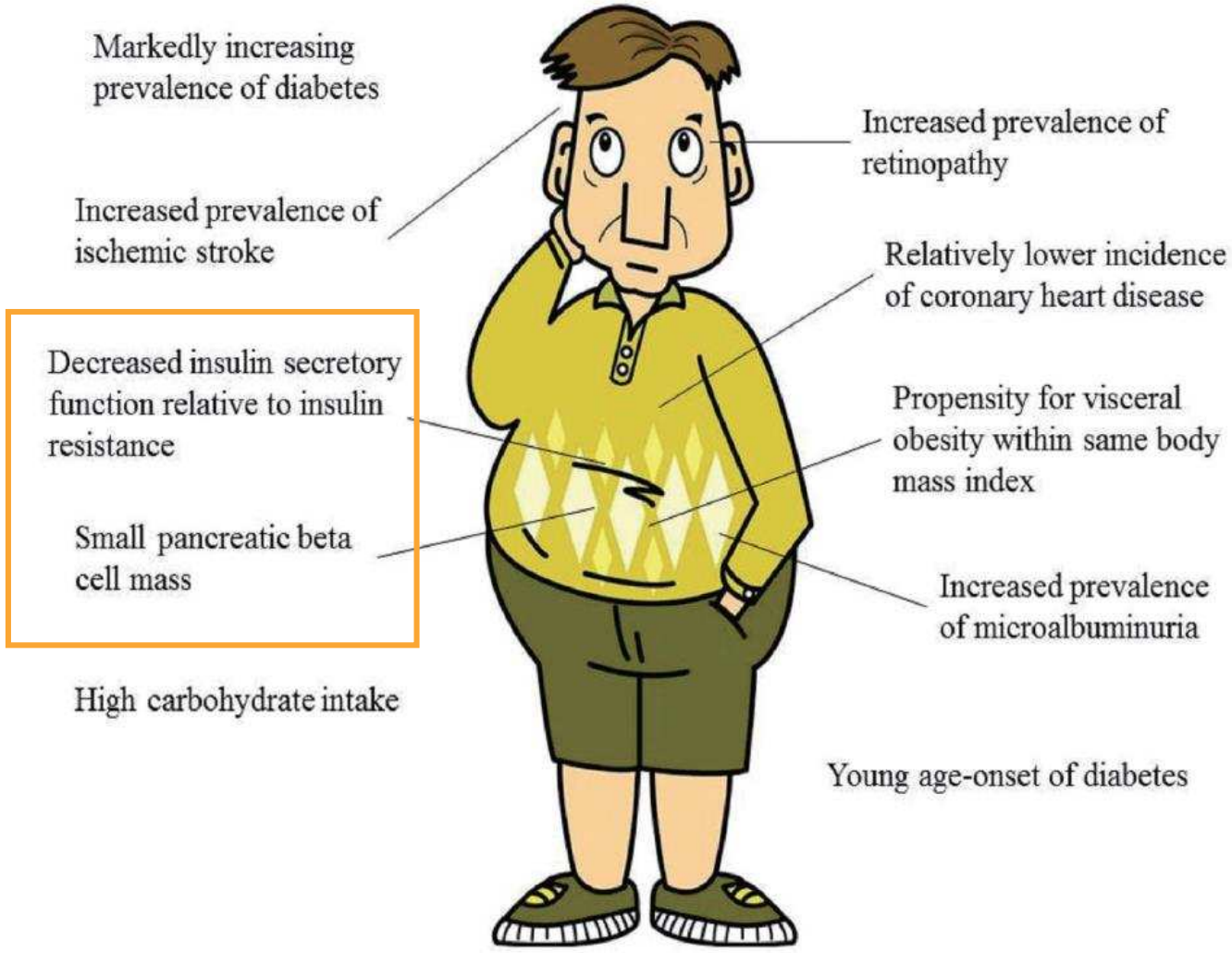


Patient Educ Couns. 2012 Apr;87(1):74-80.

Preserve beta-cell

Unique feature in Asians

- ***Young age of disease onset*** *is also a distinctive characteristic*
- *Asians are known for* ***dysfunctional pancreatic insulin secretory function***
- *Asians have a higher risk of developing diabetes due to genetic defects affecting insulin secretory function and β-cell mass*
- *Asians could benefit from treatment that* ***preserve pancreatic islet functioning***



Endocrinol Metab (Seoul). 2015 Sep; 30(3): 263–269.

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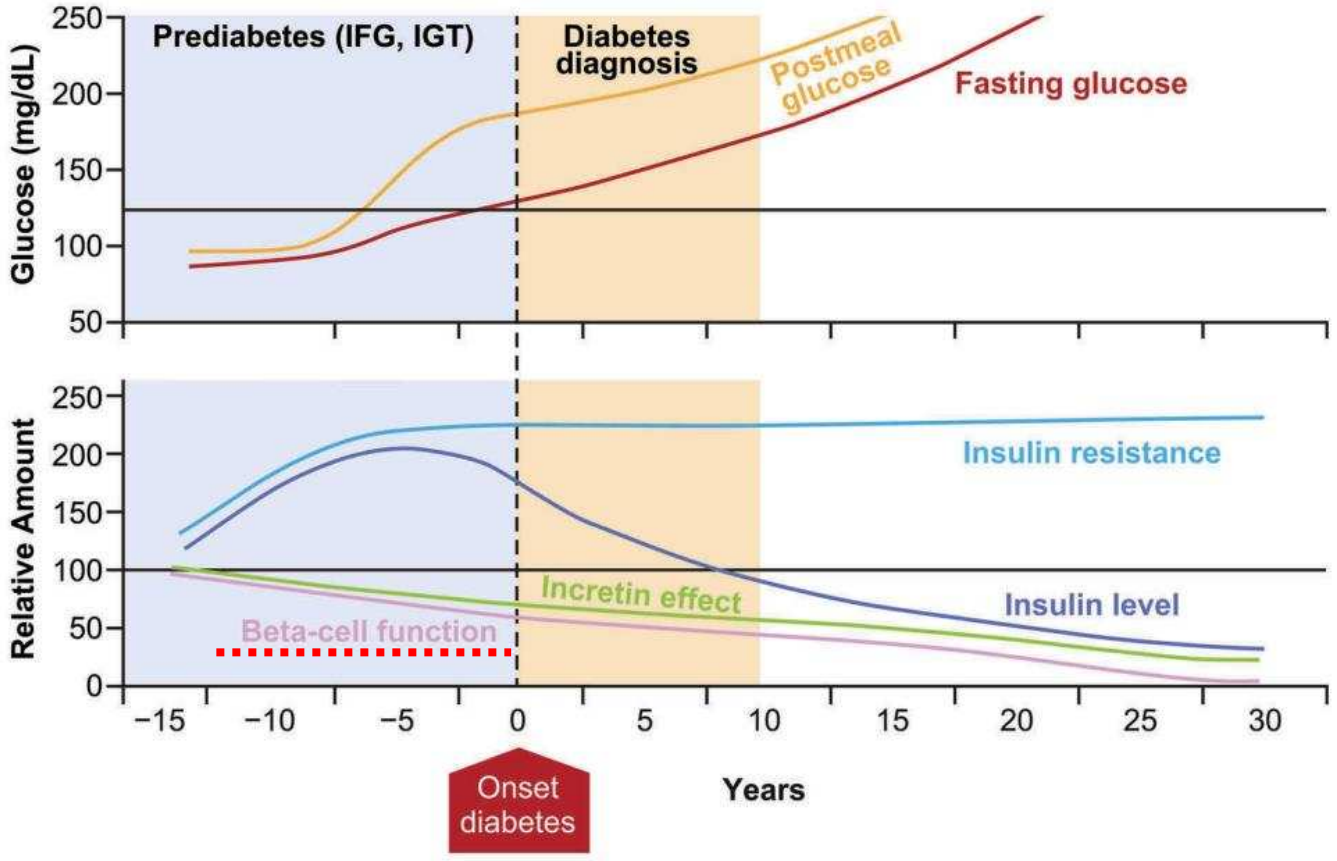
Natural history of type 2 diabetes:
Preserving beta cell might be noticed as earlier as possible!

