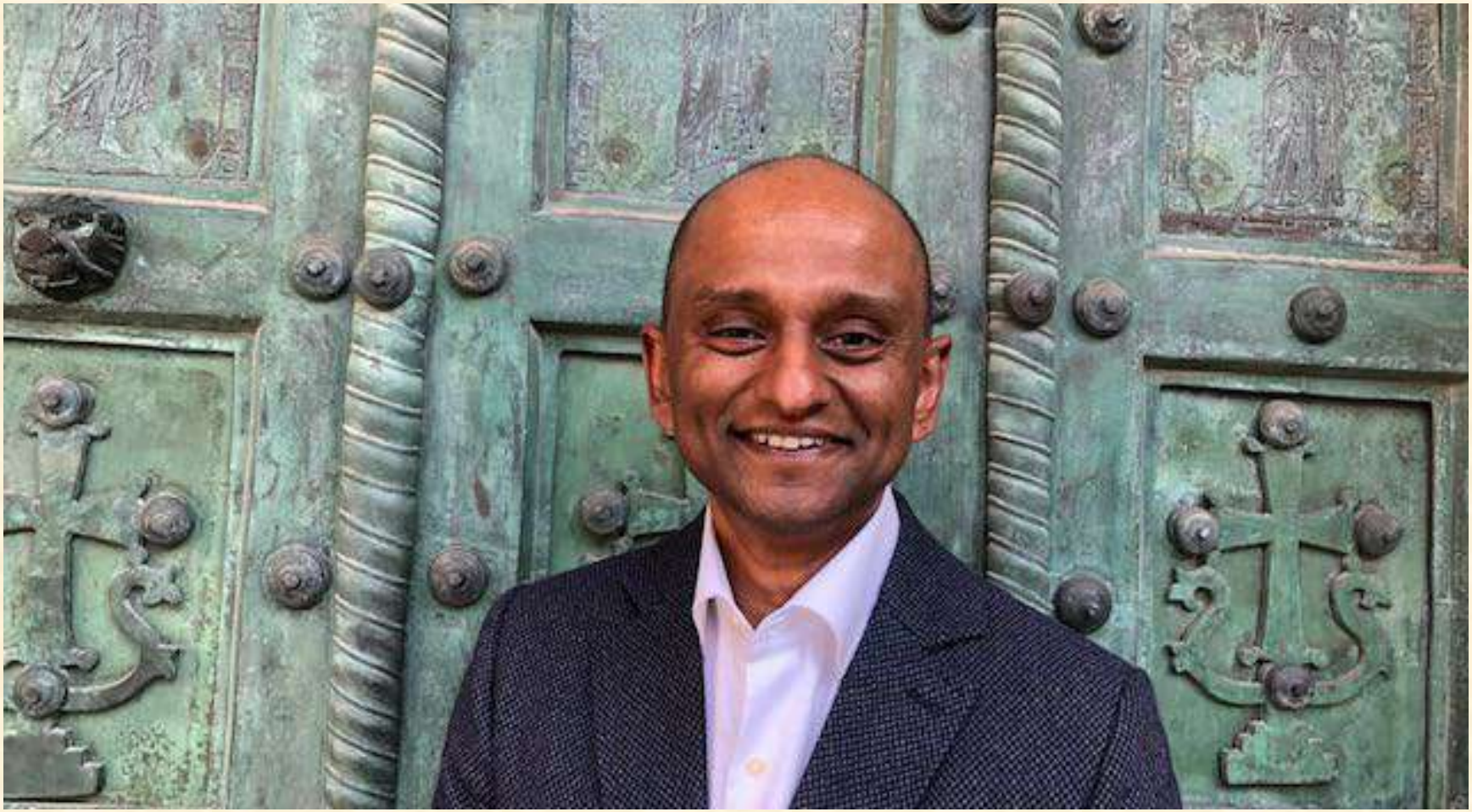
Why Are People Fat ?

A/Prof Harsha Chandraratna
Obesity Surgery WA
Subiaco / Murdoch / Mandurah / Booragoon

Who am I ?



So what's the big deal …..?

Medical Complications of Obesity

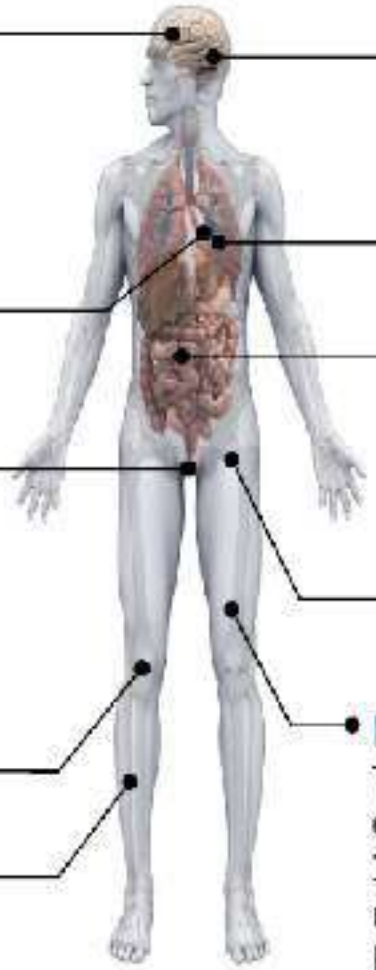
- Metabolic
- Structural
- Inflammatory
- Degenerative
- Neoplastic
- Psychological

236

comorbidities affecting EVERY organ system and medical specialty

Yuen M … Kaplan LM , Obesity Week 2016

OBESITY: A MAJOR CONTRIBUTOR TO DISEASE



Psychological[1]
Depression
Poor self-image
Poor quality of life
Eating disorder

Neurologic[1]
Stroke
Intracranial hypertension
Dementia

Cardiovascular[1]
Atherosclerosis
Hypertension
Dyslipidemia
CHF

Pulmonary[1]
Obstructive sleep apnea
Hypoventilation syndrome
Asthma
Pulmonary hypertension
Dyspnea

Gastrointestinal[1]
Nonalcoholic fatty liver disease
Gall bladder disease
GERD
Hernia

Genitourinary[1]
PCOS
Abnormal menses
Infertility
Urinary incontinence
Low testosterone

Cancer[2]
Esophagus
Stomach
Colorectal
Liver
Gallbladder
Pancreas
Breast
Corpus uteri
Ovary
Kidney
Meningioma
Thyroid
Multiple myeloma

Metabolic[1]
Type 2 diabetes
Gout
Insulin resistance
Metabolic syndrome

Musculoskeletal[1]
Low back pain
Osteoarthritis
Restrictive mobility

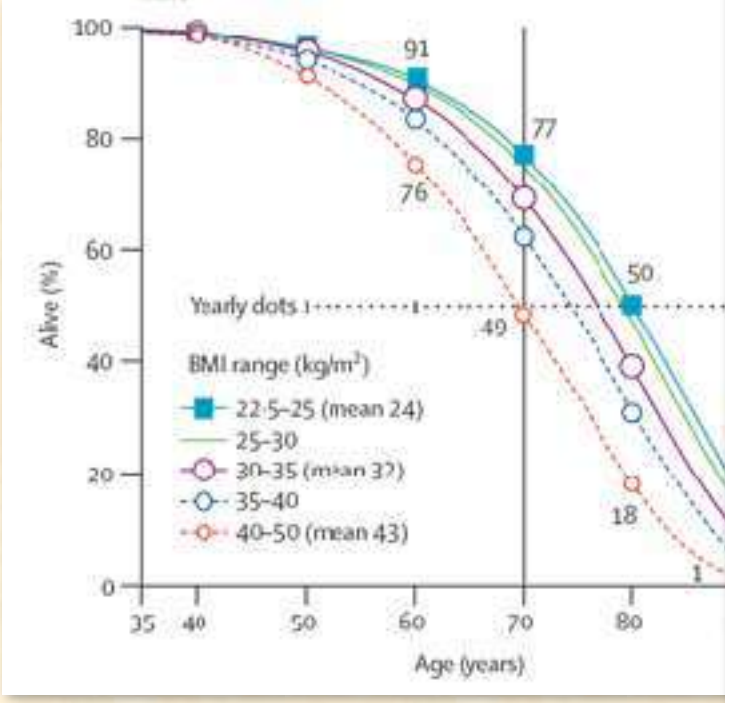
Dermatologic[1]
Venous stasis
Cellulitis

CHF=congestive heart failure; GERD=gastroesophageal reflux disease; PCOS=polycystic ovarian syndrome.

1. Catenacci VA et al. *Clin Chest Med*. 2009;30:415-444. 2 Lauby-Secretan B et al. *N Engl J Med*. 2016;375:794-798.

Obesity shortens life expectancy

Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects

Lars Sjöström, M.D., Ph.D., Kristina Narbro, Ph.D., C. David Sjöström, M.D., Ph.D., Kristjan Karason, M.D., Ph.D., Bo Larsson, M.D., Ph.D., Hans Wedel, Ph.D., Ted Lystig, Ph.D., Marianne Sullivan, Ph.D., Claude Bouchard, Ph.D., Björn Carlsson, M.D., Ph.D., Calle Bengtsson, M.D., Ph.D., Sven Dahlgren, M.D., Ph.D., Anders Gummesson, M.D., Peter Jacobson, M.D., Ph.D., Jan Karlsson, Ph.D., Anna-Karin Lindroos, Ph.D., Hans Lönroth, M.D., Ph.D., Ingmar Näslund, M.D., Ph.D., Torsten Olbers, M.D., Ph.D., Kaj Stenlöf, M.D., Ph.D., Jari Torgerson, M.D., Ph.D., Göran Ågren, M.D., and Lena M.S. Carlsson, M.D., Ph.D., for the Swedish Obese Subjects Study

ABSTRACT

BACKGROUND

Obesity is associated with increased mortality. Weight loss improves cardiovascular risk factors, but no prospective interventional studies have reported whether weight loss decreases overall mortality. In fact, many observational studies suggest that weight reduction is associated with increased mortality.

METHODS

The prospective, controlled Swedish Obese Subjects study involved 4047 obese subjects. Of these subjects, 2010 underwent bariatric surgery (surgery group) and 2037 received conventional treatment (matched control group). We report on overall mortality during an average of 10.9 years of follow-up. At the time of the analysis (December 1, 2006), vital status was known for all but three subjects (follow-up rate, 99.9%).

