“เอกสารและสื่อนี้ ใช้เพื่อประกอบการเรียนการสอน
ในหลักสูตรแพทยศาสตรบัณฑิต
คณะแพทยศาสตร์ศิริราชพยาบาลเท่านั้น
ห้ามผู้ใดนำไปใช้ในวัตถุประสงค์อื่น
หากฝ่าฝืนอาจมีความผิดตามพระราชบัญญัติลิขสิทธิ์”

Management of obesity

รศ. ดร. พญ.ฉันทชา สิทธิจรูญ
ภาควิชาสรีรวิทยา

ผศ. นพ.พรพจน์ เปรมโยธิน
ภาควิชาอายุรศาสตร์

ผศ. พญ.พิณพิไล จูทะสมพากร
ภาควิชาเภสัชวิทยา

ดร. พญ.ปัทมาสน์ นิติวรางกูร
ภาควิชาสรีรวิทยา

Email: chantacha.sit@mahidol.ac.th, pornpoj.pra@mahidol.ac.th, pinpilai.jut@mahidol.ac.th, patamat.pat@mahidol.ac.th

Faculty of Medicine Siriraj Hospital, Mahidol University

จุดประสงค์การเรียนการสอน

1. บอกวิธีและอธิบายหลักการในการลดความอ้วน โดยการควบคุมอาหาร การใช้ยา การผ่าตัด และวิธีอื่น ๆ ได้
2. อธิบายกลไกการออกฤทธิ์ เภสัชจลนศาสตร์ที่มีความสำคัญ ข้อควรระวัง และผลข้างเคียงของยาลดความอ้วนได้

Outline

- การควบคุมความอ้วนโดยการควบคุมอาหาร
- การควบคุมความอ้วนโดยวิธีผ่าตัดและอื่น ๆ
- การควบคุมความอ้วนโดยยา

สำหรับตอบคำถาม/ซักถามในคาบเรียน

https://forms.gle/5GGfeL5rfJBdgj9L8

Principle of Weight Management

กิจกรรมการเรียนในคาบ

Mentimeter

https://www.menti.com/

Principle of Weight Management

1. Inspiration and determination
2. Goal setting: short-term goal & long-term goal
3. Choosing a diet that's right for you
4. Increased energy expenditure
5. Self-monitoring
6. Sleep
7. Probiotics
8. Stress
9. Support
10. Positive attitude

Principle of Weight Management

1. Inspiration and determination
   - The most important factor
   - Drives behavior

2. Goal setting
   - Short term-goal for goal achievement
   - Long term-goal for optimum BW/BMI
   - Limit setting

3. Choosing a diet that's right for you
   - Could be done continuously in a long term
   - Too hungry → over-eating!!!
   - Method alternating

Weight loss diet regimens

1. General Recommendation (↓Carbohydrate, ↓Sugar, ↑Protein, ↓Fat, ↑Vegetable/Fiber, ↑Drinking water)
   - Metabolism boosting meals (High protein, Low fat, No carb with 1 day cheating/week)
   - Plate method
2. Calories reduction
3. Paleolithic diet
4. Mediterranean diet
5. "Eating breakfast like a king, lunch like a prince, and dinner like a pauper"
6. Intermittent fasting (including Time-restricted eating, TRF)
7. Ketogenic Diet

Principle of Weight Management

4. Increased energy expenditure
   - ↑EAT or exercise
     - ↑EE, lean mass, BMR, lipolysis, GH
   - ↑NEAT
   - Aerobic exercise
     - Moderate intensity 150 min/week (walking)
     - Vigorous intensity 75 min/week (running)
   - Muscle strengthening, all muscle groups
     - ≥2 days/week (8-12 repetitions, 2-3 sets)
   - Pedometer goal:
     - 5,000-10,000 steps/day

Principle of Weight Management

5. Self-monitoring

- Weighing
- Bathroom scale
- Feedback (self-awareness)
- Fat → light weight → stepwise
- Food Record
- Calories
- Response
- Feedback

6. Sleep

- Deep sleep → GH → ↑lipolysis
- Lack of sleep
- Sleep deprived people → ↓leptin, ↑ghrelin → ↑appetite

GH = growth hormone

Principle of Weight Management

7. Probiotics

- Faster gut & colonic transit time
- ↑Stool frequency
- ↑Stool consistency
- ↓Flatulence
- ↑recovery of tight junction between epithelial cells → prevent bacterial movement & ↓inflammation from LPS →↑insulin sensitivity at hypothalamus → ↑satiety
- ↑GLP-1 & PPY in intestine→ ↓appetite, ↑fullness

LPS = lipopolysaccharide, GLP-1 = glucagon-like peptide 1, PYY = peptide YY

Principle of Weight Management

8. Adjust behavior when stressed

- Stress ⌦ eat

9. Support

- Friend, family
- Social
- Environment

10. Positive attitude

- Don’t give up
- Can always start over

Weight regain

Weight Regain

- **Weight reduction 5-10% within 3-6 months**
- **Weight Regain**
  - **Obvious in ~6-12 months after weight loss**
  - **>25% within the first year**
  - **>50% within 2 years**
  - **>80% within 5 years**
- **Causes**
  - **↓Fat → ↓Insulin & leptin → ↑appetite**
  - **↓TEE (REE & non-REE) from ↓body composition (↓ metabolically active component e.g. FFM)**
  - **↓FFM → high risk of weight regain or even ↑BW**

TEE = total energy expenditure, REE = resting energy expenditure, FFM = fat-free mass

Weight Regain

- Causes
  - ↓Thermogenesis not associated with BW & body composition called "adaptive thermogenesis" (AT) or ↓EE > ↓body composition
    - Occurring
      - Eating less >2 weeks
      - Optimum ~10% weight loss of initial BW or after 12-20 weeks of loosing weight
  - ↓T3
  - ↓SNS
  - Unlimited eating→ rapid weight regain
    - ↑Energy intake
    - ↓Energy expenditure from ↓FFM and prolong AT
    - 4 weeks → normal BMR (new body composition)

AT = adaptive thermogenesis, EE = energy expenditure, BW = body weight, T3 = Triiodothyronine,

SNS = sympathetic nervous system, FFM = fat-free mass, BMR = basal metabolic rate

Diet break or Cheat days

Diet break or Cheat days

- Eating less >2 weeks
  - ↓RMR
  - Adaptive thermogenesis
    - Could be normal after diet refeed
- Diet break or cheat days
  - Eucaloric or ~5-10% a little bit ↑ or ↓ than current BW, not initial BW
  - Diet control, not over eating
  - Short term ~1-3 days
  - Or prolong >4 days to several weeks
  - Maintain BW to stimulate RMR & thermogenesis
  - More effectiveness in weight loss

RMR = resting metabolic rate, BW = body weight

Weight loss maintenance

Weight loss maintenance

- Voluntary weight loss at least 10% of initial BW and maintain at least 1 year
- Voluntary weight loss at least 5% of initial BW and maintain at least 2 years
- Generally, weight loss ~7-10% of initial BW in 6 months after that ~5-6% of initial BW
- Within 5 years, 13-20% of people can maintain weight loss

BW = body weight

Factors associated with successful weight maintenance

1. Inspiration
2. Reaching a self-determined goal weight
3. Autonomy
4. Initial weight loss → more initial weight loss, more successful weight maintenance
5. Calorie Reduction and Portioning of food eaten
6. Eating breakfast regularly
7. Control of over-eating with eating restraint
8. Physically active lifestyle

- Elfhag K, Rössner S. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. Obes Rev. 2005;6(1):67-85.
- Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. Med Clin North Am. 2018;102(1):183-97.
- Wing RR, Phelan S. Long-term weight loss maintenance. Am J Clin Nutr. 2005;82(1 Suppl):222S-5S.

Factors associated with successful weight maintenance

9. Self-monitoring → weighing & food record

10. Psychological strength and stability

11. Self-efficacy

12. Ability to handle life stress & coping strategy

13. Socialization & thinking flexibility

14. Social support

15. Being able to maintain weight after prolong weight loss

- Elfhag K, Rössner S. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. Obes Rev. 2005;6(1):67-85.
- Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. Med Clin North Am. 2018;102(1):183-97.
- Wing RR, Phelan S. Long-term weight loss maintenance. Am J Clin Nutr. 2005;82(1 Suppl):222S-5S.

Percentage of total weight loss

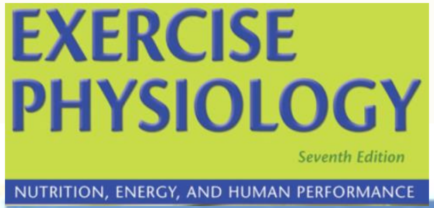


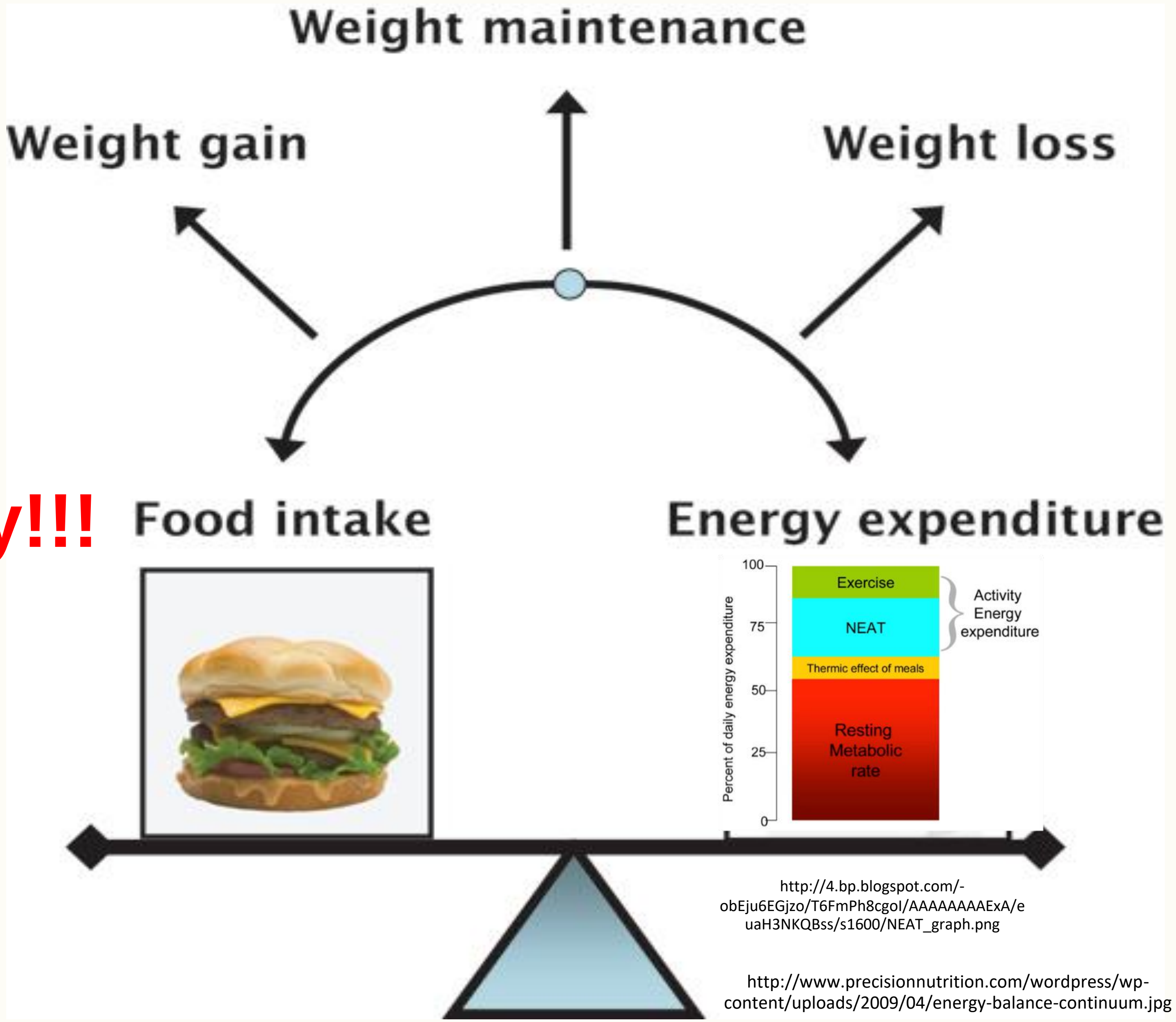
Figure 30.22 • General trend for the percentage composition of the weight lost during 4 weeks of caloric restriction.

The fasting state

- When fat reserves are gone.
  - Degradation of essential proteins begins
  - Loss of heart and liver function
  - Prolonged starvation → death

- Stored fat → provides adequate energy during fast or rigid diet, but vitamins and minerals must be provided.
- Sufficient dietary glucogenic amino acids are needed to replace those being used for gluconeogenesis.
- Rations for those on a weight-reduction diet are commonly fortified with vitamins, minerals and amino acids or proteins.

Energy balance



Obesity!!!

http://4.bp.blogspot.com/-obEju6EGjzo/T6FmPh8cgoI/AAAAAAAAExA/euaH3NKQBss/s1600/NEAT_graph.png

http://www.precisionnutrition.com/wordpress/wp-content/uploads/2009/04/energy-balance-continuum.jpg

Quiz

Q1. ควรแนะนำให้รับประทานอาหารชนิดใดเพิ่มขึ้นหากต้องการลดน้ำหนัก

1. เนื้อไก่
2. หมูสามชั้น
3. ขนุน
4. น้ำผลไม้

Quiz

Q2. พฤติกรรมใด ส่งเสริมการลดน้ำหนัก

1. อดหลับอดนอน
2. จดบันทึกอาหารที่รับประทาน
3. นั่งเล่นโทรศัพท์มือถือทั้งวัน
4. กินอาหารประเภทบุฟเฟต์

Quiz

Q3. ควรชั่งน้ำหนักเวลาใด

1. เช้า
2. กลางวัน
3. เย็น
4. ก่อนนอน

Reference

ฉันทชา สิทธิจรูญ. ใน: ฉันทชา สิทธิจรูญ, บรรณาธิการ. ภาวะอ้วนและการลดน้ำหนัก.

