2022년 대한임상건강증진학회

추계학술대회

비만약물치료의 최신지견

허　　연(의정부 을지대병원)

대한임상건강증진학회
Korean Society for Health Promotion and Disease Prevention

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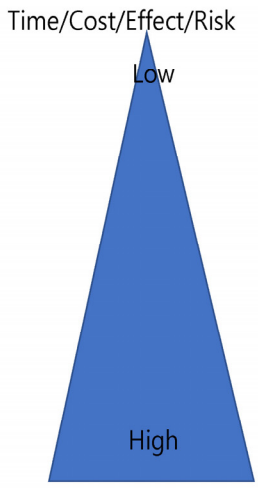
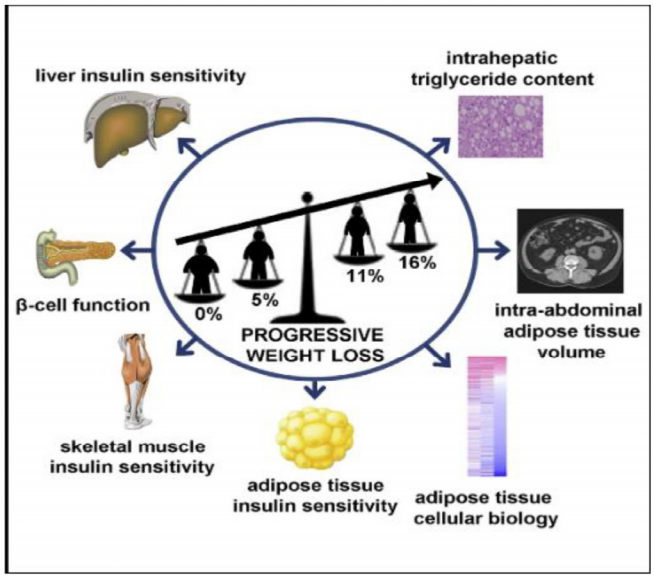
Currently Available options

1. Diet/ Exercise
2. Medication
① BMI 25kg/m^2 이상인 경우
② BMI 23kg/m^2 이상이면서 비만 합병증의 위험이 증가한 경우
3. Surgery
① BMI 35kg/m^2 이상인 경우
② BMI 30kg/m^2 이상이면서 비만 합병증이 동반된 경우
③ BMI 27.5- 30kg/m^2 이면서 비수술적 치료로 혈당이 적절히 조절되지 않는 제2형 당뇨병

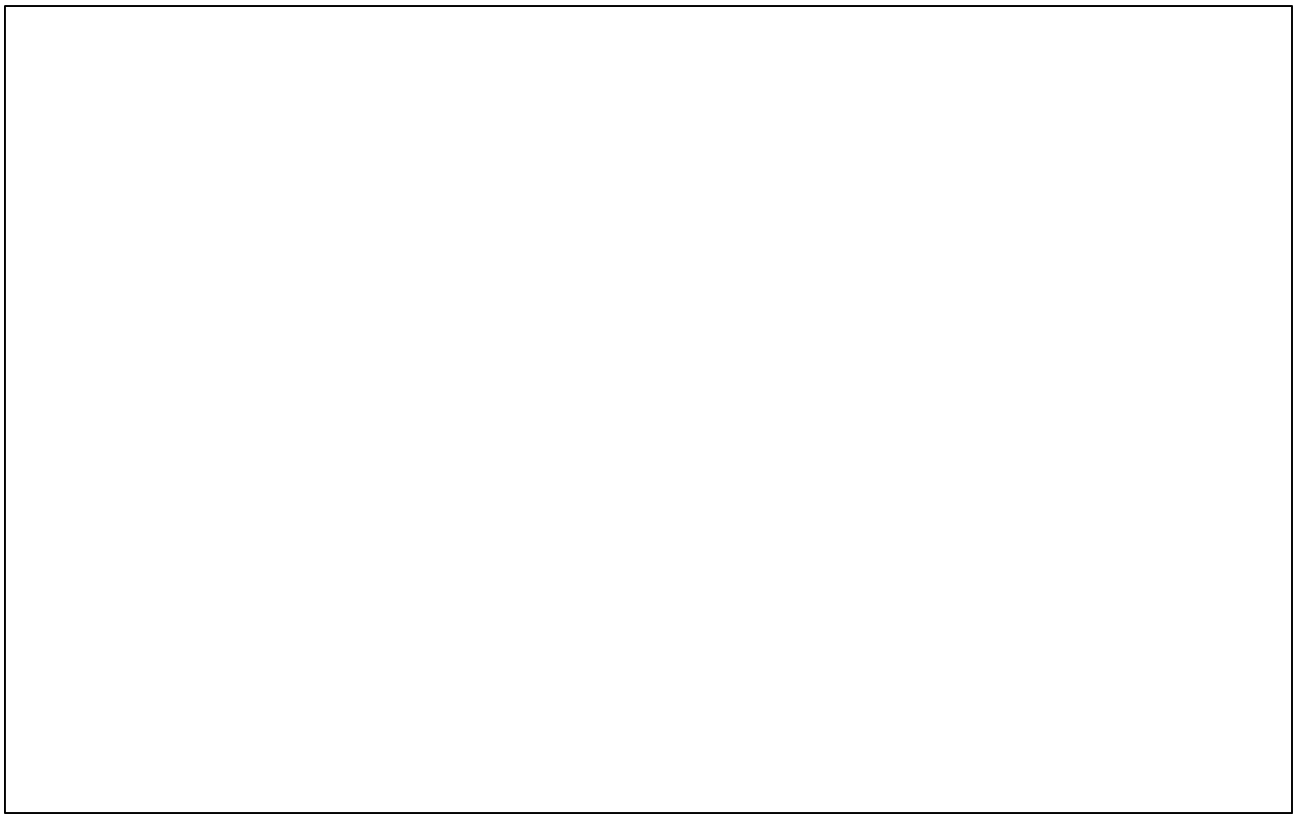


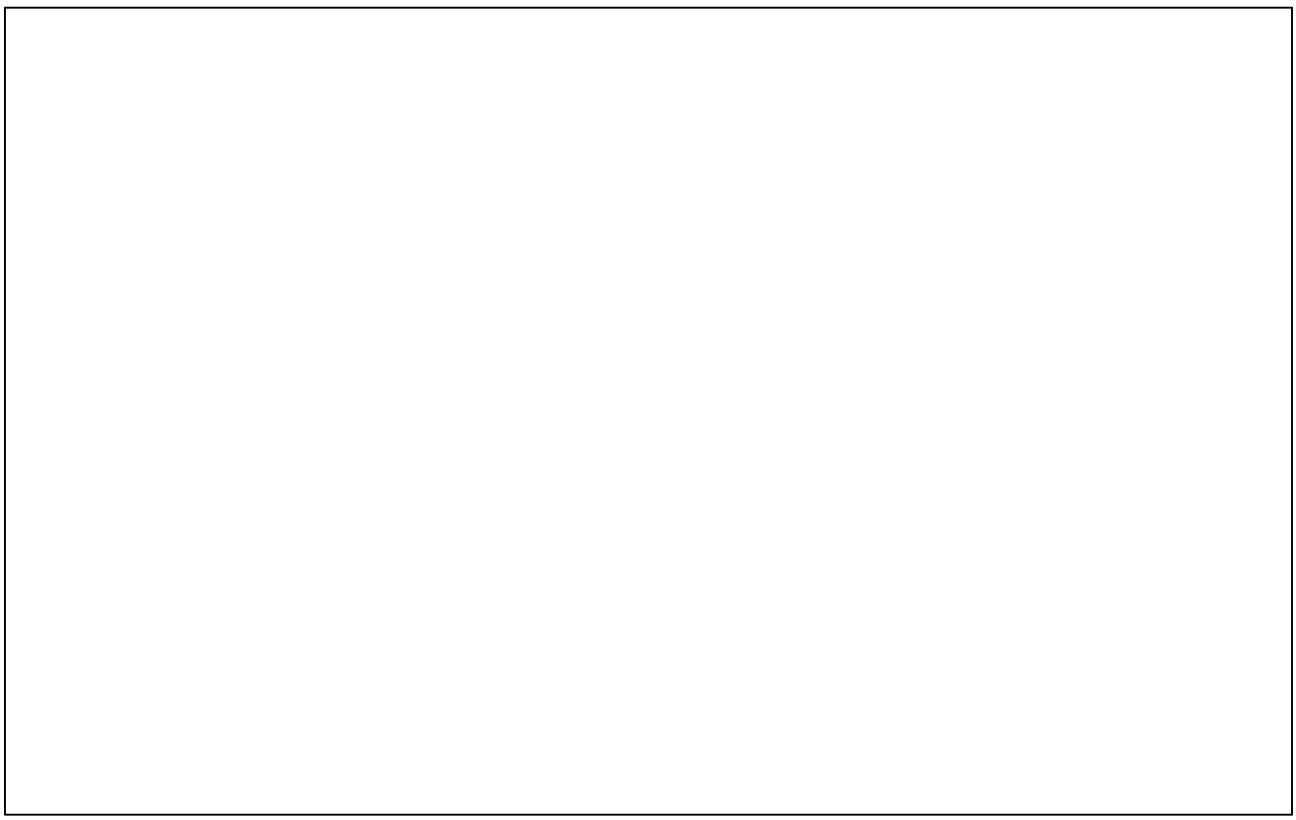
More Weight loss produces more health benefits



