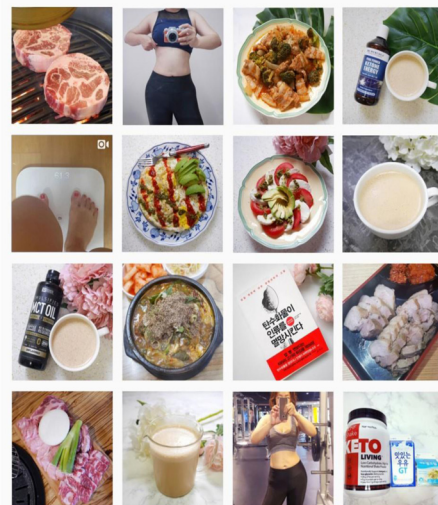
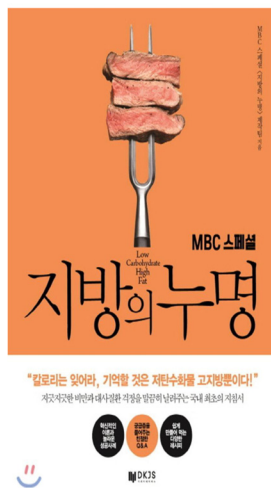
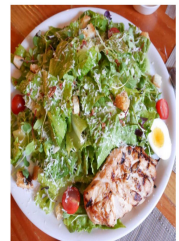
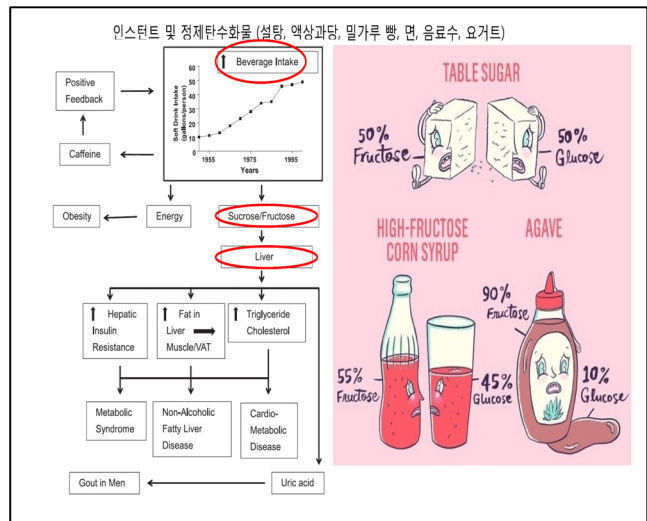
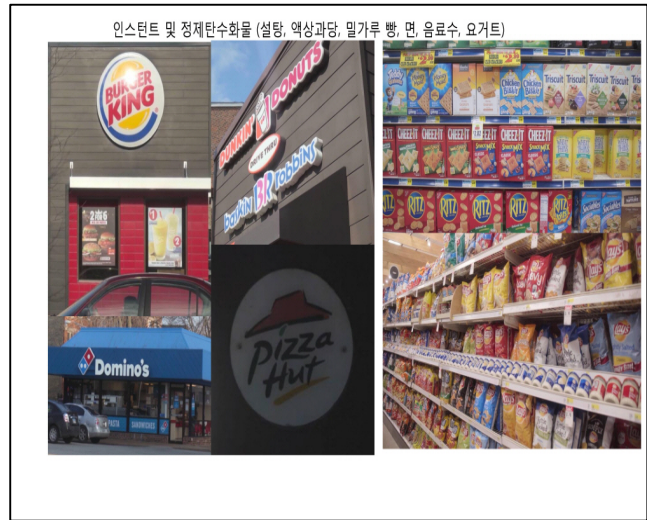
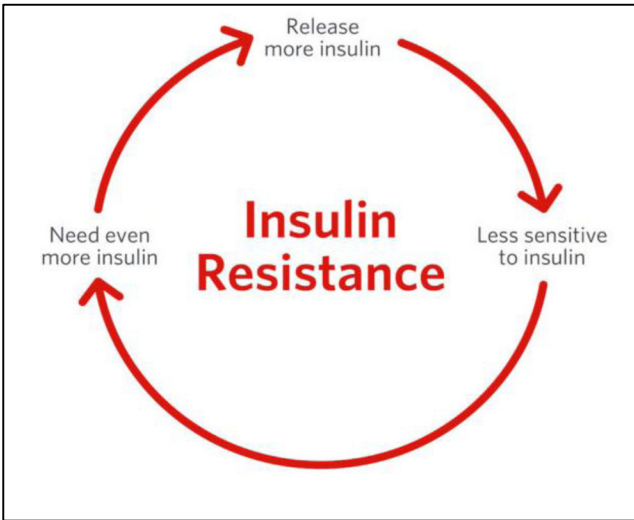
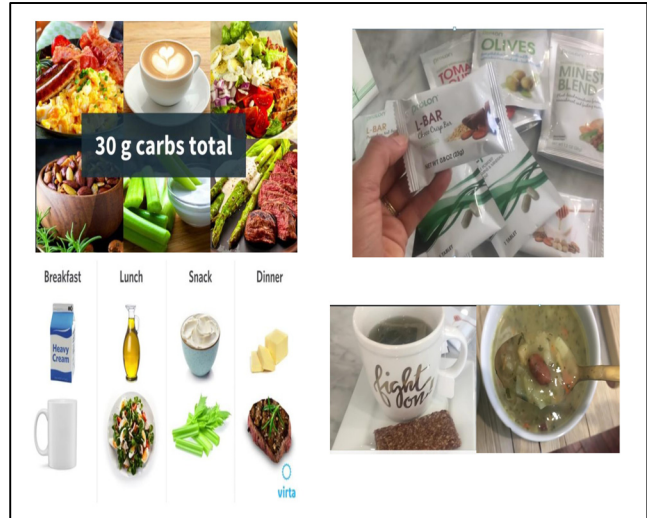


비만 치료의 최신 Update

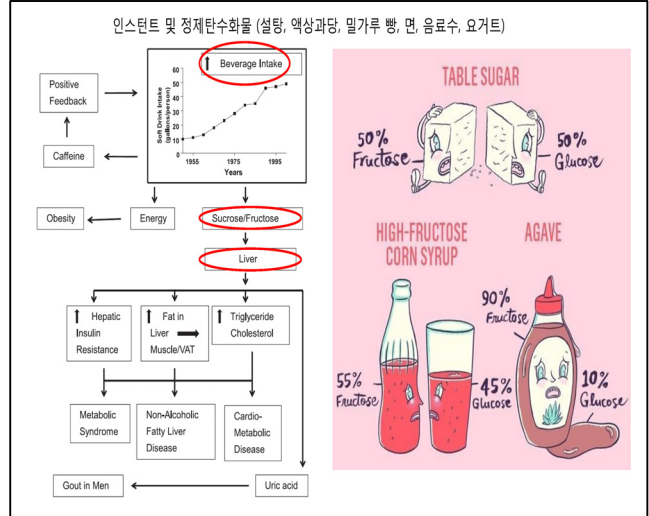
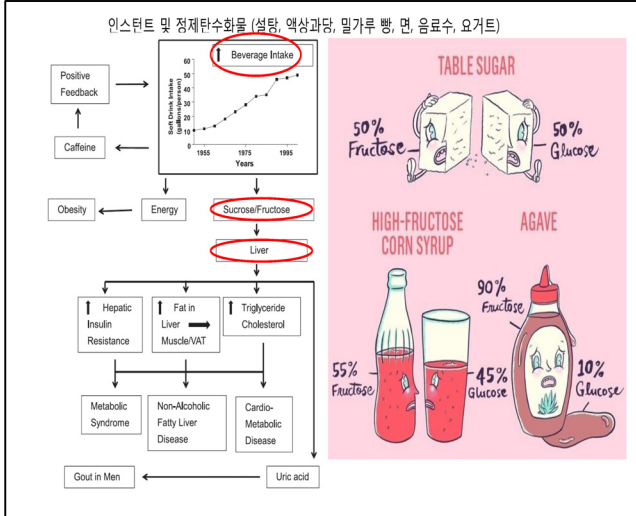
이 철 진
좋은가정의원

연수강좌





이 철 진, 비만 치료의 최신 Update

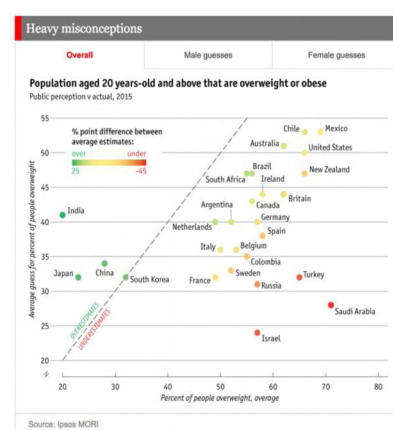
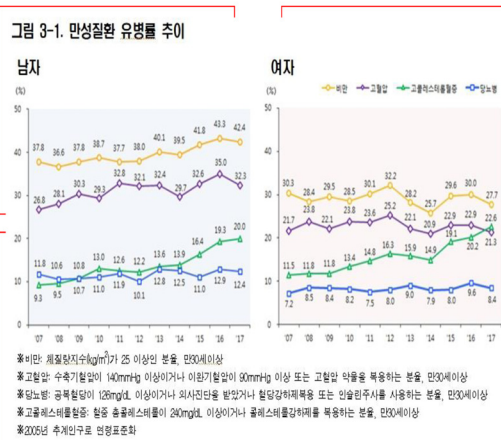


I. 총론



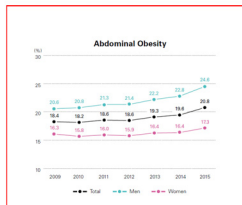
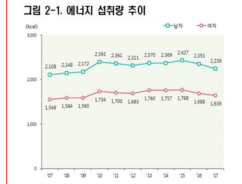
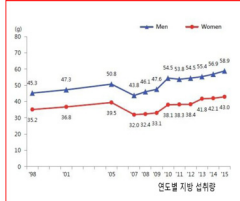
I. 총론

* Diabesity = DM + obesity

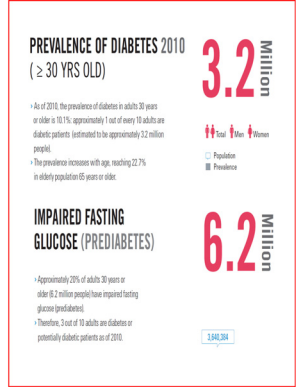


I. 총론

* Diabetes = DM + obesity



* Diabetes = DM + obesity



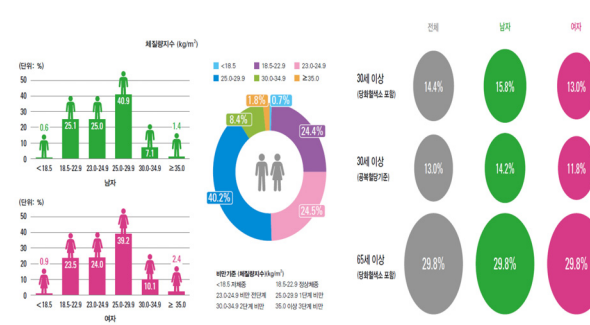
* Diabetes = DM + obesity

당뇨병과 비만 (2013-2016년 통합)

당뇨병 유병자 중 비만의 환자에서 체질량지수 25kg/m² 이상이라고, 2년에 이상의 비만을 보이는 경우는 10.2%이었다. 체질량지수 25kg/m² 이상에서 2년에 이상의 비만을 보이는 경우는 1.8%이었다.