พิมพ์ครั้งที่ 1. กรุงเทพฯ: บริษัท ไอดี ออล ดิจิตอลพริ้นท์ จำกัด; 2565.

Management of Obesity: Clinical Perspectives

ผศ. นพ.พรพจน์ เปรมโยธิน

สาขาโภชนาการคลินิก ภาควิชาอายุรศาสตร์

Today's Outline

1. How much weight do I need to lose?
2. How many calories should I eat when I try to lose weight?
3. How do I lose weight?
4. How do I avoid weight regain after successful weight loss?
5. Bariatric surgery

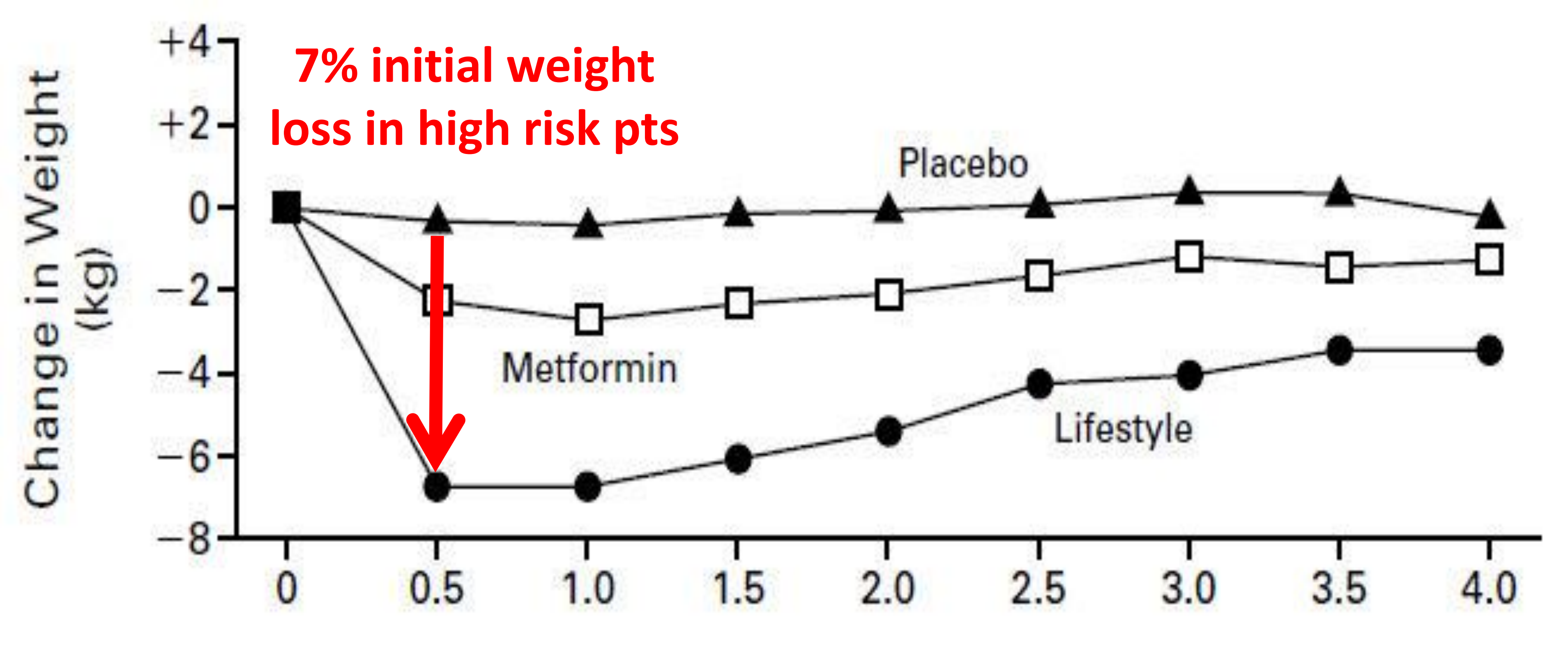
กิจกรรมการเรียนในคาบ

Mentimeter

https://www.menti.com/

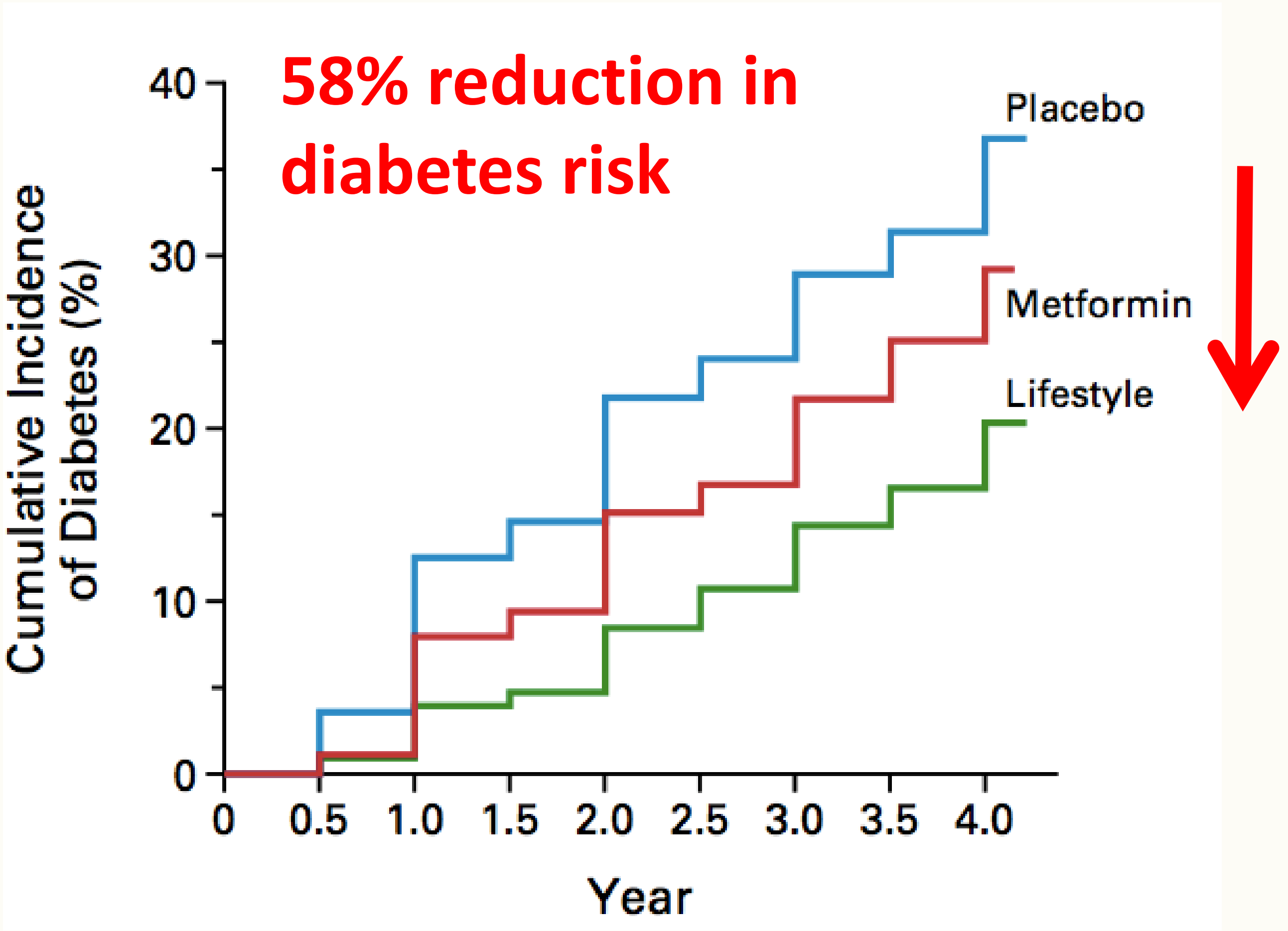
1. How much weight do I need to lose?

“Clinically meaningful weight loss”



Diabetes Prevention
Program (DPP)
NEJM. 2002 7;346(6):393-403

“Clinically meaningful weight loss”



Diabetes Prevention Program (DPP)
NEJM. 2002 7;346(6):393-403

2. How many calories should I eat when I try to lose weight?

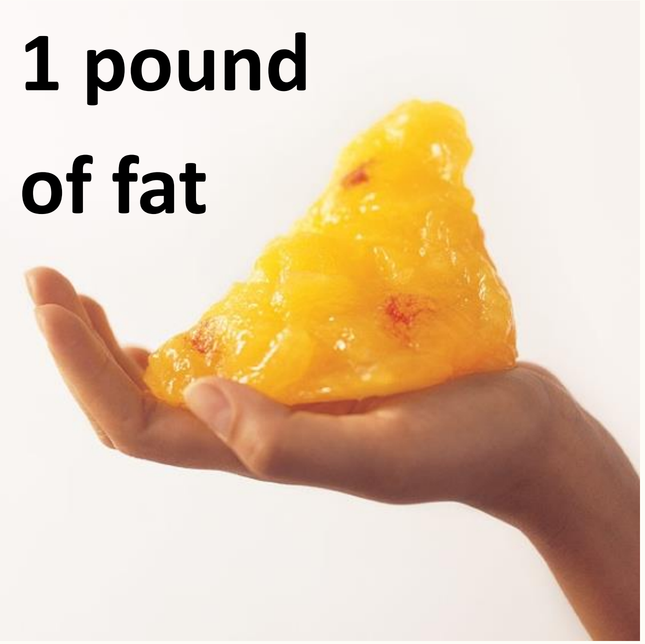
Negative energy balance

E intake < E expenditure

“3500 kcal per pound rule”

Negative 500 kcal/day or 3500 kcal/wk

→ weight loss 1 pound/wk (0.5 kg/wk)



= 3,500 kcal

E intake < $\boxed{\text{E expenditure}}$

What is my energy expenditure ?

Energy Expenditure

= BMR + PA

= BMR x activity factor (1.25)

<u>BMR Estimation by Harris-Benedict Equation</u>

M: 66.5 + (13.75 x kg) + (5.003 x cm) - (6.775 x age)

F: 655.1 + (9.563 x kg) +(1.850 x cm) - (4.676 x age)

Energy Expenditure

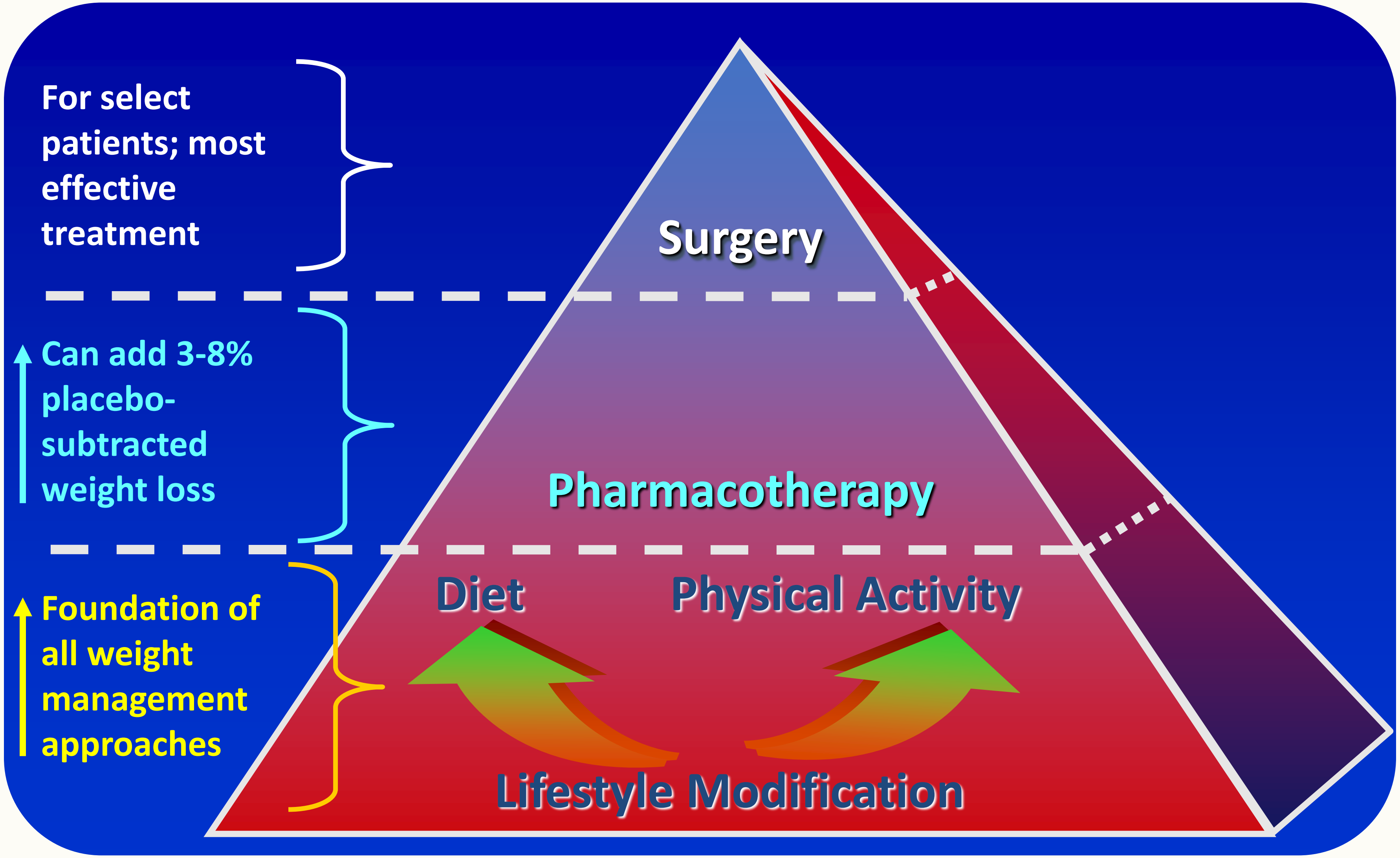
Body Weight (kg)	Male (kcal/day)	Female (kcal/day)
40	1665	1560
50	1840	1680
60	2010	1800
70	2180	1920
80	2350	2040
90	2520	2160
100	2700	2280