Beta cells eventually fail to compensate for insulin resistance, resulting in glucose intolerance and fasting hyperglycemia and overt diabetes,

When T2D diagnosed, around 40–50% of beta-cell function was already lost with a further loss of 4–5% expected each year



POSTGRADUATE MEDICINE 2020, VOL. 132, NO. 8, 676–686

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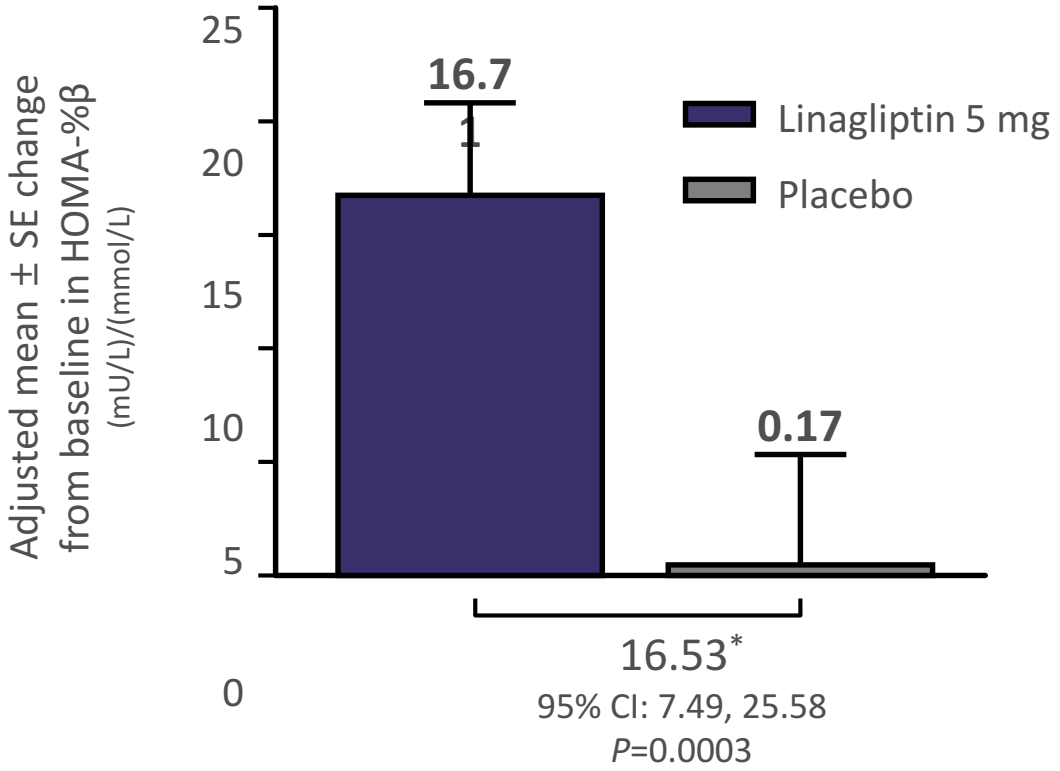
Trajenta potentially benefits Beta-cell function with improving HOMA-%B

- At Week 24, the observed improvements in HbA1c and FPG were significantly greater for Linagliptin compared with placebo (p<0.0001)
- Linagliptin significantly improved HOMA-%β, as a marker of β-cell function



A pooled analysis of six randomised, 24-week, PBO-controlled, phase III trials of LINA 5 mg qd was performed in 2701 patients with T2D (LINA, n=1905; PBO, n=796)

1. 2022台灣糖尿病治療指引 2. Diabetes Obes Metab 2014;16:1036

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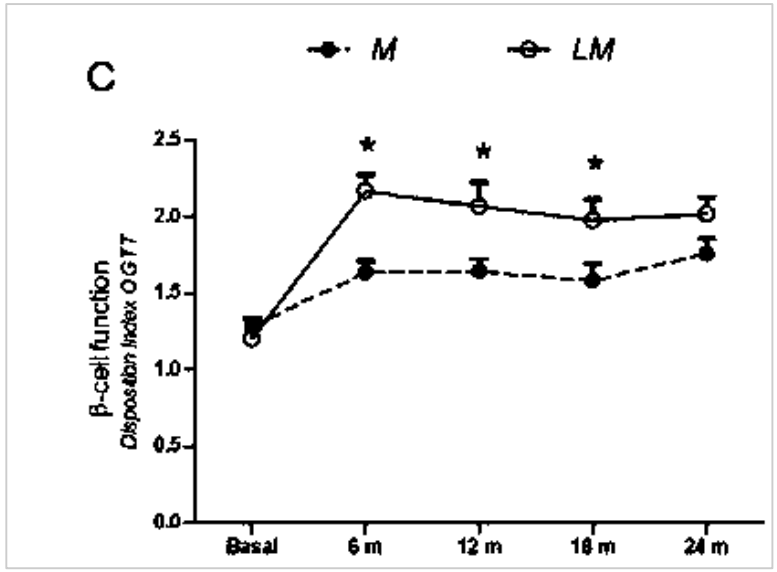
Trajenta significantly improve glucose metabolism and pancreatic β-cell function, and reduced T2D incidence in subjects with prediabetes

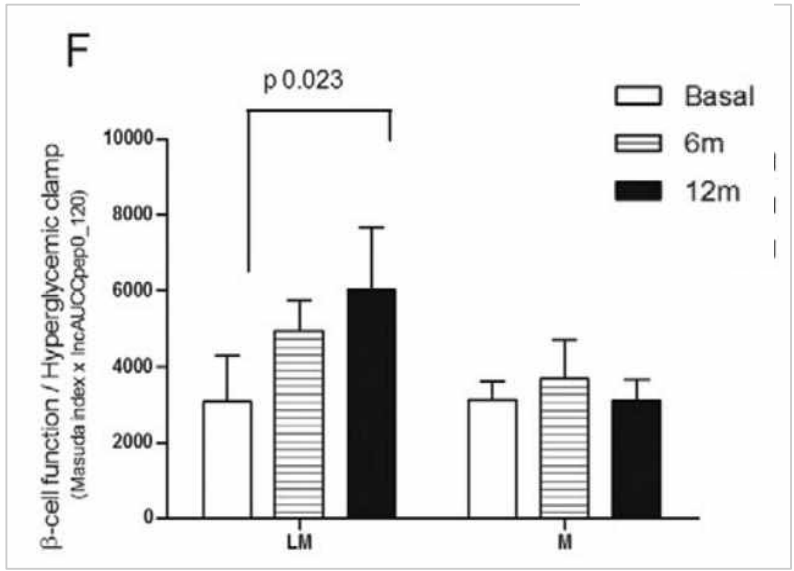
PRELLIM study

Evaluate the effect on glucose tolerance, pancreatic β-cell function and T2D incidence in prediabetes pts.

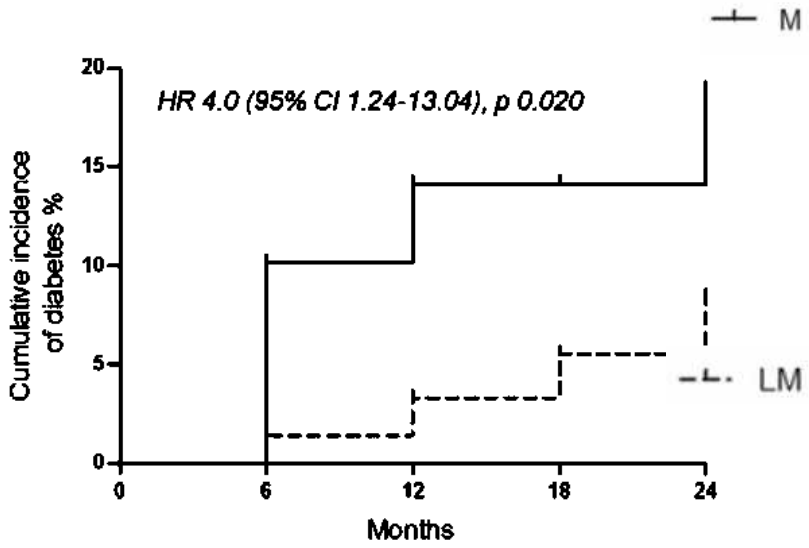
- Metformin 850 mg (M, n=70) vs Lingaliptin + Metformin 2.5/850 mg (LM, n=74)
- Prediabetes T2D
- 24 months of follow-up

↑ β-cell function





↓ T2D incidence



Metabolism. 2020 Mar;104:154054

*Trajenta is not approved for pre-diabetes treatment

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DPP4is improves β cell function, Trajenta showed improvement in pancreatic beta cell function

