



# The Battle of the Bulge: Overweight, Obesity and Adiposopathy

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# Disclosure of Multiplicity of Interests (2 years)

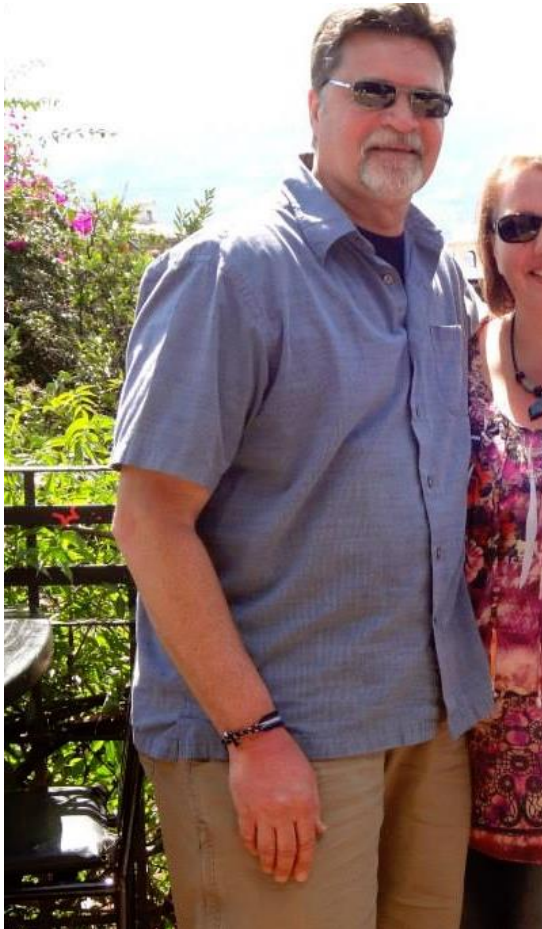


 None



# CASE

## 55 year old man



“My wife is successfully losing weight, and I want to do the same”

- ❄️ Fatigue
- ❄️ Snoring
- ❄️ Low back pain
- ❄️ Libido loss



# CASE

## 55 year old man



BMI =  $31.3 \text{ kg/m}^2$


Is he obese?

No, he is not!

Rather, he is a person who has obesity.



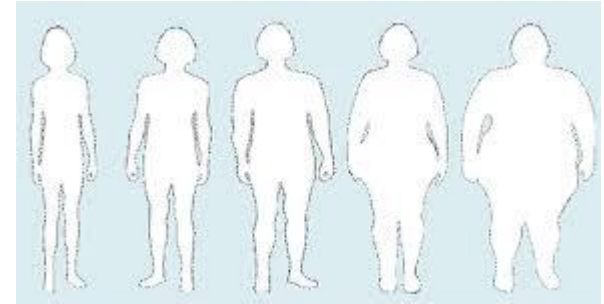
# Principles of Bariatric Endocrinology (1)

 Overweight and obesity are a continuum, and together represent a chronic, biological, preventable and treatable disease.

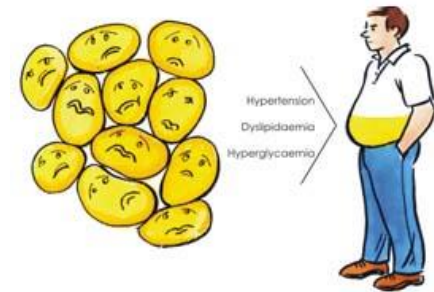


# Why is Obesity a disease?

- Physical changes (adiposity)



- Metabolic changes (adiposopathy)



- Psychological changes



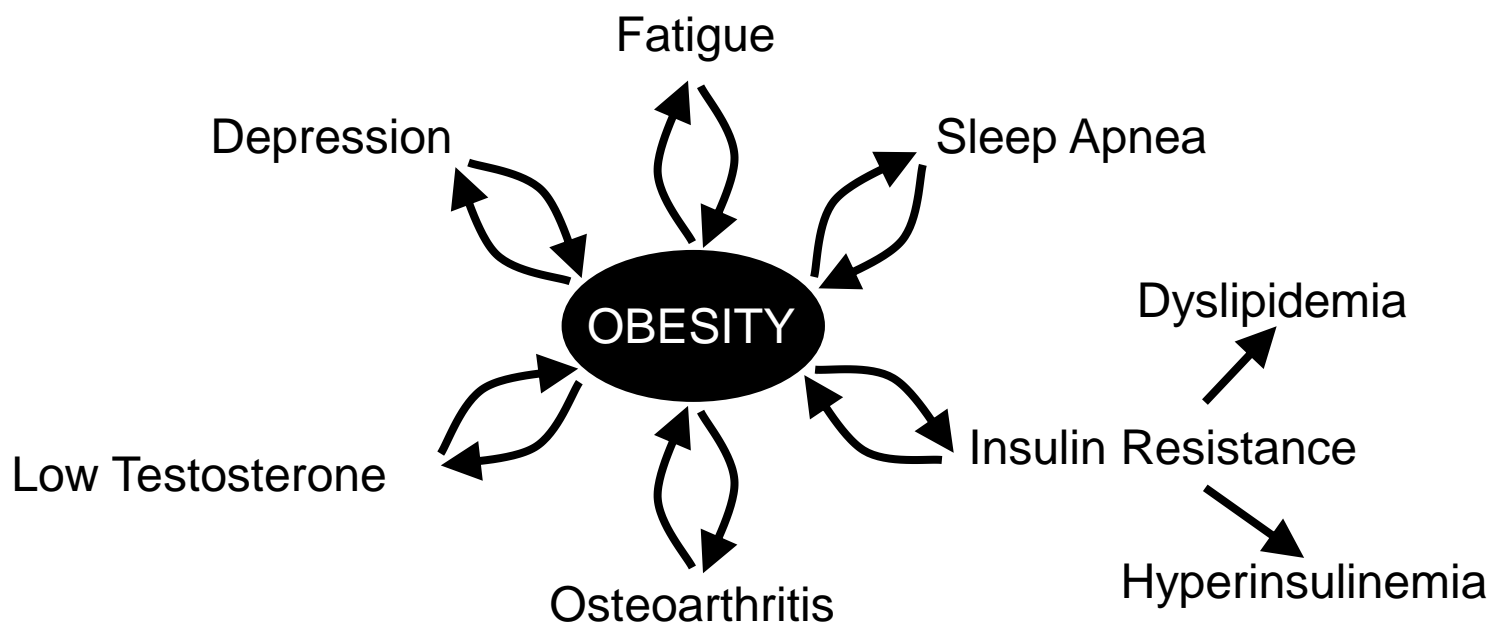


# Principles of Bariatric Endocrinology (2)

❄️ Every patient who has overweight or obesity should be thoroughly evaluated for causes and complications of weight gain, including adipose tissue dysfunction (adiposopathy)



# Obesity Vicious Cycles





# MEDS



## Promote Weight Gain

- ❄️ **Psychiatric/Neuro**
  - Antipsychotics
  - Antidepressants
  - Lithium
  - Antiepileptics
- ❄️ **Steroid hormones**
  - Prednisone
  - Estrogens, progestins
- ❄️ **Diabetic agents**
  - Sulfonylureas,
  - Thiazolidinediones,
  - Insulin
- ❄️ **Beta-adrenergic blockers**
- ❄️ **Antihistamines**

## Help Maintain or lose Weight

- ❄️ **Psychiatric/Neuro**
  - Ziprasodone
  - Celexa
  - Bupropion
  - Topiramate
- ❄️ **Steroid hormones**
  - NSAID's
  - Barrier method
- ❄️ **Diabetic agents**
  - Metformin, GLP-1 agonists,
  - Pramlintide,  $\alpha$ -glucosidase inhibitors, SGLT-2 blockers
- ❄️ **ACE Inhibitors / ARBs**
- ❄️ **Inhalers**



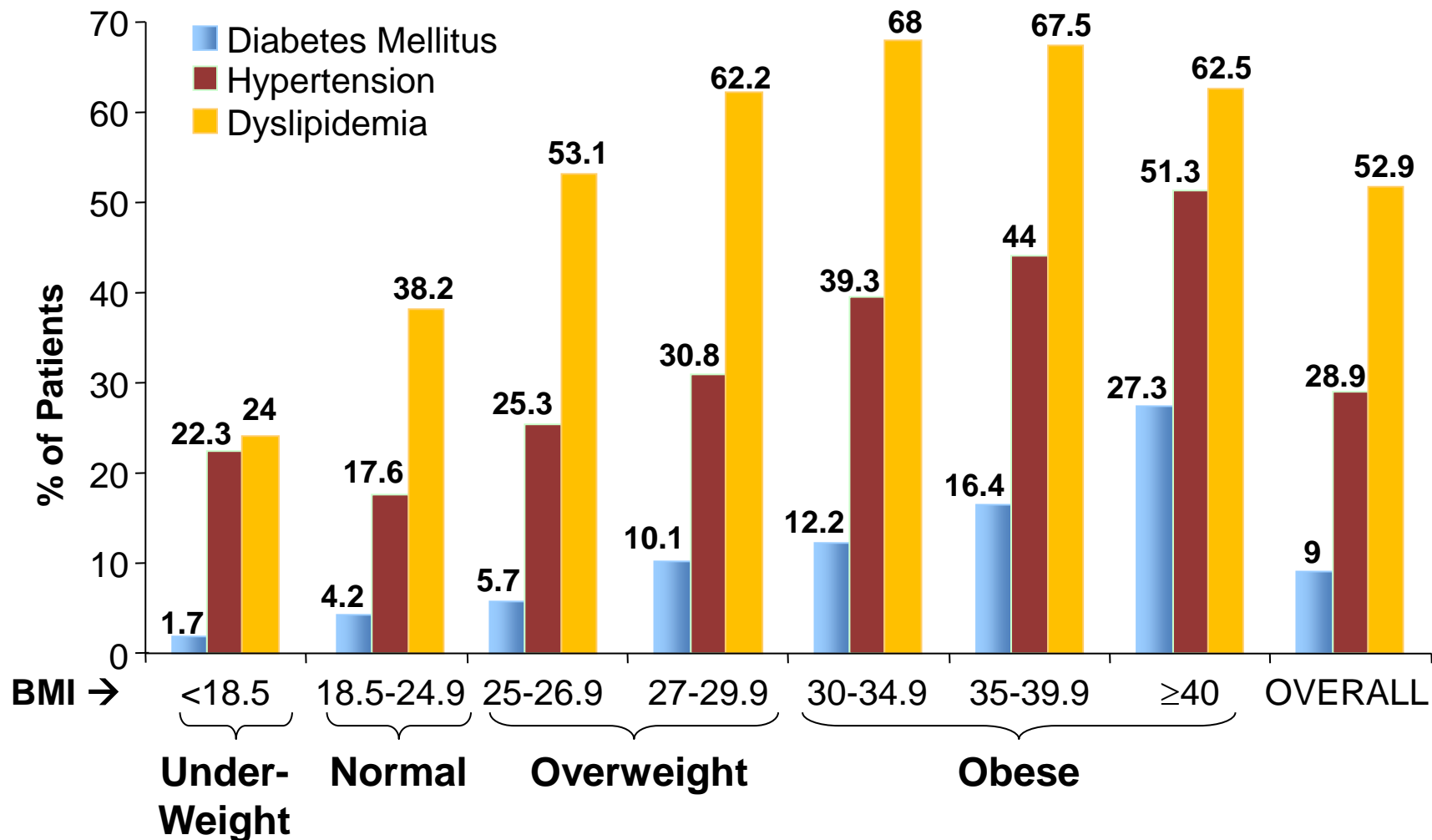
Is the classification of overweight and obesity based on BMI the best predictor of health risk?