Summary: Weight loss goals

- 5 - 10% of initial body weight
  - Minimum weight loss to achieve health benefits
- 0.5 - 1 kg/week of weight loss
  - This means that the effects of intervention are becoming apparent
- Aim for a negative energy balance of 500-750 kcal/day

3. How do I lose weight ?

Obesity Treatment Pyramid



Slide Source:
www.obesityonline.org

Slide courtesy of Dr.Caroline Apovian

Guide for Selecting Obesity Treatment

BMI Category (kg/m^2)					
Treatment	25-26.9	27-29.9	Class I 30-34.9	Class II 35-39.9	Class III ≥40
Diet, Exercise, Behavior Tx	+	+	+	+	+
Pharmaco-therapy		With co-morbidities	+	+	+
Surgery				With co-morbidities	+

Slide courtesy of Dr.Caroline Apovian

Lifestyle Modification

1. Diet
2. Physical activity
3. Behavioral therapy

3อ

Dietary Management

- 2:1:1
- 6-6-1

Plate Method

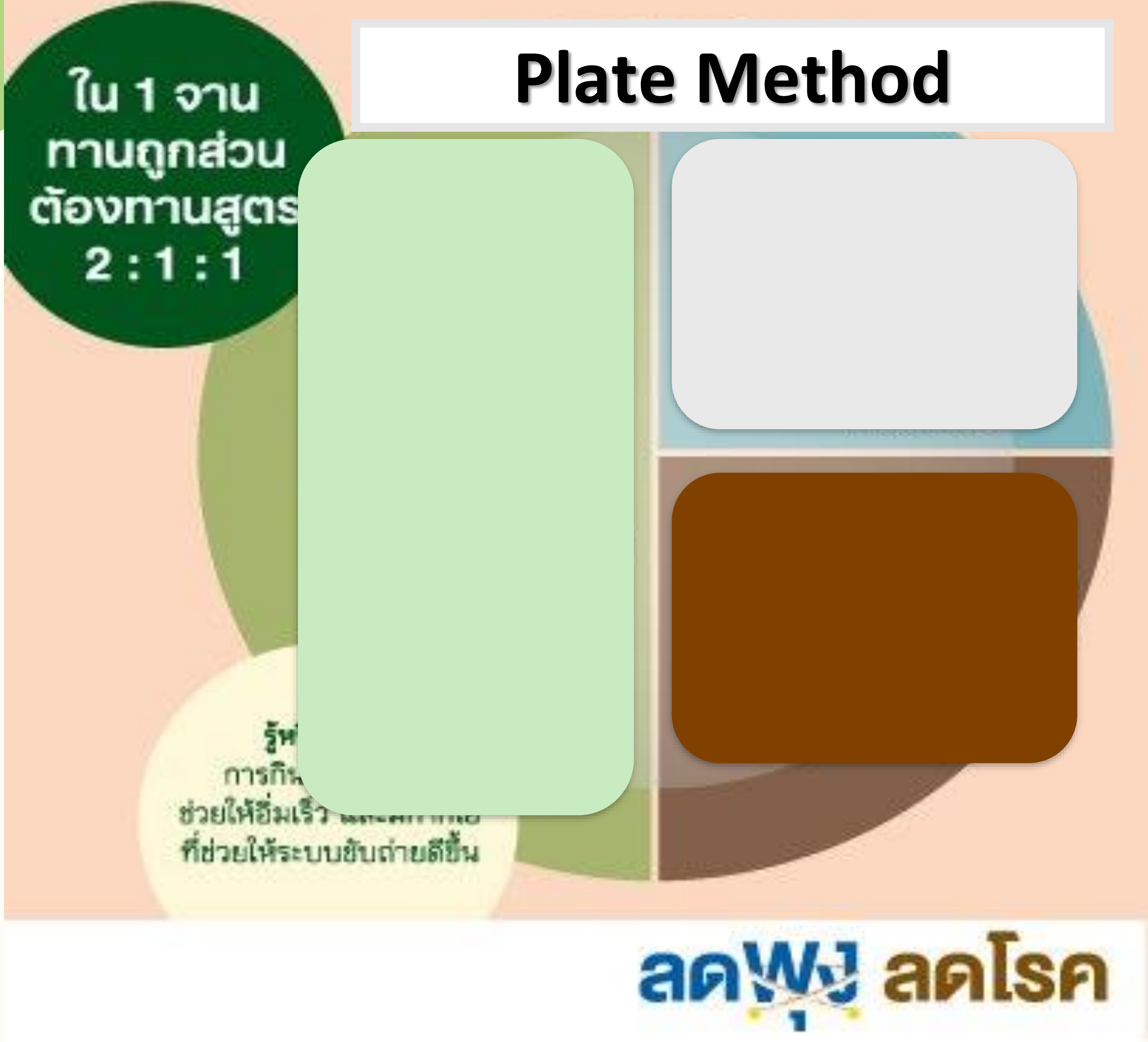


Plate Method

ลดหวาน มัน เค็ม = สูตร “6 – 6 – 1”

ขอขอบคุณศูนย์เบาหวานศิริราช สำหรับภาพประกอบ

1.

2.

ข้อใดมีน้ำตาลมากที่สุด

น้ำเปล่าดีที่สุด

3.

4.

หลีกเลี่ยง

ของทอด ของมัน

A.

B.

Which menu has more calories?

Physical Activity

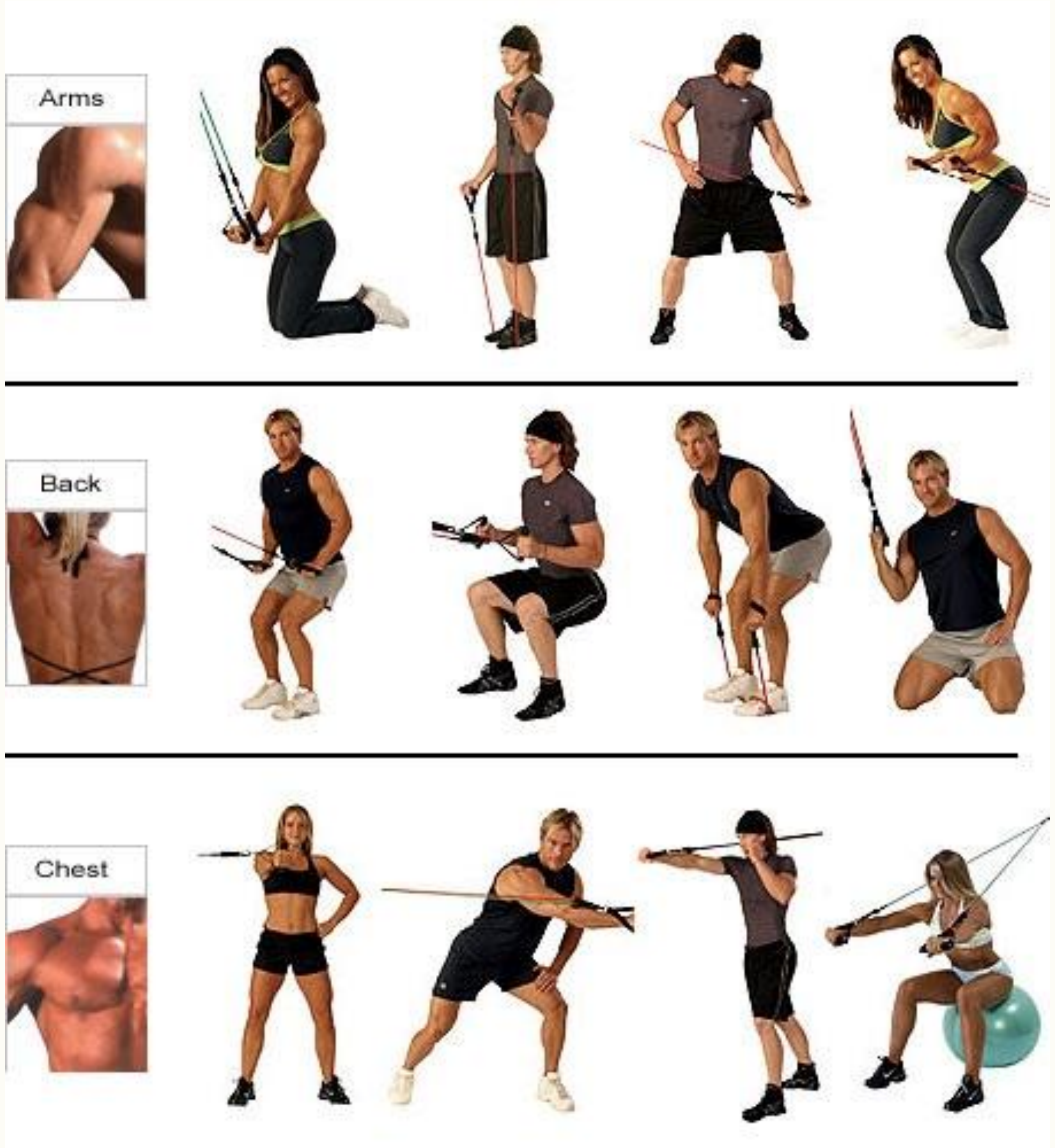
- Aerobic exercise
  - Moderate intensity 150 min/week (walking)
  - Vigorous intensity 75 min/week (running)

Physical Activity

- Aerobic exercise
  - Moderate intensity 150 min/week (walking)
  - Vigorous intensity 75 min/week (running)

- Muscle strengthening, all muscle groups,
  ≥2 days/week (8-12 repetitions, 2-3 sets)

Muscle Strengthening



Physical Activity

- Aerobic exercise
  - Moderate intensity 150 min/week (walking)
  - Vigorous intensity 75 min/week (running)

- Muscle strengthening, all muscle groups,
  ≥2 days/week (8-12 repetitions, 2-3 sets)

- Pedometer goal:
  5,000-10,000 steps/day


อาหาร
ออกกำลังกาย
อารมณ์


สกัด
สะกด
สะกิด

Bariatric Surgery


HONDA

INTERCOOL
Chang


BEFORE
AFTER

Indications for Bariatric and Metabolic Surgery

Guideline	AHA/ACC/ TOS (2013) Circulation 2014; 24; 129 (25 Suppl 2): S102-38.	IFSO-APC consensus (2011) Obes Surg 2012; 22:677–684	DSS-II (2016) FOR T2DM PATIENTS Diabetes Care 2016; 39:861–877	
Ethnicity	Did not specify	Asians	Asians	Others
No comorbid diseases	BMI ≥40 kg/m²	BMI ≥35 kg/m²	-	-
Significant obesity-related co-morbidities	BMI ≥ 35 kg/m²	Should be considered if BMI ≥ 30 kg/m²	Recommended if BMI ≥ 37.5 or ≥ 32.5 with poor glycemic control	Recommended if BMI ≥ 40 or ≥ 35 with poor glycemic control
		May be considered if BMI ≥ 27.5 kg/m²	Consider if BMI ≥ 32.5 or ≥ 27.5 with poor glycemic control	Consider if BMI ≥ 35 or ≥ 30 with poor glycemic control