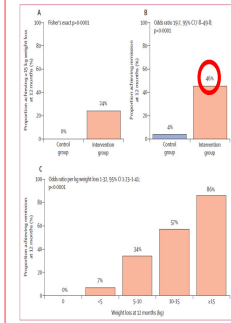
당뇨병 유병률 (2016년)

30세 이상 성인 7명 중 한 명(14.4%)이 당뇨병을 가지고 있다. 65세 이상 성인에서는 1명 중 2명으로 증가했다. 공복혈당치를 기준으로 사별한 경우 당뇨병 유병률은 13%이었다.



DM REMISSION

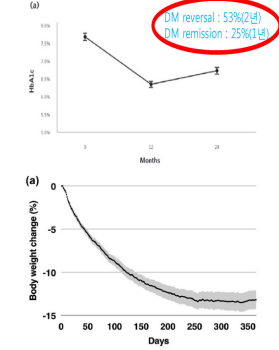
I. Primary care-led weight management for remission of type 2 diabetes: DIRECT - an open-label, cluster-randomised trial



II. 저탄고지

Efficacy and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study

Sarah J. Hallberg, Amy L. McKenzie, Paul T. Williams



III. 간헐적단식

Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin

Suleiman Furriri¹, Rami Elmasy^{2,3}, Megan Ramos⁴, Jason Fung^{4,5}

Table 1. Patient demographics

Table 1 Patient characteristics				
	Age	Sex	Years with type 2 diabetes	Existing frequency/duration
Patient 1	40	Male	20	Hypertension, hypercholesterolemia 3 times in 7 months
Patient 2	52	Male	25	Chronic kidney disease Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin Insulin 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Table 2. Change in glycemic and other health parameter for baseline to end of following

Insulin	Pre-IF	Post-IF	Insulin	Pre-IF	Post-IF	Insulin	Pre-IF	Post-IF	Insulin	Pre-IF	Post-IF
Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Year 1	11.82	11.50	11.82	11.50	11.82	11.50	11.82	11.50	11.82	11.50	11.82
Year 2	11.52	11.41	11.52	11.41	11.52	11.41	11.52	11.41	11.52	11.41	11.52
Year 3	11.82	11.43	11.82	11.43	11.82	11.43	11.82	11.43	11.82	11.43	11.82

DM REMISSION

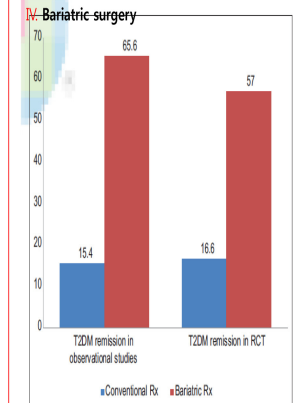
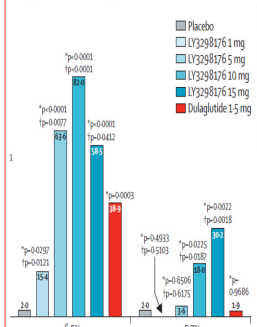


Figure 1: Type 2 diabetes mellitus remission rate (%) following bariatric surgery

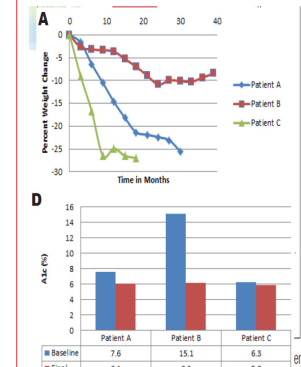
DM REMISSION

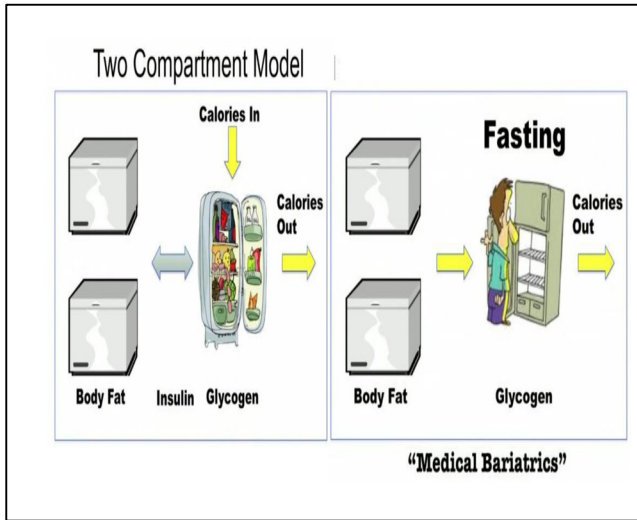
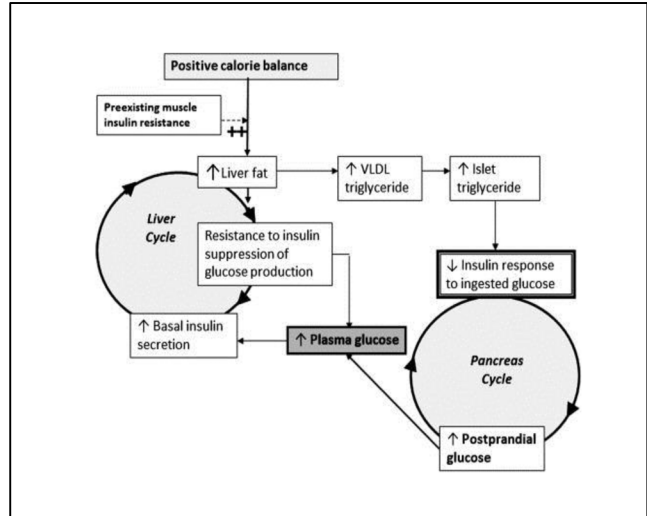
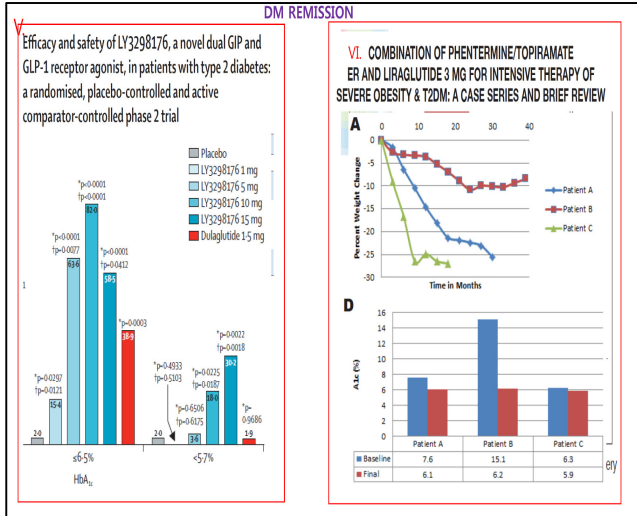
III. 간헐적단식

Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial



VI. COMBINATION OF PHENTERMINE/TOPIRAMATE AND LIRAGLUTIDE 3 MG FOR INTENSIVE THERAPY OF SEVERE OBESITY & T2DM: A CASE SERIES AND BRIEF REVIEW





CASE #1, F/37, BMI 27, 62kg CASE #2, F/23, BMI 28, 72kg

[illegible]

1504	12.0.0	36.258.55, 1366		
1208	12.0.0	36.258.55, 1366		
송 - 출기 + 반출, 단산, 반출(반산), 무출				
		stress		
		역산		
		F723		
FLU1	주요관리역출		2	2
SE1	일반관리역출		2	2
UCF	일반관리역출 25mg		2	2
XA	일반관리역출 120mg		2	2

12.0.0	69.8	> 69.6	> 67.6	> 65.1	> 63.1	> 61.4
12.0.0	69.8	> 69.6	> 67.6	> 65.1	> 63.1	> 61.4
61.4	> 61.4	> 60.5	> 62.1	> 59.8	> 56.8	> 54.8
56.8	> 56.8	> 56.1	> 56.8	> 54.8	> 52.8	> 50.8
50.8	> 50.8	> 49.7	> 51.1	> 48.2	> 45.8	> 43.5
43.5	> 43.5	> 42.5	> 44.5	> 42.5	> 40.5	> 38.5
역산, 반출 + 45						
송출 + 역산, 반출, 출기, 단산, 반출(반산), 무출, 역산 + 4700 지점						
100	12.0.0	69.8				
GM1	일반관리역출 25mg		10	2	14	14
AD1	일반관리역출 120mg		1	1	14	14

CASE #3, M/51 90kg, BMI 31.1

170/90, 0.3/1.1, 27.1/24.4, 1645
 수 월주6일 끊었다. 커피 블랙, 콜라 -, 잠금, 변배 -
 2018년 2월 A1c 5.8, FBS 74
 FBS 111, TG 395, LDL 113, GGT 85

90.0 -> 86.6 -> 86.2 - 84.4 - 83.4 - 81.7 - 79.9 - 79.1 - 78.1

푸로린캡슐		2	2	7
토라맥정 25mg	4	2	7	

CASE #4, M/32 85kg, BMI 26.3

180/85, 1/26.3, 31.7/27.0, 1752			
3년 전 운동중단후 20kg로 증가			
수 월 5~6회, 하루 한개(맥으면 힘들다), 커피 블랙한잔, 콜라			
배경마음(Stress)			
술은늦게 보고 식이성당 조절하자			
85.1 → 82.6 → 80.4 · 79.1 · 78.7			

Case #5 F/57, BMI 24.4, 62.4kg, DM for 5년

[illegible]

Case #6 M/35, BMI 33.1 101.3kg, Prediabetes

FLU1	후두인두염	175/101, 3/33, 11, 37, 2/37, 7, 1948	2	2	7	혈액
TO1	폐렴 100mg		2	2	7	혈액
	01.9.1 → 98.4.7 → 97.2.95 - 94.3.92.6 - 92.1.91.5					
	90.4 - 90.3 - 90.4 - 89.0 - 88 (7.7)					
	술, 야식					
	술 - 케피 맥스한잔, 골라-, 맨해 -					
	약보 : 80, 65kg(4년전), 운동불필요					

HbA1c 5.8(2018년 12월) → 5.5(2019년 3월)

HbA1c 5.8(2018년 12월) → 5.5(2019년 3월)