# BMI does not always reflect adiposity



- ❄️ Muscularity
- ❄️ Edema states
  - ❄️ CHF
  - ❄️ Nephrotic Syndrome
  - ❄️ Cirrhosis
  - ❄️ Lymphedema
- ❄️ Dehydration
- ❄️ Sarcopenia (especially the elderly)
- ❄️ Pregnancy

# BMI and Prevalence of Metabolic Disease by BMI -- NHANES 1999-2002



*Int J Clin Pract.* 2007;61:737-747.

*Am J Med.* 2009;122:S26-37.



Not all patients who have  
overweight or obesity by BMI  
criteria have adiposopathy  
(sick fat) with metabolic  
derangements

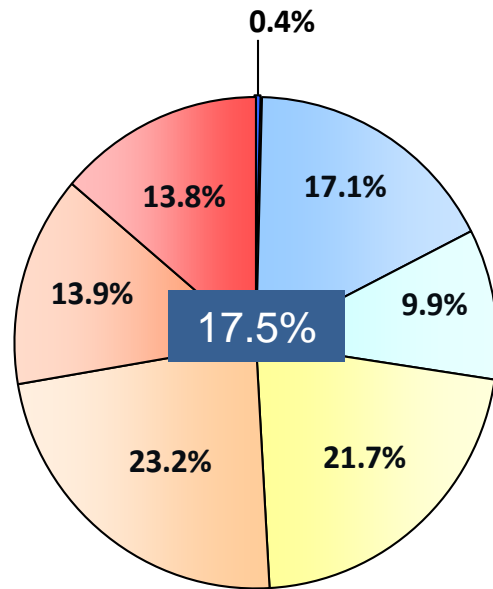


Not all patients with metabolic disease have overweight or obesity by BMI criteria

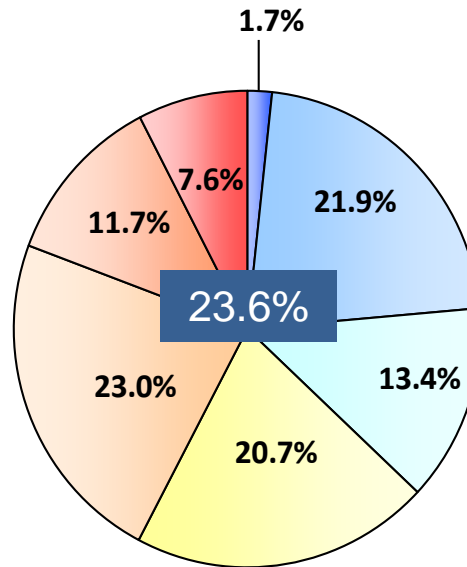
# BMI Among Patients With Metabolic Disease NHANES 1999-2002



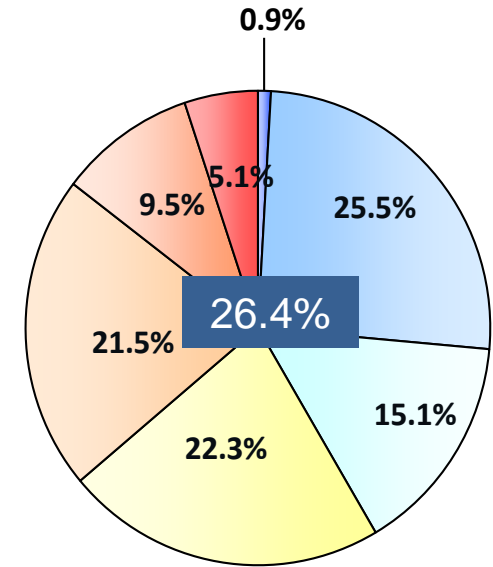
Diabetes Mellitus



Hypertension  
Percent with BMI under 25



Dyslipidemia



## Body Mass Index (BMI)

■ <18.5

■ 18.5-24.9

■ 25-26.9

■ 27-29.9

■ 30-34.9

■ 35-39.9

■ ≥40

**Under-weight**

**Normal**

**Overweight**

**Obesity**

*Int J Clin Pract.* 2007;61:737-747.

*Am J Med.* 2009;122:S26-37.



Why, for patients with a BMI under  $25 \text{ kg/m}^2$ , do so many have metabolic disorders?





# Adiposopathy



Harold Bays, MD



# Adiposopathy is functionally manifested by:

- ❄️ Impaired adipogenesis and adipocyte hypertrophy
- ❄️ Heterogeneous distribution -- visceral adiposity
- ❄️ Adipocyte lipolysis in excess of lipogenesis
  - ❄️ Increased free fatty acids
- ❄️ Pathogenic adipose tissue endocrine responses
  - ❄️ i.e. Hypoadiponectinemia // Hyperleptinemia
- ❄️ Pathogenic adipose tissue immune responses
- ❄️ Pathogenic crosstalk between fat and other organs



# Adiposopathy is anatomically manifested by:

- ❄️ Adipocyte hypertrophy
- ❄️ Visceral adiposity
- ❄️ Growth of adipose tissue beyond its vascular supply
- ❄️ Increased number of adipose tissue immune cells
- ❄️ Ectopic fat deposition (in other body tissues)

Bays HE et al. *Future Cardiology*. 2005;1(1):39-59

Bays HE. *Expert Rev Cardiovas Ther*. 2005;3(3):395-404

Bays HE, et. al. *Expert Rev Cardiovas Ther* 2008;6:343-68



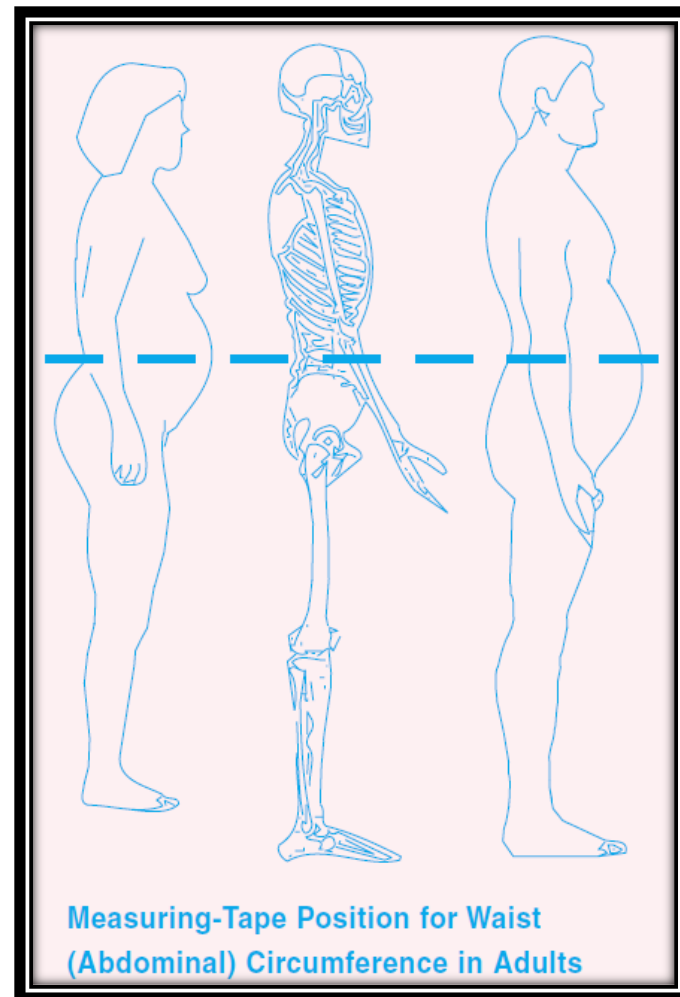
Are there alternative ways to stratify health risk for patients who have overweight or obesity by BMI criteria?



# Clinical Tools:

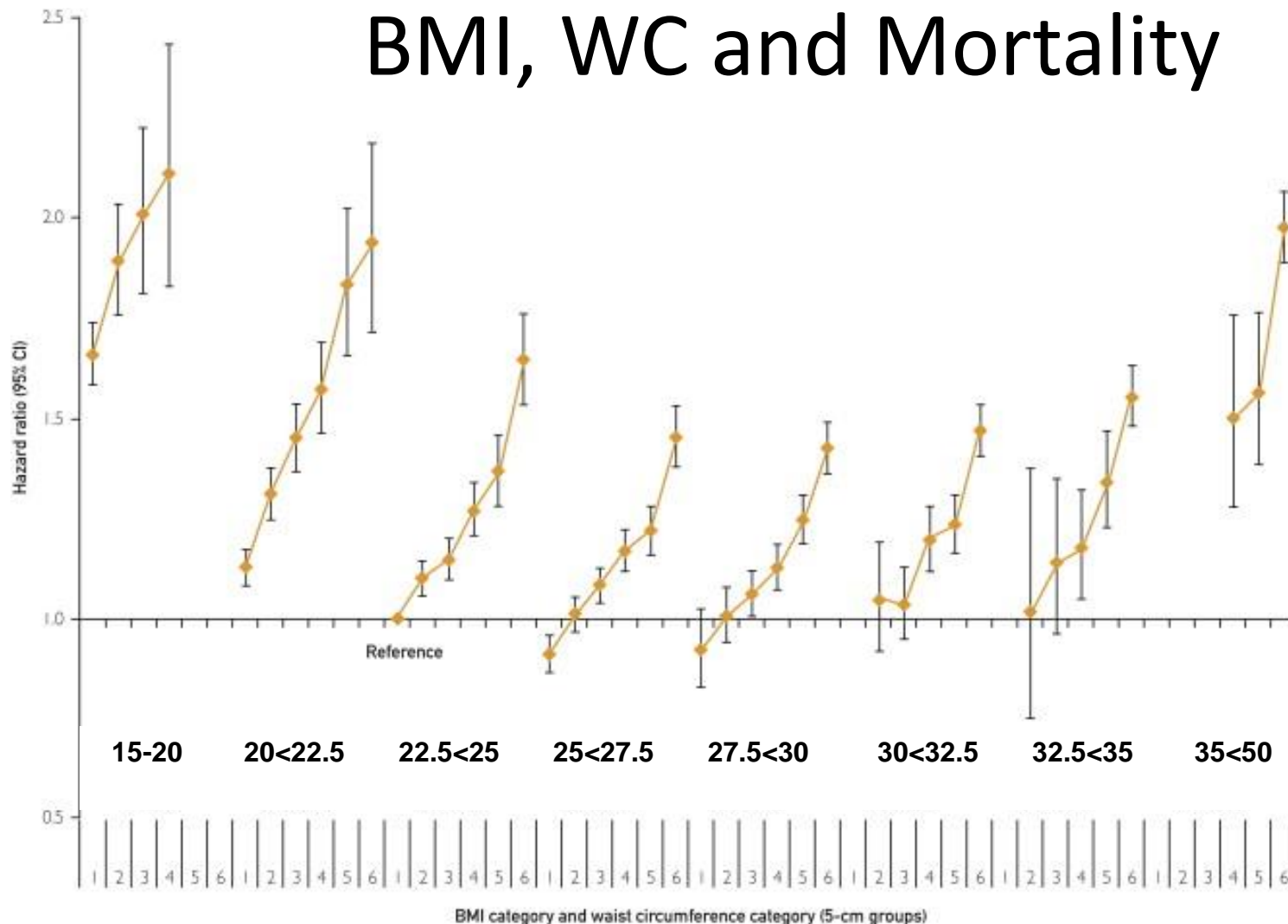
## Measuring Waist Circumference

- ❄️ Locate the superior iliac crests and the lower rib margins
- ❄️ Place measuring tape around abdomen above iliac crests, keeping it parallel to the floor
- ❄️ Ensure tape is snug but not compressing the skin





# BMI, WC and Mortality



**HR and 95% CIs for WC (5-cm increments) and all-cause mortality by BMI category** (men and women). Adjusted for educational level, marital status, smoking, alcohol, physical activity, and BMI. WC cut points were <90.0, 90.0 to 94.9, 95.0 to 99.9, 100.0 to 104.9, 105.0 to 109.9, and  $\geq 110.0$  cm for men and <70.0, 70.0 to 74.9, 75.0 to 79.9, 80.0 to 84.9, 85.0 to 89.9, and  $\geq 90.0$  cm for women.