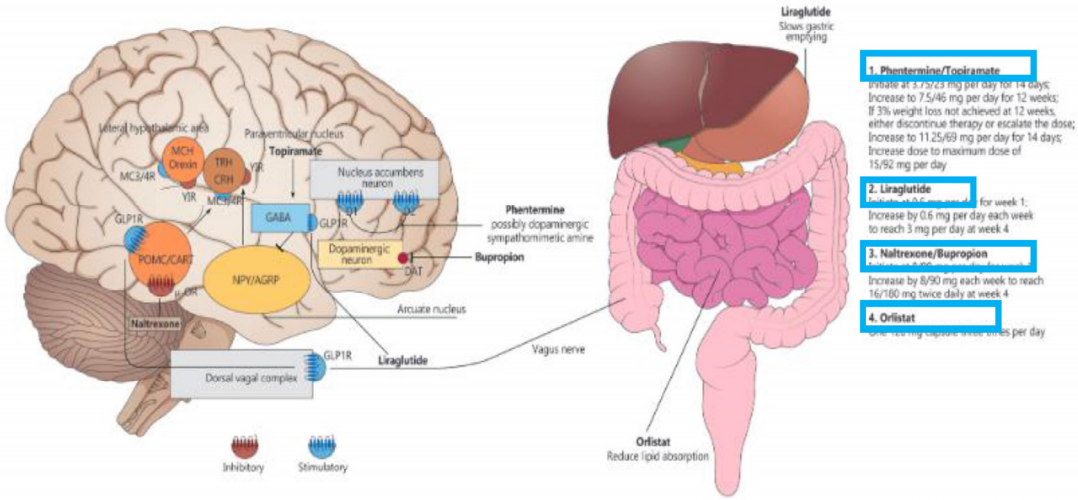
- Moderate 5% weight loss improves multi-organ insulin sensitivity and b cell function
- Additional weight loss of 11%–16% further increases insulin sensitivity in muscle
- Progressive weight loss causes stepwise changes in adipose tissue biology.

Cell Metab. 2016;23:591-600.



