Medical Treatment of Obesity

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Seattle, WA

Obesity Medicine Association

AMERICAN BOARD of OBESITY MEDICINE

Disclosures

- Novo Nordisk advisory council
- Retrofit advisory board

The Obesity Medicine Association's Definition of Obesity

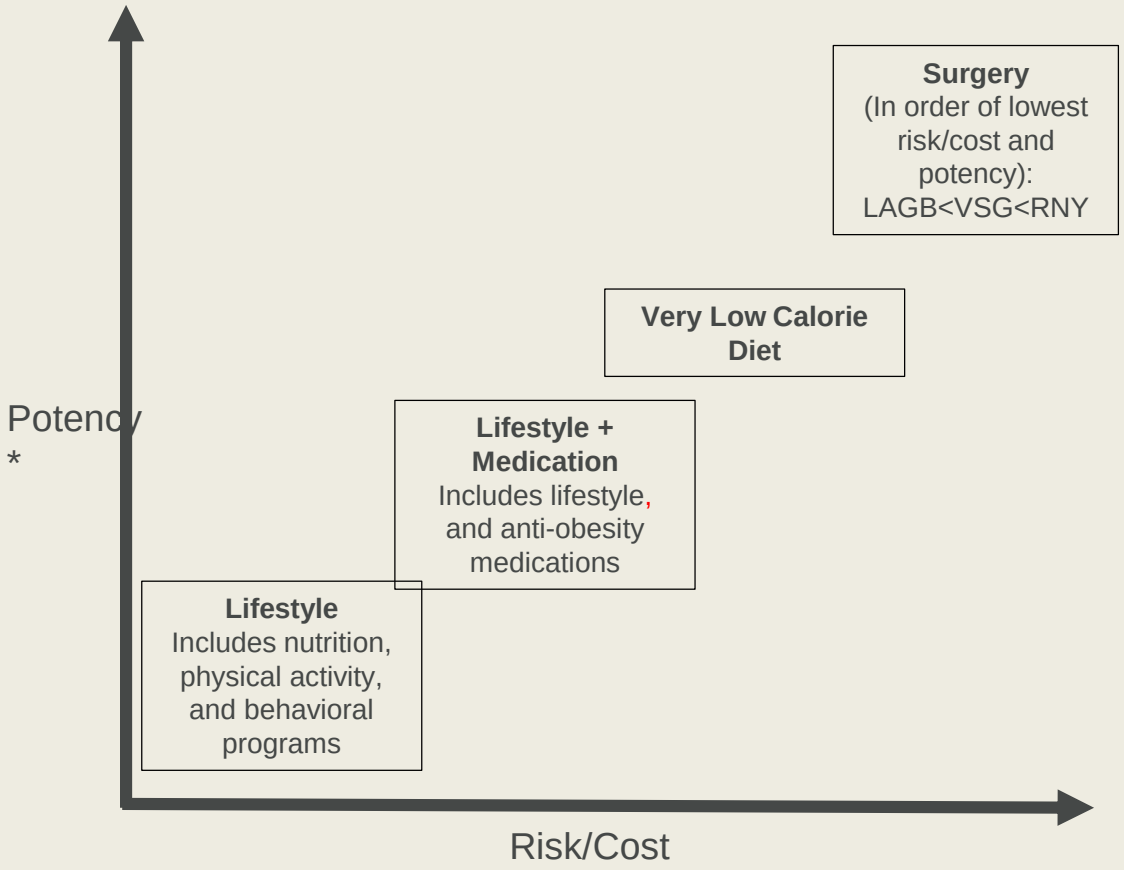
"Obesity is defined as a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes **adipose tissue dysfunction** and abnormal fat mass physical forces, resulting in **adverse metabolic**, biomechanical, and psychosocial health **consequences**."

Multiple treatment algorithms exist, with largely convergent content

- Obesity Medicine Association (OMA)
- American Heart Association/The American College of Cardiology/The Obesity Society (AHA/ACC/TOS)
- American Association of Clinical Endocrinologists(AACE/ACE)
- American Diabetes Association (ADA)

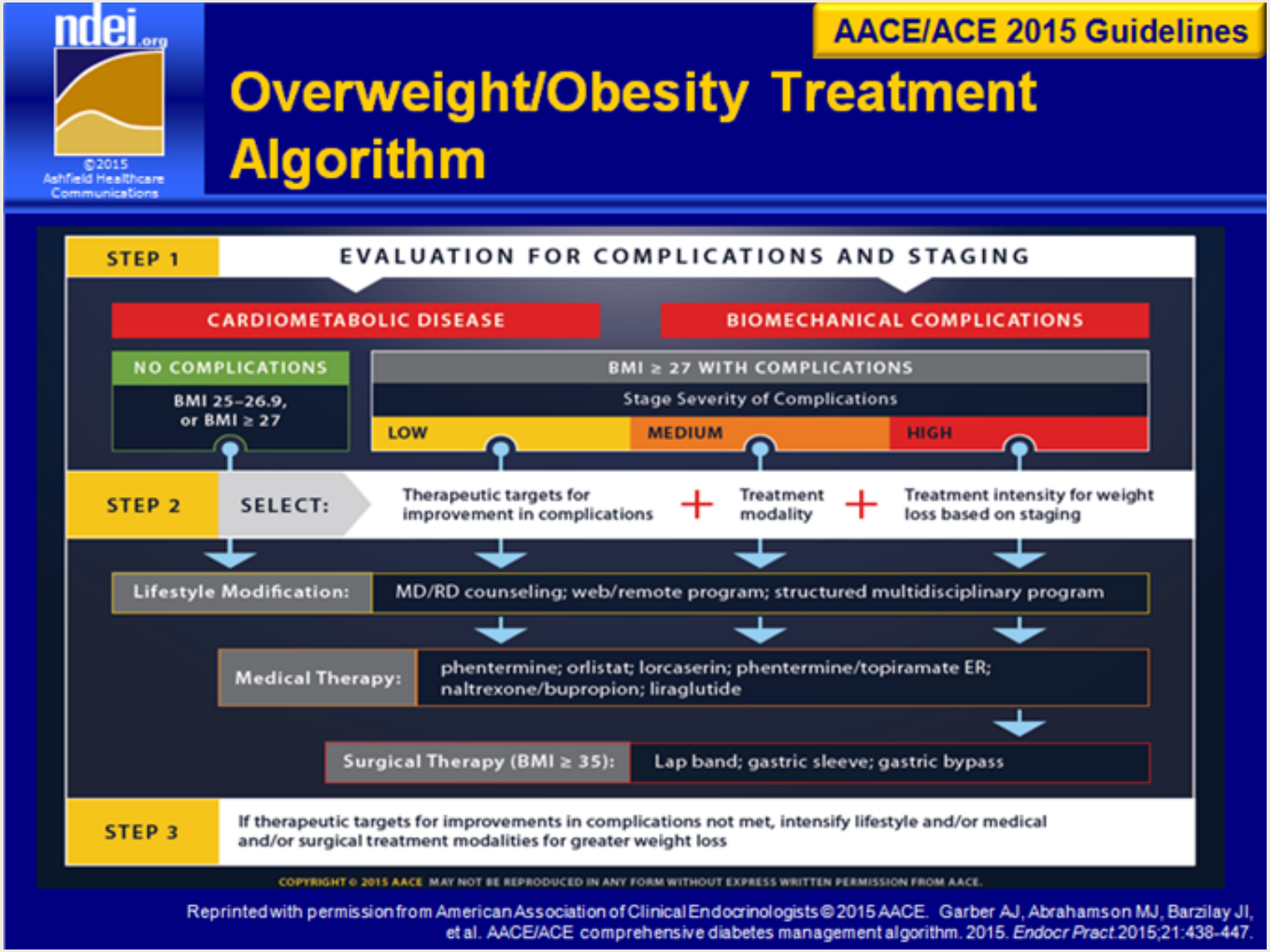
- All are open source
- Differences are largely in degree of detail
- Some variation wrt medication options
- Some variation in staging tools
- User friendliness, or lack of

Current Treatment Options for Obesity



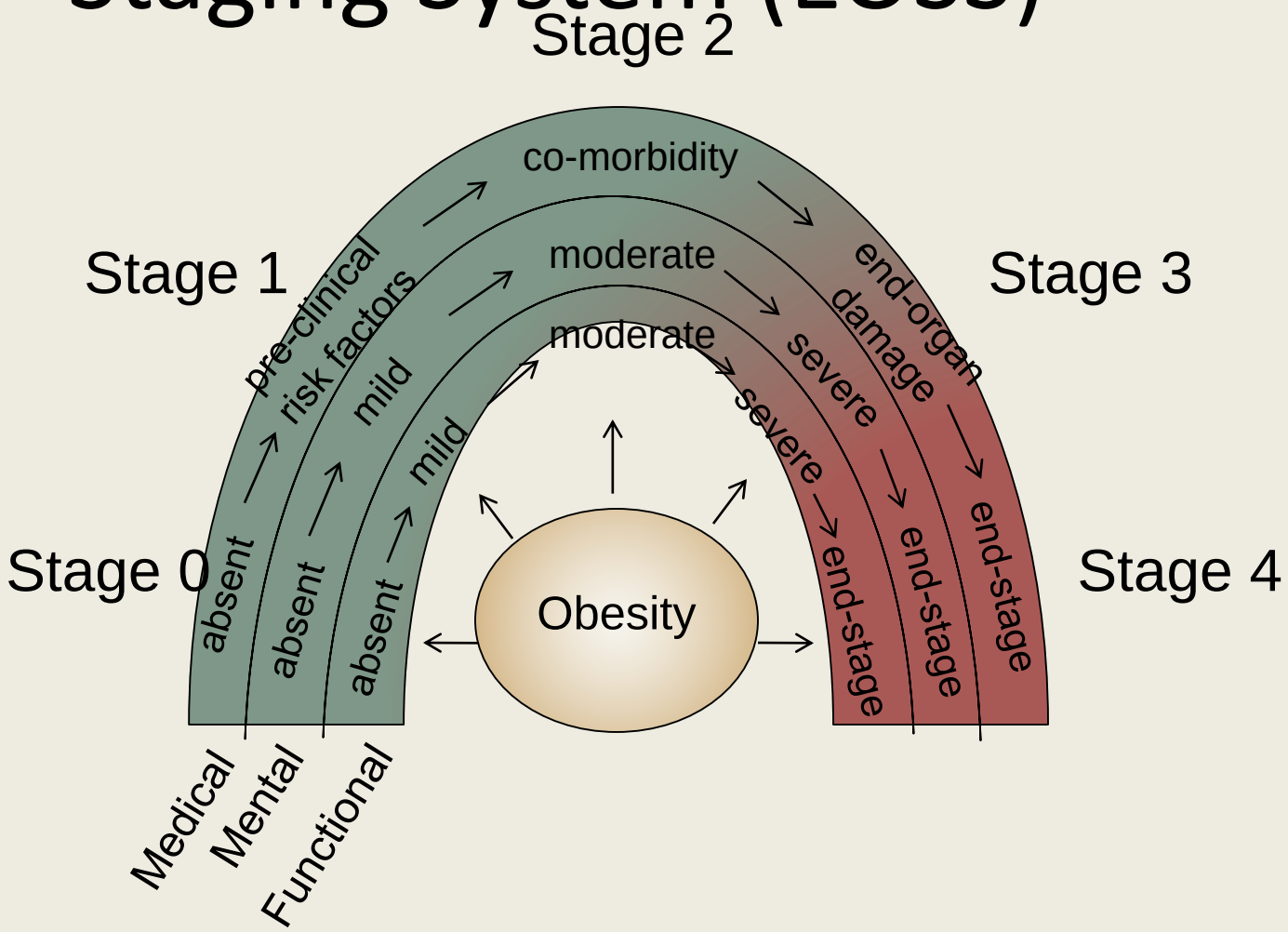
*Potency includes many factors, such as the amount, rate, and sustainability of weight loss, and the long-term resolution of adiposopathy and fat mass disease. Potency varies greatly for each individual (i.e., long-term adherence to a lifestyle program can be as potent as gastric bypass surgery).

Treatment Guidelines



Reprinted with permission from American Association of Clinical Endocrinologists © 2015 AACE. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm. 2015. *Endocr Pract* 2015;21:438-447.

Edmonton Obesity Staging System (EOSS)

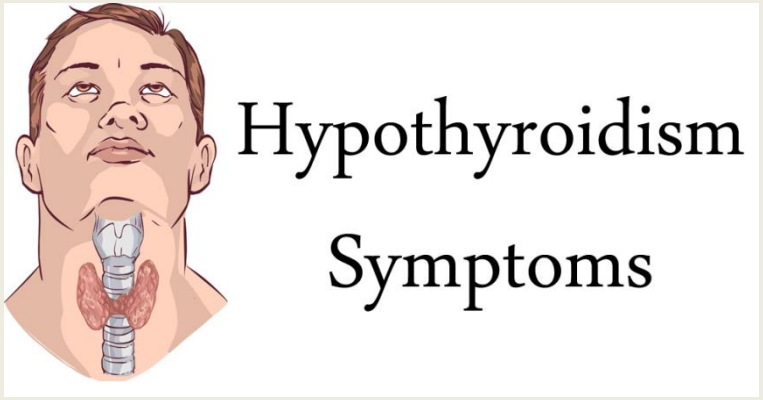


Sharma AM & Kushner RF, *Int J*

Obesity as a Chronic Disease

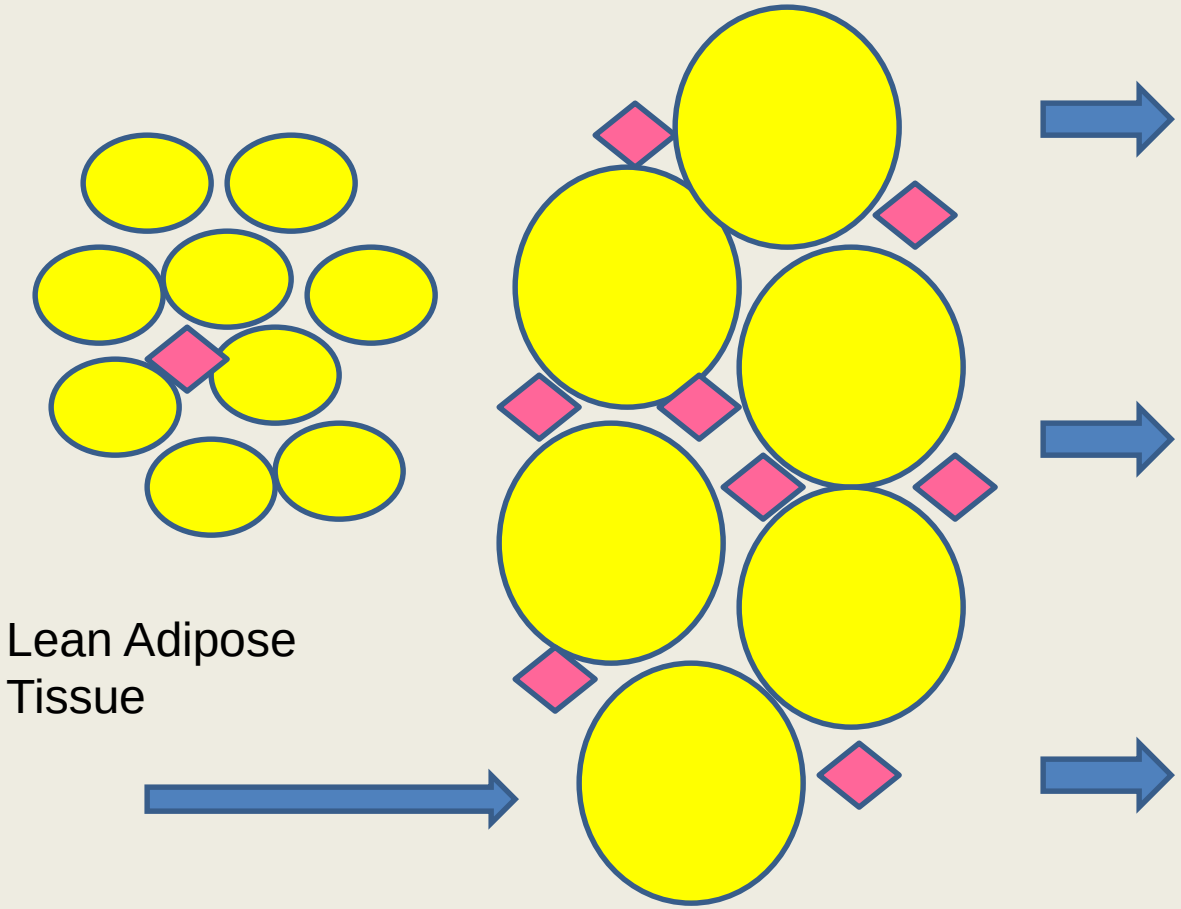
- Long term problem, not likely to improve without treatment
- Treatable and manageable, not thought of as “curable”
- Stopping treatment leads to recurrence or relapse
- Strategies are Long Term!
- Multidisciplinary care continuum approach

Chronic Disease Examples



Metabolic Syndrome

- AKA Dysmetabolic Syndrome
- AKA Syndrome X
- AKA "**Insulin Resistance**"
- ICD 10 code E88.9
- "Syndrome" of combination abnormalities:
  - Blood pressure
  - Lipids
  - Glucose
  - Increased abdominal girth
  - +/- microalbuminuria
- Metabolic Syndrome leads to **Cardiometabolic Risk**



- Inflammatory Cytokines
  - TNF-α
  - Interleukin-1
  - IL-6
  - IL-8
  - Resistin
  - Monocyte Chemotactic Protein (MCP)
  - Adipsin
  - Plasminogen Activator Inhibitor-1 (PAI-1)
  - Angiotensinogen

Cytokines and Inflammation

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  - TNF-α
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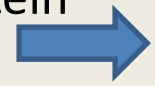
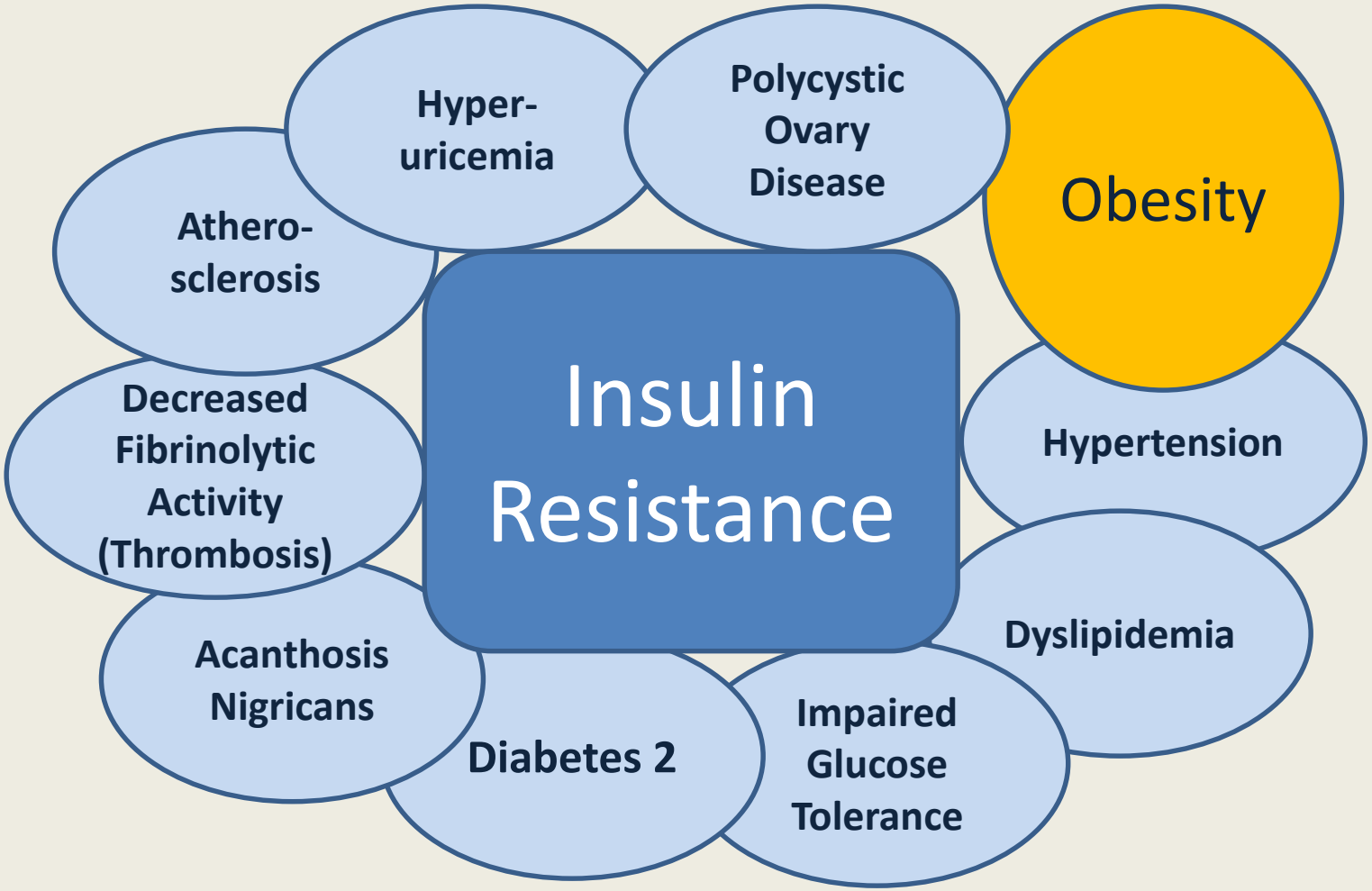
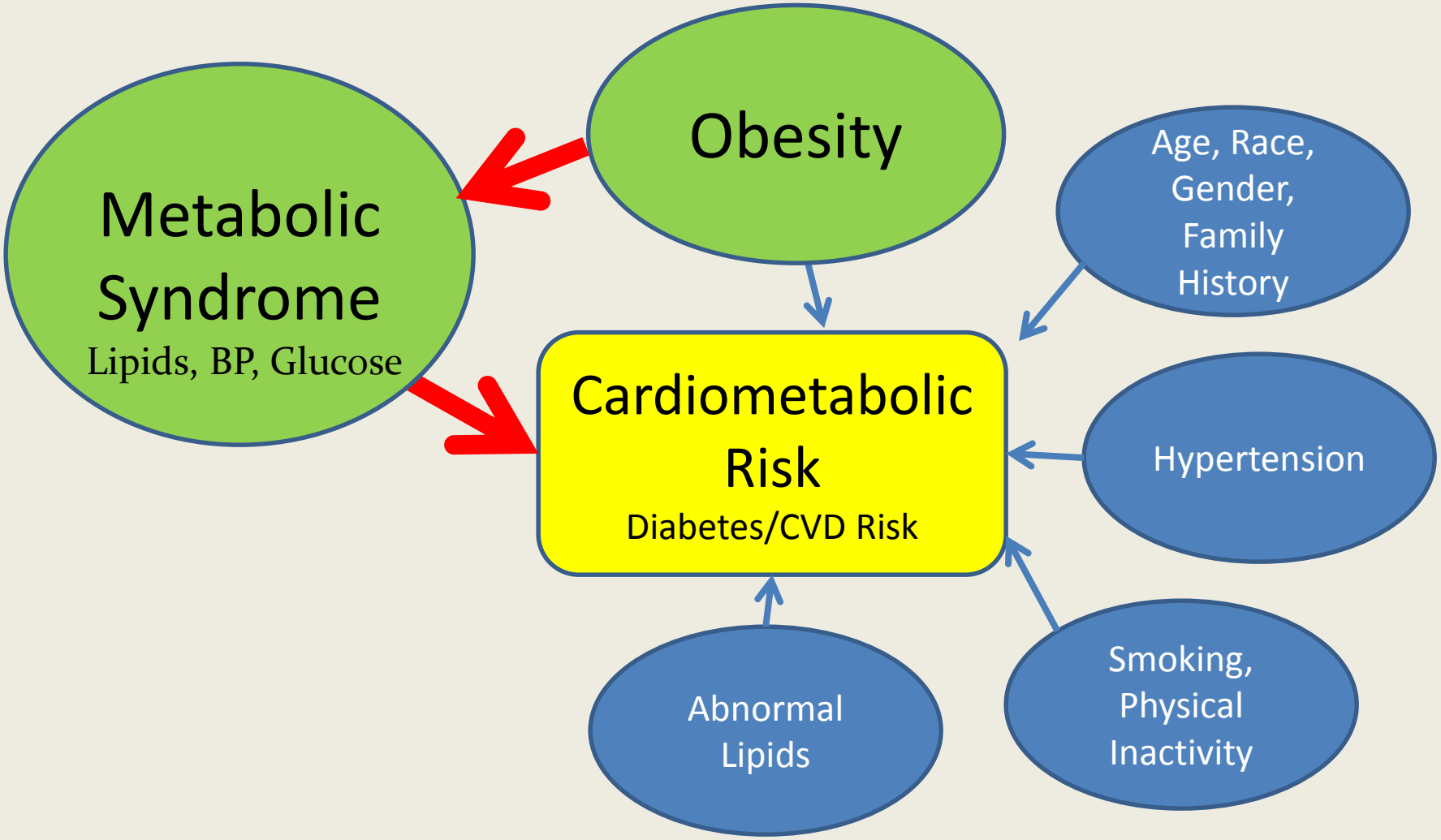


- "Downstream" Effects
  - Inflammation
    - CRP
  - Thrombosis
  - Atherosclerosis
  - Dyslipidemia
  - Type 2 Diabetes
  - Hypertension
  - Metabolic Syndrome
  - Cardio-Metabolic Dz
  - Androgen Deficiency

Insulin Resistance is Central to Multiple Pathologic Conditions

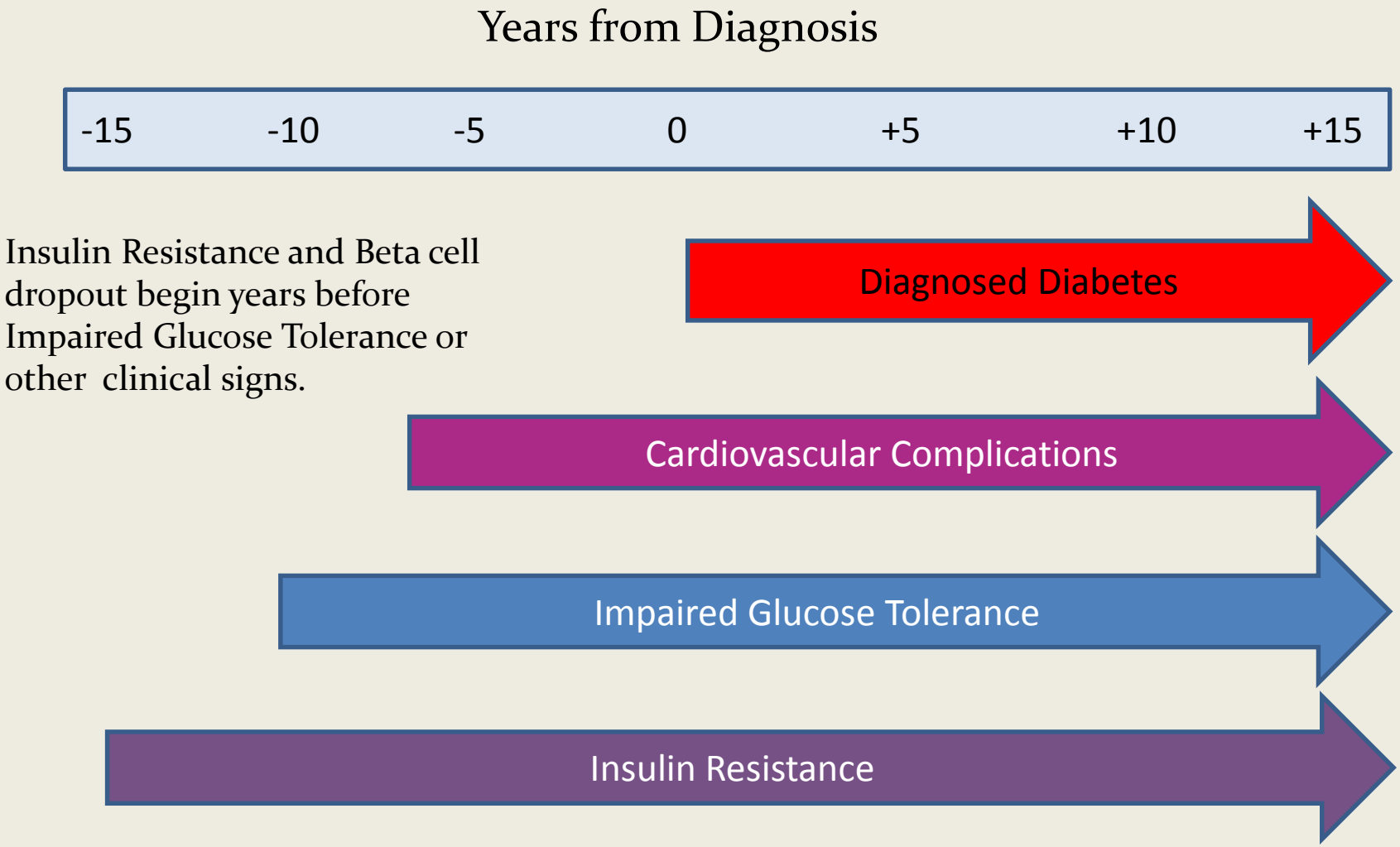


Factors Contributing to Cardiometabolic Risk



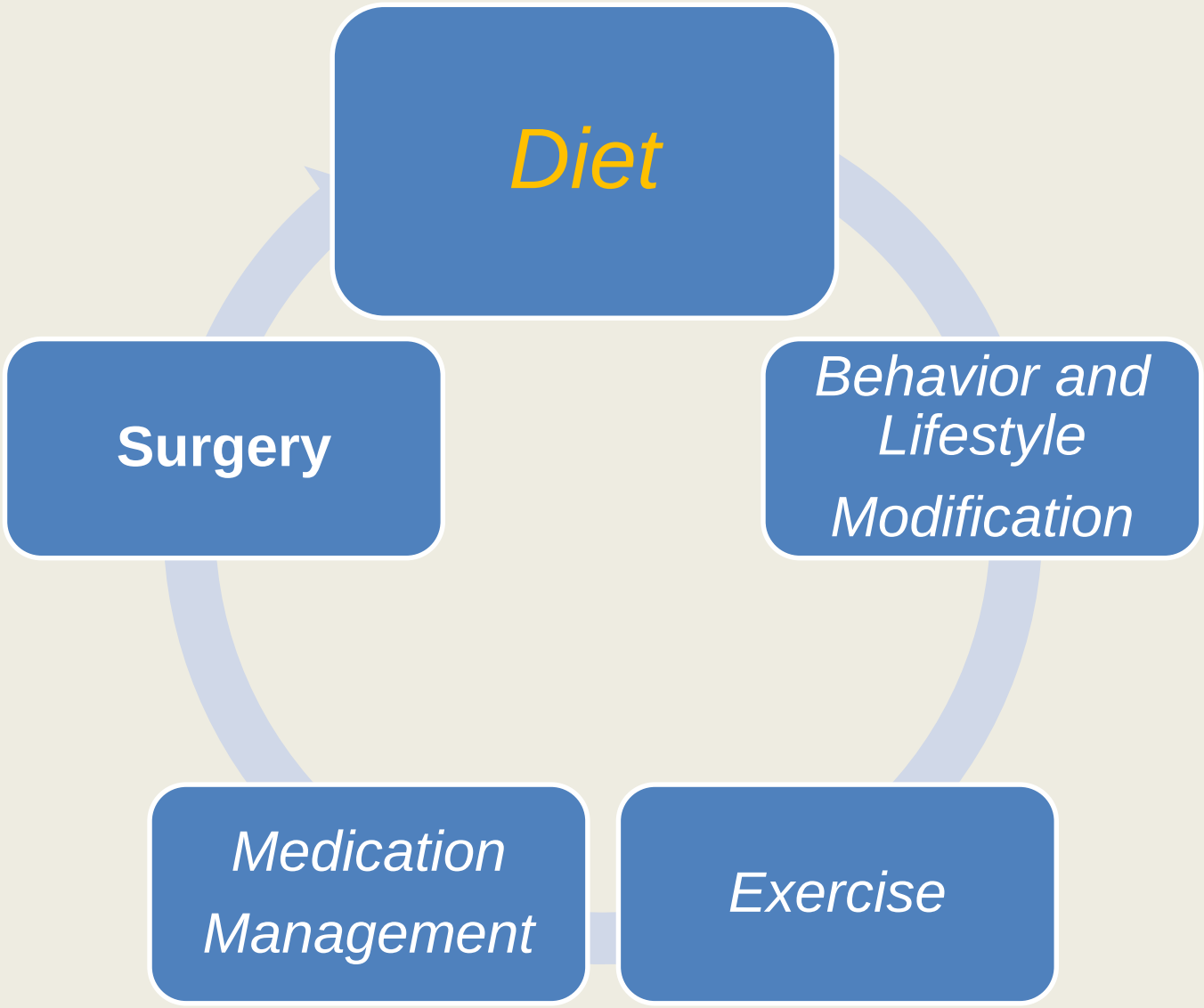
Brunzell, et al. JACC 2008; 51:1512-1524

Natural History of Type 2 Diabetes



Ramlo-Halstead, Clinical Diabetes. 2000.

Obesity Treatment Strategies



Diet – Caloric Composition

- 0-400
- 400-800
- 800-1500
- Above 1500

- Starvation or near starvation, never recommended
- Very Low Calorie Diet (VLCD)
- Low Calorie Diet (LCD)
- Balanced Deficit Diet (BDD)
  - Reduction of 500-1000 cal/day from DMR

Diet – Nutritional Composition Macronutrients

- Low Fat
  - AHA, Ornish, Pritikin
- Low Carb
  - Atkins
- High Fat
  - Atkins
- High Protein

Names associated with diets are examples only

Diet – Type or Brand

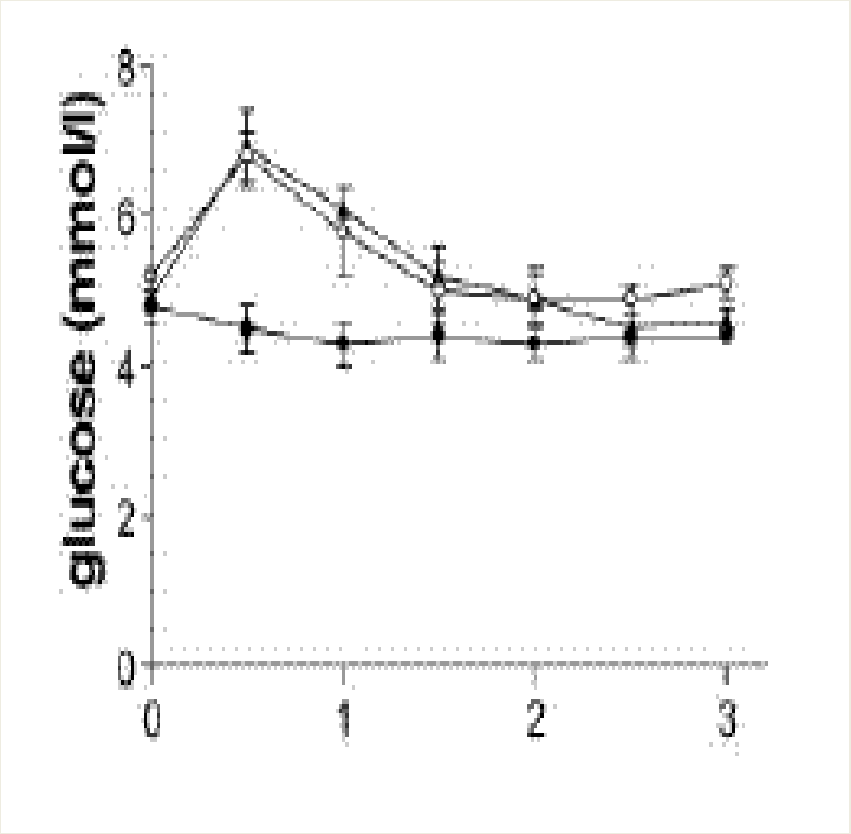
- Atkins
- Protein Power
- ZONE
- LEARN (balanced deficit)
- ADA (diabetic)
- South Beach
- Weight Watchers
- Jenny Craig
- Nutrisystems
- Optifast
- HCG
- Mediterranean
- Body for Life
- DASH
- AHA
- Pritikin
- Ornish
- “Whole Food, Plant Based”
- Vegan
- Vegetarian
- Kosher
- Halal

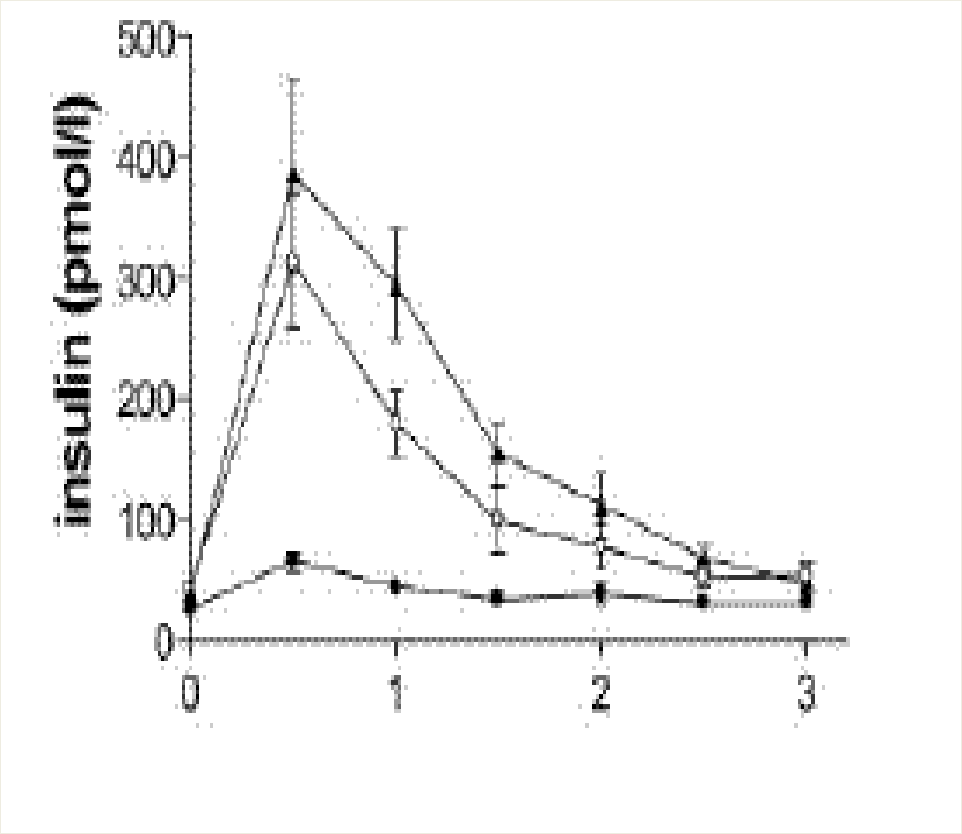
Diet – Is there a “Best” diet?

- Diet should be individualized
- All diets can be described in terms of caloric content and macronutrient content
- Many different diets have strong adherents
- All diets can be effective in weight loss
- Most obesity medicine specialists use some version of a reduced carbohydrate approach
  - All calories are not created equal

Glucose and Insulin Response to a 300 Kcal Meal

after 10 d of a high- (*triangles*), intermediate- (*open circles*), and low-carbohydrate (*closed circles*) diet (n=6).

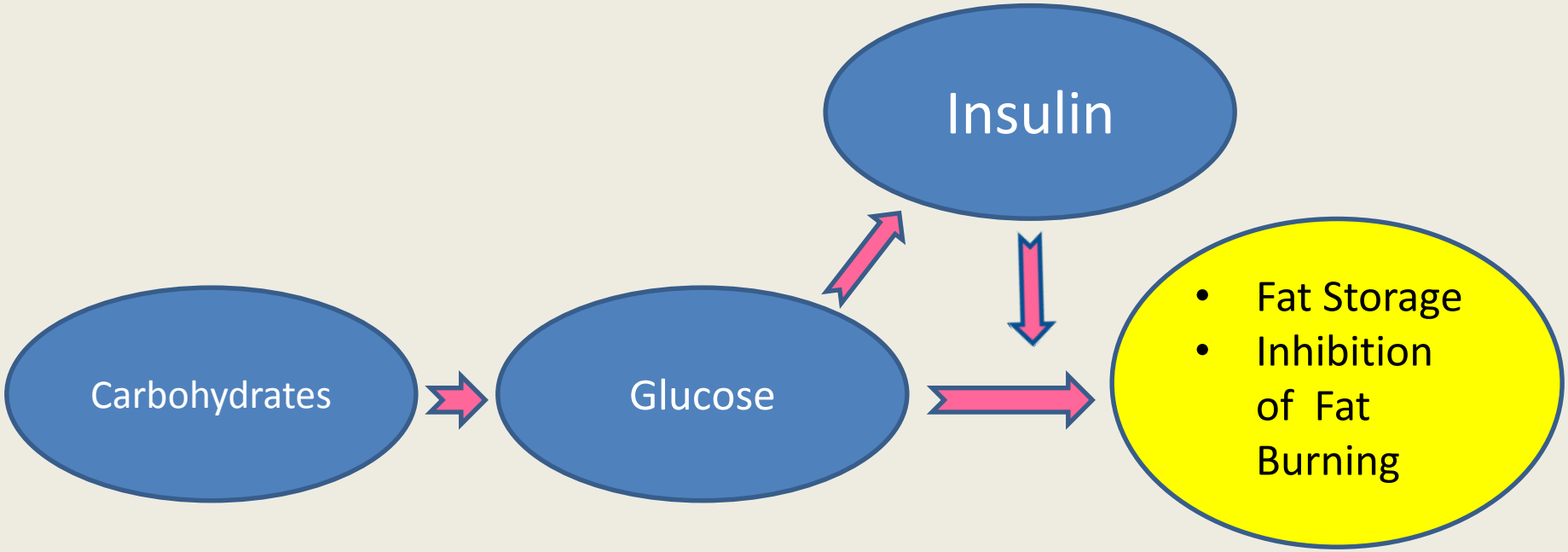


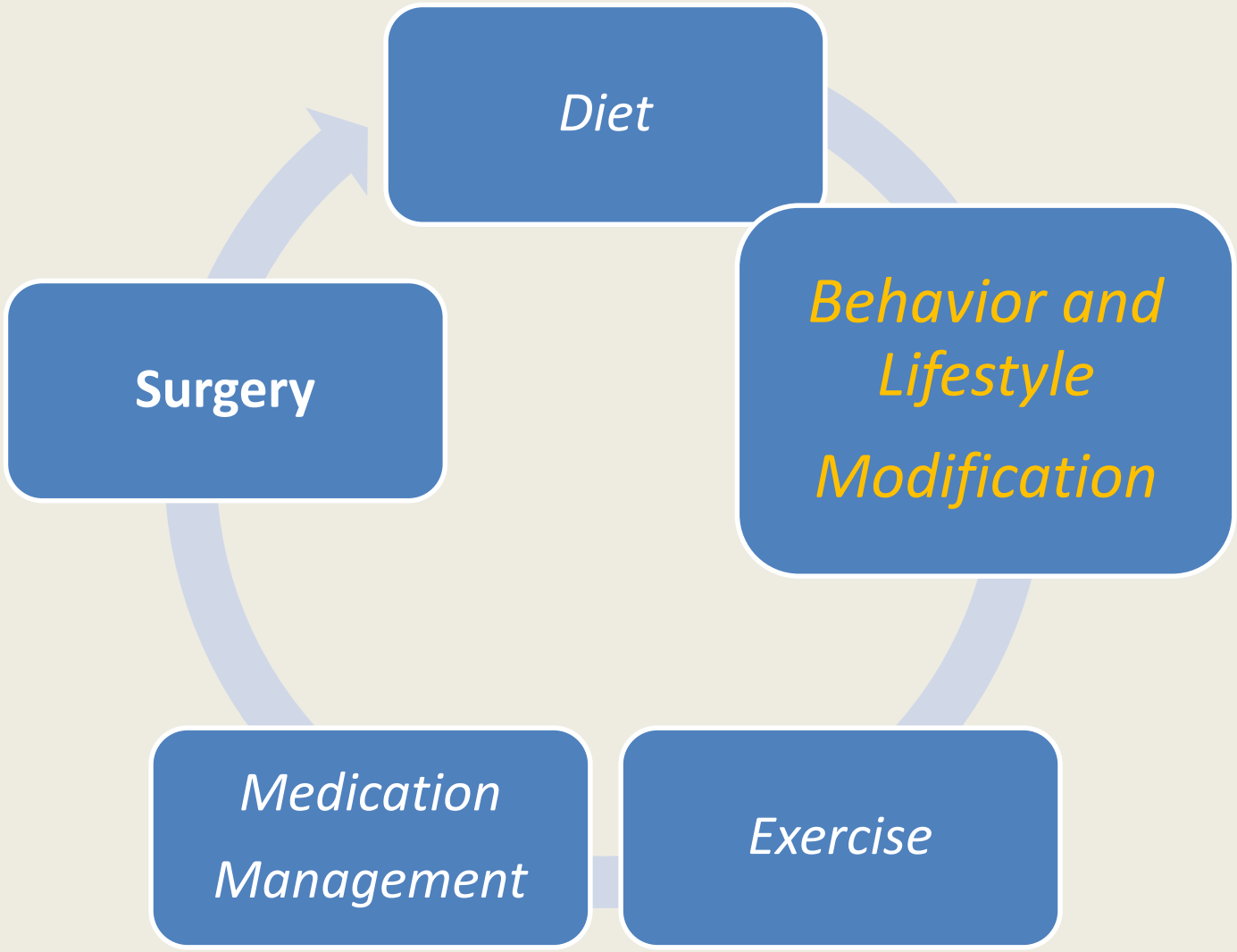


Glucose AUC was lowest for the low-carbohydrate diet (p=0.001).
Insulin AUC was different for each diet (p=0.001).