- A meta-analysis of 52 RCTs showed that DPP4i as monotherapy or add-on therapy significantly improved β cell function[1]
- **Linagliptin + metformin** + lifestyle modification improved glucose levels during OGTT and pancreatic β-cell function in patients with persistently impaired glucose tolerance after 6 months[2]

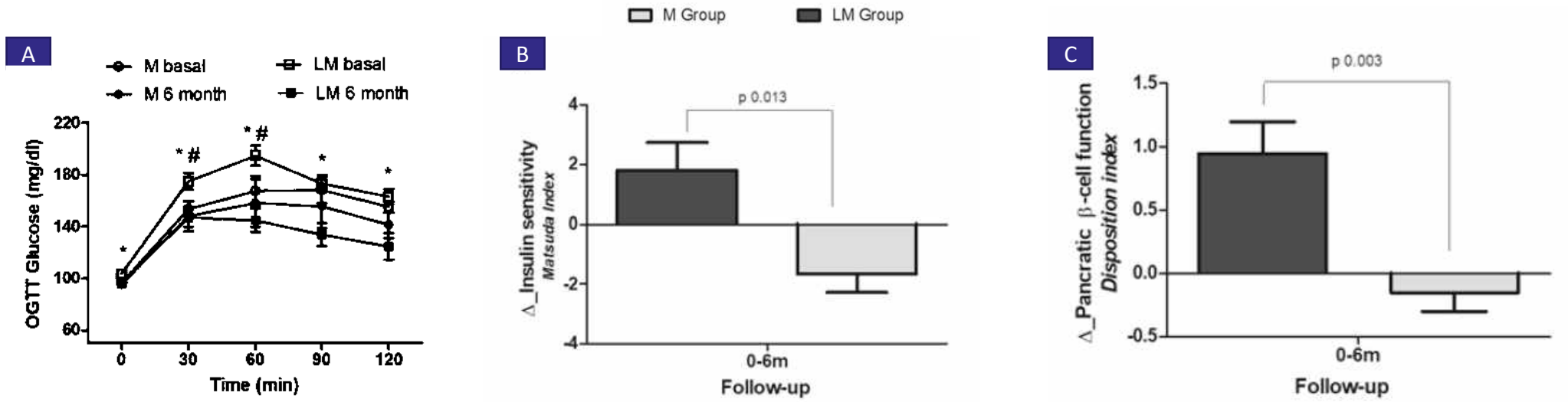

Figure (**a**) Glucose levels during OGTT at basal and after 6 months (**b**) insulin sensitivity and (**c**) pancreatic β-cell function from 0 to 6 months between the study groups M group, Metformin group; LM group, Linagliptin + Metformin group. * p<0.05 for comparisons in LM group between basal and 6 months, # p<0.05 for inter-group comparisons at basal (0 months).

1. Lyu X, et al. *Sci Rep* 2017;7:44865. **2.** Alvarez-Canalez M, et al. *Sci Rep* 2021;11:8750.

DPP4i, dipeptidyl peptidase 4 inhibitors; **OGTT**, oral glucose tolerance test; **RCT**, randomised control trial.

*Trajenta is not approved for pre-diabetes treatment

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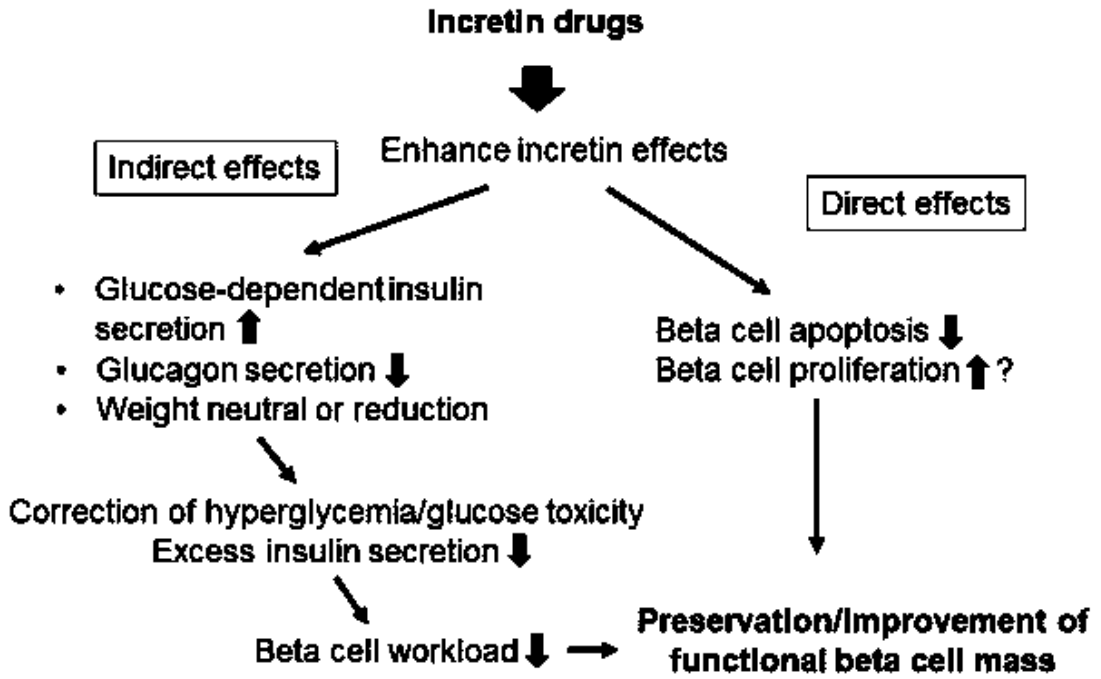
The concept for the management of type 2 diabetes with a paradigm to “beta cell-centric”

DPP-4 inhibitors are a unique class of drugs which restore islet function, a core deficit of T2DM, by direct and indirect mechanisms

Expert Opin Pharmacother. 2020 Sep;21(13):1565-1578

Linagliptin protected from gluco-, lipo-, and cytokine-toxicity and stabilized active GLP-1 secreted from human islets. This provides a direct GLP-1 mediated protective effect of linagliptin on beta-cell function and survival.

J Clin Endocrinol Metab, July 2013, 98(7):E1163–E1172



EXPERT OPINION ON PHARMACOTHERAPY 2020, VOL. 21, NO. 13, 1565–1577

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Trajenta® (linagliptin) 5mg tablets

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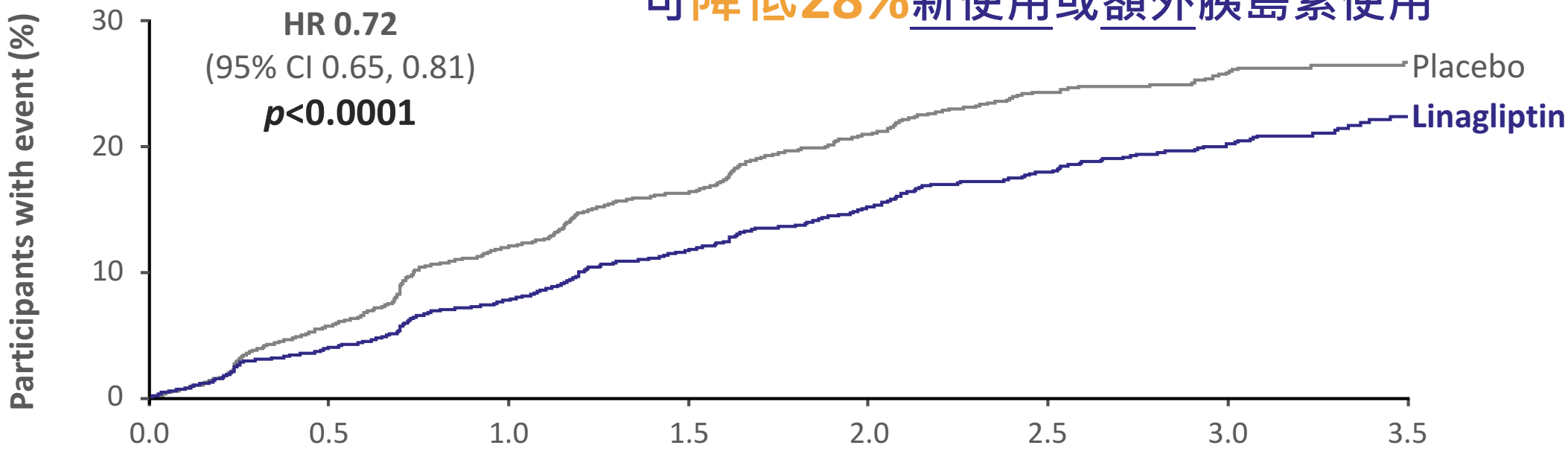
With Trajenta, fewer patients initiated or increased insulin dose

CARMELINA

Initiation or dose increase of insulin

合併 Trajenta 治療，

可降低28%新使用或額外胰島素使用



No. at risk								
Placebo (n)	3,485	3,203	2,913	2,263	1,590	1,024	613	220
Linagliptin (n)	3,494	3,271	3,072	2,411	1,746	1,140	676	242

Treated set, Kaplan-Meier estimate. Hazard ratio and 95% CI based on Cox regression model

Rosenstock J, et al. JAMA 2019; 321: 69-79.