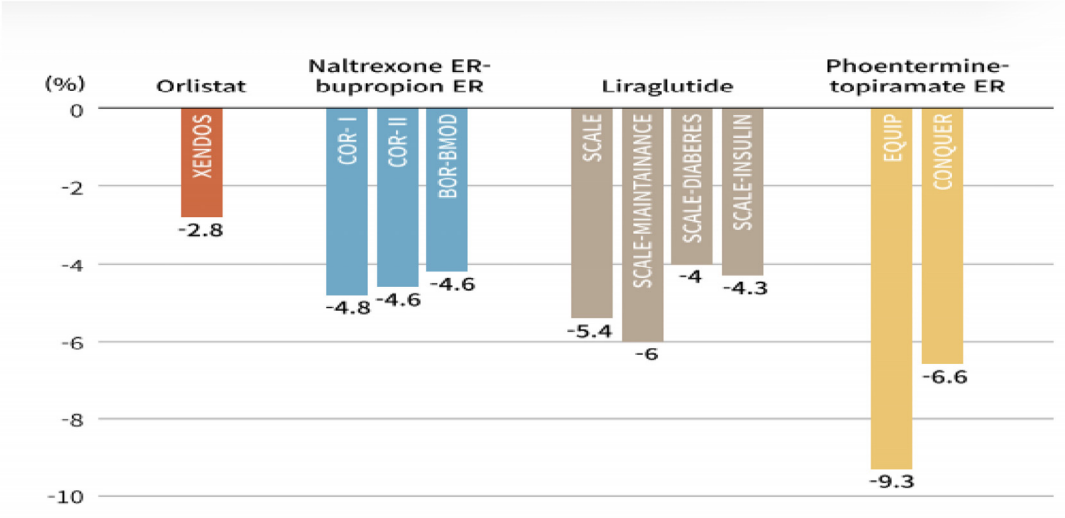


Currently approved long-term therapies for obesity

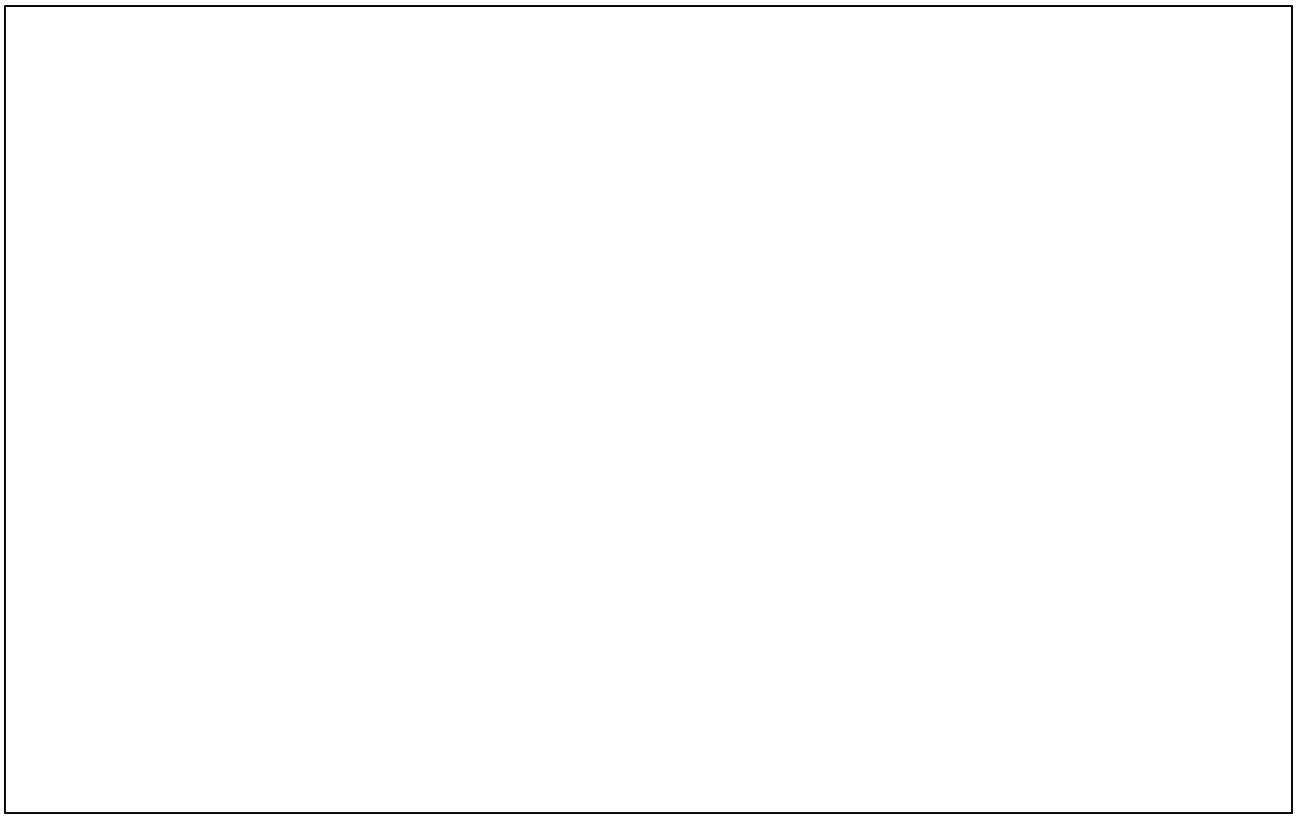


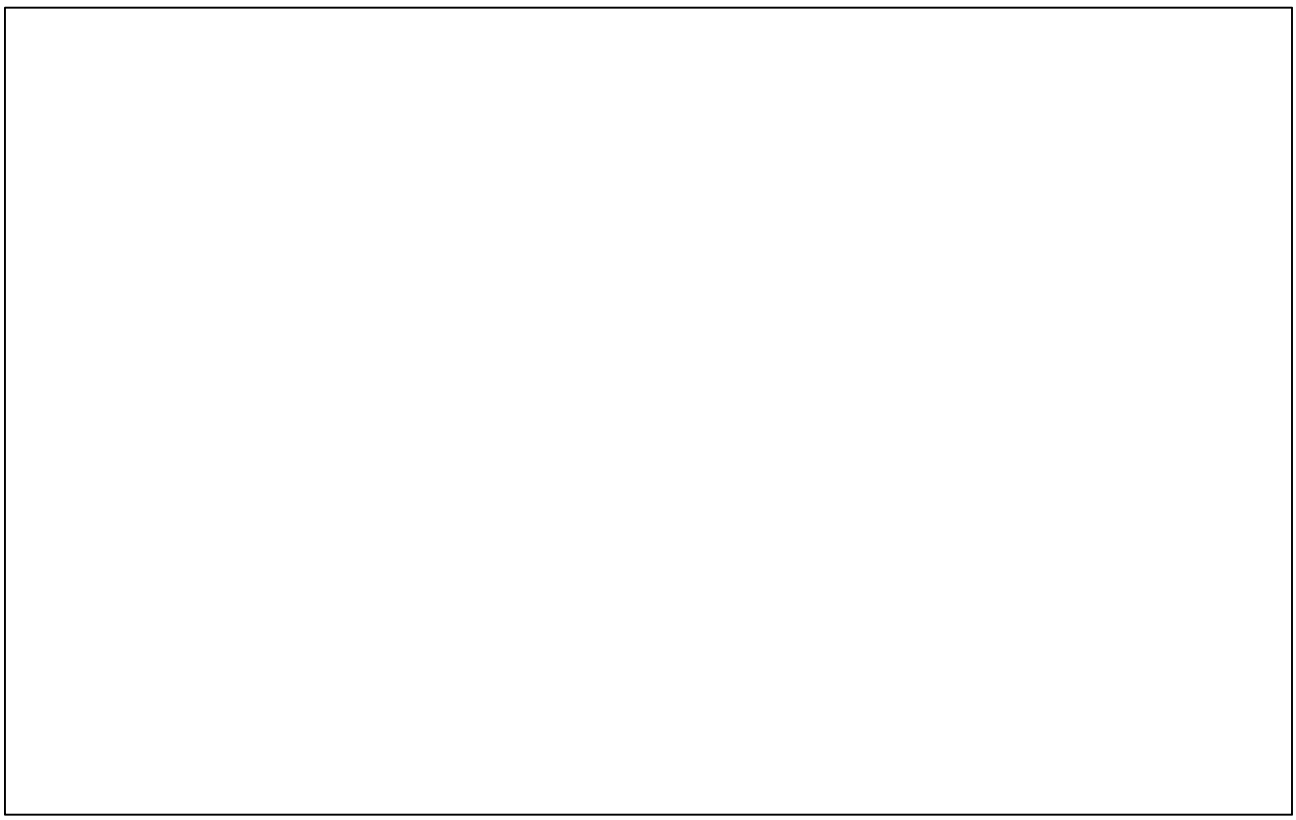
Diabetes Metab J 2020;44:802-818.

Effects of currently approved long-term therapies for obesity



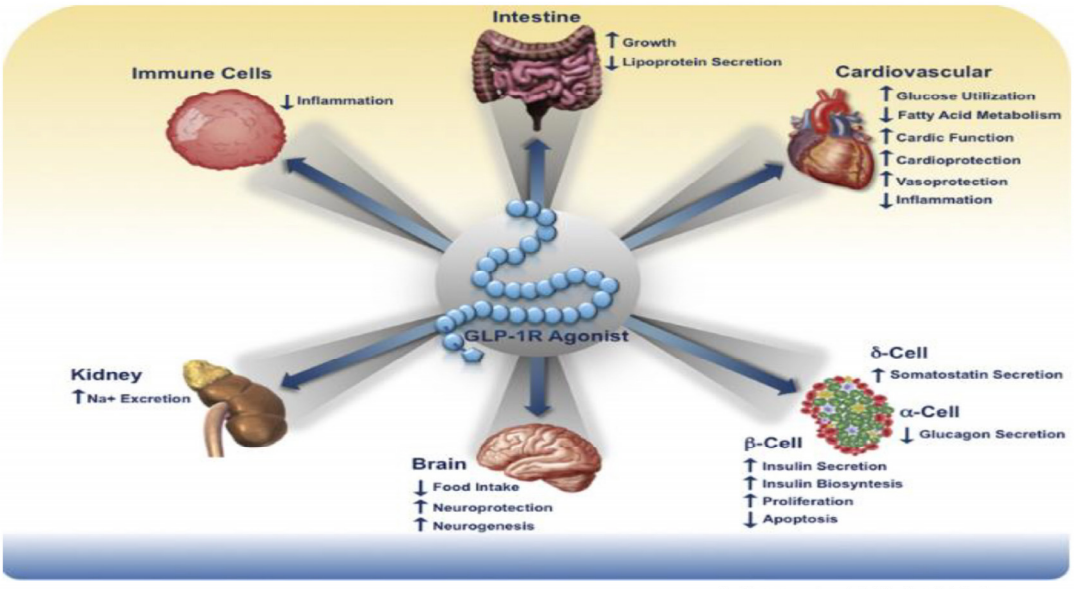
비만 진료지침 2020.





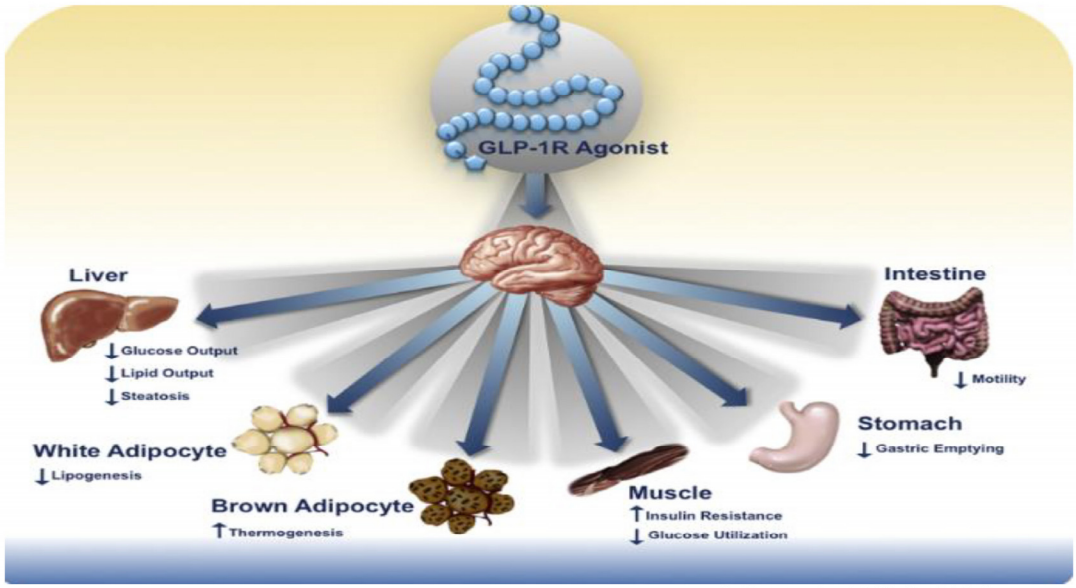
Semaglutide

Direct pharmacological actions of GLP-1R agonists



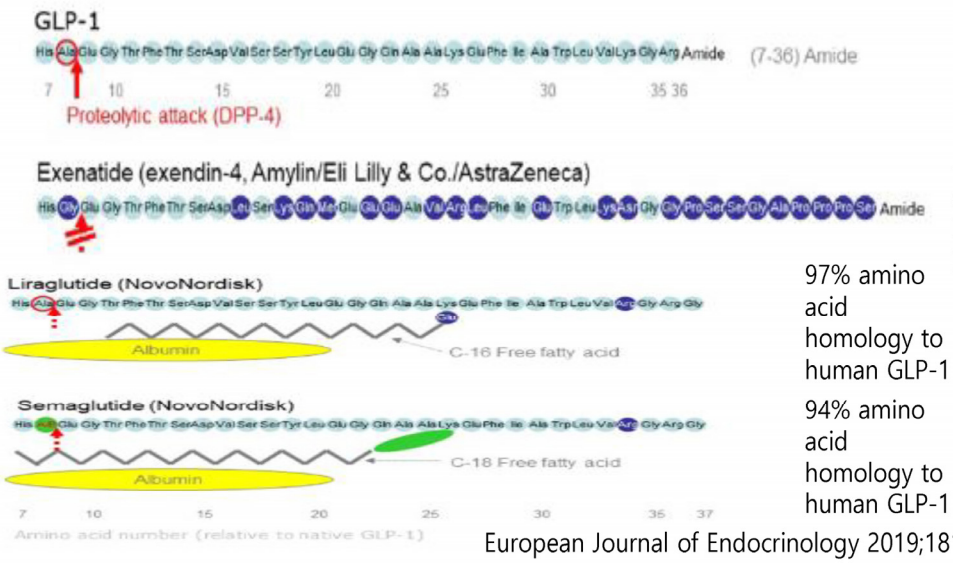
Cell Metab. 2013;17:819-37.

Indirect pharmacological actions of GLP-1R agonists



Cell Metab. 2013;17:819-37.