Bisschop et al. J Clin Endocrinol Metab;2003:88:3801–3805. Data are means (SE).

Carbohydrate Metabolism

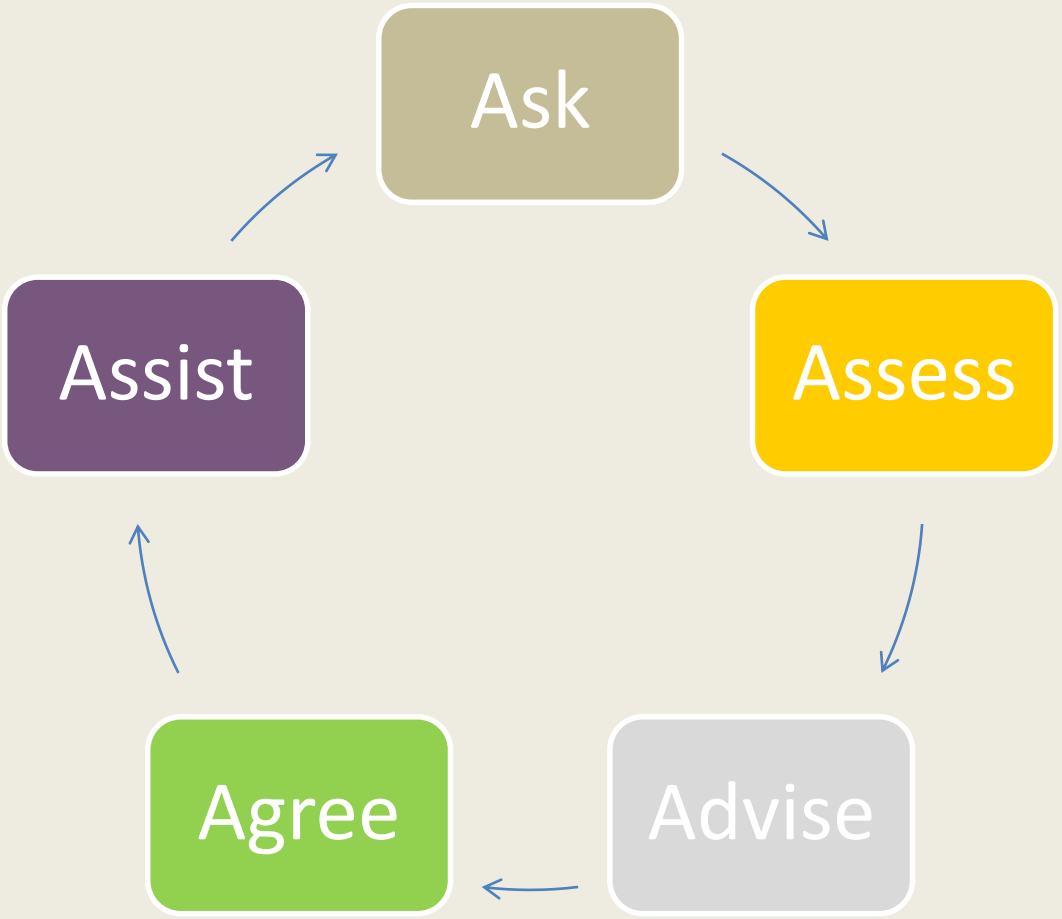



Diet
Behavior and Lifestyle Modification
Exercise
Medication Management
Surgery

Behavior and Lifestyle Modification

- Goal is to help patient learn behaviors and patterns of thinking that support weight loss and weight maintenance
- Varied counseling approaches are useful
  - Motivational Interviewing
  - Cognitive Behavioral Therapy
  - Relational/Interpersonal Therapy
- 5 A's approach currently used by Centers for Medicare and Medicaid Services (CMS)

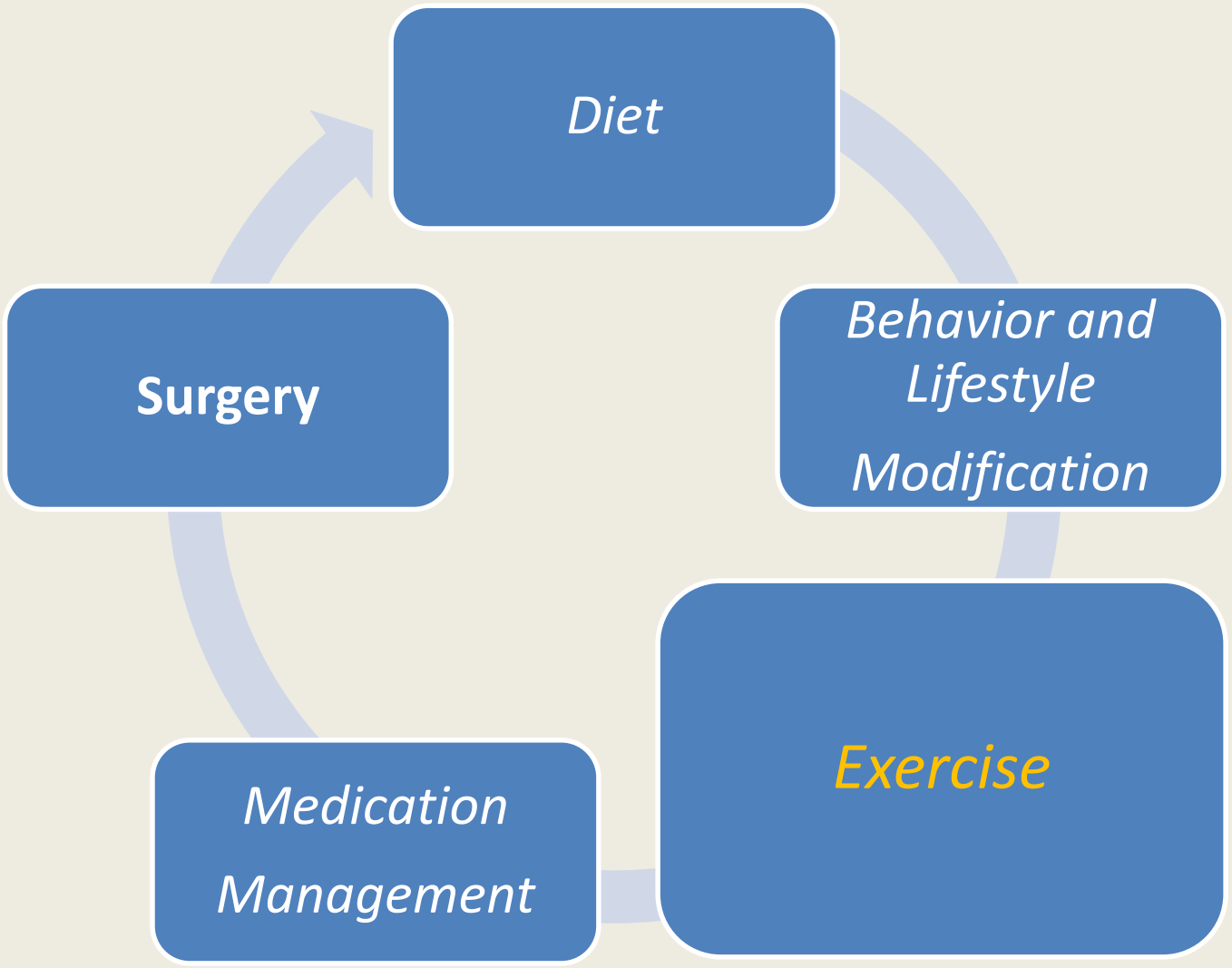
Five Major Steps to Intervention – The 5 A's



Overall Approach

Five A's of Obesity Management

Ask	Assess	Advise	Agree	Arrange/Assist
• Ask for permission to discuss body weight • Explore readiness for change	• Assess body mass index, waist circumference, and obesity stage • Explore drivers and complications of excess weight	• Advise the patient about the health risks of obesity, the benefits of modest weight loss, the need for a long-term strategy, and treatment options	• Agree on realistic weight-loss expectations, targets, behavioral changes, and specific details of the treatment plan	• Assist in identifying and addressing barriers • Provide resources • Assist in finding and consulting with appropriate providers • Arrange regular follow-ups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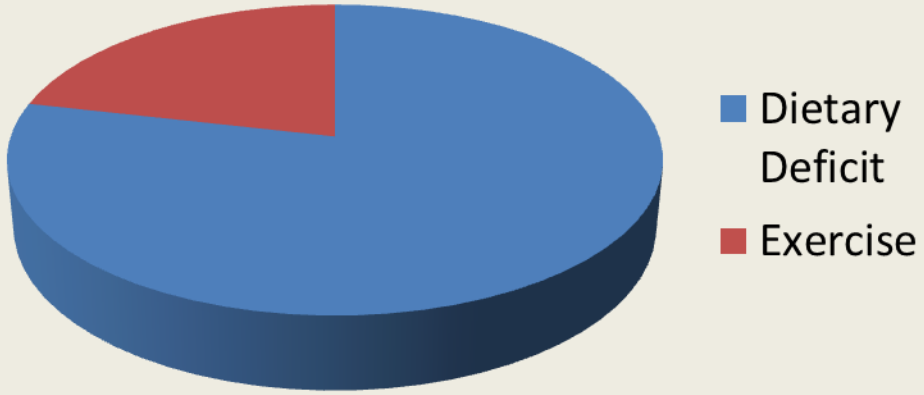
Exercise and Activity

- Part of a comprehensive plan
- More important for weight maintenance than weight loss
- Many benefits other than weight control
- Exercise Prescription

Exercise and Activity – How much does it contribute to weight loss?

- Not as much as we might think
- Example:
  - 45 yo female patient with DMR of 2200 cals per day.
  - 1100 Low Calorie Diet => diet deficit of ~1100 cal/day
  - Calories burned with 1 hour of walking ~300

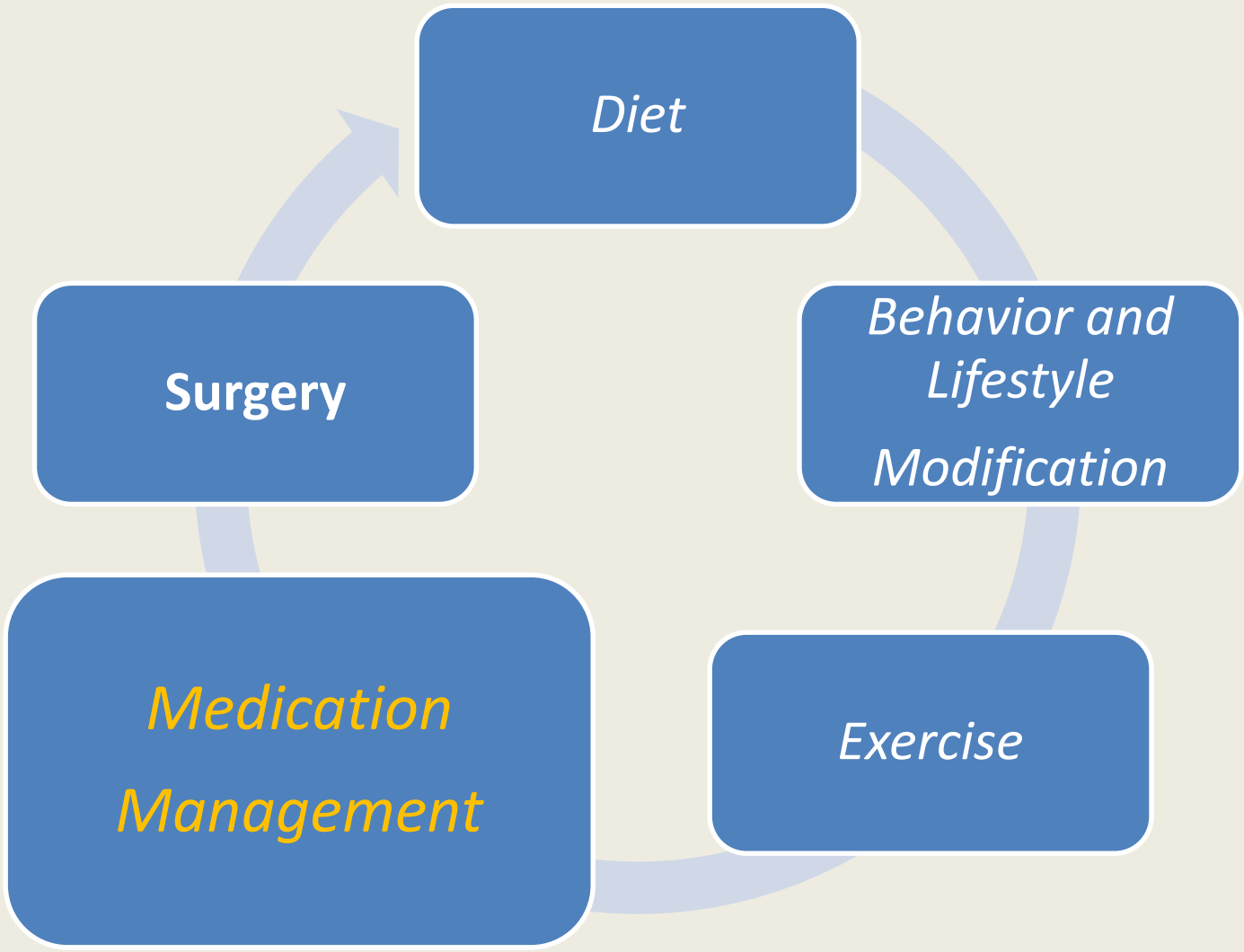


Exercise and Activity

Many benefits *other than* weight control

- Mood
- Cardiovascular fitness
- Pain
- **Glucose control**
- Dyslipidemia
- Strength
- Balance/Coordination
- ADLs (Activities of Daily Living)
- Lowers risk of some cancers

http://www.cdc.gov/physicalactivity/everyone/health/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Medications

- Medications used to treat weight
- Medications that affect weight

Medications Used to Treat Weight

- Sympathomimetics
  - Phentermine
  - Phendimetrazine
  - Diethylpropion
- Metformin
  - – Off label
- Topiramate
  - – Off label
- Gastric Lipase Inhibitor
  - Orlistat (Alli® – OTC, Xenical® –RX)
- "New" Drugs
  - GLP-1 analogues
    - Liraglutide (Saxenda®)
  - Combination
    - Phentermine/Topiramate (Qsymia®)
    - Bupropion/Naltrexone (Contrave®)
  - Serotonergic (5HT-2cR)
    - Lorcaserin (Belviq®)

Medications Used to Treat Weight Relative Advantages

- Sympathomimetics
  - Years of experience
  - Predictable
  - Inexpensive
- Newer Agents
  - Approved for extended use
  - Offer variety
  - Different mechanisms

Medications That Affect Weight

Weight Positive (Gain)

- Corticosteroids
- Antihistamines
  - Cyproheptadine(Periactin®)
- Many Antidepressants
  - MAOIs, TCAs, most SSRIs (esp paroxetine)
- Opioids
- Atypical Antipsychotics
  - risperidone, quetiapine, olanzapine, aripiprazole, ziprasidone
- Most Antiseizure meds
  - (not topiramate or zonisamide
- **Many Diabetes meds**
- Beta Blockers

Weight Negative (Lose)

- Metformin
- Nefazodone (Serzone®)
- Bupropion (Wellbutrin®)
- ?Fluoxetine (Prozac®)
- Incretins
  - Exenatide (Byetta®, Bydureon®)
  - Liraglutide (Victoza®, Saxenda®)

Weight Neutral

- Venlafaxine (Effexor®)
- Citalopram (Celexa®)
- Sertraline (Zoloft®)

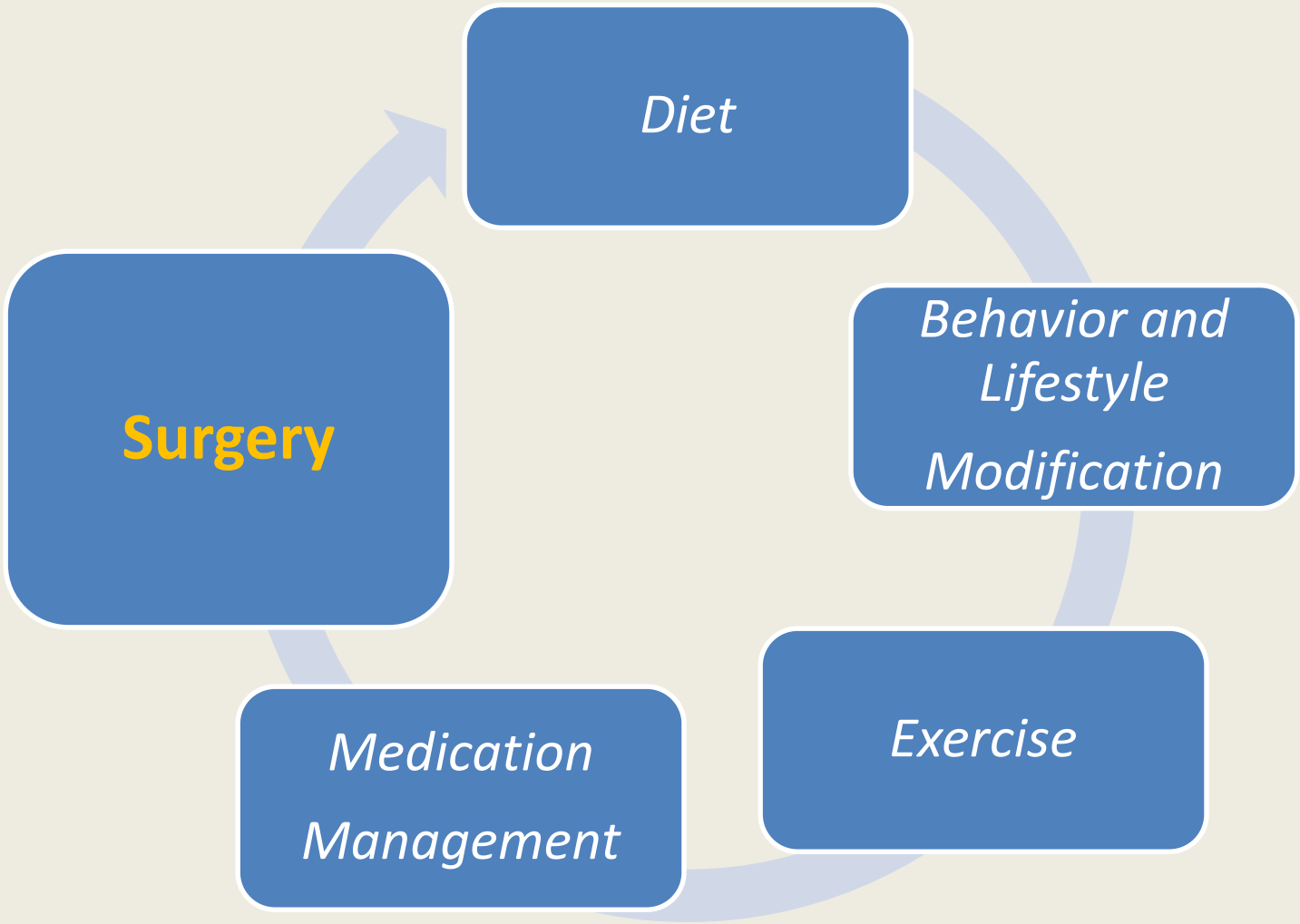
Diabetic Medications Effects on Weight

Weight Positive (gain)

- Insulins
- Thiazolidinediones (TZDs)
  - rosiglitazone (Avandia®)
  - pioglitazone (Actos®)
- Sulfonylureas
  - glimepiride (Amaryl®)
  - glipizide (Glucotrol®)
  - glyburide (DiaBeta®, Glynase®, Micronase®)
- Meglitinides
  - nateglinide (Starlix®)
  - repaglinide (Prandin®)

Weight Negative (lose)

- Metformin
- GLP-1 analogues
  - liraglutide (Victoza®, Saxenda®)
  - exenatide (Byetta®, Bydureon®)
- DPP-4 Inhibitors
  - sitagliptin (Januvia®)
- Gliflozins
  - SGLT-2 Inhibitors(sodium-glucose cotransporter 2)
    - canagliflozin (Invokana®)
    - dapagliflozin (Farxiga®)
    - empagliflozin (Jardiance®)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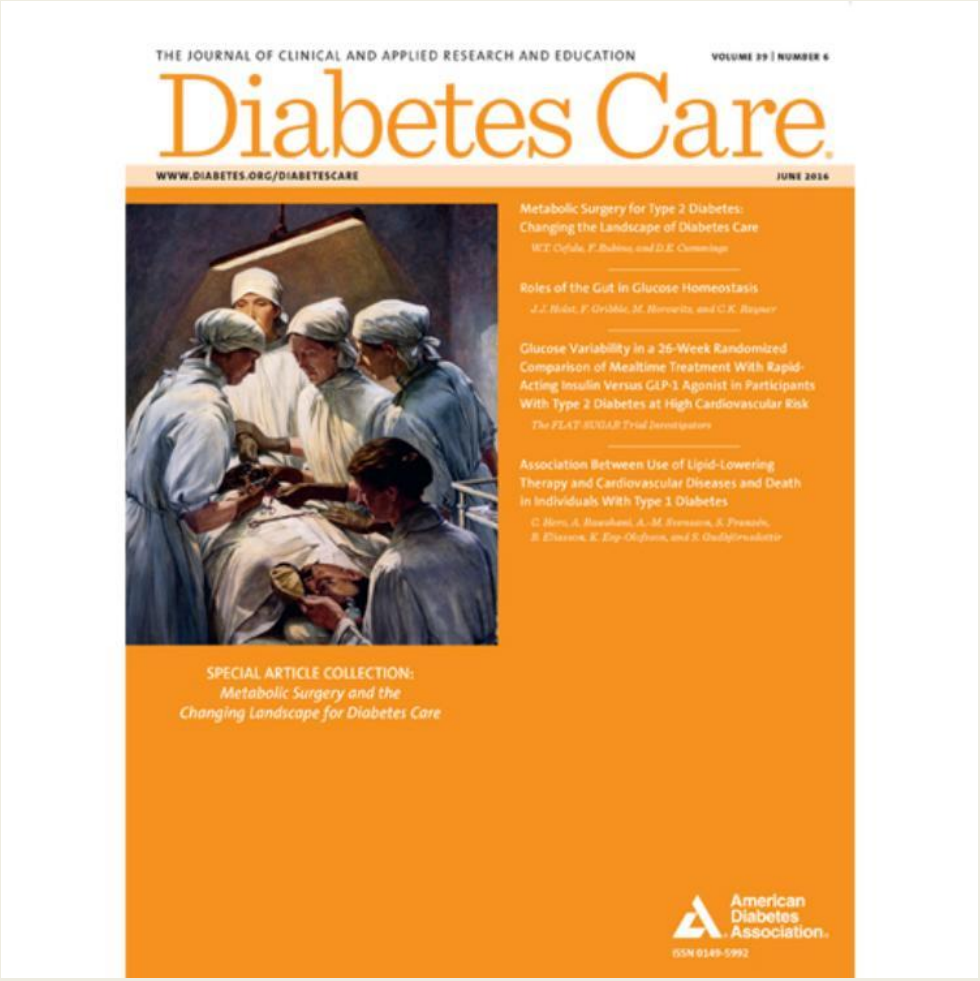
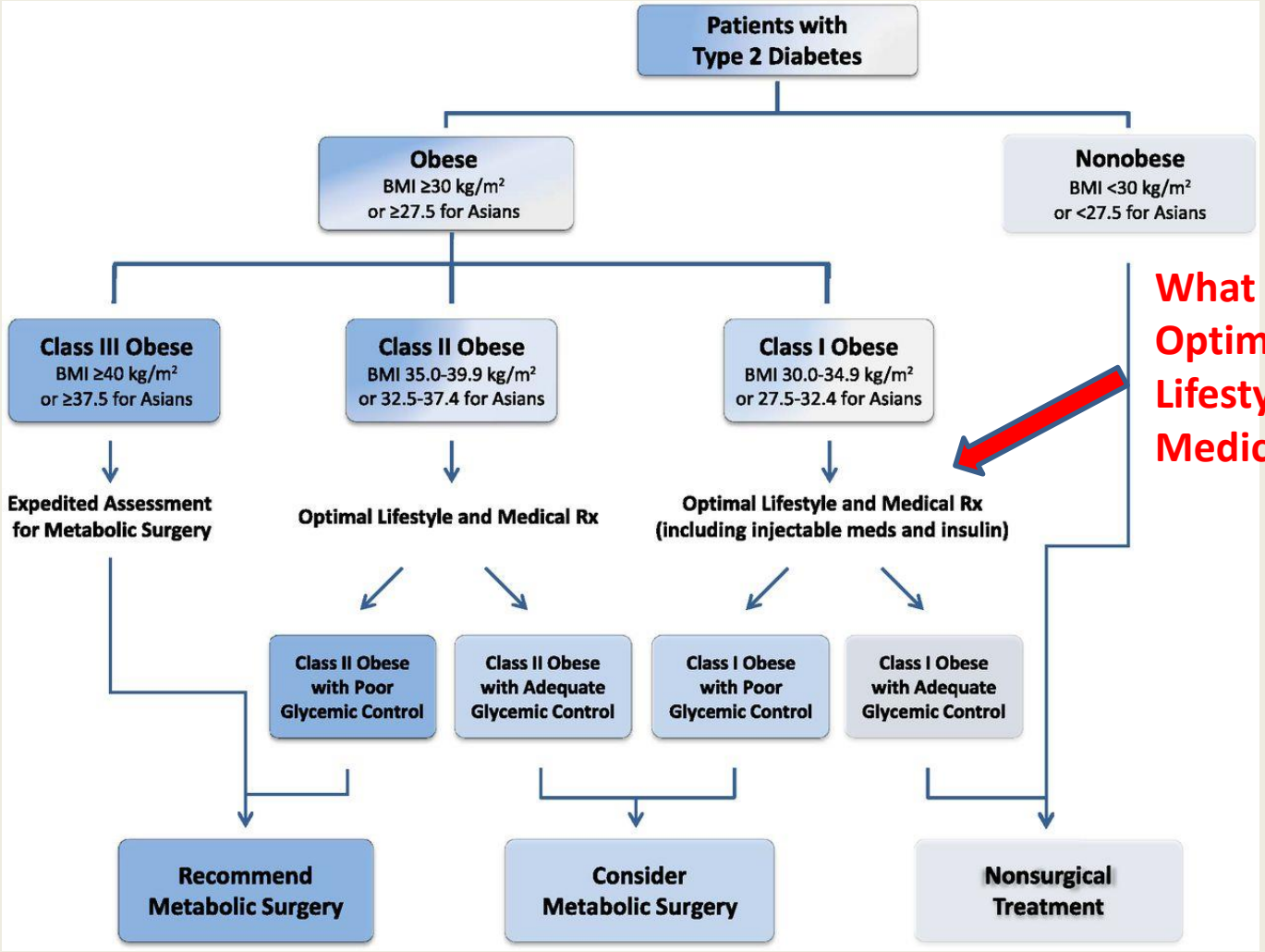
American Diabetes Association. Diabetes Care®

"The new guidelines recognize for the first time surgery as a legitimate diabetes treatment and should inform physicians and policymakers about the appropriate selection of patients for surgical treatment. Both practically and conceptually it is one of the greatest innovations in diabetes care in recent times."



Diabetes Care 2016 Jun; 39(6)

Algorithm for the treatment of T2D, as recommended by DSS-II voting delegates.



Francesco Rubino et al. Dia Care 2016;39:861-877

American Diabetes Association.

Summary

- Obesity is a chronic condition amenable to long term strategies
- Insulin resistance is central to many downstream metabolic diseases of obesity
- Carbohydrate metabolism is central to obesity and associated morbidities
- The concept of a “care continuum” is very useful and allows for combined approaches

Thank You!

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New Concepts in PCOS

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October 21, 2016

Disclosures

- None

Learning Objectives

- To review the diagnostic criteria and differential diagnosis for PCOS
- To discuss the role of environmental and genetic factors in the pathogenesis of PCOS
- To review the risk of DM, CVD, and other metabolic consequences of PCOS
- To discuss the therapeutic options for the treatment of PCOS

Definition (Rotterdam 2003)

- Diagnosis requires at least two of the following:
  - Oligo- or anovulation (oligomenorrhea)
  - Hyperandrogenemia or hyperandrogenism (acne, hirsutism)
  - Polycystic ovaries on ultrasound
- a*nd*, exclusion of other causes

Differential Diagnosis

- Non-classical (Late Onset) CAH
- Cushing’s Syndrome
- Hyperprolactinemia
- Hypothyroidism
- Premature ovarian insufficiency (POI)
- Androgen-secreting tumor

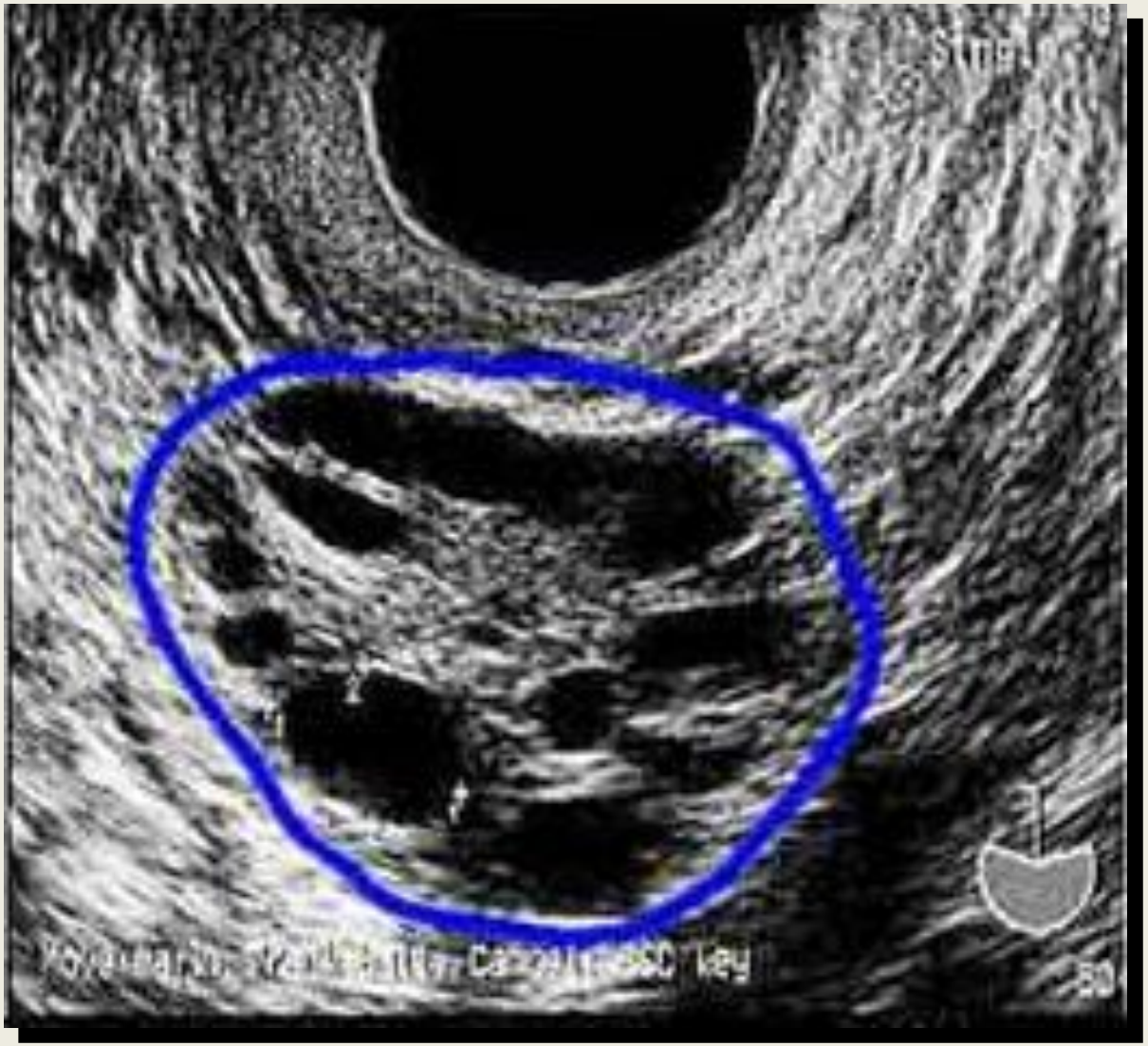
Diagnostic Work-up

- FSH, TSH, PRL, 17OHP, P4
- (LH, T, DHEAS)
- Lipids
- OGTT (FBS or HgA1C)
- (Pelvic US)
- AMH $\geq$ 5 ng/ml

Polycystic Ovaries - US Criteria

- ≥ 12 follicles measuring 2-9 mm in diameter or increased ovarian volume (>10 cm^3)

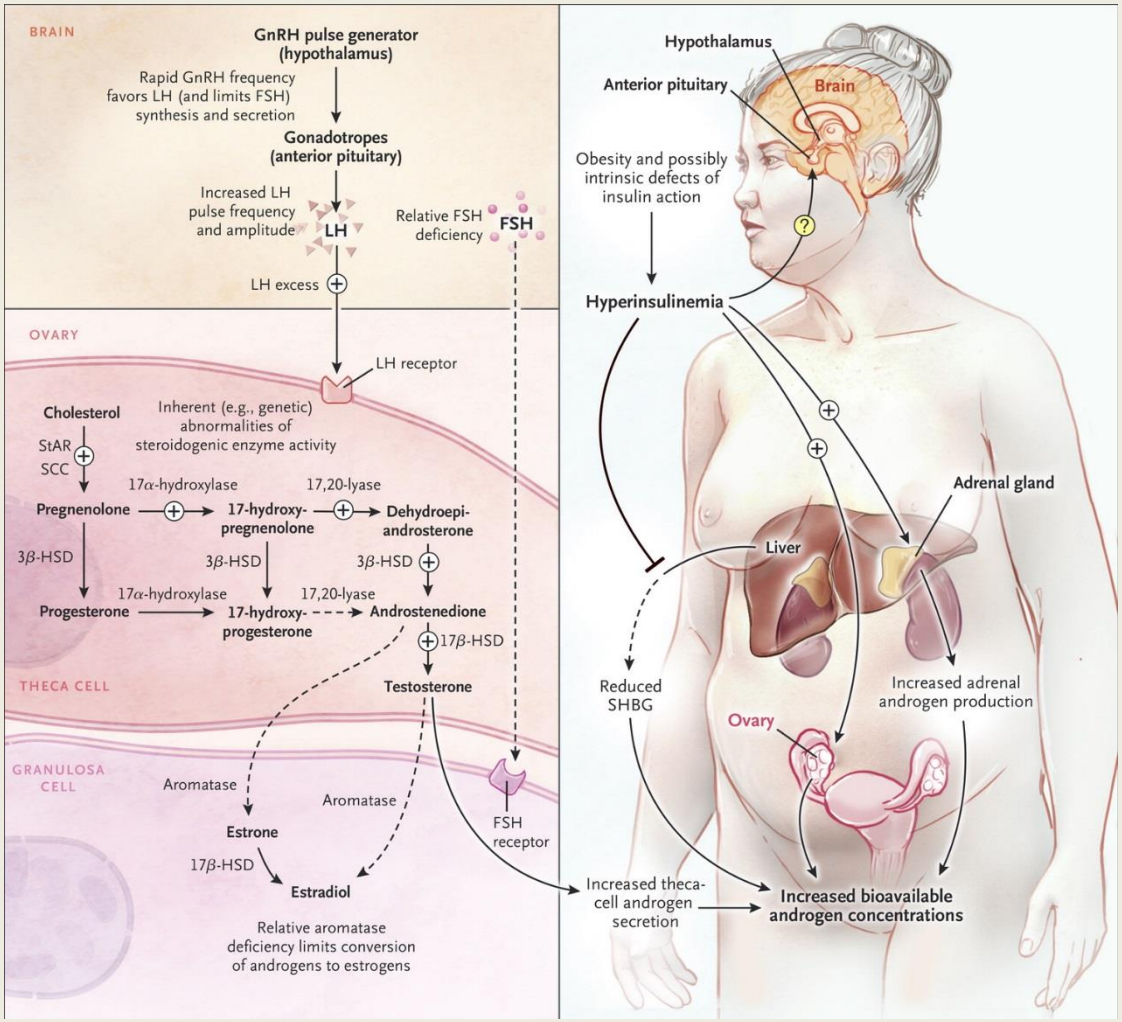
Polycystic Ovaries



Pathogenesis

- Insulin resistance/hyperinsulinemia
- Dysregulation of ovarian steroidogenic enzymes
- Gonadotropic dysfunction - ↑ GnRH pulse frequency

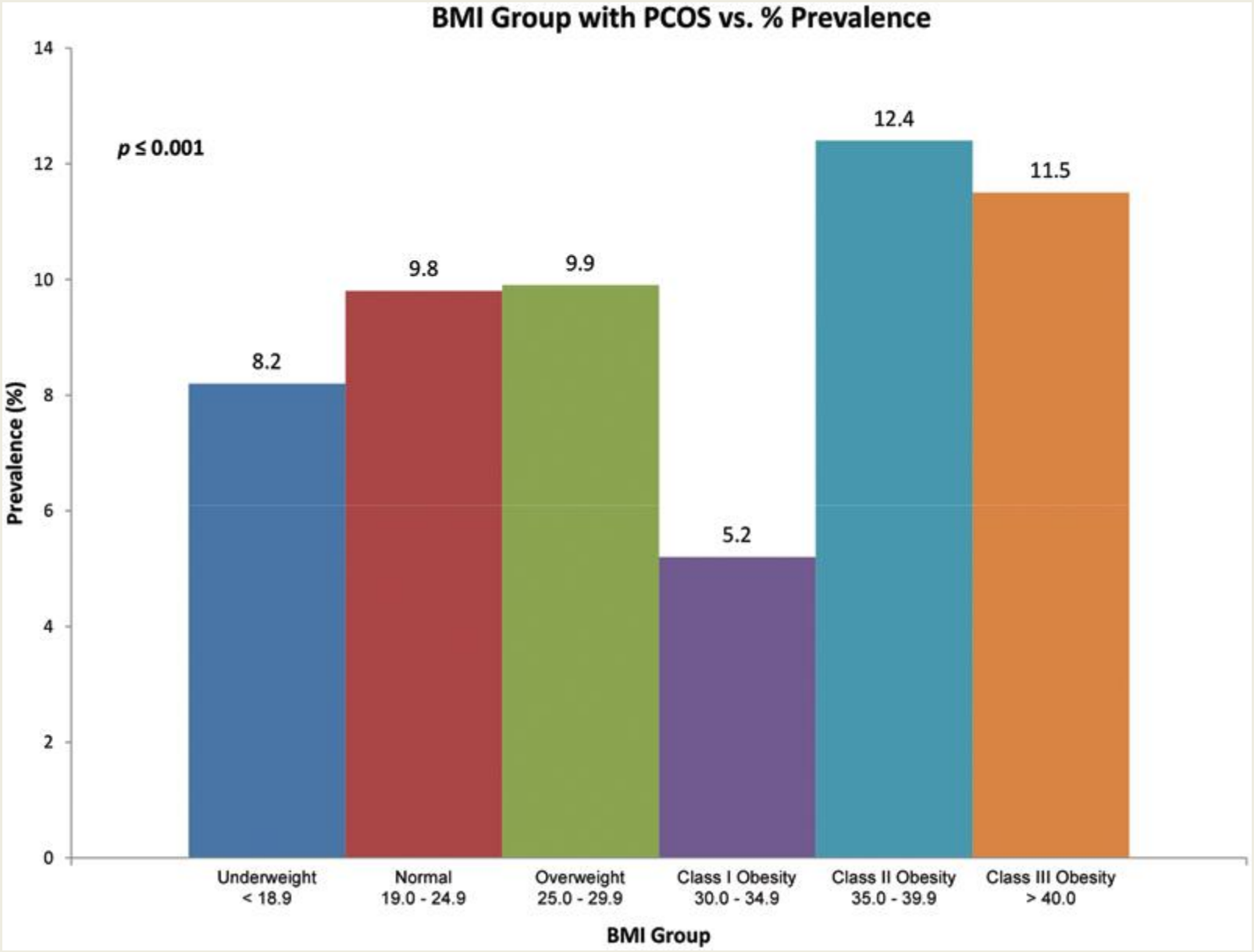
Basic Pathophysiology of Hyperandrogenemia in the Polycystic Ovary Syndrome.