CASE #7, F/47, BMI 23, 57kg

- Hx : 펜타민, 토피라메이트 intermittent medication
- 삭센다 0.6mg 으로 시작(10일간) : 57.3 → 54.3
- 1.2mg -> 1.8mg -> 2.4mg : 7-10일간격 증량, 한달 사용 : 54.3 → 52.4
- 약 가격 부담으로 펜타민으로 체인지(0.5T) 한달사용 : 52.4 → 49.9
- 토피라메이트 50mg QD로 유지중 : 마지막 체중 47.9

CASE #8, F/43 88kg, BMI 35.2

고혈압 치료중 2018년 9월 20일 DM 진단 : HbA1c 7.6
(멧포민, 자디앙)

- 88kg (9/20), 158cm,
- 80kg (10/26)
- 77kg (11/24)
- 74kg (2019년 1/4), HbA1c 6.3, BMI 29.6
- 68kg (2019년 2/2)

CASE #9, F/38 78kg, BMI 29.8, 2015년DM 진단

HbA1c

2015년 7월 18일 → 77.8 → 75.9 → 73.1 → 72.1

MIME2 10대여덟 줄

FLU1 두라클릭 25mg

TOF 두라클릭 25mg

HbA1c 7.1

10대여덟 줄

2016년 7월 18일 → HbA1c 7.0

7.0 → 7.4 → 71.8 → 72.8 → 71.7 → 69.3 → 68.8

HbA1c 8.7

2017년 10대여덟 줄

HbA1c 7.1

7.3 → 70.9 → 70.2 → 68.8

2017년 10월 HbA1c 7.9, 71kg

2018년 10대여덟 줄

7.0 → 68.8 → 70.5 → 69.6 → 68.4

58 → 56 → 57 → 56 → 57

HbA1c 7.9 → 7.0 → 6.2 → 6.0

HbA1c 7.1

7.1

7.6

6.7

7.9

5.8

2015년 7월

2016년 7월

2017년 10월

2018년 10월

HbA1c

6.0 6.2 7.0 7.3 7.1 6.7 7.6 7.1

CASE #10 정체, Yoyo

96.8 → 96.4 → 93.9 → 91.5 → 81.5 → 80.0 → 80.0

이론 → 이론실적률, 공란 → , 정답, 연비

이론 : 55

실적 : 55

공백 : 55

정답 : 55

연비 : 55

정답은 맞다. 학교 실답

TOE	부록면면출	2	2	7
FLU	국문출제 25점	6	2	7
MGM	미국출제	3	2	7

71.3 → 78.6 → 70.7 → 77.4 → 76.6 → 74.8, 74.0 → 72.8

81.6 → 71.6 → 71.6 → 70.4 → 69.8

68.8 → 69.2 → 69.5 → 69.8 → 69.8 → 68.5

3.1, 3.750, 11.08 (정답은 3.1, 3.75, 11.08)

15901, 34272, 34, 3434.4, 151

180.74, 82.92, 38, 42.72, 1318

180.71, 72.8, 0, 32, 92.3, 6, 129

180.69, 42.71, 31, 32.21, 1, 125

159.91, 32.32, 38, 33.31, 1, 151

은 원문과 다르다. 커리큘럼, 정답, 연비, 연비, 기본공

출제, 동문출제 문제 없었다

교과문도, 정답 오류 디스크 MFI



새라 지난 19개월였다...

90 ~ 96

음 +++ 기의 매일 공를수있다..

기법 : 늘음..

음은 :

163.91.9.4와 같은 해트..

163.91.9.4 ~ 163.91.9.21, 1505kcal

73 ~ 88 ~ 83 ~ 82 ~ 78

73 ~ 88 ~ 88 ~ 87 ~ 67 ~ 69 ~ 68

75 ~ 73 ~ 71 ~ 69.5 ~ 68.5 ~ 66.5 ~ 67 ~ 66 ~ 65

94.91.9.4

111 ~ 108 ~ 106 ~ 107 ~ 107 ~ 106 ~ 105 ~ 104 ~ 103

102 ~ 101 ~ 99 ~ 98 ~ 97 ~ 96.5 ~ 94.3 ~ 93 ~ 92.1

90.5 ~ 88.5 ~ 88.5 ~ 88.5 ~ 88 ~ 87.5 ~ 86.7 ~ 86.1

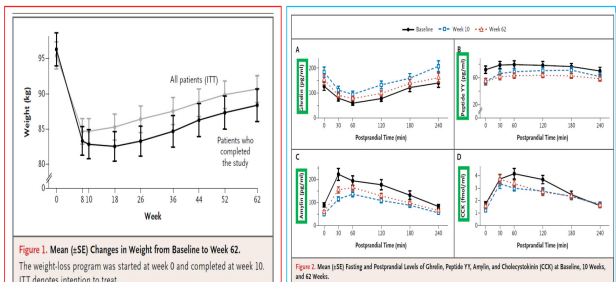
83.3 ~ 85.8 ~ 88 ~ 85.5 ~ 83.3 ~ 83.0 ~ 82 ~ 80.5 ~ 80

80 ~ 78.2 ~ 77.5 ~ 77.5 ~ 77.5 ~ 78.2 ~ 78.5 ~ 78.5 ~ 78.2 ~ 78

77 ~ 77 ~ 77 ~ 78 ~ 78 ~ 78.8 ~ 78.5 ~ 78.5 ~ 78.2 ~ 77

Long-Term Persistence of Hormonal Adaptations to Weight Loss

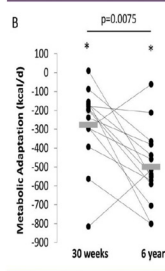
Priya Sumithran, M.B., B.S., Luke A. Prendergast, Ph.D.,
Elizabeth Delbridge, Ph.D., Katrina Purcell, B.Sc., Arthur Shulkes, Sc.D.,
Adamandia Kriketos, Ph.D., and Joseph Proietto, M.B., B.S., Ph.D.



Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition 16명

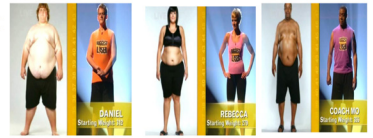


AVERAGE BIGGEST LOSER WEIGHT CHANGE

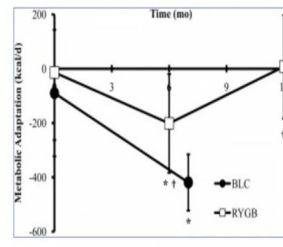


Obesity | VOLUME 24 | NUMBER 8 | AUGUST 2016

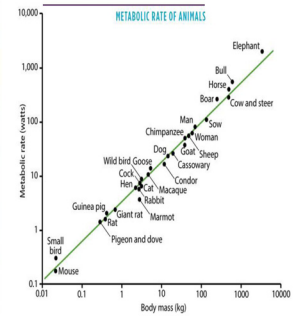
Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition 16명



Biggest Loser vs Bariatrics



Metabolic Adaptation following Massive Weight Loss
Obesity (2014) 22, 2563-2569

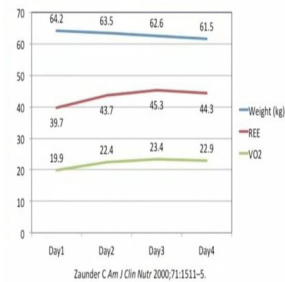


Obesity | VOLUME 24 | NUMBER 8 | AUGUST 2016

Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition 16명



Metabolic Changes over 4 days of fasting



Obesity | VOLUME 24 | NUMBER 8 | AUGUST 2016

RAPID vs GRADUAL

The effect of rate of weight loss on long-term weight management: a randomised controlled trial

Katrina Peralta, Pooja Sundares, Luke A Pendergast, Catherine Baines, Elizabeth Deleage, Joseph Proulx

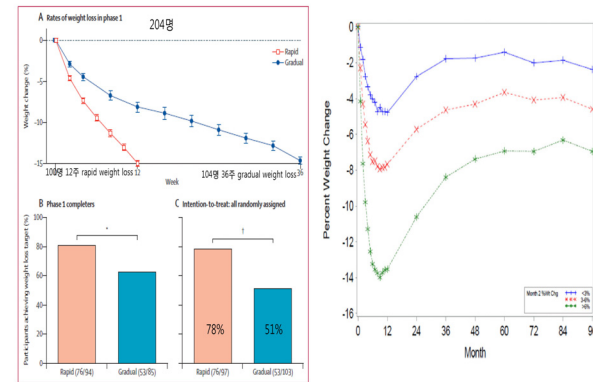


Figure 2: Rate of weight loss during phase 1 for successful participants (mean % change, 95% CI). Successful participants were those who achieved at least 12.5% weight loss from baseline to end of phase 1. *p<0.05; †p<0.001.

Lancet Diabetes Endocrinol 2014

RAPID vs GRADUAL

The effect of rate of weight loss on long-term weight management: a randomised controlled trial

Katrina Peralta, Pooja Sundares, Luke A Pendergast, Catherine Baines, Elizabeth Deleage, Joseph Proulx

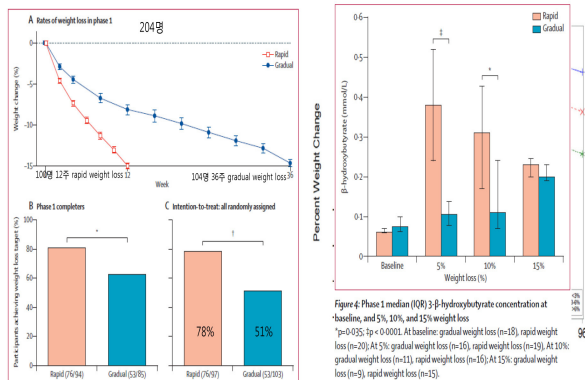


Figure 4: Phase 1 median (IQR) 3-β-hydroxybutyrate concentration at baseline, 5%, 10%, and 15% weight loss. *p=0.035; †p<0.001. At baseline: gradual weight loss (n=18); rapid weight loss (n=20); At 5%: gradual weight loss (n=16); rapid weight loss (n=19); At 10%: gradual weight loss (n=11); rapid weight loss (n=16); At 15%: gradual weight loss (n=5); rapid weight loss (n=15).

Lancet Diabetes Endocrinol 2014

Effects of anti-obesity drugs, diet, and exercise on weight-loss maintenance after a very-low-calorie diet or low-calorie diet: a systematic review and meta-analysis of randomized controlled trials¹⁻³

Kari Johansson, Martin Nowvis, and Erik Hemmingsen

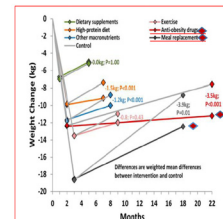
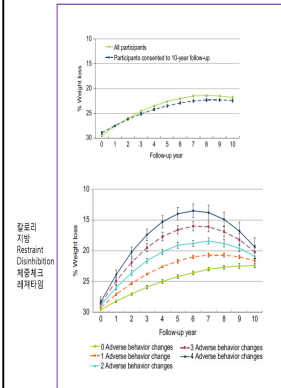


FIGURE 3. Overview of changes in body weight during the rapid weight-loss phase and the weight-loss maintenance period in 20 randomized controlled trials that evaluated different anti-obesity drug, diet, and exercise weight-loss maintenance strategies after an initial very-low-calorie diet or low-calorie diet (<1000 kcal/d). The grey lines represent the control subjects in each subcategory. Anti-obesity drugs: sibutramine and rimonabant. Dietary supplements: green tea, high fiber, oil supplement, and conjugated linoleic acid. Other macronutrients: low fat, low glycemic index, and healthy eating pyramid. The random-effects model was used to weight and pool the studies within each treatment arm (intervention and control) after the very-low-calorie diet or low-calorie diet period and maintenance period. The mean increase for each month was estimated from these 2 measurements. Weighted mean differences between the intervention and control groups at follow-up.