Molecular structures of GLP-1 receptor agonists



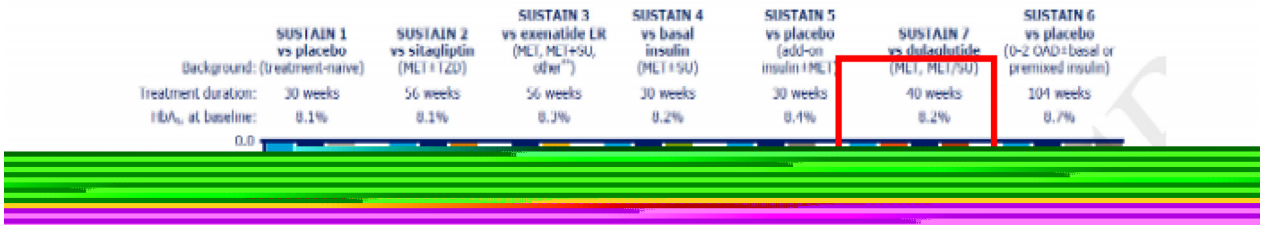
~50% amino acid homology to human GLP-1

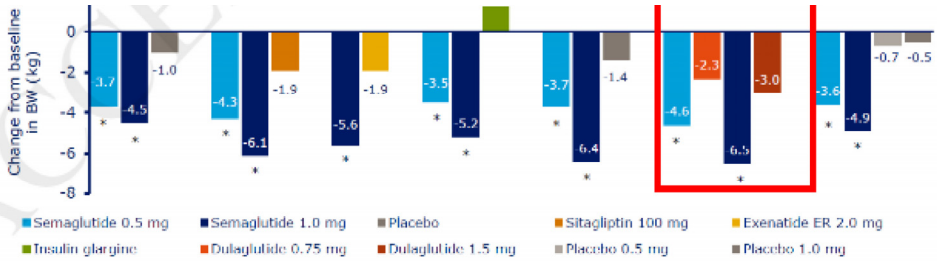
97% amino acid homology to human GLP-1

94% amino acid homology to human GLP-1

European Journal of Endocrinology 2019;181:R211-R234

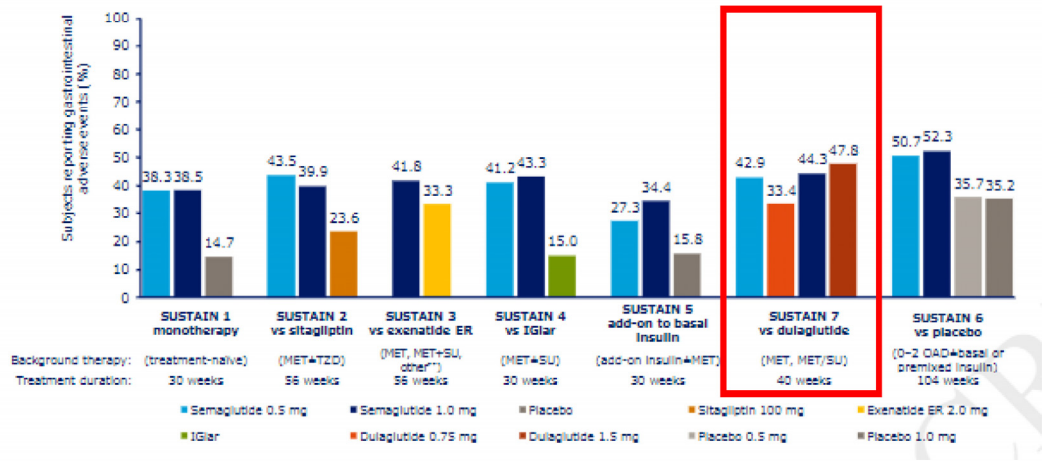
The Effect of semaglutide (HbA1c)





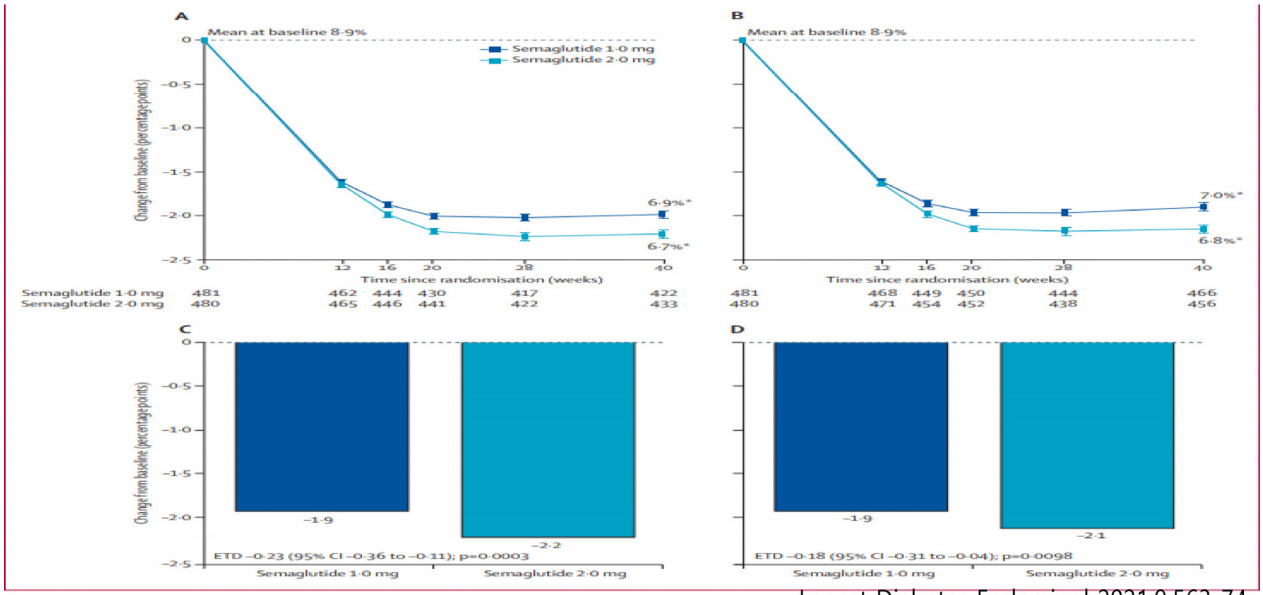
Diabetes & Metabolism 2019;45:409-418.

The GI side effect of semaglutide



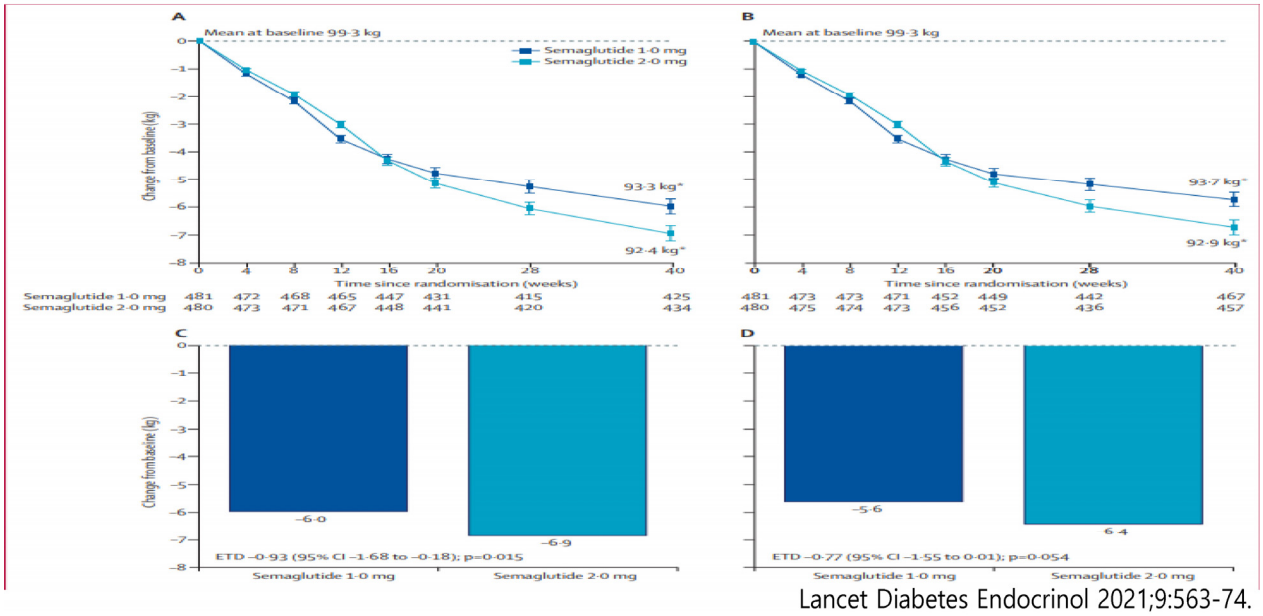
Diabetes & Metabolism 2019;45:409-418.

Semaglutide 2.0mg vs. Semaglutide 1.0mg (HbA1c)



Lancet Diabetes Endocrinol 2021;9:563-74.