Initial evaluation

Indications | Patient understanding and compliance

↓

Referral to multi-disciplinary bariatric clinic

Preoperative evaluation

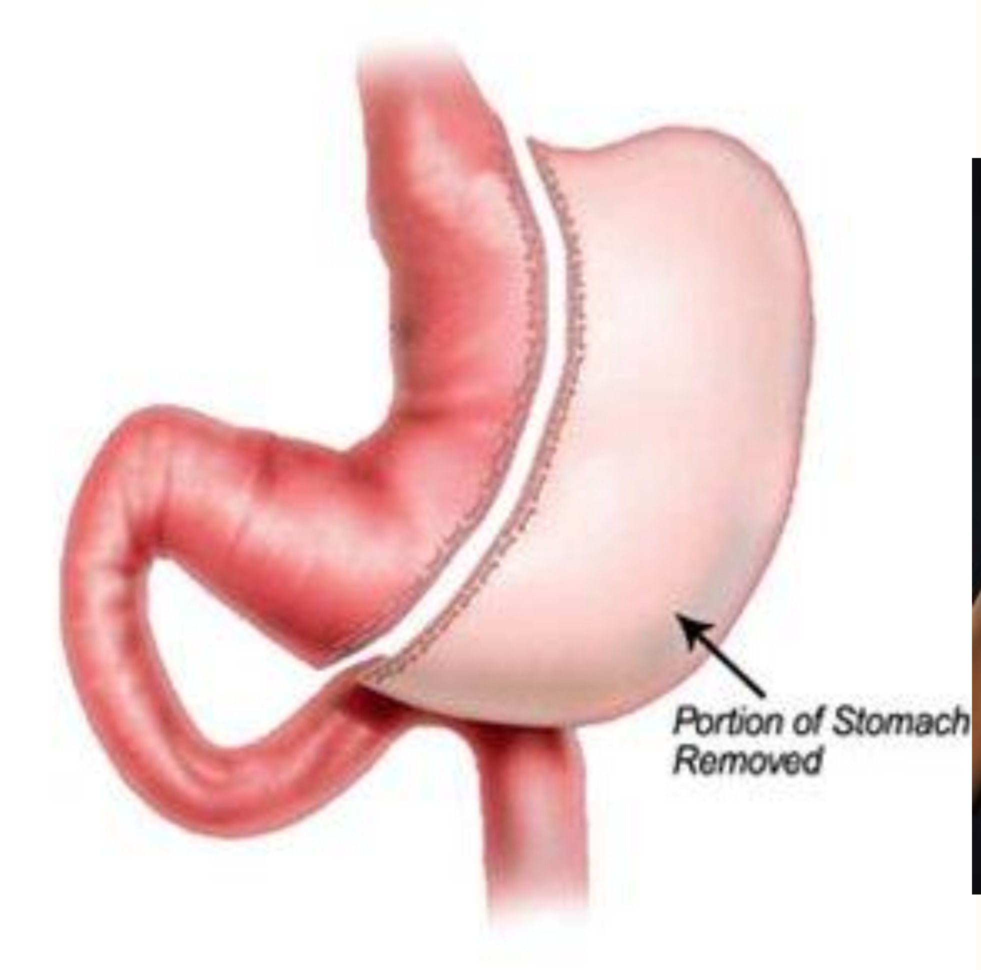
↓

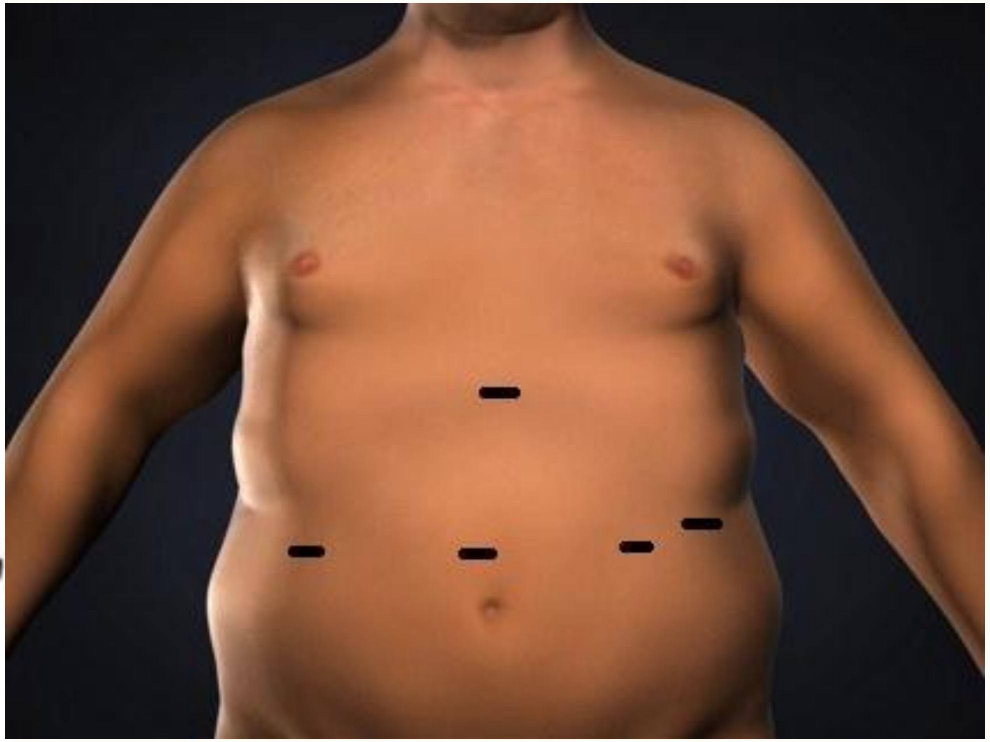
Operation

↓

Post-operative evaluation and follow-up

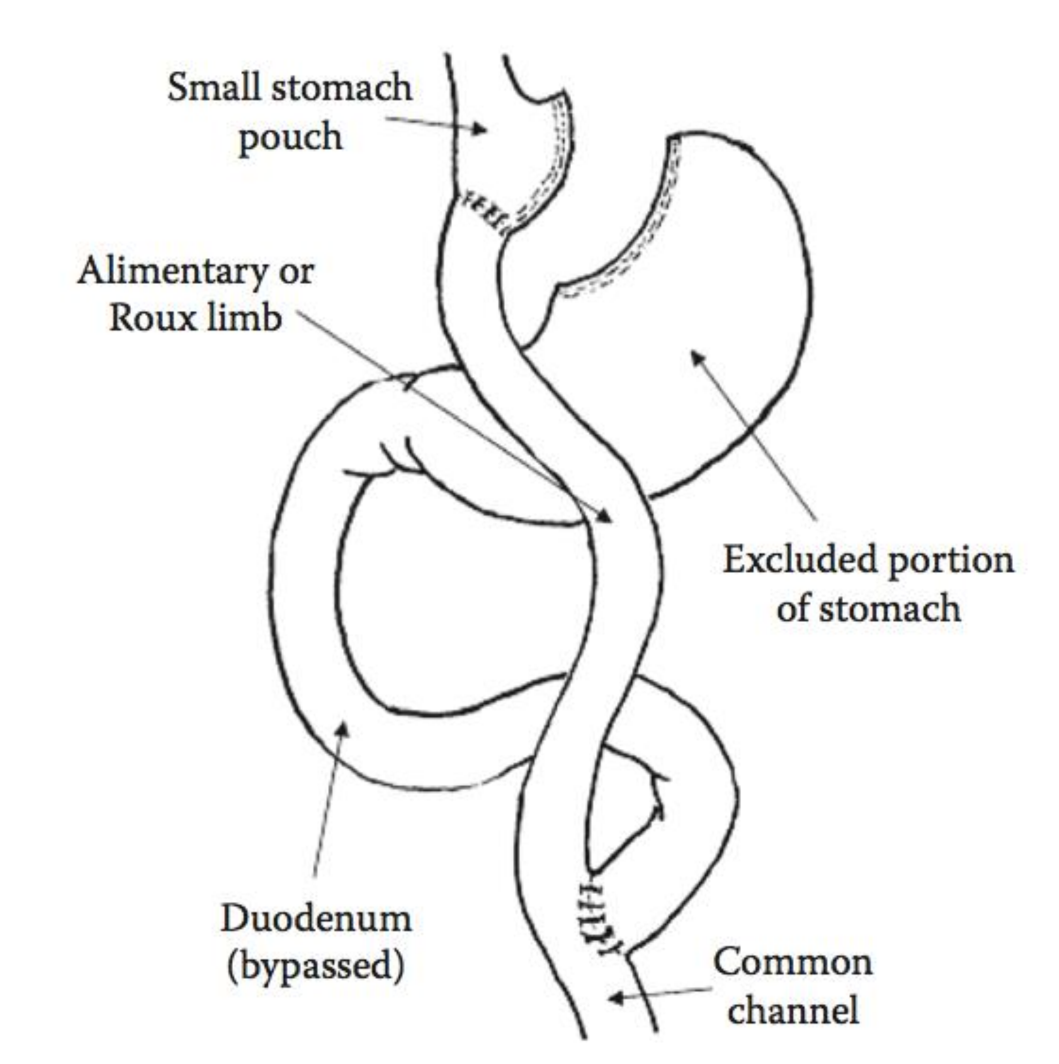
At 2 weeks, every 3 months in year 1, then every 6-12 months





Laparoscopic Sleeve Gastrectomy (LSG)

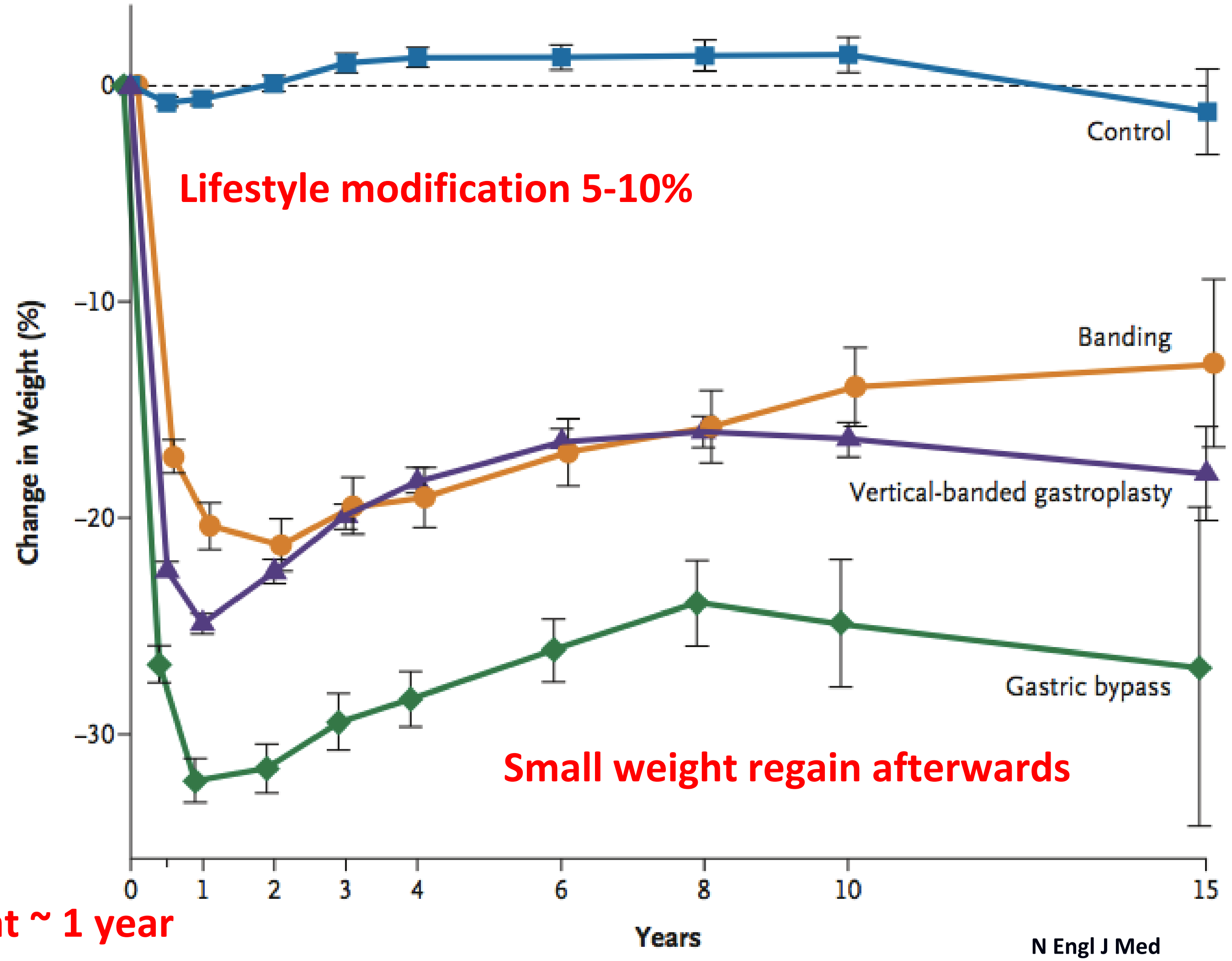
Roux-en-Y
Gastric Bypass (RYGB)



Benefits

- Short term
  - Weight loss
  - Glycemic control and diabetes remission
  - Improved quality of life

Bariatric surgery 30-40%



Max Weight Loss at ~ 1 year

N Engl J Med 2007; 357:741-52

No. Examined									
Control	2037	1768	1660	1553	1490	1281	982	886	190
Banding	376	363	357	328	333	298	267	237	52
Vertical-banded gastroplasty	1369	1298	1244	1121	1086	1004	899	746	108
Gastric bypass	265	245	245	211	209	166	92	58	10