Surgery Can Save Lives

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects

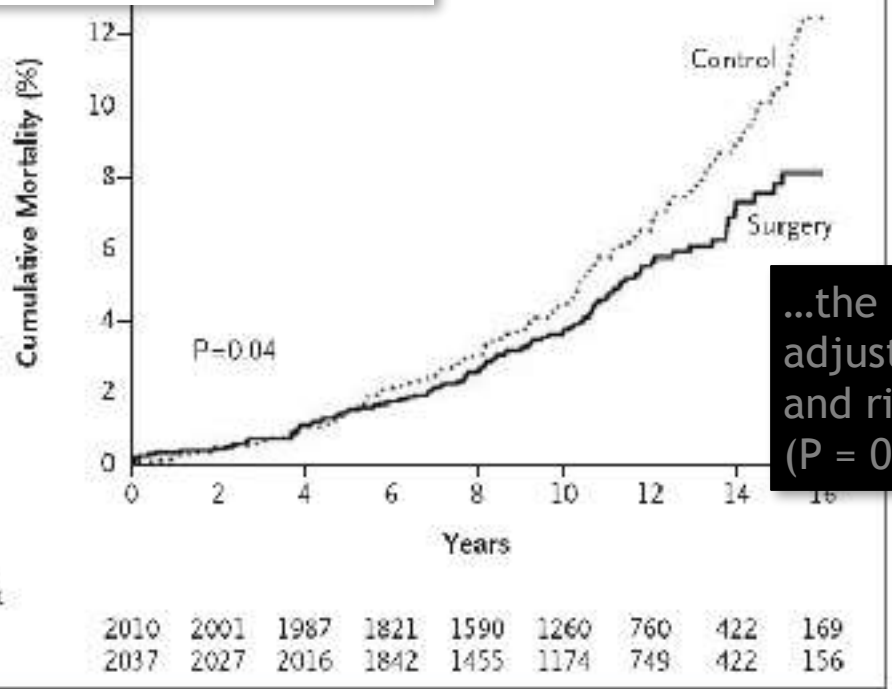
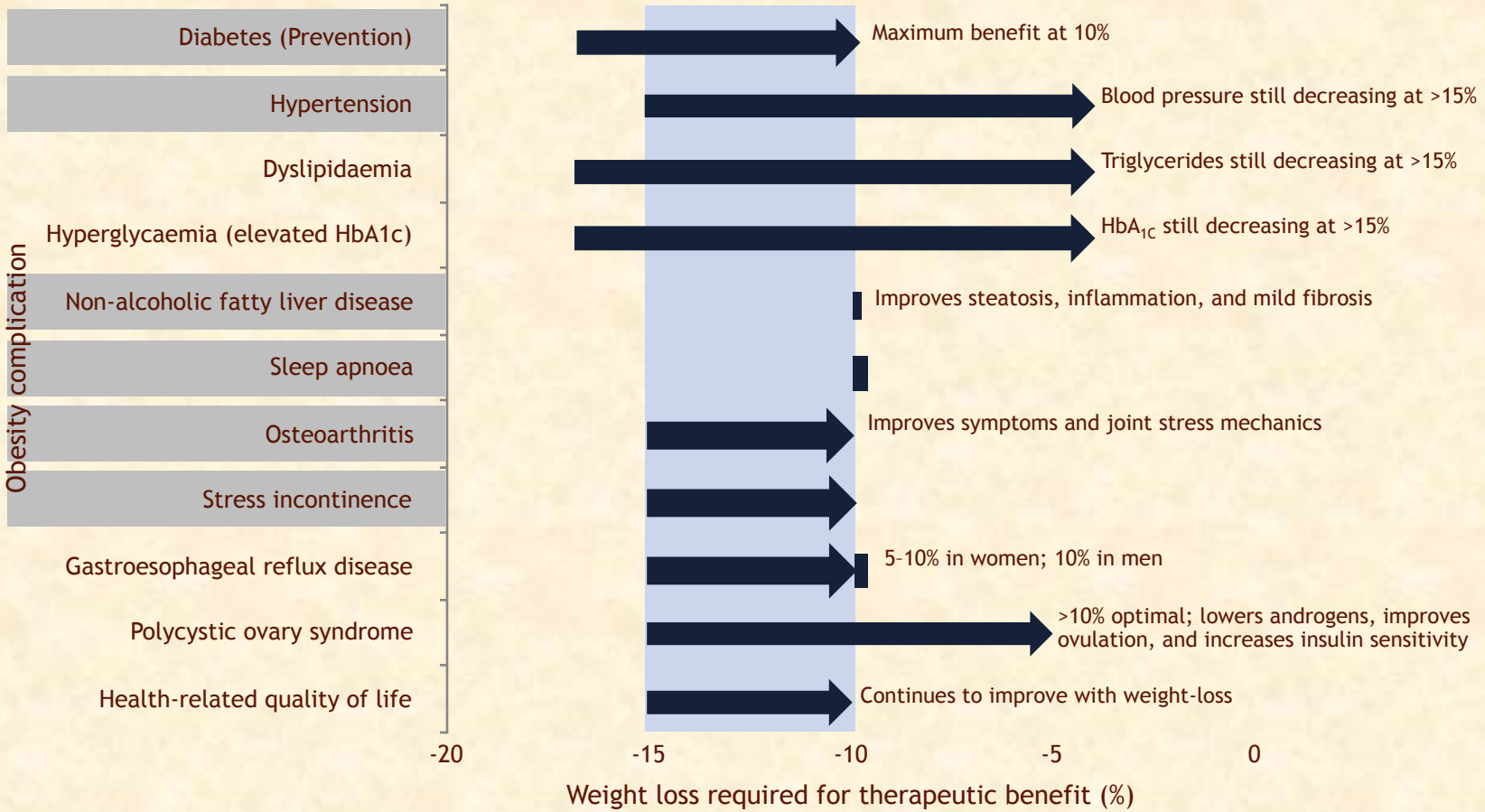


Figure 2. Unadjusted Cumulative Mortality.

The hazard ratio for subjects who underwent bariatric surgery, as compared with control subjects, was 0.76 (95% confidence interval, 0.59 to 0.99; P=0.04), with 129 deaths in the control group and 101 in the surgery group.

…the hazard ratio adjusted for sex, age, and risk factors was 0.71 (P = 0.01).

5–10% weight loss is clinically meaningful



Cefalu WT et al. Diabetes care 2015;38(8):1567-82. Wright F et al. J Health Psychol. 2013;18:574-86.

The Plan

- A series of issues
- I will try to bring things into perspective ….

Conventional Thinking

vs

Modern Thinking

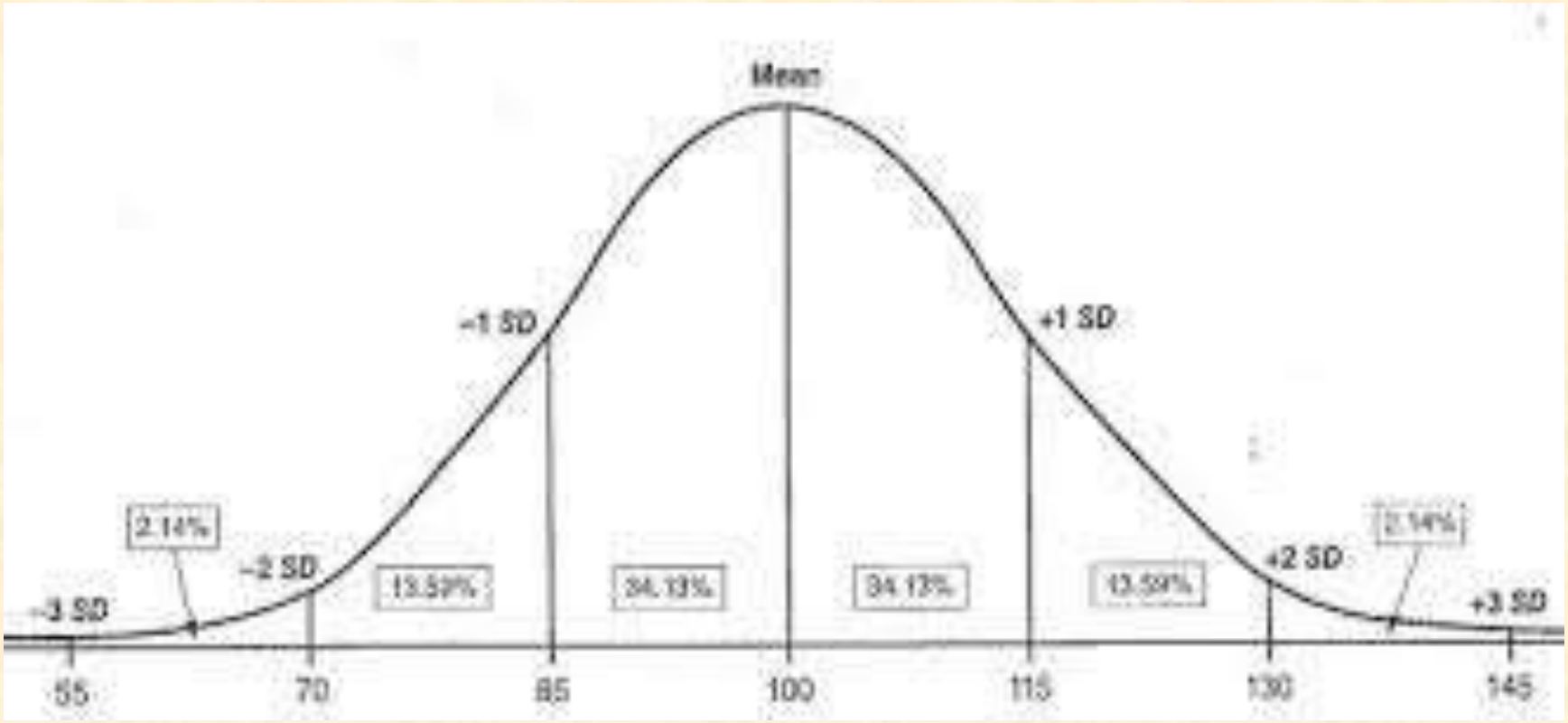
1) Everyone is different

- We knew that,

  - but what this really means is that the research is unpredictable

  - so we have to see the individual …..

Everything is a Bell Curve



2) Separating

GLUTTONY

DISEASE

Your Perception

- A patient with a disease
- Avoid judgement
- Is it there fault ?

What Really is Obesity ?

- A collection of disease processes
- Multiple processes may be at work in one individual, with additive effects
- Most are not reversible by simple means

But Even Gluttony ……

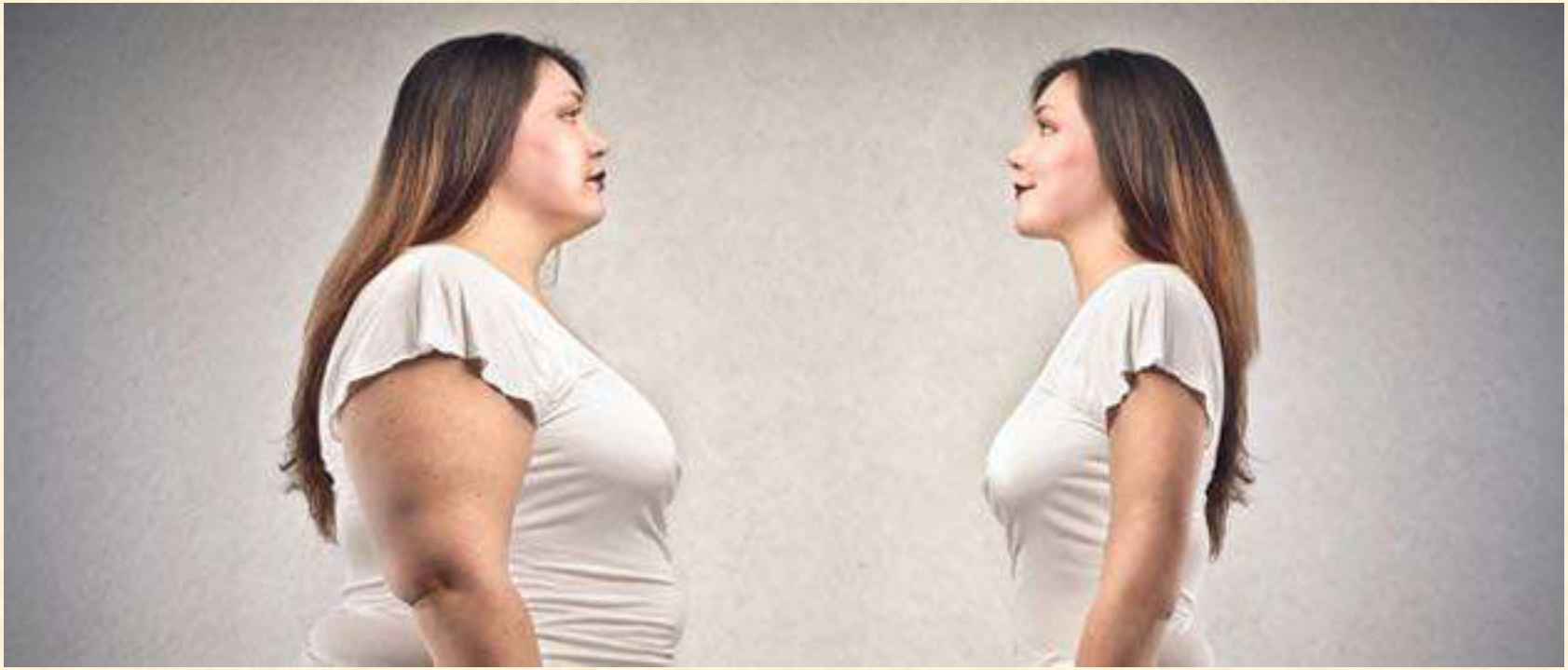
- Stress / Comfort eating

..at some point in our lives all of us will resort to food to make us feel better….