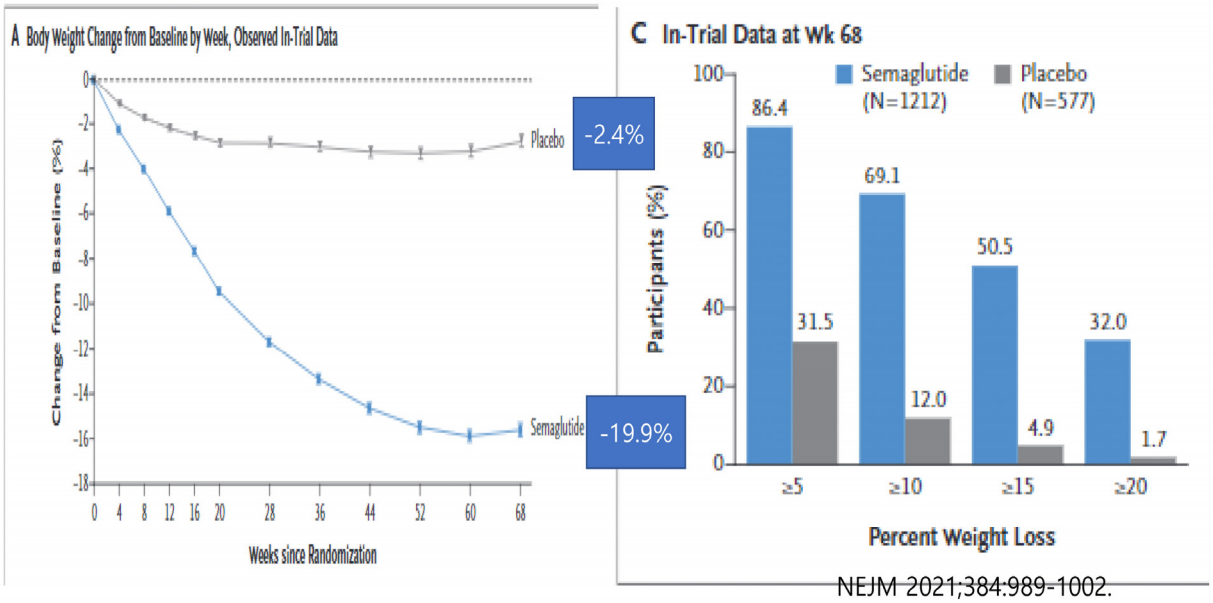
Semaglutide 2.0mg vs. Semaglutide 1.0mg (Body weight)



Lancet Diabetes Endocrinol 2021;9:563-74.

	Semaglutide 1·0 mg (n=480)			Semaglutide 2·0 mg (n=479)		
	n (%)	Events	Events per 100 patient-years of exposure	n (%)	Events	Events per 100 patient-years of exposure
Treatment-emergent adverse events	251 (52%)	828	201·4	272 (57%)	775	189·1
Severity						
Mild	199 (41%)	575	139·8	215 (45%)	552	134·7
Moderate	111 (23%)	216	52·5	108 (23%)	194	47·3
Severe	26 (5%)	37	9·0	19 (4%)	29	7·1
Serious	25 (5%)	40	9·7	21 (4%)	29	7·1
Deaths*	1 (<1%)	1	0·2	2 (<1%)	2	0·5
Treatment-emergent adverse events leading to premature treatment discontinuation						
Overall	22 (5%)	22	5·4	21 (4%)	21	5·1
Gastrointestinal adverse events						
Overall	148 (31%)	353	85·8	163 (34%)	346	84·4
Mild	121 (25%)	250	60·8	134 (28%)	247	60·3

Semaglutide 2.4mg vs. placebo (Body weight)- non DM



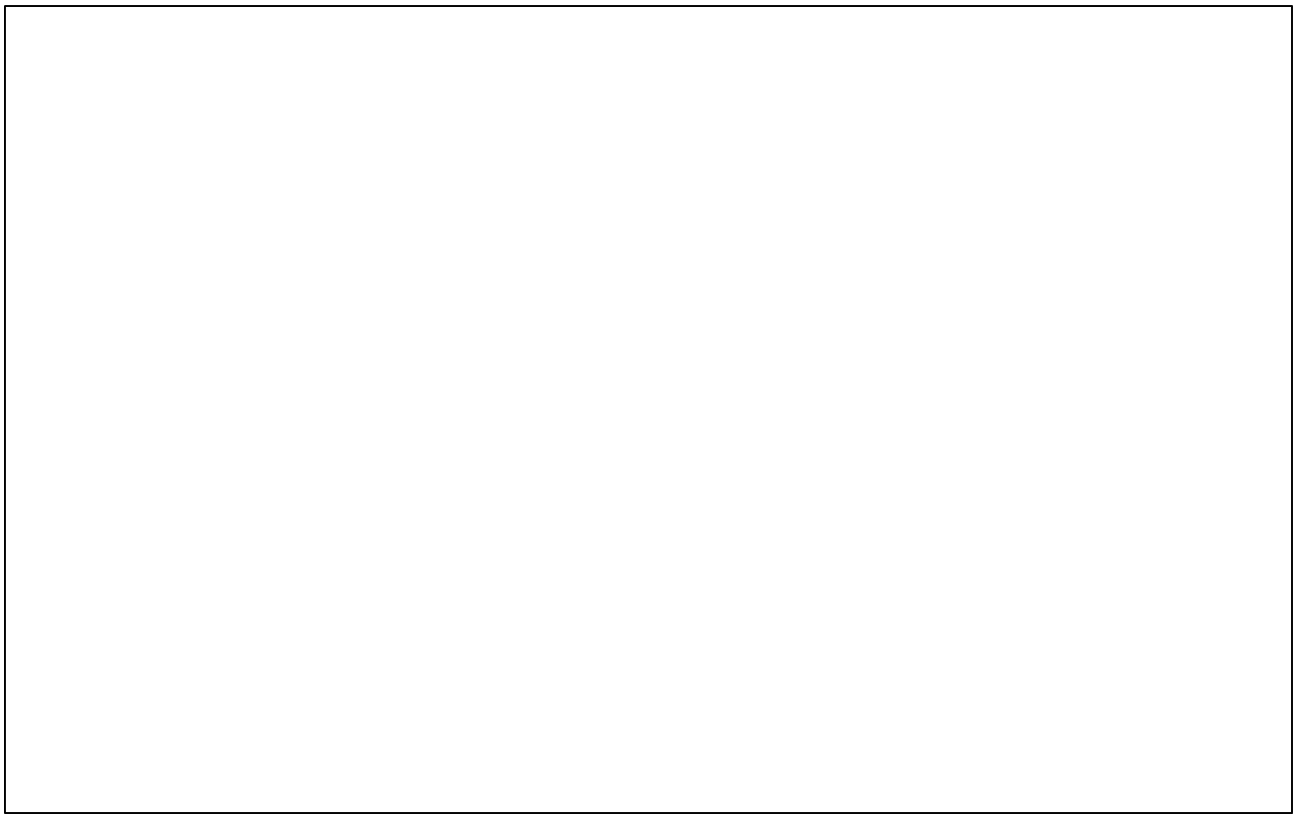
NEJM 2021;384:989-1002.

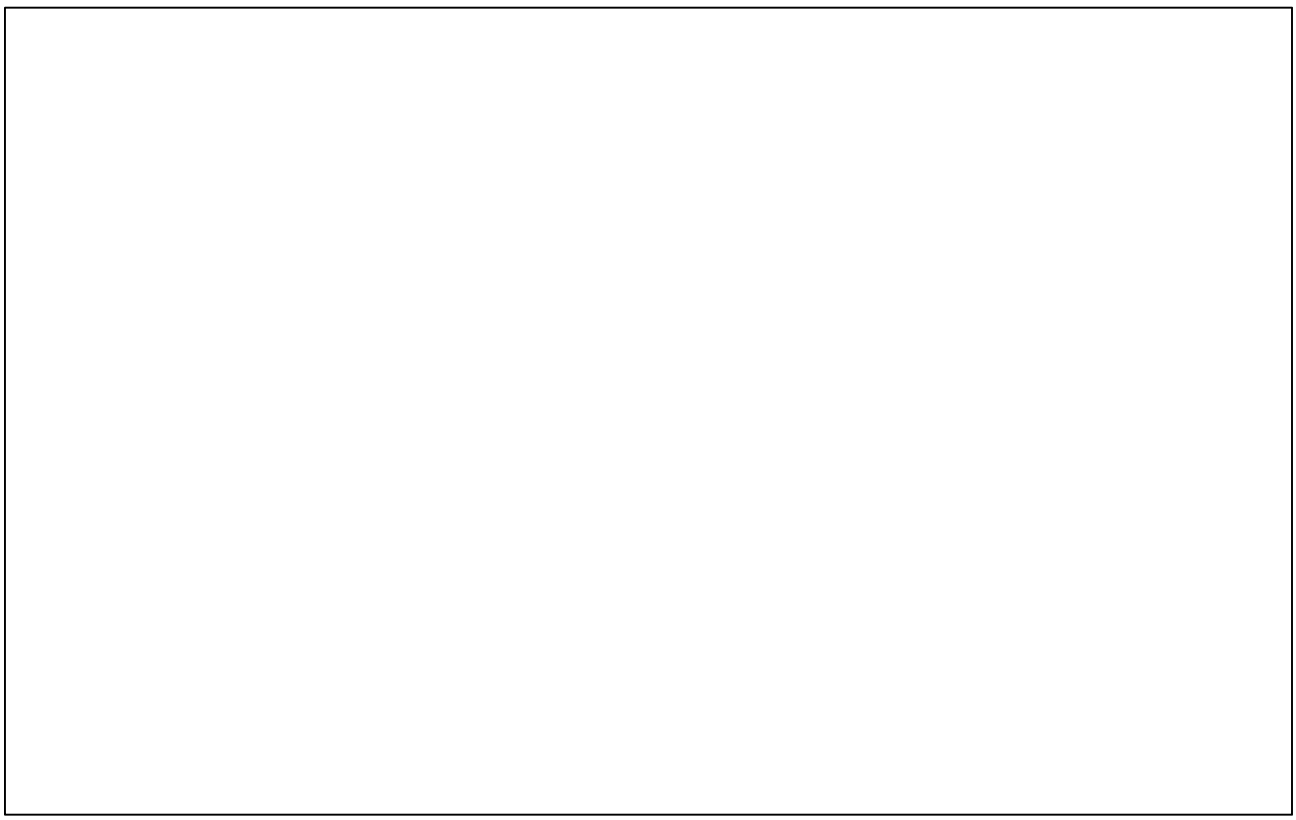
Semaglutide 2.4mg vs. placebo- non DM

Table 2. Coprimary, Confirmatory, and Selected Supportive Secondary and Exploratory End Points for the Treatment Policy Estimand.*