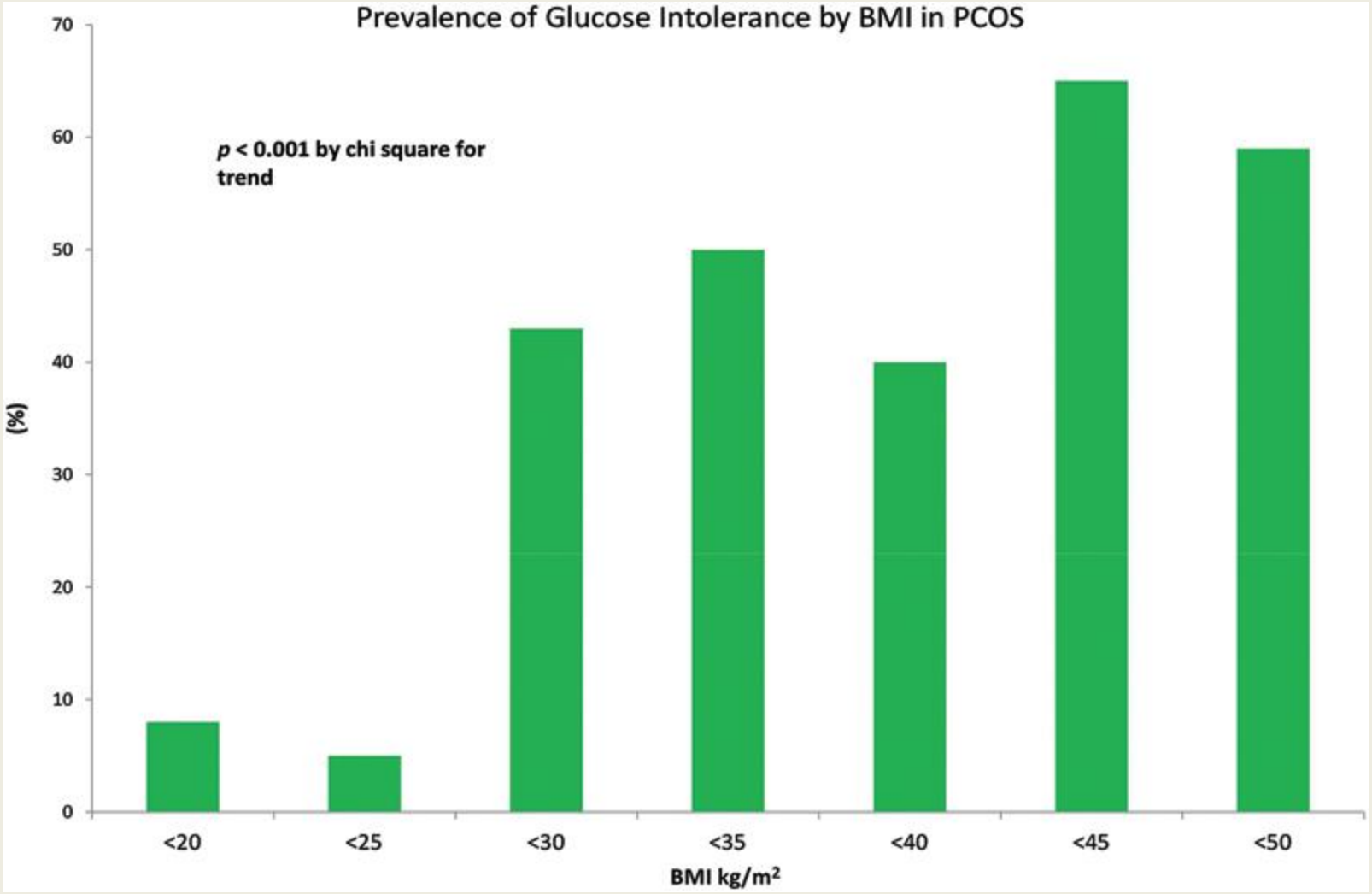


McCartney CR, Marshall JC. N Engl J Med 2016;375:54-64.

Insulin Resistance & PCOS

- Women w/ PCOS are insulin resistant compared with BMI-matched controls
- Also, defect in pancreatic β cell function
- INSR d/t post-binding defect in signal transduction; increased serine phosphorylation of INSR & IRS-1(Dunaif et al., JCI 1995)


BMI Group with PCOS vs. % Prevalence
p ≤ 0.001
Prevalence (%)
14
12
10
8
6
4
2
0
8.2
9.8
9.9
5.2
12.4
11.5
Underweight
< 18.9
Normal
19.0 - 24.9
Overweight
25.0 - 29.9
Class I Obesity
30.0 - 34.9
Class II Obesity
35.0 - 39.9
Class III Obesity
> 40.0
BMI Group


Prevalence of Glucose Intolerance by BMI in PCOS
p < 0.001 by chi square for trend
(%)
70
60
50
40
30
20
10
0
<20
<25
<30
<35
<40
<45
<50
BMI kg/m²

Insulin Resistance & PCOS

- Hyperinsulinemia enhances LH-mediated androgen secretion
- Insulin $\rightarrow \downarrow$ SHBG $\rightarrow \uparrow$ free testosterone

Ovarian Enzyme Activities in Women with PCOS

- Studies using primary ovarian tissue and cultured theca and GCs show that steroidogenic enzyme activities are upregulated in theca cells in PCOS (StAR, $P450_{SCC}$, 3β-HSD, P450C17)
- Granulosa cells underexpress aromatase and overexpress 5α-reductase
- Premature expression of LHR & $P450_{SCC}$
- Net result - ↑ androgen/estrogen ratio

Gonadotropin Dysfunction in Women with PCOS

- ↑ GnRH pulse freq - 1° vs 2° to low progesterone levels → ↑ LH pulse freq/amp → ↑ LH/FSH ratio
- LH pulse amplitude is inversely proportional to BMI
- Recent ovulation (high P4 levels) → ↓ LH levels
- Elevated LH levels are not required for increased ovarian androgen secretion

Role of Genetic Factors

- PCOS is a heterogeneous disorder
- Prevalence of 6-8% in reproductive age women
- Higher incidence in Hispanics
- Complex, multigenic disorder
- Evidence for linkage and association of a marker locus on chr 19 near INSR gene

Role of Environmental Factors

- Association btw premature pubarche (PP) & hyperinsulinemia/hyperandrogenism (Ibanez et al, 90s)
- Association btw low birth weight (LBW) & PP
- Association btw LBW and PCOS

Role of Environmental Factors

- Prenatal growth retardation → endocrine-metabolic adaptations → hyperinsulinemia → postnatal wt catch-up → ovarian hyperandrogenism → premature pubarche → PCOS (fetal programming)
- Genetic modulators

Longterm Consequences of PCOS

- Obesity (30-75% of patients) - ↑ WHR; prevalence higher in US *vs* Europe
- ↑ risk of T2DM & gestational diabetes (GDM)
- HT & vascular dysfunction
- CVD
- Hyperlipidemia
- Obstructive sleep apnea
- Endometrial hyperplasia/cancer
- Depression and anxiety

Type II DM & PCOS

- Prevalence of glucose intolerance is 30-40% and of type II DM is 10% by 4th decade
- IR, βcell dysfunction, obesity, FHx of type II DM, personal hx of GDM → risk factors for DM

Metabolic Syndrome in Women with PCOS

- High prevalence of metabolic syndrome in PCOS across all age groups
- Metabolic syndrome is associated with an increased risk of CVD and type II DM
- Most prevalent metabolic components are ↓ HDL, obesity, and HT
- Free T and SHBG are major predictors of metabolic syndrome in PCOS

Evidence for the Association between PCOS and CVD

- Recognized CVR factors
  - ↑TC, ↑LDL, ↑TG, ↓HDL
- Emerging/novel CVR factors
  - ↑CRP; ↑WBC (lymphocytes & monocytes)
- Direct measurement of subclinical CVD
  - LVH & diastolic dysfunciton, ↑IMT; endothelial dysfunction: FMD, ↑ET-1; impaired fibrinolysis (↑PAI-1)
- Increased clinical CVD
  - No increased mortality for CVD in PCOS

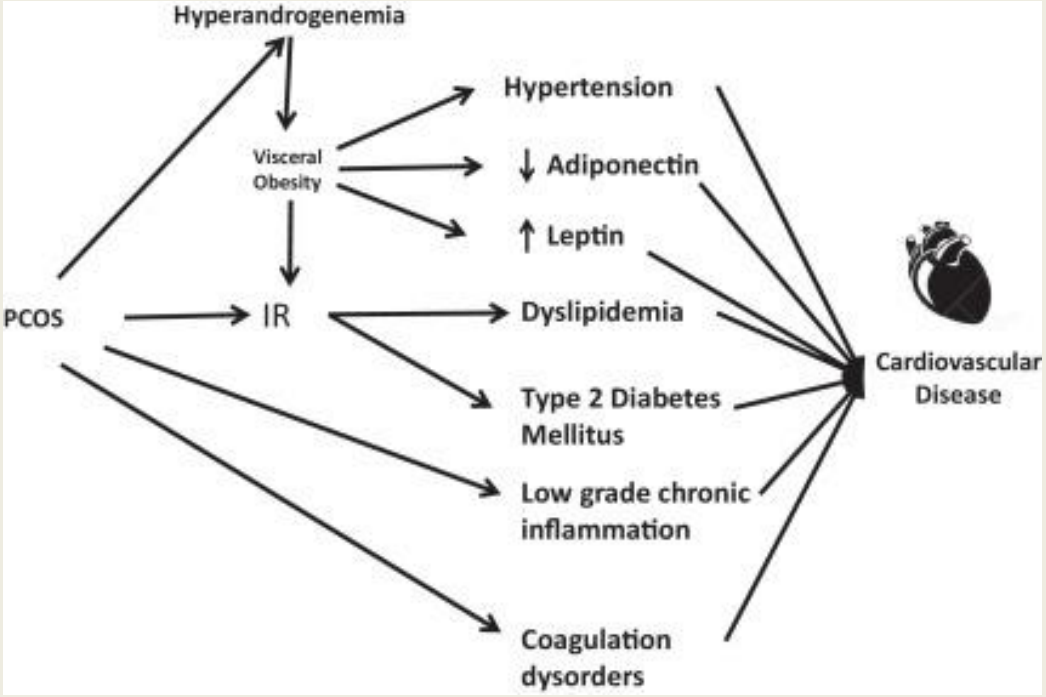


Fig. 1. Pathogenesis of cardiovascular disease in polycystic ovarian syndrome. Polycystic ovarian syndrome (PCOS) has been identified as a risk factor for cardiovascular disease. The multiple risk factors for cardiovascular disease that are associated with PCO...

Francesco Orio, Giovanna Muscogiuri, Cinar Nese, Stefano Palomba, Silvia Savastano, Domenico Tafuri, Giorgio Colarieti, Giovanbattista La Sala, Annamaria Colao, Bulent O. Yildiz

Obesity, type 2 diabetes mellitus and cardiovascular disease risk: an uptodate in the management of polycystic ovary syndrome

European Journal of Obstetrics & Gynecology and Reproductive Biology, 2016, Available online 12 August 2016

http://dx.doi.org/10.1016/j.ejogrb.2016.08.026

Treatment for Women with PCOS

- Infertility
  - CC, insulin-sensitizers, aromatase inhibitors, FSH, IVF
- Hirsutism
  - OCPs, antiandrogens
- Menstrual irregularity
  - OCPs or cyclic progestogens
- Weight/metabolic concerns
  - Diet/lifestyle modification, insulin-sensitizers, Orlistat, bariatric surgery

Treatment of Hirsutism/Acne

- OCPs
  - ↓ LH → ↓ androgen secretion
  - ↑ SHBG → ↓ free testosterone
  - Less androgenic progestins preferred (desogestrel, norgestimate, drosperinone)
- Antiandrogens
- Insulin-sensitizers

Treatment of Hirsutism/Acne

- Antiandrogens
  - Spironolactone 100-200 mg/d
  - Flutamide 250 mg/d; AR-blocker; concern re liver toxicity
  - Finasteride 5 mg/d; 5α-reductase inhibitor

Management of Oligomenorrhea

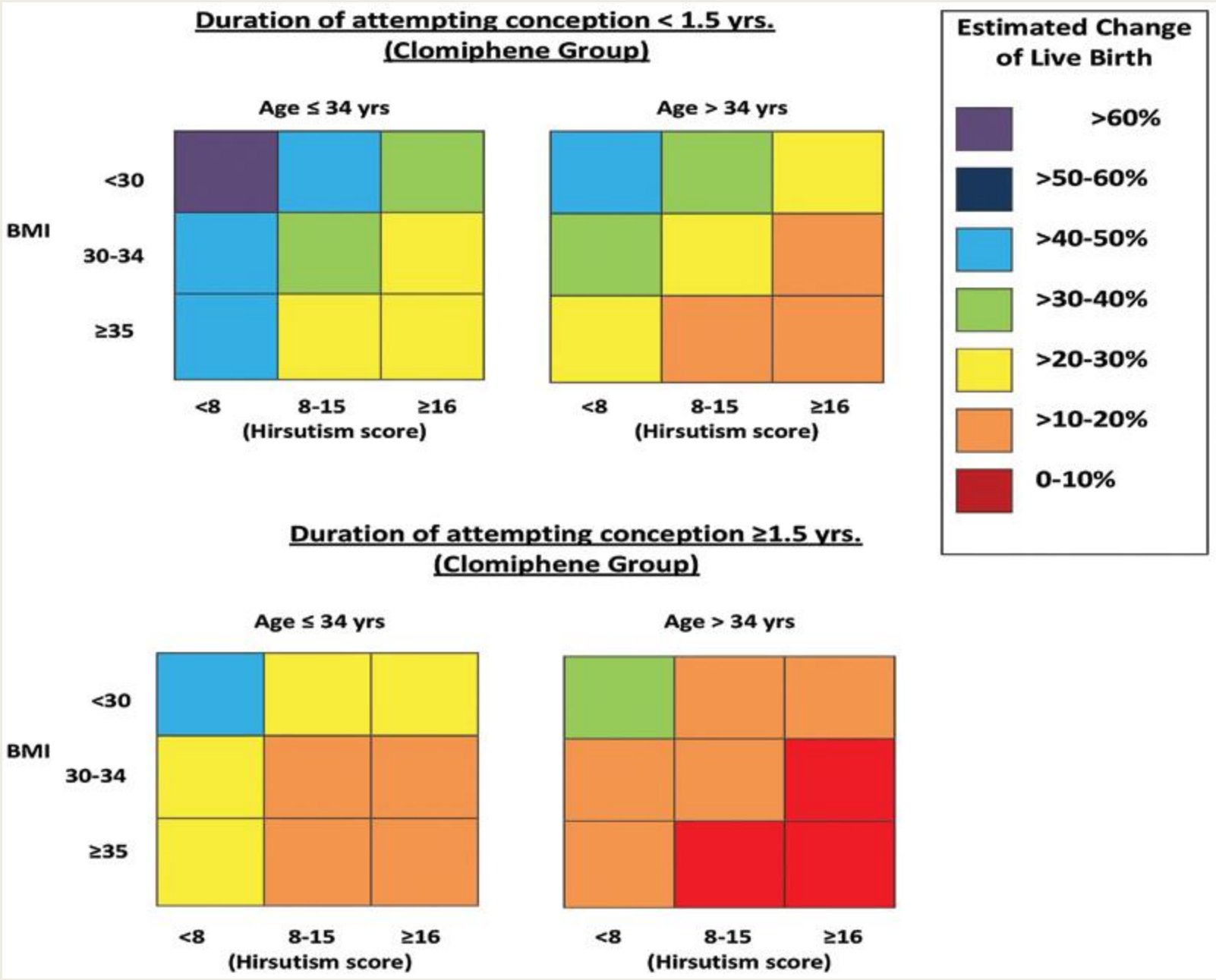
- Consider an endometrial biopsy to rule out endometrial hyperplasia
- OCPs
- Cyclic progestogens
- Levonorgestrel IUD
- Lifestyle modification/weight-loss
- Insulin-sensitizing medications

Management of the Adolescent and Young Women w/ PCOS

- Evidence that Metformin plus anti-androgen may normalize the metabolic abnormalities in PCOS
- Metformin-flutamide better than OCPs
- Metformin-flutamide + OCPs better than OCPs alone (Ibanez & de Zegher, Fertil Steril 2006)

Lifestyle Modification/Weight Loss

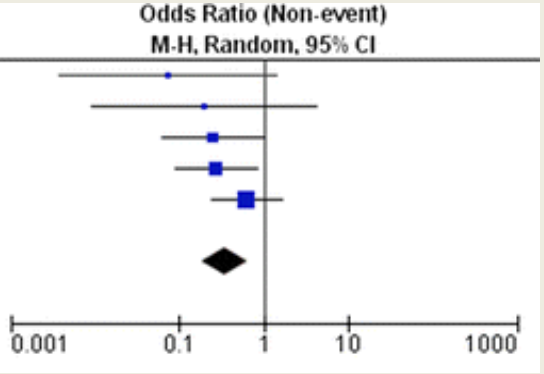
- Weight loss improves the reproductive and metabolic characteristic of overweight and obese patients with PCOS
- General recommendations:
  - Behavioral modification
  - Hypocaloric low GI diet
  - Moderate intensity aerobic exercise 30 min/d x 5d/wk
  - Orlistat can be considered
  - Metformin should be reserved for patients with T2DM
  - Consider bariatric surgery for obese PCOS patient with co-morbidities


Duration of attempting conception < 1.5 yrs.
(Clomiphene Group)
Age ≤ 34 yrs
Age > 34 yrs
BMI
<30
30-34
≥35
<8
8-15
≥16
(Hirsutism score)
Estimated Change of Live Birth
>60%
>50-60%
>40-50%
>30-40%
>20-30%
>10-20%
0-10%
Duration of attempting conception ≥1.5 yrs.
(Clomiphene Group)
Age ≤ 34 yrs
Age > 34 yrs
BMI
<30
30-34
≥35
<8
8-15
≥16
(Hirsutism score)

Study or Subgroup	Pre Bariatric Events	Total	Post Bariatric Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI
Eid 2005	5	24	0	24	4.5%	0.07 [0.00, 1.39]
Dixon2002	2	107	0	107	4.2%	0.20 [0.01, 4.14]
Jama 2012	10	20	4	20	19.7%	0.25 [0.06, 1.02]
Talebpour2011	14	254	4	254	30.7%	0.27 [0.09, 0.85]
George2013	11	156	7	156	40.9%	0.62 [0.23, 1.64]
Total (95% CI)		**561**		**561**	**100.0%**	**0.35 [0.19, 0.65]**
Total events	42		15			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.99$, $df = 4$ ($P = 0.56$); $I^2 = 0\%$

Test for overall effect: $Z = 3.31$ ($P = 0.0009$)



Management of Infertility in Women with PCOS

- Weight loss
- Optimize HgA1C and vitamin D levels pre-pregnancy
- Clomiphene citrate
- Aromatase inhibitors
- Insulin-sensitizing medications
  - Metformin
  - Thiazolinediones
- Gonadotropins
- IVF

Complications of Ovulation Induction

- Multiple pregnancy
- Ovarian hyperstimulation syndrome (OHSS)

Clomiphene Citrate (CC)

- Historically first-line drug of choice
- Antiestrogen
- Clomiphene citrate 50-150 mg D3-7
- 80% of patients with PCOS respond to CC
- Antiestrogen effects on endometrial lining and cervical mucus
- Clomiphene associated with a higher live birth rate than metformin and combination no better than clomiphene alone (Legro et al, NEJM ‘07)

Aromatase Inhibitors (Letrozole)

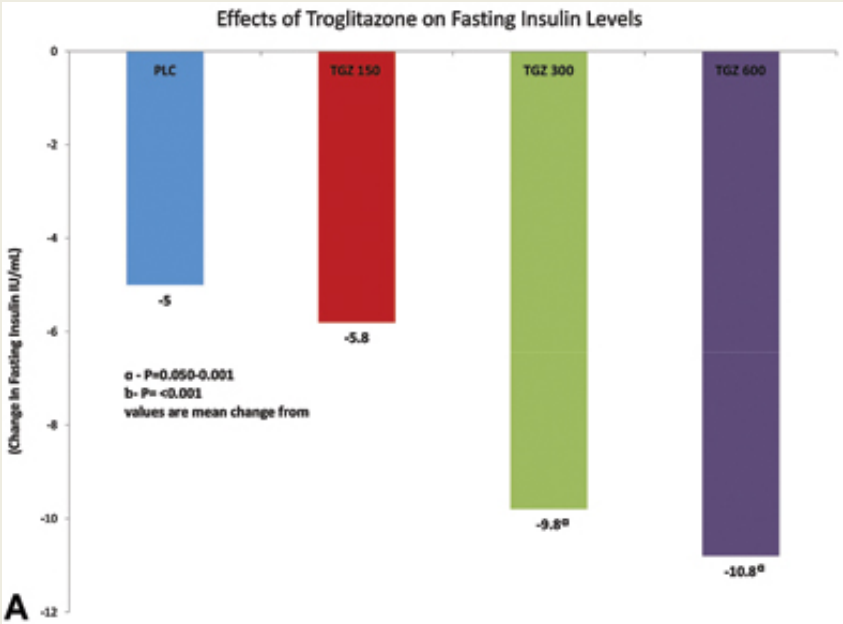
- Inhibit conversion of androgens to E2
- Letrozole 2.5-7.5 mg/d D3-7
- Letrozole associated with a higher live birth rate than clomiphene citrate (Legro et al, NEJM ‘14)
- Now considered first-line therapy in PCOS
- No antiestrogenic effects on end target tissues
- Well-tolerated
- Recent reports of teratogenicity - unsubstantiated

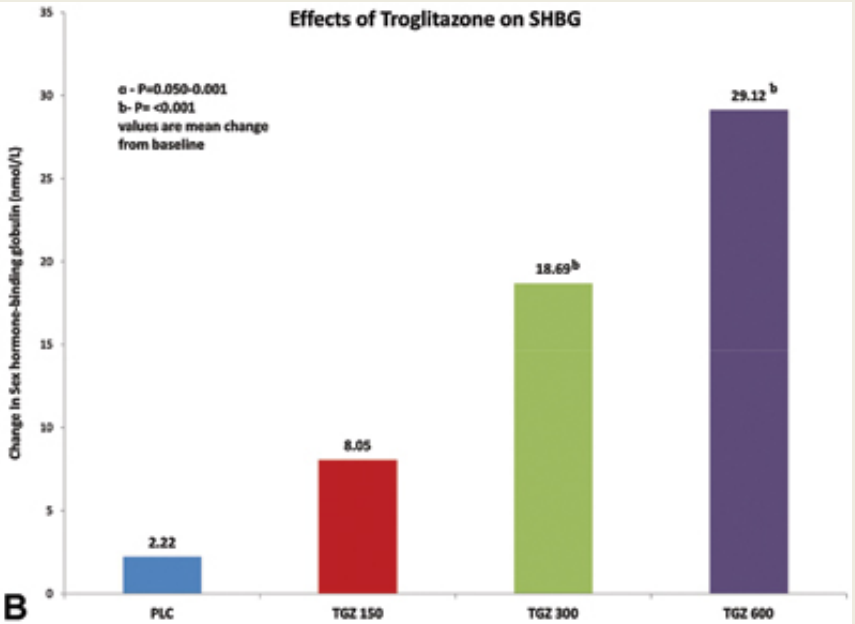
Metformin

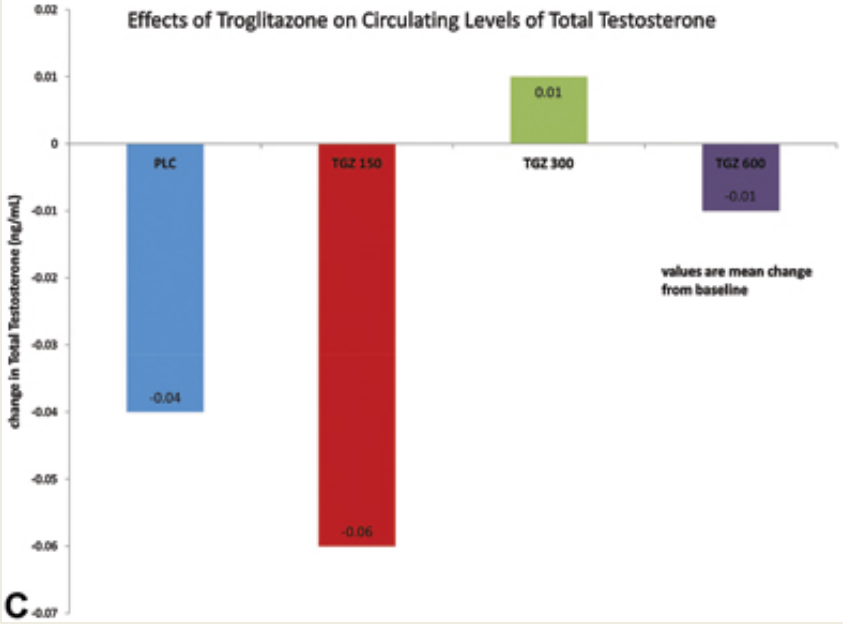
- Biguanide; dose 500 mg tid or 850 bid
- Inhibits hepatic glucose production; increases glucose uptake in muscle
- Used in combination with CC, AI, or FSH in resistant patients
- ↓ ins, ↓ T, improve ovulation, ↑ preg rates
- Used to decrease risk of OHSS in PCOS patients during IVF

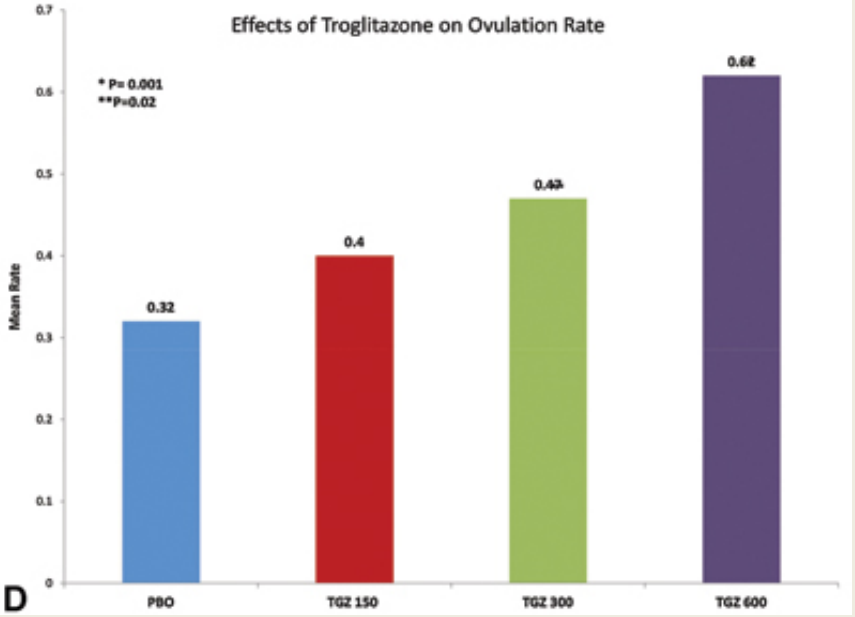
Thiazolinediones

- Results comparable to Metformin
- ? Safety in pregnancy
- Commonly cause edema & wt gain


Effects of Troglitazone on Fasting Insulin Levels
(Change in Fasting Insulin IU/mL)
PLC
TGZ 150
TGZ 300
TGZ 600
-5
-5.8
-9.8a
-10.8a
a - P=0.050-0.001
b- P= <0.001
values are mean change from
A


Effects of Troglitazone on SHBG
Change in Sex hormone-binding globulin (nmol/L)
a - P=0.050-0.001
b- P= <0.001
values are mean change from baseline
2.22
8.05
18.69b
29.12b
PLC
TGZ 150
TGZ 300
TGZ 600
B


Effects of Troglitazone on Circulating Levels of Total Testosterone
change in Total Testosterone (ng/mL)
PLC
TGZ 150
TGZ 300
TGZ 600
-0.04
-0.06
0.01
-0.01
values are mean change from baseline
C


Effects of Troglitazone on Ovulation Rate
Mean Rate
* P= 0.001
**P=0.02
0.32
0.4
0.68
PBO
TGZ 150
TGZ 300
TGZ 600
D

Gonadotropins

- “Low-slow protocol” - monofollicular development

Ovarian Drilling (LOD)

- Resumption of ovulation and menstrual cyclicity in 80% of patients
- ↓ androgen levels, ↓ LH/FSH ratio, improved ovulation
- Controversial - risk of adhesion formation
- ↓ risk of multiple preg/OHSS

In-vitro Fertilization (IVF)

- Gonadotropins ± Meformin
- Gnrh agonist (Lupron) trigger to decrease risk of OHSS
- *In vitro* oocyte maturation (experimental)

Treatment Algorithm for Infertility in Patients with PCOS

Wt loss

↓

CC or Letrozole or Metformin

↓

(CC or Letrozole) + Met

↓

Low-slow Gonadotropins ± Met

↓

IVF

Role of Obesity in PCOS

- Obesity is likely not a cause of PCOS
- However, obesity does exacerbate many aspects of the phenotype
- Obesity is associated with a poor response to infertility treatment and likely an increased risk of pregnancy complications
- Encouraging weight loss is front-line therapy
- Further studies are needed to identify the best treatment
- The role of lifestyle therapies in women of normal weight with PCOS is uncertain