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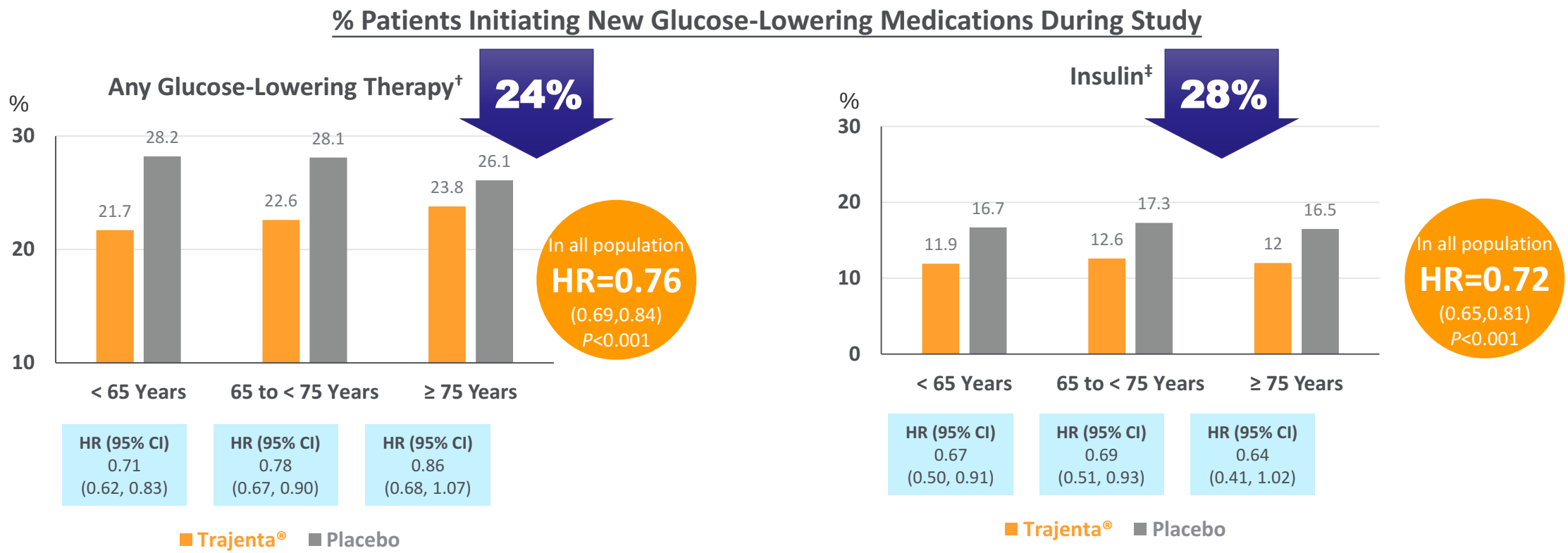
CARMELINA 次族群分析顯示，在各年齡族群中，使用 Trajenta 的組別，皆能減少後續額外加藥的比例



† P value for age group by treatment interaction = 0.3912; in the overall population[2], there was a higher use of additional glucose-lowering therapies in the placebo group (HR (95% CI) 0.76 (0.69, 0.84); p<0.001).

‡ P value for age group by treatment interaction = 0.9712; in the overall population[2], there was a higher use of insulin in the placebo group (HR (95% CI) 0.72 (0.65, 0.81); p<0.001).

P value for age group by treatment interaction = 0.1862; in the overall population[2], there was a higher use of non-insulin therapies in the placebo group (HR (95% CI) 0.75 (0.66, 0.86); p<0.001).

1. Cooper M, et al. Diabetes Obes Metab. 2020; 1–12. 2. Rosenstock J, et al. JAMA 2019; 321: 69-79.

CI: confidence interval; CV: cardiovascular; HR: Hazard ratio.

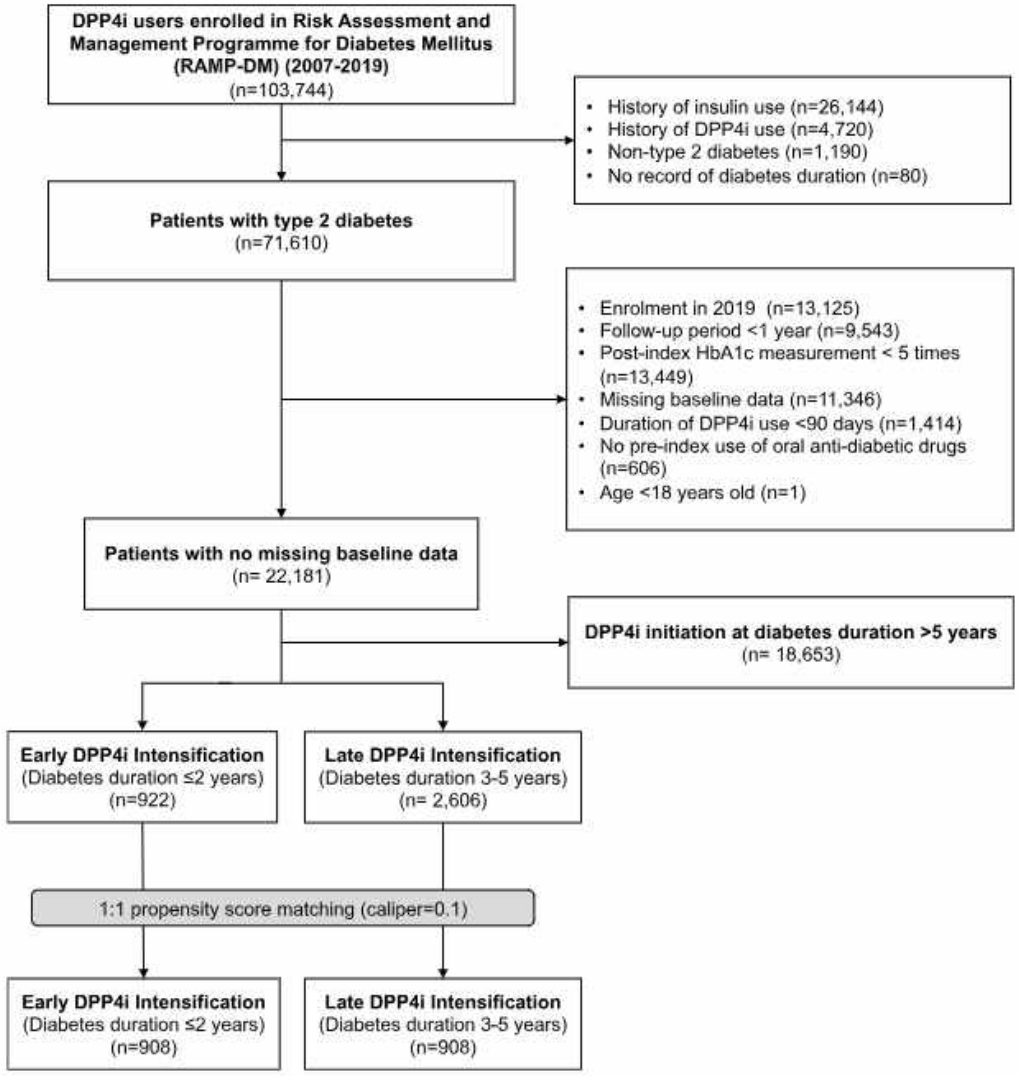
Patient Number: <65 Years: Trajenta:1467 , Placebo:1501 ; 65 to < 75 Years: Trajenta:1405 , Placebo:1395; ≥ 75 Years: Trajenta:622 , Placebo:589

Boehringer Ingelheim

Trajenta® (linagliptin) 5mg tablets

TrajentaDuo® (linagliptin/metformin HCl)

Early treatment with dipeptidyl-peptidase 4 inhibitors reduces glycaemic variability and delays insulin initiation in type 2 diabetes: A propensity score-matched cohort study



香港前瞻性研究

1:1 傾向評分匹配：
- 早期強化治療（糖尿病 0-2 年期間起始 DPP4i）(n=908)
- 晚期強化治療（糖尿病 3-5 年期間起始 DPP4i）(n=908)

追蹤時間長達 8 年

Diabetes Metab Res Rev. 2023 Aug 26;e3711.