End Point	Semaglutide (N=1306)	Placebo (N=655)	Difference between Semaglutide and Placebo (95% CI)†	Odds Ratio	P Value
Coprimary end points assessed in the overall population					
Percent body-weight change from baseline to wk 68	−14.85	−2.41	−12.44 (−13.37 to −11.51)		<0.001
Participants with body-weight reduction ≥5% at wk 68 — %‡	86.4	31.5		11.2 (8.9 to 14.2)	<0.001
Confirmatory secondary end points assessed in the overall population					
Participants with body-weight reduction ≥10% at wk 68 — %‡	69.1	12.0		14.7 (11.1 to 19.4)	<0.001
Participants with body-weight reduction ≥15% at wk 68 — %‡	50.5	4.9		19.3 (12.9 to 28.8)	<0.001
Change from baseline to wk 68					
Waist circumference — cm	−13.54	−4.13	−9.42 (−10.30 to −8.53)		<0.001
Systolic blood pressure — mm Hg	−6.16	−1.06	−5.10 (−6.34 to −3.87)		<0.001
SF-36 physical functioning score	2.21	0.41	1.80 (1.18 to 2.42)		<0.001
IWQOL-Lite-CT physical function score	14.67	5.25	9.43 (7.50 to 11.35)		<0.001
Supportive secondary end points assessed in the overall population§					
Participants with body-weight reduction ≥20% at wk 68 — %‡	32.0	1.7		26.9 (14.2 to 51.0)	
Change from baseline to wk 68					
Body weight — kg	−15.3	−2.6	−12.7 (−13.7 to −11.7)		
Body-mass index	−5.54	−0.92	−4.61 (−4.96 to −4.27)		
Glycated hemoglobin — percentage points	−0.45	−0.15	−0.29 (−0.32 to −0.26)		
Fasting plasma glucose — mg/dl	−8.35	−0.48	−7.87 (−9.04 to −6.70)		
Diastolic blood pressure — mm Hg	−2.83	−0.42	−2.41 (−3.25 to −1.57)		
Lipid levels, ratio of wk 68 value to baseline¶					
Total cholesterol	0.97	1.00	0.97 (0.95 to 0.98)		
HDL cholesterol	1.05	1.01	1.04 (1.02 to 1.05)		
LDL cholesterol	0.97	1.01	0.96 (0.94 to 0.98)		
VLDL cholesterol	0.78	0.93	0.84 (0.81 to 0.87)		
Free fatty acids	0.83	0.93	0.89 (0.83 to 0.94)		
Triglycerides	0.78	0.93	0.84 (0.81 to 0.87)		
C-reactive protein, ratio of wk 68 value to baseline¶	0.47	0.85	0.56 (0.51 to 0.61)		

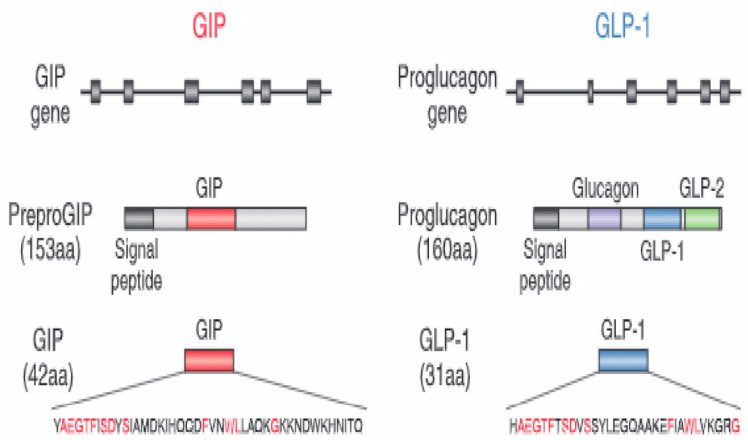
NEJM 2021;384:989-1002.





Tirzepatide

GLP-1 and GIP



GIP: glucose-dependent insulinotropic polypepide
GLP-1: glucagon-like peptide

J Diabetes Investig.2010;1:8-23.

GLP-1 and GIP

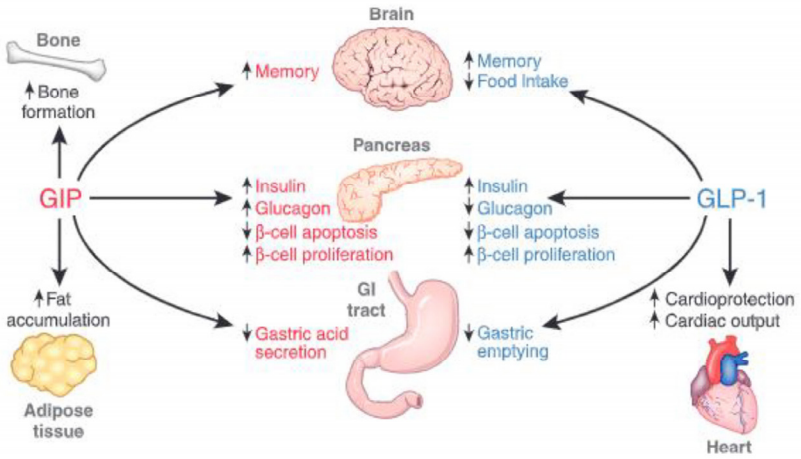
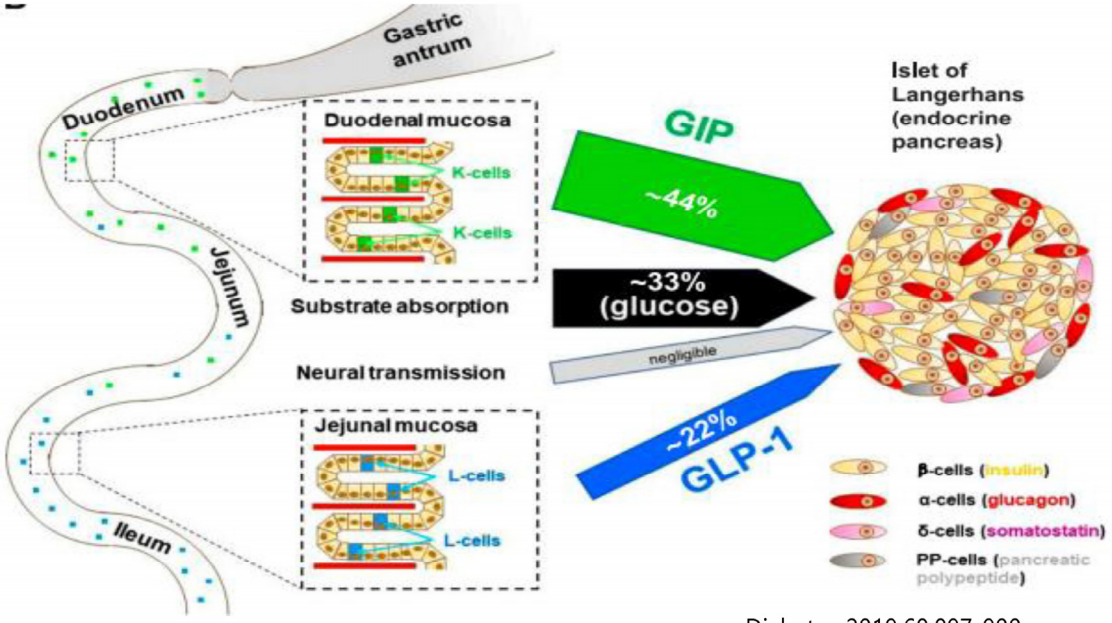


Figure 2 | Pancreatic and exopancreatic function of glucose-dependent insulinotropic polypepide (GIP) and glucagon-like peptide (GLP)-1. GIP acts

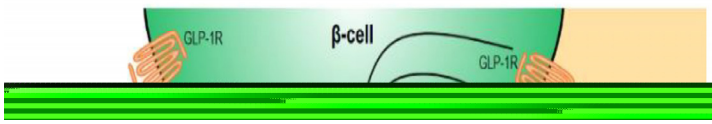
Cell Metab. 2013;17:819-37.