OHSU

Obesity and Cancer

Bruce M. Wolfe, M.D., FACS, FASMBS

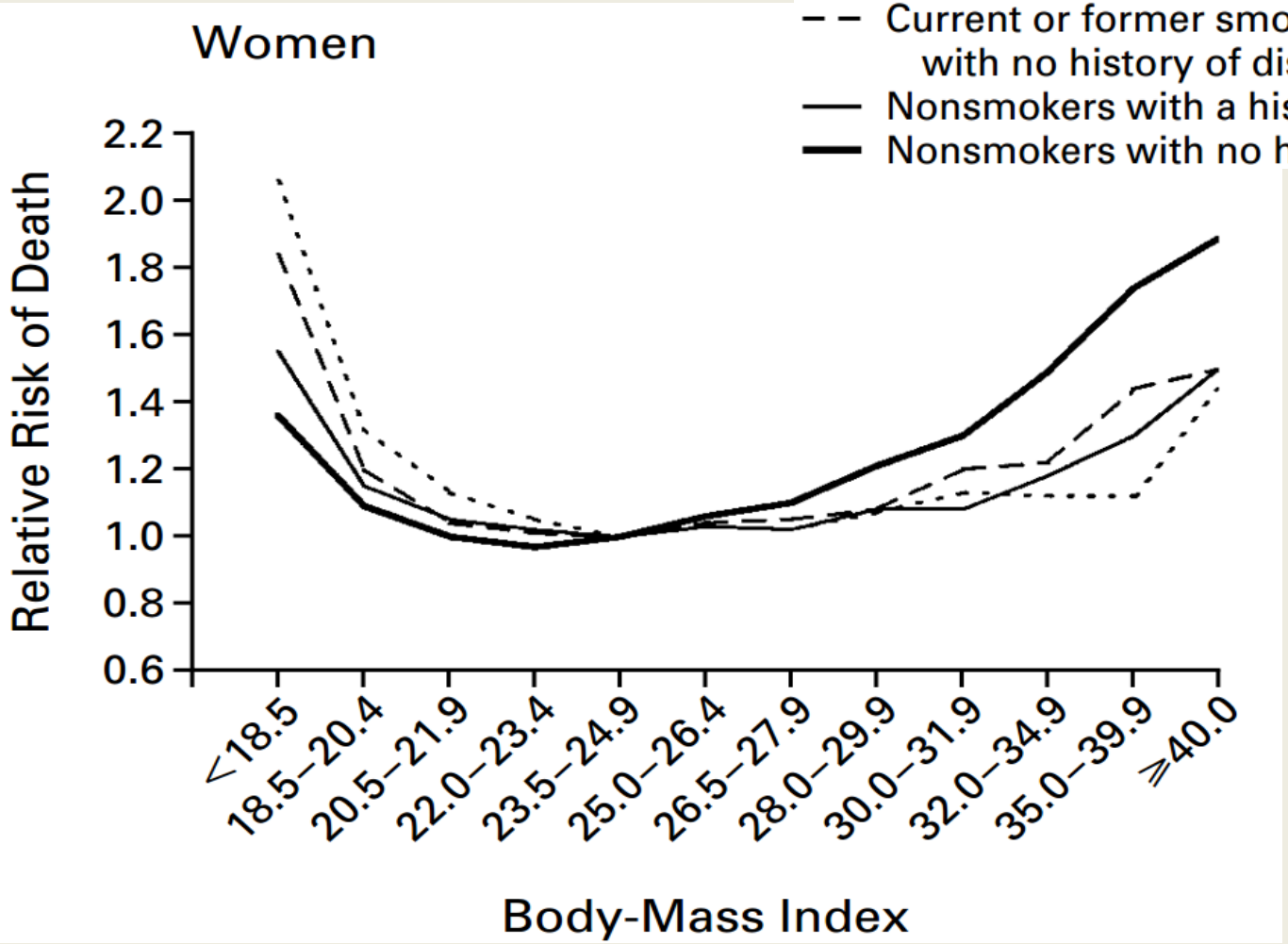
Portland, OR

Disclosures

EnteroMedics – consultant

BMI v. Mortality

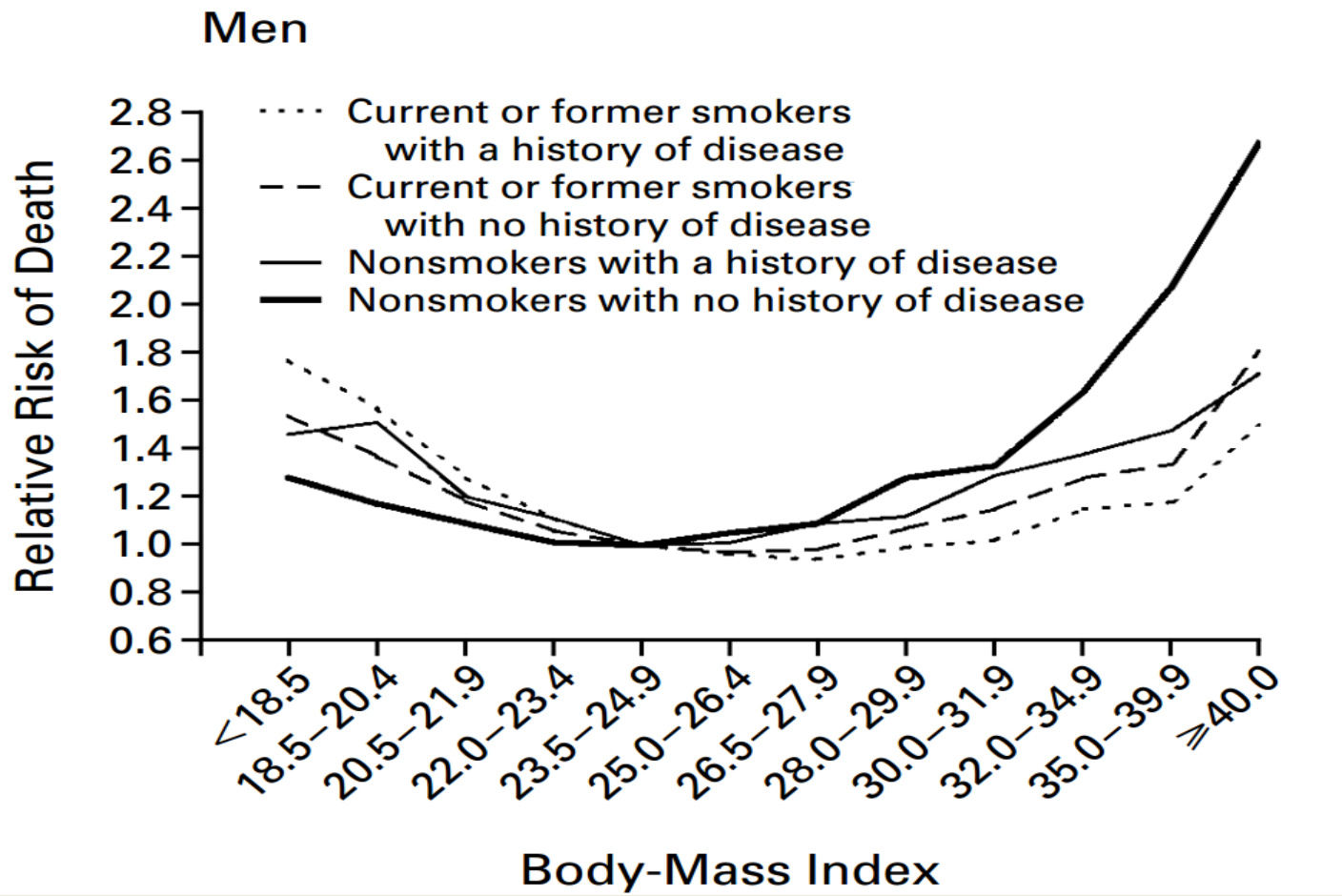
Women



Calle: NEJM(1999);341:1097

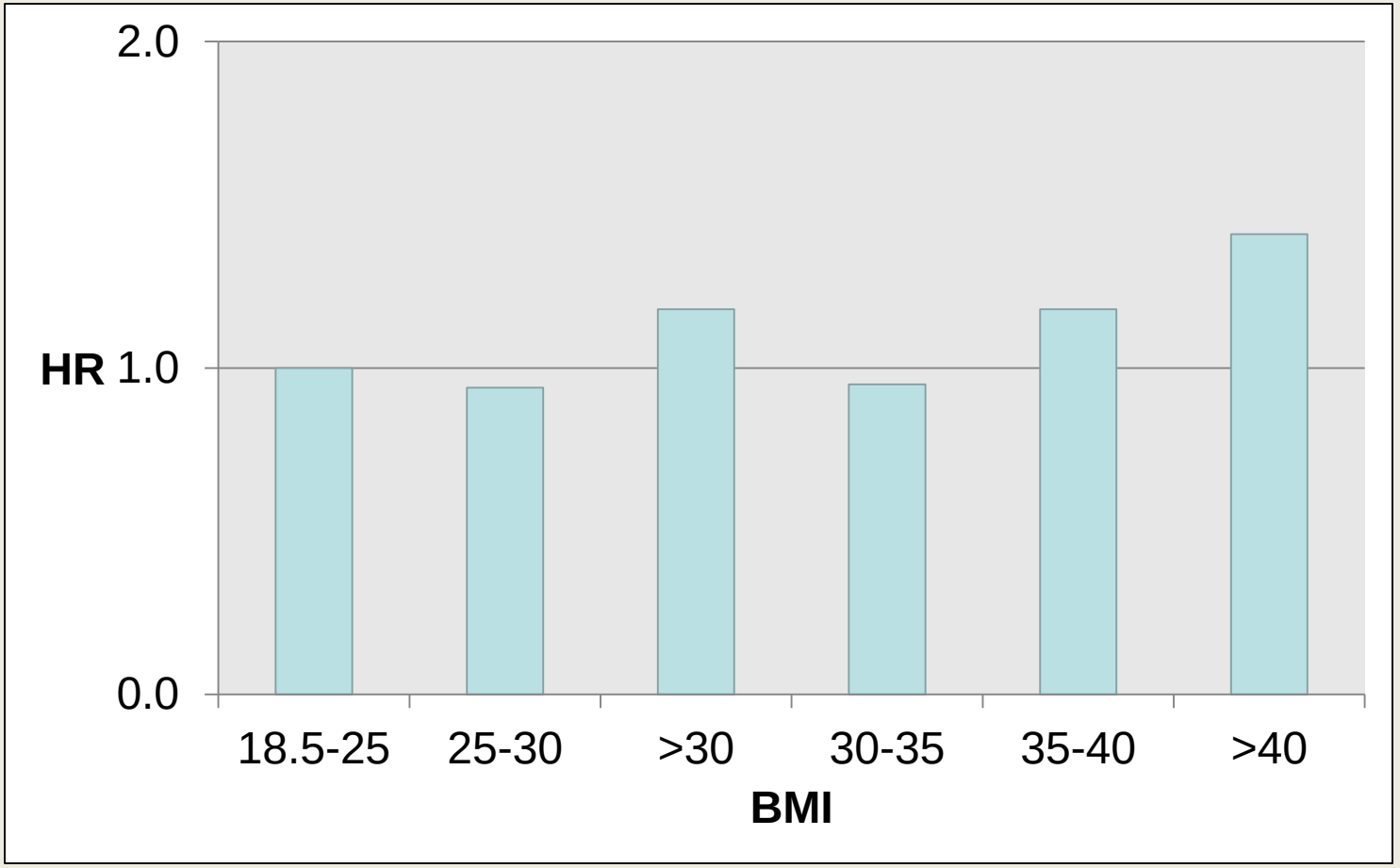
BMI v. Mortality

Men



Calle: NEJM(1999);341:1097

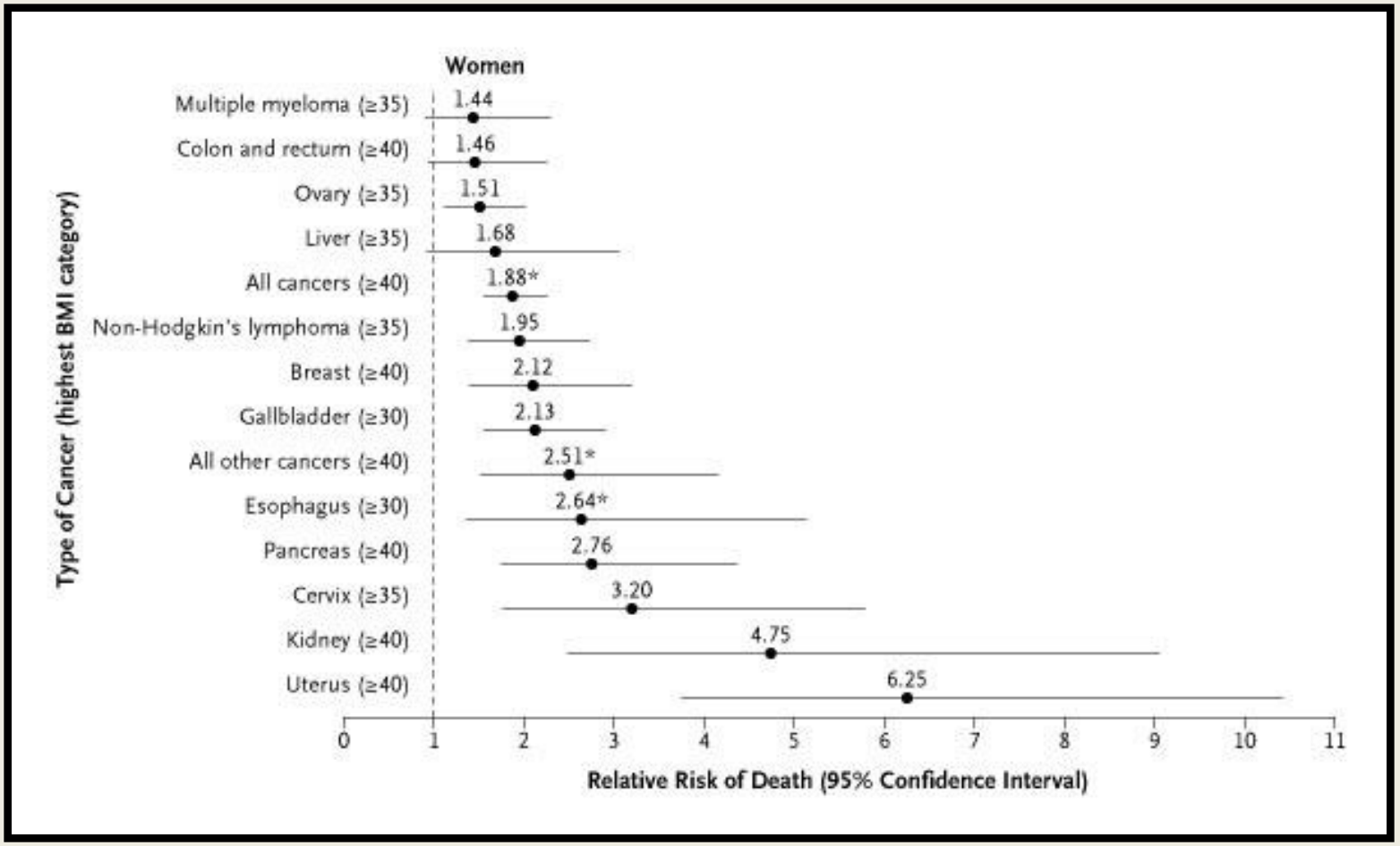
All Cause Mortality vs. BMI



Flegal: JAMA(2013);309:71

Obesity: Cancer

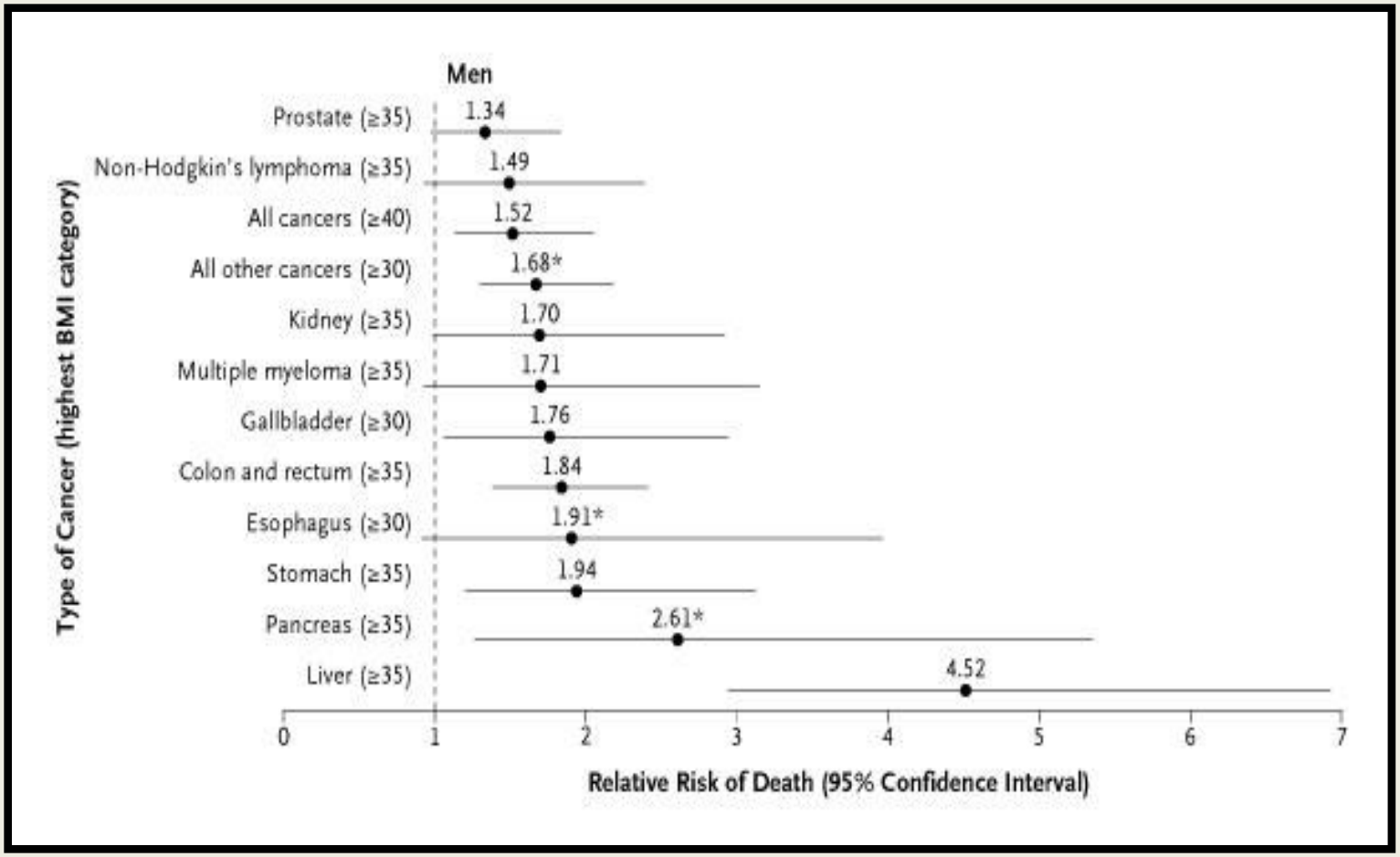
Women



Calle: NEJM(2003);348:17

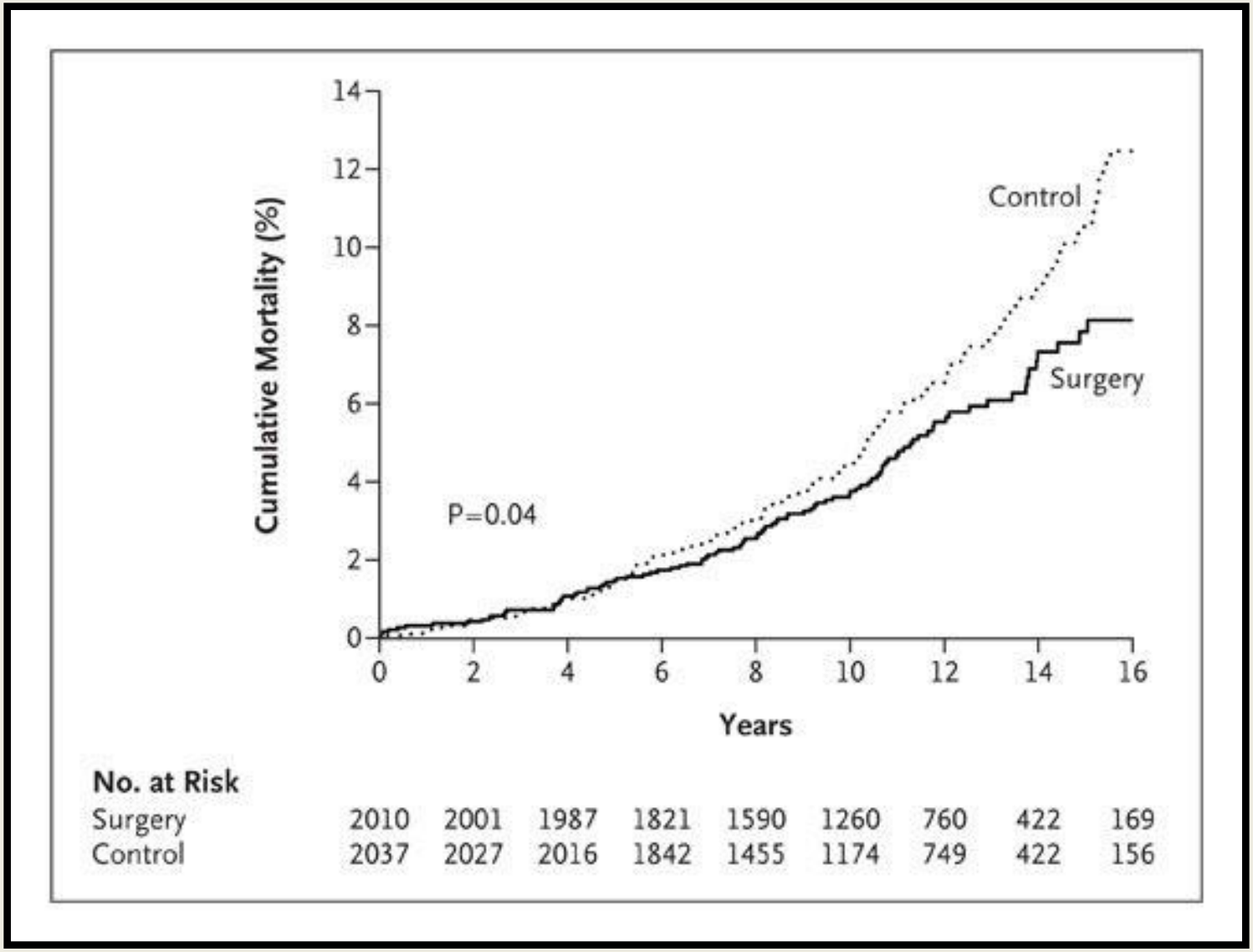
Obesity: Cancer

Men



Calle: NEJM(2003);348:17

Unadjusted Cumulative Mortality



Sjostrom: NEJM 2007;357:741-52

Cause of Death: SOS

	Control	Surgery	HR
Number of subjects	2037	2010	
Cardiovascular event	53	43	↓ 19%
Tumor	48	29	↓ 40%
Other	28	29	
Total	**129**	**101**	**0.76**

Sjostrom: N Engl J Med 2007;357:741

Cause of Death: Utah

Number/10,000 person.yrs

	Control	Surgery	% Decrease
Cardiovascular	18.5	9.7	48%
Cancer	13.3	5.5	60%
Other	25.3	22.4	11%
Total	**57.1**	**37.6**	**34%**

Adams: NEJM (2007);357:753

Weight Loss Decreases Cancer Mortality
Possible Explanations

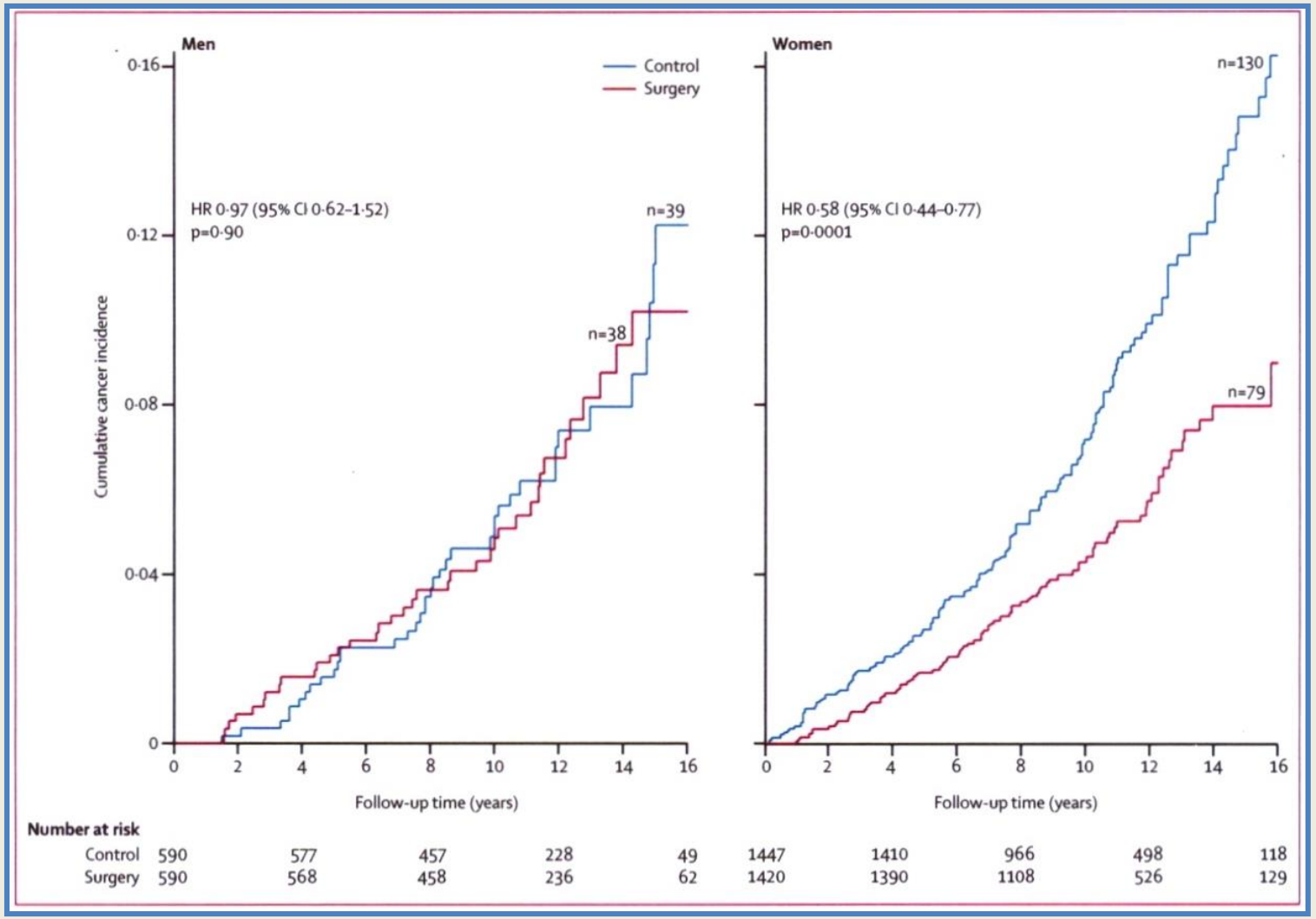
- Decreased cancer incidence
- Enhanced cancer survival
- Process of care

Bariatric Surgery: Effect on Cancer Incidence

	Control (n)	Surgery (n)	f/u, year	RR
Quebec[1]	5746	1035	5	0.22
Utah[2]	9442	6596	12.5	0.76
Sweden[3]	2037	2010	10.9	0.67

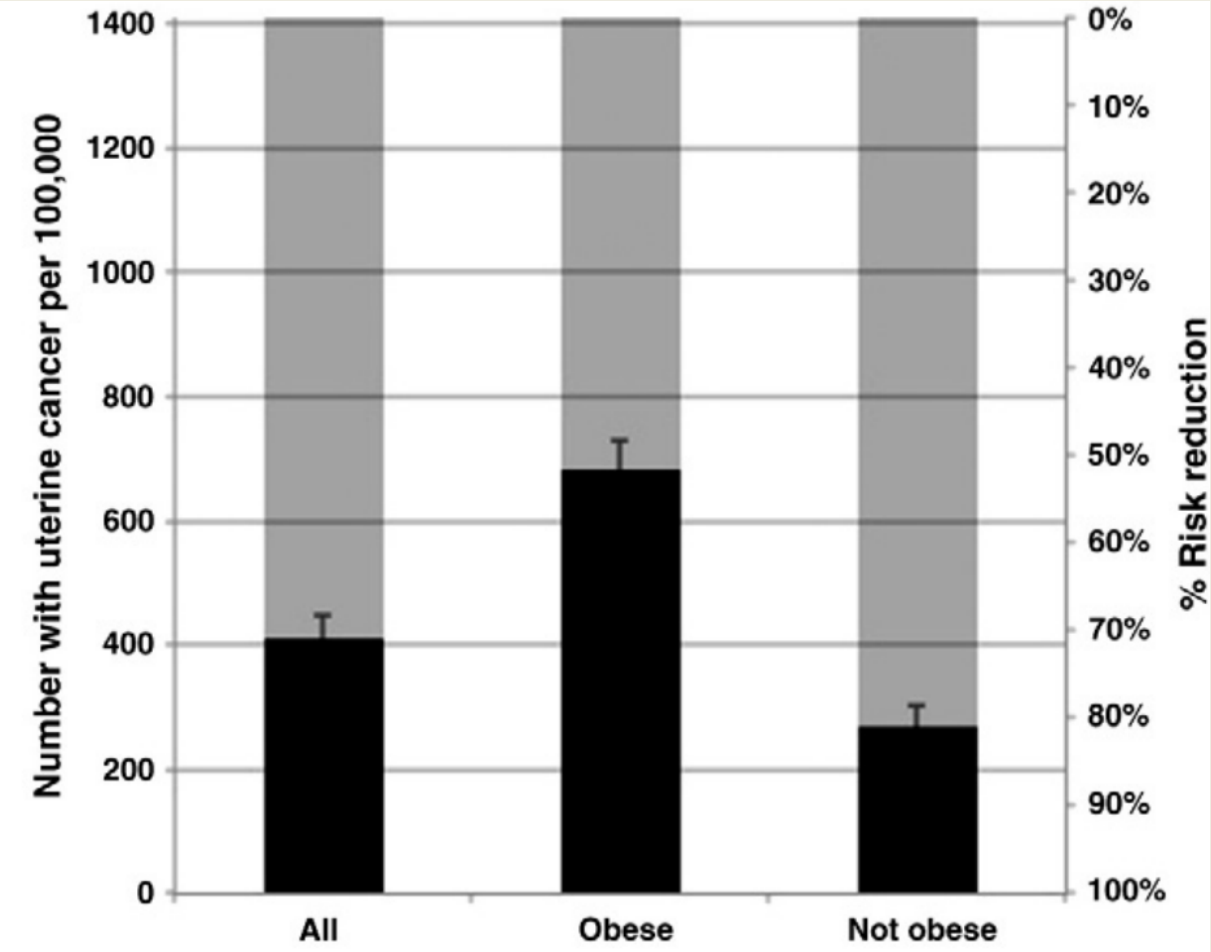
1. Christou: Surg Obes Relat Dis 2008;4:691
2. Adams: Obesity 2009;17:796
3. Sjostrom: Lancet Oncol 2009;10:653

Fatal and Non-Fatal Cancer Incidence: SOS



Sjostrom: Lancet Oncol 2009;10:653

Uterine Malignancy: Bariatric Surgery



Ward: Gyn Oncol 2014;144:63-65

Incidence of Cancers by Stage

	Surgery (n)	Control (n)	HR
In Situ	44	73	0.86
Local	128	219	0.86
Regional	49	98	0.61
Distant	28	68	0.61

Adams: Obesity 2009;17:796

Nutrition and Cancer

Diet

Overweight/Obesity

ACS Data: 20% cancer women

14% cancer men

Weight Loss: Bariatric Surgery

Cancer mortality reduced 60-80%

Obesity – Cancer

Plausible Mediators

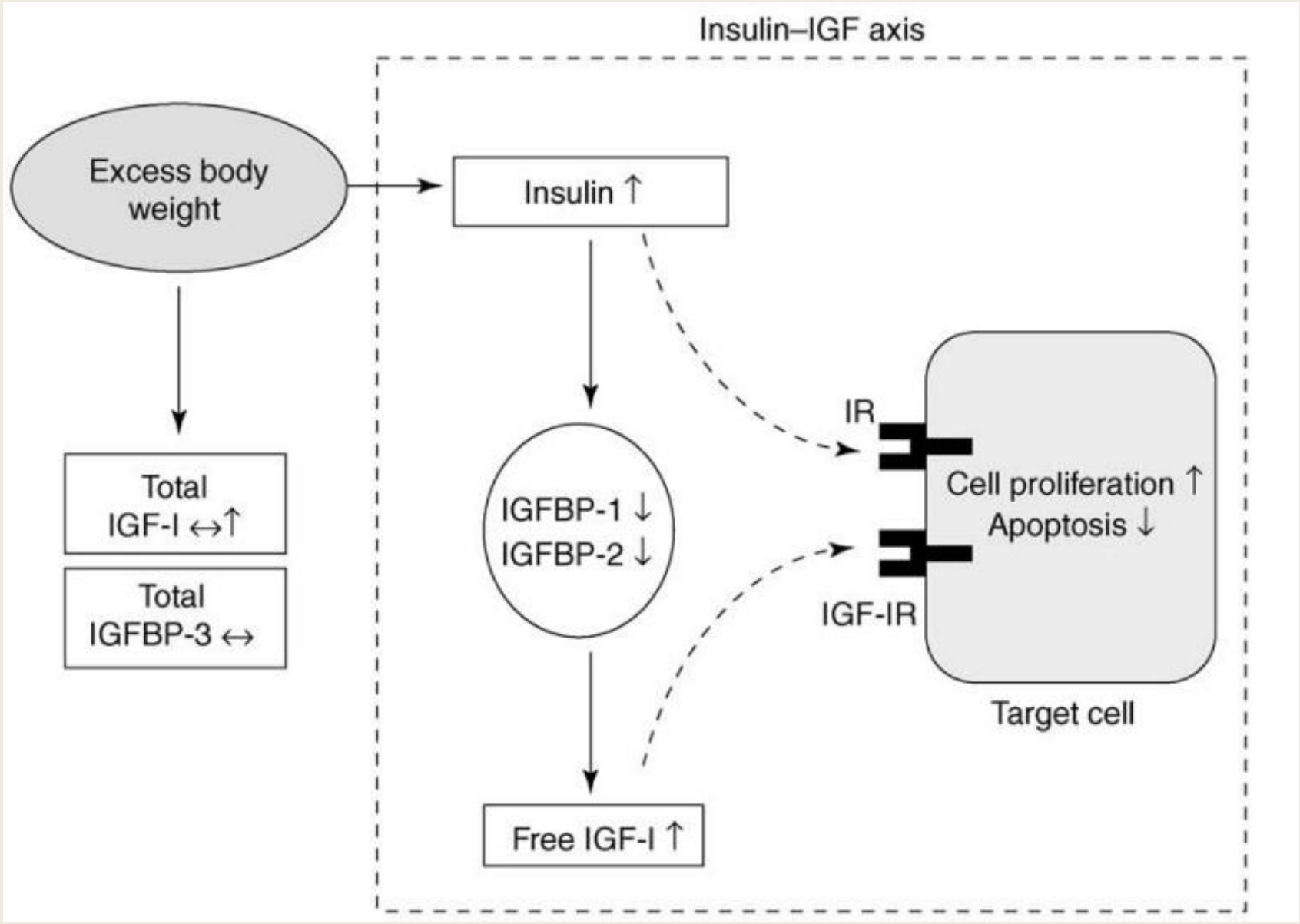
- Insulin
- Estrogens
- Adipokines
- Inflammation

Insulin Related Compounds

Insulin: pancreatic islets

Insulin- like growth factor 1 (IGF-1): liver

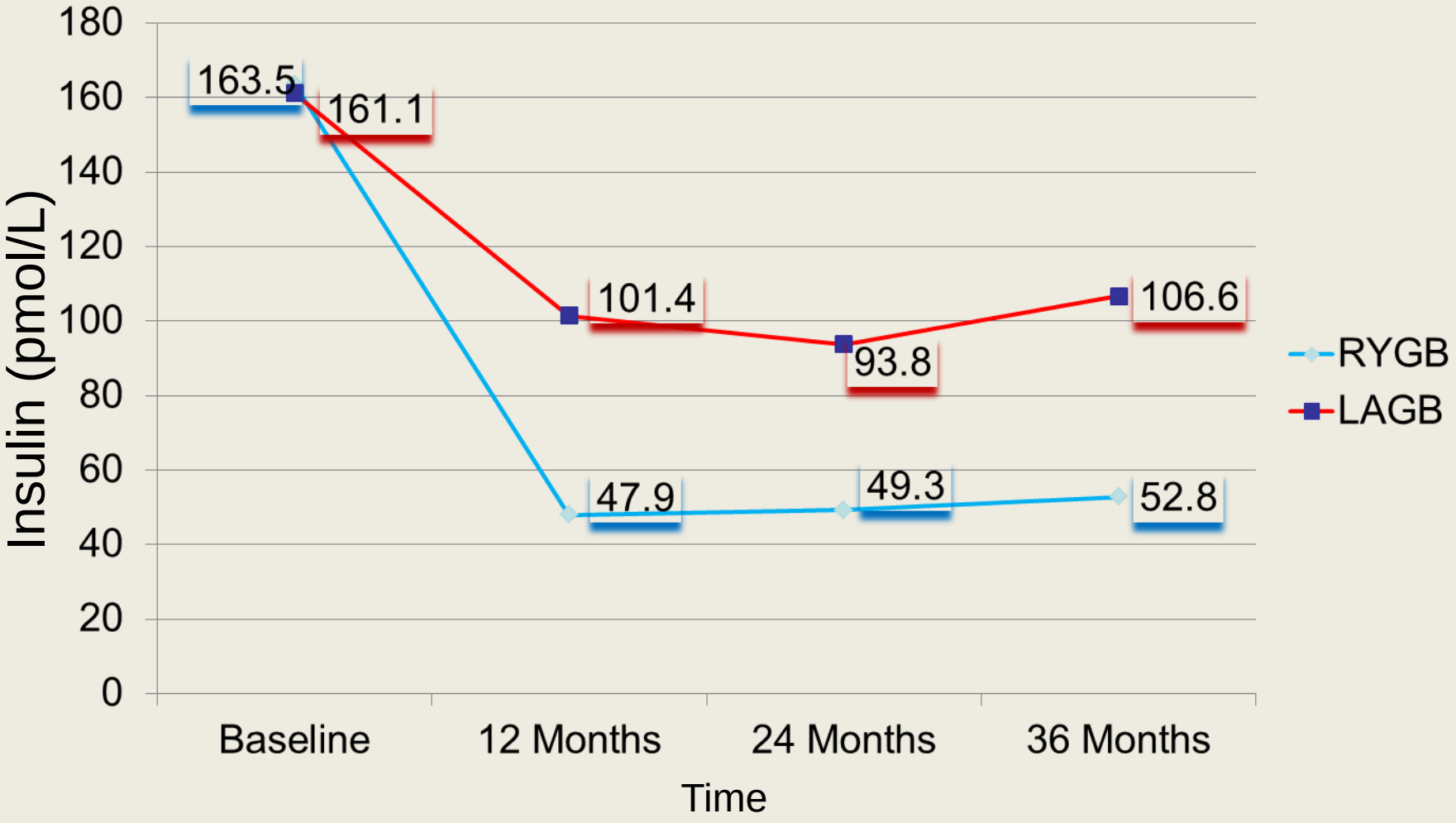
Insulin-like growth factor binding protein (IGFBP-1)



Trends in Endocrinol & Metab 2006;17(8):328-336.

Pre-Op & Post-Op Insulin, by Procedure

LABS-2



Cancer and Diabetes

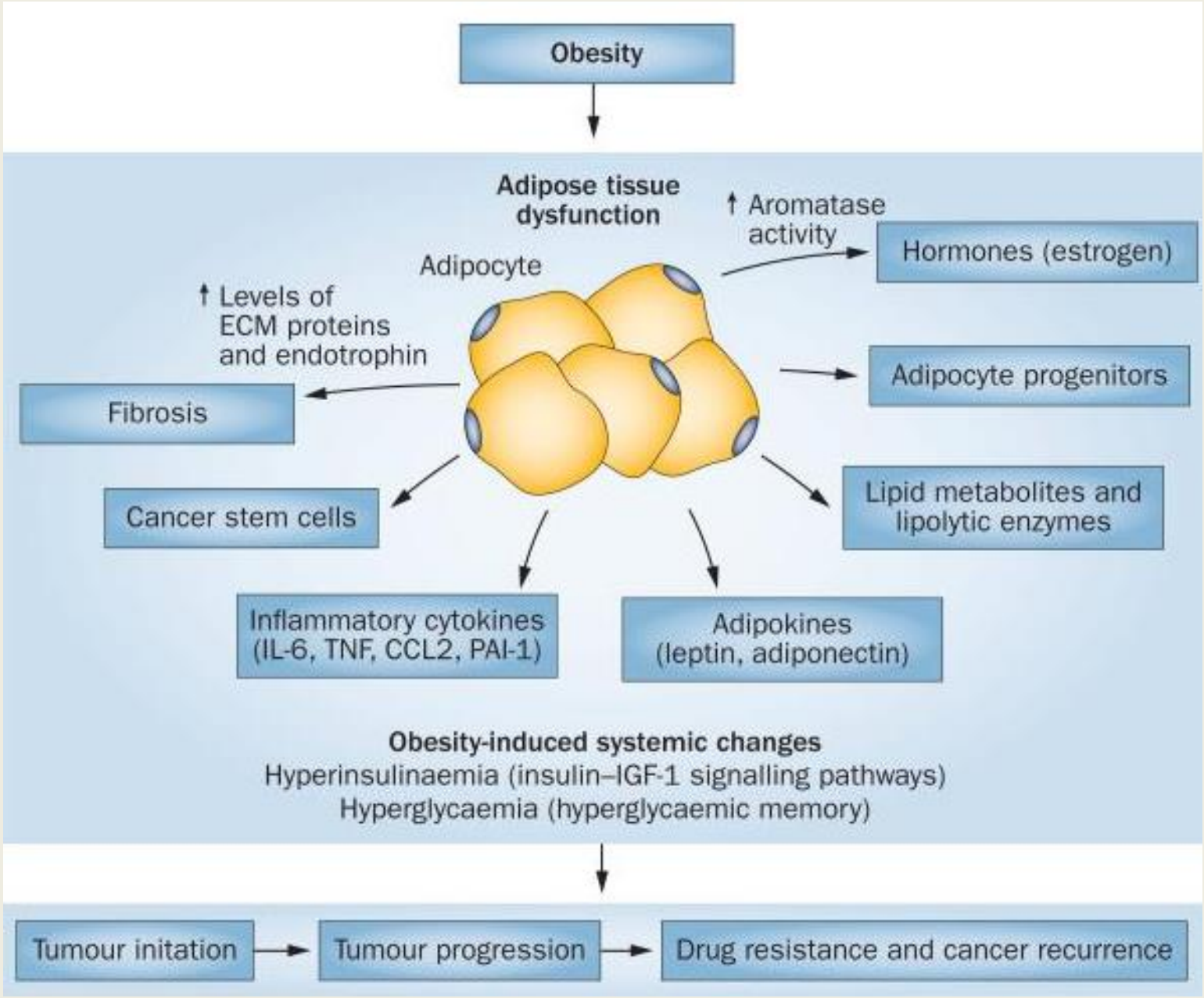
Diabetes associated with cancer of:

Liver, Pancreas, Endometrium, Colon/Rectum, Breast, Kidney

Glucose v. Insulin

T2DM: insulin ⟶ ↑ cancer (OR 1.97)

Chang: J Clin Endocrinol Metab 2012;97:E1170



Nat Rev Endocrinol. 2014 August; 10(8): 455–465.

Sex Hormones and Cancer

Androgens $\xrightarrow{\text{Cytochrome P450 aromatase}}$ Estrogens

Premenopause: ovaries

Postmenopause: adipose, skin

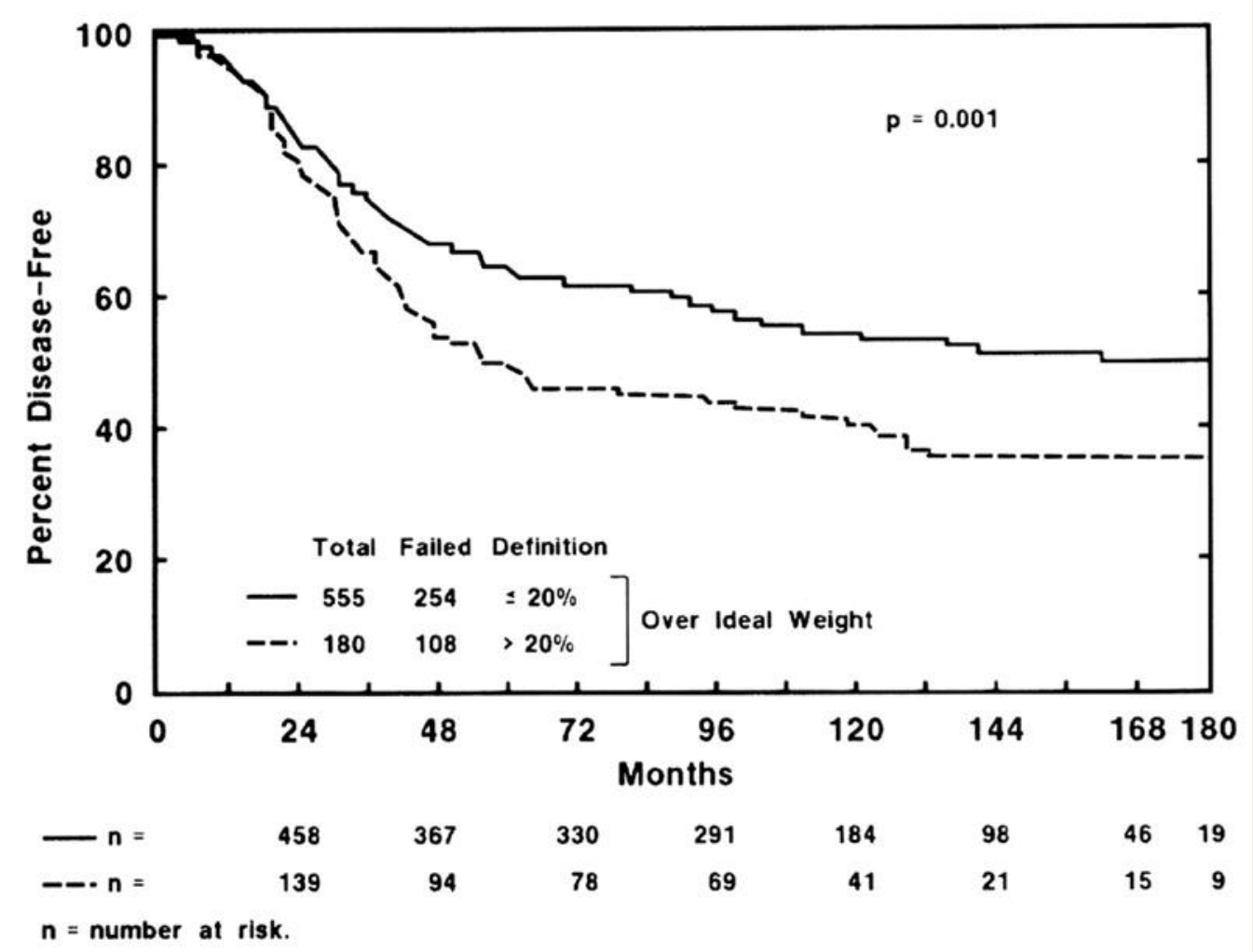
Obesity $\longrightarrow$ ↑ Aromatase, ↑ Estrogens

Adiponectin

- Adipokine
- ↓ Obesity, ↑ with Weight Loss
- ↑ Insulin Sensitivity
- Cancer Inhibition
- ↑ Apoptosis

Breast Cancer Disease Free Interval

>20% Above Ideal BW, Adjuvant Chemotherapy



Bastarrachea: Ann Int Med 1994;120:18

Women's Intervention Nutrition Study (WINS)

Early stage breast cancer survivors (n=2437) low fat diet, 5 years

	Control	**Low fat**
Weight loss	0	~3%
Recurrence		HR 0.76
Recurrence ER (-)		HR 0.58

Pierce: JNCI 2006; 98:1767

Women's Health Eating & Lifestyle (WHEL)

Early stage breast cancer survivors

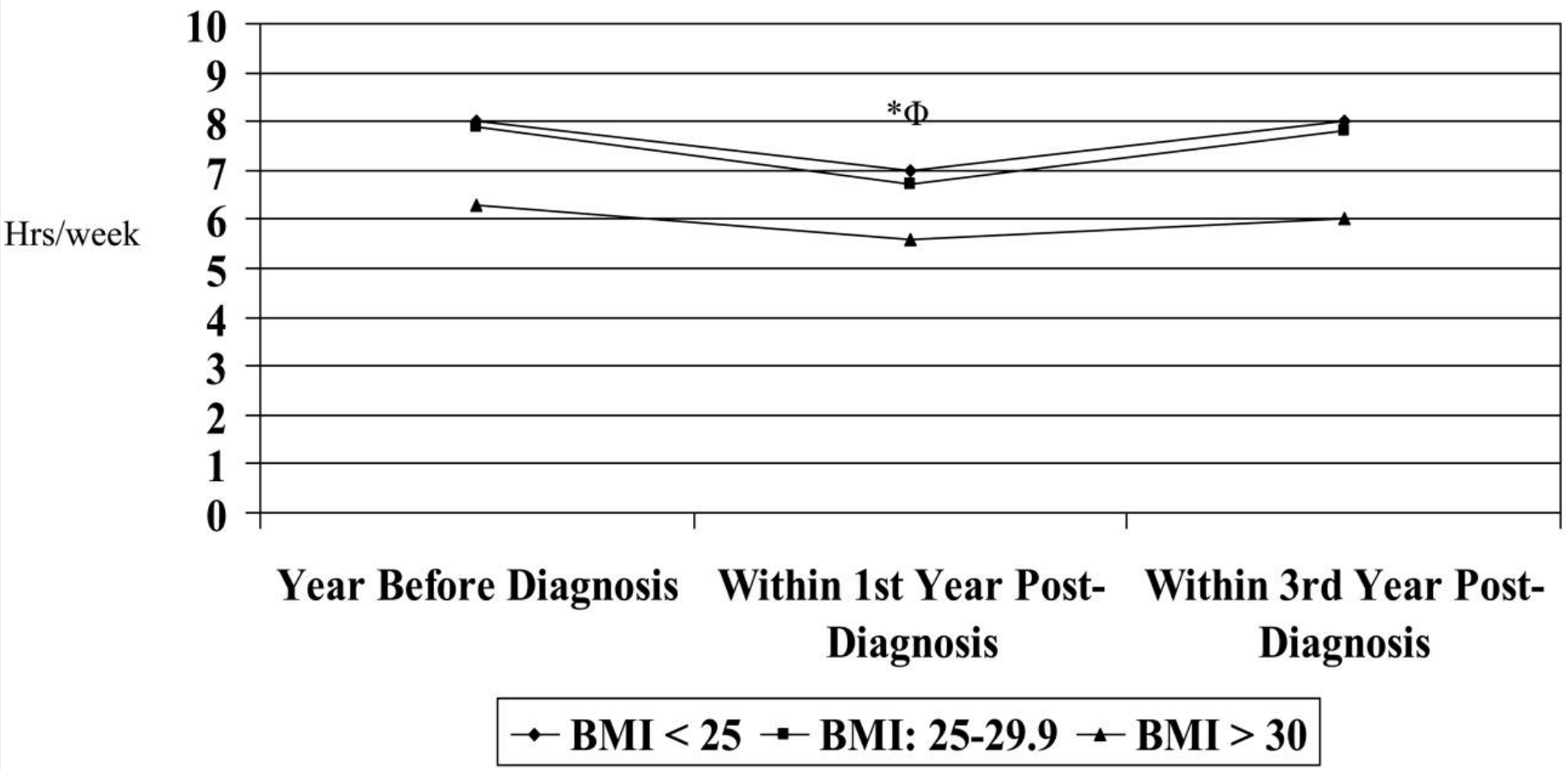
↑ vegetable, fruit n = 3088

f/u median 7.3 years, 518 relapse events

	Control	**Vegetable/Fruit**
Weight Change	No difference	
Recurrence	16.7%	16.9%
Survival	10.1%	10.3%

Chlebowski: J Natl Cancer Inst 2006; 98:167

Physical Activity Levels/BMI



Med Sci Sports Exerc. 2004 Sep; 36(9): 1484–1491.