# Ethnic Variations in Waist Circumference Risk Thresholds

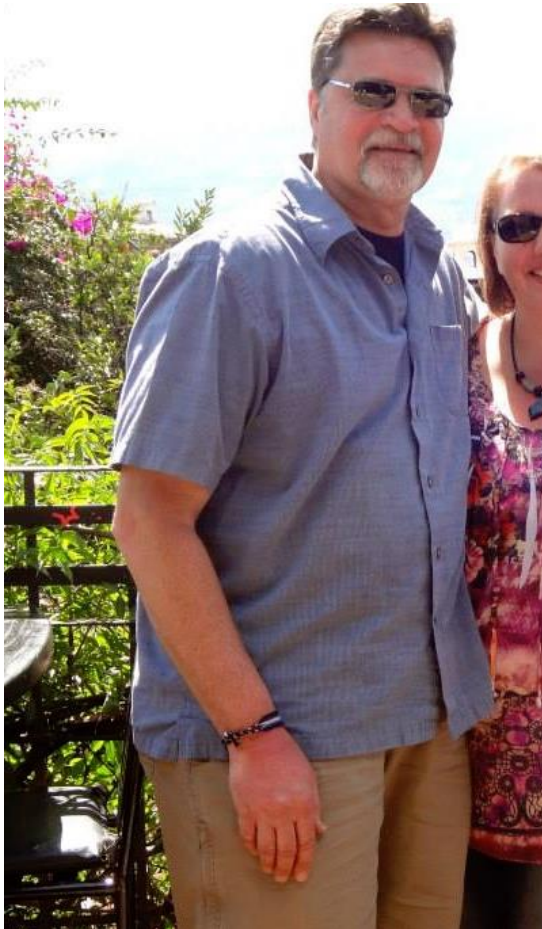
**Joint Recommendations of the  
IDF, NHLBI, AHA, WHF, IAS, and IASO**

<b>Ethnic/Regional Origin</b>	<b>Men, in (cm)</b>	<b>Women, in (cm)</b>
Europid	≥37 (94)	≥31 (80)
Caucasian	≥37 (94)	≥31 (80)
North American, European	≥40 (102)	≥35 (88)
Asian	≥35 (90)	≥31 (80)
Middle Eastern, Mediterranean	≥37 (94)	≥31 (80)
Sub-Saharan African	≥37 (94)	≥31 (80)
Central and South American	≥37 (94)	≥31 (80)



# CASE

## 55 year old man



BMI = 31.3 kg/m<sup>2</sup>

WC = 44 inches





# Physical Examination

## The Patient with Obesity

### **Examination for complications of obesity**

- Height, weight, and BMI
- Distribution of adiposity – neck, WC, WHR
- Abdomen – liver
- Cardiovascular – SBP/DBP, heart, vessels, dyspnea
- Muscular-skeletal – joints and gait
- Extremities – edema, lymphedema, venous stasis
- Skin – acanthosis nigricans, hirsutism, skin tags

### **Endocrine exam for causes of obesity**

- Insulin resistance, thyroid, Cushing's syndrome

# Physical Examination

## Acanthosis and skin tags



# Physical Examination

## Acanthosis and skin tags

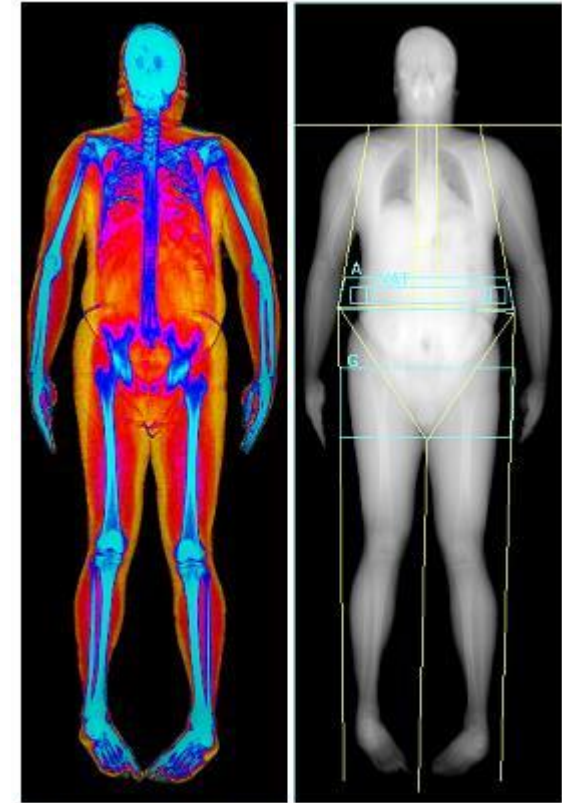




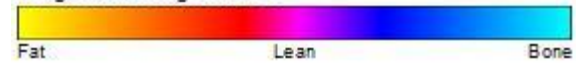
# Assessment of Body Composition

Method	Feature measured	Advantages	Limitations
Bioelectrical impedance analysis (BIA)	Total body water Extracellular and intracellular fluid spaces	Ease of use Low cost Speed (fast)	Population specific, poor accuracy in individuals
Dual-energy X-ray absorptiometry (DXA)	Total and regional body fat Total and regional lean mass	Ease of use Low radiation exposure Accurate	Biased for body size, sex, fatness High equipment cost Specially trained personnel
Dilution techniques	Total body water Extracellular fluid	Ease of use OK for all ages	Inaccurate in disease High equipment cost Labor-intensive analysis
Air displacement plethysmography	Total body volume Total body fat	Relatively good accuracy Speed (fast)	Less accurate in disease High equipment cost
3D photonic scanning	Total and regional body volume	OK for very obese Ease of use	Limited availability
Quantitative magnetic resonance	Total body water Total body fat	Ease of use Safety Speed (fast)	High equipment cost Limited availability
Magnetic resonance imaging (MRI)	Total and regional adipose tissue Skeletal muscle	Highly accurate and reproducible	Costly

# DXA - BCA



Images not for diagnostic use





# Fat Mass Index

Minnesota Center for Obesity, Metabolism & Endocrinology, PA

1185 Town Centre Drive  
Eagan, MN 55123

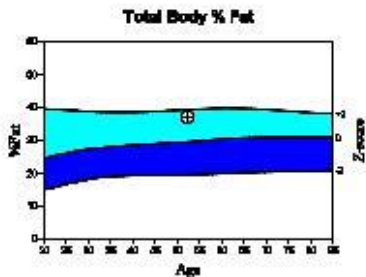
Telephone: 651 379 1600

Fax: 651 379 1650

Name: Gonzalez-Campoy, Michael      Sex: Male      Height: 68.7 in  
Patient ID:      Ethnicity: Hispanic      Weight: 217.6 lb  
DOB: October 20, 1960      Age: 52



Images not for diagnostic use  
Fat      Lean      Bone



Source: 2008 NHANES Hispanic Male

World Health Organization Body Mass Index Classification  
BMI = 32.4 WHO Classification Obesity I

Underweight    Normal    Overweight    Obese I    Obese II    Obese III



## Body Composition Results

Region	Fat Mass (g)	Lean + BMC (g)	Total Mass (g)	% Fat	% Fat	% Fat Percentile
					YN	AM
L. Arm	22.95	27.49	50.44	29.0	98	99
R. Arm	20.22	24.81	45.03	26.9	97	97
Trunk	190.27	284.11	474.38	40.1	97	92
L. Leg	52.27	96.28	148.55	35.2	91	92
R. Leg	56.62	102.82	159.45	35.5	91	92
Subtotal	242.64	355.62	598.26	38.2	96	95
Head	14.95	45.69	60.64	24.5		
Total	558.59	894.21	1452.80	37.2	96	94
Android (A)	24.62	42.28	66.90	36.8		
Gynoid (G)	55.28	79.89	135.17	40.9		

Scan Date: January 28, 2012 ID: A01281309  
Scan Type: 1 Whole Body  
Analysis: January 28, 2012 16:25 Version 12.4  
Auto Whole Body  
Operator: RM  
Modet: Discovery 70 (SN 12045)  
Comments:

## Adipose Indices

Measure	Result	YN	Percentile	AM
Total Body % Fat	37.2	96	94	
Fat Mass/Height <sup>2</sup> (kg/m <sup>2</sup> )	11.8	93	87	
Android/Gynoid Ratio	1.10			
% Fat Trunk/% Fat Legs	1.13			
Trunk/Limb Fat Mass Ratio	1.24			
Est. VAT Mass (g)	1095			
Est. VAT Volume (cm <sup>3</sup> )	1184			
Est. VAT Area (cm <sup>2</sup> )	227			

## Lean Indices

Measure	Result	YN	Percentile	AM
Lean Weight (kg/m <sup>2</sup> )	17.1	55	19	
Approx. Lean Weight (kg/m <sup>2</sup> )	8.26	53	45	

Est. VAT = Estimated Visceral Adipose Tissue  
YN = Young Normal  
AM = Age Matched

## Adipose Indices

Measure	Result	Percentile	
		YN	AM
Total Body % Fat	37.2	96	94
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Android/Gynoid Ratio	1.10		
% Fat Trunk/% Fat Legs	1.13	85	40
Trunk/Limb Fat Mass Ratio	1.24	78	23
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Fat weight (in kilograms), divided by the height (in meters squared).