Allain de Botton

3) Genetics vs Environment

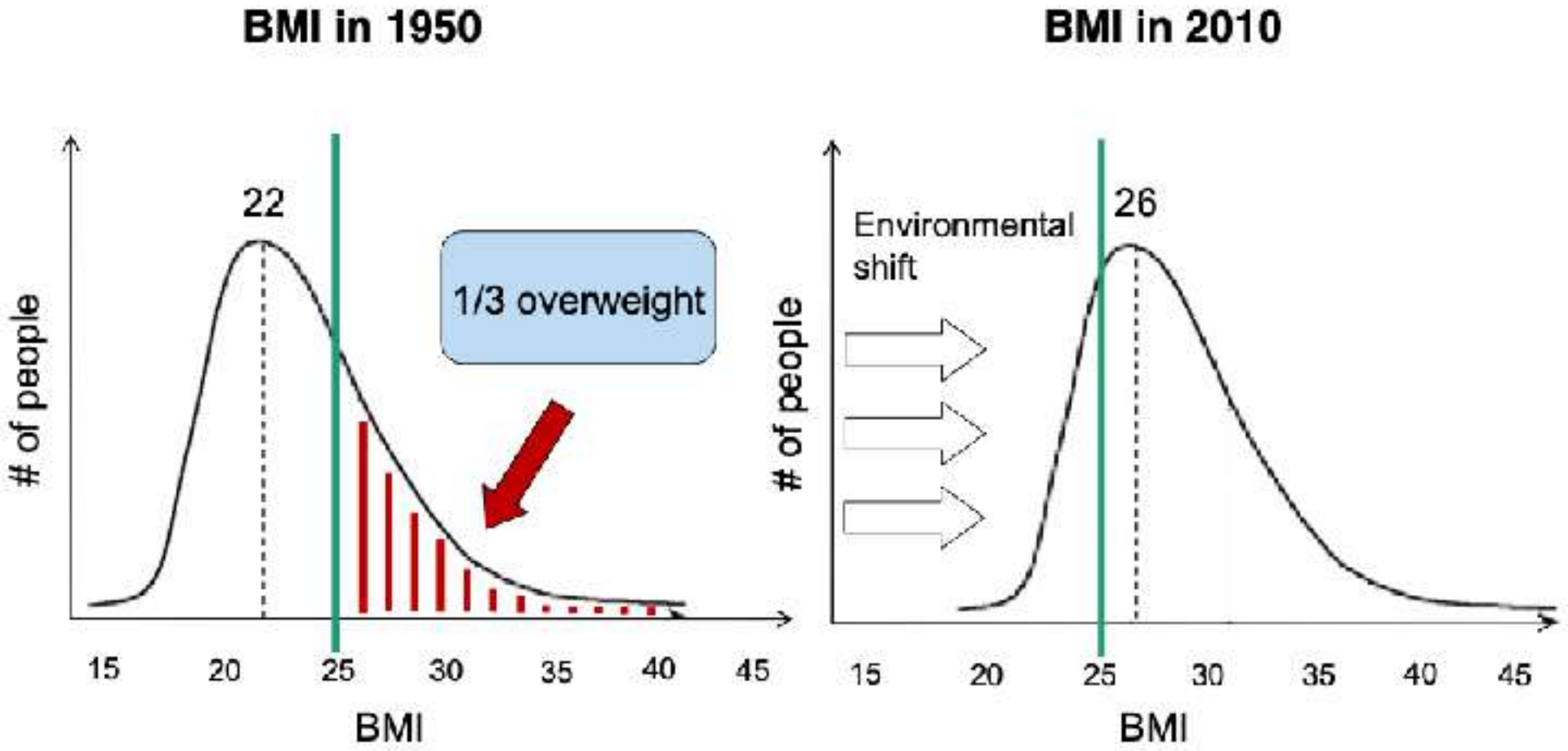
- We now live in an Obesio-genic Environment



Environment

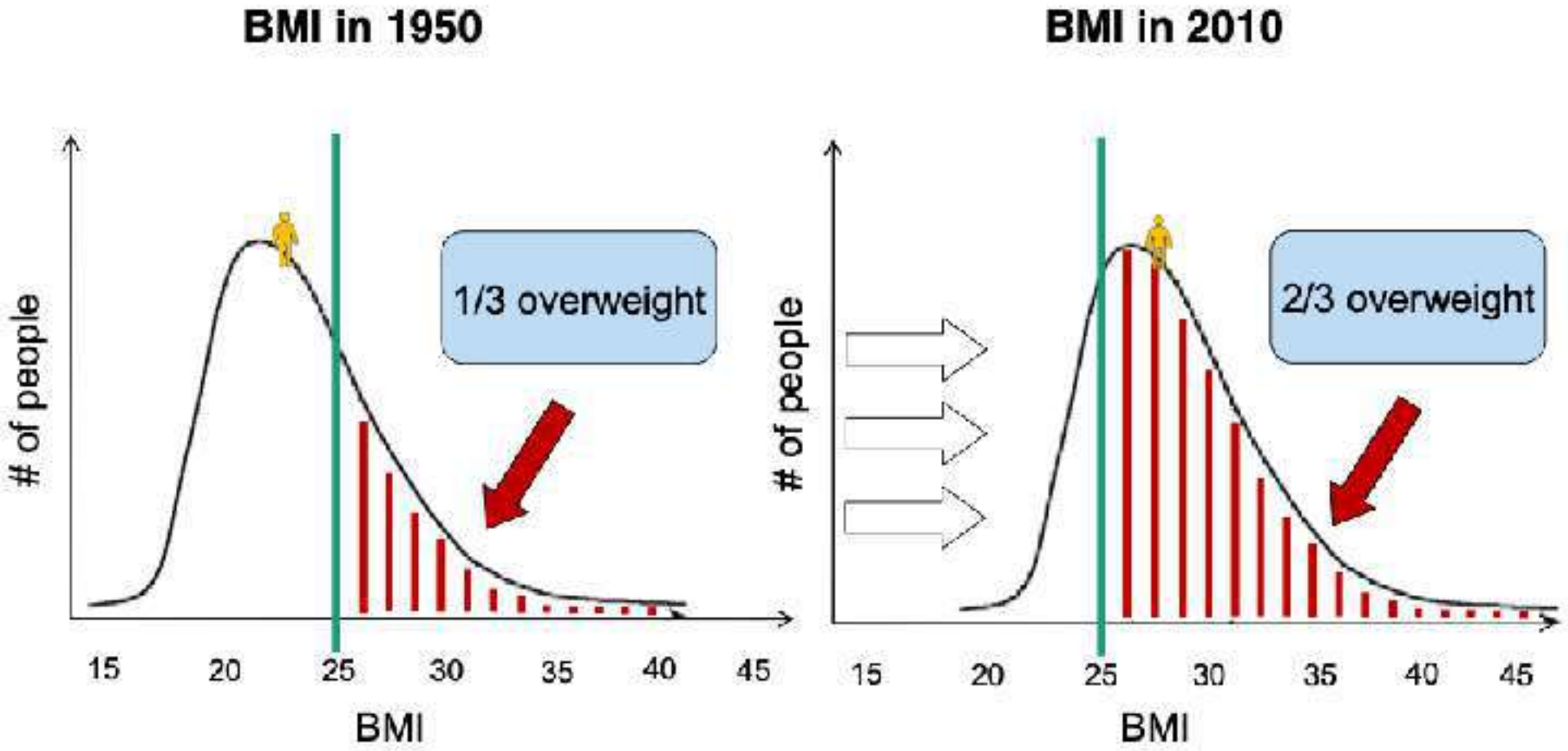
- Abundant Calorie Dense Food
- Bad social behaviours
- Eat to enjoy / Eat to live
- Diet in childhood