Obesity – Cancer

Clinical Implications:

1) Current cancer screening

2) Consider bariatric surgery when fully recovered from primary cancer treatment

Breast Cancer Screening
American Cancer Society 2016

Age	Risk	Recommendation	Frequency
40-44[1]	Average	Mammogram Choice	1 yr
45-54	Average	Mammogram	1 yr
>55	Average	Mammogram	2, 1 choice
>30[2]	(+) BCRA	Mammogram + MRI	1 yr
>30	20-25% Lifetime	Mammogram	1 yr

1. ACS Breast Cancer Screening Guidelines (2016). http://www.cancer.org/healthy/informationforhealthcareprofessionals/acsguidelines/breastcancerscreeningguidelines/index
2. Smith: CA: Cancer Journal for Clinicians (2015);65:31

Cervical & Endometrial Cancer Screening

American Cancer Society 2016

Cervical:

Age	Risk	Recommendation	Frequency
21-29	Average	PAP Test; HPV if needed	3 yr
30-65	Average	PAP + HPV	3 yr
>65	NL in past	None	----
>65	Past pre-cancer	Pap	3, 20 more years

Endometrial:

Age	Risk	Recommendation	Frequency
Menopause	Average	Advise	----
35	High	Endometrial Bx	1 yr

American Cancer Society Guidelines for the Early Detection of Cancer (2016).
http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer

Colorectal Cancer Screening

American Cancer Society 2016

Age	Risk	Recommendation	Frequency
>50	Average	Flexible Sigmoidoscopy or	5 yrs
		Colonoscopy or	10 yrs
		Barium Enema or	5 yrs
		CT Colonoscopy	5 yrs

1. ACS Colorectal Cancer Screening Tests (2016).
http://www.cancer.org/cancer/colonandrectumcancer/moreinformation/colonandrectumcancerearlydetection/colorectal-cancer-early-detection-screening-tests-used

Prostate & Lung Cancer Screening

American Cancer Society 2016

Prostate:

Age	Risk	Recommendation	Frequency
50	Average	Discuss with Patient	
45	African American, 1° relative	Discuss	Depends

Lung:

Age	Risk	Recommendation	Frequency
55-74	>30 pk/yrs	LDCT	----

American Cancer Society Guidelines for the Early Detection of Cancer (2016).
http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer

Pharmacotherapy in Obesity

Richard Lindquist M.D.
Seattle, WA

Obesity Medicine Association

AMERICAN BOARD of OBESITY MEDICINE

Disclosures

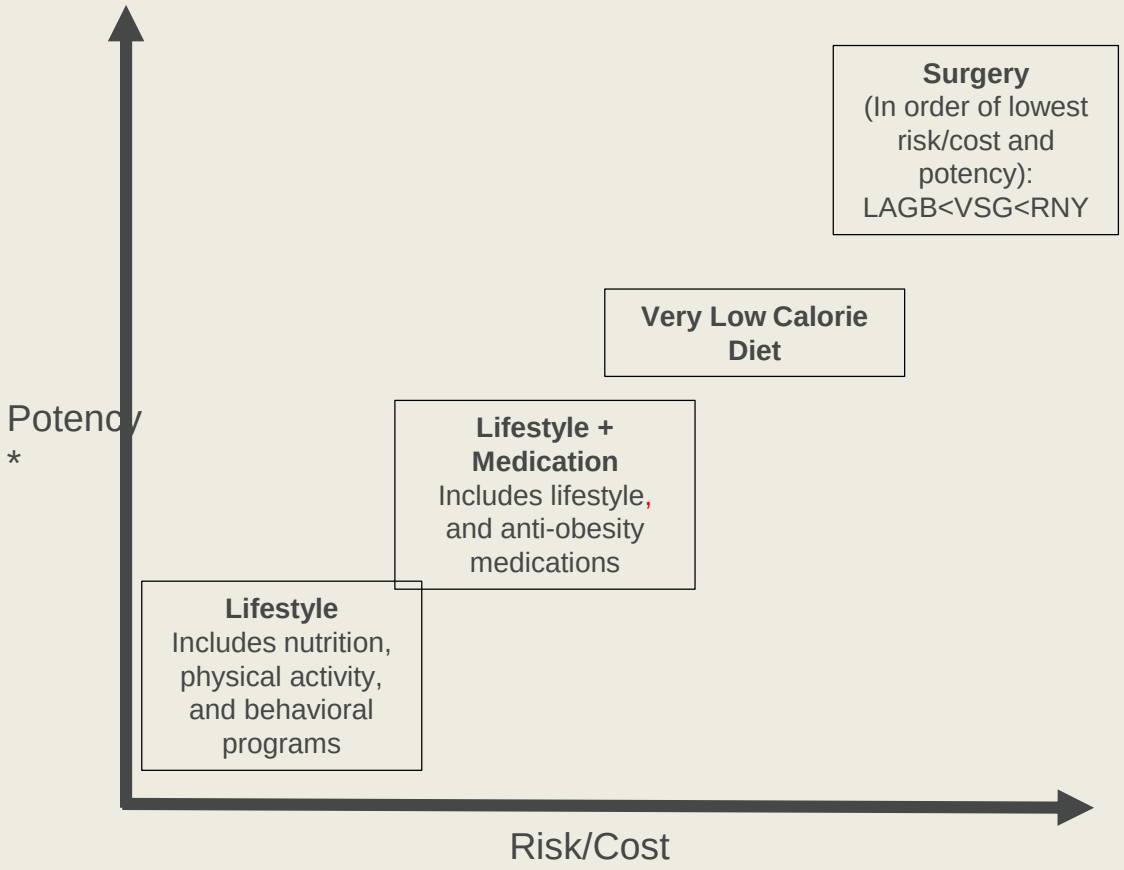
- Novo Nordisk advisory council
- Retrofit advisory board

Multiple treatment algorithms exist, with largely convergent content

- Obesity Medicine Association (OMA)
- American Heart Association/The American College of Cardiology/The Obesity Society (AHA/ACC/TOS)
- American Association of Clinical Endocrinologists(AACE/ACE)
- American Diabetes Association (ADA)

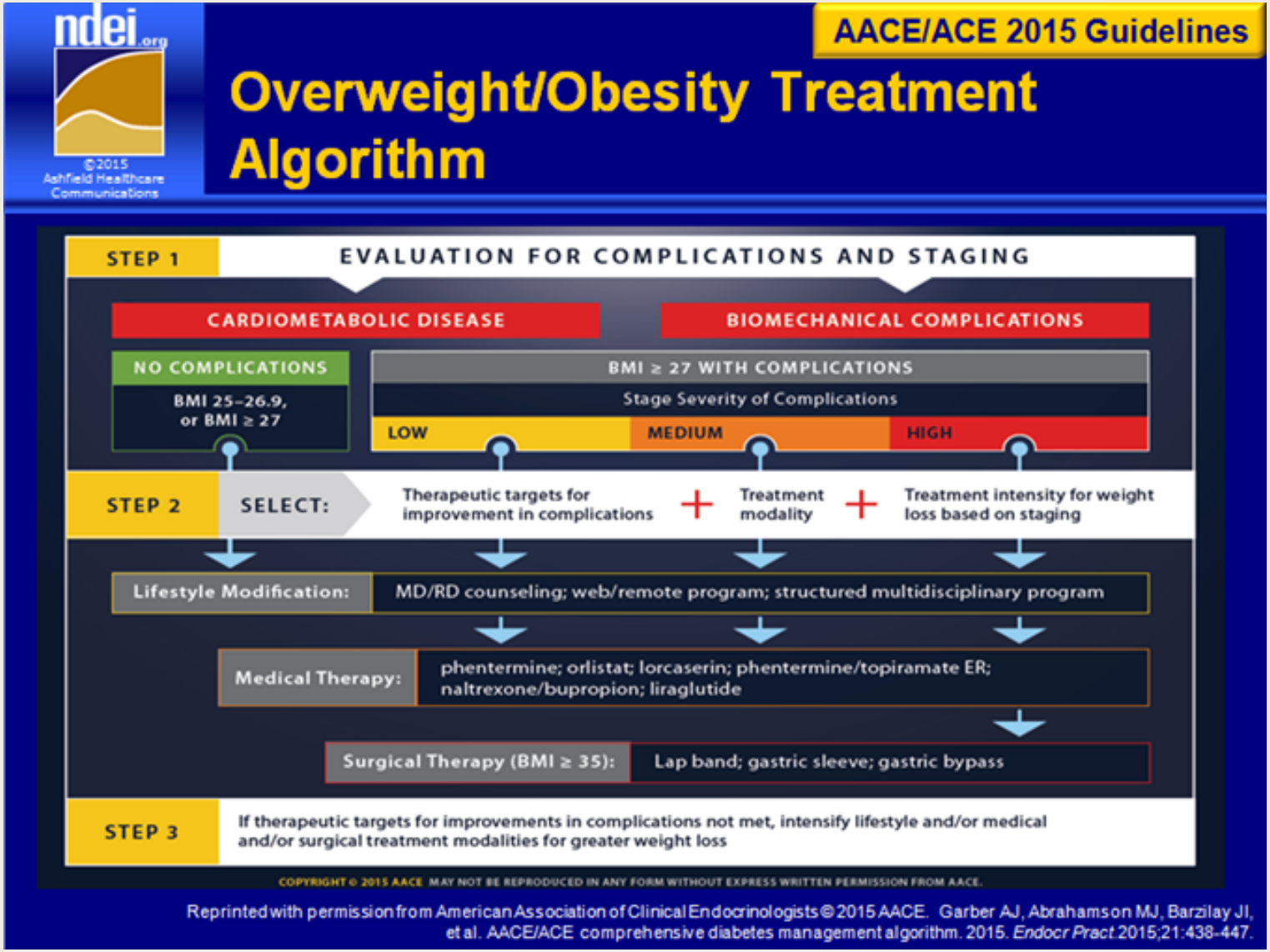
- All are open source
- Differences are largely in degree of detail
- Some variation wrt medication options
- Some variation in staging tools
- User friendliness, or lack of

Current Treatment Options for Obesity

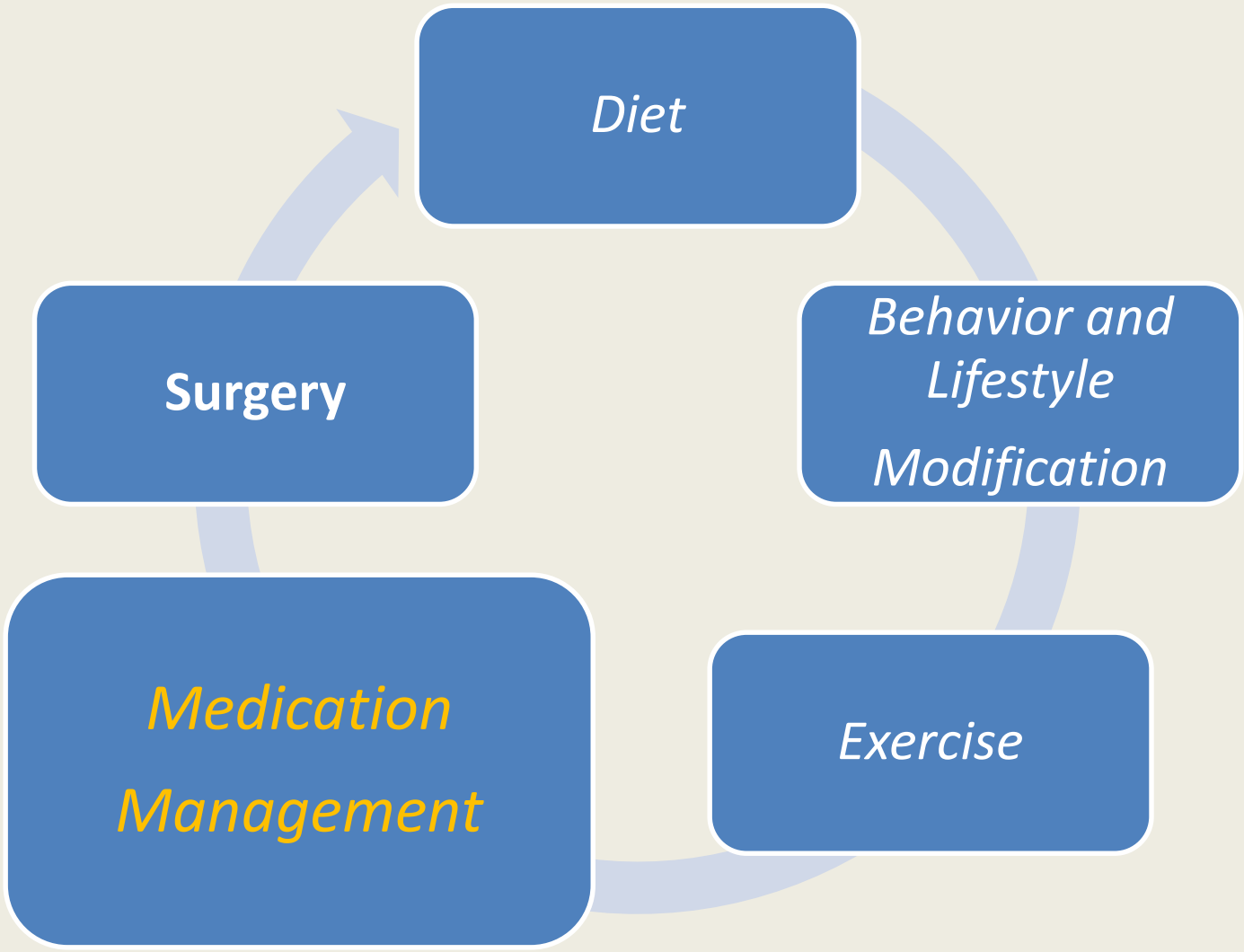


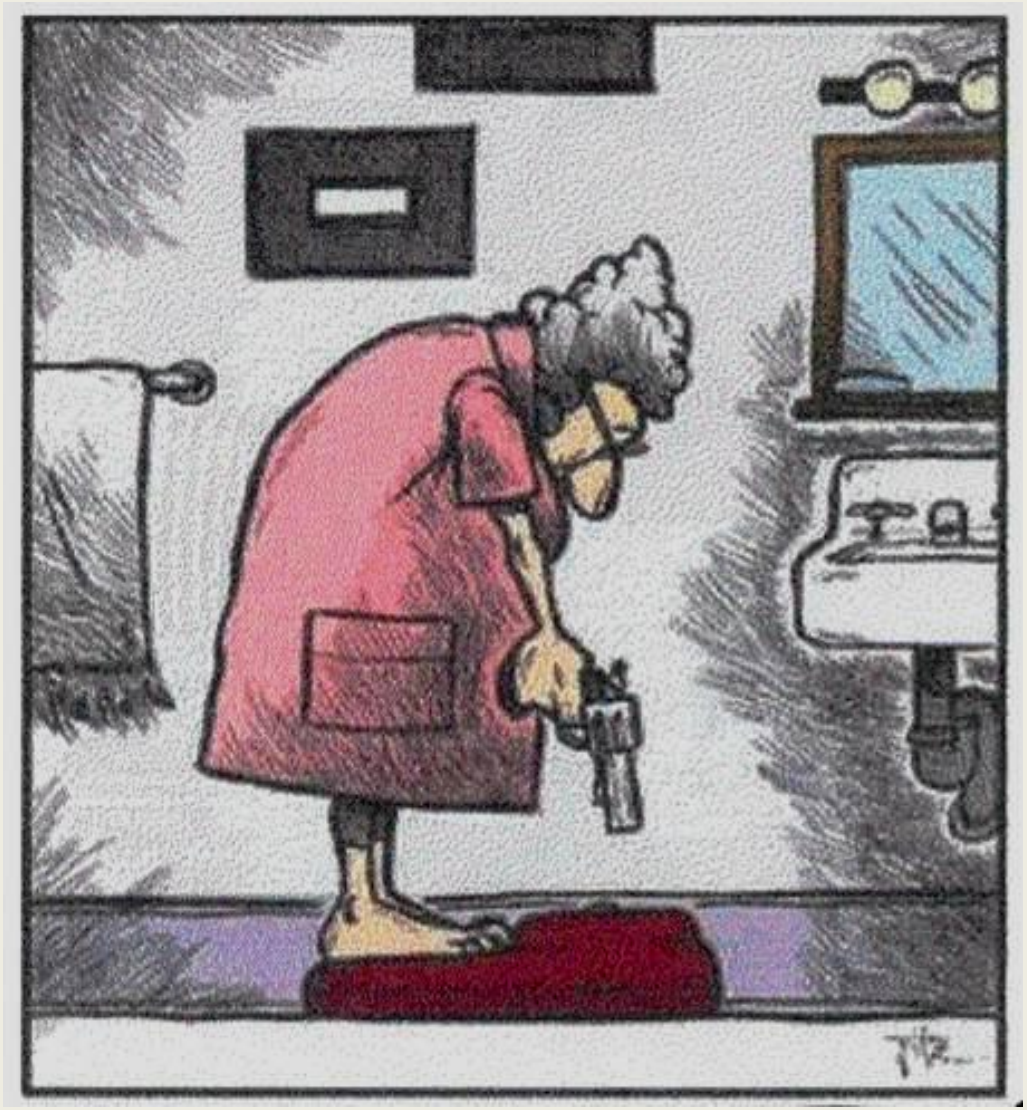
*Potency includes many factors, such as the amount, rate, and sustainability of weight loss, and the long-term resolution of adiposopathy and fat mass disease. Potency varies greatly for each individual (i.e., long-term adherence to a lifestyle program can be as potent as gastric bypass surgery).

Treatment Guidelines

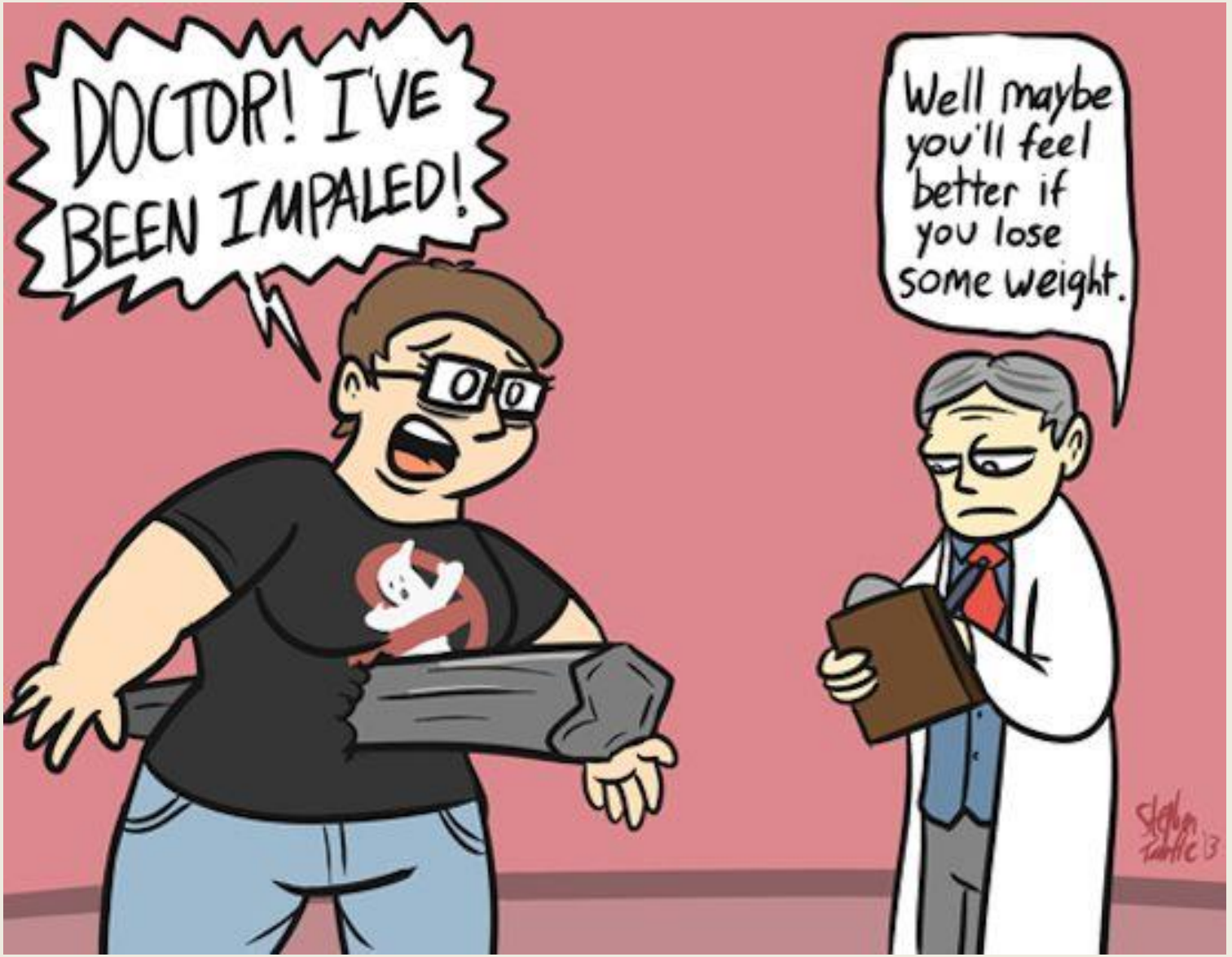


Reprinted with permission from American Association of Clinical Endocrinologists © 2015 AACE. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm. 2015. *Endocr Pract* 2015;21:438-447.


Diet
Behavior and Lifestyle Modification
Exercise
Medication Management
Surgery



Fed up with how her diet is going Charlene takes a more serious aim at her target weight


DOCTOR! I'VE BEEN IMPALED!
Well maybe you'll feel better if you lose some weight.

Chronic treatment of hypertension as a model

- In 1960s hypertension was felt to be a disease of stress
- We now have 120+ various medication combinations for HTN
- We treat it as a chronic disease

Barriers to the Use of Medication in Treating Obesity

- Perception that obesity is a disorder of willpower
- Professional perception that weight regain after termination of treatment reflects the failure of the medication; that is, medication is expected to cure obesity
- Prior problems with available medications
  - (Fen-Phen, Sibutramine)
- Regulatory rigidity that limits medication to a few weeks – varies by state
- Licensing boards that persecute physicians for alleged misuse of appetite suppressants – varies by state
- Legislative grandstanding
- Inadequate funding for clinical work in obesity

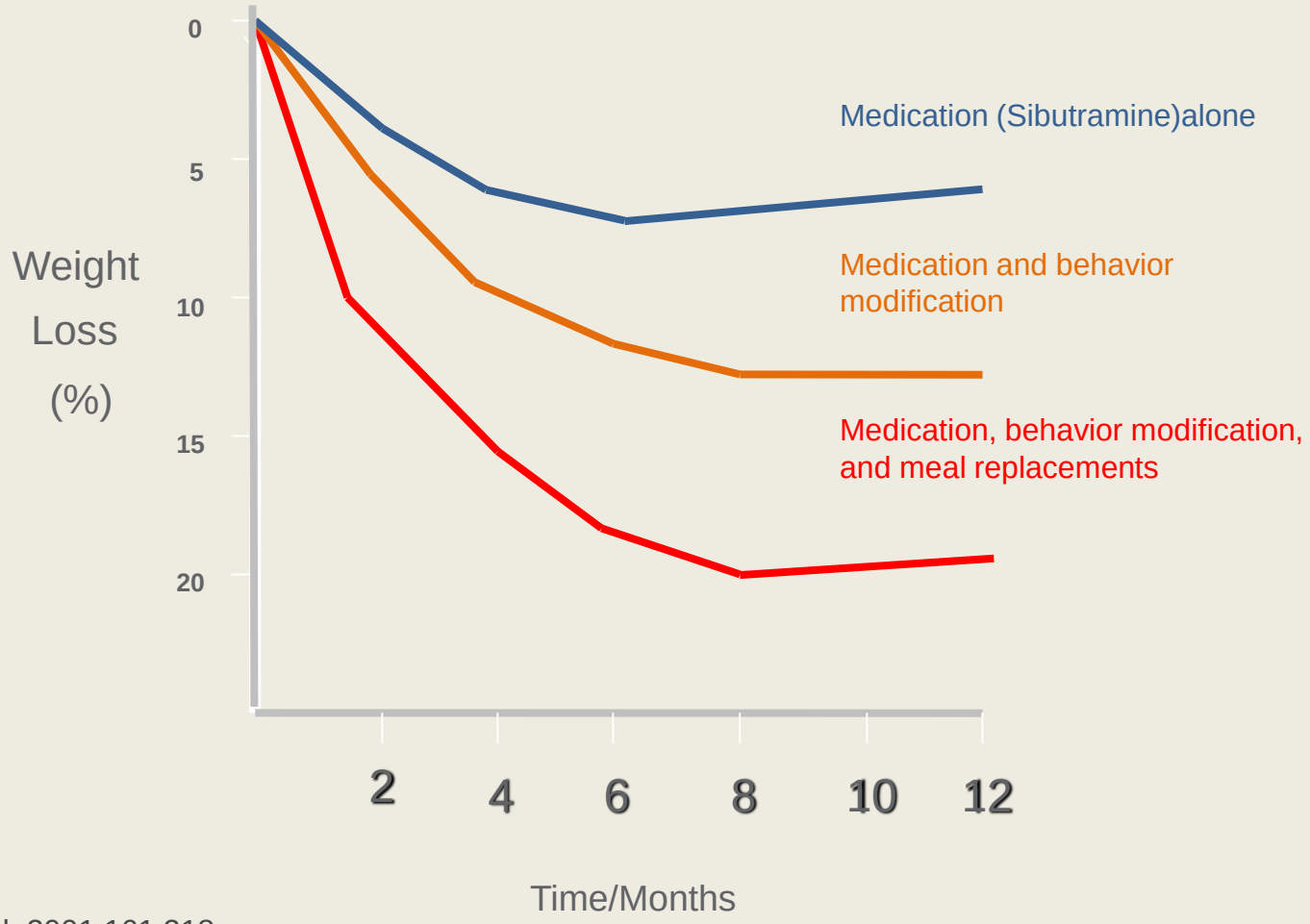
Bray GA, Ann Intern Med. 1993;119:707

Some key points

- Medications are effective adjuncts
  - Important to manage expectations
  - Awareness of prior problems
    - (Fen-Phen, sibutramine)
- Can choose based on mechanism of action
- Can and should be considered for chronic use
  - As with any chronic disease
- Current medical-legal status can be a minefield
  - Oregon – Washington – Ohio examples

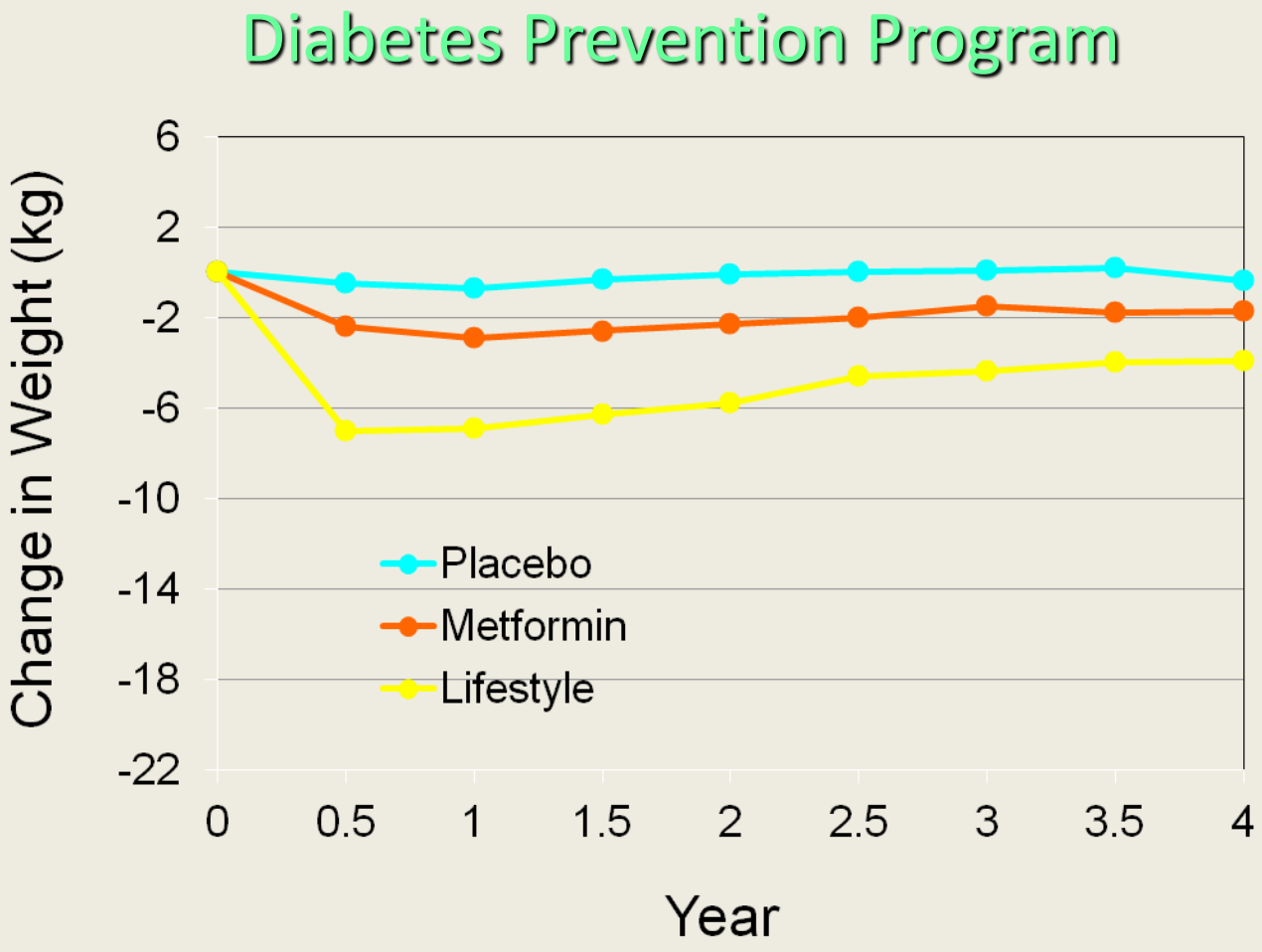
Combine Diet, Medication, and Behavior Modification

Additive effects of behavior and meal replacement therapy with pharmacotherapy for obesity



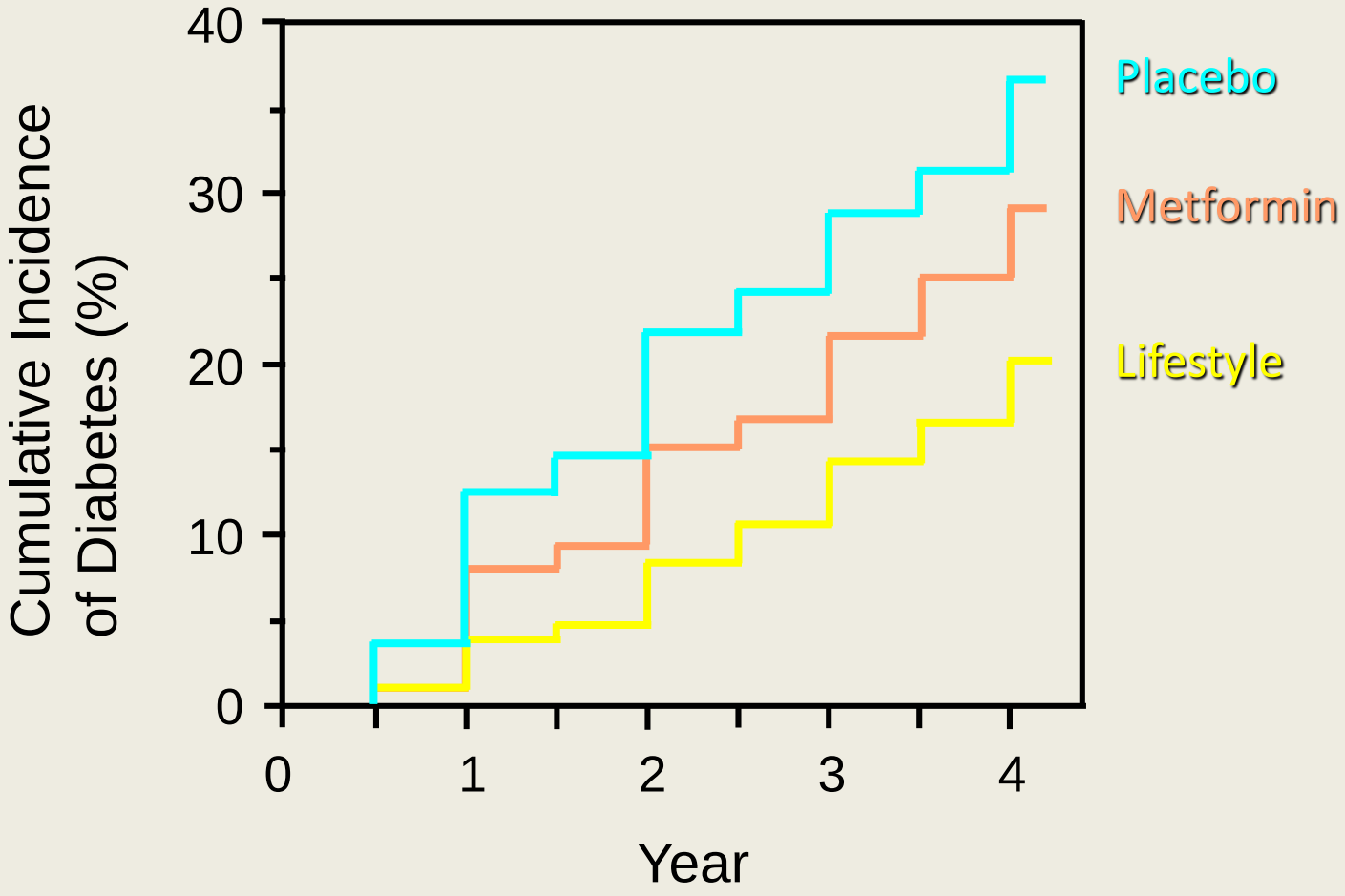
Wadden, Arch Int Med. 2001;161:218

Benefits of Intensive Medical Intervention



DPP Research Group, N Engl J Med, 2002

Diabetes Prevention



Diabetes Prevention Program Research Group
N Engl J Med, 2002

Medications That *Affect* Weight

Weight Positive (Gain)

- Corticosteroids
- Antihistamines
  - Cyproheptadine(Periactin®)
- Many Antidepressants
  - MAOIs, TCAs, most SSRIs (esp paroxetine)
- Opioids
- Atypical Antipsychotics
  - risperidone, quetiapine, olanzapine, aripiprazole, ziprasidone
- Most Antiseizure meds
  - (not topiramate or zonisamide
- **Many Diabetes meds**
- Beta Blockers

Weight Negative (Lose)

- Metformin
- Nefazodone (Serzone®)
- Bupropion (Wellbutrin®)
- ?Fluoxetine (Prozac®)
- Incretins
  - Exenatide (Byetta®, Bydureon®)
  - Liraglutide (Victoza®, Saxenda®)

Weight Neutral

- Venlafaxine (Effexor®)
- Citalopram (Celexa®)
- Sertraline (Zoloft®)

Diabetic Medications *Affect* Weight

Weight Positive (gain)

- Insulins
- Thiazolidinediones (TZDs)
  - rosiglitazone (Avandia®)
  - pioglitazone (Actos®)
- Sulfonylureas
  - glimepiride (Amaryl®)
  - glipizide (Glucotrol®)
  - glyburide (DiaBeta®, Glynase®, Micronase®)
- Meglitinides
  - nateglinide (Starlix®)
  - repaglinide (Prandin®)

Weight Negative (lose)

- Metformin
- GLP-1 analogues
  - liraglutide (Victoza®, Saxenda®)
  - exenatide (Byetta®, Bydureon®)
- DPP-4 Inhibitors
  - sitagliptin (Januvia®)
- Gliflozins
  - SGLT-2 Inhibitors(sodium-glucose cotransporter 2)
    - canagliflozin (Invokana®)
    - dapagliflozin (Farxiga®)
    - empagliflozin (Jardiance®)

Changes in paradigm

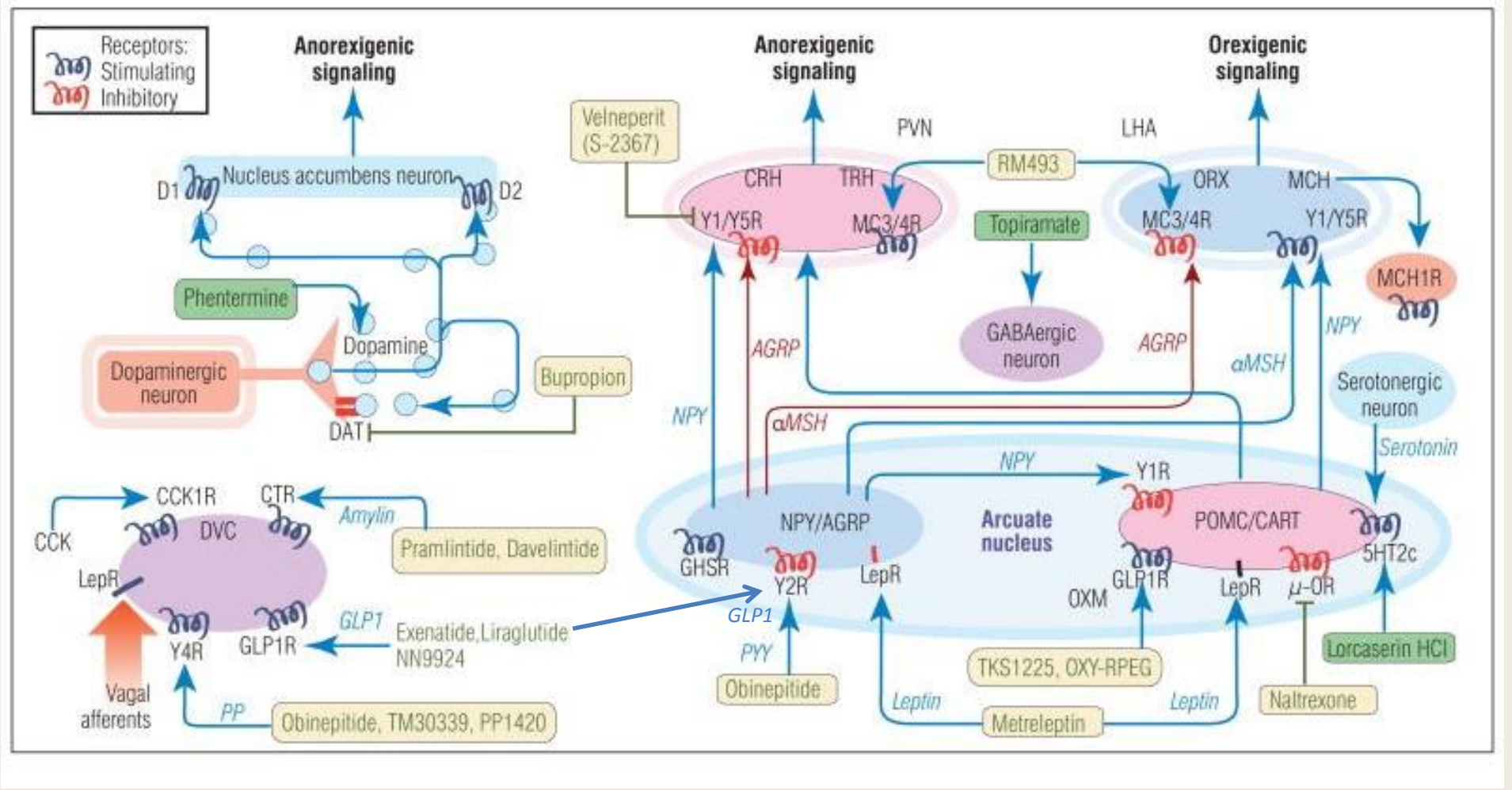
- Initially a “nothing we can do” approach to medication related weight gain
- Gradually learned to avoid weight positive medications if possible
- Now choosing medications based on co effects
  - Metformin in diabetes and prediabetes
    - Note: recommended but not approved for prediabetes or PCOS
  - SGLT-2 inhibitors, Liraglutide in diabetes
  - Topiramate, Zonisamide in migraines and seizure disorders

Medications Used to *Treat* Weight

- Sympathomimetics
  - Phentermine (1959)
  - Phendimetrazine
  - Diethylpropion
- Metformin
  - – Off label
- Topiramate
  - – Off label
- Gastric Lipase Inhibitor
  - Orlistat (Alli® – OTC, Xenical® –RX)

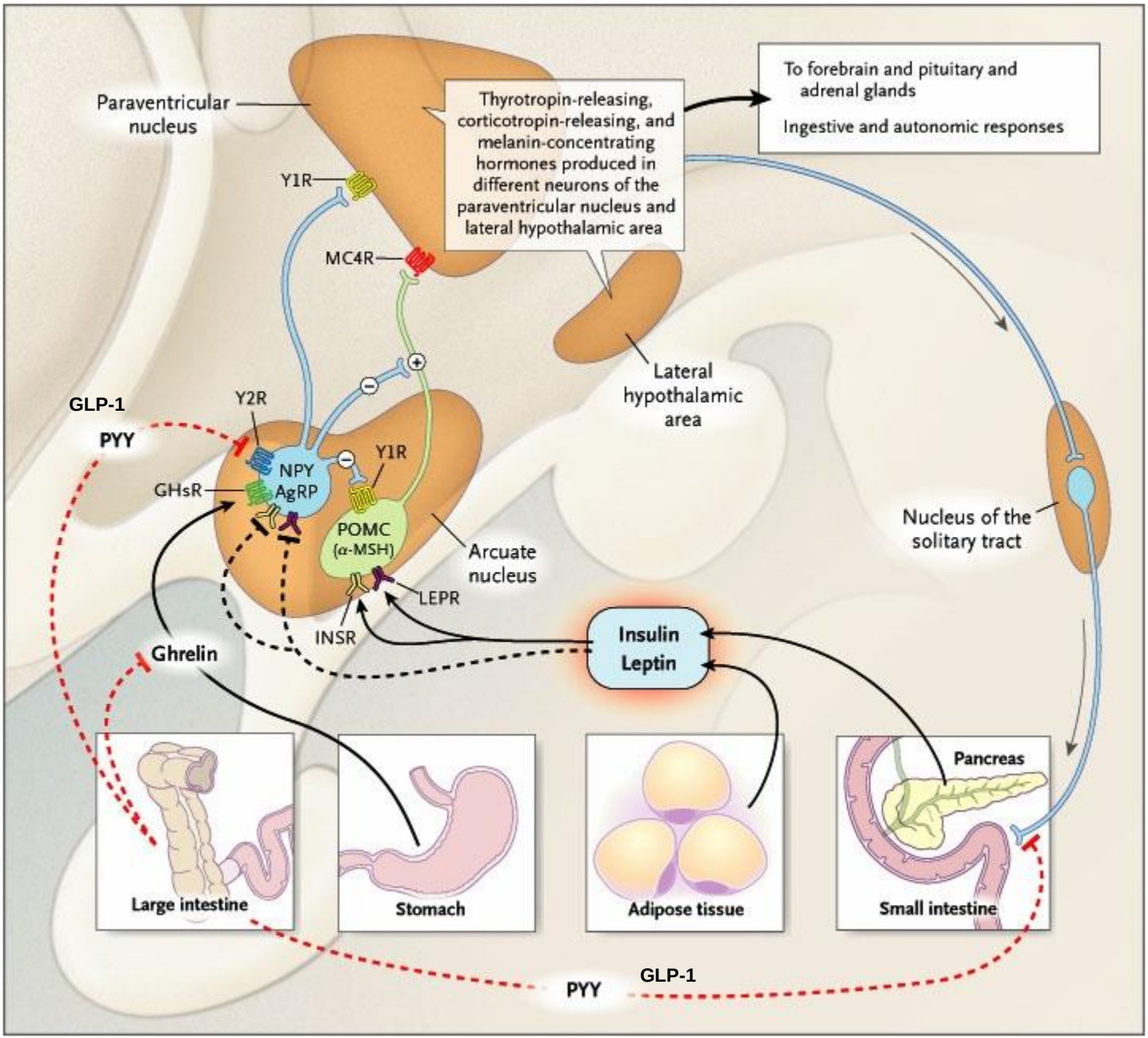
- "New" Drugs (since 2012)
  - GLP-1 analogues
    - Liraglutide (Saxenda®)
  - Combination
    - Phentermine/Topiramate (Qsymia®)
    - Bupropion/Naltrexone (Contrave®)
  - Serotonergic (5HT-2cR)
    - Lorcaserin (Belviq®)

Anti Obesity Agents and Mechanism of Action



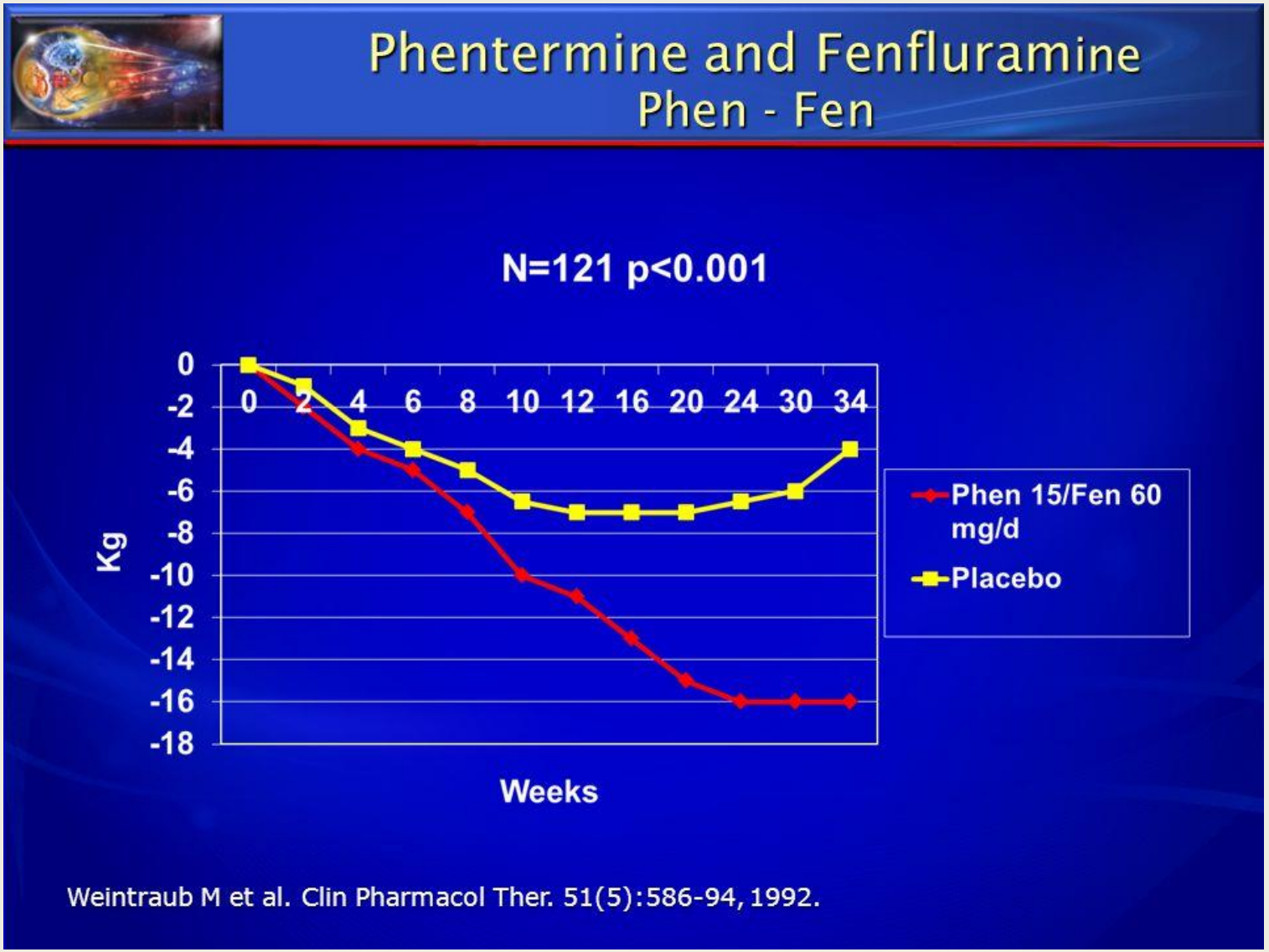
Clin Pharmacol Ther. 2014 Jan; 95(1): 53–66.