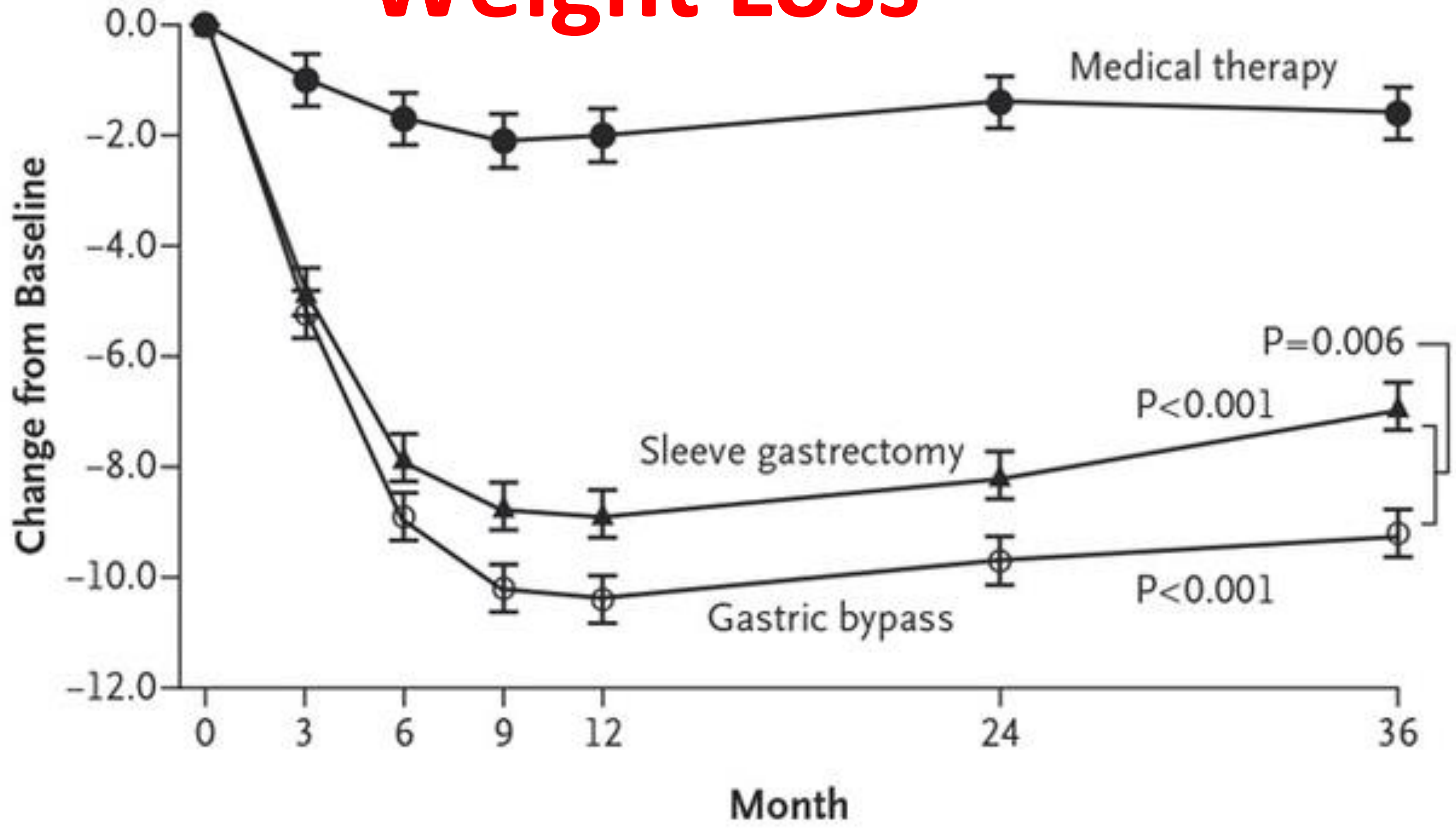
igure 1. Mean Percent Weight Change during a 15-Year Period in the Control Group and the Surgery Group, ccording to the Method of Bariatric Surgery.

LSG and RYGB

Operation	Laparoscopic sleeve gastrectomy (LSG)	Laparoscopic Roux-en-Y gastric bypass (RYGB)
Weight loss	++	+++
Diabetes remission	++	+++
Complexities and operative time	+	+++

Weight Loss

D Body-Mass Index

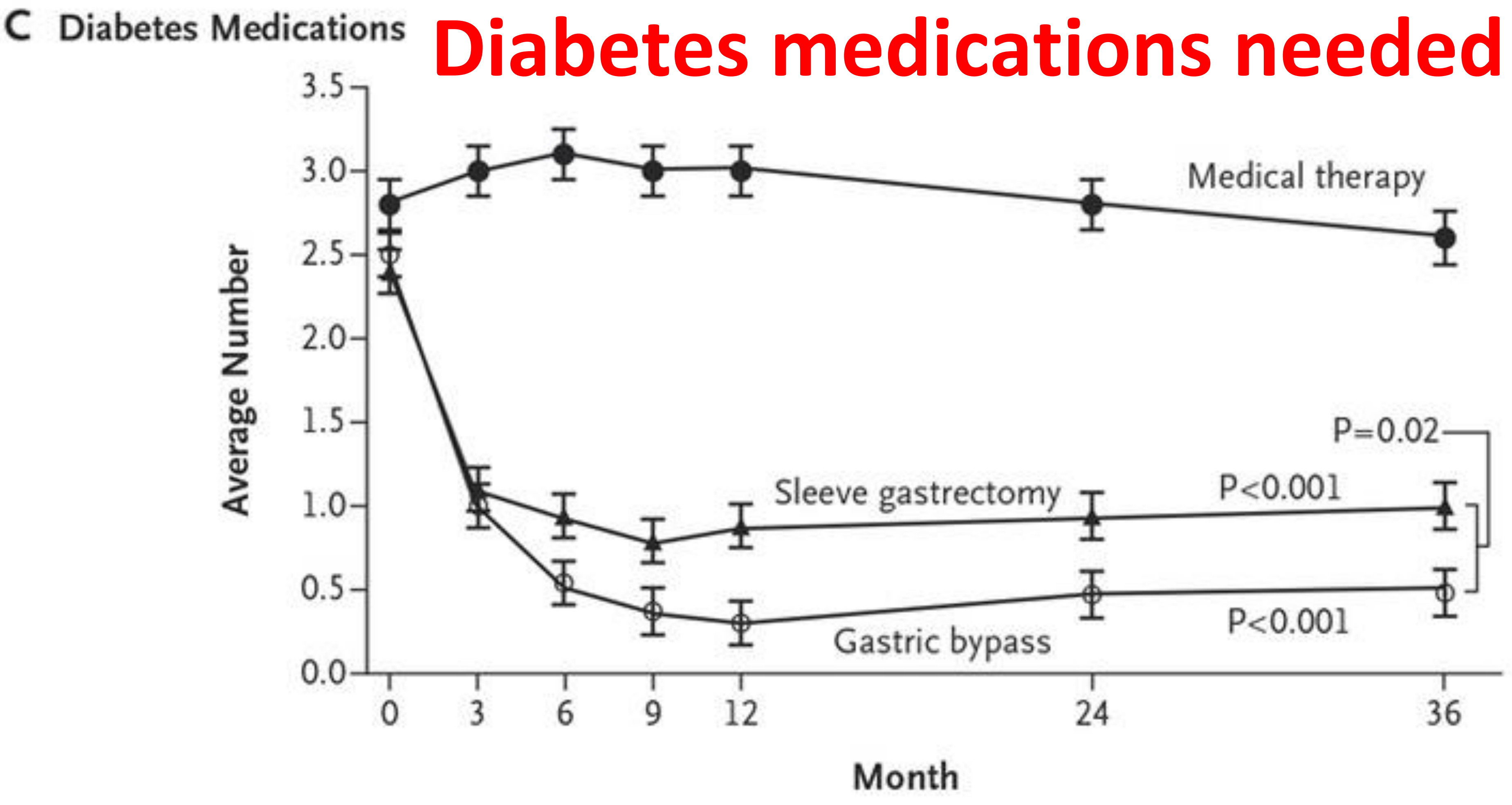


Value at Visit

Medical therapy	36.4	34.6	34.2	35.0	34.8
Sleeve gastrectomy	36.1	28.3	27.1	27.9	29.2
Gastric bypass	37.1	28.2	26.7	27.3	27.9

Schauer PR et al. N Engl J Med 2014;370:2002-2013.

Diabetes medications needed



Value at Visit

Medical therapy	2.8	3.1	3.0	2.8	2.6
Sleeve gastrectomy	2.4	0.94	0.88	0.94	1.0
Gastric bypass	2.5	0.54	0.3	0.47	0.48

Schauer PR et al. N Engl J Med 2014;370:2002-2013.

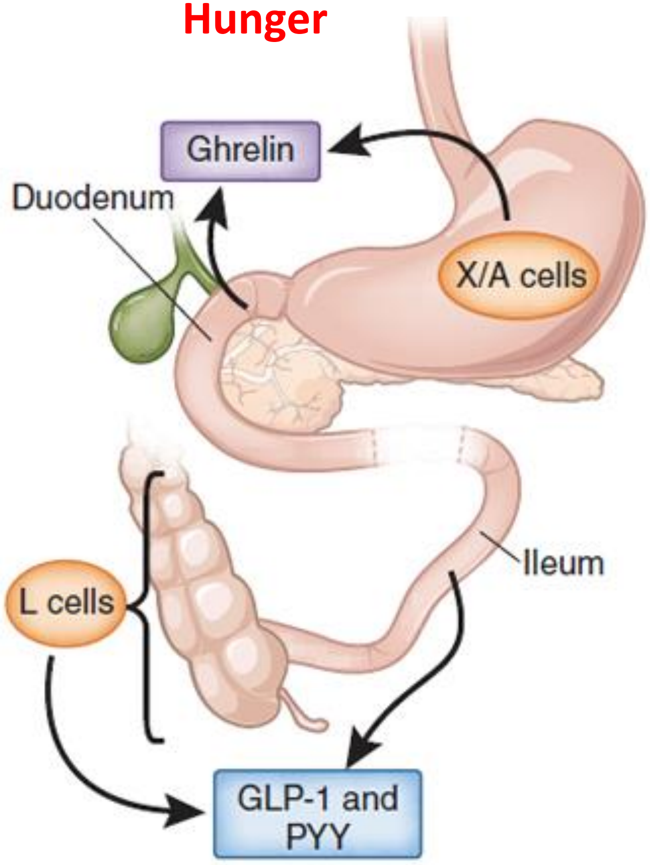
BENCH TO BEDSIDE

Metabolic insights from cutting the gut

VOLUME 18 | NUMBER 5 | MAY 2012 NATURE MEDICINE

Keval Chandarana & Rachel L Batterham

Hunger



Satiety

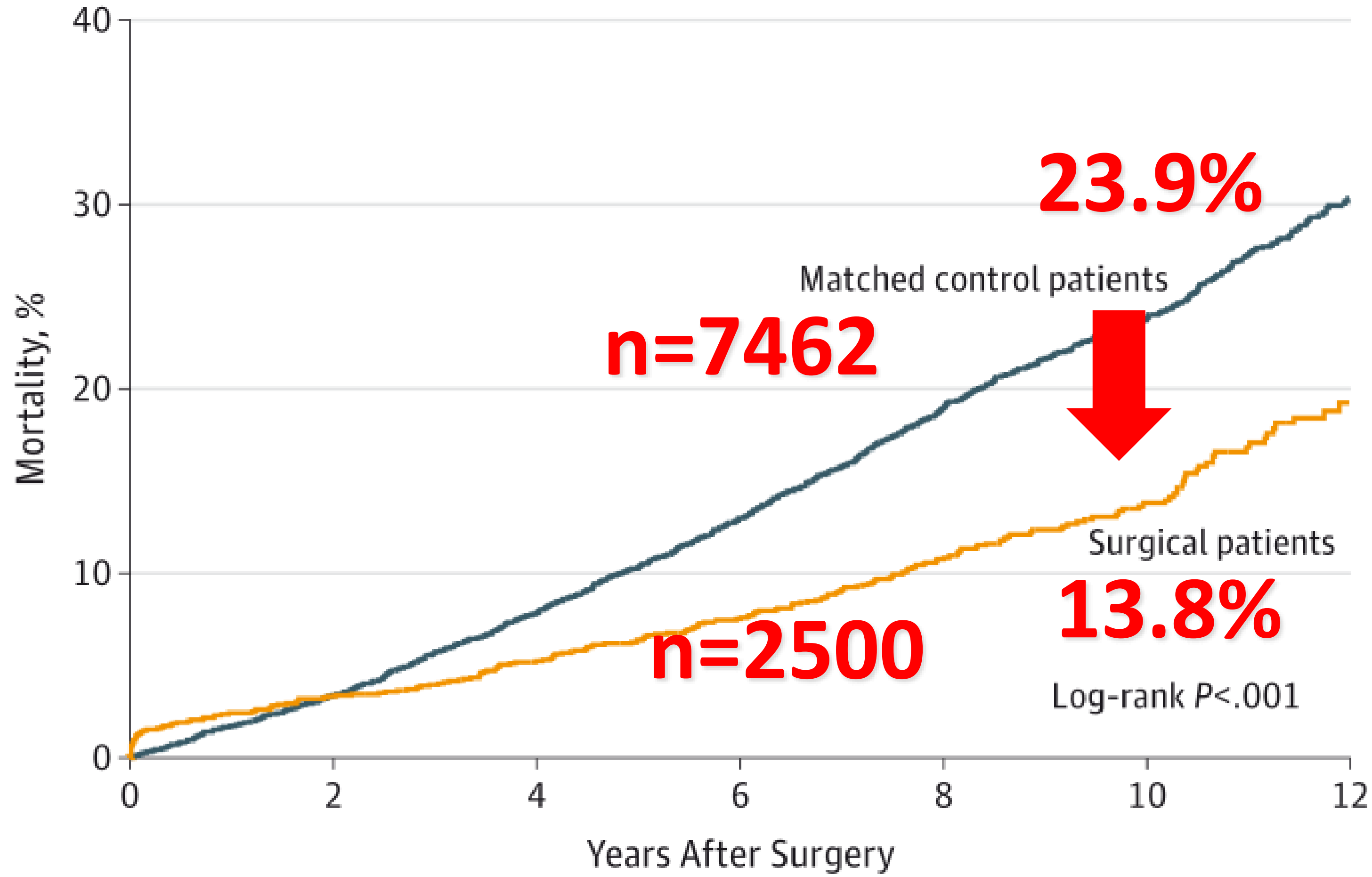
Bile acids & FXR

Gut microbiota

Benefits

- Short term
  - Weight loss
  - Glycemic control and diabetes remission
  - Improved quality of life
- Long term
  - Decreased mortality
  - Decreased CV events
  - Decreased cancer incidence