Am J Clin Nutr 2014;99:14-23.

Predictor

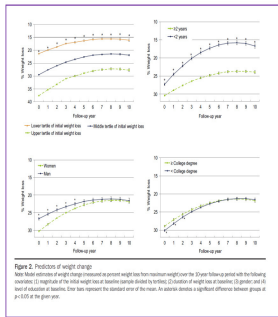
NWCR



Weight-Loss Maintenance for 10 Years in the National Weight Control Registry

J. Graham Thomas, PhD, Dale S. Bond, PhD, Suzanne Phelan, PhD
James O. Hill, PhD, Rena R. Wing, PhD

- * Enroll : 1년이상 13.6kg이상 체중감소 있었던 2886명(여 : 78%, 48세)
- * 평균체중감소 : 31.3kg(0년) 23.8 kg(5년) 23.1kg(10년)
- * 87% 가 10%이상 체중감소



Am J Prev Med 2014;46(1):17-23

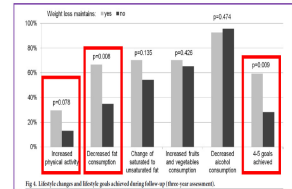
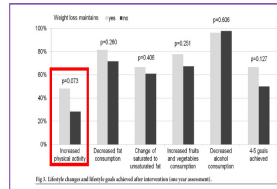
Predictor

DEPLAN

	Baseline		Change from baseline to 1 year		Change from baseline to 2 years		p
	Maintained Non-maintained	p-value	Maintained Non-maintained	p-value	Maintained Non-maintained	p-value	
Age (yr)	50.1 (22.4)	0.94	7.3 (8)	0.73	7.8 (8)	0.68	
Weight (kg)	94.1 (24.4)	0.03	-10.2 (10.1)	0.0001	-10.2 (10.1)	0.0001	
%fat	32.2 (4.2)	0.03	-1.9 (2.1)	0.0001	-1.9 (2.1)	0.0001	
%fat (range)	24.1-42.4		-3.9-10.1		-3.9-10.1		
%fat (mean)	32.2 (4.2)		-1.9 (2.1)		-1.9 (2.1)		
%fat (range)	24.1-42.4		-3.9-10.1		-3.9-10.1		
%fat (mean)	32.2 (4.2)		-1.9 (2.1)		-1.9 (2.1)		
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Predictors of long term weight loss maintenance in patients at high risk of type 2 diabetes participating in a lifestyle intervention program in primary health care: The DE-PLAN study

5명 DM 진행 : 1명(maintainers),
4명(non-maintainers)



PLOS ONE March 23, 2018

Predictor

동기부여

Predictors of long term weight loss maintenance in patients at high risk of type 2 diabetes participating in a lifestyle intervention program in primary health care: The DE-PLAN study

Long-term weight loss maintenance¹

Rena R Wing and Suzanne Phelan *Am J Clin Nutr* 2005;82(suppl):222S-5S

	Unadjusted model		Adjusted model	
	OR ^a	95% CI ^b	OR ^a	95% CI ^b
Age				
<40 (ref)	1.00	(0.97, 1.12)	1.00	(0.88, 1.08)
40-49	4.61	(0.81, 25.31)	3.67	(0.81, 16.47)
Education				
(Basic and medium/high)	2.19	(0.33, 13.19)		
Marital status				
(Married or having a partner/single or widow)	1.73	(0.41, 7.23)		
BMI ^c				
<25 (ref)	1.05	(0.89, 1.22)		
Weight circumference				
History of increased glucose	4.47	(0.75, 26.51)	4.53	(1.13, 18.15)
Family history of Diabetes	1.49	(0.33, 6.59)		
History of hypertension	1.19	(0.21, 6.71)		
Smoking status	1.21	(0.53, 2.80)		
FINDRSC ^d	0.96	(0.72, 1.27)		
Increased physical activity over past year	2.18	(0.49, 9.90)		
Decreased consumption of fat over past year	5.99	(1.17, 30.58)	4.28	(1.41, 12.98)
Decreased consumption of fruit and vegetables over past year	0.46	(0.08, 2.26)		
>5% weight loss during intervention period	2.18	(0.49, 9.90)		

*NWCR study

- 83%가 체중감소 trigger가 있었다:
Medical triggers (23%), 최고체중
(21.3%), 거울에 비친 모습(12.7%)

- Medical triggers : longterm behavior change → 초기 체중감소, 체중유지와
연관 : 36kg loss vs 32kg loss(non medical), regain(4kg vs 6kg)

Predictor

동기부여

[illegible]

157/74/40/68.0, 57.9/29.4, 131/8

523년(간지) : 송 왕조(대위) 왕조간, 개화, 덕성, 불라, ~, 삼국,
연배, 개국군, 양자지(비부자 협상), 불라, 궁극적
mother : DM, 장년 결핵성
200/170 ~ 185/120, 궁극적비자
박지석

46/F

FLUI	부동비합출	2	2	7
TOF	도리박출 25mg	8	2	7

LDL 187, total cholest 267

→ 25mg, 호르몬(비부자 협상) 스타틴
74.4 → 71.1
150/115.

FLUI	부동비합출	2	2	7
TOF	도리박출 25mg	8	2	7

130/95

Predictor

동기부여

PUI	토라력 25mg	0.5	1	7.1
TOF		1	2	7

FAN	Wi-charger				
	송-, 케리 필릭, 클라, 잠실양자, 가문로, 연변- 회파우터와 완동, 도라강, 역 보아주세요 결론번호 : 108H, 사정 : 68H				
	180.0/67.2T, 32.0/22.3, 1436				
	60.7 - 60.5				
FLUIT	무로비트출	2	2	7	H
SUA	클러미안성	2	2	7	H
TGFI	도라북형 25mg	1	2	7	H
MGI	대그나스체	2	2	7	H
B	올림피아드출	1	1	7.1	L
	송-, 케리 필릭, 클라, 잠실양자, 가문로, 연변- 회파우터와 완동, 도라강, 역 보아주세요 결론번호 : 108H, 사정 : 68H				
	180.0/67.2T, 32.0/22.3, 1436				
	60.7 - 60.7 > 65.8 - 65.9 - 64.5 - 64.1 - 63.3 - 62.6 < 61.5				
	문종 서남호 : 55H, 호라프스 : 68H서 남극 육지, 황려제 연선, 육각 : 55				
FLUIT	무로비트출	2	2	7	H
SUA	클러미안성	2	2	7	H
TOI	도라북형 100mg	2	2	7	H
MGI	대그나스체	2	2	7	H
B	올림피아드출	1	1	7.1	L

II. 각론

이 철 진. 비만 치료의 최신 Update

식이조절

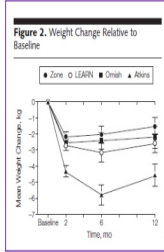
Non-compliance : unconscious

Table 2. Mean Energy Intake and Energy Expenditure by Diet Group and Time Point*

	Atkins	Zone	LEARN	Ornish	Atkins
Energy intake	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy expenditure	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy balance	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Energy intake	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy expenditure	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy balance	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Energy intake	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy expenditure	1888 (51)	1875 (50)	1875 (50)	1875 (50)	1875 (50)
Energy balance	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women

The A TO Z Weight Loss Study: A Randomized Trial



A : 탄수화물 20g/40하, 그 이후에도 50g 이하
Z : 4-3-3
T : 탄수화물 55%-60%, 지방 10%이하
O : 지방 10%이하

JAMA, March 7, 2007—Vol 297, No 9

식이조절

Comparison of Weight Loss Among Named Diet Programs in Overweight and Obese Adults

A Meta-analysis

Figure 1. Difference in Mean Weight Loss at 6- and 12-Month Follow-up Across All Diet Classes With 95% Credible Intervals

Diet Class	12-mo Weight Loss, kg			
	Zone	LEARN	Ornish	Atkins
Low carb	6.07 (4.21 to 7.94)	5.16 (3.48 to 6.84)	5.70 (4.18 to 7.22)	7.27 (5.26 to 9.28)
Moderate carb	6.78 (5.09 to 8.47)	6.71 (4.97 to 8.45)	6.71 (4.97 to 8.45)	6.71 (4.97 to 8.45)
High carb	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)

The values above the diet classes (blue boxes) correspond to the difference in mean weight loss between the columns and row at 12 months follow-up. The difference in average weight loss between moderate macronutrients and no diet at 6 months is 6.78 kg. LEARN indicates Lifestyle, Exercise, Attitudes, Relationships, and Nutrition.



→ "내가 믿는 Diet 하나만 꼭 지속할 수 있으면 성공한다"

JAMA, September 3, 2014, Volume 312, Number 9

식이조절

Comparison of Weight Loss Among Named Diet Programs in Overweight and Obese Adults

A Meta-analysis

Figure 2. Difference in Mean Weight Loss Across Diet With 95% Credible Intervals

Diet Class	12-mo Weight Loss, kg			
	Zone	LEARN	Ornish	Atkins
Low carb	6.07 (4.21 to 7.94)	5.16 (3.48 to 6.84)	5.70 (4.18 to 7.22)	7.27 (5.26 to 9.28)
Moderate carb	6.78 (5.09 to 8.47)	6.71 (4.97 to 8.45)	6.71 (4.97 to 8.45)	6.71 (4.97 to 8.45)
High carb	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)	6.73 (4.97 to 8.49)

The values above the diet classes (blue boxes) correspond to the difference in mean weight loss between the columns and row at 12 months follow-up. The difference in average weight loss between moderate macronutrients and no diet at 6 months is 6.78 kg. LEARN indicates Lifestyle, Exercise, Attitudes, Relationships, and Nutrition.