J Clin Endocrinol Metab, February 2015, 100(2):342–362



Korner: NEJM Vol 349(10). Sept 2003. 926-928

A challenging history – Fen-Phen



A challenging history – Fen-Phen

- Caused right and left heart valve lesions and pulmonary hypertension
- ? Incidence “23%”
- Fortunately, most regressed once off of the drug combination
- Subsequently linked to Fenfluramine, a 5-HT **2B** receptor agonist

N Engl J Med 1997; 337:581-588

Pharmacology & Therapeutics; 132 (2):146–157, 2011

More challenging history – SCOUT Trial

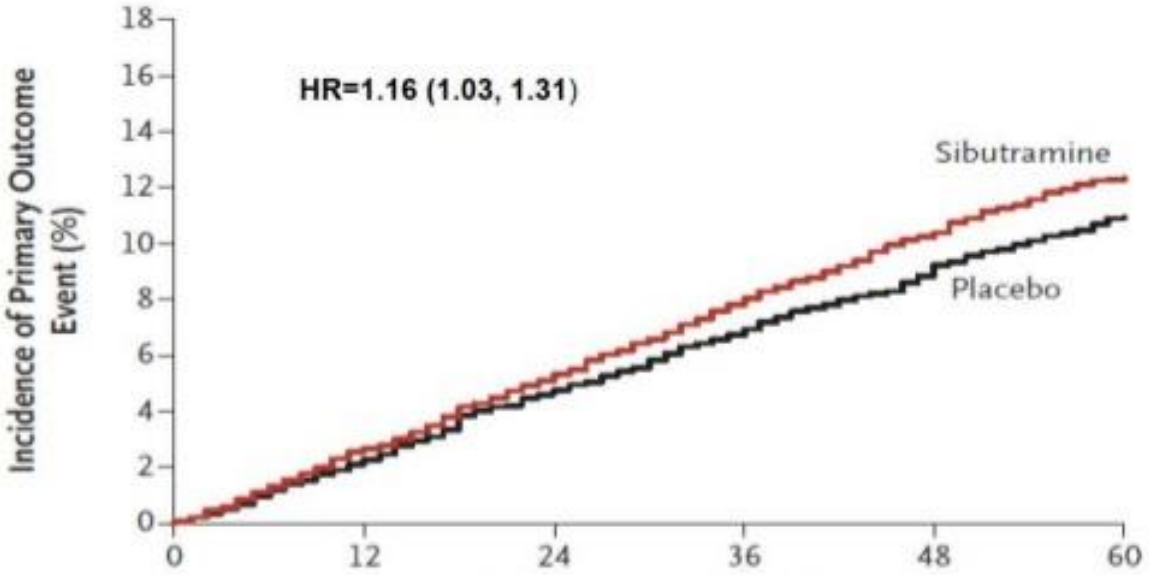
SCOUT

- **S**ibutramine **C**ardiovascular **Out**comes trial
- Randomized, double-blind, placebo-controlled trial ~ 10,000 subjects
- Primary endpoint
  - MACE: CV death, non-fatal MI, non-fatal stroke, resuscitated cardiac arrest
- January 2003 – March 2009

More challenging history – SCOUT Trial

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

SCOUT
MACE - Overall Population

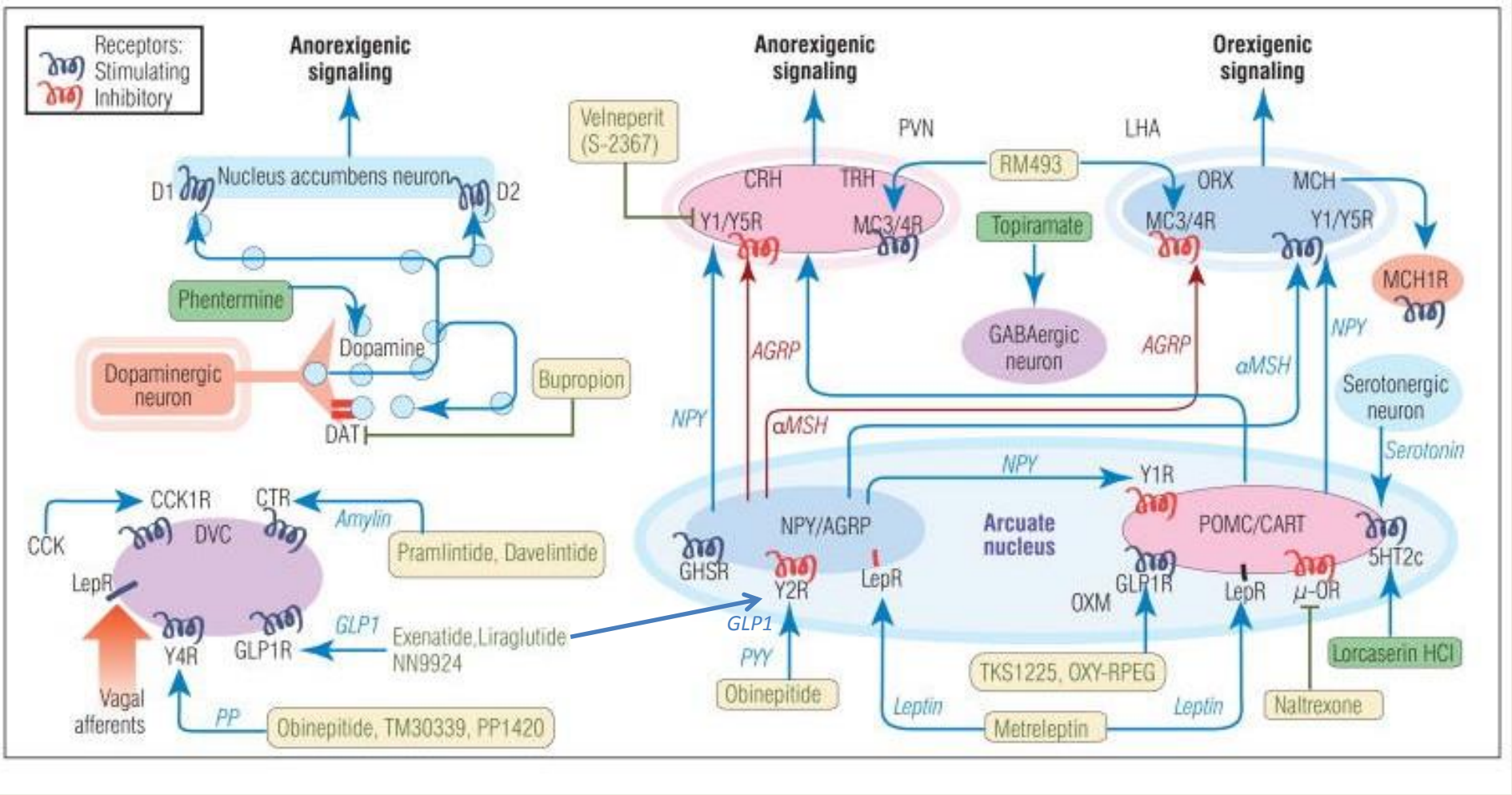


No. at Risk						
Placebo	4898	4776	4623	4482	3467	1730
Sibutramine	4906	4749	4601	4427	3403	1720

Kaplan-Meier curves for time to first occurrence of MACE

James, NEJM, 2010

Anti Obesity Agents and Mechanism of Action

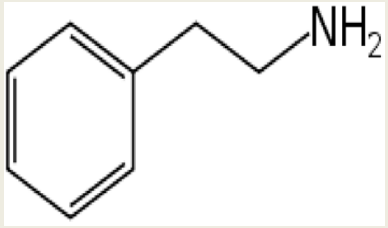


Clin Pharmacol Ther. 2014 Jan; 95(1): 53–66.

J Clin Endocrinol Metab, February 2015, 100(2):342–362

Sympathomimetics (SMPs)

- Drug class: phenethylamines – includes amphetamine, methamphetamine, **phentermine**, diethylpropion, epinephrine, dopamine, and many others.
- Phentermine is not "an amphetamine"
  - Does have phenyl ethylamine backbone



- Phentermine FDA approval in 1959 during a U.S. epidemic of amphetamine addiction. Presumption then – all SMPs shared same adverse effects including addiction potential.
- All obesity drugs reapproved in 1970s for "short-term use" only due to continuing concerns of addiction despite the fact that addiction had occurred *only* with amphetamine.

Phentermine: Effects

- Weight loss
- Maintenance of weight loss
- Diminution or disappearance of cravings
- Changes in eating behaviors
  - Obsessive eating
  - Improved eating control and diet adherence
- Possible elevation of mood (a mild antidepressant)
- Often increased energy
- Possible improvement in ADD and ADHD

Phentermine: Common Misperceptions on Adverse Effects

- Addiction
  - Addiction potential in clinical setting – nil
  - Withdrawal – no amphetamine-like withdrawal
- Adverse cardiovascular effects
  - Hypertension – no evidence
  - Cardiac valvulopathy – no evidence
  - Pulmonary hypertension – no evidence
  - Arrhythmias – no established relationship
  - Cardiovascular disease – no direct evidence but recall SCOUT Trial experience with sibutramine

Rothman AJT 2010, Hendricks Obes 2011

Phentermine: Actual Adverse Effects

Most Common

- Dry mouth – weak anticholinergic agent; usually tolerable
- Insomnia – early, usually fades; if not melatonin may help
- Constipation

Less Common

- Bruxism
- Palpitations
- Difficulty with urination in males with prostatic hyperplasia
- Headache

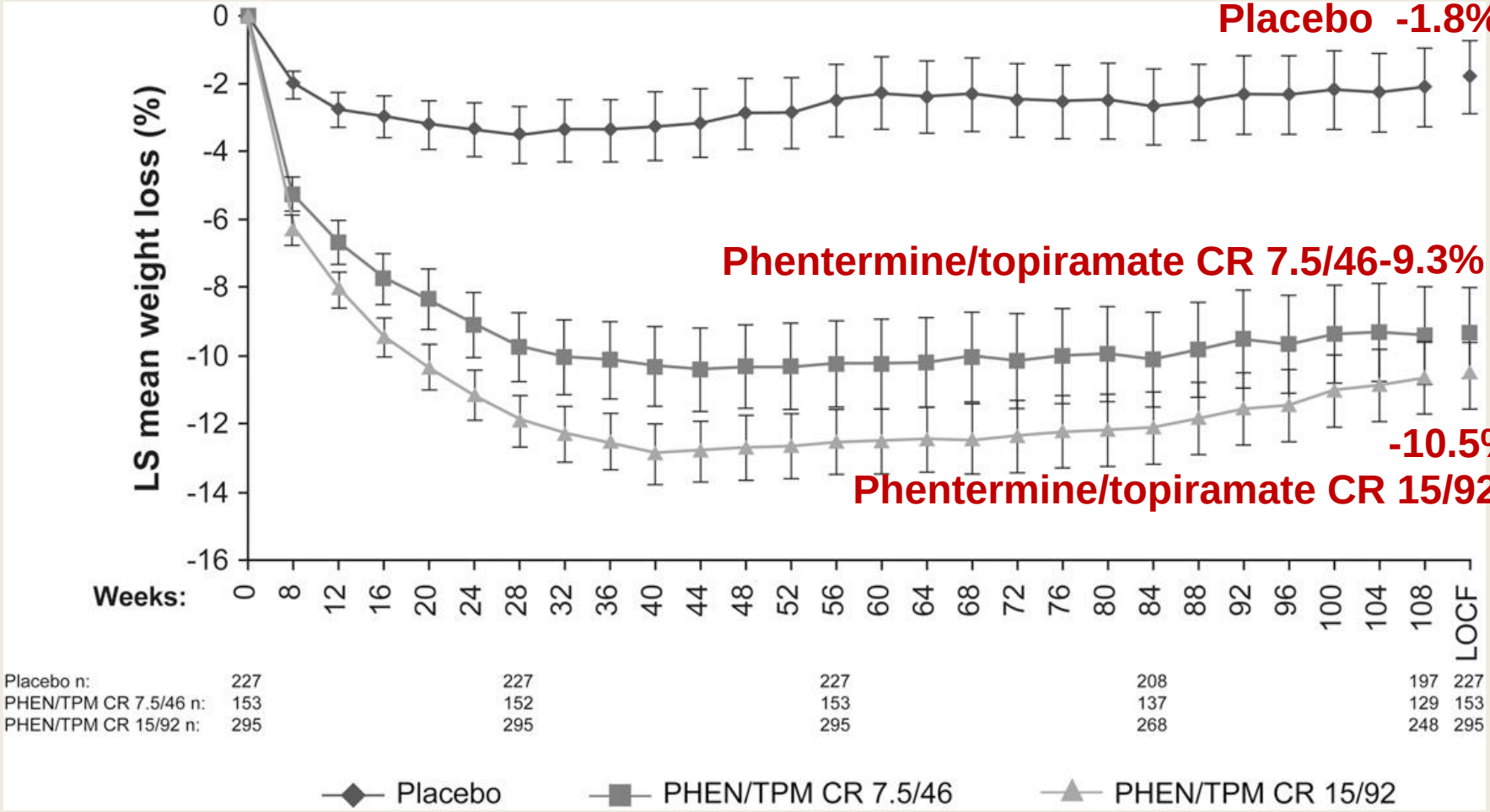
Uncommon

- Impotence, changes in libido
- Dysphoria
- Irritability

Typical dosage: 15 -37.5 mg daily in single or split doses

Effect of **Phentermine/Topiramate ER** on Weight Loss in Obese Adults Over 2 Years

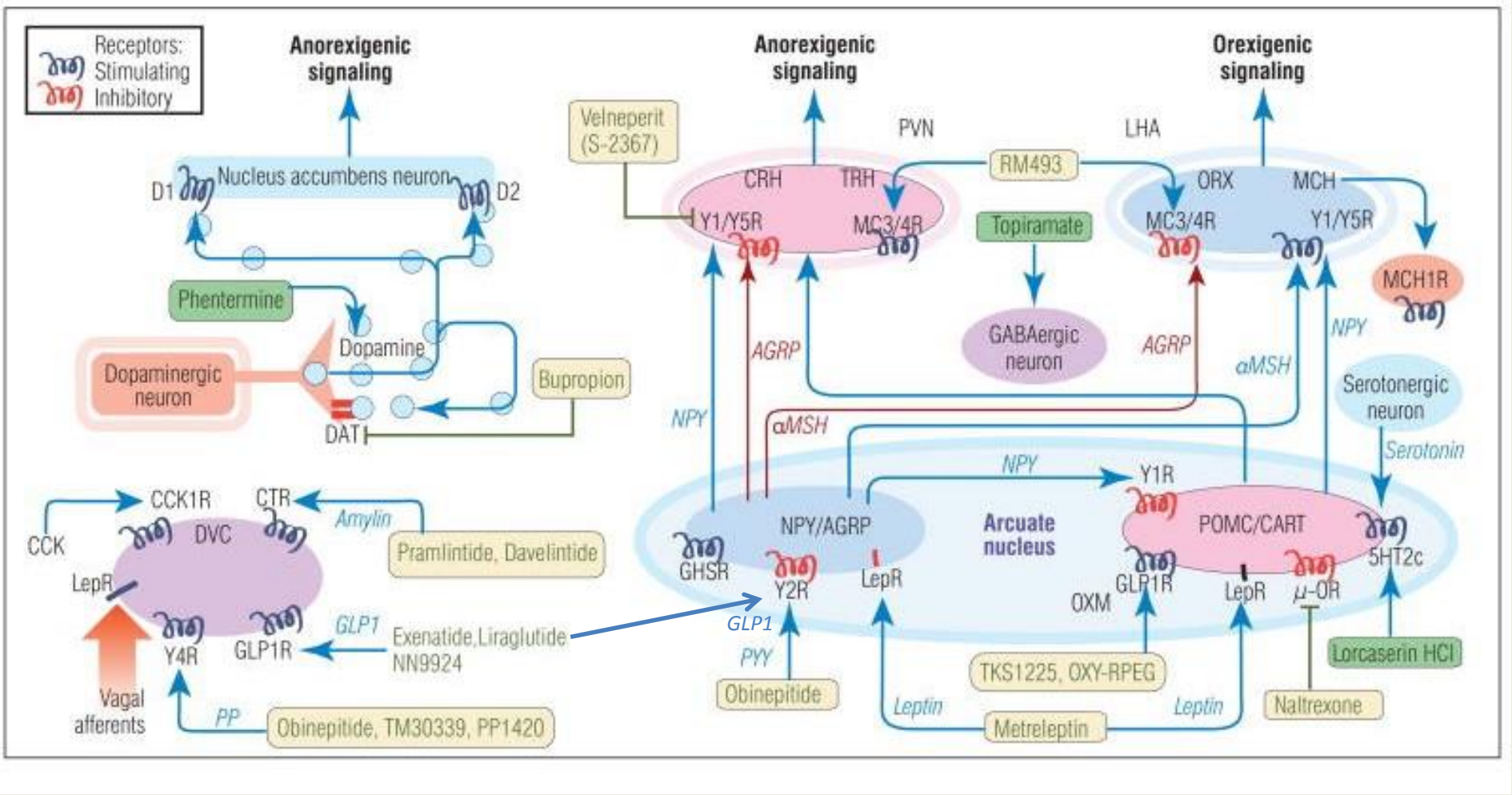
SEQUEL Study



Data are shown with least squares mean (95% CI).

Garvey WT, et al. *Am J Clin Nutr*. 2012;95:297-308.

Anti Obesity Agents and Mechanism of Action



Clin Pharmacol Ther. 2014 Jan; 95(1): 53–66.

J Clin Endocrinol Metab, February 2015, 100(2):342–362

Phentermine HCL/Topiramate Extended Release

Completion of Risk Evaluation and Mitigation Strategy (REMS) program to inform prescribers and female patients about the increased risk of congenital malformations (especially orofacial clefts) in infants exposed to phentermine HCL/topiramate extended release during the first trimester of pregnancy*

Indications and Use

- Drug Enforcement Agency Schedule IV drug
- Phentermine is a shorter-acting sympathomimetic amine approved as monotherapy as a weight-management drug
- Topiramate is a longer-acting neurostabilizer approved as monotherapy for seizure disorders and migraine headache prevention
- Doses = Once daily in the morning with or without food
  - Starting dose = 3.75 mg/23 mg (phentermine/topiramate extended release)
  - After 14-day intervals, and as clinically indicated, escalate doses to:
    - Recommended dose = 7.5 mg/46 mg
    - Titration dose = 11.25 mg/69 mg
    - Top dose = 15 mg/92 mg

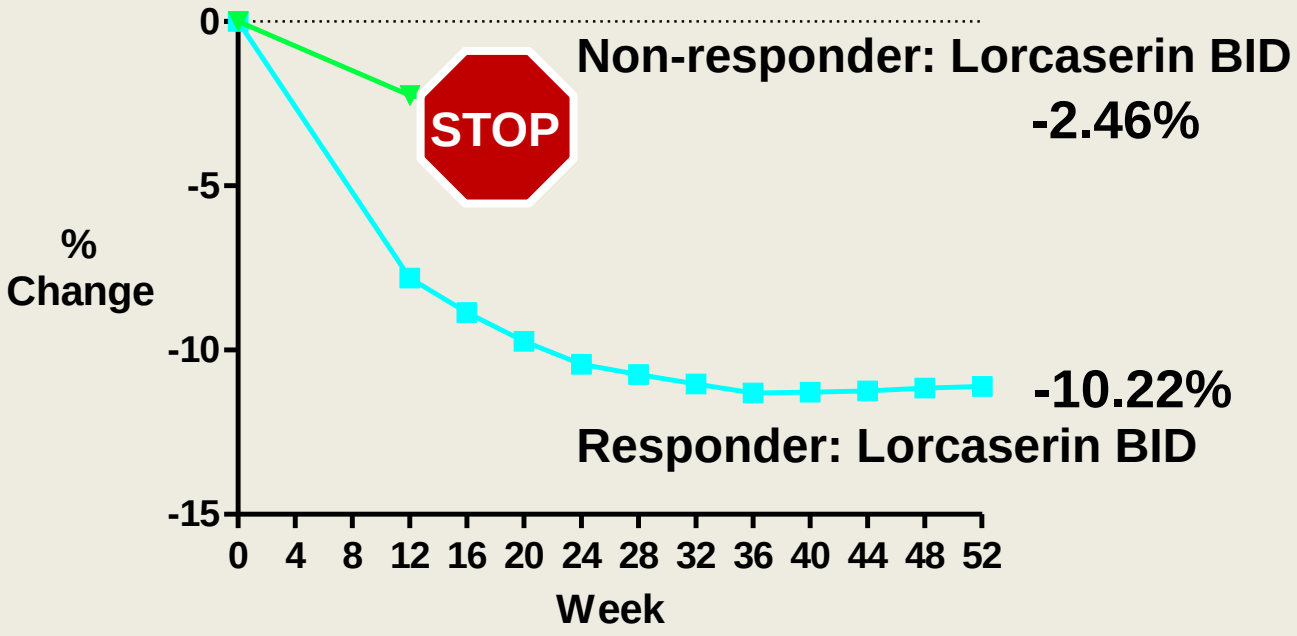
*Completion of the FDA-mandated REMS program is optional and not required prior to prescribing phentermine HCL/topiramate extended release. Implementation of a REMS program by clinicians and pharmacies is intended to provide appropriate safety information to females with reproductive potential.

From Obesity Medicine Association Algorithm –open access

Reference/s: [174] [175] [504]

Lorcaserin: Those Who Lost ≥ 4.5% Total Body Weight by Week 12 Were Week 52 Responders

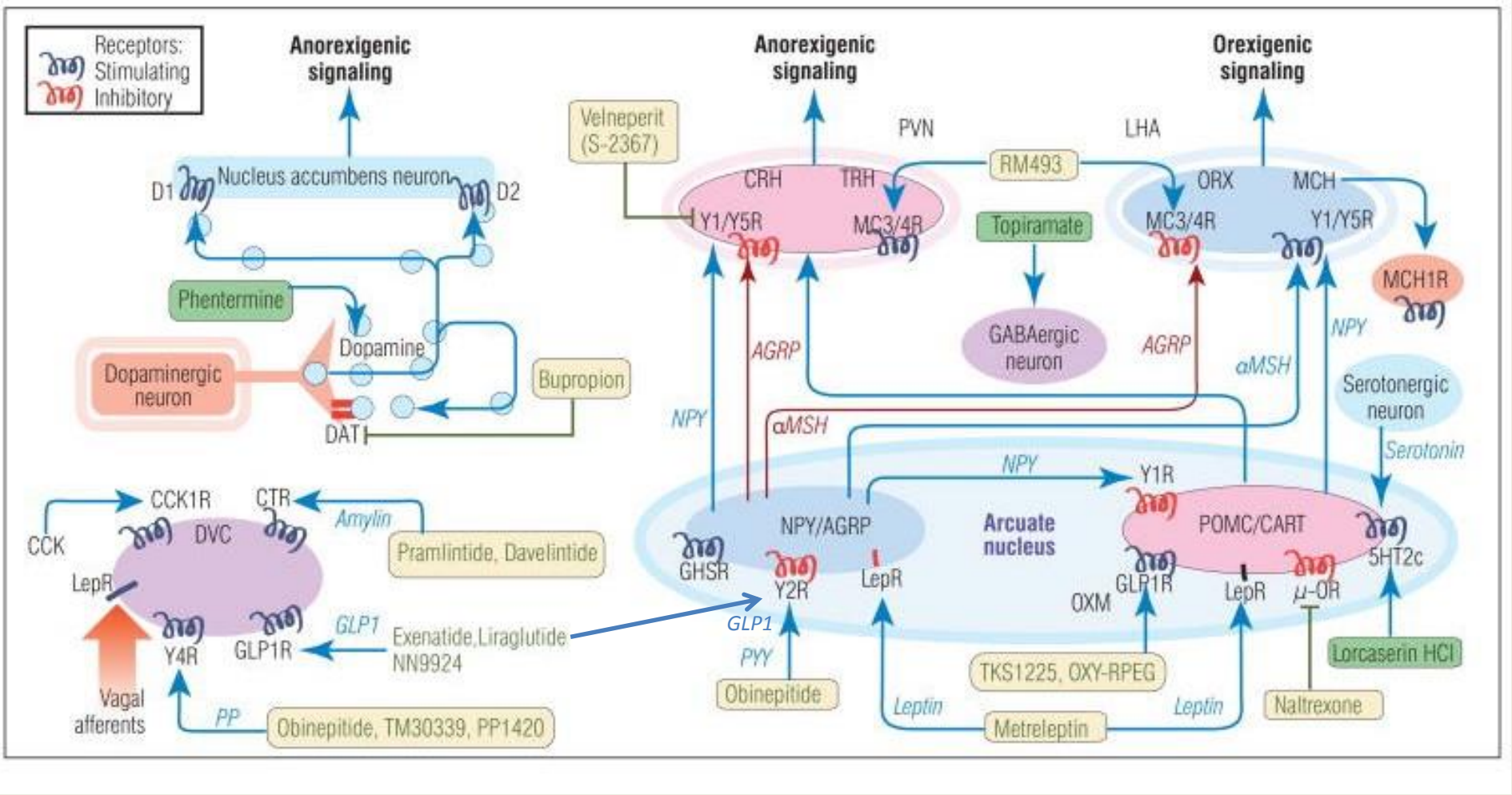
Studies 009 and 011, MITT



MITT Lorcaserin BID	Week 12	Completed Week 12	Completed Week 52
N = 3097	≥4.5% wt loss	1369/3097 (44.2%)	1083/1369 (79.1%)
	<4.5% wt loss	1168/3097 (37.7%)	680/1168 (58.2%)

Slide courtesy Dr. Steve Smith; May 10, 2012 FDA Advisory Committee Meeting

Anti Obesity Agents and Mechanism of Action



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Lorcaserin

Indications and Use

- Serotonin (5-hydroxytryptamine) 2c receptor agonist anti-obesity medication
- Drug Enforcement Agency Schedule IV drug
- **Dose = 10 milligrams (mg) twice per day**

Potential Drug Interactions

- The safety of lorcaserin co-administration with other serotonergic or anti-dopaminergic agents is not yet established, which includes selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, triptans, bupropion, dextromethorphan, St. John's Wort

Pharmacokinetics

- Lorcaserin is metabolized in the liver with metabolites excreted in the urine

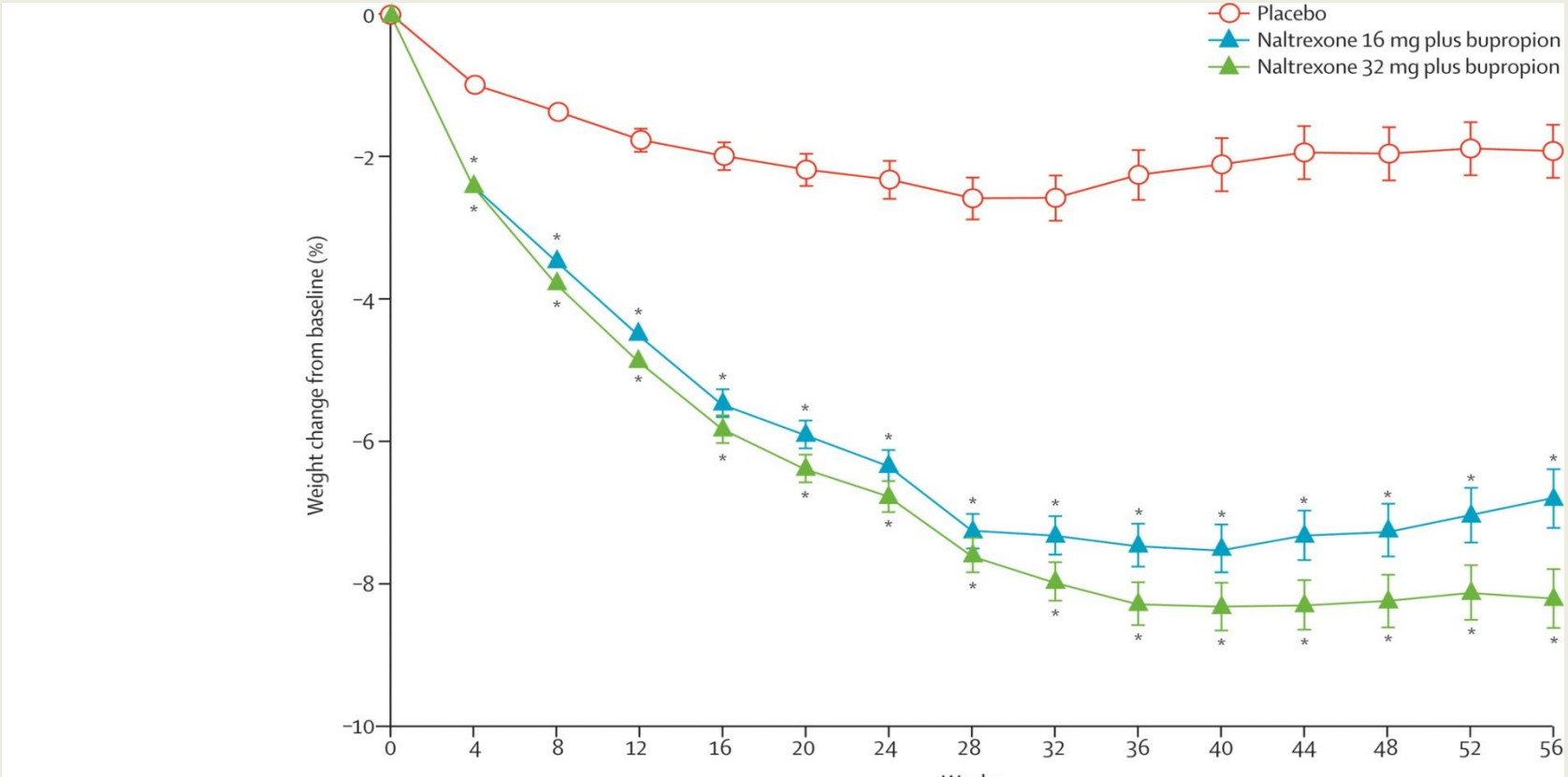
Reference/s:[172] [173] [503]

Mean Weight Loss

Naltrexone/ Bupropion

COR-I Phase 3

56 Weeks – Completer Population

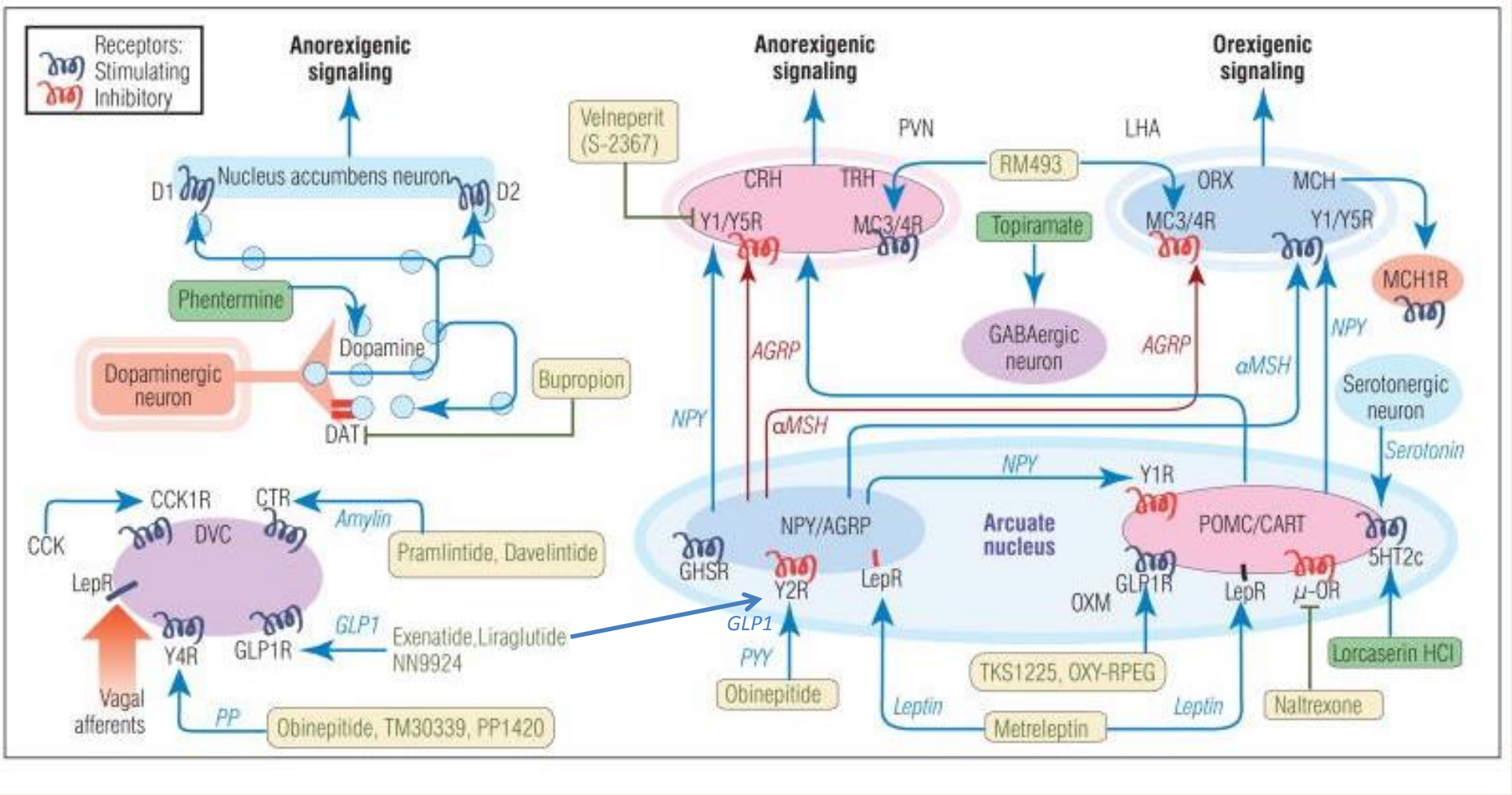


Number of participants by visit (observed)

	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56
Placebo	507	463	420	394	365	353	327	318	308	302	296	291	289	277	
Naltrexone 16 mg plus bupropion	467	410	373	351	346	341	311	311	302	297	300	284	283	273	
Naltrexone 32 mg plus bupropion	467	411	391	372	365	361	343	327	321	316	311	305	298	284	

Greenway FL, et al. *Lancet* 2010 Aug 21; 376:595. DOI:10.1016/S0140-6736(10)60888-4.

Anti Obesity Agents and Mechanism of Action



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J Clin Endocrinol Metab, February 2015, 100(2):342–362

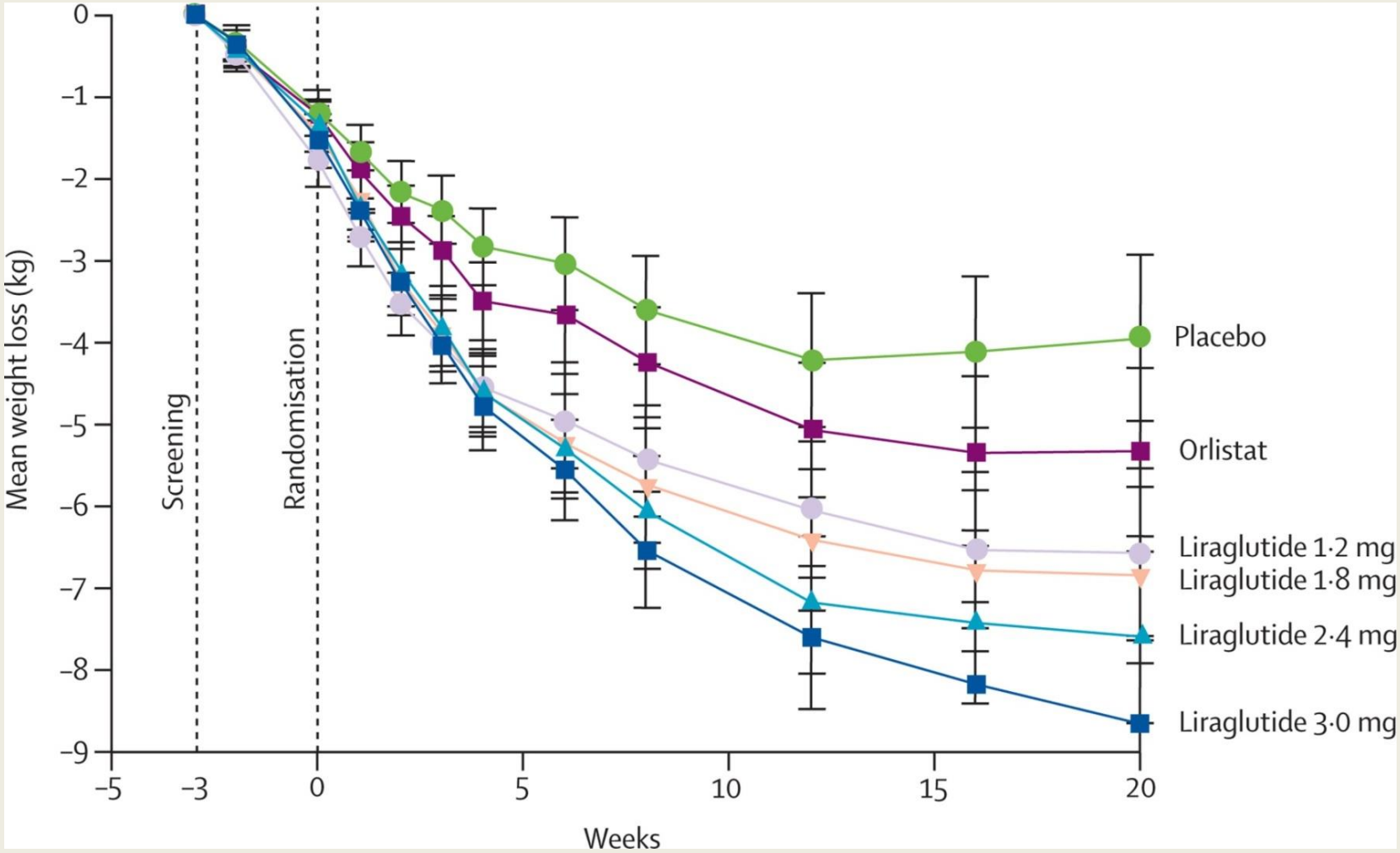
Naltrexone HCL/Bupropion HCL Extended Release

Indications and Use

- Naltrexone is an opioid antagonist
- Bupropion is an aminoketone antidepressant
- Drug Enforcement Agency Schedule: Not a scheduled drug
- Tablets = 8 mg/90 mg (naltrexone HCL/bupropion HCL extended release)
- Dosing:
  - Week 1 = 1 tablet in AM, no tablets in PM
  - Week 2 = 1 tablet in AM, 1 tablet in PM
  - Week 3 = 2 tablets in AM, 1 tablet in PM
  - Week 4 and beyond = 2 tablets in AM, 2 tablets in PM

Reference/s: [505]

Effects of **Liraglutide** and Orlistat on Body Weight in Nondiabetic Obese Adults

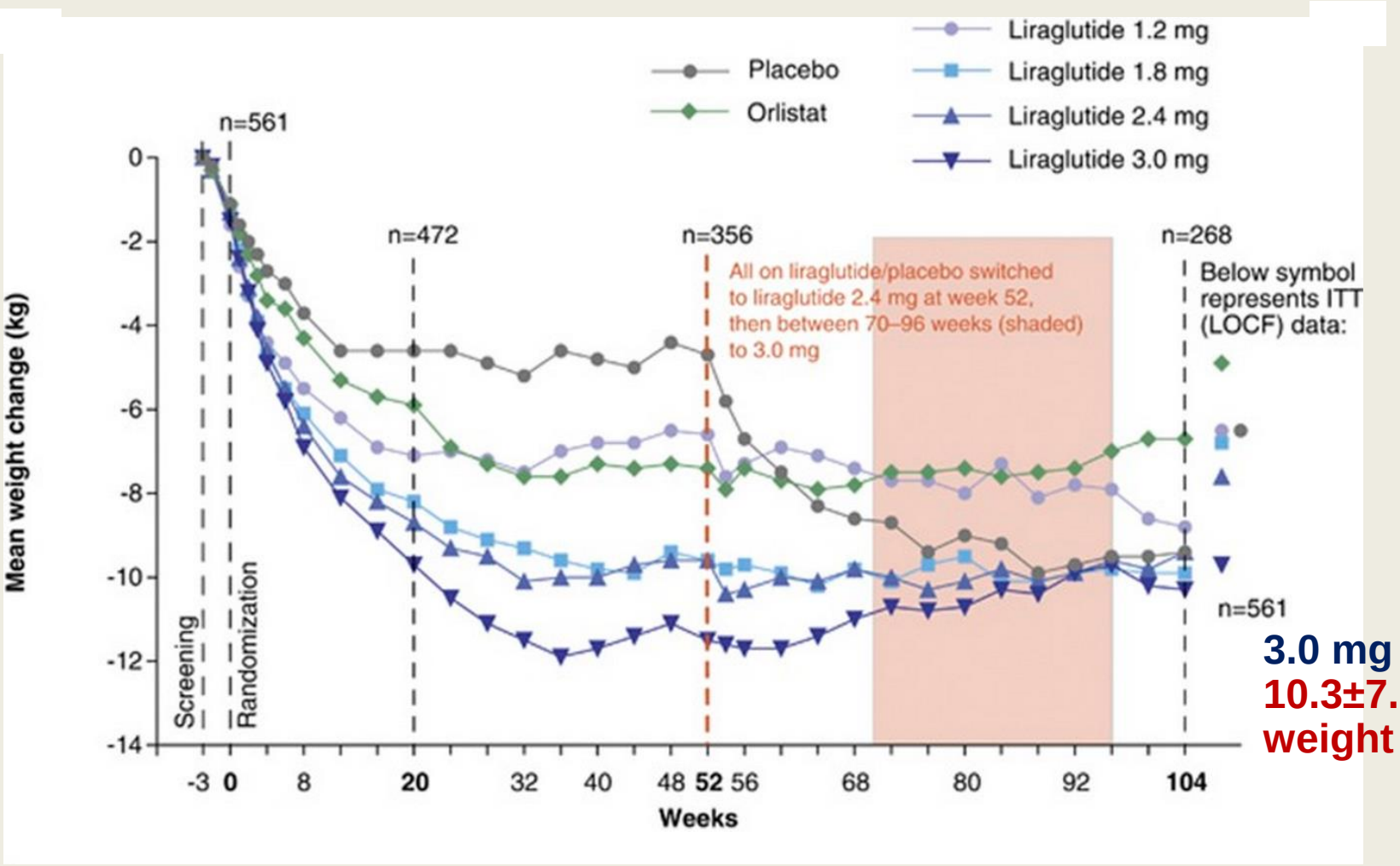


Data are mean (95% CI) for the ITT population

Astrup A, et al. *Lancet*. 2009 Nov 7;374(9701):1606-16.