Bariatric Surgery and Long-Term Mortality

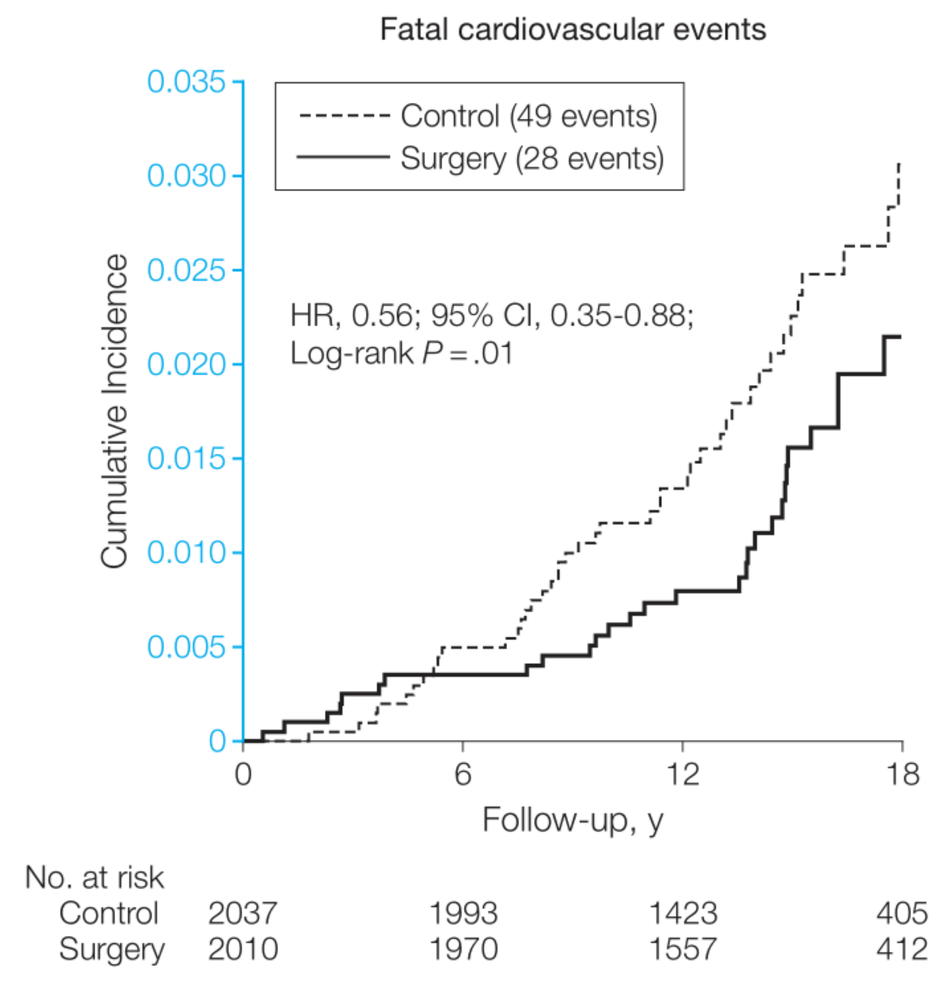


No. at risk							
Matched control patients	7462	7114	5306	3878	2641	1407	472
Surgical patients	2500	2416	1868	1412	1004	552	185

Arterburn DE et al. JAMA. 2015; 6;313(1):62-70.

Fatal CV events

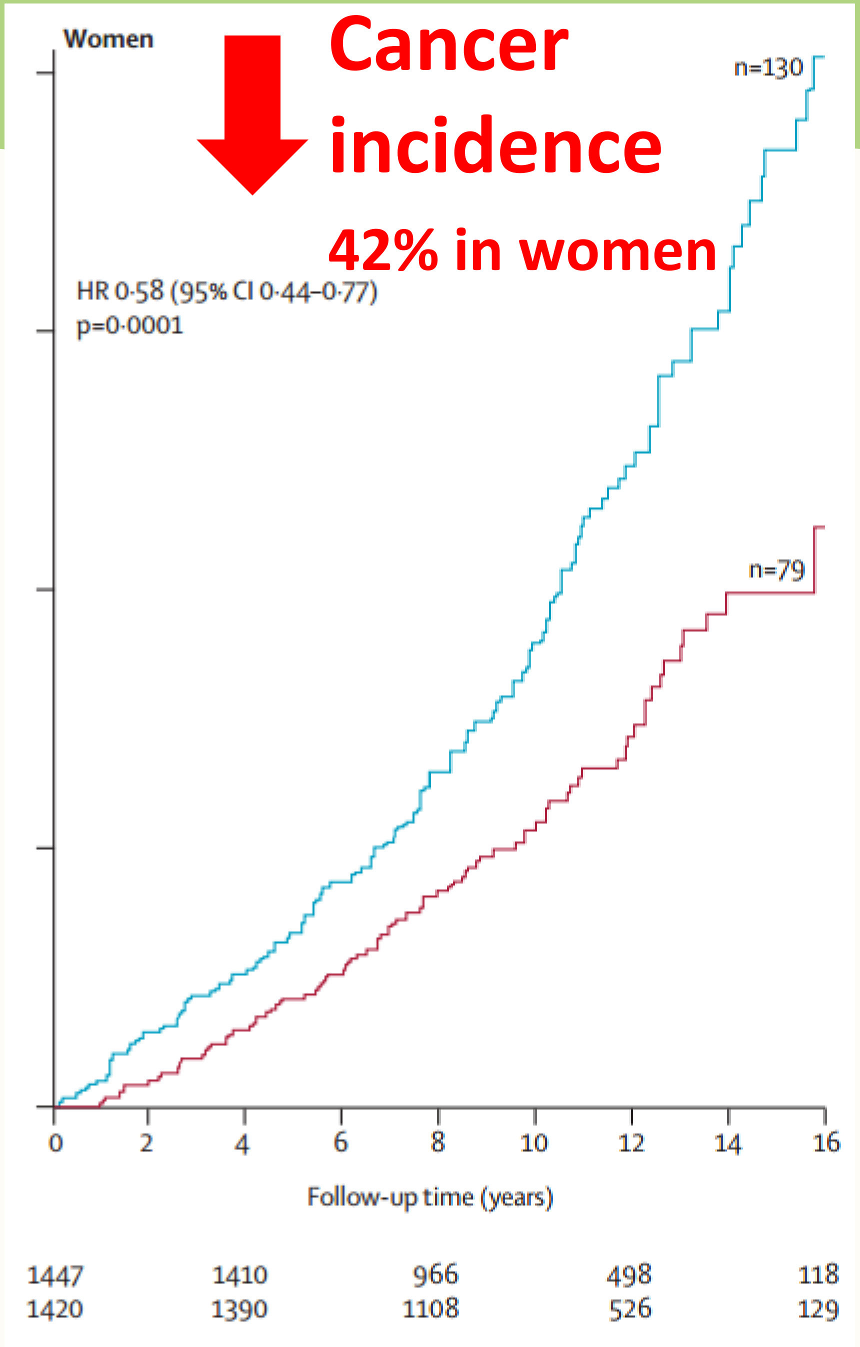
44%



Sjostrom et al. JAMA. 2012; 4;307(1):56-65.

Cancer incidence

42% in women



Sjostrom et al. Lancet Oncol. 2009;10(7):653-62.

Benefits

- Short term
  - Weight loss
  - Glycemic control and diabetes remission
  - Improved quality of life
- Long term
  - Decreased mortality
  - Decreased CV events
  - Decreased cancer incidence

Limitations

- Require patient compliance
- Cost
- Complications
  - Surgical and peri-operative
  - Nutritional and metabolic

Early post-op diet

วันที่ 1	จิบน้ำเปล่า
วันที่ 2	น้ำซุปใส
วันที่ 3-14	<u>เป้าหมาย</u> – โปรตีน 50-60 กรัม/วัน - ของเหลว 2 ลิตร/วัน (น้ำเปล่า 1ล., อาหารเหลว 1ล.) • จิบน้ำเปล่าอย่างน้อย 1 ลิตร/วัน • Neomune 6 ช้อนตวง+น้ำ 250 มล. x 2 มื้อ (โปรตีน 30 ก.), 120 บาท • ซุปไข่: น้ำซุปไก่หรือหมู 250 มล. + ไข่ทั้งฟอง 2 ฟอง คนจนสุก (โปรตีน 14 ก.) • โยเกิร์ต: (ปราศจากไขมันและน้ำตาล) 250 มล. (โปรตีน 8-10 ก.)

Early post-op diet

วันที่ 15-45	เป้าหมาย – อาหารอ่อน, โปรตีน 60 กรัม/วัน - ดื่มน้ำ 2 ลิตร/วัน ● โปรตีน 9 ส่วน/วัน = 18 ช้อนโต๊ะ/วัน ○ รับประทานเนื้อสัตว์ล้วน 3 ช้อนโต๊ะ/มื้อ x 6 มื้อ/วัน ○ ได้แก่ ปลานึ่ง, ไก่ต้ม, หมูตุ๋น, กุ้ง, ปู, เต้าหู้ ○ นมวัว (0% ไขมัน) 250 mL ทดแทนเนื้อสัตว์ได้ 2 ช้อนโต๊ะ ○ ไข่ทั้งฟอง 1 ฟอง ทดแทนเนื้อสัตว์ได้ 2 ช้อนโต๊ะ ○ โปรตีน whey 2 ช้อนตวง ทดแทนเนื้อสัตว์ได้ 2 ช้อนโต๊ะ ● ค่อยๆเริ่มรับประทานผักนิ่มหั่นซอยชิ้นเล็กฝอย ได้แก่ ฟักต้ม, บวบสุก, ผักกาดขาวสุก, น้ำเต้าสุก, กวางตุ้งสุก, ฟักทองสุก เสริม x 10 วัน จากนั้นเริ่มรับประทานผลไม้นิ่มชิ้นเล็ก เช่น แตงโม, กล้วยสุก, มะละกอสุก, เชอร์รี่ เสริม x 10 วัน จากนั้นเริ่มรับประทานข้าว ● เคี้ยวอาหารให้ละเอียดเสมอ

Post-operative vitamin supplementation

- **Centrum 1 tablet po bid**
- **FeSO4 1 tablet po OD**
- **Vitmain B12 (1000 mcg) 1 tablet po OD**
- **Vitamin D2 (20,000 IU) 1 capsule po weekly**
- **$CaCO_3$ (1,500 mg) 1 tablet po bid**

- **Total cost 330 baht/month = 11 baht/day**

Today's Outline

1. How much weight do I need to lose?
2. How many calories should I eat when I try to lose weight?
3. How do I lose weight?
4. How do I avoid weight regain after successful weight loss?
5. Bariatric surgery

Quiz

Q4. จะต้องลดน้ำหนักอย่างน้อยเท่าไร จึงจะมีความสำคัญทางคลินิก?

1. 1-5% of initial weight
2. 5-10% of initial weight
3. 10-15% of initial weight

Quiz

Q5. How many calories should I eat when I try to lose 0.5 kg of weight per week?

1. **-100 Calories per day**
2. **-500 Calories per day**
3. **+100 Calories per day**
4. **+500 Calories per day**

Quiz

Q6. What is the appropriate proportion of protein: CHO: vegetable in the plate method?

1. 1:1:1
2. 1:1:2
3. 1:2:1
4. 2:1:1

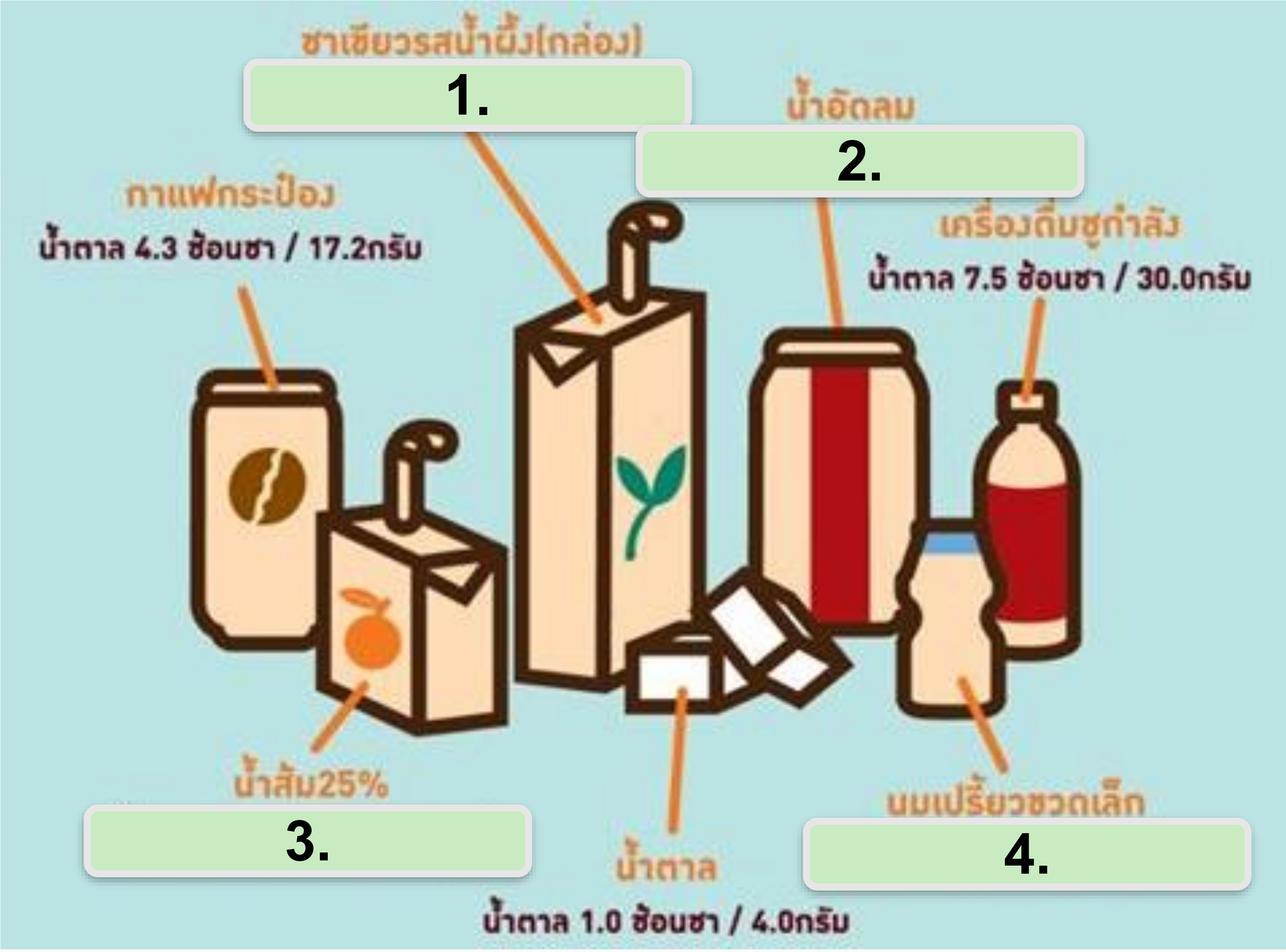
Quiz

Q7. What is the appropriate amount of sugar: fat: salt in 1 day?