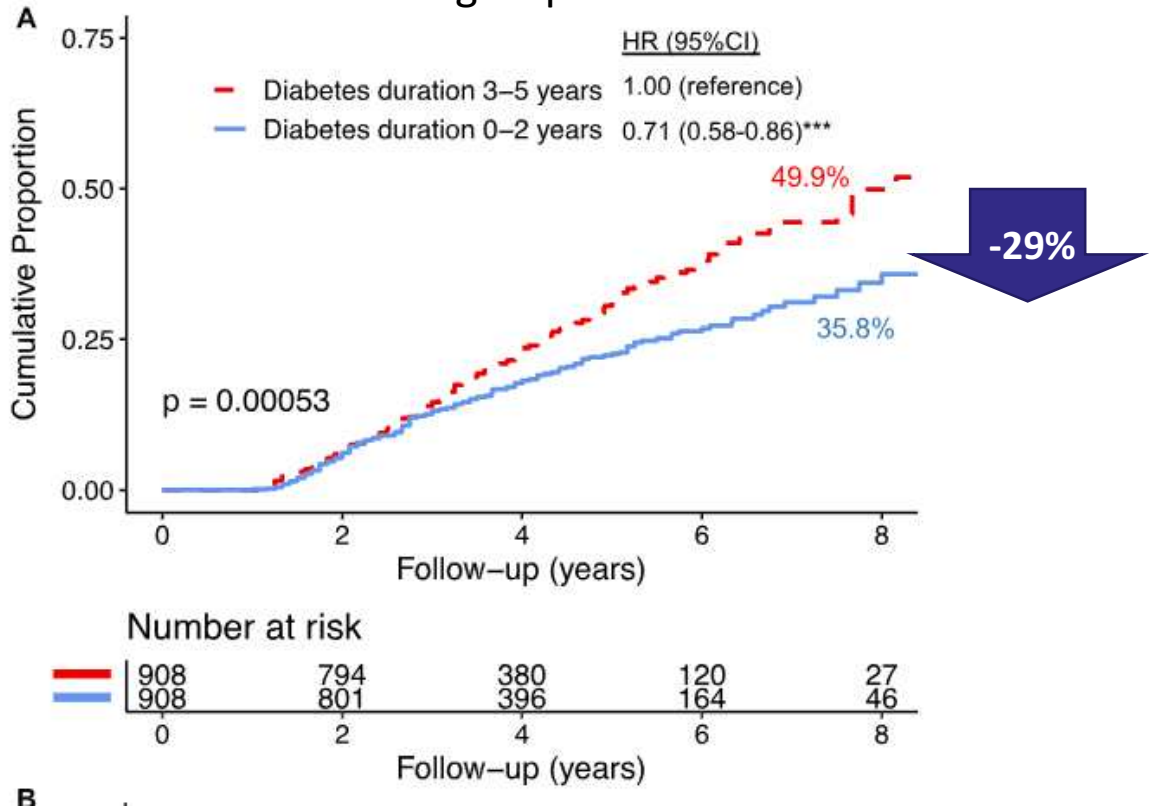
Boehringer Ingelheim

Trajenta® (linagliptin) 5mg tablets

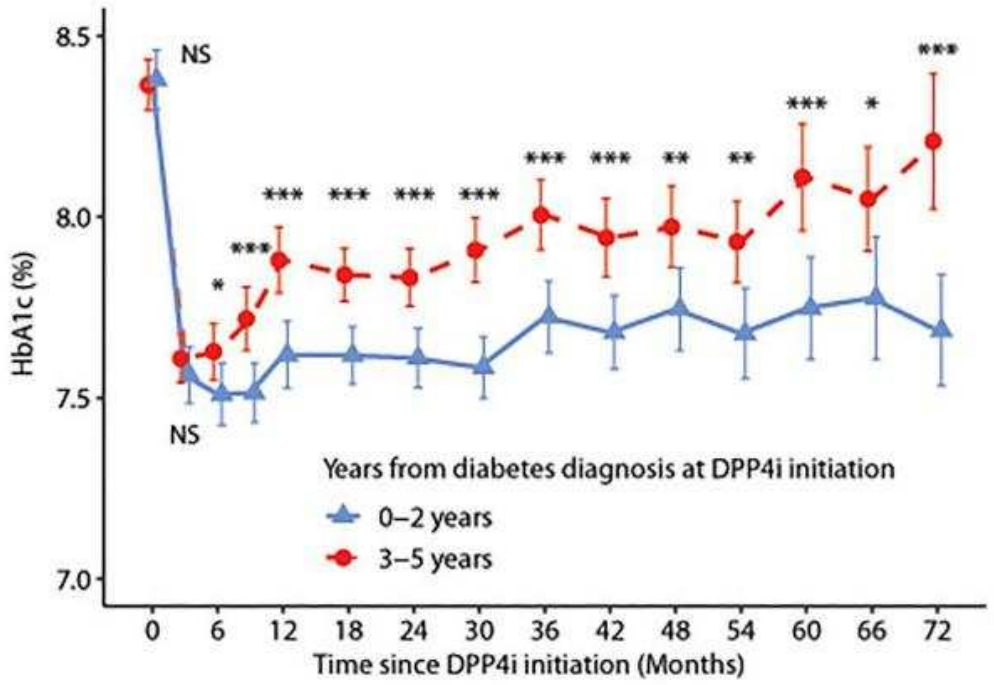
TrajentaDuo® (linagliptin/metformin HCl)

Early DPP4i intensification delayed insulin initiation and displayed stable glycemic control

Early intensification group had **29% lower risk** of insulin initiation vs late group



The trajectory of mean HbA1c after DPP4i intensification in early and late intensification groups