→ "내가 믿는 Diet 하나만 꼭 지속할 수 있으면 성공한다"

JAMA, September 3, 2014, Volume 312, Number 9

Macronutrient
- PURE

Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

>35~70세, 18개국, 평균 7.4년, 153,355명>

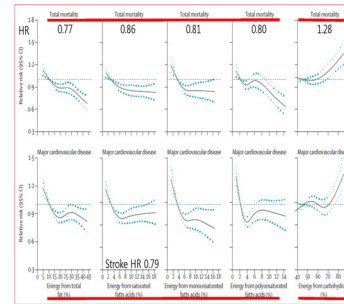


Figure 2. Association between estimated percentage energy from nutrients and total mortality and major cardiovascular disease (n=153,355). Adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, centre, geographical region, and energy intake.

www.thelancet.com, Vol 390, November 4, 2017

Macronutrient
- ARIC

Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis

1543명, 1987년-1999년 시작, 25년 뒤, 6283명 사망

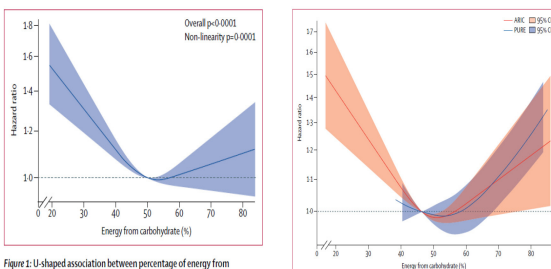


Figure 1. U-shaped association between percentage of energy from carbohydrate and all-cause mortality in the ARIC cohort. The reference level is 50% energy from carbohydrate. Results are adjusted for age, sex, race, ARIC test centre, total energy consumption, diabetes, cigarette smoking, physical activity, income level, and education. ARIC=Atherosclerosis Risk in Communities.

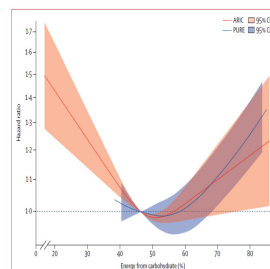


Figure 3. U-shaped association between percentage of energy from carbohydrate and all-cause mortality in the ARIC and PURE cohort studies. The reference level is 45% energy from carbohydrate. ARIC results are adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, ARIC test centre, and energy intake. PURE results are adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, centre, geographical region, and energy intake. The mean percentage of energy from carbohydrate in ARIC is 45%, and from PURE is 50%. ARIC=Atherosclerosis Risk in Communities, PURE=Prospective Urban Rural Epidemiology.

Lancet Public Health 2018; 3: e419-28

Macronutrient
- ARIC

Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis

15428명, 1987년-1999년 시작, 25년 뒤, 6283명 사망

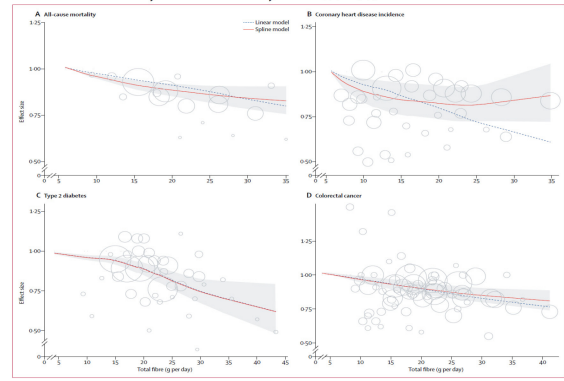


Figure 3. Dose-response relationships between total dietary fibre and critical clinical outcomes based on data from prospective studies. (A) Total fibre and all-cause mortality. 68,183 deaths over 12.5 million person-years. Assuming linearity a risk ratio of 0.92 (95% CI 0.91-0.93) was observed for every 8 g more fibre consumed per day. (B) Total fibre and incidence of coronary heart disease. 6489 deaths over 2.5 million person-years. Assuming linearity a risk ratio of 0.81 (95% CI 0.79-0.83) was observed for every 8 g more fibre consumed per day. (C) Total fibre and incidence of type 2 diabetes. 22,426 cases over 3.7 million person-years. Assuming linearity a risk ratio of 0.85 (95% CI 0.83-0.87) was observed for every 8 g more fibre consumed per day. (D) Total fibre and incidence of colorectal cancer. 20,009 cases over 20.9 million person-years. Assuming linearity a risk ratio of 0.92 (95% CI 0.89-0.95) was observed for every 8 g more fibre consumed per day.

h 2018; 3: e419-28

중추신경계 비만약물

1) Noradrenergic agents

Phentermine, Phendimetrazine, Diethylpropion, Mazindol

2) Serotonergic agents :

Fenfluramine (5-HT stimulator: 1997년 FDA승인취소)

Sibutramine(SNR) : 2010년 승인취소

Fluoxetine: 5-HT reuptake inhibitor : 우울증 및 신경성 식욕 과잉증에 승인

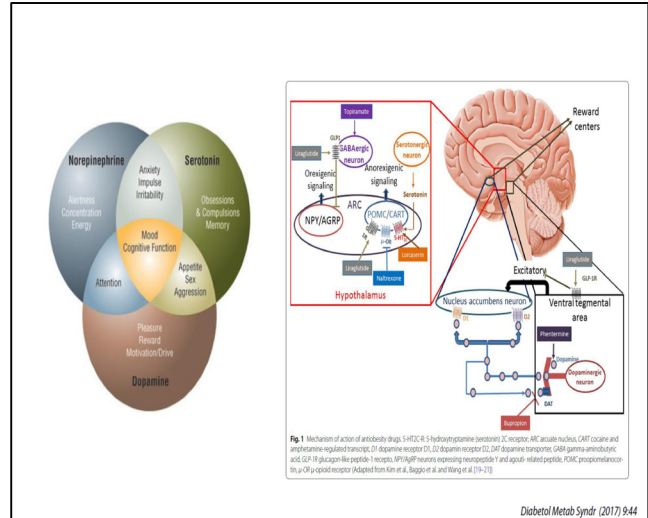
Lorcaserin: selective 5-HT 2c receptor agonist : 2012년 승인

3) Dopaminergic agents :

Bupropion: D2 agonist, dopamine reuptake inhibitor

4) GLP-1 agonist : Liraglutide

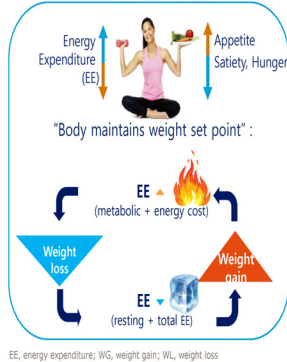
5) GABA, Glutamate : Topiramate



Diabetol Metab Syndr (2017) 9:44

Homeostatic vs. hedonic appetite regulation

Two systems simultaneously influence appetite
Homeostatic regulation (실용적 식욕)



EE, energy expenditure; WG, weight gain; WL, weight loss

Hall et al. *Am J Public Health* 2014;104(1):69-75

Hedonic regulation (쾌락적 식욕)



- Reward of eating through pleasure
- Acts even in satiety
- Eating beyond needed
- Attraction to high calorie foods



Pharmacology of weight-loss agents

Compound	Releasing Agent			Reuptake Inhibitor		
	5-HT	NA	DA	5-HT	NA	DA
Amphetamine						
Fenfluramine						
Fluoxetine						
Sibutramine						
Lorcaserin(5HT-2C)						
Diethylpropion						
Phendimetrazine						
Phentermine						
Topiramate						
Venlafaxine						
Bupropion						
Naltrexone						

Endogenous opioid의 negative feedback 억제

각 약제 간 비교

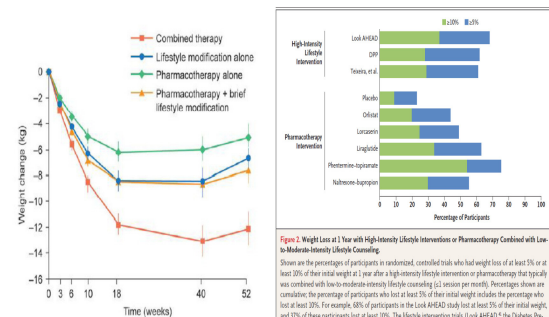
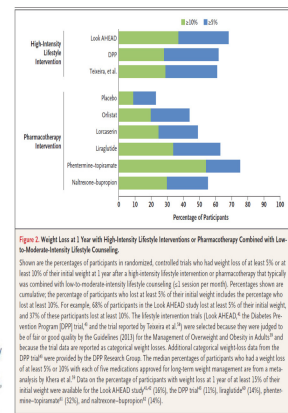


Figure 1 Weight change in response to lifestyle and pharmacotherapy modifications. © 2015. Source: Reproduced with permission from New England Journal of Medicine, from Wadden et al., 2005.



각 약제 간 비교

Figure 4. SUCRAs for Weight Loss and Adverse Event Outcomes

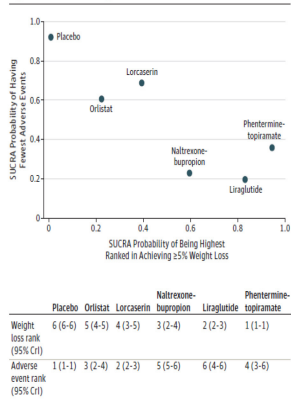


Figure 2 | **Efficacy of anti-obesity drugs.** The percentage estimated weight loss (drug minus placebo) for the six currently available anti-obesity drugs is depicted. ER, extended release; SR, sustained release.

각 약제 간 비교

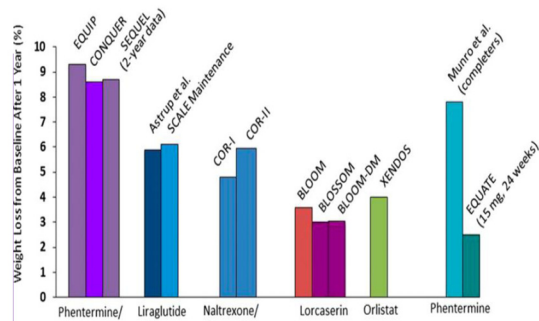
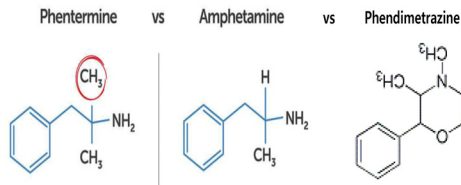


Figure 4—Comparative efficacy of weight-loss medications. All data are placebo-subtracted, maximal dose, 1-year results in intention-to-treat populations using last-observation-carried-forward method unless otherwise indicated (144–154,160–162).