1. 6 teaspoon: 6 teaspoon: 1 teaspoon
2. 6 teaspoon: 6 teaspoon: 6 teaspoon
3. 6 tablespoon: 1 tablespoon: 1 tablespoon
4. 6 tablespoon: 6 tablespoon: 1 tablespoon

Quiz

Q8. Which one has the highest sugar content?

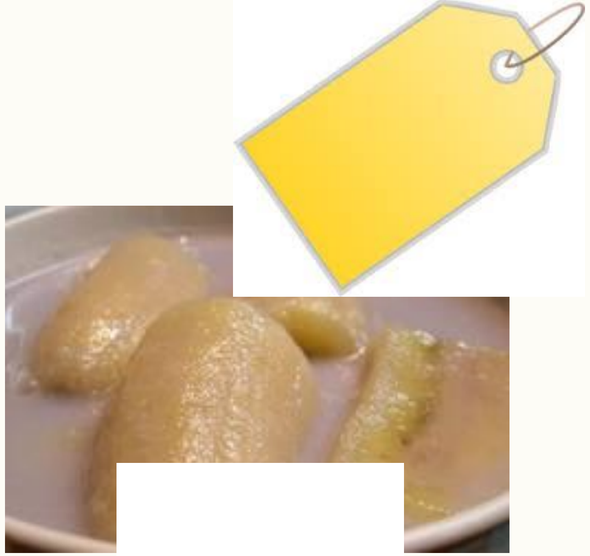


Q9. Which menu has the highest calories?

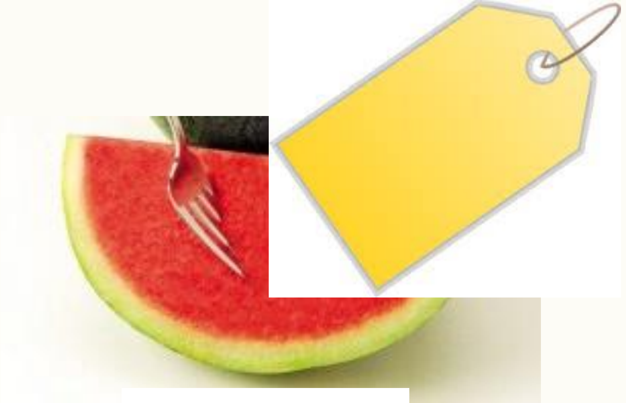
Quiz

Q10. Which menu has more calories?

A.



B.



Drug for Treatment of Obesity

- Pinpilai Jutasompakorn, MD
- Department of Pharmacology
- Faculty of Medicine Siriraj Hospital

กิจกรรมการเรียนในคาบ

Mentimeter

https://www.menti.com/

"ยาลดอ้วน" มรณะ สาวแม่ลูกอ่อนชาวอ่างทอง สั่งซื้อออนไลน์-กินช็อกดับ

ข่าว ทั่วไทย

ไทยรัฐฉบับพิมพ์

6 ก.ค. 2562 05:21 น.

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สาวแบงก์กินยาลดความอ้วนเสียชีวิต ล่าสุดแม่ตรอมใจสิ้นลม เผยพบสารอันตราย

วันที่ 13 พฤษภาคม 2561 - 15:18 น.

ข่าวสด

“ดูลูกแม่เป็นตัวอย่าง ถ้าไม่อยากตาย” สาวม.4 กินยาลดความอ้วน สิ้นใจสุดสลด

วันที่ 6 กันยายน 2562 - 19:29 น.

ข่าวสด

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บุกทลาย!!โรงงานผลิตยาลดอ้วน **OHO by** ปูนิ่ม ปนเปื้อน "Sibutramine"

http://crime.tnews.co.th/content/118288

ข่าวสด

อย.บุกจับ โรงงานผลิตกาแฟลดน้ำหนัก เจอแอบใส่สารไซบูทรามีน

วันที่ 3 ตุลาคม 2561 - 18:33 น.

นพ.ธเรศ กรัษนัยรวิวงค์ รองปลัดสธ. นำตรวจค้น

Daily Mail

60p

Pizzas. Nachos. Rice pud...

2 DAY SUMMER DIET recipes your family will love

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MORE GREAT OFFERS INSIDE

Coroner attacks online dealers who target the vulnerable

BANNED SLIMMING DRUG KILLS MEDICAL STUDENT

Death of medical student Sarah Houston after taking banned slimming drug “Dinitrophenol” highlights dangers of buying pills online

Eloise Parry, 21, who had battled with bulimia, bought tablets containing “Dinitrophenol” via the internet using her online payment account

Anti-obesity drugs

- **Medicinal strategies in treatment of obesity**
- **History of anti-obesity drugs**
- **Current anti-obesity drugs**

Medicinal strategies in the treatment of obesity

- Reduce calories in

  - Reduce food intake (anorexigenic agents)

  - Reduce caloric absorption (block fat absorption)

- Increase energy expenditure: increase metabolism

Drugs that have been introduced into the market

Before 1900 — **Thyroid hormone**

Reduced lean body mass
cardiac arrhythmias & arrest

1920s — **Dinitrophenol**

Agranulocytosis, dermatitis, cataracts, fatal hyperthermia

↑energy expenditure

↓calories in

1930s — **First amphetamine*** **introduced**

1959 — **FDA approval of Phentermine***

1992 — **Fenfluramine***

Pulmonary hypertension,
heart valve disease

1997 — **FDA approval of Sibutramine***

Increase risk for stroke and myocardial infarction

1999 — **FDA approval of Orlistat**

possible↑ risk of cancer

2006 — **EMA approval of Rimonabant**
(Cannabinoid receptor antagonist)

Depression, suicide ideation

2012 — **FDA approval of Lorcaserin & Phentermin/topiramate**

FDA approval of liraglutide & Natrexone/bupropion

Current anti-obesity drugs

Block fat absorption

- Orlistat

Reduce food intake

- Amphetamine-like drugs
- Phentermine and topiramate (Qsymia®)
- Natrexone/bupropion
- Glucagon-like peptide-1 (GLP-1) agonist
- Dual GLP-1 and GIP receptor agonist

All drugs can be use as adjunctive therapy for chronic weight management except for Amphetamine-like drugs

Indication and usage

Patients at high risk from obesity

- BMI ≥ 30 kg/m^2 or
- BMI ≥ 27 kg/m^2 with other risk factors: HTN, DM, DLP

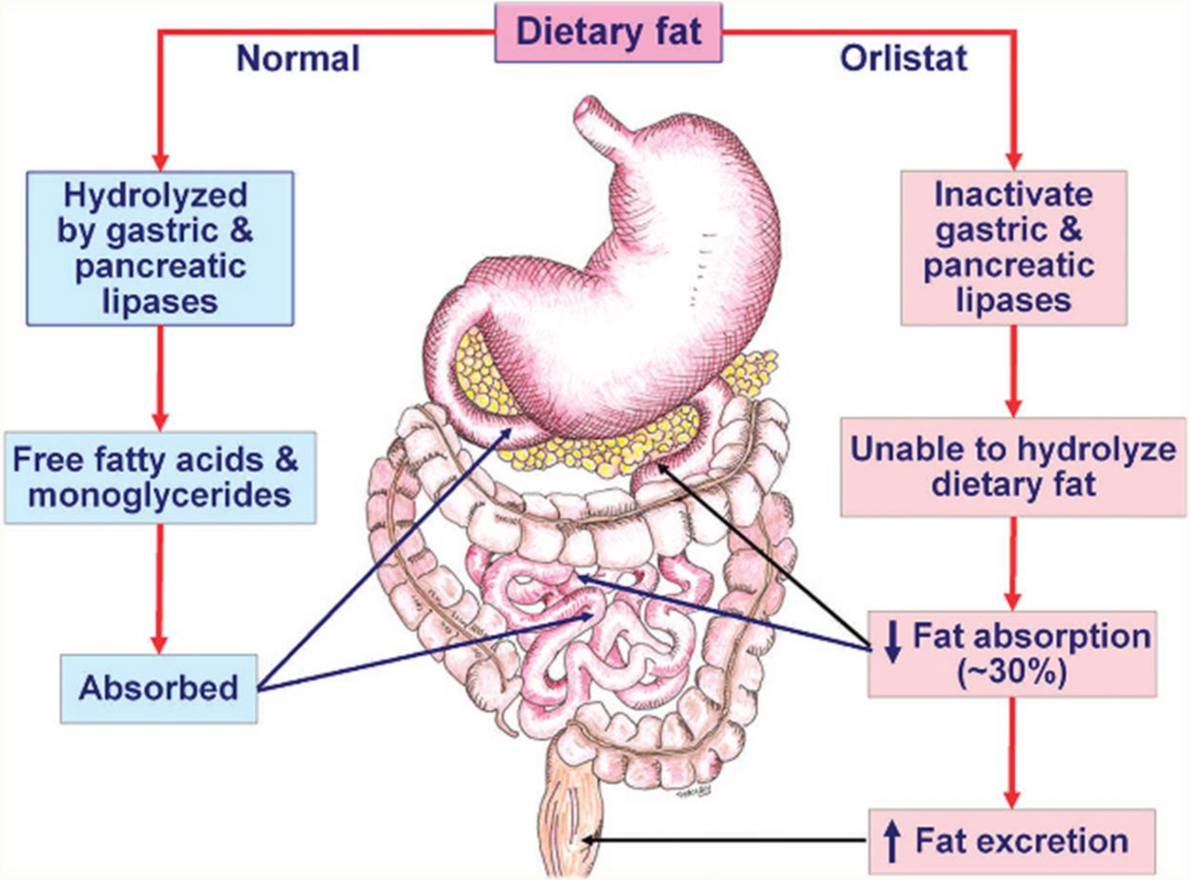
And diet/exercise have not achieved acceptable weight loss

Drugs are used as an adjunct to a reduced-calorie diet and increased physical activity

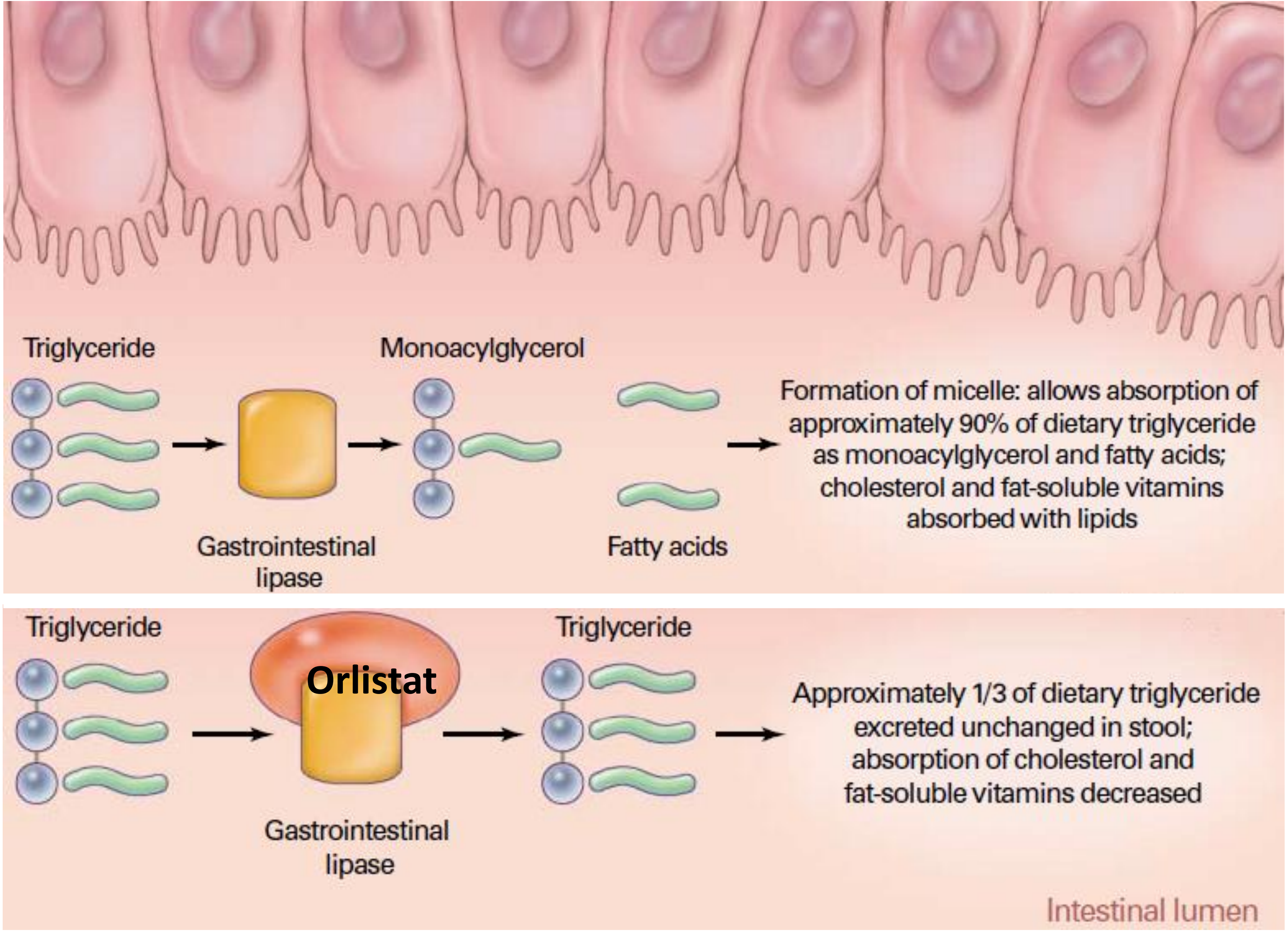
Block fat absorption

Orlistat

- Gastric & pancreatic lipase inhibitor



Elangbam CS. Vet Pathol. 2009 Jan;46(1):10-24.