Liraglutide Weight Loss: Two Years

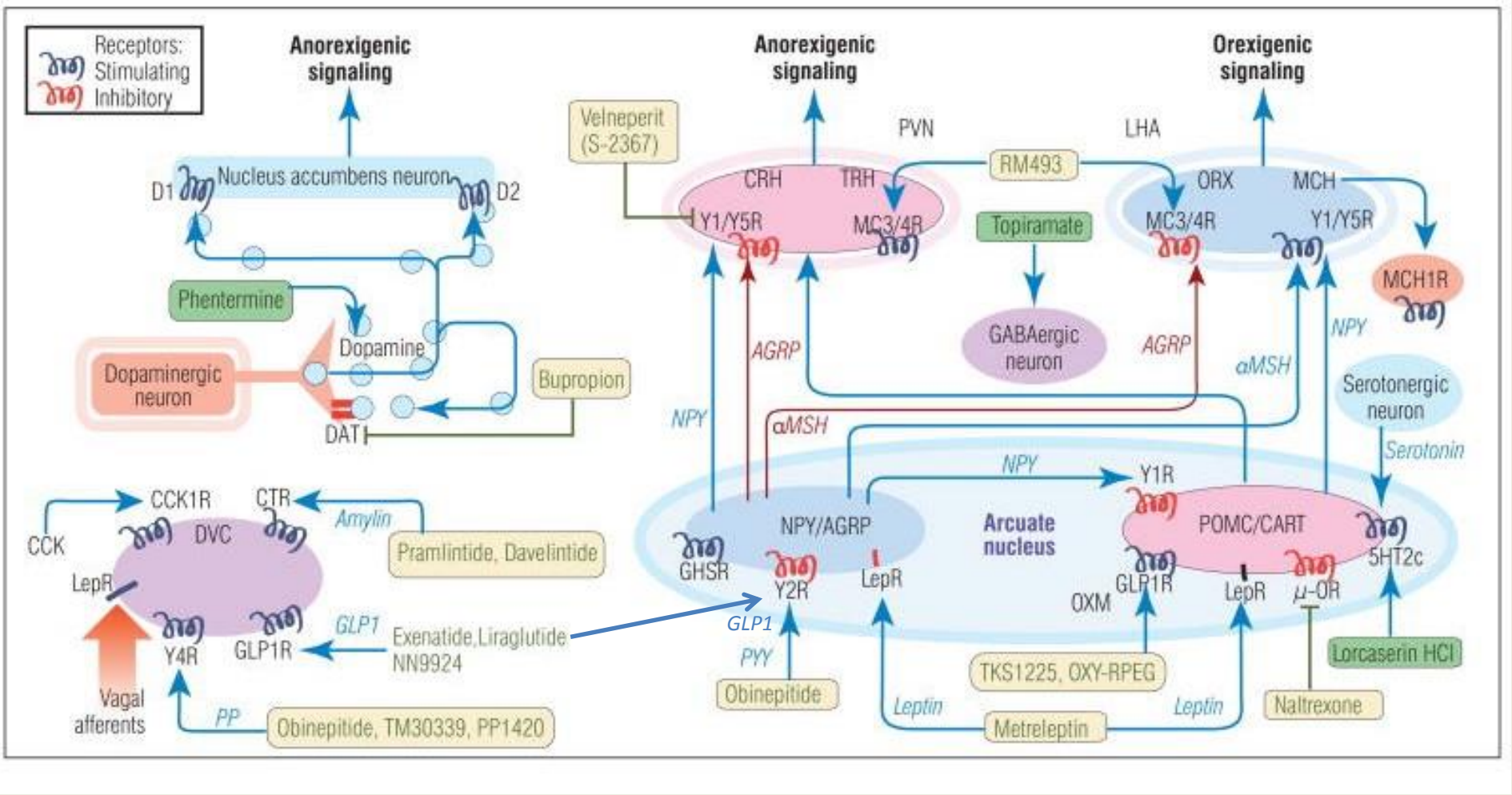
Liraglutide 3.0 mg for 1 year (and then maintained on 2.4/3.0 mg for the second year) maintained a mean weight loss of 10.3±7.1 kg from screening over 2 years



3.0 mg
10.3±7.1 kg weight loss

Astrup A, et al. *Int J Obes (Lond).* Jun 2012; 36(6): 843–854.

Anti Obesity Agents and Mechanism of Action



Clin Pharmacol Ther. 2014 Jan; 95(1): 53–66.

J Clin Endocrinol Metab, February 2015, 100(2):342–362

Liraglutide

Indications and Use

- Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist
- Drug Enforcement Agency Schedule: Not a scheduled drug
- Solution for subcutaneous injection, pre-filled, multi-dose pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg, or 3 mg
- Inject subcutaneously in the abdomen, thigh, or upper arm; the injection site and timing can be changed without dose adjustment
- Recommended dose of liraglutide for treatment of obesity is 3 mg daily, any time of day, without regard to the timing of meals
- Dosing:
  - Week 1 = 0.6 mg per day
  - Week 2 = 1.2 mg per day
  - Week 3 = 1.8 mg per day
  - Week 4 and beyond = 3.0 mg per day

*Completion of the FDA mandated REMS program is optional and not required prior to prescribing liraglutide. Implementation of the REMS program by clinicians and pharmacies is intended to provide appropriate safety information pertaining to the potential serious risks of taking liraglutide, which include medullary thyroid carcinoma (MTC) and acute pancreatitis.

Reference/s: [506]

Other rational combinations?

- All are approved in some usages, but not approved as combinations
- Lorcaserin-Phentermine
- Pramlintide-Phentermine
- SGLT inhibitor combinations

Other indications?

- Is it reasonable to start or continue use after bariatric surgery? (regain)

Drugs approved for 'long term" treatment AACE/ACE 1 of 2

WEIGHT-LOSS MEDICATIONS APPROVED BY THE FDA FOR LONG-TERM TREATMENT OF OBESITY

Anti-obesity Medication (Trade Name) Year of FDA Approval	Mechanism of Action, Study Name, Study Duration: % TBWL Greater Than Placebo	Dose	Common Side Effects	Contraindications, Cautions, and Safety Concerns ✓ Contraindication • Warning, Safety Concern	Monitoring and Comments

Orlistat
 	
(Xenical™)
(Alli™) – OTC
 	
1999
	Lipase inhibitor
	
	XENDOS
	
	1 yr: 4.0%
	4 yr: 2.6%
		120 mg PO TID (before meals)
		
		OTC: 60 mg PO TID (before meals)
			• Steatorrhea
			• Fecal urgency
			• Incontinence
			• Flatulence
			• Oily spotting
			• Frequent bowel movements
			• Abdominal pain
			• Headache
				✓ Pregnancy and breastfeeding
				✓ Chronic malabsorption syndrome
				✓ Cholestasis
				✓ Oxalate nephrolithiasis
				• Rare severe liver injury
				• Cholelithiasis
				• Malabsorption of fat-soluble vitamins
				• Effects on other medications:
				  • Warfarin (enhance)
				  • Antiepileptics (decrease)
				  • Levothyroxine (decrease)
				  • Cyclosporine (decrease)
					Monitor for:
					• Cholelithiasis
					• Nephrolithiasis
					
					- Recommend standard multivitamin (to include vitamins A, D, E, and K) at bedtime or 2 hours after orlistat dose
					- Eating >30% kcal from fat results in greater GI side effects
					- FDA-approved for children ≥12 years old
					- Administer levothyroxine and orlistat 4 hours apart

Lorcaserin (Belviq®) 2012	Serotonin (5HT2c) receptor agonist BLOSSOM BLOOM 1 yr: 3.0%-3.6% 2 yr: 3.1%	10 mg PO BID	• Headache • Nausea • Dizziness • Fatigue • Xerostomia • Dry eye • Constipation • Diarrhea • Back pain • Nasopharyngitis • Hyperprolactinemia	✓ Pregnancy and breastfeeding ✓ Serotonin syndrome or neuroleptic malignant syndrome • Safety data lacking in patients who have depression • Concomitant use of SSRI, SNRI, MAOI, bupropion, St. John's wort as may increase risk of developing serotonin syndrome • Uncontrolled mood disorder • Cognitive impairment • Avoid in patients with severe liver injury or renal insufficiency • Caution with patients with bradycardia, heart block, or heart failure • Unproven concern for potential cardiac valvulopathy • Leukopenia	**Monitor for:** • Symptoms of cardiac valve disease • Bradycardia • Serotonin syndrome • Neuroleptic malignant syndrome • Depression • Severe mood alteration, euphoria, dissociative state • Confusion/somnolence • Priapism • Leukopenia • Euphoria at high doses could predispose to abuse • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas
Phentermine/ Topiramate ER (Qsymia®) 2012	NE-releasing agent (phentermine) GABA receptor modulation (topiramate) EQUIP CONQUER SEQUEL 1 yr: 8.6%-9.3% on high dose; 6.6% on treatment dose 2 yr: 8.7% on high dose; 7.5% on treatment dose	**Starting dose:** 3.75/23 mg PO QD for 2 weeks **Recommended dose:** 7.5/46 mg PO QD **Escalation dose:** 11.25/69 mg PO QD **Maximum dose:** 15/92 mg PO QD	• Headache • Paresthesia • Insomnia • Decreased bicarbonate • Xerostomia • Constipation • Nasopharyngitis • Anxiety • Depression • Cognitive impairment (concentration and memory) • Dizziness • Nausea • Dysgeusia	✓ Pregnancy and breastfeeding (topiramate teratogenicity) ✓ Hyperthyroidism ✓ Acute angle-closure glaucoma ✓ Concomitant MAOI use (within 14 days) • Tachyarrhythmias • Decreased cognition • Seizure disorder • Anxiety and panic attacks • Nephrolithiasis • Hyperchloremic metabolic acidosis • Dose adjustment with hepatic and renal impairment • Concern for abuse potential • Combined use with alcohol or depressant drugs can worsen cognitive impairment	**Monitor for:** • Increased heart rate • Depressive symptomatology or worsening depression especially on maximum dose • Hypokalemia (especially with HCTZ or furosemide) • Acute myopia and/or ocular pain • Acute kidney stone formation • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas - Potential for lactic acidosis (hyperchloremic non-anion gap) in combination with metformin - MAOI (allow ≥ 14 days between discontinuation) - 15 mg/92 mg dose should not be discontinued abruptly (increased risk of seizure); taper over at least 1 week - Health care professional should check βHCG before initiating, followed by monthly self-testing at home - Monitor electrolytes and creatinine before and during treatment - Can cause menstrual spotting in women taking birth control pills due to altered metabolism of estrogen and progestins

Drugs approved for 'long term" treatment AACE/ACE 2/2

Anti-obesity Medication (Trade Name) Year of FDA Approval	Mechanism of Action, Study Name, Study Duration: % TBWL Greater Than Placebo	Dose	Common Side Effects	Contraindications, Cautions, and Safety Concerns	Monitoring and Comments
Naltrexone ER/ Bupropion ER (Contrave®) 2014	Opiate antagonist (naltrexone) Reuptake inhibitor of DA and NE (bupropion) COR-I COR-II COR-BMOD **1 yr: 4.2%-5.2%**	**Titrate dose:** **Week 1:** 1 tab (8/90 mg) PO QAM **Week 2:** 1 tab (8/90 mg) PO BID **Week 3:** 2 tabs (total 16/180 mg) PO QAM and 1 tab (8/90 mg) PO QHS **Week 4:** 2 tabs (total 16/180 mg) PO QHS	• Nausea • Headache • Insomnia • Vomiting • Constipation • Diarrhea • Dizziness • Anxiety • Xerostomia	✓ Pregnancy and breastfeeding ✓ Uncontrolled hypertension ✓ Seizure disorder ✓ Anorexia nervosa ✓ Bulimia nervosa ✓ Severe depression ✓ Drug or alcohol withdrawal ✓ Concomitant MAOI (within 14 days) ✓ Chronic opioid use • Cardiac arrhythmia • Dose adjustment for liver and kidney impairment • Narrow-angle glaucoma • Uncontrolled migraine disorder • Generalized anxiety disorder • Bipolar disorder • Safety data lacking in patients who have depression • Seizures (bupropion lowers seizure threshold)	**Monitor for:** • Increased heart rate and blood pressure • Worsening depression and suicidal ideation • Worsening of migraines • Liver injury (naltrexone) • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas • Seizures (bupropion lowers seizure threshold) - MAOI (allow ≥ 14 days between discontinuation) - Dose adjustment for patients with renal and hepatic impairment - Avoid taking medication with a high-fat meal - Can cause false positive urine test for amphetamine - Bupropion inhibits CYP2D6
Liraglutide 3 mg (Saxenda®) 2014	GLP-1 analog SCALE Obesity & Prediabetes **1 yr: 5.6%**	**Titrate dose weekly by 0.6 mg as tolerated by patient (side effects):** 0.6 mg SC QD→ 1.2 mg SC QD→ 1.8 mg SC QD→ 2.4 mg SC QD→ 3.0 mg SC QD	• Nausea • Vomiting • Diarrhea • Constipation • Headache • Dyspepsia • Increased heart rate	✓ Pregnancy and breastfeeding ✓ Personal or family history of medullary thyroid cancer or MEN2 ✓ Pancreatitis ✓ Acute gallbladder disease • Gastroparesis • Severe renal impairment can result from vomiting and dehydration • Use caution in patients with history of pancreatitis • Use caution in patients with cholelithiasis • Suicidal ideation and behavior • Injection site reactions	**Monitor for:** • Pancreatitis • Cholelithiasis and Cholecystitis • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas • Increased heart rate • Dehydration from nausea/vomiting • Injection site reactions - Titrate dose based on tolerability (nausea and GI side effects)

Abbreviations: BID = twice daily; DA = dopamine; FDA = US Food and Drug Administration; GI = gastrointestinal; HCTZ = hydrochlorothiazide; MAOI = monoxidase inhibitor; MEN2 = multiple endocrine neoplasia type 2; NE = norepinephrine; OTC = over-the-counter medication; %TBWL = percent total body weight loss from baseline over that observed in the placebo group; PO = oral; QAM = every morning; QD = daily; QHS = every bedtime; SC = subcutaneous; SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TID = 3 times a day; T2DM = type 2 diabetes mellitus.

FDA indication for all medications: BMI >30 kg/m^2 or BMI ≥27kg/m^2 with significant comorbidity.

After 3 to 4 months of treatment with antiobesity medication:

- **For naltrexone ER/bupropion ER and lorcaserin:**
  If the patient has not lost at least 5% of their baseline body weight at 12 weeks on the maintenance dose, the medication should be discontinued.
- **For phentermine/topiramate ER:**
  Continue medication if the patient has lost >5% body weight after 12 weeks on recommended dose (7.5 mg/42 mg); if the patient has not lost at least 3% of body weight after being on the recommended dose for 12 weeks then the medication should be discontinued, or the patient can be transitioned to maximum dose (15 mg/92 mg); if patient has not lost at least 5% after 12 additional weeks on the maximum dose, the medication should be discontinued.
- **For liraglutide 3 mg:**
  If the patient has not lost at least 4% of body weight 16 weeks after initiation, the medication should be discontinued.

References:

1–4 and package inserts for each medication

1. Wyatt HR. Update on treatment strategies for obesity. *J Clin Endocrinol Metab*. 2013;98(4):1299-1306.
2. Garvey WT, Garber AJ, Mechanick JI, Bray GA, Dagogo-Jack S, Einhorn D, et al. American Association of Clinical Endocrinologists and American College of Endocrinology position statement on the 2014 advanced framework for a new diagnosis of obesity as a chronic disease. *Endocr Pract*. 2014;20(9):977-989.
3. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA*. 2014;311(1):74-86.
4. Fujioka K. Current and emerging medications for overweight and obesity in people with comorbidities. *Diabetes Obes Metab*. 2015;17(11):1021-1032.

Summary

- Use of Anti Obesity Medications is a valuable adjunct to other treatment modalities
- It is important to understand barriers to use of medications
- Learning correct usage takes time but resources are available
- Managing expections is important – even small amounts of weight loss have large effects

Thank You!

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Bariatric Surgery Updates

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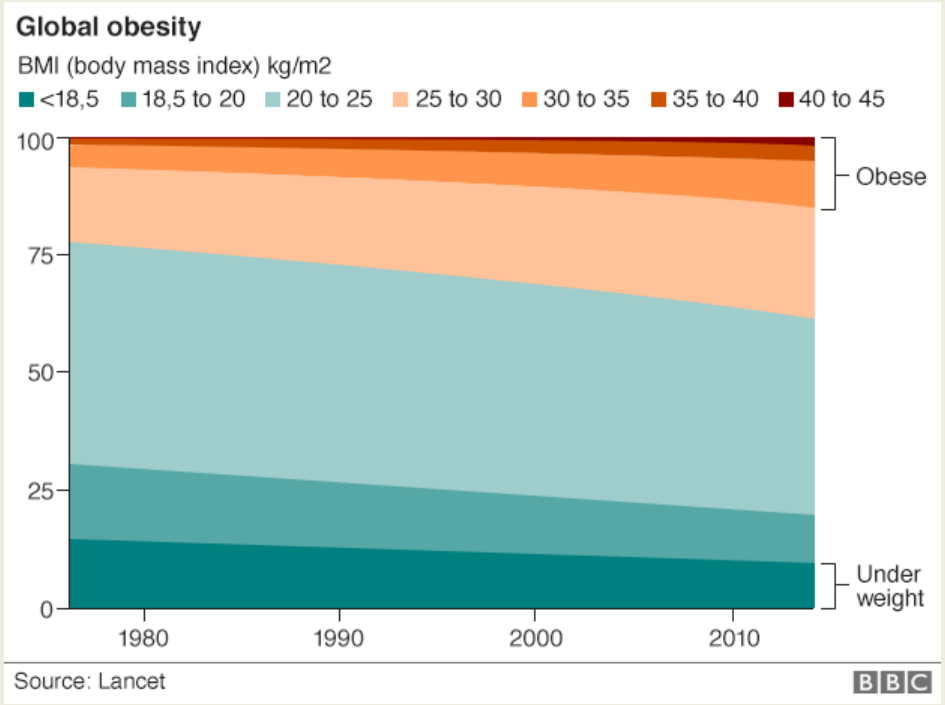
2016

Obesity in 2016 (from WHO)

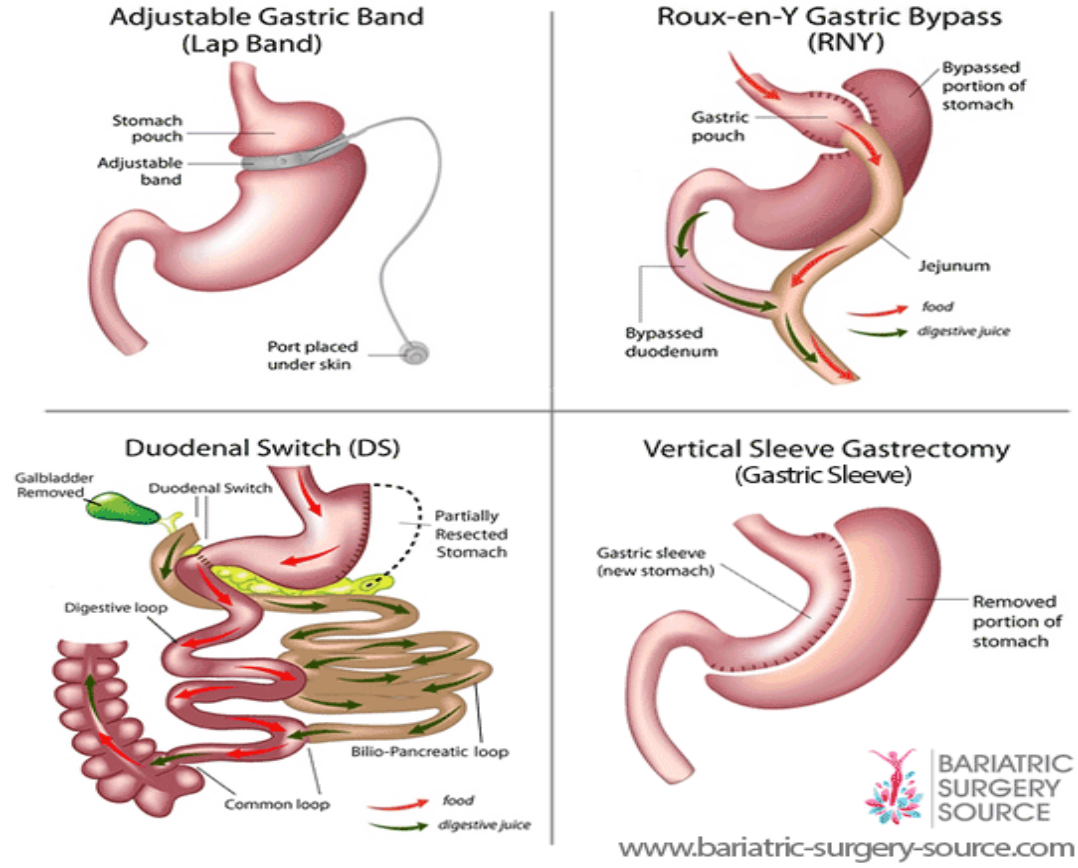
- Worldwide obesity has more than doubled since 1980.
- Undernutrition and obesity can exist together- “double burden”
- 39% overweight and 14% obese



Objectives

- Become familiar with the most common surgical procedures for weight loss
- Awareness of endoscopic treatments for obesity

4 Most Common Weight Loss Surgery Procedures in the United States



Key Surgical Points

- Most procedures are done laparoscopically, OR time ranges 45 min- 3 hours on average
- Very safe, minimal blood los
- <0.2% mortality
- 0-2 night hospital stays

Key Surgical Points

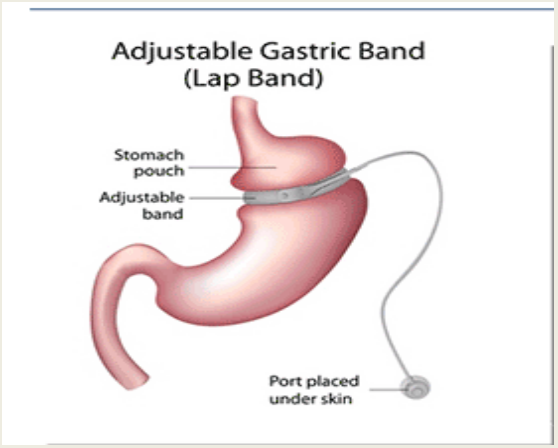
- Early ambulation (within 4hours postop)
  - can shower
  - use of IS and CPAP immediately postop
- Hydrate
  - Goal 64
- Start MV

when able to tolerate (

Laparoscopic Adjustable Gastric Band

- Less utilized now

- Band concerns
  - Slip
  - Erosion

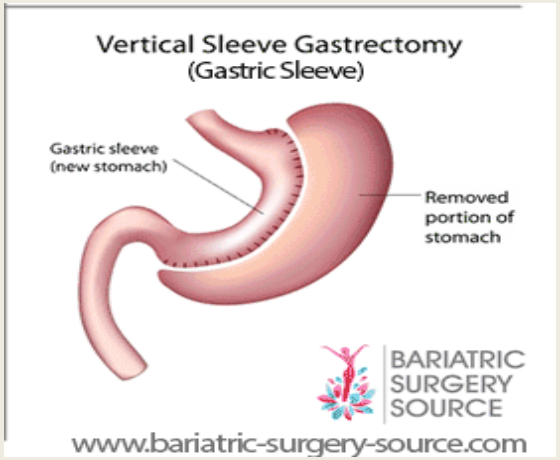


- Port site concerns
  - Access only with a huber needle

Laparoscopic Sleeve Gastrectomy

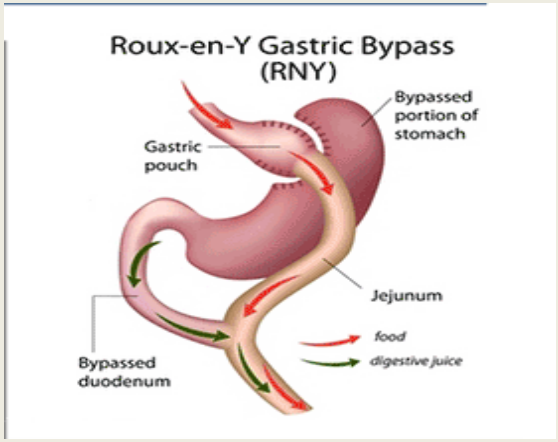
- Most commonly performed now

- Types of complications
  - Leak
  - Bleeding
  - Obstruction/stenosis
  - GERD



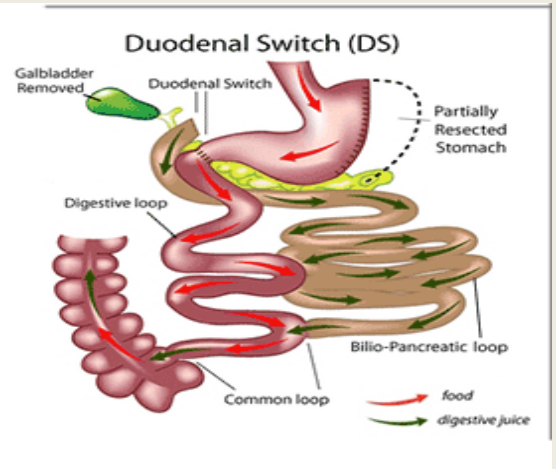
Laparoscopic Roux-en-Y Gastric Bypass (LRYGB)

- Longest history/evolution
- Types of complications
  - Leak
  - Bleeding
  - SBO/Internal hernia
  - Marginal ulcers
- Malabsorption component



Laparoscopic Duodenal Switch (DS)

- Starting to increase in numbers
- Most malabsorptive
- Vitamin compliance/Dietary compliance



Original Investigation

Five-Year Outcomes After Laparoscopic Gastric Bypass and Laparoscopic Duodenal Switch in Patients With Body Mass Index of 50 to 60

A Randomized Clinical Trial

Hilde Risstad, MD; Torgeir T. Søvik, MD, PhD; My Engström, RN, PhD; Erlend T. Aasheim, MD, PhD; Morten W. Fagerland, MSc, PhD; Monika Fagevik Olsén, RPT, PhD; Jon A. Kristinsson, MD, PhD; Carel W. le Roux, MD, PhD; Thomas Bøhmer, MD, PhD; Kåre I. Birkeland, MD, PhD; Tom Mala, MD, PhD; Torsten Olbers, MD, PhD

BMI 50-60, 30 pts duodenal switch vs 30pt LRYGB

- DS greater weight loss and greater improvements in low-density lipoprotein cholesterol, triglyceride, and glucose levels 5 years
- Improvements in health-related quality of life were similar
- Duodenal switch was associated with more surgical, nutritional, and gastrointestinal adverse effects.

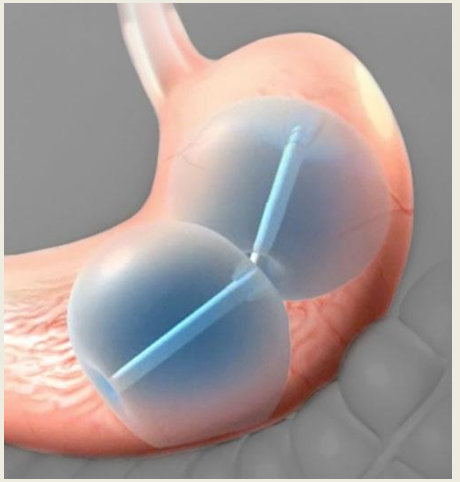
Key Diet Education

- 45-60 grams of protein daily
- Start with slow drinks/bites all day, but progress to 3 meals
  - Over 2-3 months
- Exercising immediately- low impact, light weights (1-5lbs)
- MVI for everyone
- Other vitamins
  - B12 and/or B-complex
  - Vitamin D3
  - Calcium citrate
  - ADEK- DS only

Endoscopic treatments

Intragastric Balloons

- Double balloon and single balloon available (Orbera, ReShape, Allurion)
- Space occupying
- Nausea
- 3-6 month duration
- FDA approval BMI 30-40



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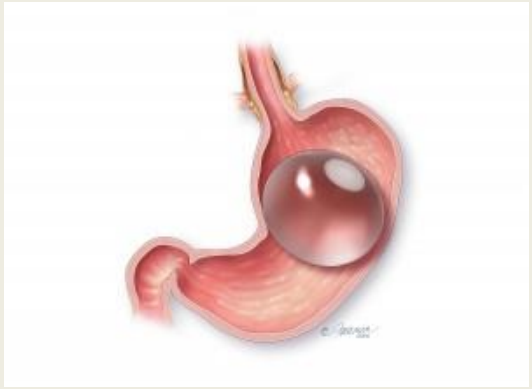
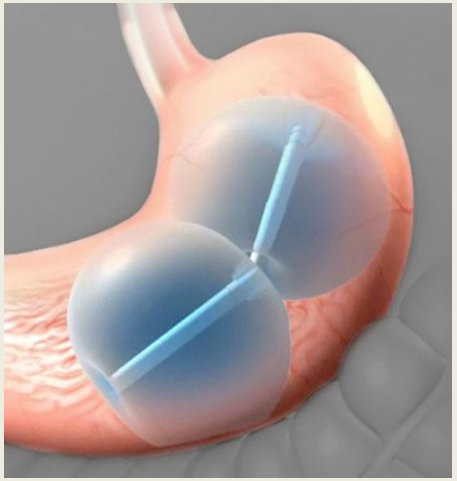




Endoscopic treatments

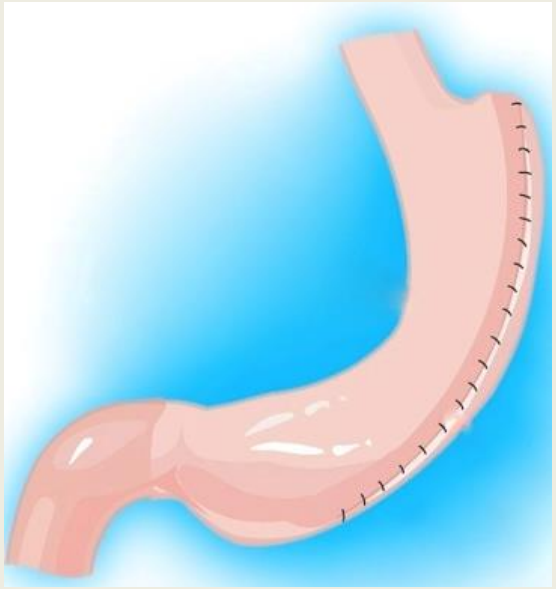
Endoscopic gastric plication

- Suturing done with the endoscope

- 3-4hour procedure

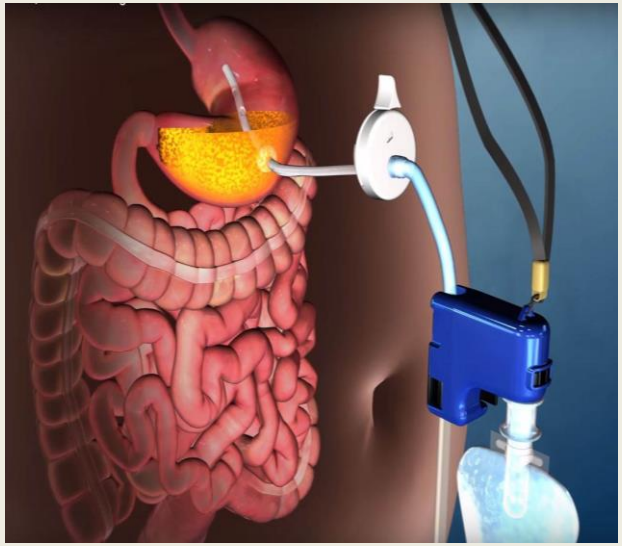
- Requires GETA

- DDW 242 patient, 19.8% TBW at 18 months



Additional Treatments

- AspireAssist- FDA approved
  - 111 pts, 37.2% EBW

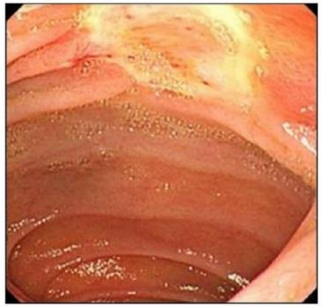


- GI Windows
  - Magnets- jejunoileal anastomosis
  - Placed in GI lab
  - Czech 10pts, 28.3% EBW
  - HgA1c improved
- Revita
  - Duodenal mucosal resurfacing
  - Hot balloon
  - Type 2 DM- 1.2%

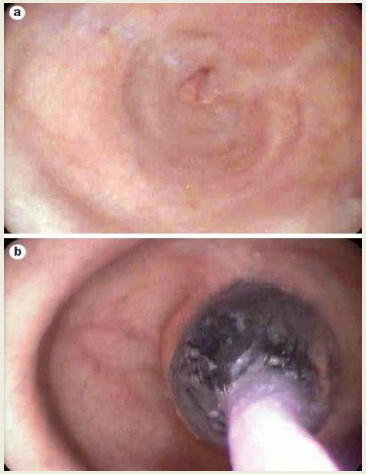
Questions?

Late complications (>30 days)

- Marginal Ulcers- Gastric Bypass and Duodenal Switch
  - PPI +/- H2 blocker
  - Carafate slurry qid
  - EGD



- Stricture- Gastric Bypass and Duodenal Switch
  - EGD with dilation +/- kenalog injection, BIOPSY
  - Hypertrophic scar vs ischemic



Health Equity and Obesity Disparities: Social Causes and Consequences

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Oct. 21, 2016

Social Determinants of Health

- ***Social Determinants of Health***: the economic and social conditions that influence individual and group differences in health status.
- "Social determinants of health reflect the social factors and physical conditions of the environment in which people are born, live, learn, play, work, and age. Also known as social and physical determinants of health, they impact a wide range of health, functioning, and quality-of-life outcomes." (Healthy People 2020) http://www.healthypeople.gov/2020/about/foundation-health-measures/Determinants-of-Health

Health Disparities

- ***Health Disparities***: "a particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage."
  - Avoidable gaps between subgroups
- Persistent disparities in numerous health outcomes are observed on the basis of:
  - Race/ethnicity
  - Sex/Gender
  - Disability Status
  - Age
  - Socioeconomic Status/Position

Sources: Healthy People 2020 (https://www.healthypeople.gov/2020/about/foundation-health-measures/Disparities)
CDC. *MMWR* 2013; 62(Suppl 3).

Disparities in Obesity

- No groups have been immune to increasing levels of obesity
- Who is disproportionately affected?
  - Generally > Women, Black and Hispanic, those with lower incomes and education
  - Various social positions interact to produce a more complicated picture:
    - The most socially disadvantaged (low-educ/income Black women) have highest rates of BMI growth, while most socially advantaged have lowest rates (high educ/income White men) (Ailshire & House. *Social Forces* 2011. 90(2): 397-423)

Obesity in the U.S.

- Obesity is an immensely complex issue
- Intense debate surrounds the extent to which various factors have led to such increases in obesity
- Factors include:
  - Major shifts in lifestyle patterns (sedentary, meals away from home, snacking); Western diet
  - Abundant use of additives in food supply
  - Overabundance of food
  - Lack of access to healthy options
  - Lack of information or misleading information

Social Determinants of Obesity

- Lack of available resources, e.g. affordability of healthy options
- Neighborhood disorder: safety, access to space
- Socio-cultural factors: social support, health behaviors and attitudes
- Concentrated disadvantage: poverty, segregation
- Political Factors: food policy (subsidies), lack of regulation of food industry

The Food Environment

- Recognize the influence of the food environment
  - ***Toxic/Obesogenic Food Environment***: the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals and populations
  - What we are seeing is a normal response to an abnormal environment (Egger & Swinburn. *BMJ* 1997; 315(7106): 477-480)
  - An ecological approach reduces emphasis on obesity as an individual problem (Story et al. *Annu. Rev. Public Health* 2008. 29:253–72)

The Food Environment

- ***Food Desert***: a term used to describe areas that have poorer access to healthy choices
  - Less grocery store availability and more fast food in urban areas
  - Obesity in disadvantaged groups is influenced by acess to supermarkets and safety of neighborhoods (Lovasi et al. *Epidemiol Rev* 2009. 31:7-20)

- Common approach to obesity takes a downstream approach, i.e. focus on and modify behavior/diet instead of the food environment

Social Consequences

- A prevalent message is that obesity is mainly an issue of personal choice (or a lack of will power)
  - But, keep in mind that obesity has increased despite increased knowledge, awareness, and education about nutrition and exercise
- People with obesity suffer from bias and discrimination in multiple settings

Source: Puhl, Rebecca, and Kelly D. Brownell. *Obes Res* 2001; 9(12): 788-805.

Weight Bias and Stigma

- Stigma (a representation of society's negative perceptions)
  - Weight bias leads to: lower wages over life course, hiring prejudice, disparities in educational outcomes, and bullying
  - Health Setting: Patients feel stigmatized and may avoid care
    - Associations with increased rates of depression and anxiety
    - Evidence of less intervention, less time spent

Sources: Sobal, J. *A Soc of Food and Nutrition* 2004; 383-402.
Puhl & Brownell. *Obes Rev* 2003; 4:213-227.
Friedman & Puhl. Weight Bias: A Social Justice Issue.
http://www.uconnruddcenter.org/files/Pdfs/Rudd_Policy_Brief_Weight_Bias.pdf

Weight Bias and Stigma

- Media Messages
  - Promotes intense fear of weight gain, overweight, and obesity
  - Stereotypical representations of those with obesity
  - http://www.uconnruddcenter.org/media-gallery
- No productivity differences observed in those with obesity vs. without

Research Findings

- Better working alliance was associated with increased patient activation, regardless of weight
- Perceived weight bias lowered patient activation
- Patient activation is a promising avenue through which to promote the adoption and maintenance of healthy behaviors

Source: Gonzales, Garcia, et al. Under Review – *Health Education Research*, "Patient-provider relationship, weight bias, and patient activation among American Indians and Alaska Natives,"

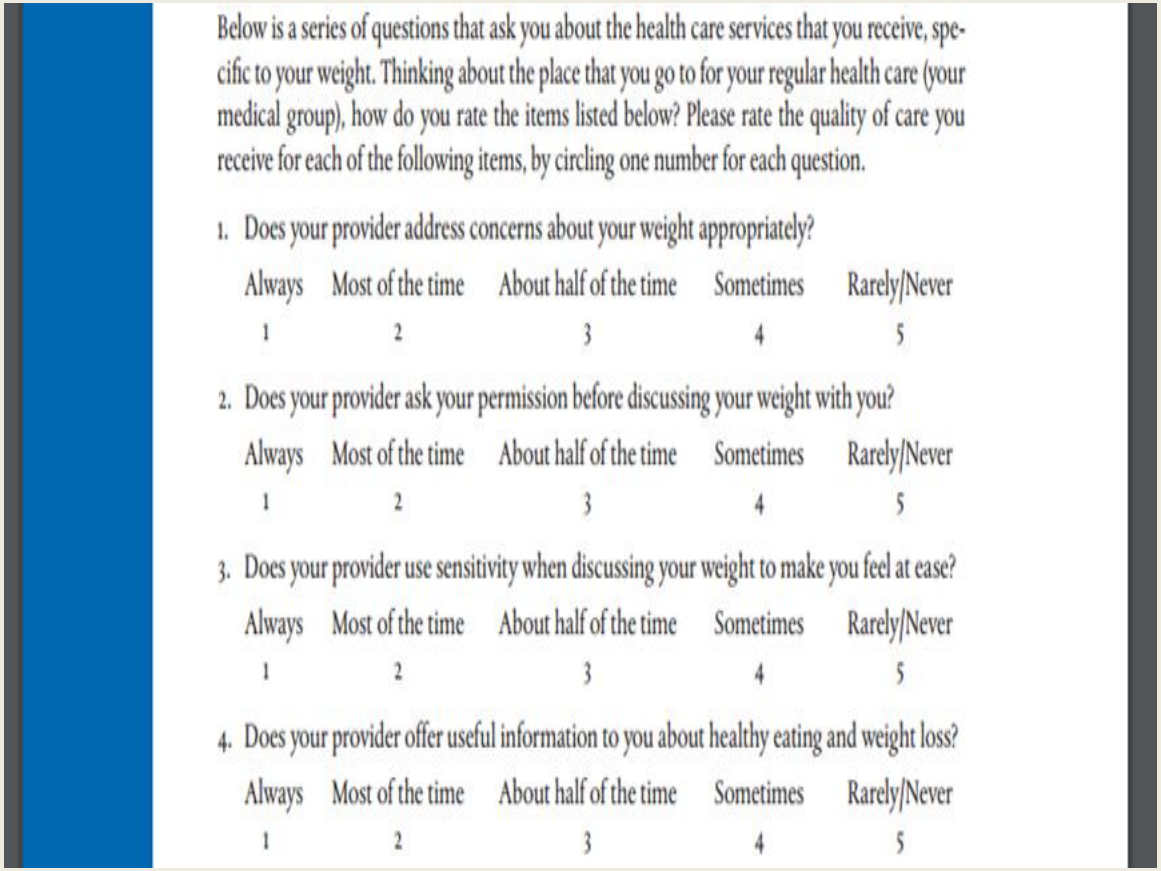
Recommendations

- Recognize the role of external forces and the complexity of the issue
- Examine/consider findings that suggest obesity on its own may not be directly connected to ill-health/mortality (see resources for suggested reading)
- Keep focus on health promotion and adoption of healthy behaviors
- Acknowledge possible biases

Recommendations

- Issues of best practice
  - Offer support with weight management
  - Promote healthy eating and active lifestyles/wellness to all patients
  - Increase accessibility if possible (comfortable chairs, etc.)
  - Provide access to resources for patients that increase their knowledge/agency (improve working alliance and patient activation) – empower your patients
  - Use appropriate language: “People with obesity”
  - Help with development of wellness policies

- Administer surveys to assess your practice: http://biastoolkit.uconnruddcenter.org/toolkit/Module-8/8-05-SurveyWeightSensitive.pdf



Below is a series of questions that ask you about the health care services that you receive, specific to your weight. Thinking about the place that you go to for your regular health care (your medical group), how do you rate the items listed below? Please rate the quality of care you receive for each of the following items, by circling one number for each question.