각 약제 간 비교

Weight loss %	% patients on liraglutide 3mg (Saxenda®)	% patients on semaglutide 0.4mg daily (Phase II)	% patients on phentermine/topiramate 15/92mg (Qsymia®)	% patients on lorcaserin (Belviq®) 10mg BID	% patients on bupropion/naltrexone (Contrave®)
> 5%	63%	80%	67%	47%	42%
> 10%	33%	65%	47%	22%	21%
> 15%			32%		10%
> 20%	6%	40%			

II-1. Phentermine, Phendimetrazine



F/26, BMI 28.7, 72.6kg

72	→ 69.8 → 69.6 → 67.6 → 65.1 → 65.1 → 64.5
65.1 → 64.8 → 62.0 → 61.7 → 64.6 → 65.5 → 64.0 → 63.2	
63.2 → 65.0 → 62.5 → 62.5 → 61.5 → 59.0 → 55.7 → 56.8	
56.8 → 57.2 → 61.0 → 59.0 → 58.8 → 58.0 → 58.8 → 57.7 → 56.1	
53.1 → 52.8 → 51.7 → 57.1 → 56.2 → 55.1 → 56.8 → 55.5 → 55	
54.4 → 55.5 → 60.0 → 58.8 → 58.4 → 57.4 → 55.4 → 55.52	
55.52	
43	
연락처 : 45	
주소 : 태산	
수출업종 : 과일, 꿀, 견과류, 탄산수, 과일(우유, 과일, 빵)	
TA	2 2 14 14
SO1	2 2 14 14
AG1	4 2 14 14
MD1	1 1 14 14
KE1	2 2 14 14
150/72/62/7.7, 36.5/26.5, 1366	

F/27, BMI 26.4, 65.8kg

	150/65, 8/26.4, 28.3/18.6, 1325				
	최근 제재 다음 약 먹었다 : 안발락(구 솔 - 케티 - 골다 - 골강 변백약)도 먹고 있다. 같은 이이런만 다음, 임신 계획				
FLU1	두로비렌솔	2	2	7	내적
SA	불로강	2	2	7	내적
TOF	두로비렌솔 25mg	1	2	7	내적
<hr/>					
	55.3 > 62.3 - 61.8 - 60.4 - 60.0 - 59.1 - 58.9 - 58.9				
	57.9 - 57.4 - 57.3 - 57.6 - 56.6 - 53.7 - 54.3 - 52 - 53				
	52 - 52 - 51 - 53 - 52				
SA	불로강	2	2	7	내적
TO1	두로강 100mg	2	2	7	내적
PUI	불로강	1.5	1	7.1	내적
P02	두로비렌솔	2	1	7.1	내적

Phentermine

- 하루 37.5 mg (1T) 하루 1번
또는 18.75mg(1T) 하루 2번,
- 1959년 FDA 승인
- 1990년대에 Fenfluramine +
Phen복합제(Fen+Phen)
- DEA IV



Phendimetrazine

- 1정 (35 mg 또는 17.5mg)을 1일 2-3회
- DEA III



Contraindication

- Hx of cardiovascular disease (coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension)
- MAOI inhibitor 복용자(최근 14일 이내)
- Hyperthyroidism, - Glaucoma
- Agitated states
- History of drug abuse, - Pregnancy, 수유부
- Known hypersensitivity, or idiosyncrasy to the sympathomimetic

항경신성 식욕억제제 4개 성분 공급량

(단위 : 천개, 백만원)

구분	마진돌		펜디메트라진		펜터민		디아키프로피온 (일피프라운)	
	수량	금액	수량	금액	수량	금액	수량	금액
2010	2160	1176	85,396	26,418	34,422	25,931	7,156	1,943
2011	2,609	1,456	85,486	29,622	44,103	34,500	7,536	2,048
2012	2,397	1,360	105,246	32,483	52,090	40,419	7,623	2,010
2013.상	1,143	658	56,974	17,713	29,805	23,253	4,059	1,088

2013년 : 총 1억 7천만개
2014년 : 총 1억 8천만개
2015년 : 총 2억 3천만개

자료 출처 : 건강보험심사평가원

How Physician Obesity Specialists Use Drugs to Treat Obesity

Ed J. Hendricks¹, Richard B. Rothman² and Frank L. Greenway³

Medication	% Frequency of use
Phentermine/Topiramate	97
Diethylpropion	64
Phendimetrazine	60
Mefenorex (Mefenorex)	3
Stimulant/Topiramate	43
Orlistat/Topiramate	43
Topiramate/Topiramate	50
Zonisamide (Zonisamide)	9
5-HTP/Carbidopa	20

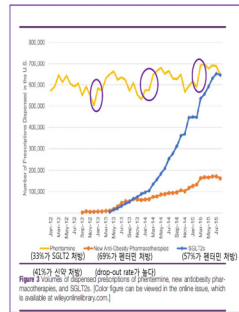
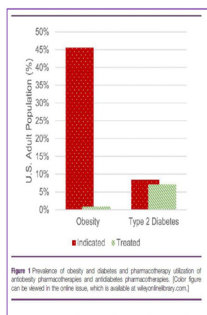
Medication	Highest average dose (mg/d)	Lowest average dose (mg/d)	Approved dose
Stimulant	17	9	10-15mg/d
Orlistat	271	138	360mg/d
Phentermine	56	17	15-37.5mg/d
Diethylpropion	77	27	75mg/d
Phendimetrazine	122	38	35-210mg/d
5-HTP/Carbidopa	82	21	N/A (5400mg/d)
Zonisamide	95	35	N/A (5400mg/d)
Bupropion	288	14	N/A (5400mg/d)
Mefenorex	1,662	527	N/A (52g/d)

5-HTP, 5-hydroxytryptophan; N/A, not available.

* 56% 이상의 의사가 펜터민 장기 처방중이었음

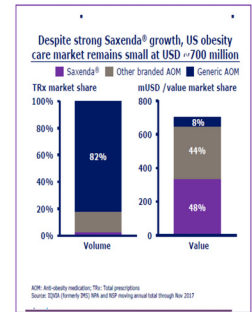
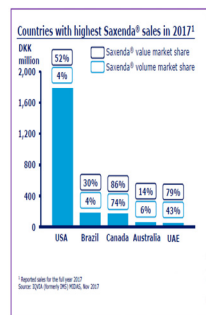
Obesity (2009) 17, 1730-1735.

Low Adoption of Weight Loss Medications: A Comparison of Prescribing Patterns of Antiobesity Pharmacotherapies and SGLT2s



Obesity | VOLUME 24 | NUMBER 9 | SEPTEMBER 2016
2018 Novo Nordisk IR자료

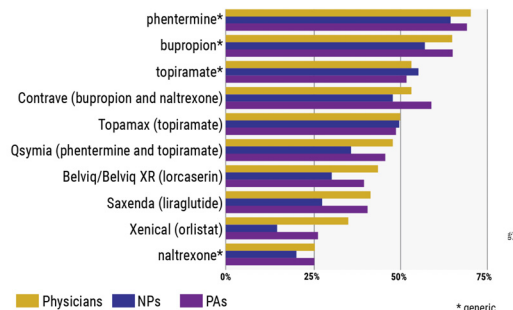
Low Adoption of Weight Loss Medications: A Comparison of Prescribing Patterns of Antiobesity Pharmacotherapies and SGLT2s



Obesity | VOLUME 24 | NUMBER 9 | SEPTEMBER 2016
2018 Novo Nordisk IR자료

Low Adoption of Weight Loss Medications: A Comparison of Prescribing Patterns of Antiobesity Pharmacotherapies and SGLT2s

Which drugs are used the most?



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Low Adoption of Weight Loss Medications: A Comparison of Prescribing Patterns of Antiobesity Pharmacotherapies and SGLT2s

Low cost alternative to Qsymia®

Know your state laws!!!

- Replicate 15mg phentermine and 92mg topiramate with generics
- Doses of phentermine
 - 8mg tablets Lomaira® (more expensive, more flexible dosing) \$45 for 90 tabs
 - 15mg and 30mg capsules \$30 for 30 caps
 - 37.5mg tablets (can use 1/2 tab and save \$) \$30 for 30 tabs lasting 60 days
- Cheapest option is 1/2 of 37.5mg tab daily (as low as \$4/mo)
- Topiramate start at 25mg once a day for 2 weeks then increase to 25mg BID and then to 50mg BID as tolerated. Can consider XR version if patient has coverage
- Phentermine longer than 3 months is off label but sanctioned by medical experts

Obesity | VOLUME 24 | NUMBER 9 | SEPTEMBER 2016
2018 Novo Nordisk IR자료

THE COST-EFFECTIVENESS OF PHARMACOTHERAPY IN OBESE PATIENTS

Minyi Lee, Tiannan Zhan, Jin Choi, Matthew Klebanoff, Dorothy Kim, Barham K. Abu Dayyeh, Kathleen E. Corey, Lee M. Kaplan, Chin Hur

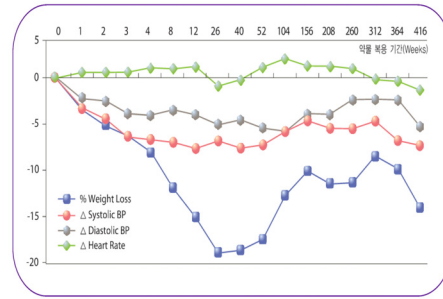
	TBWL Year 1 (%)	TBWL Year 3 (%)	TBWL Year 5 (%)	Non-Adherence Rate Year 1 (%)	Non-Adherence Rate Year 2-5 (%)	Yearly Cost (\$)	QALYs/100ME
Intensive Lifestyle Intervention	-8.5	-5.1	-5.3	7.8	2.2	409	0.0067
Phenamine	-34.4	-17.2	-0.0	75.3	51.1	725	0.01
Phenamine/Tegaserod	-7.8	-7.6	-7.4	30.9	17.6	1,871	0.021
Erythraide	-11.6	-8.1	-6.7	26.4	19.0	16,734	0.011
Osibat	-7.7	-2.5	3.0	27.7	22.1	2,069	0.009
Lacosarin	-7.5	-3.1	1.3	44.6	2.7	2,572	0.019

phentermine was the cost-effective strategy

Table 2: Incremental cost effectiveness ratios per QALY gained for years one, three and five

	Cost (\$)	Incremental Cost (\$)	QALY	Incremental QALY	ICER (\$/QALY)
	Year 1				
Offbeat	720.67		0.0393		Dominate
Intensive Lifestyle Intervention	454.82	-265.85	0.06209	0.09215	Dominate
Phonemic/Phonotactic	625.67	19.044	0.04802	0.00353	Dominate
Locutone	609.79	66.13	0.07213	0.08810	Dominate
Locutone	96.01	-59.79	0.07321	0.08114	Dominate
Phonotactic/Phonemic	5739.27	5188.26	0.07737	0.06408	1,379,776
Offbeat	2329.40		2.48331		Dominate
Intensive Lifestyle Intervention	1268.72	-1,580.08	2.48375	0.00005	Dominate
Phonemic/Phonotactic	265.12	12,588.28	0.08893	0.01446	Dominate
Locutone	265.45	-2,941.37	2.51681	0.06819	Dominate
Locutone	2268.15	2,403.15	2.25441	0.08842	255,641.30
Phonotactic/Phonemic	2268.80	19,396.54	2.56221	0.07779	513,319.40
Intensive Lifestyle Intervention	2,232.37		3.97508		Dominate
Offbeat	4201.75	1,977.41	3.58842	0.01144	Dominate
Phonemic/Phonotactic	329.26	-3,872.22	0.04494	0.02251	Dominate
Locutone	3678.89	3,340.43	0.0204	0.00619	214,707.85
Phonotactic/Phonemic	3352.48	253.99	0.0426	0.02027	122,476.49
Locutone	3242.26	28,495.49	0.38688	0.07799	466,148.78