Yanovski & Yanovski. NEJM 2002

Block fat absorption

Orlistat

- Adverse effects

- Absorption is minimal.

- GI side effects: oily, loose stools, fecal incontinence, frequent bowel movements, and flatulence

Vitamin supplements is recommended in long term use.

Drug reduce food intake

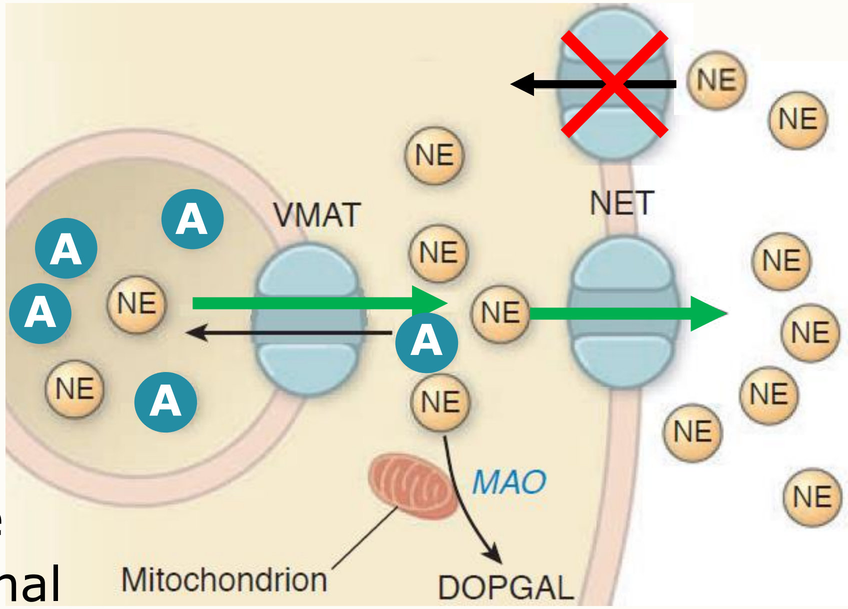
Amphetamine-like drugs: phentermine, diethypropion

- ↓Reuptake and ↑release of NE (Sympathomimetic)

- Appetite suppression: Activation of α1 and β2-adrenoceptors at paraventricular hypothalamic nucleus

- Lipolysis: Activation of β3-adrenoceptor at adipocyte

Nerve terminal



NET: norepinephrine transporter
VMAT: Vesicular monoamine tranportors

Principle of Pharmacology: The Pathophysiologic Basis of Drug Therapy. 3rd ed.

Drug reduce food intake

Amphetamine-like drugs

- Short term treatment (up to 12 weeks)
- Adverse effects
  - Headache, restlessness, insomnia and dry mouth
  - Increase heart rate and blood pressure
  - Dependence
- Contraindication
  - Coronary artery disease
  - Uncontrolled hypertension
  - Hyperthyroidism
  - Co-administration with MAOIs
  - History of drug abuse

Drug reduce food intake

Phentermine/topiramate extended release (Qsymia®)

Phentermine (Amphetamines derivatives)

- ↑Release of NE: promote satiety

Topiramate

- Treatment of epilepsy/migraine prophylaxis
- Demonstrated unexpected weight loss benefit
- Mechanism of ↓food intake: not entirely understood

Combining low dose phentermine & low dose topiramate

: additive effect on weight loss and fewer side effects

Drug reduce food intake

Phentermine/topiramate extended release (Qsymia®)

- Adverse effects
  - Paresthesia, altered taste
  - Dry mouth, constipation, insomnia
- Contraindications
  - Pregnancy (increased risk of oral clefts)
  - Glaucoma
  - Hyperthyroidism
  - Co-administration with MAOIs

Drug reduce food intake

Glucagon-like peptide-1 (GLP-1) agonist

- Initially developed for the treatment of type 2 DM

- Stimulate GLP-1 receptor at pancreas:

  ↑insulin secretion (β-cell) ↓glucagon secretion (α-cell)

- Mechanisms of weight reduction: decrease food intake

- Stimulate GLP-1 receptor at vagal afferent neuron: inhibit GI motility (tachyphylaxis)

- Stimulate GLP-1 receptor at **POMC/CART neurons**: **increase POMC/CART neurons activities**

J Clin Invest. 2014 Oct;124(10):4223-6.

Drug reduce food intake

Glucagon-like peptide-1 (GLP-1) agonist

- Liraglutide (Saxenda®): once-daily subcutaneous injection
- Semaglutide (Wegovy®): once-weekly subcutaneous injection

(oral semaglutide for weight management – waiting for approval)

- Adverse effect
  - Common: nausea, vomiting, diarrhea (transient)
  - Cholelithiasis
  - Hypoglycemia: in combination with sulfonylureas/insulin
- Contraindication: Medullary thyroid carcinoma/MEN 2

Drug reduce food intake

Dual GLP-1 and GIP receptor agonist

- Terzepatide (Zepbound®): once-weekly subcutaneous injection

Glucose-dependent insulinotropic polypeptide (GIP)

- Treatment of type 2 DM
  - ↑insulin secretion and ↓glucagon secretion
  - ↑glucagon levels in euglycemic/hypoglycemic conditions
  - Improve insulin sensitivity
- Enhance lipid-buffering capacity of white adipose tissue
- Decrease food intake (CNS)

Investigational drugs

Nutrient-Stimulated Hormone-Based Medication

Stimulate metabolic effects of enterohepatic hormones:

- Glucagon-like peptide-1 (GLP-1)
- Glucose dependent insulinotropic polypeptide (GIP)
- Glucagon
- Amylin

Spotlight on the pipeline

- Triple GIP, GLP-1, and glucagon receptor agonist
- Dual GLP-1 and glucagon receptor agonists
- Dual GLP-1 and amylin agonist

Current anti-obesity drugs

Drugs	Dose	Average weight loss (%) ≈1year placebo-subtracted weight loss
**Amphetamine-like drugs	-	NA
**Orlistat	120 mg TID	2.9-3.4
*Phentermine/topiramate	15/92 mg daily	8.6-9.3
Naltrexone/bupropion	32/360 mg daily	4.8-5.2
**Liraglutide	3 mg SC daily	5.4
**Semaglutide	2.4 mg SC weekly	12.4
**Terzepatide	15 mg SC weekly	17.8
Retatrutide (Triple-hormone RA)	**12 mg SC weekly**	**22.1** (phase II)

Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. JCEM 2015.
A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. NEJM 2015.
Once-Weekly Semaglutide in Adults with Overweight or obesity. NEJM 2021.
Tirzepatide Once Weekly for the Treatment of Obesity. NEJM 2022.

Can drugs cause weight gain?

	Drugs cause weight gain	Alternatives- weight reducing
Antidepressants	**TCAs:** Amytriptyline, Nortriptyline **SSRIs:** Paroxetine **NaSSA**: Mirtazapine	**NDRIs**: Bupropion↓ short term **SSRIs**: Fluoxetine↓ 4-12 wks Sertraline↓
Mood stabilizers	Lithium	
Atypical Antipsychotic	Clozapine, Olanzapine, Quetiapine, Risperidone	Ziprasidone, Aripiprazole
Anticonvulsants	Carbamazepine, Valproate, Gabapentin, Pregabalin, Vigabatrin,	felbamate↓, topiramate↓, zonisamide↓
Diabetes drugs	**Insulin, Sulfonylureas, Thiazolidinediones**	**GLP-1 agonists↓, Metformin↓, SGLT-2 inhibitors↓**

Other drugs that cause weight gain include Protease inhibitors, Corticosteroids, antihistamines with CNS activity (sedation)

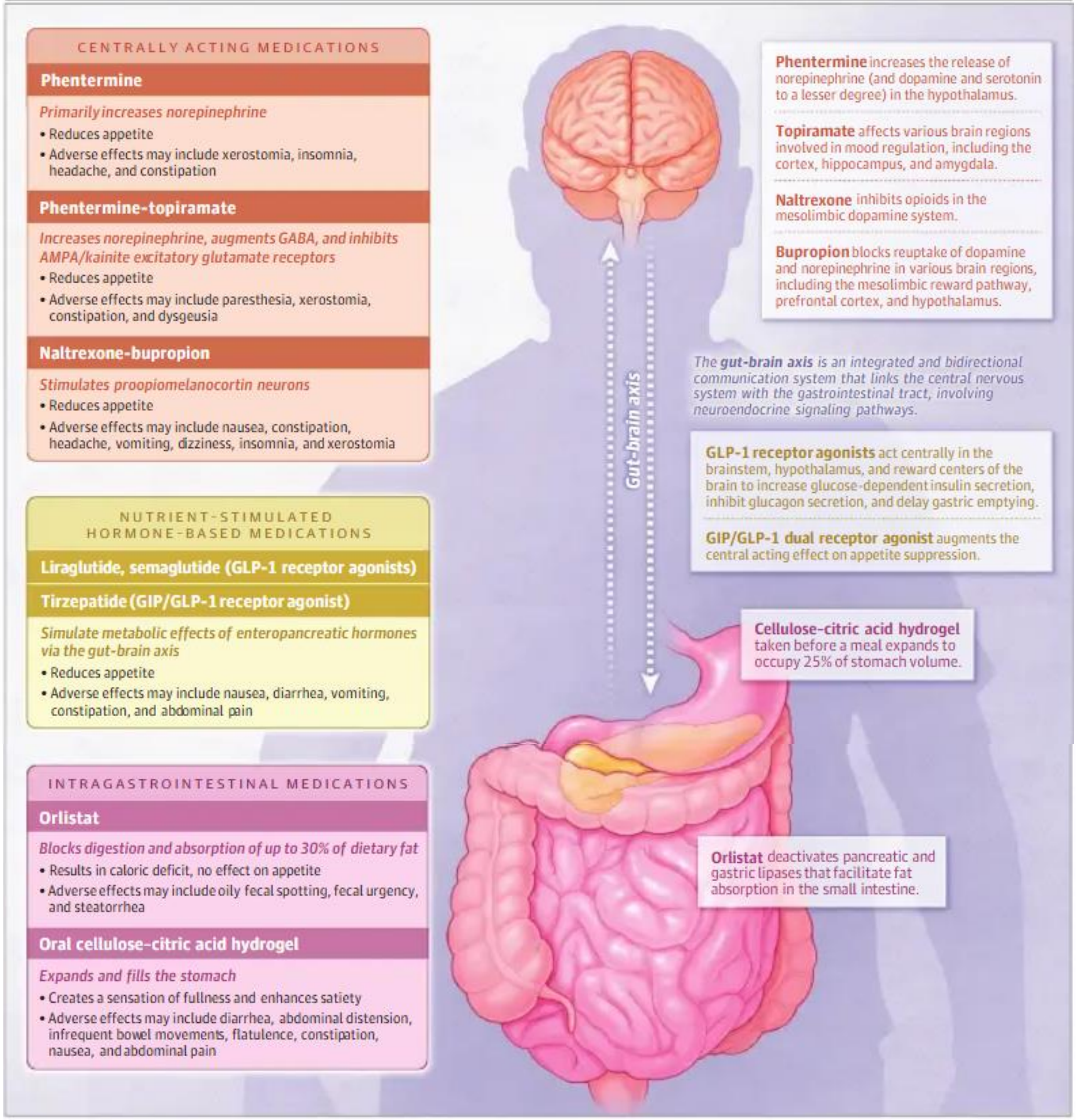
JAMA | Review

Medications for Obesity
A Review

Kimberly A. Gudzune, MD, MPH; Robert F. Kushner, MD, MS

JAMA. 2024;332(7):571-584.

Figure 1. Mechanisms of Action and Common Adverse Effects of 3 Classes of Antiobesity Medication



AMPA indicates α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA, γ-aminobutyric acid; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide 1.

Quiz

Choose 1 if a statement is true and

choose 2 if a statement is false.

11 . Anti-obesity drugs can be used instead of exercise and behavior changes.

Quiz

12. Anti-obesity drug is indicated in which of the followings?

1. BMI 35 kg/m^2
2. BMI 30 kg/m^2, diet and exercise have not achieved acceptable weight loss
3. BMI 27 kg/m^2 with type 2 diabetes mellitus

Quiz

13. Which of the following drugs directly reduces caloric absorption?

1. **Oristat**
2. **Liraglutide**
3. **Phentermine**

Quiz

14. Which of the following glucose lowering drugs causes weight gain?

1. Liraglutide
2. Metformin
3. Sulfonylureas
4. GLP-1 agonists

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https://forms.gle/5GGfeL5rfJBdgj9L8