# Fat Mass Index Classification

Fat Mass Index (FMI) Class	Male	Female
Severe fat deficit	<2	<3.5
Moderate fat deficit	2 to <2.3	3.5-<4
Mild fat deficit	2.3 to <3	4 to < 5
Normal	3 to 6	5 to 9
Excess fat	>6 to 9	>9-13
Obese class I	> 9 to 12	>13 to 17
Obese class II	> 12 to 15	>17 to 21
Obese class III	> 15	>21

# Visceral Adipose Tissue (VAT)



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1185 Town Centre Drive  
Eagan, MN 55123

Telephone: 651 379 1600

Fax: 651 379 1650

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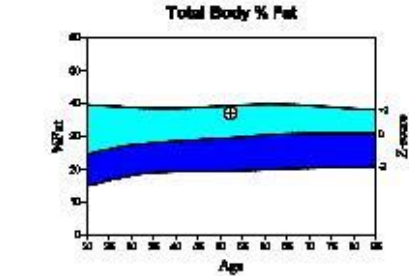


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U.S. Adult      H.      Overweight I      Overweight II      Obese I      Obese II      Obese III



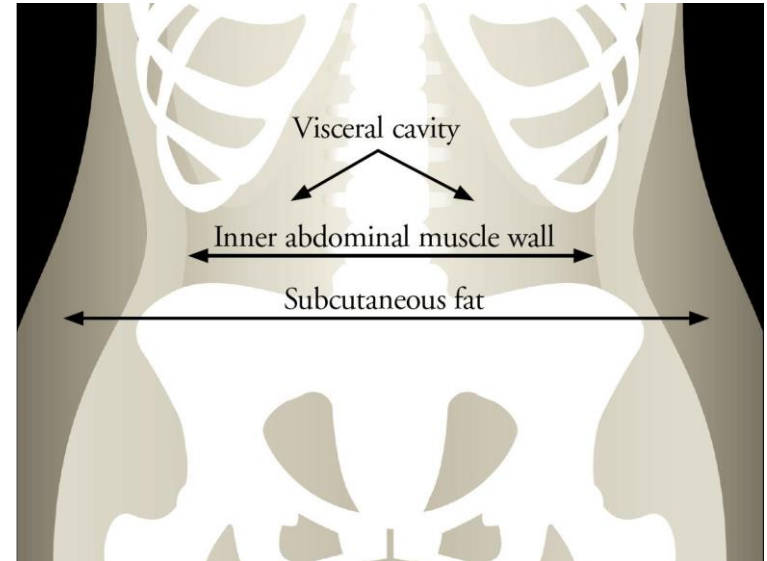
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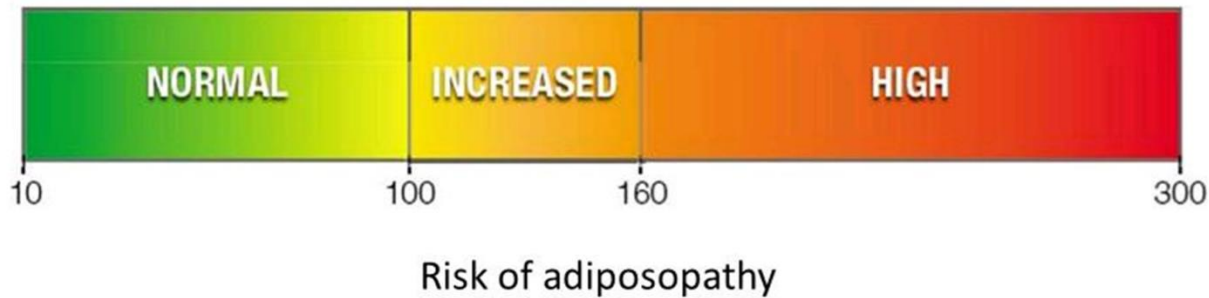
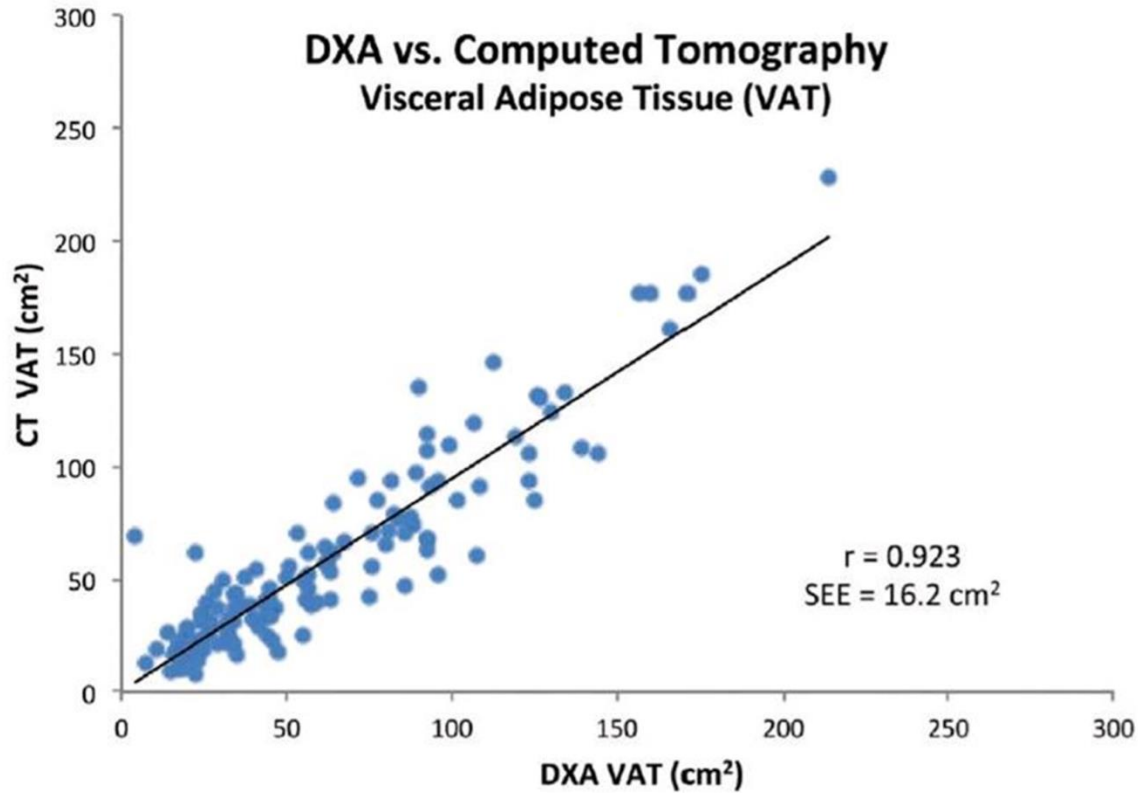


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# Visceral Tissue Area





What laboratory tests are appropriate to evaluate patients with overweight and obesity?



# Laboratory Testing

## **Primary screening tests**

- CBC
- A1c
- Complete metabolic panel
- Lipids

## **Secondary tests based on History and Exam**

- Overnight oximetry
- TSH
- Testosterone
- 25-hydroxyvitamin D
- Indirect calorimetry



# Evaluation of Patients with Overweight or Obesity: Staging

Diagnosis	Anthropometric Component: BMI kg/m <sup>2</sup>	Clinical Component	Prevention and/or Treatment
Normal	< 25		Primary
Overweight	25 -29.9 (≥ 23 some ethnicities)	No obesity-related complications	Secondary
Obesity Stage 0	≥ 30	No obesity-related complications	Secondary
Obesity Stage 1	≥ 25	Presence of one or more mild to moderate obesity-related complications	Tertiary
Obesity Stage 2	≥ 25	Presence of one or more severe obesity-related complications	Tertiary



# Laboratory Testing in bariatric endocrinology

- ❄️ C-reactive protein
- ❄️ 11 pm salivary cortisol
- ❄️ Gonadal axis evaluation
- ❄️ Fasting insulin or c-peptide
- ❄️ Leptin to adiponectin ratio



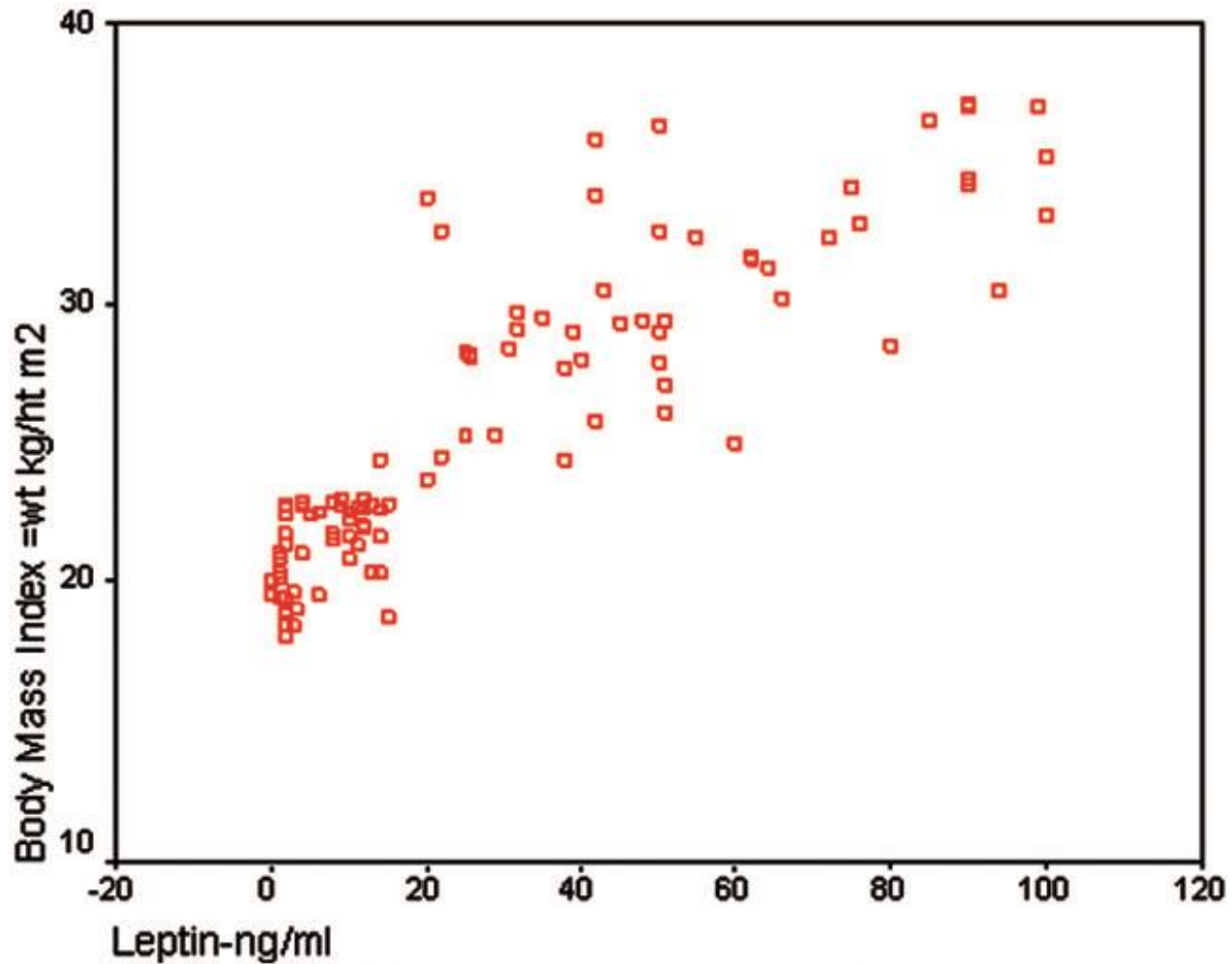
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## 55 year old man