Blood Pressure and Heart Rate Effects, Weight Loss and Maintenance During Long-Term Phentermine Pharmacotherapy for Obesity

Ed J. Hendricks^{1,2}, Frank L. Greenway³, Eric C. Westman⁴ and Alok K. Gupta¹

Obesity (2011) doi:10.1038/oby.2011.94

비만 환자에서 펜터민 (Phentermine)의 유효성 및 안전성

성균관대학교 의과대학 가정의학교실

우 오 하

Efficacy and Safety of Phentermine for Obese Patients : A Preliminary Open-Label Study

Park, Yong-Woo

Department of Family Medicine, Sanghyunkwan University School of Medicine

<63명, BMI 25이상, 3개월>

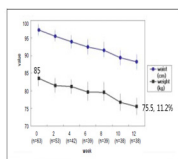


Fig. 1. Weight and Waist Changes During 12 Weeks

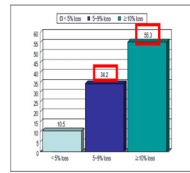


Fig. 2. Distribution of % Weight Loss in Subjects with 12-week Medication

대한비만학회지 제 14 권 제 1 호 2005

Phentermine 장기 연구

TABLE 18.1
Longer-Term, Placebo-Controlled Studies with Phentermine or Diethylpropion

Author(s) and Reference [3]	Year	Number Started Phase I/IIa	Number Completed Phase I/IIa	Duration (Days)	Weight Loss (g)	Weight Loss (%)	Weight Loss (%) Pharm	Weight Loss (%) Drug	Comments
Shelton and Salzman [3] Dihydroergot 75 mg/day McKun [7]	1985	16/16	6/5	52	-10.3	-4.8	-13.3	-11.0	Moderate gross nausea.
Shelton and Salzman [3] Dihydroergot 75 mg/day Moore et al. [7]	1987	10/10	6/10	24	-2.5	-1.7	-2.6	-2.3	
Phentermine 30 mg b.i.d. or alternating doses of 30 mg/day with placebo	1968	36/36	29/32	36	-4.8	-12.0	-11.0		Complete results given phentermine group allowing results had equivalent efficacy.
Langdon et al. [5] Phentermine 30 mg/day Williams and Salzman [3] Phentermine 30 mg/day	1981	20/10	23/26	14	-1.7	-7.4	-2.0	-8.7	
10/10 10/10	1981	15/15	10/11	24	-4.5	-6.3	-9.2	-12.6	Enriched patients with concomitant ulcers.
10/10, 20/20 10/10, 20/20 Phentermine 15 mg per day	2002	200 subjects in four treatment arms	136 subjects; 24/1 and 18/0 discontinued in the phentermine and placebo arms, respectively	28			-2.1%	-4.6%	Randomized comparison of phentermine 150 mg and phentermine 150 mg and phentermine plus vitamin B1200
Pearl et al. [5] 10/10, 20/20 Phentermine 15 mg or 15 mg per day	2003	756 subjects in two treatment arms	458 subjects in two treatment arms	28			-1.71%	-5.65 (7.5 mg) -6.86% (15 mg)	Randomized comparison of placebo, phentermine 150 mg, phentermine 150 mg, or phentermine 150 mg and vitamin B1200 phentermine 150 mg phentermine 150 mg phentermine 150 mg phentermine 150 mg
Prochla Hollander Phentermine 150mg or Placebo	2017	334 subjects		26					

Handbook of obesity, volume2, 235

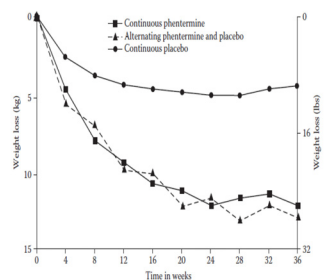


FIGURE 18.2 Mean weight loss over 36 weeks with placebo, continuous rhenstermine, and intermittent rhenstermine (1 month phen-
stermine alternating with 1 month placebo). (From Munro JF et al., *Br. Med. J.* 1, 352-356, 1968.)

EQUATE

Evaluation of Phentermine and Topiramate versus Phentermine/Topiramate Extended-Release in Obese Adults

Louis J. Aronne¹, Thomas A. Wadden², Craig Peterson¹, David Winslow⁴, Sarah Odell³ and Kishore M. Gadde⁵

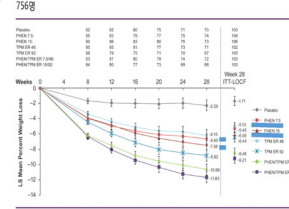


FIGURE 2 LS mean percent weight loss overtime (mTTS; $P < 0.05$ vs. placebo at all time points except week 0 for all comparisons between PHEN/TPM ER and placebo or the individual components except PHEN/TPM ER 7.5/45 vs. topiramate ER 92 at weeks 2 and 28 in the mITT population. At week 28 comparisons between PHEN/TPM ER and placebo or the individual components in the LOCF population were significant. LS, least squares; PHEN/TPM ER 15/92, phenentermine 15 mg and topiramate extended release 92 mg; PHEN 15, phenentermine 15 mg; TPM ER 92, topiramate extended-release 92 mg; PHEN/TPM ER 7.5/45, phenentermine 7.5 mg and topiramate extended-release 45 mg; PHEN 7.5, phenentermine 7.5 mg; TPM ER 45, topiramate extended-release 45 mg.

TABLE 2 Percentage of subjects achieving $\geq 5\%$ or $\geq 10\%$ weight loss from baseline to week 28 (ITT-LOCI)

Variable	Placebo (n = 123)	Phentermine 7.5 (n = 104)	Topiramate ER 45 (n = 102)	PHEN/TPM ER 7.5/45 (n = 103)	Phentermine 15 (n = 100)	Topiramate ER 92 (n = 105)	PHEN/TPM ER 15/92 (n = 103)
≥5% weight loss, n (%)	16 (13.5)	45 (43.3)	40 (39.2)	64 (62.1) [†]	49 (48.7)	51 (48.8)	66 (66.0) ^{††}
≥10% weight loss, n (%)	7 (5.8)	13 (12.5)	11 (10.8)	40 (39.0) ^{††}	25 (25.0)	35 (33.3)	47 (46.6) ^{††}

ITT, intention-to-treat; LOS, last observation carried forward; PHEN/TPR (R 150), phenitoin 15-mg and topiramate extended-release 32-mg; PHEN/TPR (R 30), phenitoin 15-mg and topiramate extended-release 48-mg.
 * $p < 0.05$ vs. placebo.
 † $p < 0.01$ vs. phenitoin (R 15).
 ‡ $p < 0.01$ vs. topiramate (R 48).
 § $p < 0.05$ vs. phenitoin (R 15).
 ¶ $p < 0.023$ vs. topiramate (R 48).

Obesity | VOLUME 21 | NUMBER 11 | NOVEMBER 2013

Combination Therapy

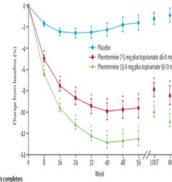


1. Qsymia®

2,487명

Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial

Shibori L, et al. Lancet. 2012;380(9849):1136-45.



5% 이상 체중감소: 62% vs 21% (7.5 - 15 - placebo)
10% 이상 체중감소: 57% vs 48% vs 7% (7.5 - 15 - placebo)
HbA1c: 6.8% -> 6.4%

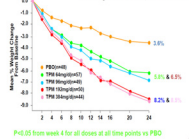
Figure 2. Effects of phentermine plus topiramate on bodyweight, LCOF, last observation carried forward; MI, myocardial infarction. (Reprinted with permission from Gaudin et al. (2011). Copyright © 2011 Elsevier Science Ltd.) (BMI 27-45 with two or more comorbidities)

www.thelancet.com Vol 377 April 16, 2011

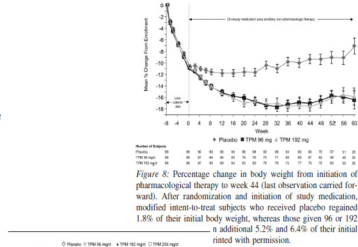
Topiramate

A 6-month randomized, placebo-controlled, dose-ranging trial of topiramate for weight loss in obesity

obesity Res 2003;11:722-733



P<0.05 from week 4 for all doses at all time points vs PBO



P<0.05 from week 4 for all doses at all time points vs PBO

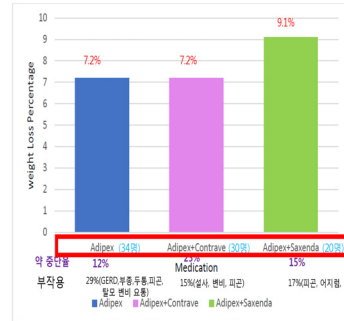
Figure 6: Mean percentage change in body weight over time for subjects in the modified intent-to-treat population who completed at least 40 weeks of treatment (last observation carried forward). After randomization and initiation of study medication, modified intent-to-treat subjects who received placebo regained 1.8% of their initial body weight, whereas those given 96 or 192 mg additional 5.2% and 6.4% of their initial weight with permission.

2. Phen + Contrave

Phen + Saxenda

A Retrospective Comparative Analysis on the Effectiveness of Pharmacologic Weight Loss

84명, 평균 BMI 36, 6개월
동반질환: HTN(37%), DM & PreDM 20%

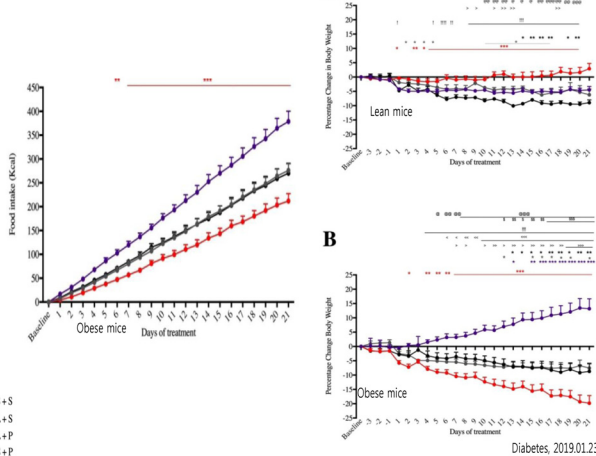


약 중단율: 12%
부작용: 29%(GERD, 부정맥, 두통, 피로), 15%(설사, 변비, 피로), 17%(피로, 어지럼, 변비, 설사)

(2018). DNP Projects 209.