Genetic Susceptibility Influenced by the Environment



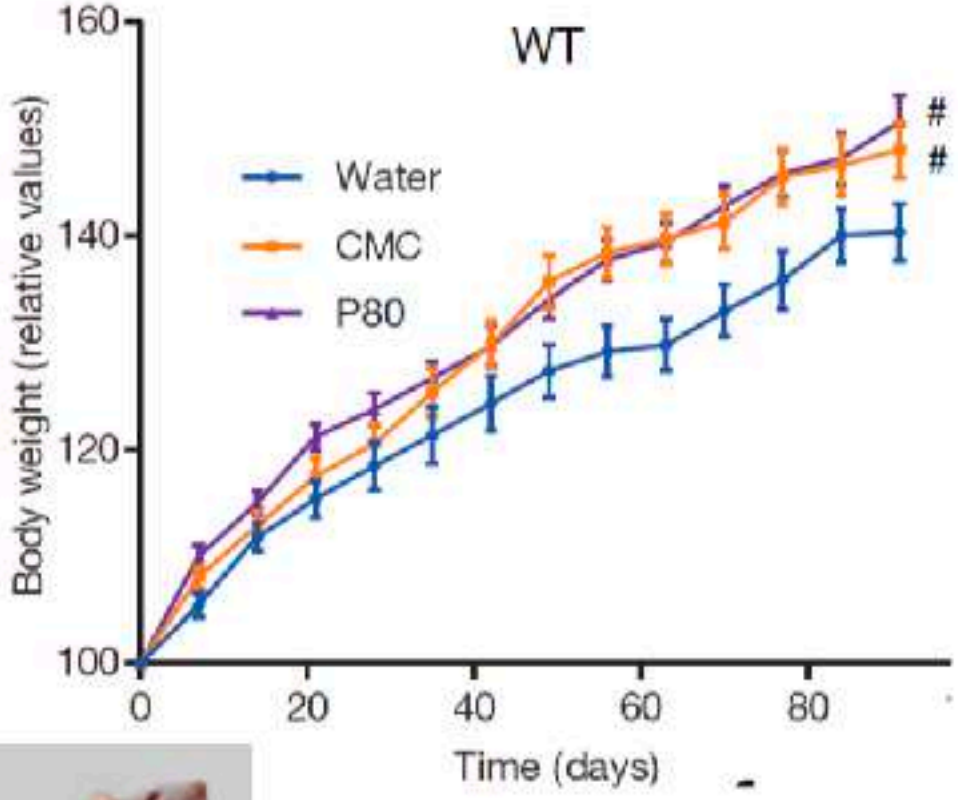
Slide provided by Ida Hatoum

Genetic Susceptibility Influenced by the Environment

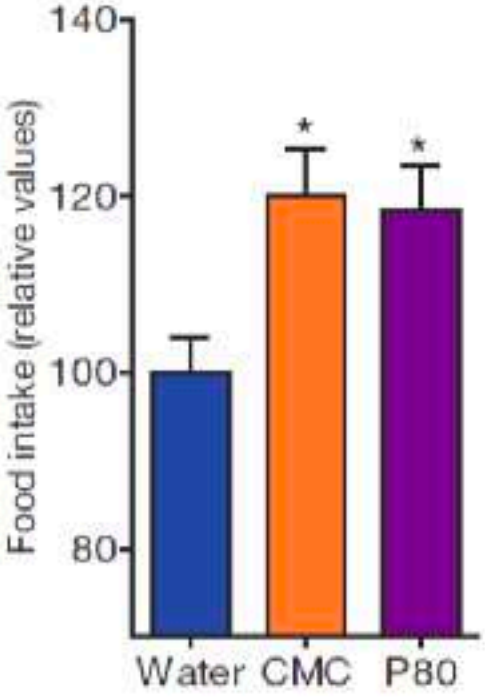


Slide provided by Ida Hatoum

Food Emulsifiers Cause Increase in Appetite



CMC: Carboxy methyl cellulose
P80 : Polysorbate 80



Chassaing B, et al. Nature, 2015. PMID: 25731162

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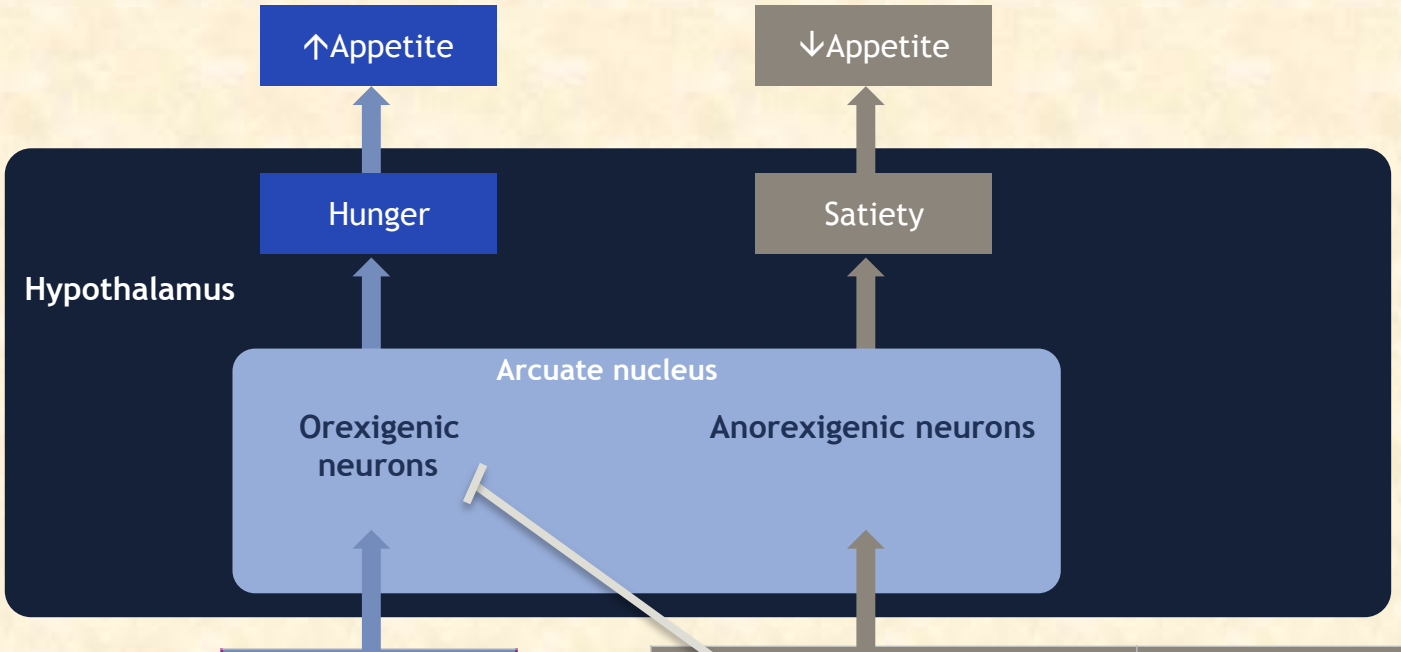
4) Weight regulation by the hypothalamus

- Set point in weight

THE HYPOTHALAMUS

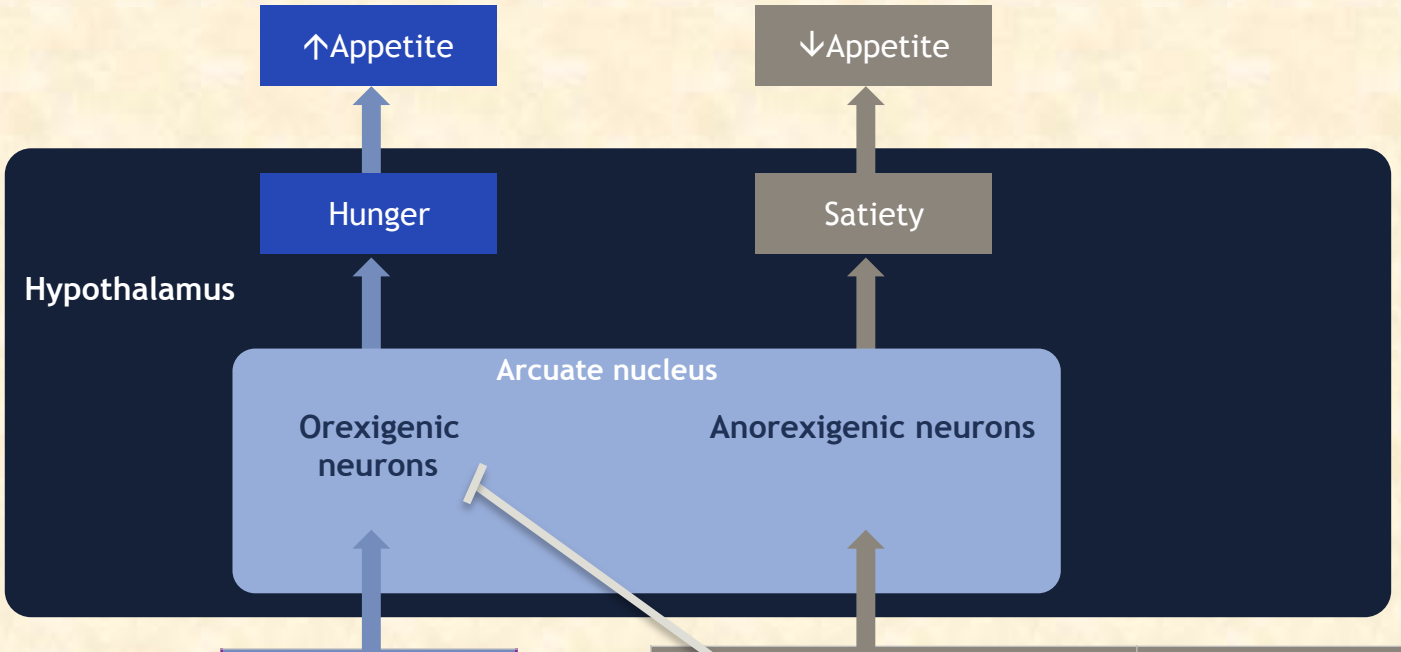


Ghrelin	GLP-1, CCK, PYY, OXM	Leptin	Insulin, Amylin, PP
Gut	Gut	Adipose tissue	Pancreas
Hunger signal	Satiety signals		

GLP-1, glucagon-like peptide-1; CCK, cholecystokinin; OXM, oxyntomodulin; PP, pancreatic polypeptide; PYY, peptide YY

Badman MK and Flier JS Science 2005;307:1909-14

THE HYPOTHALAMUS



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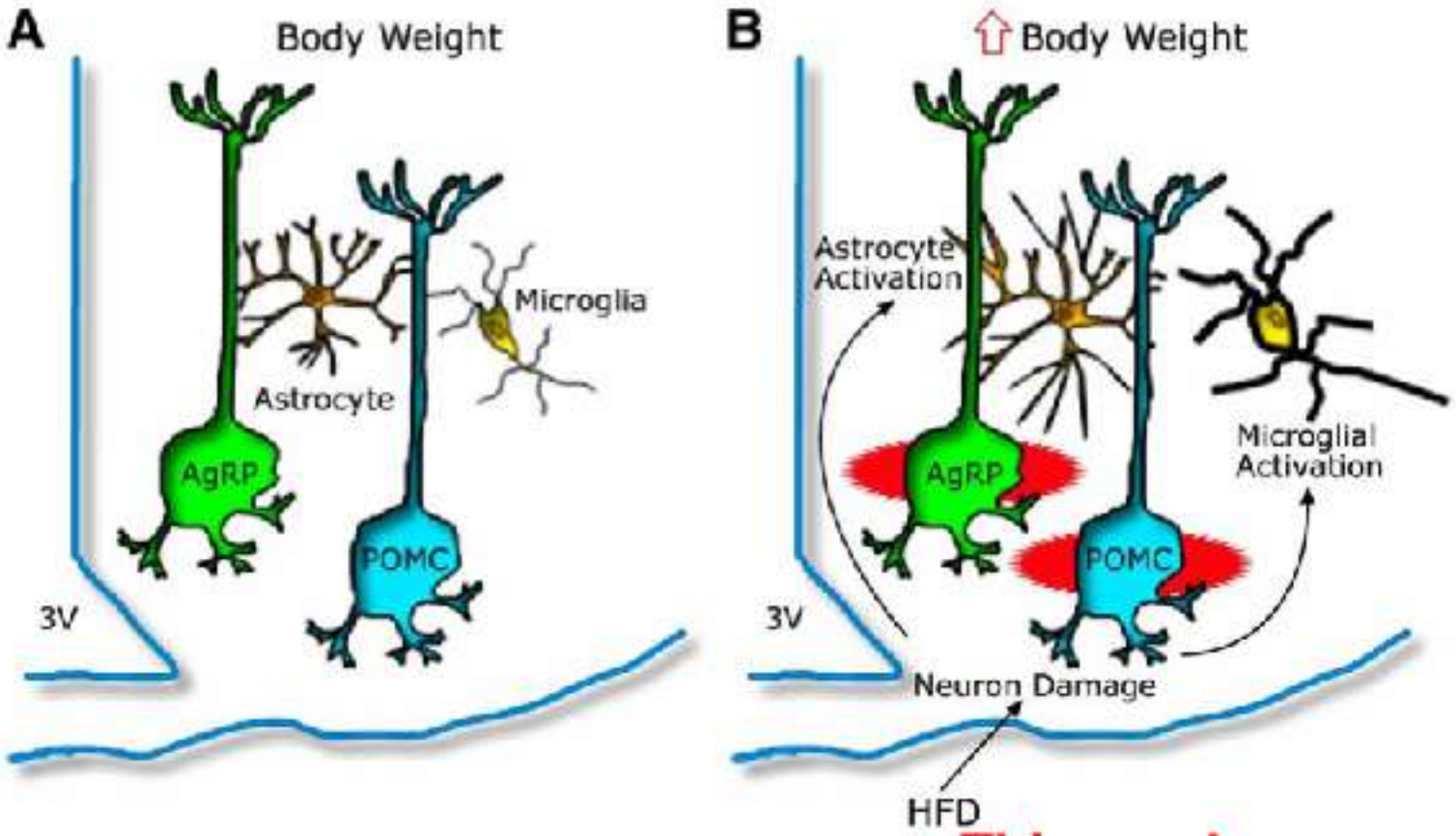
GLP-1, glucagon-like peptide-1; CCK, cholecystokinin; OXM, oxyntomodulin; PP, pancreatic polypeptide; PYY, peptide YY

Badman MK and Flier JS Science 2005;307:1909-14

4a) Outside Effectors

- High Fat Diet (Mouse Models)
  - causes inflammation and scarring in the hypothalamus
  - protected by exercise

High fat diet causes hypothalamic inflammation



JP Thaler et al., Diabetes, 2013

This can be seen on MRI

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Exercise Reduces Inflammation Caused by High Fat Diet

Normal high fiber diet	Processed high fat diet	Processed high fat diet + Running wheel
Normal food intake	↑ food intake	Normal food intake
No hypothal. Inflam.	↑ Hypothal. Inflam.	**Reduced hypothal. Inflam.**
No weight gain	↑ weight	No weight gain
Normal leptin signaling	↓Leptin signaling	**Restored leptin signaling**

Krawczewski, K., et al. Endocrinology 2011. PMID: 21586558

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4b) Body weight should be stable

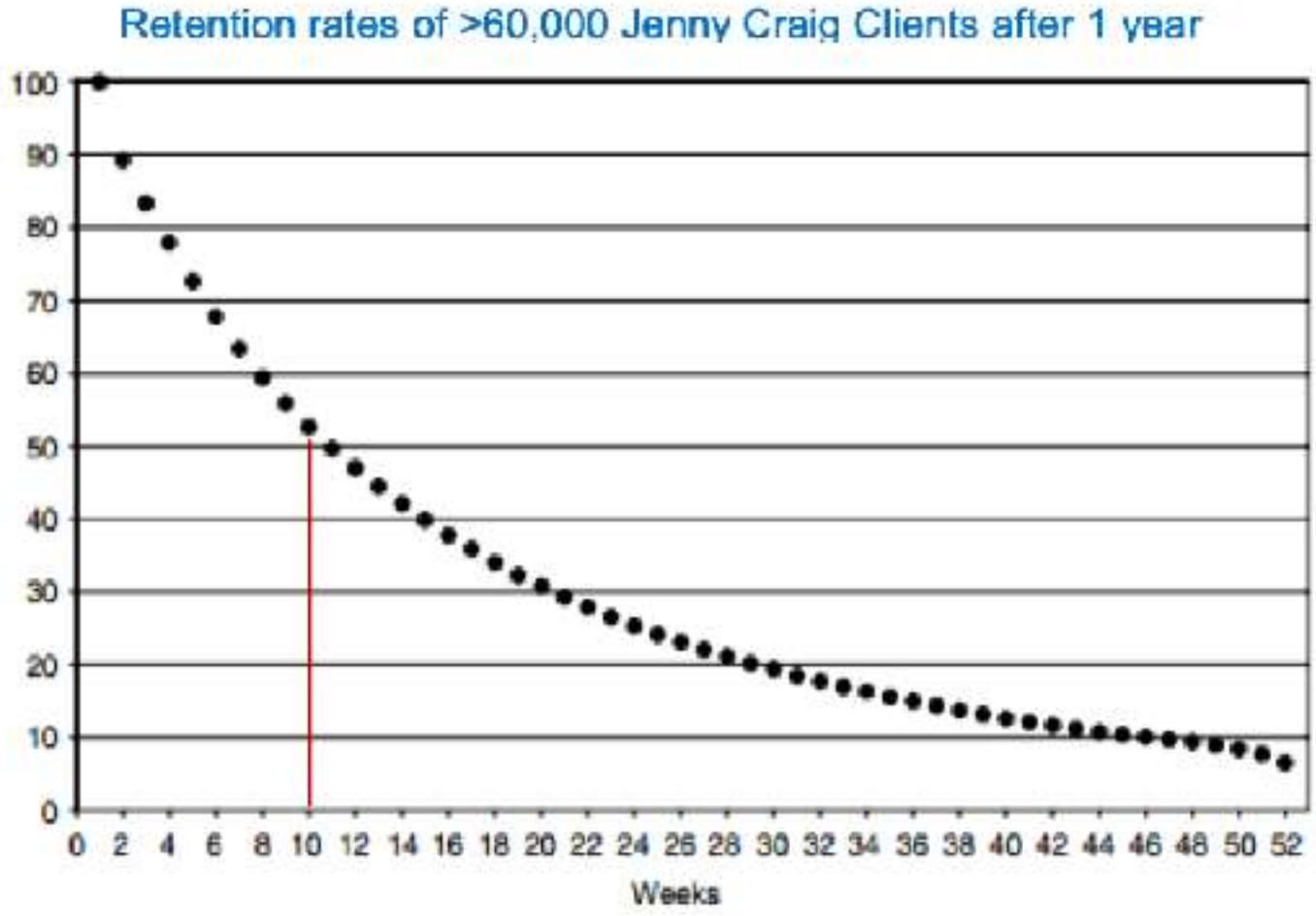
- All about homeostasis
- Your body fights to keep your weight stable
- Your hypothalamus uses orixigenic hormones
  - To change behaviour to make you eat