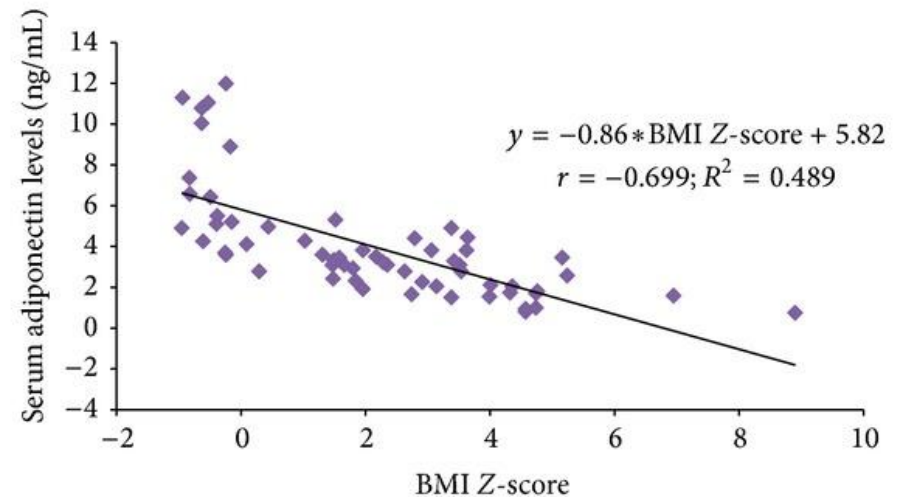
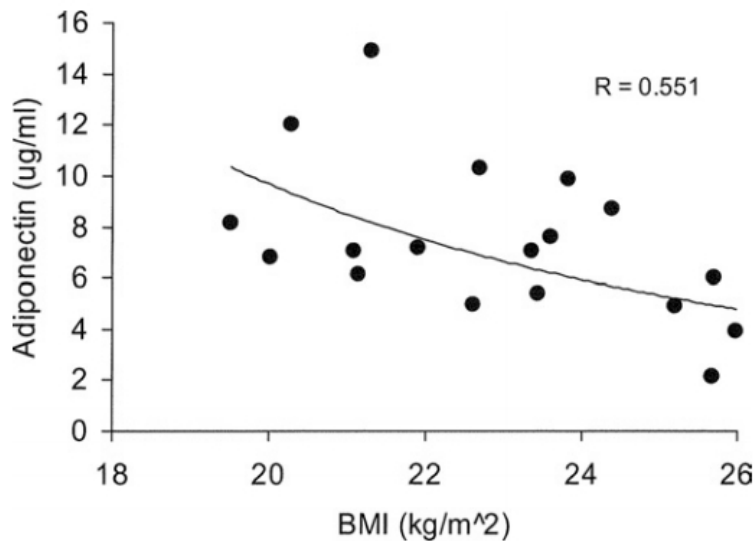


- ❄️ Adiponectin =  $3.6 \mu\text{g/mL}$   
( $2.2 - 19.9$ )
- ❄️ Leptin =  $10.6 \text{ ng/mL}$
- ❄️ Leptin to adiponectin  
ratio =  $2.9$

# Leptin levels rise with increasing BMI



# Adiponectin levels fall with increasing BMI





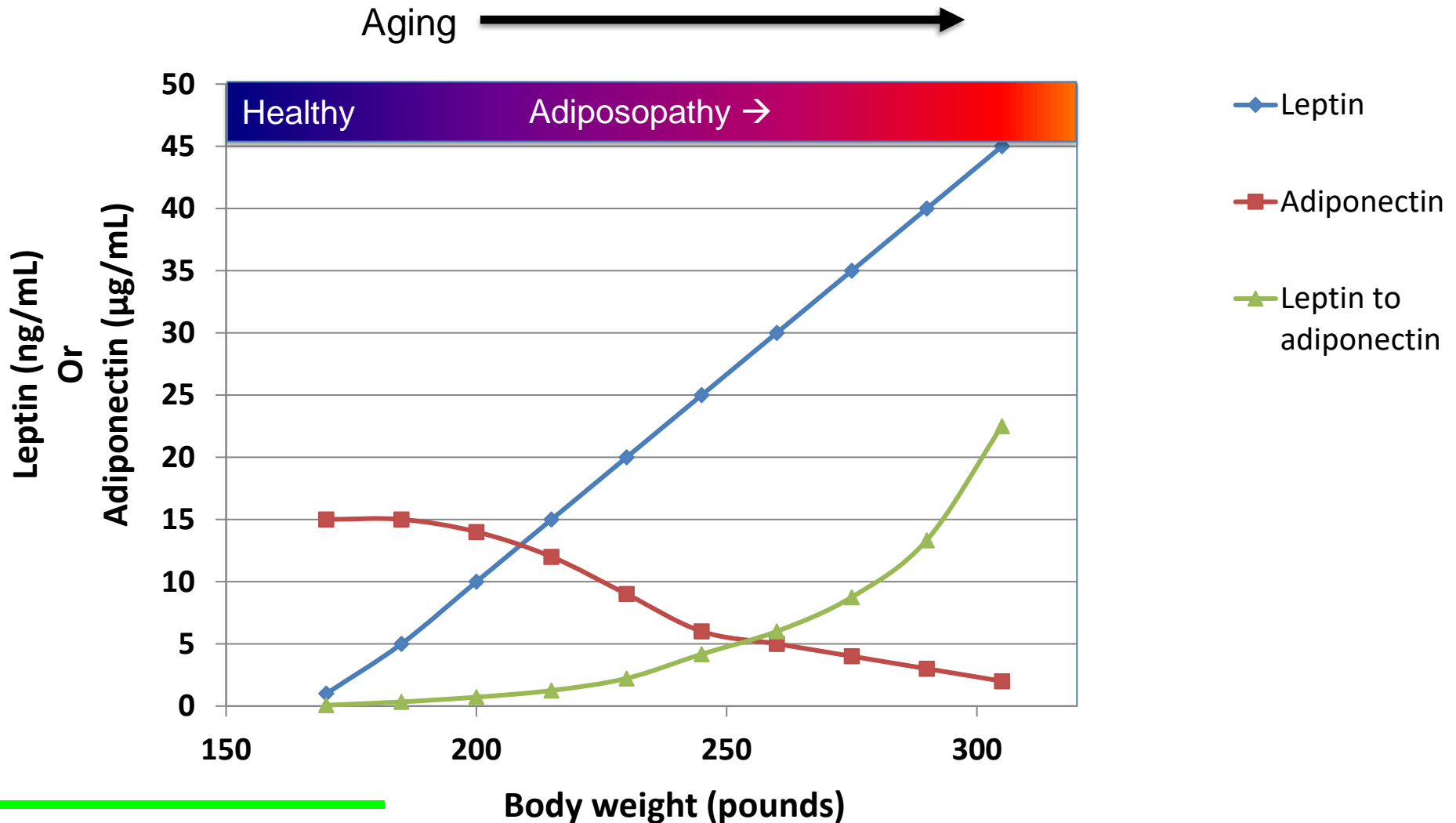


# Principles of Bariatric Endocrinology (3)

- ❄️ Every patient who has overweight or obesity should have a thorough risk re-stratification on a periodic basis