Contribution of GIP on insulin release

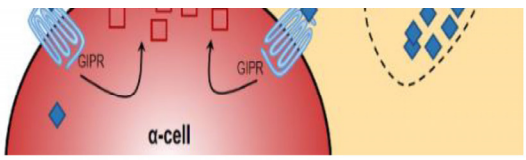


Diabetes 2019;68:897-900.

The role of GIP on glucagon secretion

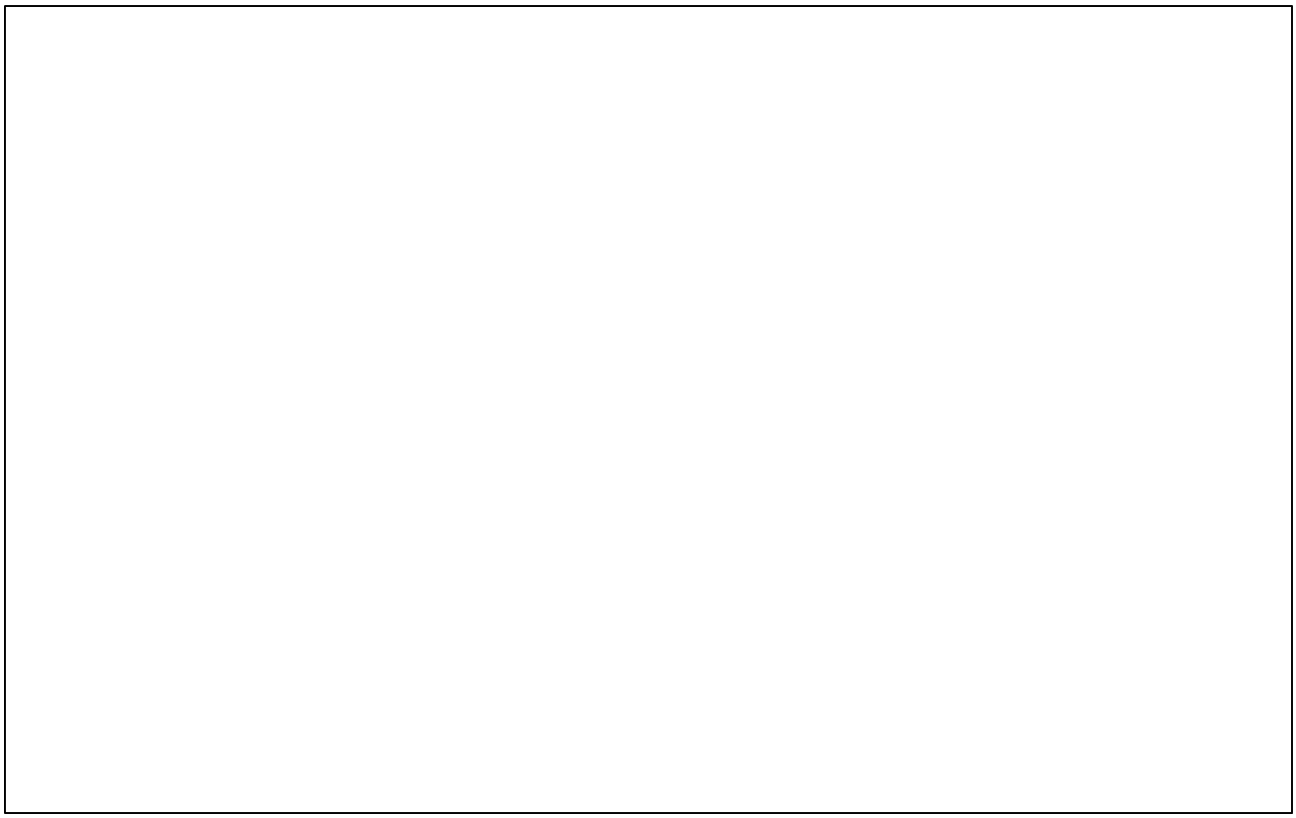


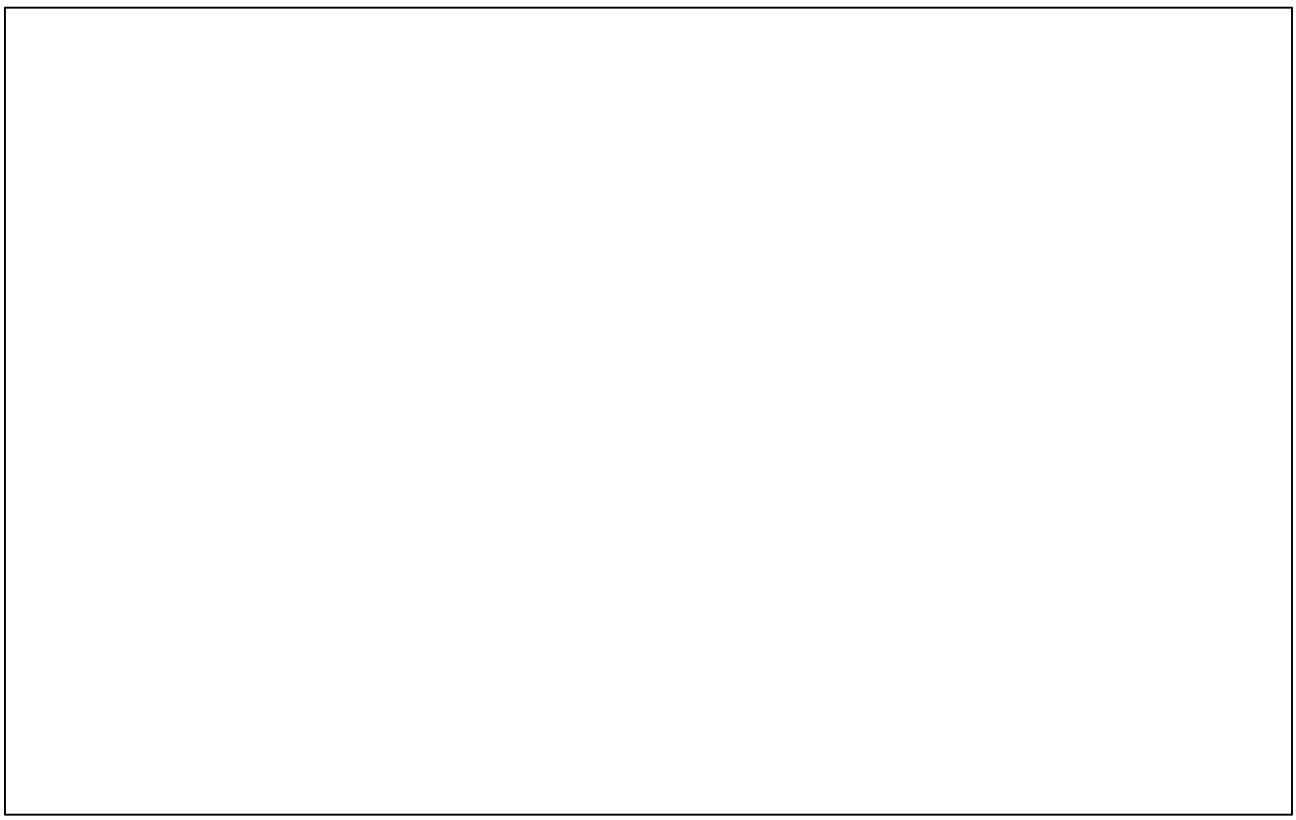
GIP stimulates glucagon secretion in a glucose-dependent manner.



inhibitory tone from β-cells, which suppress α-cell activity and thereby limit GIP-stimulated glucose secretion