Failure of dietary modalities.

"The best average weight loss achieved by the majority of diet interventions is 10kg all of which is regained within 6 months."

NIH consensus statement.

Taking a Diet History



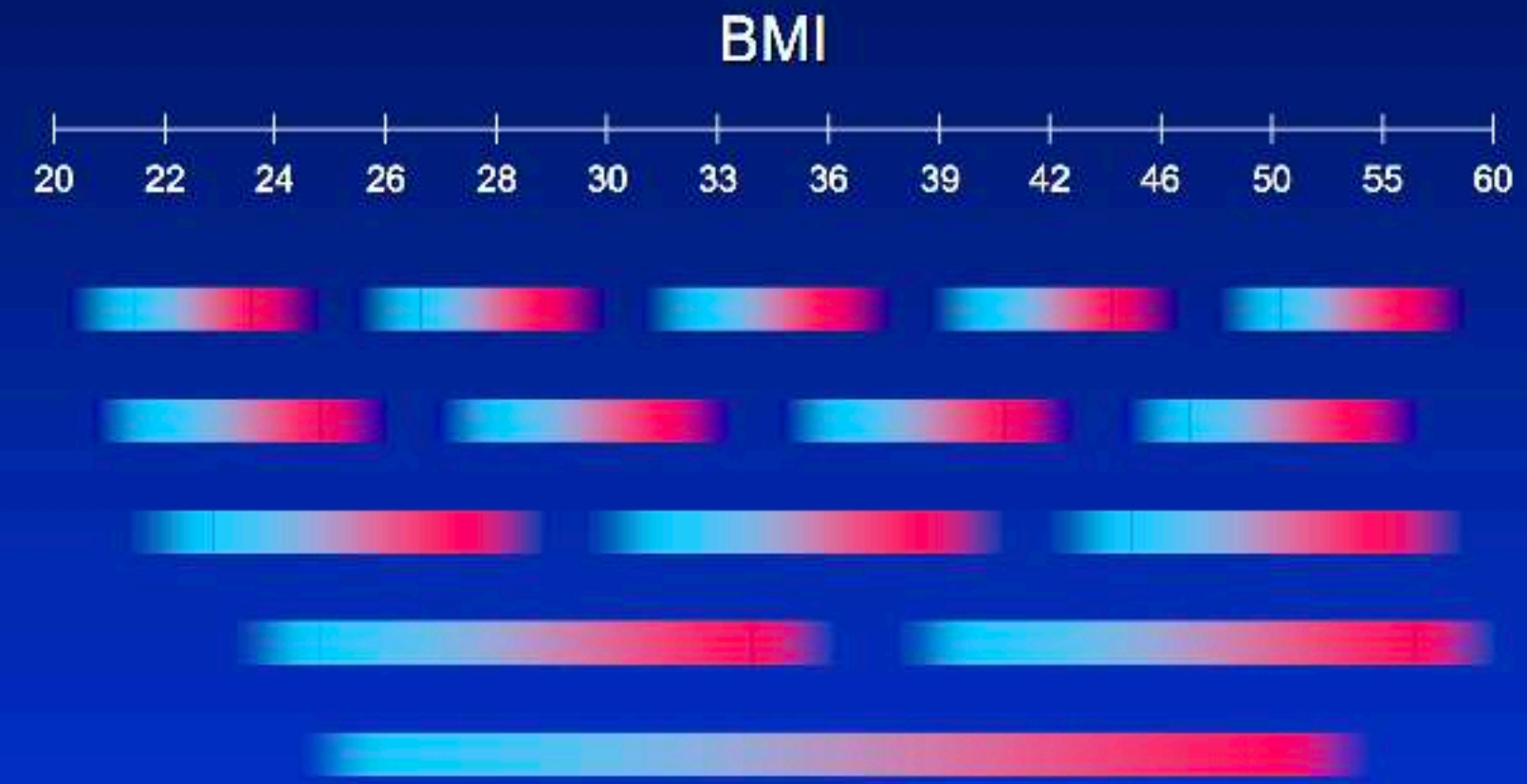
Finley CE et al;. Int J Obes, 2007;31:292-8

Cleveland Clinic

5) Everyone lives within a range

- Normal for body weight fluctuations
  - Consider a holiday
  - Consider being healthy

Natural Variation and Zones of Lifestyle Opportunity



Our Medical Aim

- Keep people at the bottom end
  - At the healthy end
- Give general health advice
  - Eating / exercise
- But don’t expect to get people out of the range without help .....

Reduced Metabolism

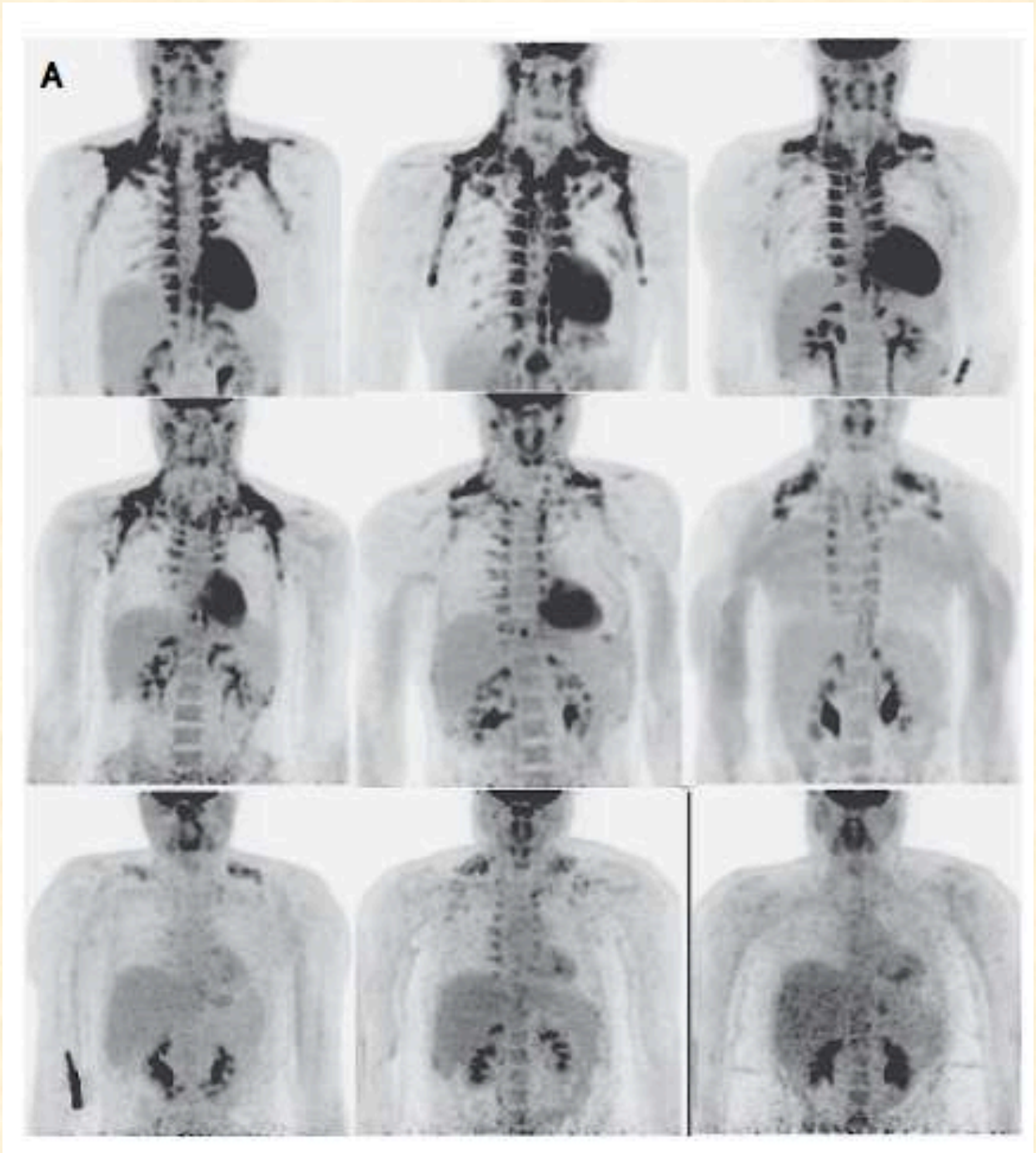
- Calories in = Calories out

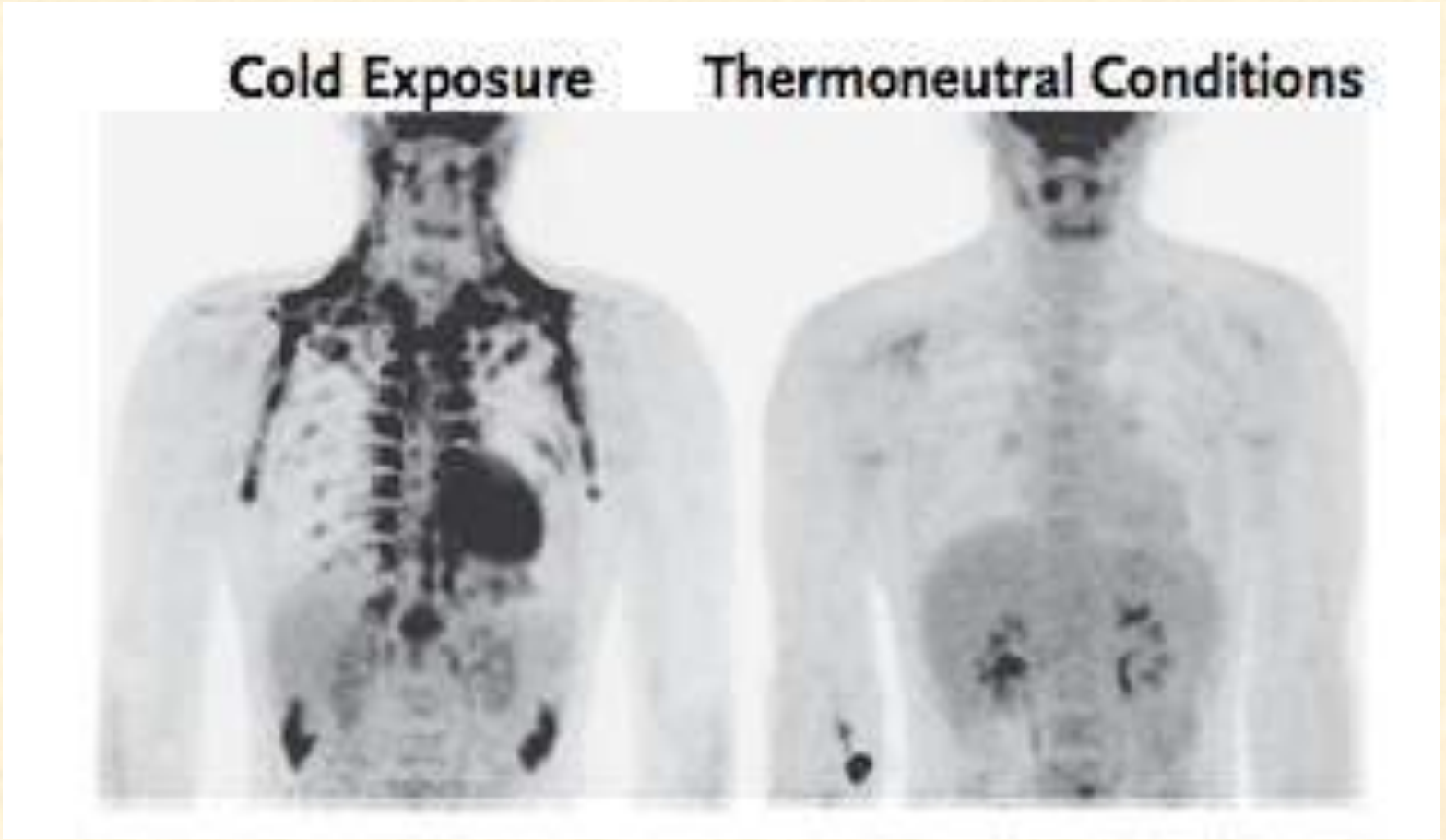
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cold-Activated Brown Adipose Tissue in Healthy Men