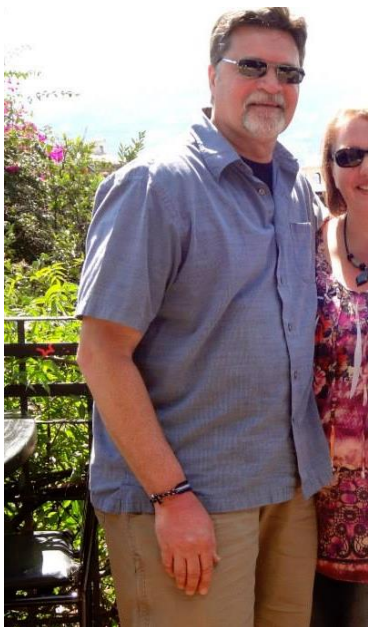


# Leptin to Adiponectin Ratio

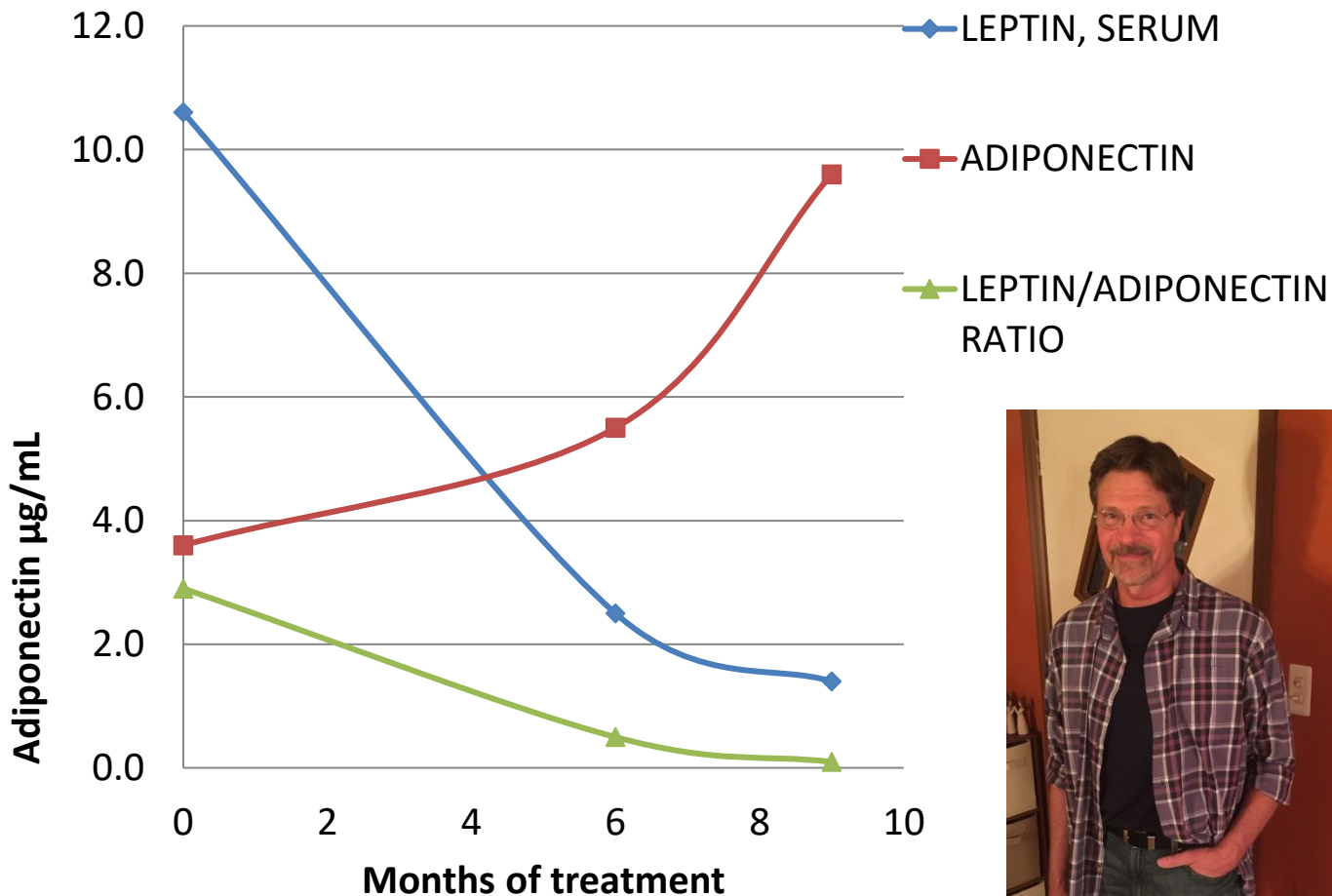




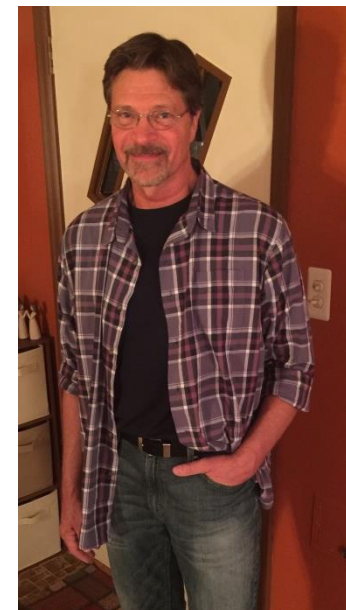
# Leptin to Adiponectin Ratio Trending



Leptin ng/mL  
Or  
Adiponectin µg/mL



CRP mg/L	7.48 (Abn)	6.40 (Abn)	4.10
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# Principles of Bariatric Endocrinology (4)

- ❄️ Overweight and obesity should be treated with the same model of chronic disease management that we use for other chronic diseases

# A Successful Model of Care



<b>Diabetes Mellitus</b>	<b>Overweight and Obesity</b>
<b>Initial Workup/Risk Assessment</b>	<b>Initial Workup/Risk Assessment</b>
<b>Institute Treatment</b>	<b>Institute Treatment</b>
<b>Patient &amp; Family Education</b>	<b>Patient &amp; Family Education</b>
<b>Glucose Self-Monitoring</b>	<b>Step Count &amp; Weekly Weight</b>
<b>Quarterly Office Assessments Follow A1c, BMI, BP</b>	<b>Quarterly Office Assessments Follow BMI, BP, WC</b>
<b>Periodic Screening for complications and risk re-stratification</b>	<b>Periodic Screening for complications and risk re-stratification</b>



# Principles of Bariatric Endocrinology (5)

- ❄ Effective behavior modification to achieve a negative energy balance is the primary long-term goal of the medical treatment of overweight and obesity



# Conditions for success

- ❄️ Engagement with the health team
- ❄️ Support at home (and at work)
- ❄️ Patience
- ❄️ Persistence
- ❄️ Realism – set goals



- Beginning today, the weight treatment goal is to lose 5 to 10% of current body weight over the next 6 to 12 months.
- Perpetual goal until BMI is 18.5 to 24.9



# Principles of Bariatric Endocrinology (6)

- ❄️ The team approach to overweight and obesity should be offered to all patients to provide nutrition education and physical activity coaching







# Healthy Eating

**CLINICAL PRACTICE GUIDELINES FOR HEALTHY EATING FOR  
THE PREVENTION AND TREATMENT OF METABOLIC  
AND ENDOCRINE DISEASES IN ADULTS:  
COSPONSORED BY  
THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/  
THE AMERICAN COLLEGE OF ENDOCRINOLOGY  
AND THE OBESITY SOCIETY**

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Karmella T. Thomas, RD<sup>17</sup>*



# Healthy Eating

- ❄️ 🌱 Portion Control
- ❄️ 🌱 Freshness
- ❄️ 🌱 Plant-based meals
- ❄️ 🌱 Limit of animal fats
- ❄️ 🌱 Water to drink



# Physical Activity

- ❄️ Not “exercise”
- ❄️ Start with limited amount, repeatedly during the day
- ❄️ Realistic, achievable, sustainable and incremental

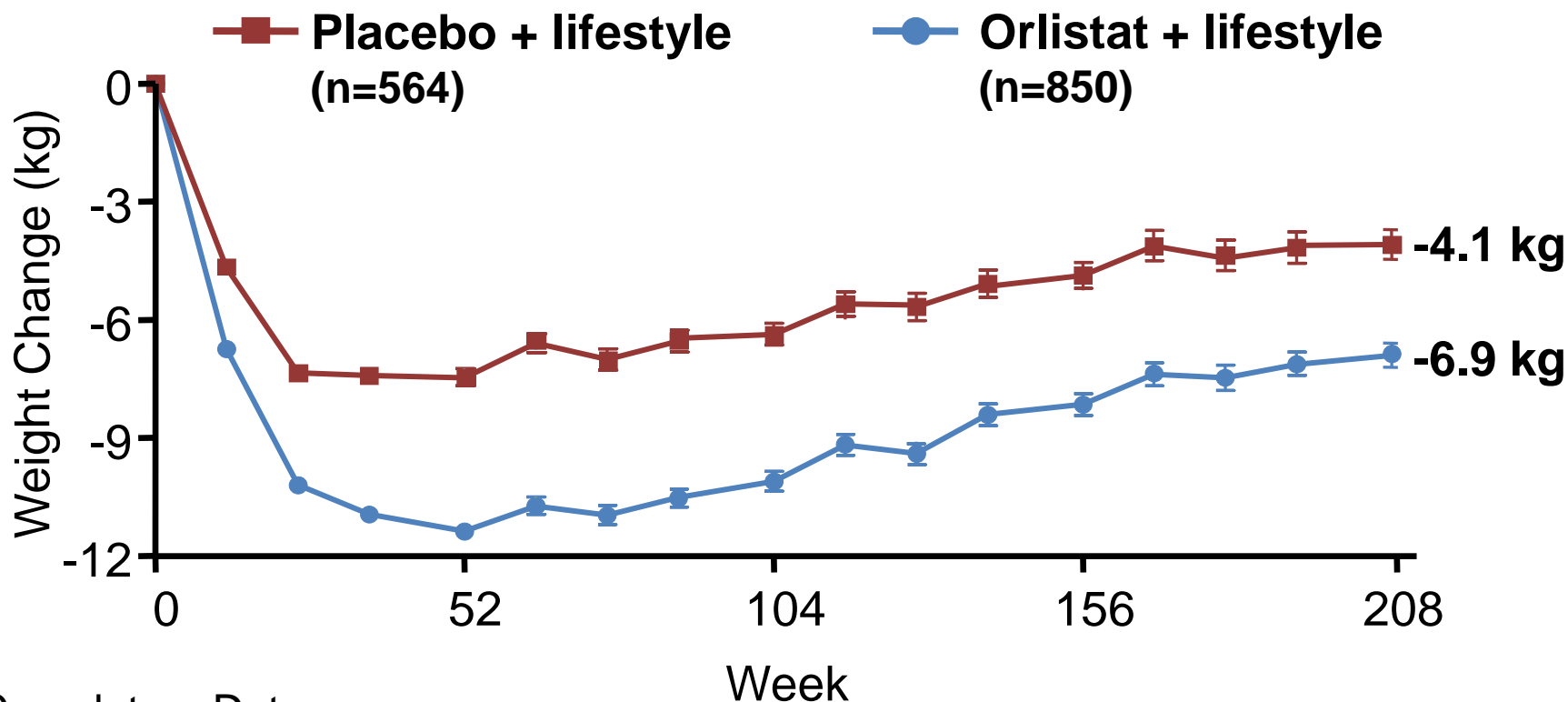


# Principles of Bariatric Endocrinology (7)

- ❄️ Pharmacotherapy to optimize metabolism and to reset the hypothalamic and CNS controls over energy balance and energy stores should be used indefinitely in the management of overweight and obesity (i.e. achieving a treatment goal is not a reason to stop treatment)



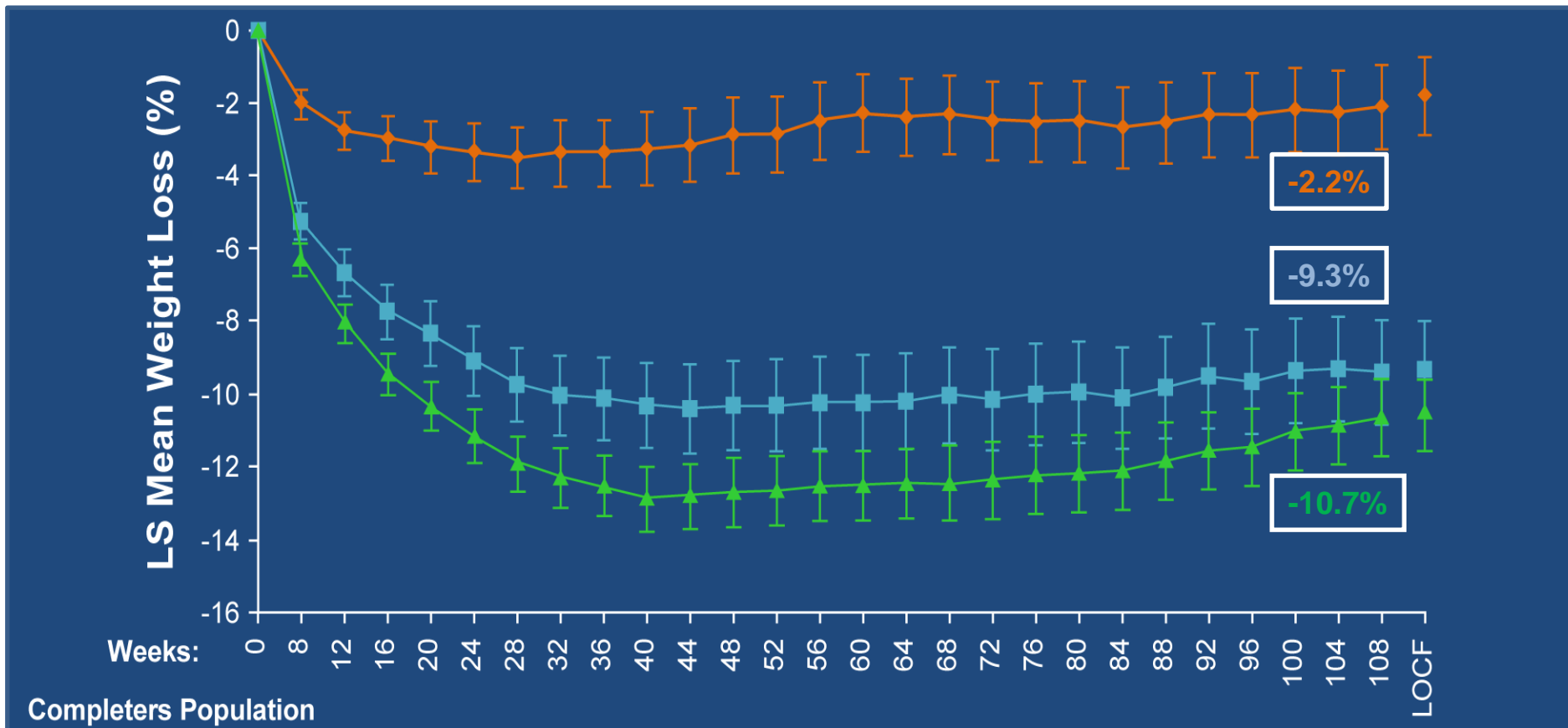
# Effect of Long-Term Treatment With Orlistat: XENDOS Study