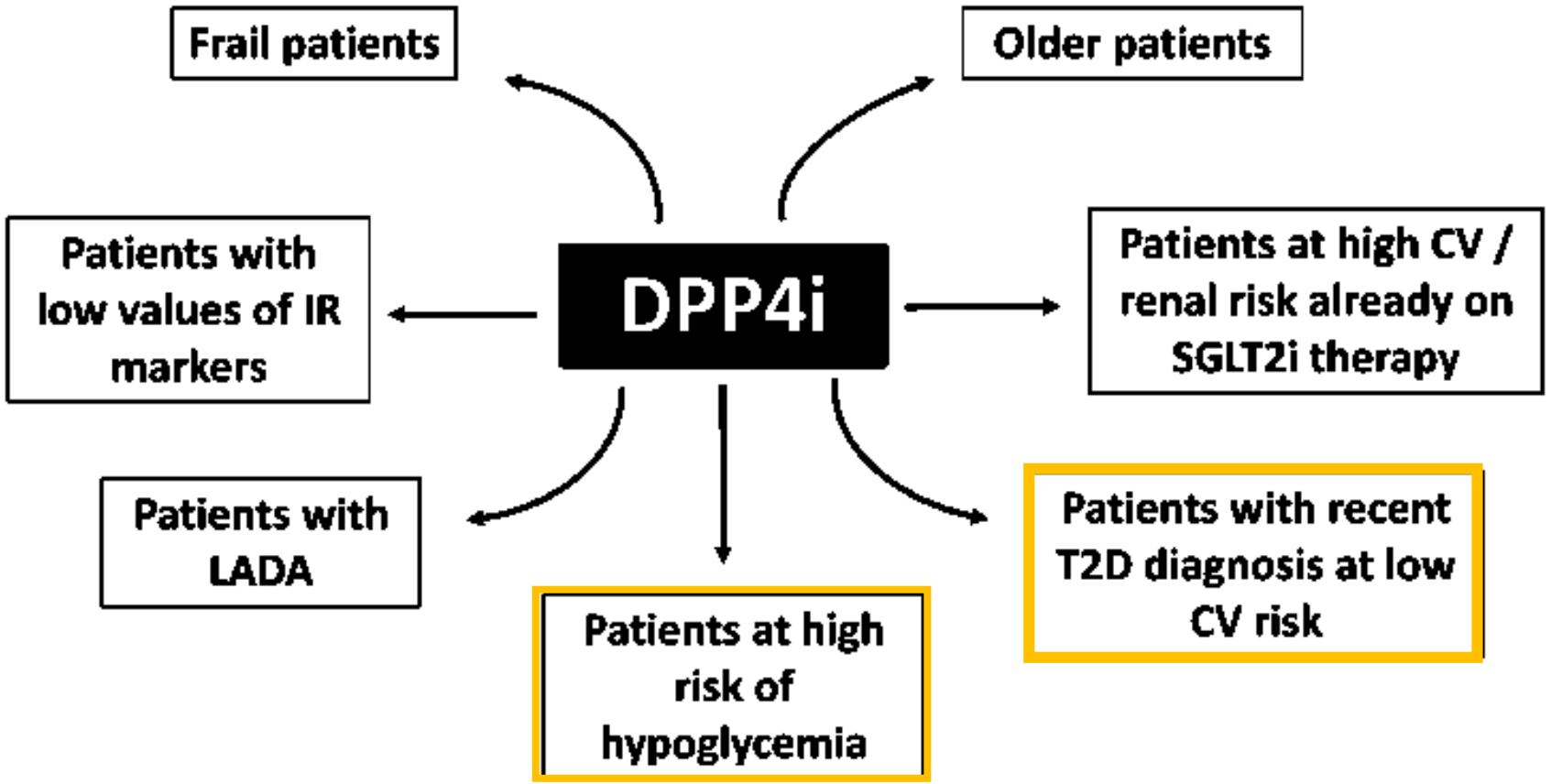
*HbA1c variabilityscore (HVS)

Diabetes Metab Res Rev. 2023 Aug 26;e3711.

Trajenta® (linagliptin) 5mg tablets
TrajentaDuo® (linagliptin/metformin HCl)

PC-TW-105985-19-Dec-2023

Patient profiles who would benefit most from DPP4i treatment



Am J Cardiovasc Drugs. 2023 Nov;23(6):601-608.

Trajenta® (linagliptin) 5mg tablets TrajentaDuo® (linagliptin/metformin HCl)

PC-TW-105985-19-Dec-2023

Trajenat 一錠適用各階段肝腎功能不全之 T2D 病人, Easy start easy control

Absorption:

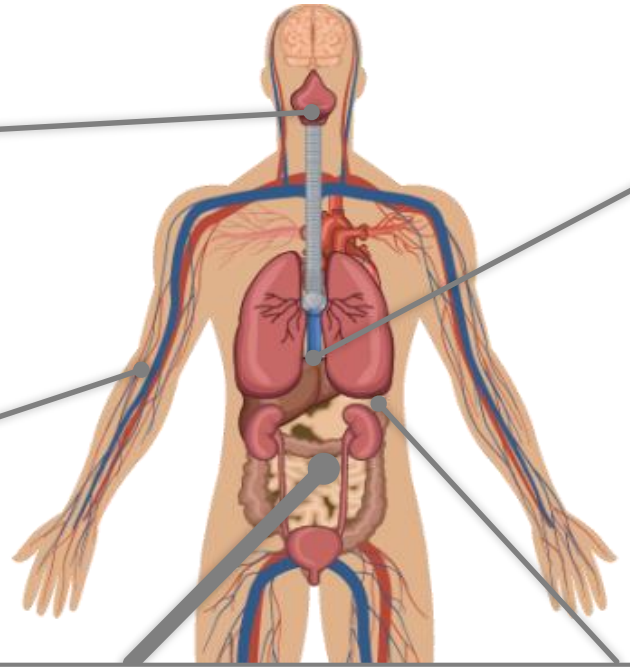
Tablet intake: 5 mg qd independent of food

↓

Absolute bioavailability:
~30%, with or without food

↓

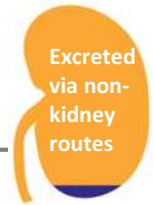
~95% bound to plasma proteins (in essence, DPP4)*



Metabolism:

~10% (inactive) metabolite

~90% transferred **unchanged**



Excretion:†

>80% of orally administered linagliptin is excreted via **the bile and gut**

~5% of orally administered linagliptin is excreted via the kidneys

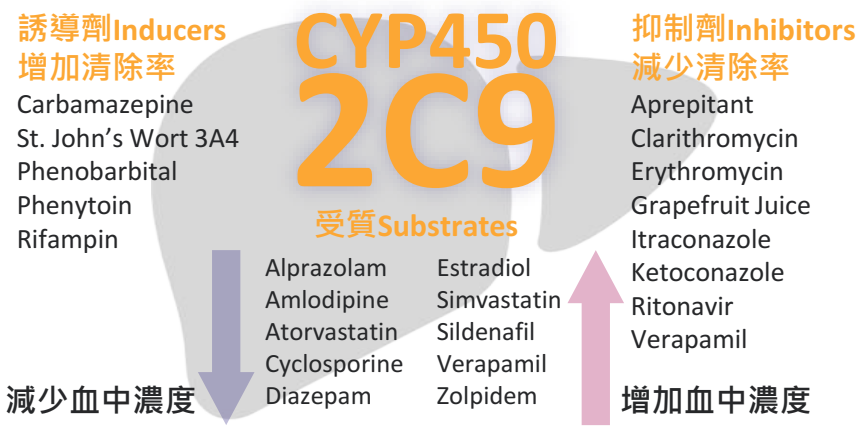
In contrast, for each of the other globally-available DPP4i, 75% or more of the drug is excreted via kidneys.[2-5]

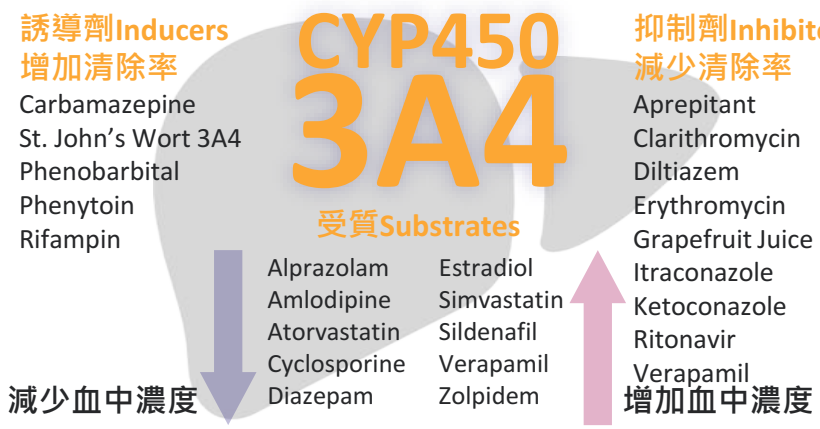
*Protein binding is concentration-dependent: 99% at 1 nmol/l to 75–89% at ≥30 nmol/l; †At steady state. Note that the label statement describes single-dose analyses that do not add up to 100% (a common effect for this type of analysis); following administration of an oral [^{14}C]-linagliptin dose to healthy patients, ~85% of the administered radioactivity is eliminated via the enterohepatic system (80%) or urine (5%) within 4 days of dosing
DPP4, dipeptidyl peptidase-4; DPP4i, dipeptidyl peptidase-4 inhibitor
Boehringer Ingelheim and Eli Lilly. Trajenta® (linagliptin) summary of product characteristics. 2019

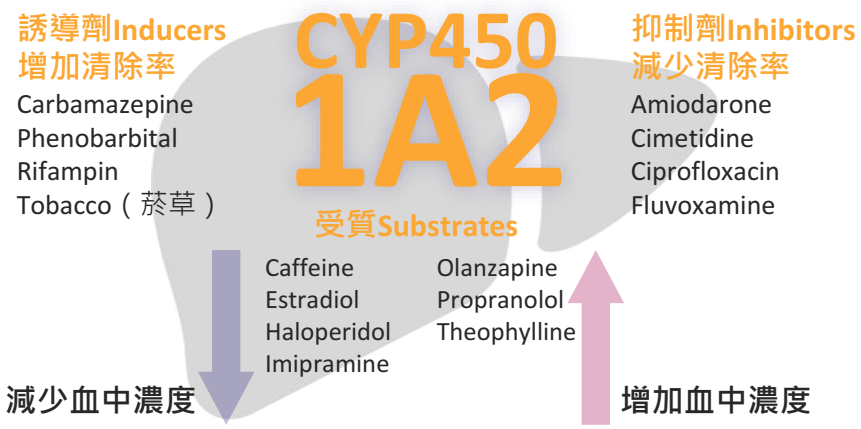
Trajenta® (linagliptin) 5mg tablets
TrajentaDuo® (linagliptin/metformin HCl)

PC-TW-105985-19-Dec-2023

Trajenta with lower drug-drug interaction risk in CYP450 fits the T2D patients co-existing comorbidities







Trajenta® with low metabolic rate in liver, you don't need to worry about hepatic DDI.