Wouter D. van Marken Lichtenbelt, Ph.D., Joost W. Vanhommerig, M.S., Nanda M. Smulders, M.D., Jamie M.A.F.L. Drossaerts, B.S., Gerrit J. Kemerink, Ph.D., Nicole D. Bouvy, M.D., Ph.D., Patrick Schrauwen, Ph.D., and G.J. Jaap Teule, M.D., Ph.D.

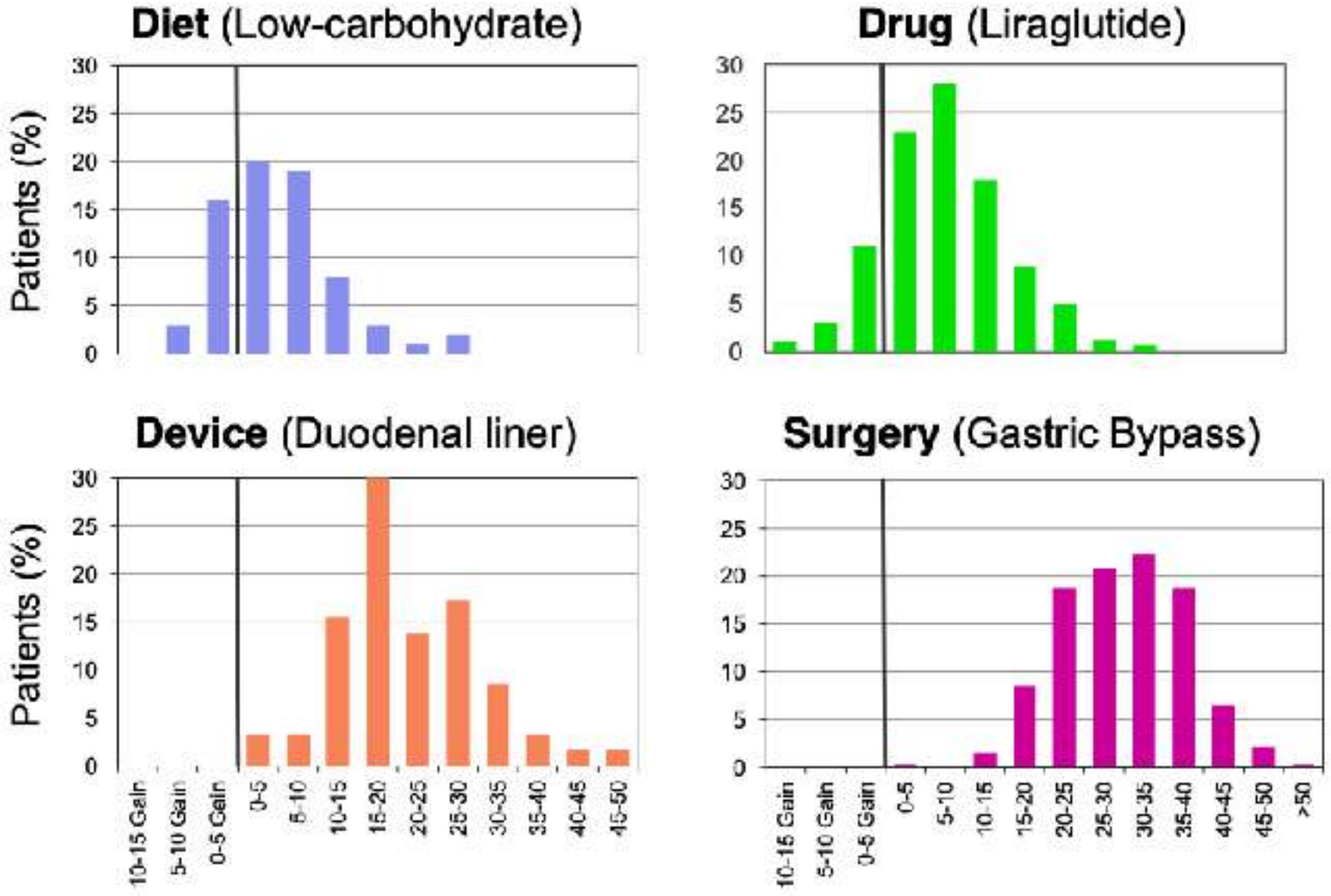

A


Cold Exposure
Thermoneutral Conditions

What about therapies ……

- Weight loss varies from individual to individual
  - So what works for one person may not work for another

Weight Loss Varies Widely Among Patients



Anti Obesity Management Plan

Encourage Healthy Living

- Eat well
- Exercise
- Sleep well
- Avoid Stress

- Psychological health / help

Sleep Hygiene

1. Avoid caffeine, nicotine, alcohol
2. Make bedroom sleep-inducing
3. Establish soothing pre-sleep routine
4. Go to bed when truly tired
5. Don't be a night-time clock-watcher
6. Use light to your advantage
7. Be consistent with sleep schedule
8. Nap early or not at all
9. Lighten up on evening meals
10. Balance fluid intake
11. Exercise early
12. Follow thru

http://healthysleep.med.harvard.edu/healthy/getting/overcoming/tips

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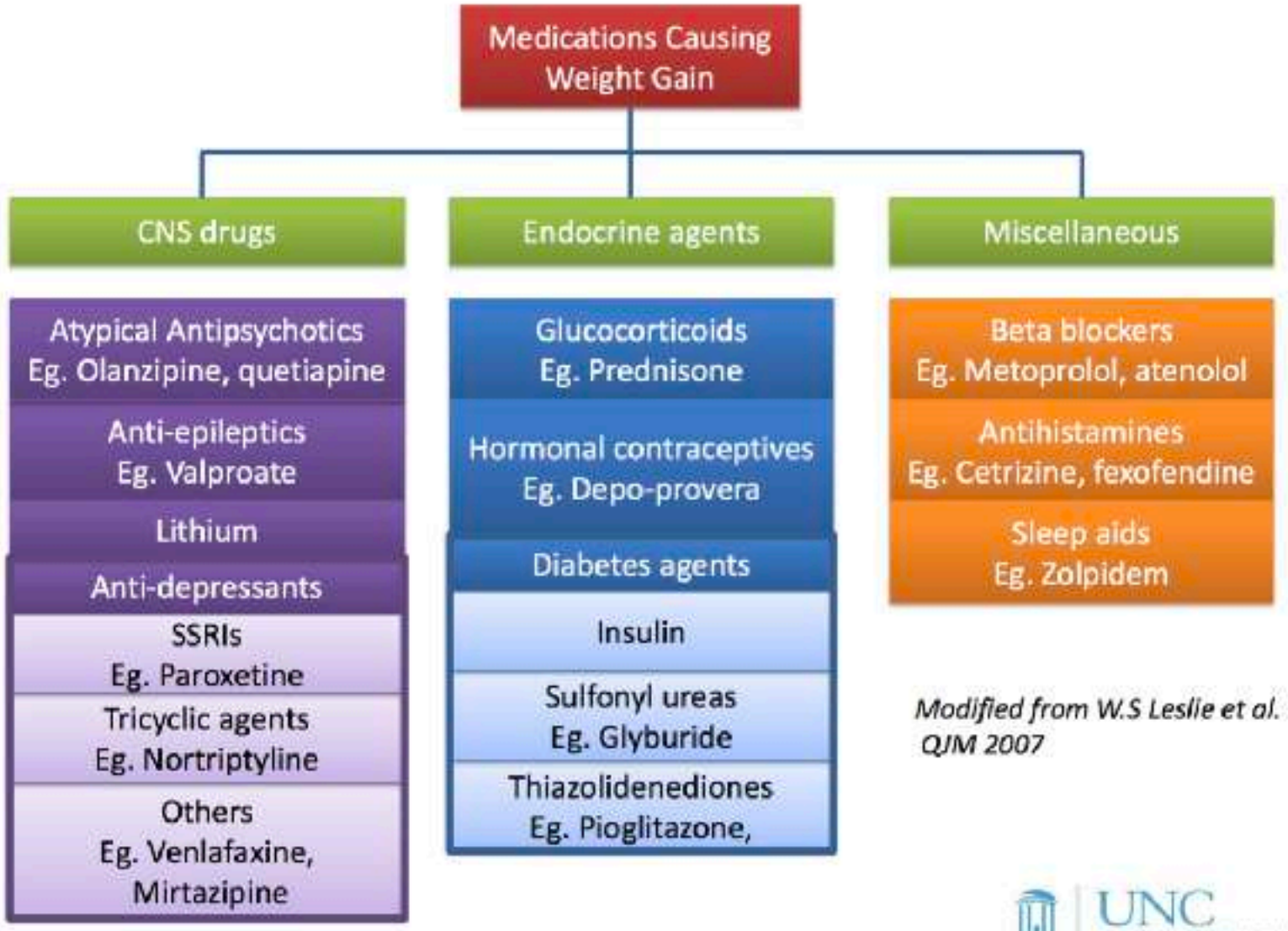
Avoid Things That Cause Weight Gain

- Bad Social Behaviours
- Medication
  - causes 10% of obesity
- Other
  - Food Emulsifiers



Modified from W.S Leslie et al. QJM 2007

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and only then…..Specific Therapies

- Education
- Behavioural Change
- Medication
- Surgery

But

- We are happy to see anyone
- It all starts with a chat

Questions ?