1. Does your provider address concerns about your weight appropriately?

Always	Most of the time	About half of the time	Sometimes	Rarely/Never
1	2	3	4	5

2. Does your provider ask your permission before discussing your weight with you?

Always	Most of the time	About half of the time	Sometimes	Rarely/Never
1	2	3	4	5

3. Does your provider use sensitivity when discussing your weight to make you feel at ease?

Always	Most of the time	About half of the time	Sometimes	Rarely/Never
1	2	3	4	5

4. Does your provider offer useful information to you about healthy eating and weight loss?

Always	Most of the time	About half of the time	Sometimes	Rarely/Never
1	2	3	4	5

Survey Excerpt (Bias Toolkit)

Source: Bias Toolkit, UCONN Rudd Center for Food Policy and Obesity, accessed at: http://biastoolkit.uconnruddcenter.org/toolkit/Module-8/8-05-SurveyWeightSensitive.pdf

Resources

- Toolkit for Healthcare Providers
  - UCONN Rudd Policy Center makes available a comprehensive toolkit for providers that includes:
    - Ways to improve patient-provider interactions
      - Example scripts for discussing weight
    - Recommended changes to office environments
    - Resources for Patients – how to empower
    - Available at: http://biastoolkit.uconnruddcenter.org/

Resources

- Implicit Association Test (IAT):
  - https://implicit.harvard.edu/implicit/education.html
- Harvard Center for Public Health > Webcast: Why We Overeat: The Toxic Food Environment and Obesity
  - https://theforum.sph.harvard.edu/events/why-we-overeat/
- Suggested Readings:
  - Brownell, Kelly D., et al. 2010. "Personal responsibility and obesity: a constructive approach to a controversial issue." *Health Affairs* 29(3): 379-387.
  - Campos et al. 2006. “The epidemiology of overweight and obesity: Public Health Crisis or Moral Panic?” *Int J Epid* 35(1): 55-60.


15 MILLION CHILDREN

Addressing Food Insecurity in Health Care

Health Care Partnerships Program

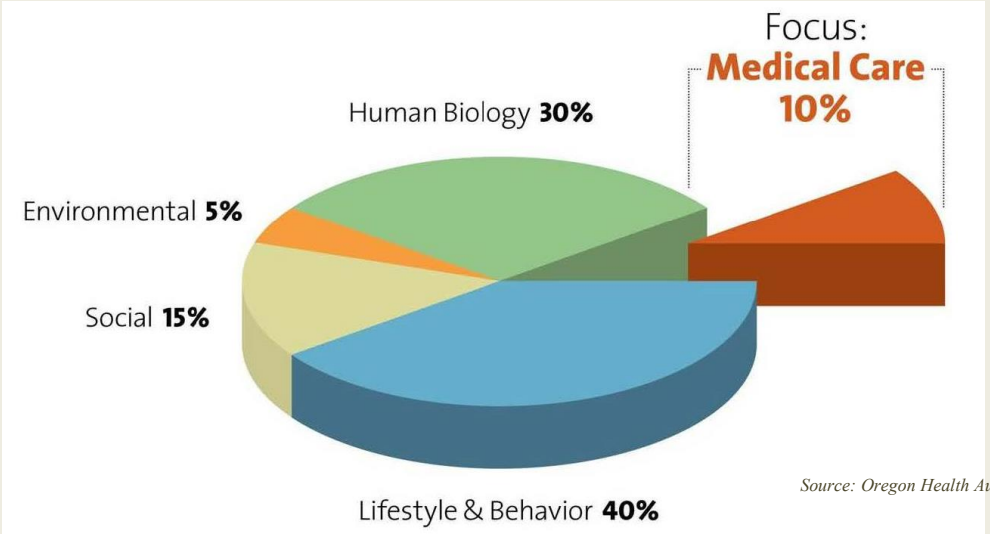
Oregon Food Bank

Summer 2016

OREGON FOOD BANK

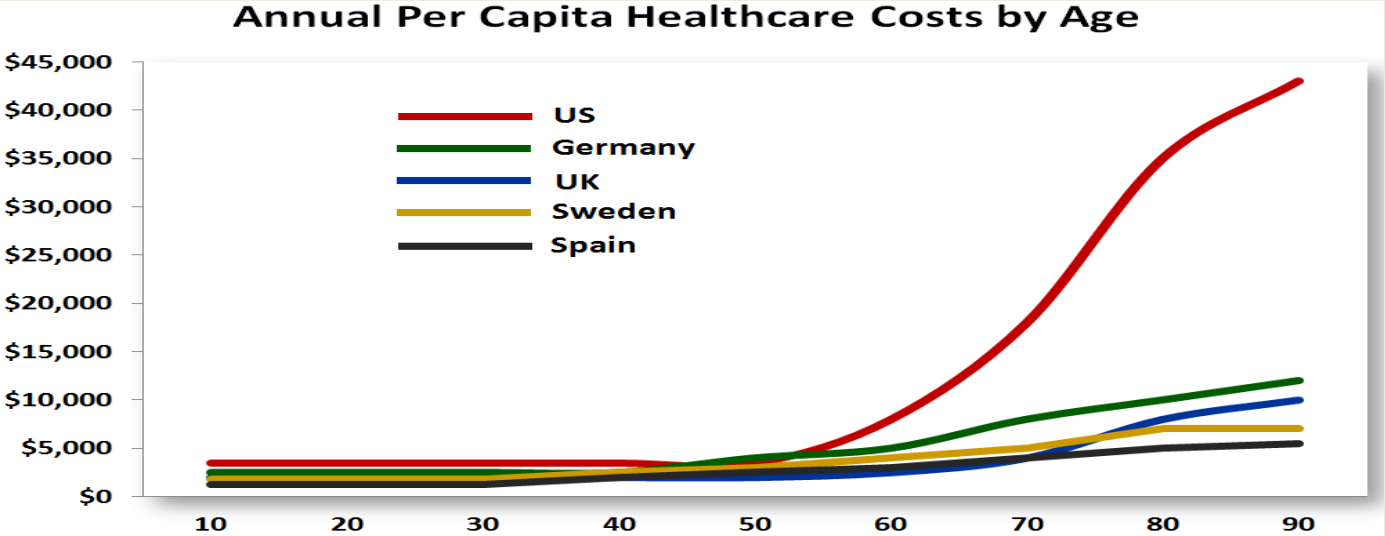
Social Determinants of Health

Narrow Focus = Deficient Results



Source: Oregon Health Authority

Health System Cost Driver: Chronic Disease



- CDC says 86% of Health Care costs due to diet-related chronic disease
- 71% of Medicaid population is food insecure (2014 MBRFS)
- 72% learn about new resource with post screening assistance

(according to preliminary evaluations)

FOOD INSECURITY IN OREGON

- Food insecurity has grown in OR more than all states except Louisiana and Mississippi
- 51 % of kids qualify for free/Reduced lunch
- Oregon has one of the greatest problems of income inequality; between rich and poor and between whites and people of color
- Lower than average wages and higher than average housing costs
- Job growth primarily in low wage jobs
- Un/underemployment still up to 30% for certain for populations of color

Motivated System - Metrics

Try Nutrition First!

High correlation between food insecurity, which = poor diet and:

- Poor child physical & mental development
- Depression & ADHD in all ages
- Cancer, Hypertension, High Blood Pressure, Obesity, and Diabetes
- Poor academic performance & childhood behavior problems
- Problems in pregnancy with smaller, sicker babies
- Seniors who are food insecure have a decreased capacity to maintain independence.

First Thing's First

- Assess your population
- Targeting special assistance and interventions, depending on setting, 30-65% screening positive
- Positives most motivated to act, 78% screened and assisted with resources find something new
- 60% of over 60 not even on SNAP
- Drive people to existing resources before developing new ones, efficient use of limited resources, avoid duplication and learn about gaps and weaknesses in existing resources
- **Clinicians need food insecurity info for accurate diagnosis & treatment**

Simple Screening & Intervention Quickly Spreading in Oregon

TOOLS: 1 page overview, 2 validated questions, 1 page EHR ready local resource handout in many languages, ICD codes, EHR support

MODEL: On-going written screening integrated into clinic flow
Results to clinician for exam
Resource handout in AVS
Immediate review with patient by staff, intern, or volunteer

FOLLOW-UP: phone check-in a week later, provider check-in at next visit, review handout for other possible actions

Screen for Food Insecurity

Screen for Food Insecurity

For each statement, please tell me whether the statement was “often true, sometimes true, or never true” for your household:

(Any patient answering with a 1 or 2 response is considered food insecure)

A. Within the past 12 months we worried whether our food would run out before we got money to buy more. *1. often true* *2. sometimes true* *3. never true* *4. don’t know or refused*

B. Within the past 12 months the food we bought just didn’t last and we didn’t have money to get more. *1. often true* *2. some- times true* *3. never true* *4. don’t know or refused*

NOT ENOUGH FOOD FOR YOUR FAMILY?
NEED HELP COOKING/SHOPPING FOR
HEALTHY FOOD ON A BUDGET?

You might qualify for SNAP (Supplemental nutritional Assistance Program, formerly known as Food Stamps)

- **Go to http://www.oregon.gov/dhs/assistance/pages/foodstamps/foodstamps.aspx or call 211***

If you are pregnant or have children under five, you may qualify for WIC (The ***Special Supplemental Nutrition Program for Women, Infants, and Children)***

- **Go to http://jacksoncountyor.org/hhs/Public-Health/Women-Infants-and-Children**
- **Or call 541-774-8203 and schedule an appointment**

If you are a senior 60+, you may qualify for a senior food program: Call Peggy at 541-774-4309

Most farmer's markets accept SNAP & WIC, several will add to SNAP dollars so you can buy more!

- **http://rvgrowersmarkets.com/** (find market near you that takes SNAP/WIC/Senior Direct

There may be a food pantry in your neighborhood where you can get a box of food for free!

- **Go to http://www.accesshelps.org/Page.asp?NavID=420 or call 541-774-4336**

Summer meals for kids Go to http://www.summerfoodoregon.org/ or call 211*

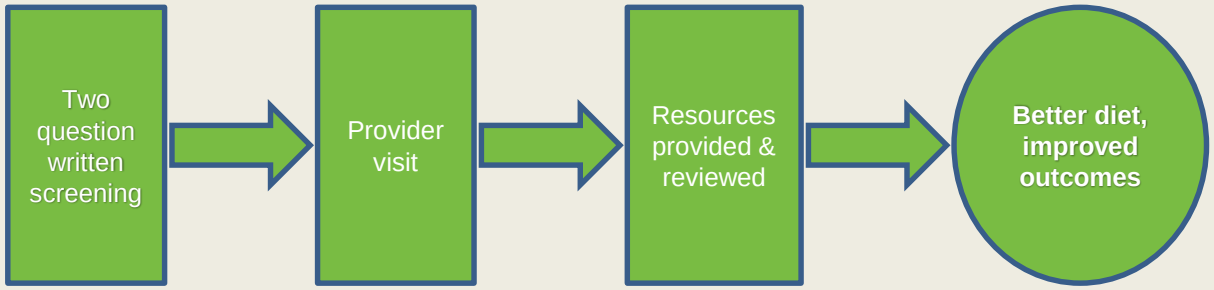
Volunteer, learn how to garden and take some produce home with you!

- **ACCESS Food Share Gardens, 541-779-6691 ext. 309**

Learn to cook healthy food and shop on a budget: Call Robin 541-690-3989 & visit https://www.foodhero.org/

Flexible Implementation

1. Stand Alone: Add questions in writing to check-in process or give to patients in exam room. Then, provide food insecure patients with resource handout and have someone review it with them and connect to new resources.
2. Integrated: Questions added to comprehensive health assessment with resource information & supported follow-up for the food insecure



Current Status

- About 280 clinics & hospitals screening, plus Head Start & WIC
- Urban & Rural Success
- Now an Oregon Performance Improvement Metric,

model screening process developed by CCO TAG

What More Can A Clinic or Hospital Do?

- Cooking & smart shopping classes
- Gardening classes & assistance
- Diabetes clinic/pantry partnerships
- On-site produce distributions
- Veggie Rx programs

- Convening of human services & health care communities to address social determinants of health

Possible New Funders for Food Assistance and Nutrition Education Initiatives

- **Local Hospital Community Benefit Funds**
  - CCO Incentive Fund Grants
  - Grants from Health Insurers, Kaiser, Anthem, Blue, Providence, Pacific Source…
- Medical Equipment Companies
- Electronic Health Record Providers
- Condition specific Medicaid billing (flex funds)

OREGON FOOD BANK

Contact

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Healthy Weight Management in Primary Care: Considering the Whole Person

Helen Bellanca, MD, MPH

October 2016

I have no financial relationships to disclose

Message #1

The idea that overweight and obesity are due to solely to calorie imbalance is a gross oversimplification.

Viruses

Gut microbiome

Resistance to leptin

Artificial sweeteners and food additives

Genetic programming

Chronic stress

WHERE DOES STRESS FACTOR INTO OBESITY?

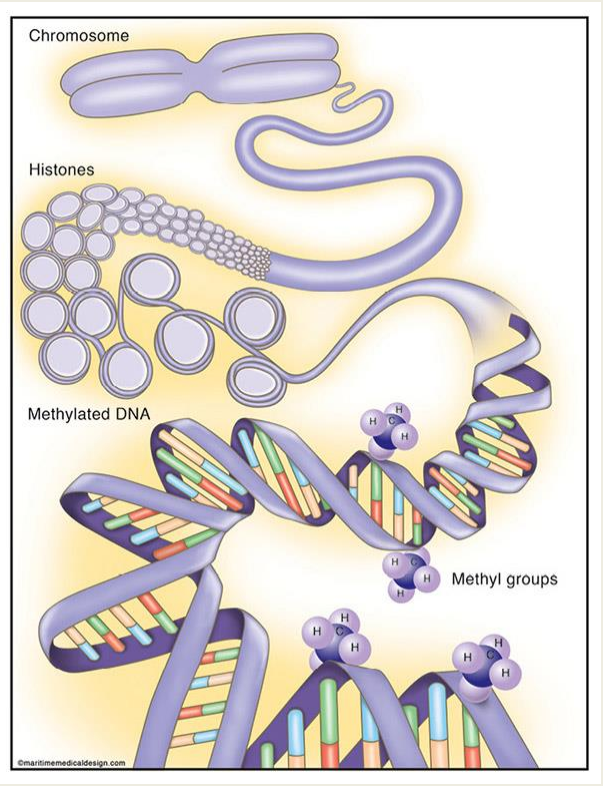
Pregnancy	Early childhood	Adolescence	Adulthood
Epigenetics	Adverse childhood events	Discrimination due to weight, culture of thinness	Poverty, racism, futility of weight loss programs, sleep deprivation

Epigenetics

Epigenetics are heritable changes to gene function.

Severe stress from previous generations affects your risk of obesity.[3]

Some populations (Native Americans, African Americans, refugees, war and famine survivors) have persistent, intractable obesity driven by survival instincts that are embedded in their genes



3. Herrera BM, Keildson S, Lindgren CM. Genetics and epigenetics of obesity Maturitas. 2011 May; 69(1): 41–49

ACEs Study

- 1995-1997 Kaiser/CDC study in California
- 17,000 participants, all HMO members
  - 75% white
  - 66% over age 50
  - 39% college graduates
  - All employed
- Asked about childhood experiences and current health status

https://www.cdc.gov/violenceprevention/acestudy

Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the adverse childhood experiences (ACE) study. *Am J Prev Med.* 1998;14:245–258.

Adverse childhood Experiences (ACEs)

Three categories

Abuse

- physical abuse
- emotional abuse
- sexual abuse

Neglect

- physical neglect
- emotional neglect

Household Dysfunction

- mental illness
- substance use disorder
- incarceration
- domestic violence
- parent abandonment

Adverse childhood Experiences (ACEs)

Three categories

Abuse

physical abuse (28%)

emotional abuse (21%)

sexual abuse (11%)

Neglect

physical neglect (10%)

emotional neglect (15%)

Household Dysfunction

mental illness (19%)

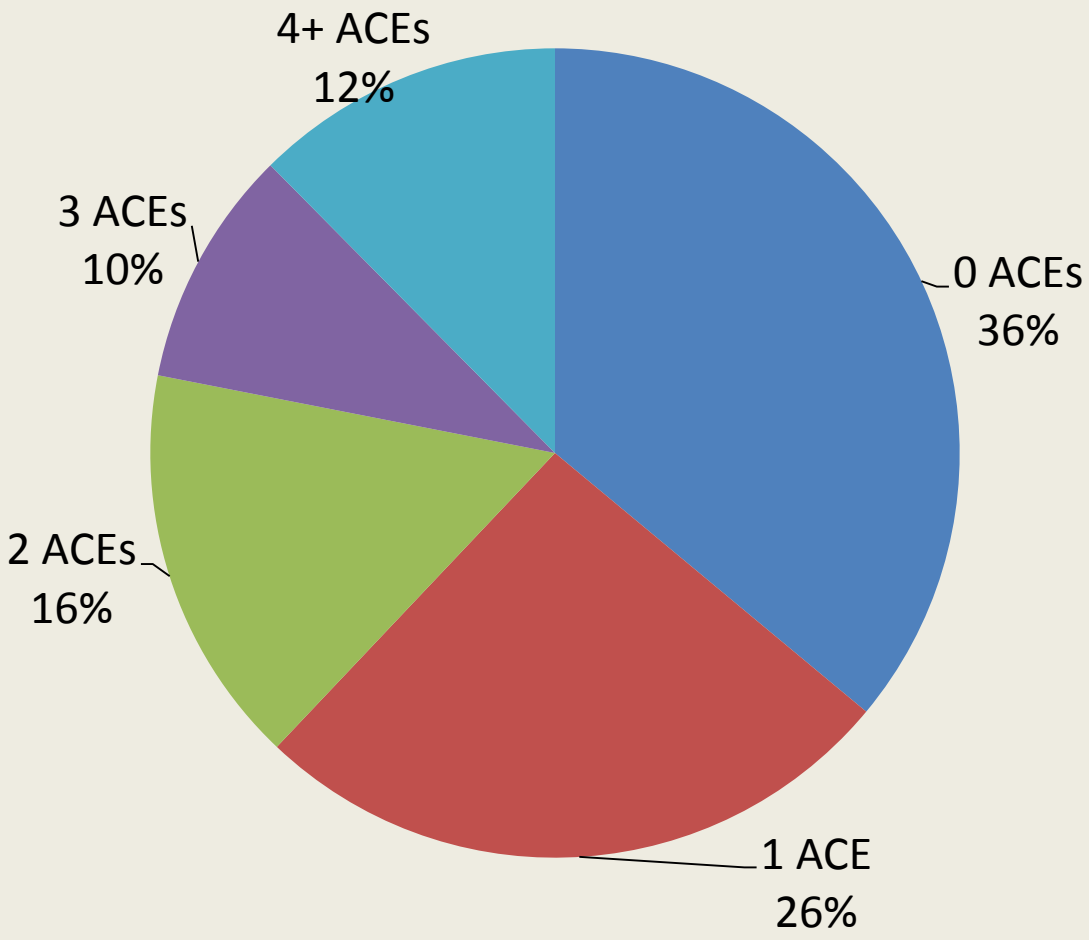
substance use disorder (27%)

incarceration (5%)

domestic violence (13%)

parent abandonment (23%)

Prevalence of ACEs



Anda, ACE interface 2013

Childhood Abuse and obesity

Adults with a history of physical, emotional or sexual abuse were 34% more likely to be obese than adults without that history[1]

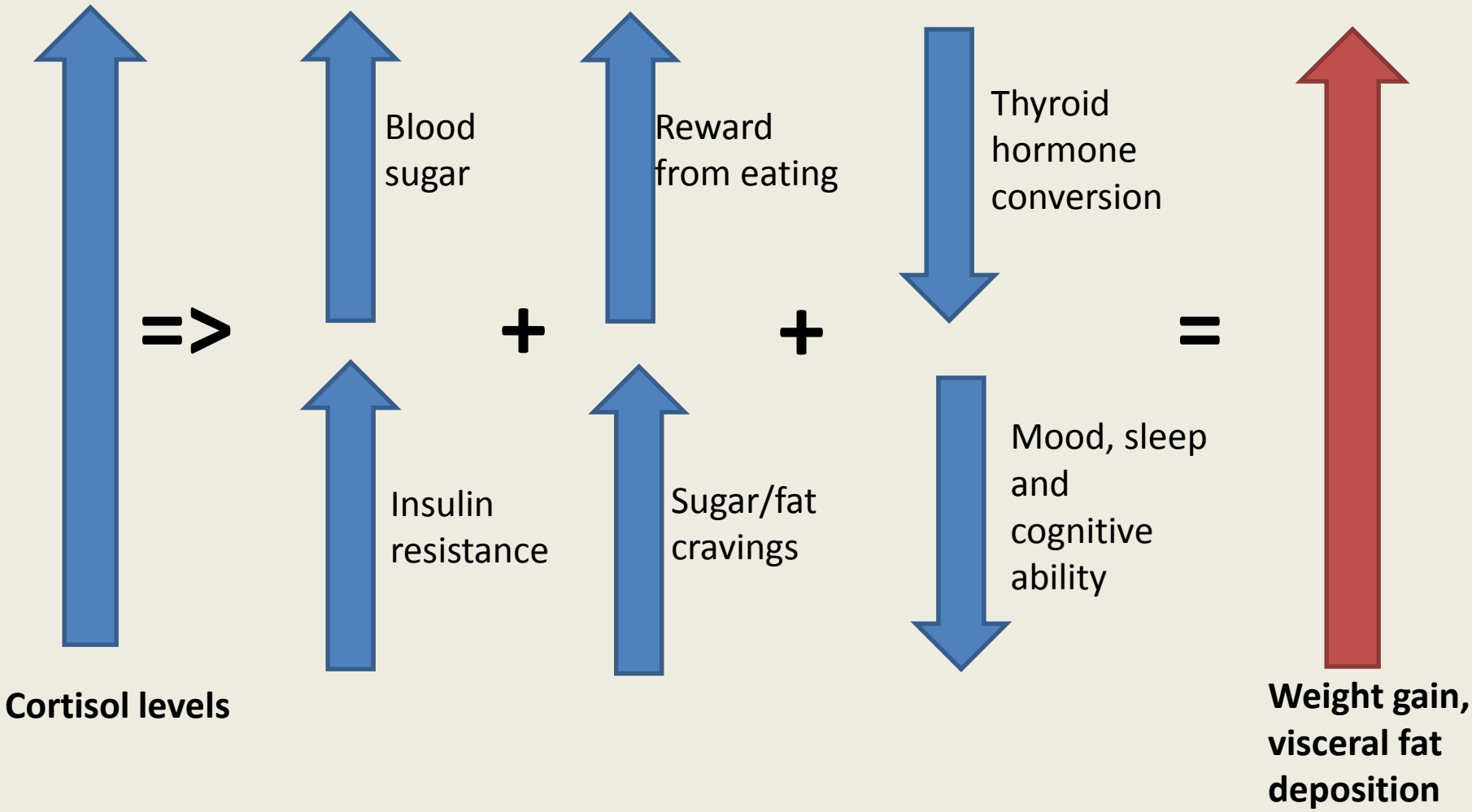
Among adults undergoing gastric bypass surgery, 69% reported childhood abuse[2]

1. Hemmingsson E, et al. Effects of childhood abuse on adult obesity: a systematic review and meta-analysis *Obesity reviews* (2014) 15, 882–893
2. Grilo CM, et al. Childhood maltreatment in extremely obese male and female bariatric surgery candidates. *Obes Res* 2005; 13: 123–130

Additional sources of STRESS

- Poverty
- Racism
- Violence in the community
- Discrimination based on weight
- Futile cycle of weight loss and gain

How does stress cause weight gain?



Why would obesity be a physiological response to severe, persistent stress?

Doesn’t excess weight cause more health problems?

Surprising benefits of overweight and obesity

Disease	Overweight and obese people have:
Coronary heart disease	Lower mortality in hospital and at one year, fewer complications
Diabetes	Lower mortality and lower amputation risk
Stroke	Better survival rates
Peripheral arterial disease	Decreasing mortality with increasing BMI
COPD	Improved prognosis from acute exacerbation
Stroke	Better survival
Non-bariatric general surgery	Lower mortality

Hainer V, Aldhoon-Hainerova I. Obesity Paradox Does Exist. *Diabetes Care* Aug 2013 vol 36 no. suppl 2 S276-S281

Mortality Data

JAMA meta-analysis of all-cause mortality by weight category published 2013

- **Lowest mortality in <u>overweight</u> people (BMI 25-30)**
- **Equal mortality rates for normal weight (18-25) and Grade 1 obesity (30-35)**
- **Mortality only increased for Grade 2 obesity (BMI >35) and higher**

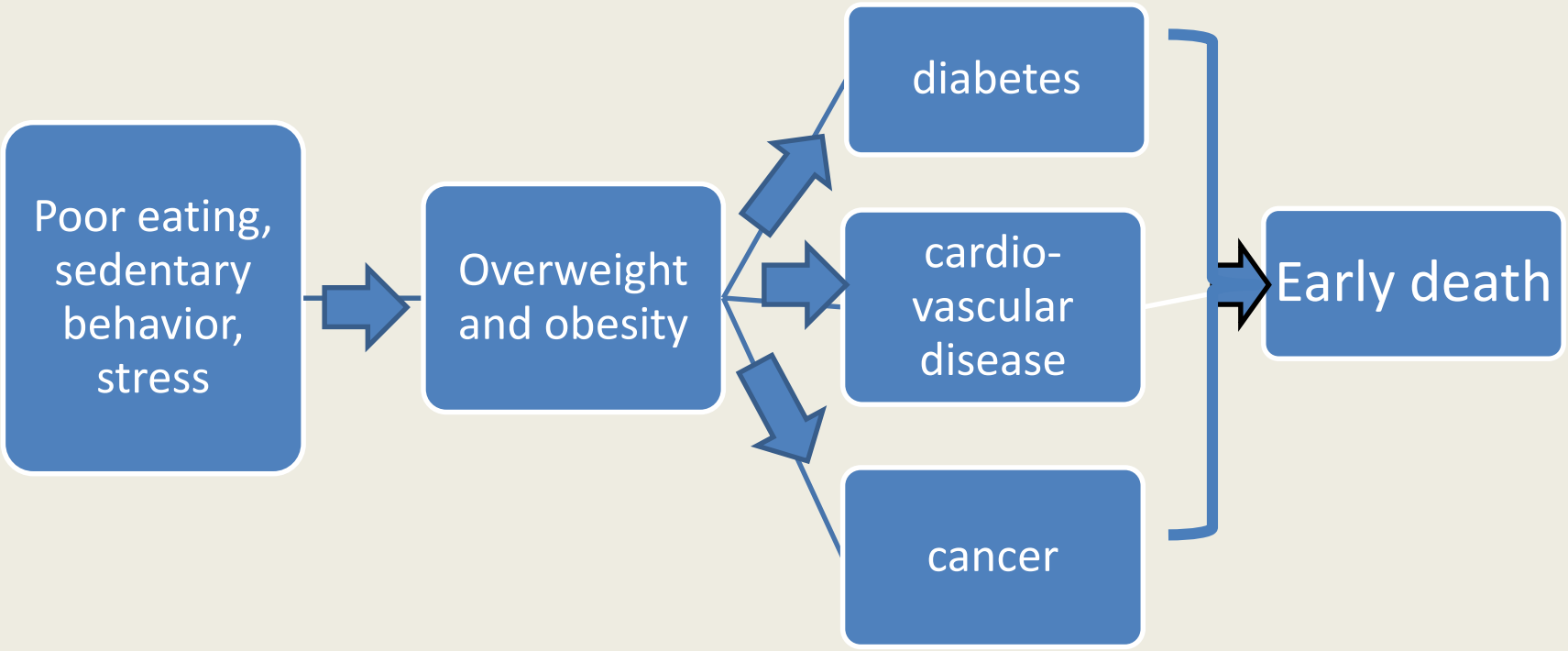
Flegal KM, et al. Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories: A Systematic Review and Meta-analysis *JAMA* 2013;309(1):71-82

Message #2

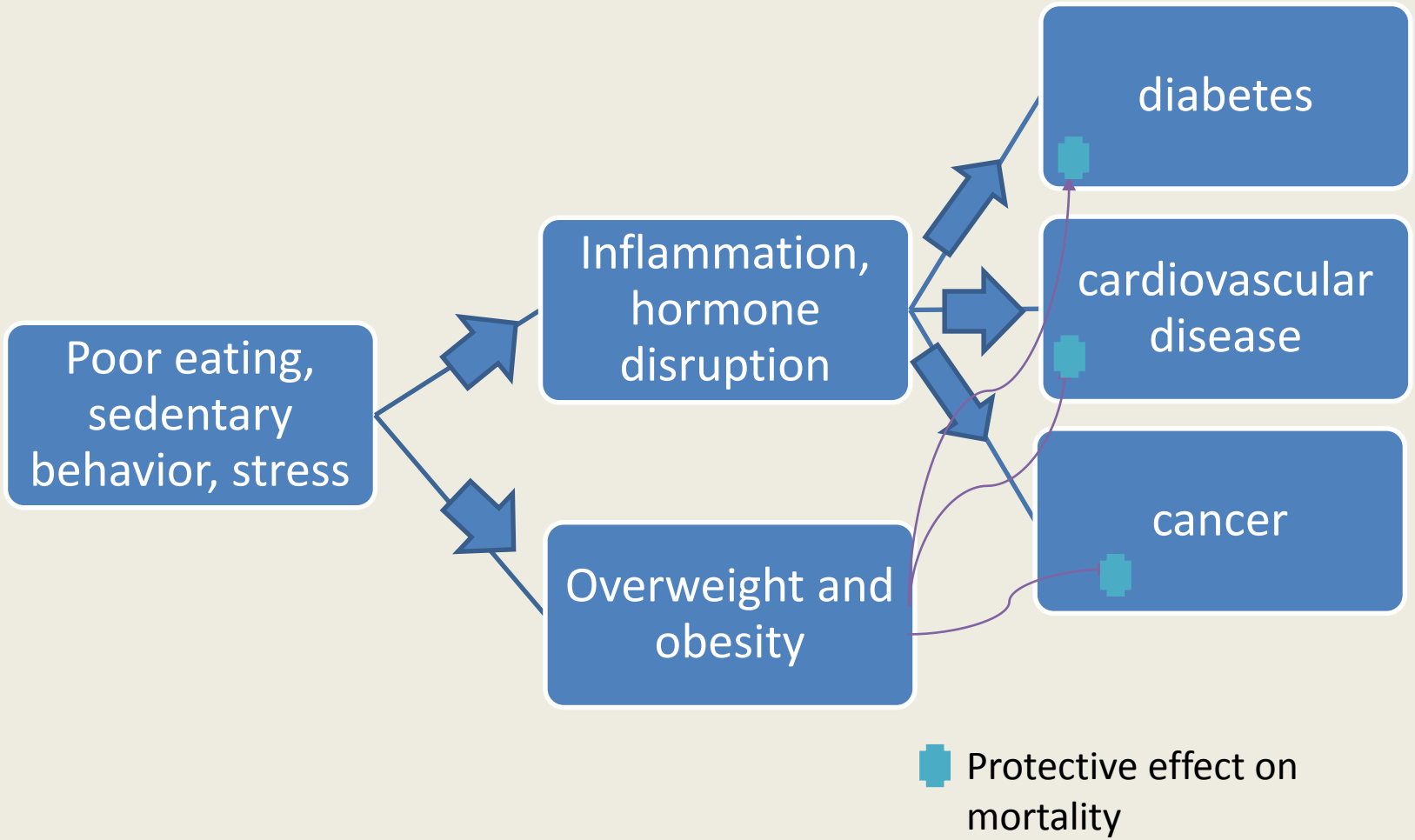
Excess weight is not the problem.

Excess weight is the response to the problem.

Old paradigm: Poor Health Behavior Causes Obesity Which Causes Disease



New paradigm: Poor Health Behavior Causes Disease and Obesity

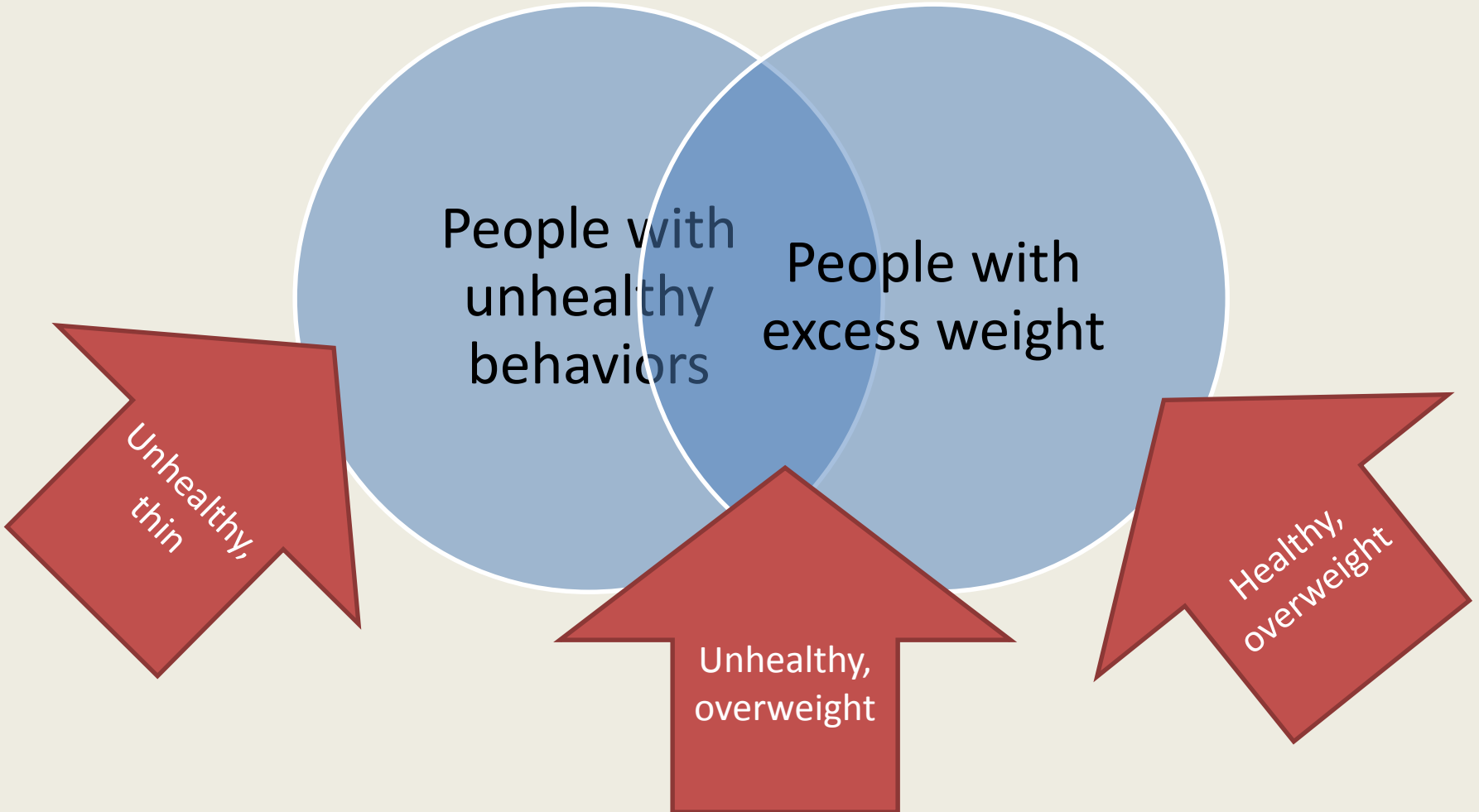


Obesity May Not Be the Problem
It May Be the Solution

- Obesity may be a <u>self protective</u> mechanism to mitigate high-stress environment
  - low quality diet
  - lack of sufficient sleep
  - toxins/viruses in the environment
  - trauma, abuse, violence, oppression, poverty

- **Metabolic disturbances** lead to disease and poor outcomes
- Excess weight is creating resilience

It’s not the weight that is the problem



BIAS

- Our culture has a very strong anti-overweight bias
  - Schools
  - Employment
  - Media
- Health care providers are not immune from this bias, and we can hide behind a health argument

Message #3

Change your practice

- Guard against attribution bias
  - Not all symptoms are related to weight
- Stop weighing people routinely
  - Exceptions: pregnancy, children, preop, medication dosing
  - If you must weigh: Ask permission, weigh at end of visit, keep results private (including from patient)
- Stop counseling people to lose weight
  - Instead, ask everyone about health behaviors, and counsel on improvement of those behaviors. Weight loss may happen incidentally but it is not the goal.

First, do no harm

- The stress of being overweight and attempting to lose weight is worse for one's health than the weight itself
- Health care providers contribute to this discriminatory, shaming culture by weighing people routinely and endorsing a narrative that blames the patient for their weight and attributes all problems to excess weight
- People routinely avoid needed health care because they do not want to be weighed
- We should stop focusing on the weight and instead focus on promoting healthy behaviors with EVERYONE

WEIGHT STIGMA in Health Care

False assumptions

- Obese individuals are entirely responsible for their weight
- All overweight individuals eat unhealthy food and eat too much
- All overweight individuals are lazy and sedentary
- Stigmatizing overweight patients may help because it will motivate them to make necessary behavior changes
- Diet and exercise can result in permanent weight loss if you stick with it

Behavior Change recommendations For Every Patient

- Ask everyone about behaviors (don't assume)

- Counsel to modify behaviors that are unhealthy
  - Insufficient sleep (need 7-9 hours a night)
  - Excessive stress, poor coping (exercise, mindfulness)
  - Insufficient activity (30-60 minutes of moderate activity every day)
  - Poor nutrition (watch beverages, increase fiber, vegetables, legumes, whole grains, limit meat, dairy, and processed foods)
- Measure behavior changes instead of weight to track progress

Health At Any Size

Regardless of weight or BMI, you can mitigate metabolic disturbances that lead to disease through exercise, sleep, stress reduction, and healthy eating.

Healthy Weight Management

Weight loss

- Short-term
- Focused on getting to a certain number
- Success defined by pounds lost
- The more pounds you lose, the better
- Aim to get to a “normal” weight
- Weight-specific reward and punishment
- **People who are overweight work to lose weight**

Healthy Weight Management

- Lifelong
- Focused on health
- Success defined by reaching behavior goals
- Halting weight gain is a successful outcome
- Fit and healthy at any size
- Weight-neutral self-care
- **Everyone works to adopt healthy habits**

Thank you!

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Developing Culturally Competent Health Communication Strategies

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Associate Professor of Clinical Psychology, Pacific University
October 21, 2016


One Size
Does Not Fit All

The importance of culturally competent communication: Three reasons

- Keep in mind that conservative estimates are that 50% of medical advice goes unheeded
- The majority (60 to 80 percent) of medical diagnoses and treatment decisions are made from the medical consultation processes
- Discrepancy in views of communication

What is cultural competence in healthcare?

- The goal of culturally competent health care services is to provide the highest quality of care to every patient, regardless of race, ethnicity, cultural background, English proficiency or literacy.
- The ability of providers and organizations to understand and integrate these factors into the delivery and structure of the health care system.

The ADRESSING model

Age

Disability

Religion

Ethnicity

Social & Economical Class

Sexual Orientation

Indigenous Background

National Origin

Gender

Culturally Competent Communication in the Delivery of Healthcare Services

- "…does **not** imply knowing everything about all cultures we are engaged with…it does, however, require **demonstration** of **respect** for differences, eagerness to learn about other cultures, acceptance of different epistemologies, and a **flexibility** and willingness to **adjust**, change and reorient where required" (Le Roux, 2002)

Cultural Competence & Communication: What we bring to the table

- Communication strategies that we employ that focus only on facts are limited
- Basic attitudes that have the potential to help the clinical relationship: Curiosity, empathy, respect, and humility
- An approach that focuses on inquiry, reflection, and analysis throughout the care process is most useful for acknowledging that culture is just one of many factors that influence an individual's health beliefs and

Cultural Competence & Communication: What we bring to the table

- Awareness of the influences of sociocultural factors
- Acceptance of the physician's responsibility to understand the cultural aspects of health and illness
- Recognition of personal biases
- Respect and tolerance for cultural differences
- Acceptance of the responsibility to combat racism, classism, ageism, sexism, homophobia, and other kinds of biases and discrimination that occur in health care settings

Strategies for culturally competent communication

- Provide interpreter services
- Recruit and retain minority staff
- Provide training to increase cultural awareness, knowledge, and skills
- Coordinate with traditional healers
- Use community health workers

Strategies for culturally competent communication

- Incorporate culture-specific attitudes and values into health promotion tools
- Include family and community members in health care decision making
- Expand hours of operation
- Provide linguistic competency that extends beyond the clinical encounter to the appointment desk, advice lines, medical billing, and other written materials

The Process ASK Questions…

- **Awareness:** Am I aware of my biases and prejudices towards other cultural groups, as well as racism and other "isms" in healthcare?
- **Skill:** Do I have the skill of conducting a cultural assessment in a sensitive manner?
- **Knowledge:** Am I knowledgeable about the worldviews of different cultural and ethnic groups?
- **Encounters:** Do I seek out face-to-face and other types of interactions with individuals who are different from myself?
- **Desire:** Do I really "want to" become culturally competent?

Cultural Competence & Communication: Key Points to Take Home

- There is a growing movement to make health services more culturally competent and to assure that global health work is culturally informed.
- Cultural competency has been defined in many different ways, and it has provoked considerable controversy over its assumptions, effects, and necessity.
- Cultural competency models have varied considerably, ranging simply awareness to more dynamic ways of interacting with patients.
- More than knowing exactly how to perform, it is more important to ask the right questions.