Boehringer

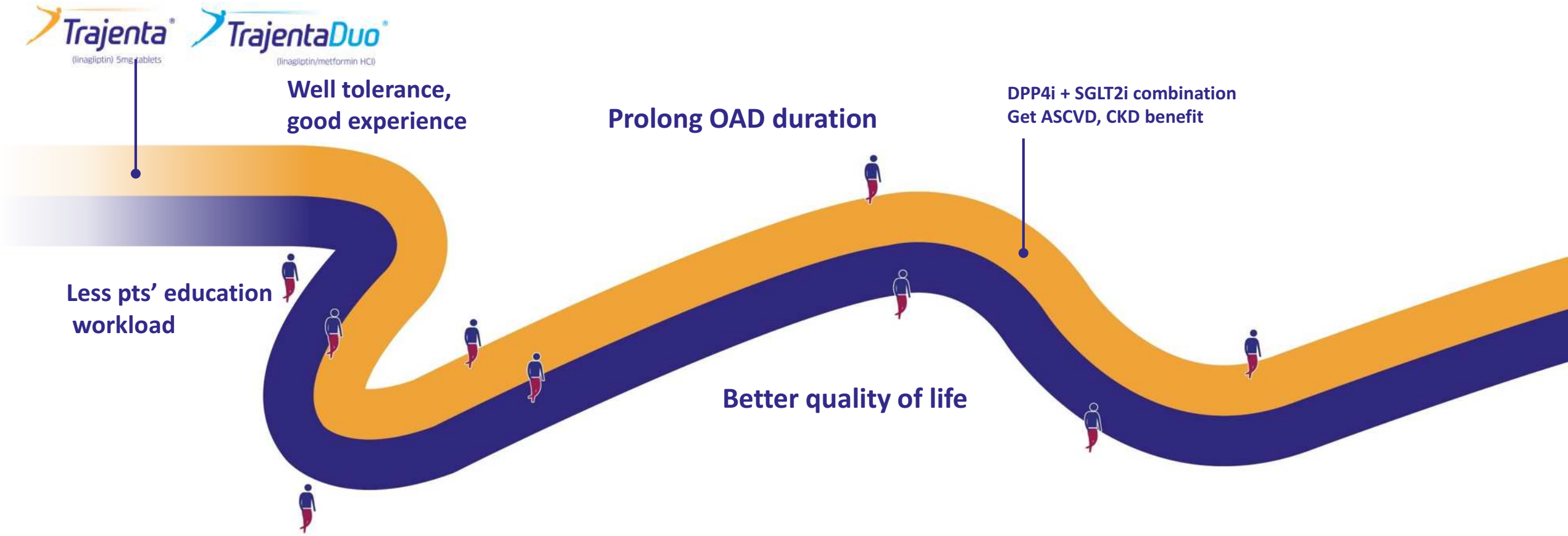
Am Fam Physician. 2007 Aug 1;76(3):391-396.

Trajenta® (linagliptin) 5mg tablets

TrajentaDuo® (linagliptin/metformin HCl)

PC-TW-105985-19-Dec-2023

The earlier the better !
及早加上 Trajenta 延緩病程， 簡單控糖 start simple stay simple



Boehringer Ingelheim

Trajenta (linagliptin) 5mg tablets
TrajentaDuo (linagliptin/metformin HCl)

Glyxambi®
(empagliflozin/ linagliptin)

Glyxambi健保給付條件

衛福部適應症

適用於配合飲食控制及運動，以改善下列第二型糖尿病患者的血糖控制：使用metformin合併empagliflozin或linagliptin未能達到適當血糖控制者；或已在使用empagliflozin及linagliptin合併治療者。

Empagliflozin用於具第二型糖尿病且已有心血管疾病的成人病人時，可降低心血管原因死亡的風險。然而，本品糖順平用於具第二型糖尿病且已有心血管疾病的成人病人時，其降低心血管原因死亡的風險的有效性尚未被建立。

健保給付條件 (2020.05.01起)

1. 每日限處方1粒。
2. 限用於已接受過最大耐受劑量的metformin，且併用empagliflozin或linagliptin治療至少六個月，糖化血色素值(HbA1c)仍高於於7.5%者。

健保價: 35.1元/顆

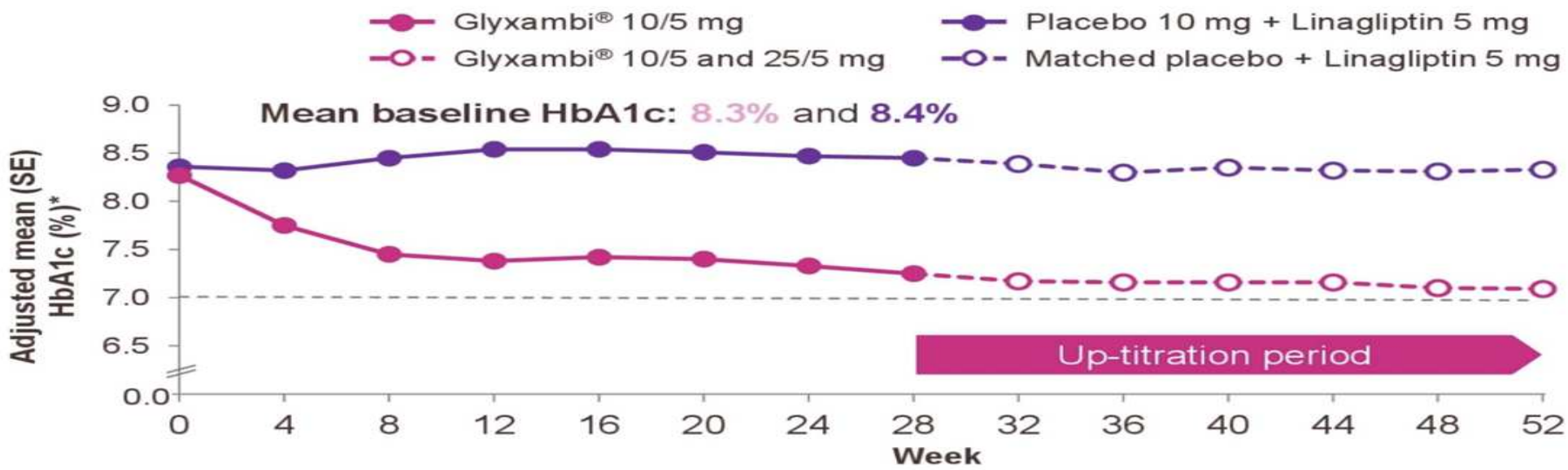
Glyxambi®
(empagliflozin/
linagliptin)

Boehringer Ingelheim

Trajenta®
(linagliptin) 5mg tablets

TrajentaDuo®
(linagliptin/metformin HCl)

一項日本研究顯示:
Trajenta後接用Glyxambi還可再降 1.2% HbA1c



FDC, fixed-dose combination
Kawamori R *et al. Diabetes Obes Metab* 2018;20:2200

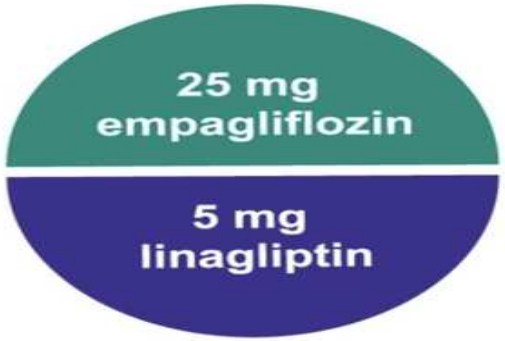
Glyxambi (empagliflozin/linagliptin)