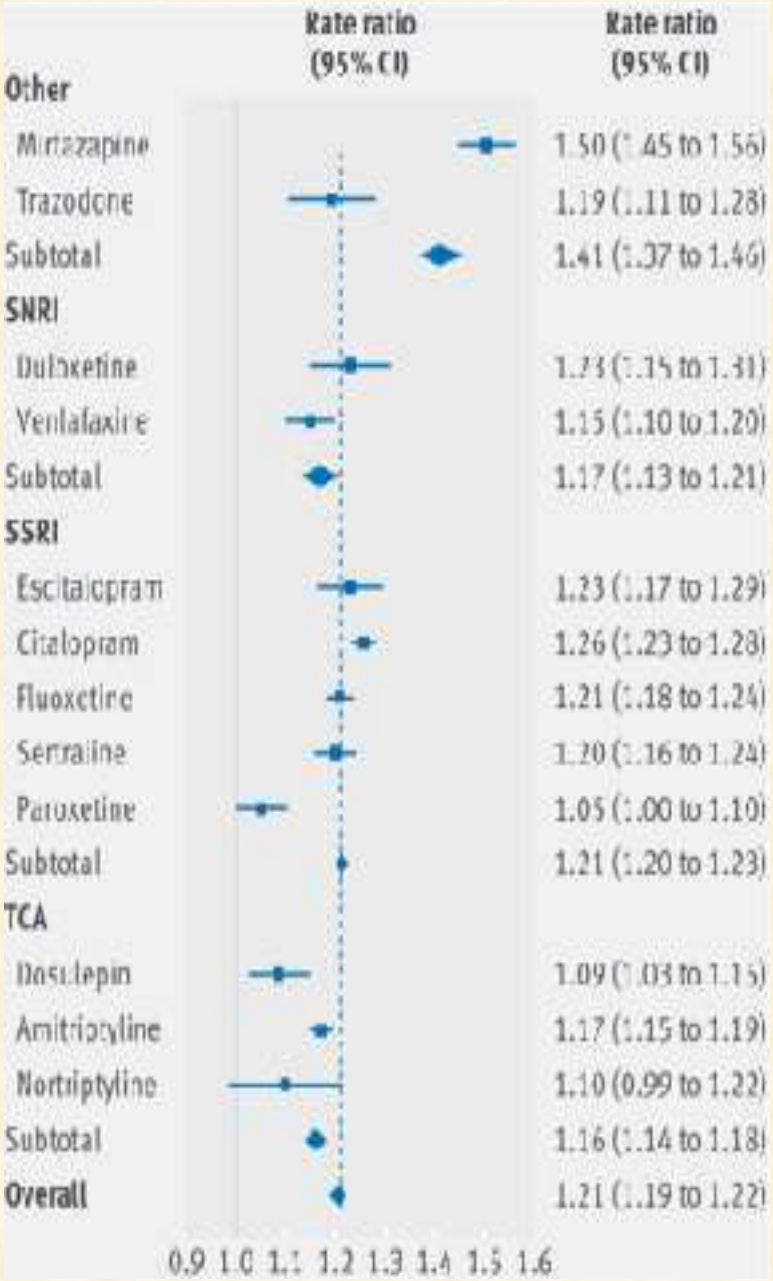
Increased U.S. Overall Use of Antidepressants

7.7% in the past month (1999–2002) to 12.7% (2011–2014)

https://www.cdc.gov/nchs/data/databriefs/db283.pdf

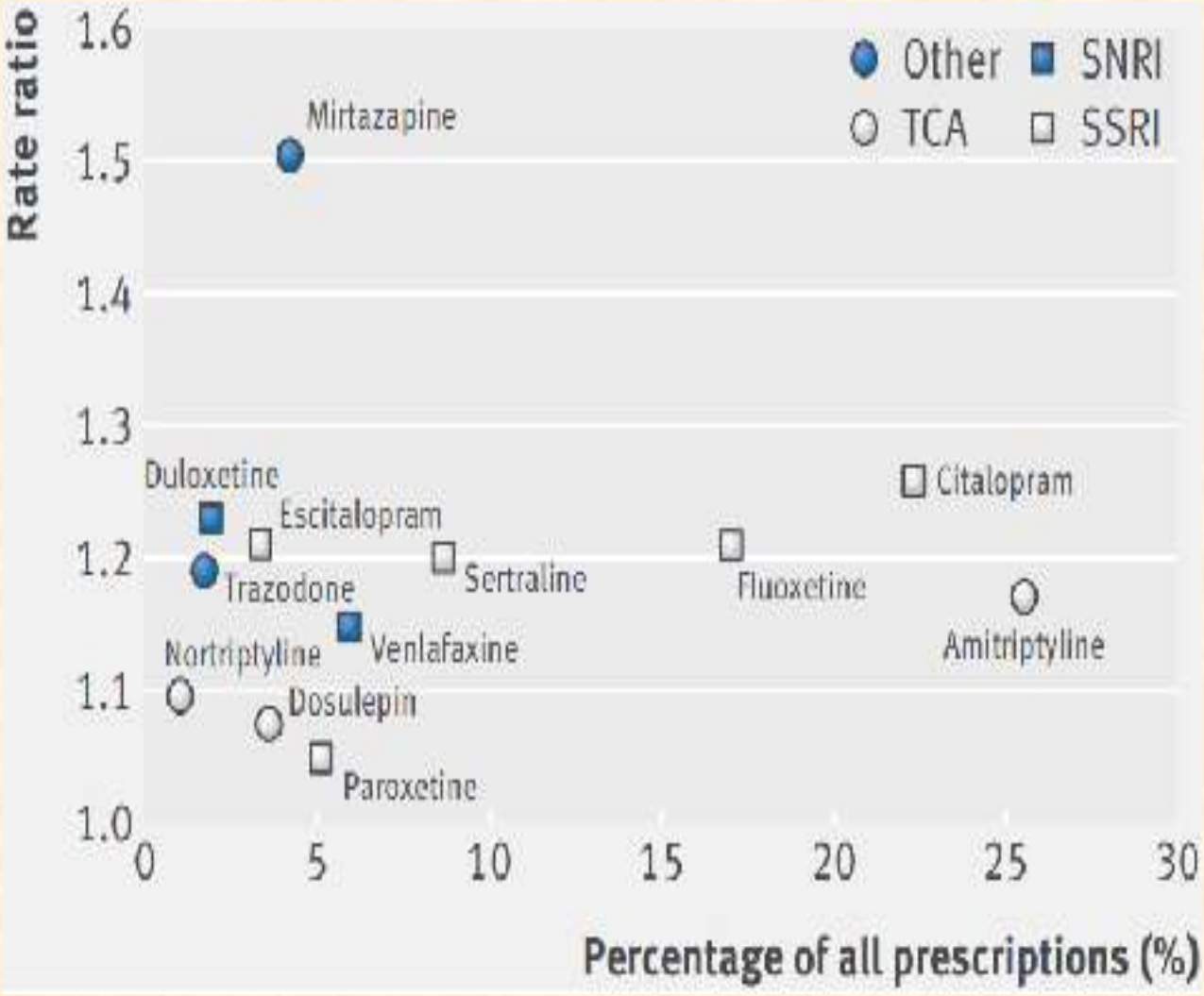
Adjusted Rate Ratios for ≥5% Weight Gain *By Antidepressant Type*

Considering the entire period of follow-up (10 years), participants who were prescribed an antidepressant had an increased risk of ≥5% weight gain compared with those who had never been prescribed an antidepressant. This association was consistently observed across a wide range of population subgroups.



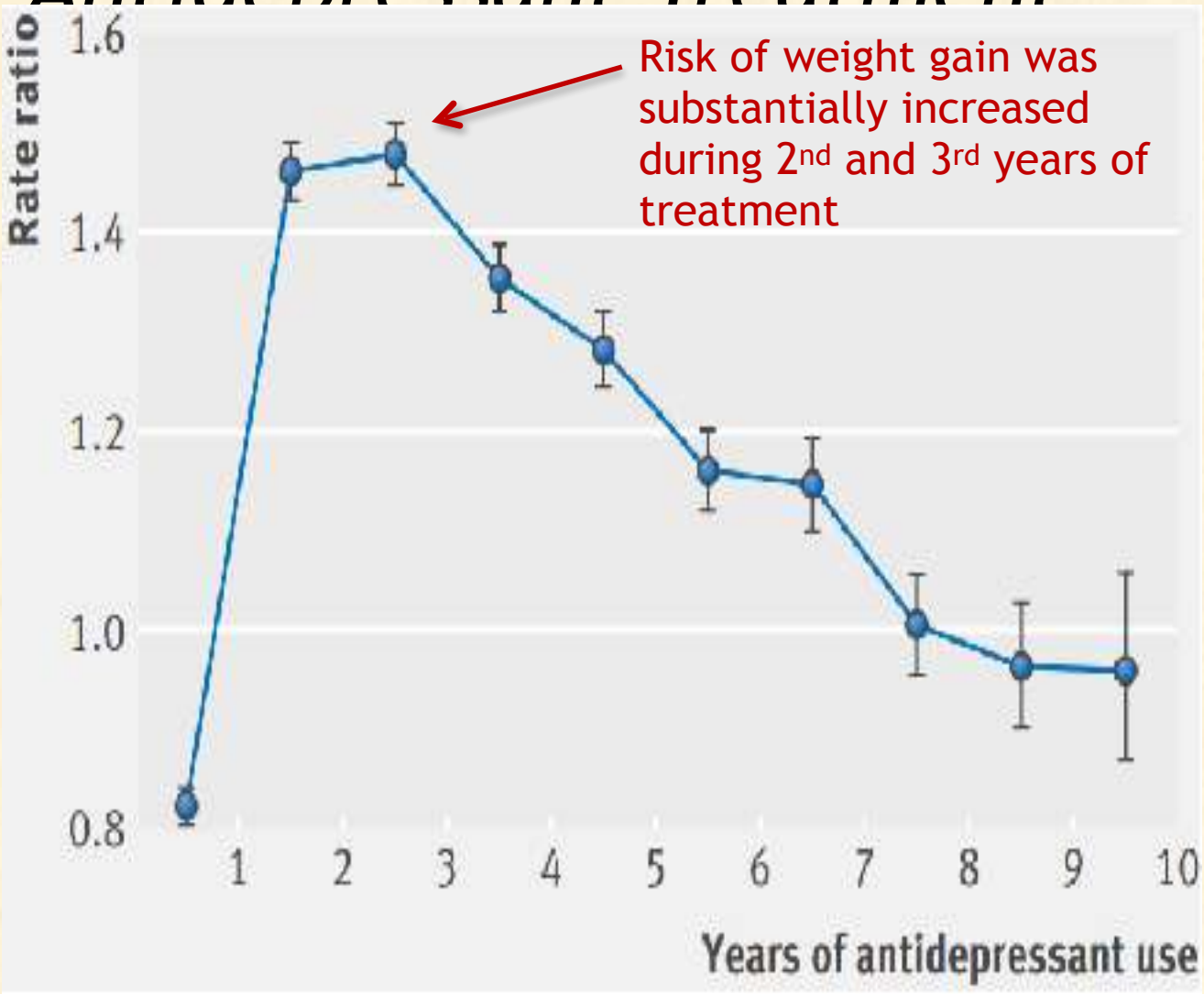
Gafoor R, et al. BMJ 2018;361:k1951

Adjusted Rate Ratios For ≥5% Weight Gain *By Number of Prescriptions*



Gafoor R, et al. BMJ 2018;361:k1951

Adjusted Rate Ratios For ≥5% Weight Gain *By Years of Antidepressant Treatment*



Gafoor R, et al. BMJ 2018;361:k1951

Drugs Associated With Weight Gain and Suggested Alternatives[1]

Category	Drug Class	Weight Gain	Alternatives
Psychiatric agents	Antipsychotic	Clozapine, risperidone, olanzapine, quetiapine, haloperidol, perphenazine	Ziprasidone, aripiprazole
	Antidepressants/mood stabilizers: tricyclic antidepressants	Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine	Bupropion[a], nefazodone, fluoxetine (short term), sertraline (<1 year)
	Antidepressants/mood stabilizers: SSRIs	Fluoxetine?, sertraline?, paroxetine, fluvoxamine	
	Antidepressants/mood stabilizers: MAOIs	Phenylzine, tranylcypromine	
	Lithium	—	
Neurologic agents	Anticonvulsants	Carbamazepine, gabapentin, valproate	Lamotrigine?, topiramate[a], zonisamide[a]
Endocrinologic agents	Diabetes drugs	Insulin (weight gain differs with type and regimen used), sulfonylureas, thiazolidinediones, sitagliptin?, metiglinide	Metformin[a], acarbose[a], miglitol[a], pramlintide[a], edenatide[a], liraglutide[a]

[a] Weight-reducing.

MAOI: monoamine oxidase inhibitor; SSRI: selective serotonin reuptake inhibitor.