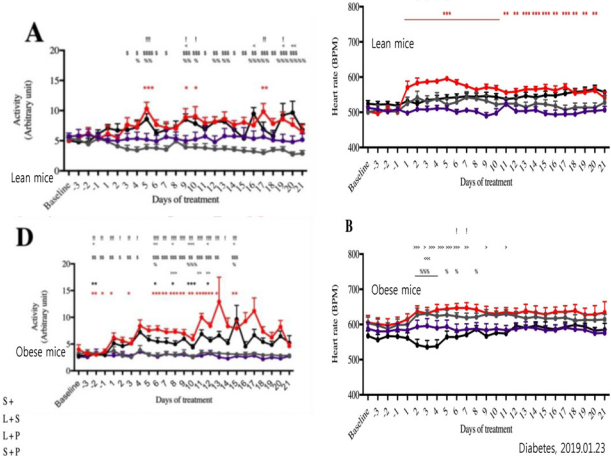
2. Phen + Saxenda

Determining the effects of combined liraglutide and phentermine on metabolic parameters, blood pressure and heart rate in lean and obese male mice.



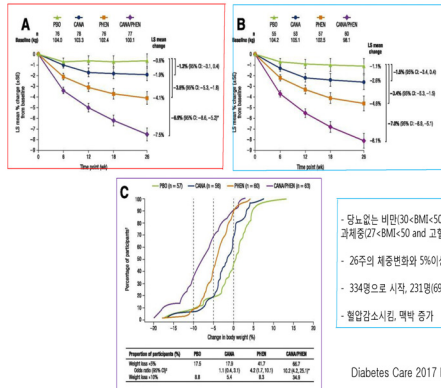
2. Phen + Saxenda

Determining the effects of combined liraglutide and phentermine on metabolic parameters, blood pressure and heart rate in lean and obese male mice.



3. Phen + Cana

Coadministration of **Canagliflozin** and **Phentermine** for Weight Management in **Overweight and Obese** Individuals Without Diabetes: A Randomized Clinical Trial



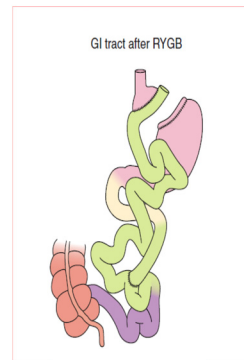
Diabetes Care 2017 May; 40(5): 632-639

II-2. Saxenda

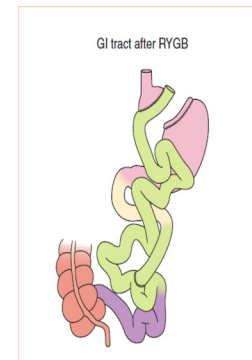
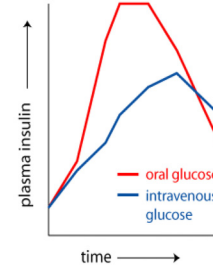
Diabetes = Obesity + Diabetes



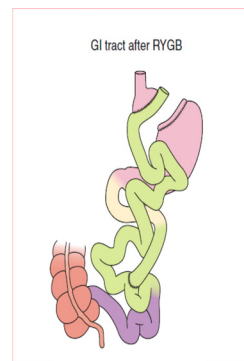
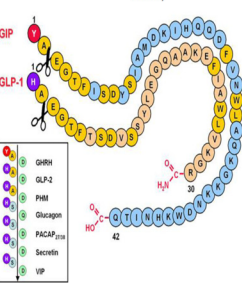
1902년 secretin,
1906년 Moore : 소장 갈아먹여 당뇨 치료
1921년 인슐린 발견



Diabetes = Obesity + Diabetes



Diabetes = Obesity + Diabetes



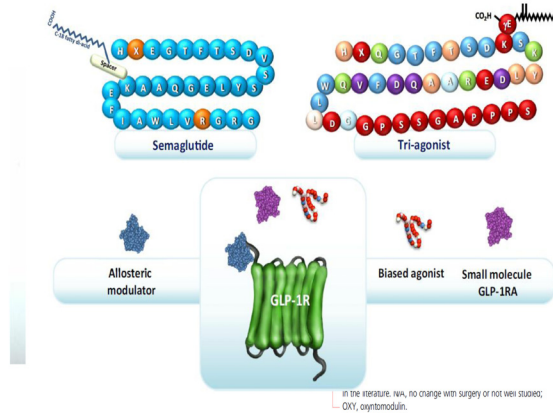
Diabetes = Obesity + Diabetes



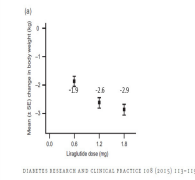
Biomarkers	VSG	RYGB
GLP-1	↑↑↑	↑↑↑
GIP	↑↑↑	↑↑↑
PYY	↑↑↑	↑↑↑
Ghrelin	↑↑↑	↑↑↑
CCK	↑↑↑	↑↑↑
OXY	N/A	N/A
Bile acids	↑↑↑	↑↑↑
Insulin	↑↑↑	↑↑↑

Figure 1. Summary of peptide responses after VSG and RYGB in human and animal models. Horizontal arrow indicates mixed results in the literature. N/A, no change with surgery or not well studied; OXY, oxyntomodulin.

Diabesity = Obesity + Diabetes



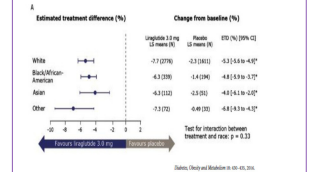
Liraglutide pharmacokinetics and dose-exposure response in Asian subjects with Type 2 diabetes from China, India and South Korea <605명, 16주>



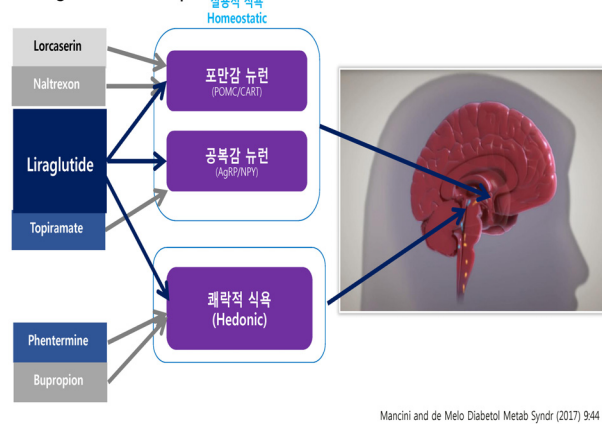
Dose-dependent improvement in glycemia with once-daily liraglutide without hypoglycemia or weight gain: A double-blind, randomized, controlled trial in Japanese patients with type 2 diabetes <226명 14주>

	Placebo	0.5 mg	0.3 mg	0.6 mg	0.9 mg
Body weight (kg, mean (SD))					
Baseline	62.00 (10.05)	64.26 (10.40)	63.34 (10.36)	63.32 (9.48)	61.40 (10.03)
Week 14	61.00 (10.04)	64.31 (10.47)	63.07 (10.36)	62.62 (9.48)	61.00 (10.03)
Liraglutide placebo	-	0.87 (0.16, 1.55)	1.00 (0.45, 1.75)	0.94 (0.35, 1.53)	0.46 (-0.22, 1.14)

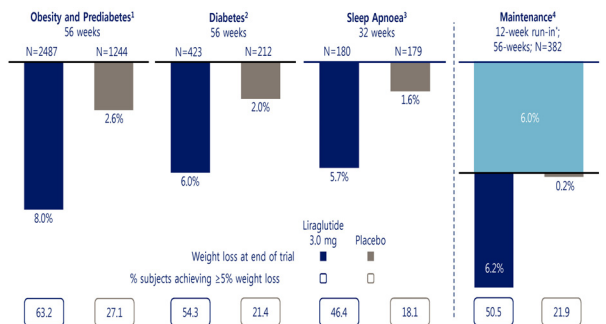
Efficacy and safety of liraglutide 3.0 mg for weight management are similar across races: subgroup analysis across the SCALE and phase II randomized trials <5325명 56주>



Liraglutide has triple actions in brain

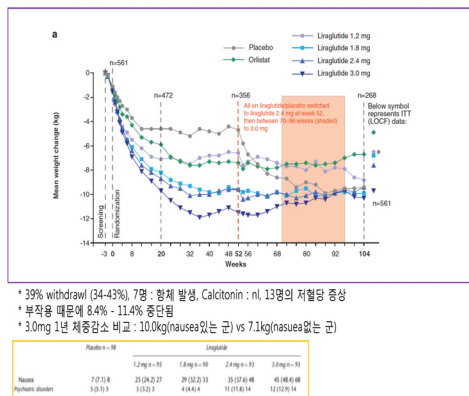


Weight loss across SCALE trials

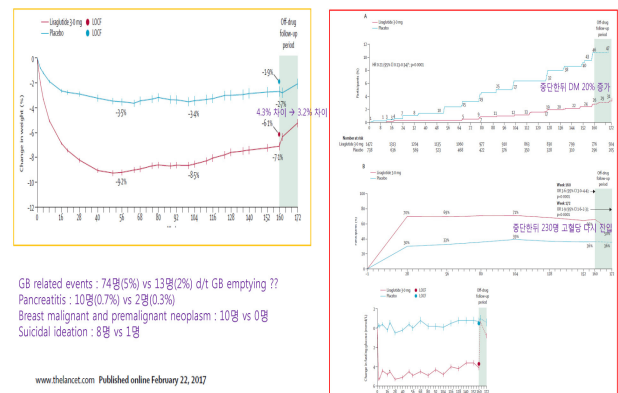


Data are observed means/proportions (except SCALE Diabetes estimated LS means/proportions); LOCF at end of trial.
¹ low calorie diet (total energy intake 1200–1400 kcal/day); ² LOCF, last observation carried forward; LS, least-squares; N, number contributing to the analysis
 1. Pi-Sunyer et al. *N Engl J Med* 2015;373:11–22; 2. Davies et al. *JAMA* 2015;314:687–99; 3. Blackman et al. *Int J Obes (Lond)* 2016;40:1310–9; 4. Wadden et al. *Int J Obes (Lond)* 2013;37:1443–51

Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide

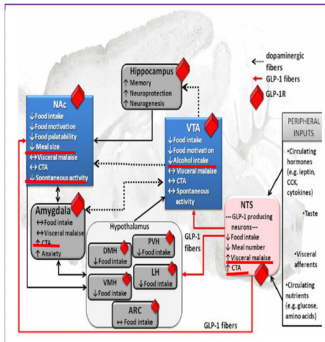


3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial



Hedonic (reward-related, NA VTA) signal vs Homeostatic (hunger-driven) signal

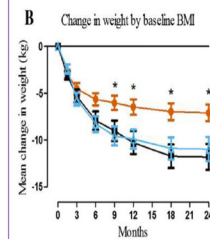
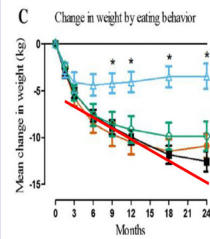
The central GLP-1: implications for food and drug reward



* 비만인에서 GLP-1 IV후 Food picture → fMRI increased response (insula, amygdala)

Frontiers in Neuroscience 14 October 2013

The effects of GLP-1 analogues in obese, insulin-using type 2 diabetes in relation to eating behaviour <151명, 2년>



Int J Clin Pharm (2016) 38:144-151