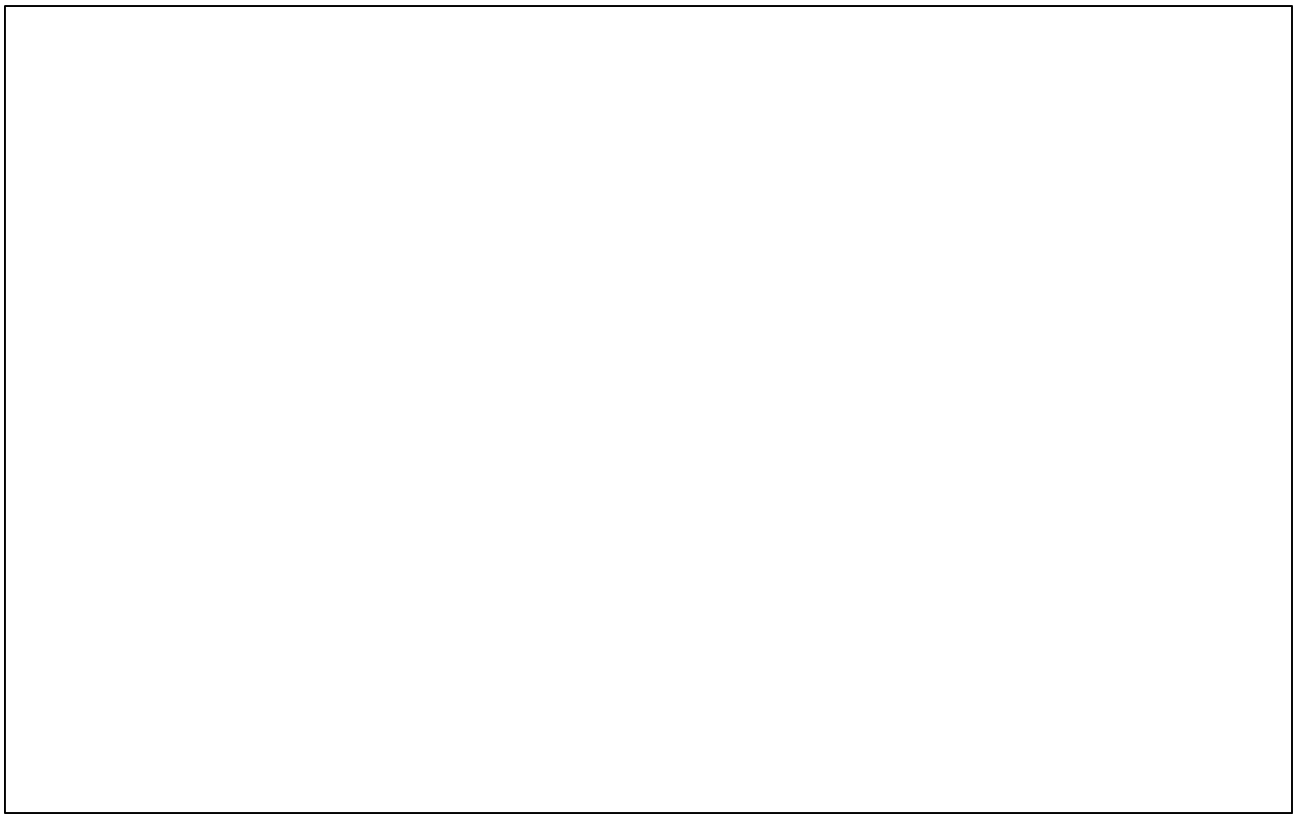
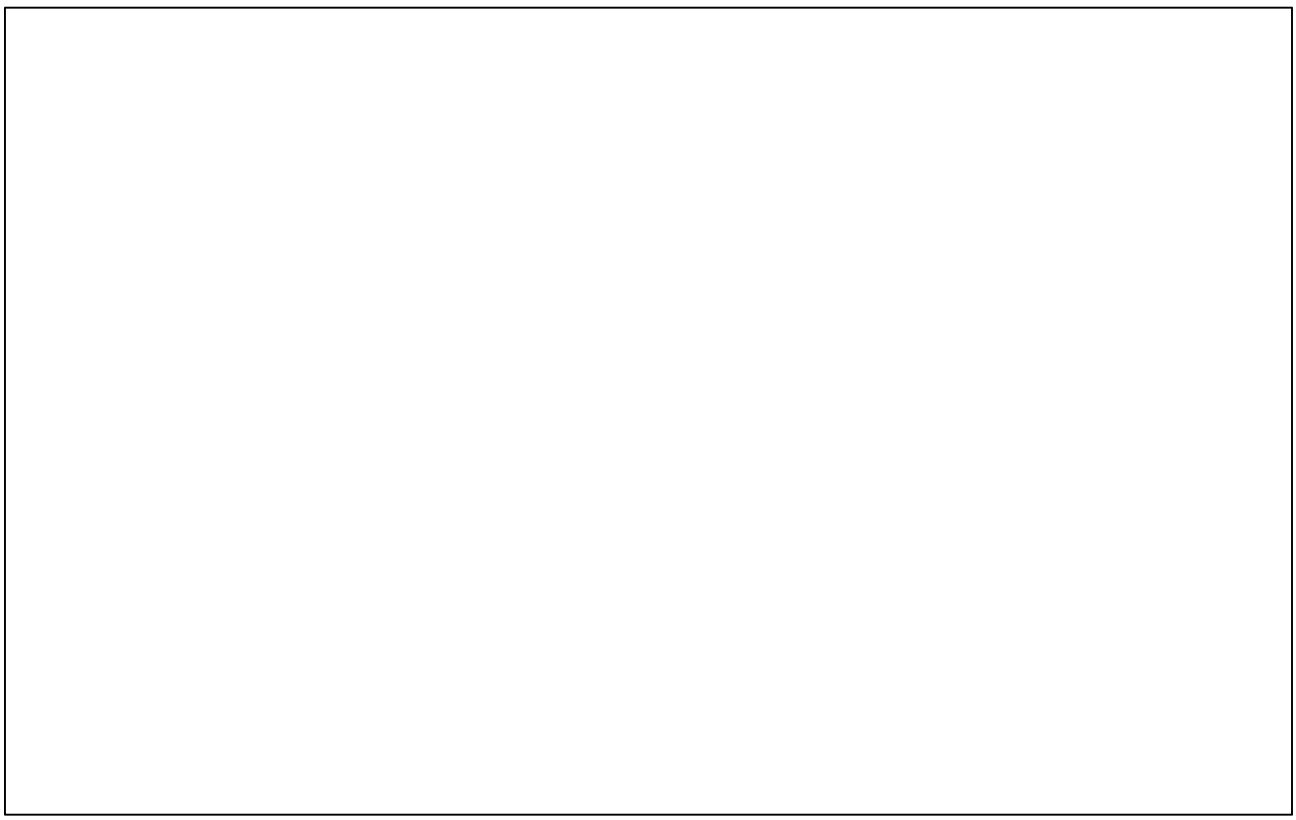
Peptides. 2020;125:170213.





Effect of once-weekly tirzepatide compared with semaglutide

Table 2. Adverse Events and Safety.

Event	Tirzepatide						Semaglutide		Total (N=1878)	
	5 mg (N=470)		10 mg (N=469)		15 mg (N=470)		1 mg (N=469)			
	No. of patients (%)	No. of events	No. of patients (%)	No. of events	No. of patients (%)	No. of events	No. of patients (%)	No. of events	No. of patients (%)	No. of events
Patients with ≥1 adverse event	299 (63.6)	—	322 (68.7)	—	324 (68.9)	—	301 (64.2)	—	1246 (66.3)	—
Patients with ≥1 serious adverse event	33 (7.0)	—	25 (5.3)	—	27 (5.7)	—	13 (2.8)	—	98 (5.2)	—
Death†	4 (0.9)	—	4 (0.9)	—	4 (0.9)	—	1 (0.2)	—	13 (0.7)	—
Adverse events leading to discontinuation of tirzepatide or semaglutide	28 (6.0)	—	40 (8.5)	—	40 (8.5)	—	19 (4.1)	—	127 (6.8)	—
Adverse events occurring in ≥0.2% of the overall population (i.e., 3 patients) and leading to discontinuation of tirzepatide or semaglutide										
Nausea	6 (1.3)		7 (1.5)		4 (0.9)		4 (0.9)			
Diarrhea										
Vomiting	27 (5.7)	35	40 (8.5)	56	46 (9.8)	61	39 (8.3)	53	152 (8.1)	205
Dyspepsia	34 (7.2)	—	29 (6.2)	—	43 (9.1)	—	31 (6.6)	—	137 (7.3)	—
Decreased appetite	35 (7.4)	—	34 (7.2)	—	42 (8.9)	—	25 (5.3)	—	136 (7.2)	—
Constipation	32 (6.8)	—	21 (4.5)	—	21 (4.5)	—	27 (5.8)	—	101 (5.4)	—
Abdominal pain	14 (3.0)	—	21 (4.5)	—	24 (5.1)	—	24 (5.1)	—	83 (4.4)	—
All gastrointestinal adverse events	188 (40.0)	—	216 (46.1)	—	211 (44.9)	—	193 (41.2)	—	808 (43.0)	—
Other adverse events										
Hypoglycemia, blood glucose level <54 mg/dl	3 (0.6)	3	1 (0.2)	2	8 (1.7)	10	2 (0.4)	2	14 (0.7)	17
Severe hypoglycemia	1 (0.2)	1	0	0	1 (0.2)‡	1‡	0	0	2 (0.1)	2
Injection-site reaction	9 (1.9)	—	13 (2.8)	—	21 (4.5)	—	1 (0.2)	—	44 (2.3)	—
Adjudicated pancreatitis	0	—	2 (0.4)	—	2 (0.4)	—	3 (0.6)	—	7 (0.4)	—
Cholelithiasis	4 (0.9)	—	4 (0.9)	—	4 (0.9)	—	2 (0.4)	—	14 (0.7)	—
Hypersensitivity§	9 (1.9)	—	13 (2.8)	—	8 (1.7)	—	11 (2.3)	—	41 (2.2)	—
Diabetic retinopathy¶	0	—	2 (0.4)	—	0	—	0	—	2 (0.1)	—

NEJM 2021;385:503-515.