1. Apovian CM et al. *J Clin Endocrinol Metab.* 2015;100:342-362.

Screen Shot 2019-01-10 at 7.32.50 am.png

But Remember

- Everyone is different
- Not everyone will increase weight
- Just like not everyone will respond

Think About Micronutrients

- Fat people have been dieting for ……ever
- Dietary fads are bad

U.S. Adults have Below Average Intake of Micronutrients

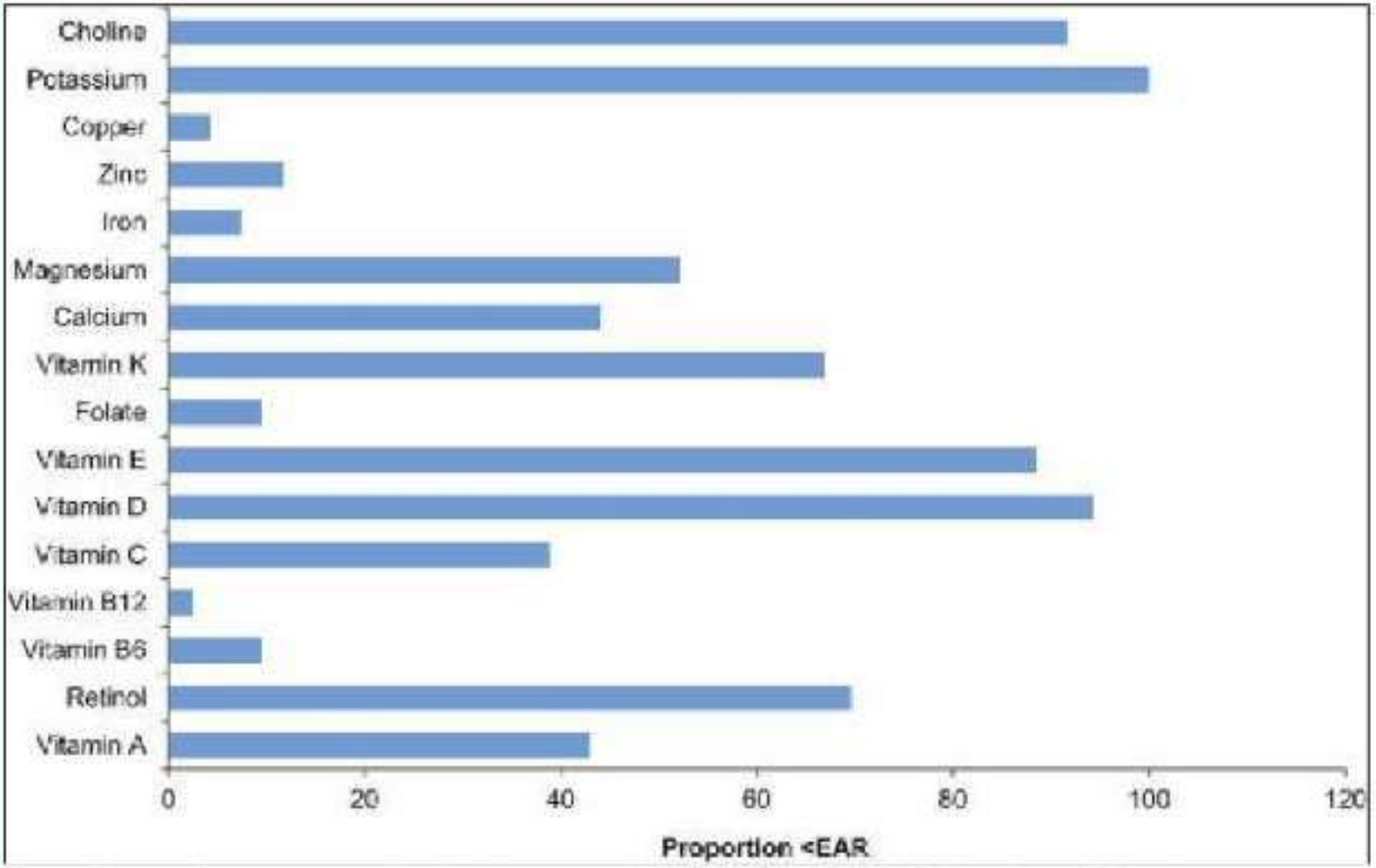


Figure 1. Percentage of Americans >=1 years of age with selected micronutrient intakes from food alone <EAR (Wallace et al., 2014). EAR = estimated average requirement.

Wright, W., Zelman, K. JAANP 2018; 30(3):160-177.

Cleveland Clinic

Medications for Weight Loss

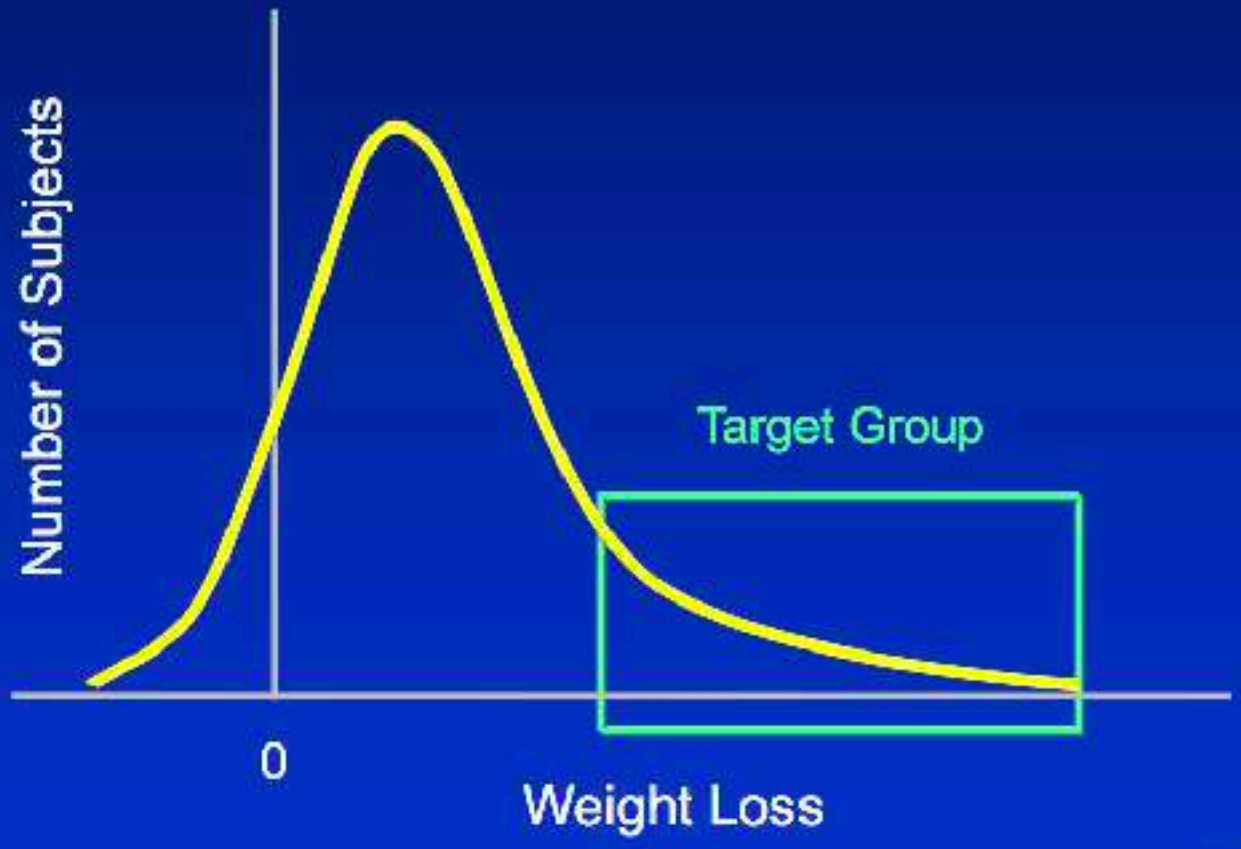
- Four Available
- No Wrong / Wright choice
- Assess Response / Side effects
- Change if necessary
- Long term therapy is possible

- Expect 10% total body weight loss

Medications for Weight Loss

- May help people stay on a diet
- Use a dietitian / psychologist

Heterogeneity of Response



Saxenda (Liraglutide)

- CI – MEN / Pancreatitis
- Start with 0.6 ug and titrate up

Side effects

  - Nausea
  - Pancreatitis
- Cost – $200-$400/month

Duromine (Phenterimine)

- CI : IHD / Anxierty / Hypertension / Glaucoma

SIDE EFFECTS

- insomnia
- agitation
- hypertension

COST - $80/month

Xenical (Orlistat)

- Safe (bit nasty)

SIDE EFFECTS

- diarhoea
- flatulance

COST:

Contrave (Bupropion / Naltrexone)

- Seizures / Hypertension / Alcohol / MAO-I
- Expect 5% by 16 weeks
- CI: Seizures

SIDE EFFECTS

- Nausea / Constipation / Headache / Vomiting
- Dizziness /

COST : $225 / month

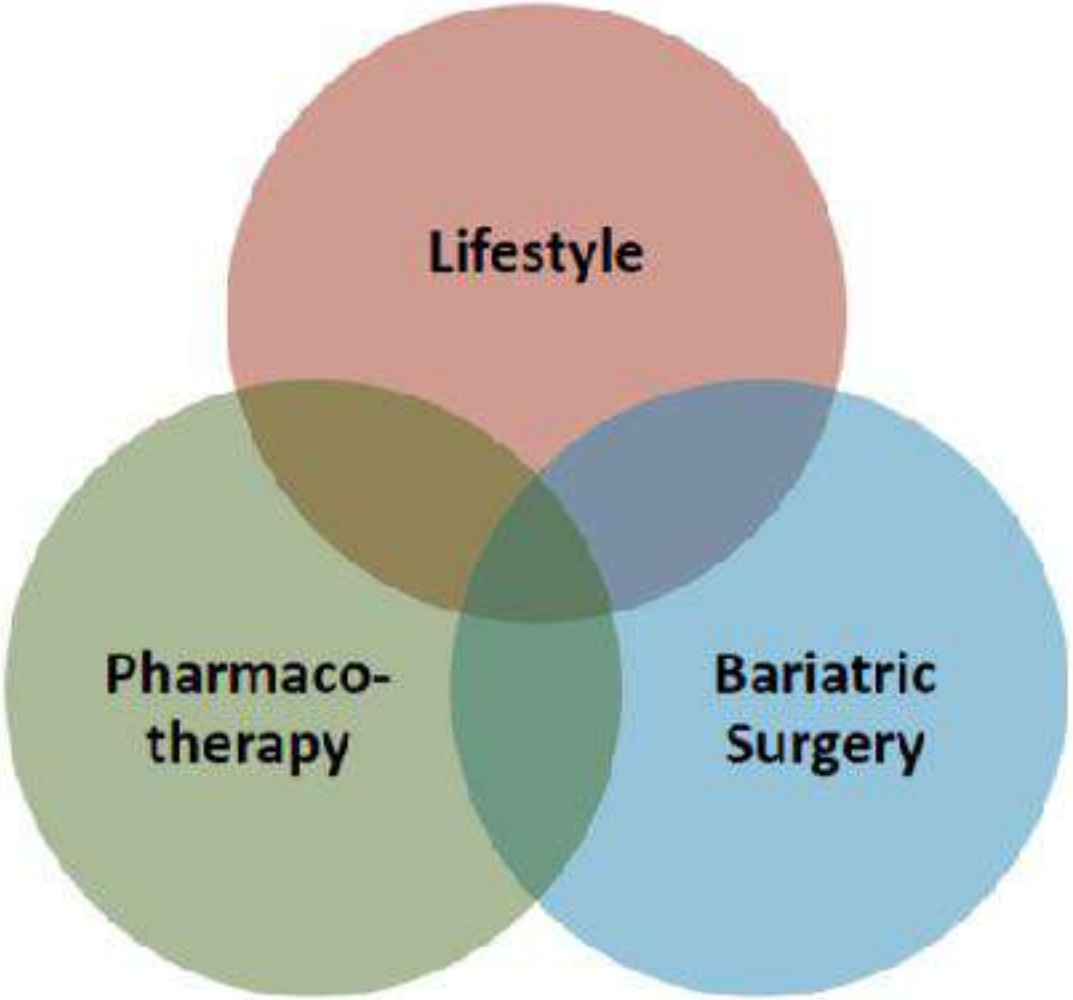
Topiramate

- By itself or with Duromine
- Used for migraine control / smoking cessation
- CI – glaucoma / kidney stones

COST: PBS – Authority Script

Private -

Combinations of Therapies Are Generally Required for Effective Obesity Management



Jensen SD, et al. *Circulation*. 2014;129(25 suppl 2):S102-S138.

What about surgery ?

- It’s not for everyone
- But ….

Who is an Operative Candidate?

- BMI > 35
- BMI 30- 35 + Obesity Co morbidity
- Age 18- 65*
- Reasonable attempts at weight loss >2 yrs
- Ability to comprehend implications of Surgery
- No Alcohol or Drug Dependency
- No desire to fall pregnant < 1yrs Post Op.

Obesity Surgery WA