Boehringer Ingelheim

Trajenta (linagliptin) 5mg tablets

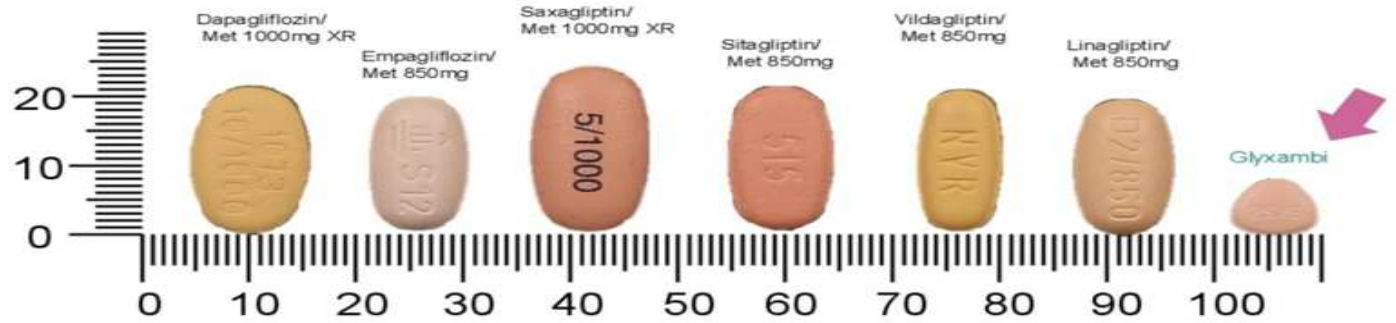
TrajentaDuo (linagliptin/metformin HCl)

GLYXAMBI can be taken...



...any time of day, with or without food

...by patients with **eGFR ≥30 ml/min/1.73 m²** with **no dose adjustment** required



Glyxambi® is **not recommended** for use in patients with **persistent eGFR <30 ml/min/1.73 m²**

Boehringer Ingelheim and Eli Lilly. Glyxambi® (empagliflozin and linagliptin) Prescribing Information. 2020

Glyxambi (empagliflozin/linagliptin)

Boehringer Ingelheim

Trajenta (linagliptin) 5mg tablets

TrajentaDuo (linagliptin/metformin HCl)

Simple.
Every Day.

Trajenta Duo Prescribing Information†
糖倍平®膜衣錠2.5/850毫克, 衛署藥輸字第025792號;
適應症:與飲食控制及運動配合治療, 藉以改善下列第2型糖尿病成人病人的血糖控制效果: (1) 已在合併使用linagliptin與metformin治療且受到良好控制效果的病人(2)單獨使用metformin未能達到適當控制效果的病人(3)與sulphonylurea併用(亦即第三重合併療法), 用於治療使用最高耐受劑量之metformin與sulphonylurea仍未達到適當控制效果的病人。
建議劑量:TRAJENTA DUO的劑量應根據有效性及耐受性進行個人化之調整, 但不可超過最高建議劑量(2.5mg linagliptin / 1000mg metformin hydrochloride, 一天兩次)。劑量調整
應採漸進式，以降低metformin引發的腸胃副作用。禁忌症:TRAJENTA DUO不可用於有下列狀況的病人：重度腎功能不全（eGFR低於30 mL/min/1.73 m2）。
急性或慢性代謝性酸中毒，包括糖尿病酮酸中毒。對於linagliptin、metformin或是TRAJENTA DUO之賦形劑過敏者，過敏反應例如急性過敏、血管性水腫、鱗片狀脫落性皮膚疾病、蕁麻疹或支氣管過敏曾發生於linagliptin。警語及注意事項:乳酸酸中毒 曾有與metformin有關之乳酸酸中毒的上市後病例，包括導致死亡的病例。Metformin會降低肝臟的乳酸吸收，升高血中乳酸濃度，因而增高乳酸酸中毒的風險。若懷疑發生與metformin有關之乳酸酸中毒，應立即停止使用TRAJENTA DUO，並儘速住院接受一般的支持性治療措施。在接受TRAJENTA DUO治療且經確診或強烈懷疑有乳酸酸中毒的病人，建議應立即進行血液透析，以矯正酸中毒與移除蓄積的metformin。胰臟炎 曾有服用 linagliptin的病人發生急性胰臟炎(包括致命案例)的報告。在CARMELINA試驗中，有9名（0.3%）接受linagliptin治療的病人和5名（0.1%）接受安慰劑治療的病人發生急性胰臟炎。在CARMELINA試驗中有2名接受linagliptin治療的病人發生急性胰臟炎並因而致死。與已知可能引發低血糖症的藥物併用在一項臨床試驗中，相較於安慰劑，linagliptin與胰島素促分泌劑（例如磺醯尿素類藥物）或胰島素併用有較高之低血糖症發生率。Metformin與胰島素與／或胰島素促泌劑併用時，低血糖症的風險可能增加。因此，在與TRAJENTA DUO併用時，為降低低血糖症風險，可能必須降低胰島素促分泌劑或胰島素的劑量。過敏反應 Linagliptin的上市後報告中曾有嚴重過敏反應的案例，包括急性過敏、血管水腫和鱗片狀脫落性皮膚疾病。維他命B12 濃度接受metformin長期治療的病人發生血清維他命B12降至正常濃度以下的風險較高，且曾有不良血液學及神經學反應的上市後報告。嚴重和致行動不便之關節疼痛DPP-4抑制劑的上市後報告中曾有嚴重和造成行動不便之關節疼痛案例。大皰性類天皰瘡 DPP-4抑制劑的上市後報告中曾有需要住院的大皰性類天皰瘡案例。修正日期 2020年12月

Trajenta Prescribing Information*
糖漸平®膜衣錠5毫克衛署藥輸字第025537號
適應症:第二型糖尿病。建議劑量:TRAJENTA的建議劑量為5mg，成人每天一次。可單獨使用亦可與metformin、sulfonylurea、insulin、PPARγ作用劑(如thiazolidinediones)合併使用，作為飲食控制及運動的輔助療法，以改善血糖的控制。TRAJENTA錠劑可與食物一起服用，亦可空腹服用。在特定族群的使用:腎功能不全 對於腎功能不全病人並無劑量調整建議。肝功能不全 對於肝功能不全病人並無劑量調整建議。老年人整體而言在安全性或有效性上，老年人與較年輕的受試者並無差異。懷孕在懷孕婦女使用TRAJENTA的現有資料極少，因此無法據以判定藥物與重大先天缺陷和流產風險之間是否具有相關性。懷孕期間糖尿病控制不佳可能對母體和胎兒造成風險。禁忌症:TRAJENTA禁用於對linagliptin或其賦形劑出現過敏反應的病人（例如：急性過敏、血管性水腫、鱗片狀脫落性皮膚疾病、蕁麻疹或支氣管過敏）警語及注意事項:胰臟炎 於TRAJENTA上市後，使用的病人中曾通報發生急性胰臟炎的案例，目前仍不瞭解具有胰臟炎病史的病人使用TRAJENTA，是否會增加發生胰臟炎的風險。與已知會造成低血糖症的藥物併用 已知胰島素促分泌物質或胰島素會造成低血糖症。在臨床試驗中，相較於安慰劑，TRAJENTA與胰島素促分泌物質（例如，磺醯尿素類藥物）或胰島素併用時的低血糖症發生率較高，而嚴重腎功能障礙之受試者併用TRAJENTA與胰島素時，低血糖症發生率較高；因此，與TRAJENTA併用時，可能須降低胰島素促分泌物質或胰島素的劑量，以減少低血糖症的風險。過敏反應 TRAJENTA的上市後報告中曾有嚴重過敏反應的案例，包括急性過敏、血管水腫和鱗片狀脫落性皮膚疾病。嚴重和行動不便之關節疼痛 DPP-4抑制劑的上市後報告中曾有嚴重和造成行動不便之關節疼痛案例。大皰性類天皰瘡 DPP-4抑制劑的上市後報告中曾有需要住院的大皰性類天皰瘡案例。核准日期2022年9月

Trajenta® (linagliptin) 5mg tablets
TrajentaDuo® (linagliptin/metformin HCl)

PC-TW-105771-17-Oct-2023