Completers Data

$P < 0.001$  vs placebo

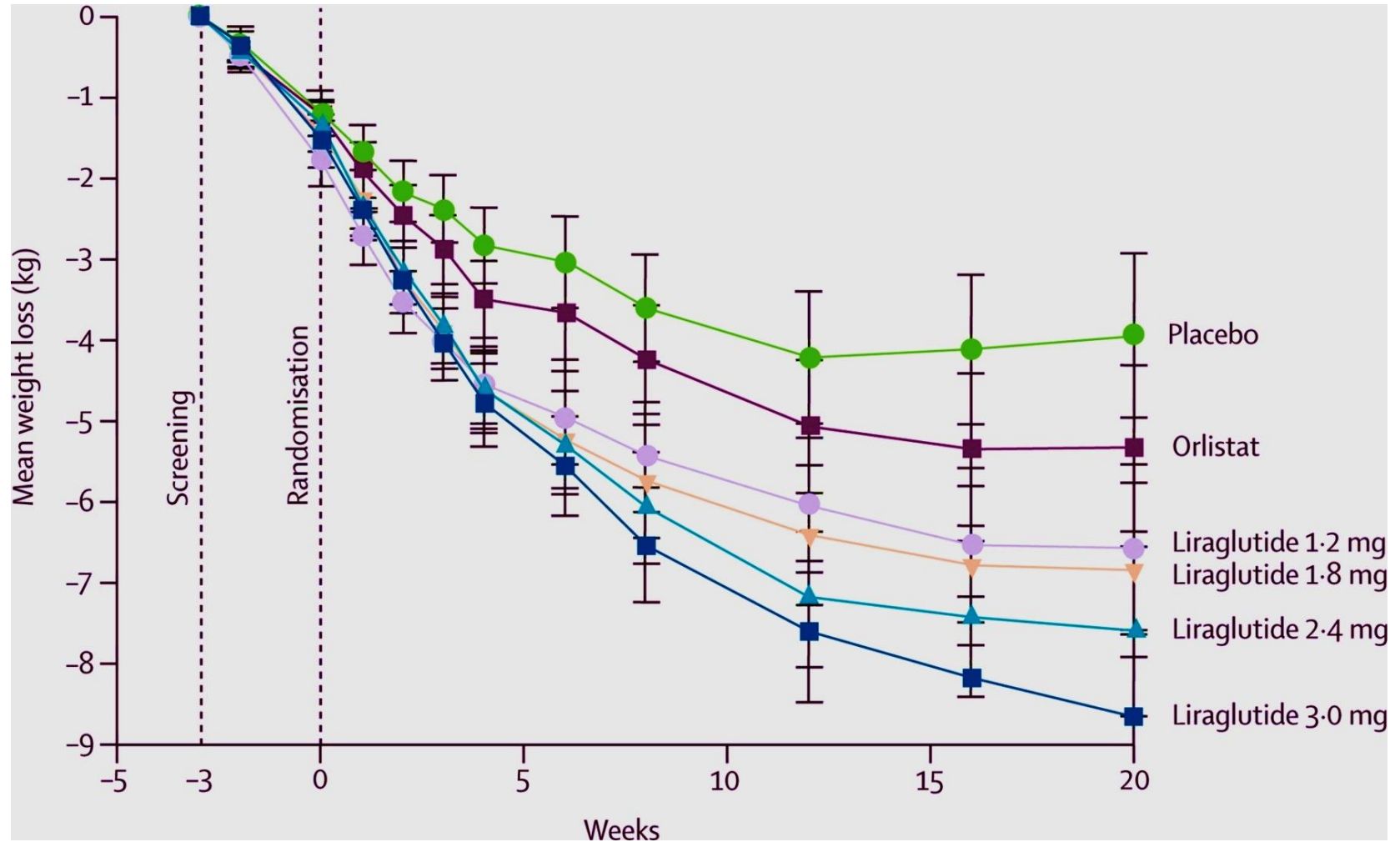
# Weight Change Over 2 Years With Phentermine/Topiramate ER



◆ **Placebo**     
 ■ **PHEN/TPM ER 7.5/46**     
 ▲ **PHEN/TPM ER 15/92**

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

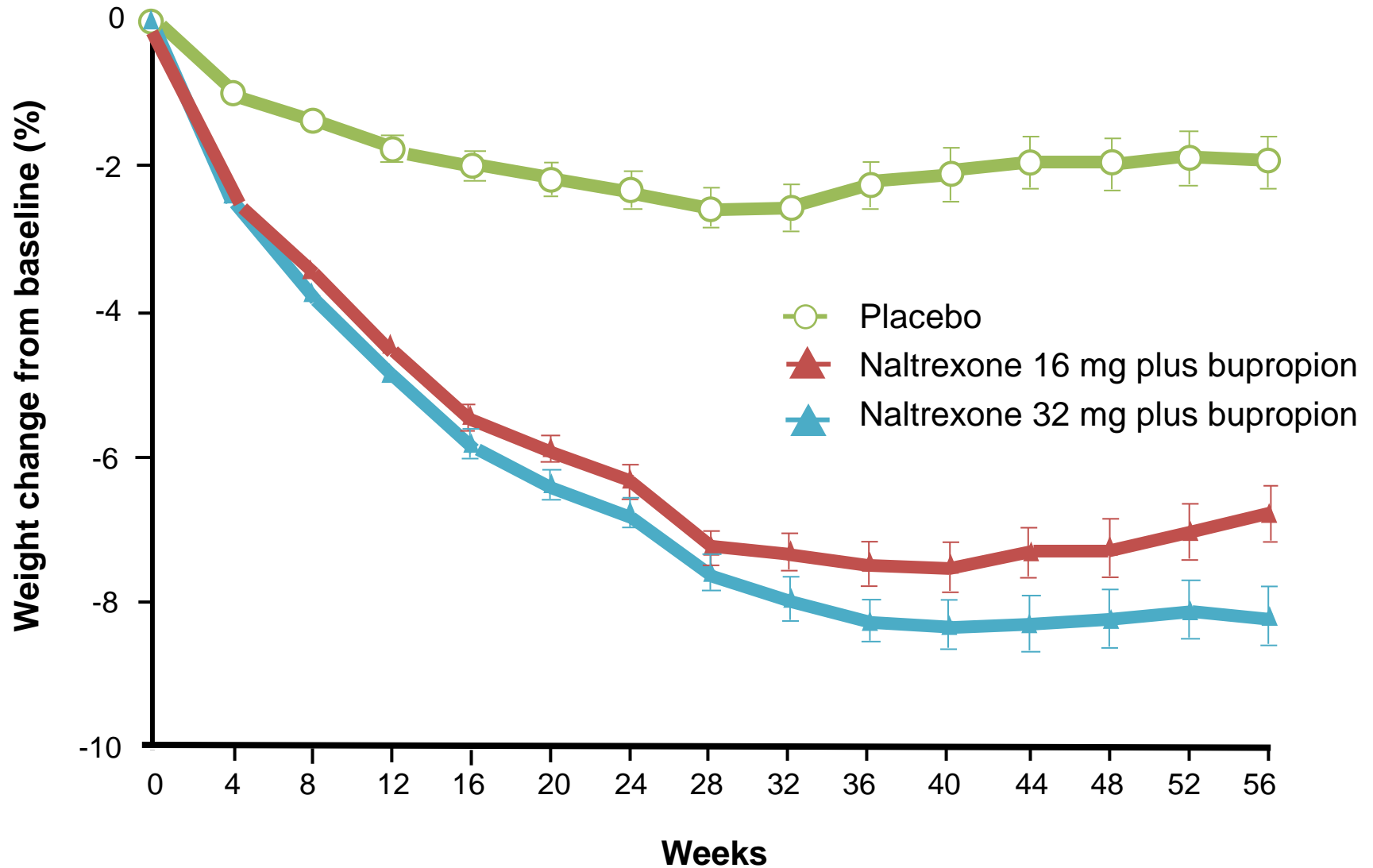
# Effects of Liraglutide and Orlistat on Body Weight in Non-diabetic Obese Adults



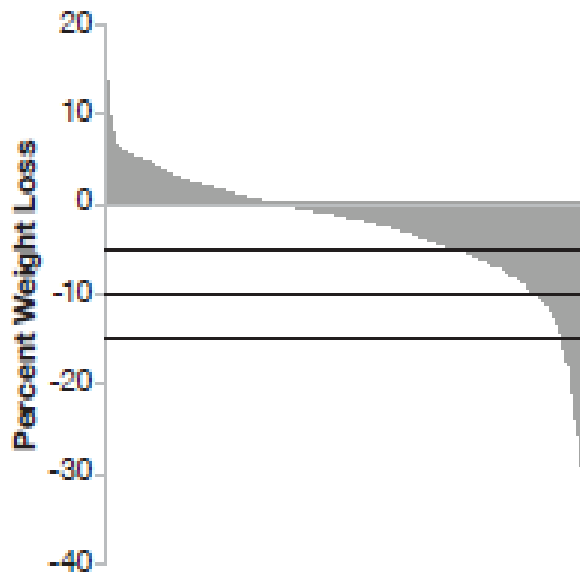
Data are mean (95% CI) for the ITT population



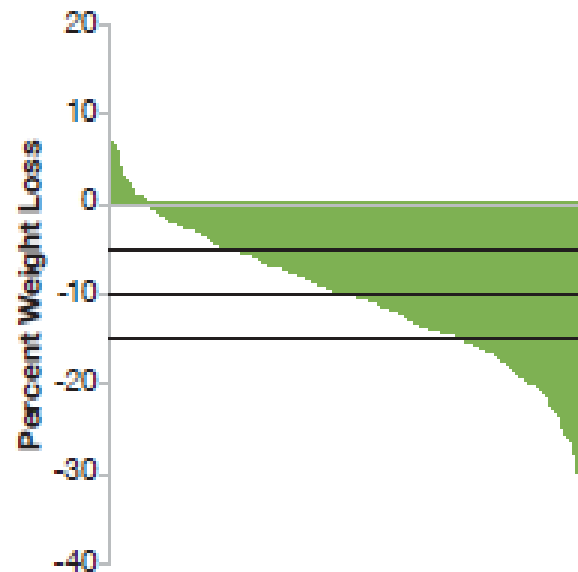
# Bupropion – Naltrexone



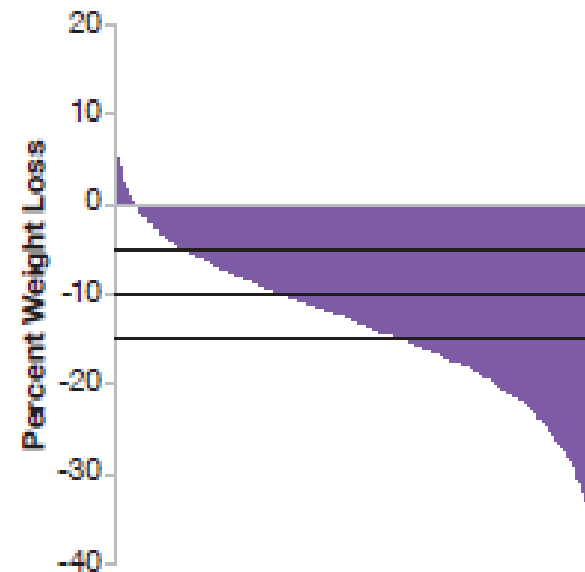
# When individual weight loss is displayed, it looks like this:



Lifestyle Modifications Alone (n=557)



PHEN/TPM ER 7.5/46 (n=338)



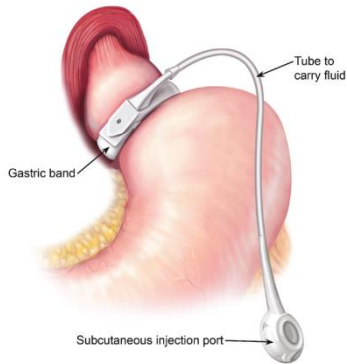
PHEN/TPM ER 15/92 (n=625)

Each vertical bar represents a single subject experience in subjects completing 56 weeks on study drug

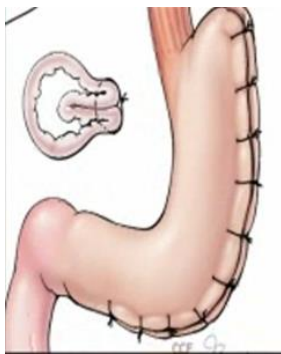
# Bariatric Surgery Procedures



## Gastric Restriction Procedures

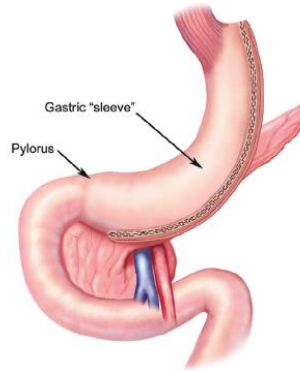


**Laparoscopic Adjustable Gastric Band (LAGB)**

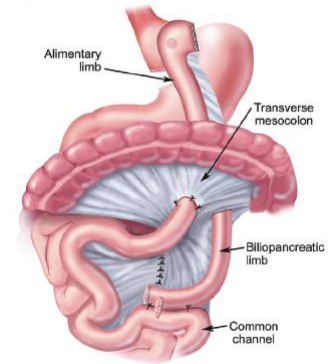


**Gastric Plication (Experimental)**

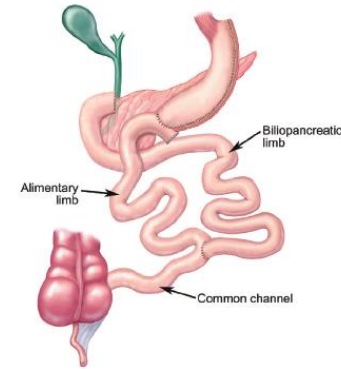
## Metabolic Procedures



**Laparoscopic Sleeve Gastrectomy (LSG)**



**Roux-en-Y Gastric Bypass (RYGB)**



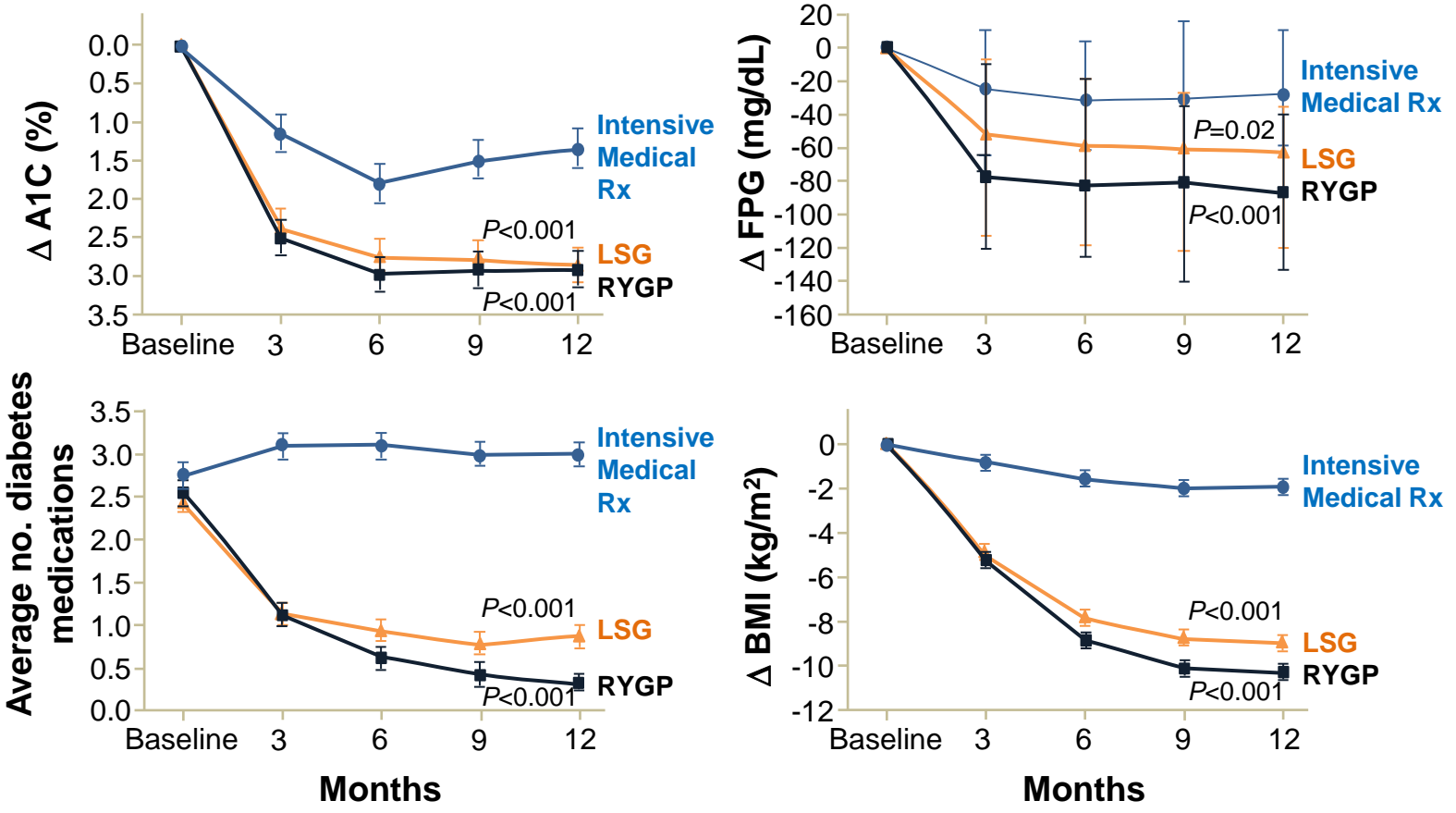
**Biliopancreatic Diversion (BPD)**

# Bariatric Surgery Outcomes

## Patients With Type 2 Diabetes

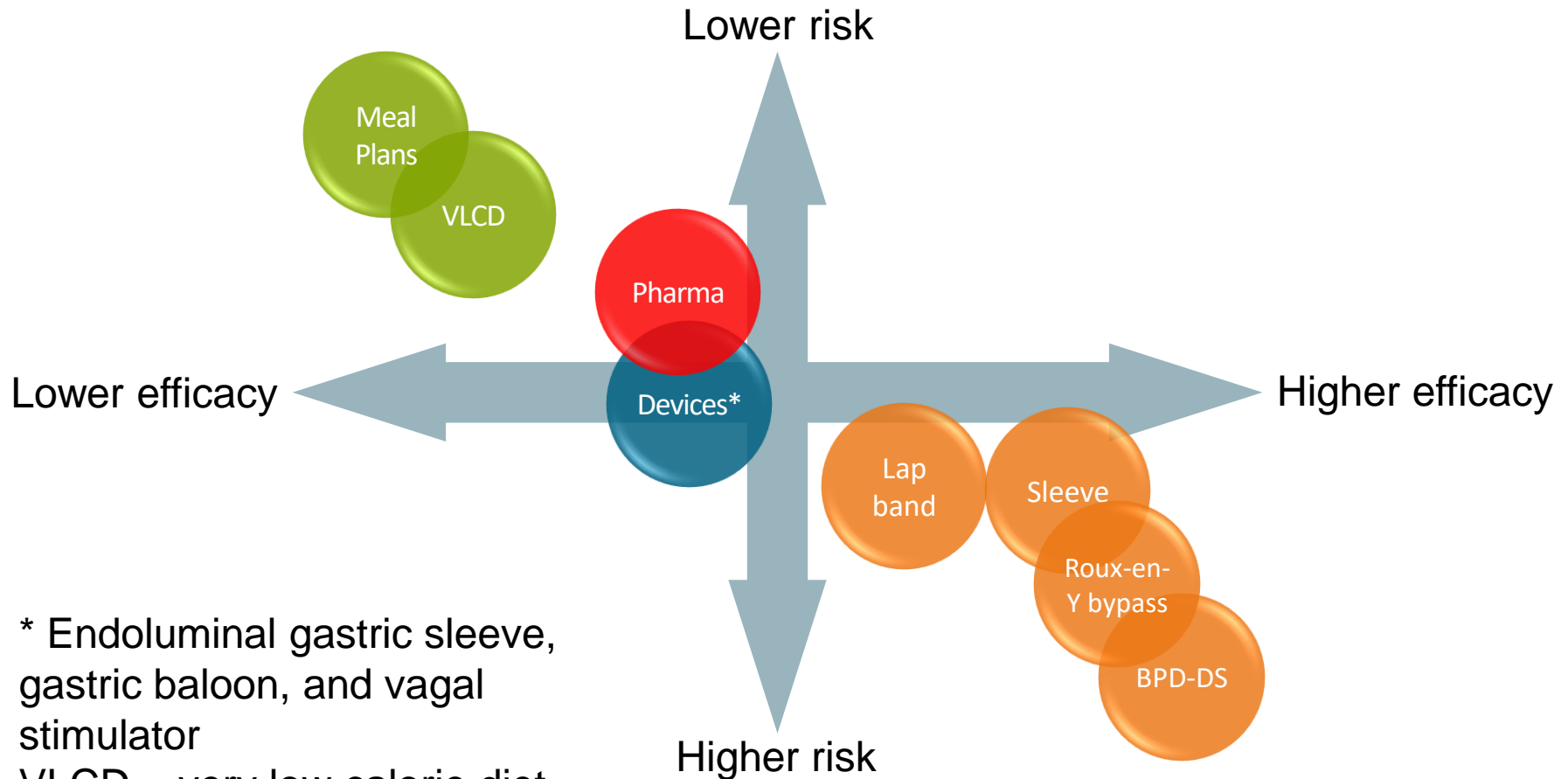


● Intensive medical therapy 
 ▲ Sleeve gastrectomy 
 ■ Roux-en-Y gastric bypass





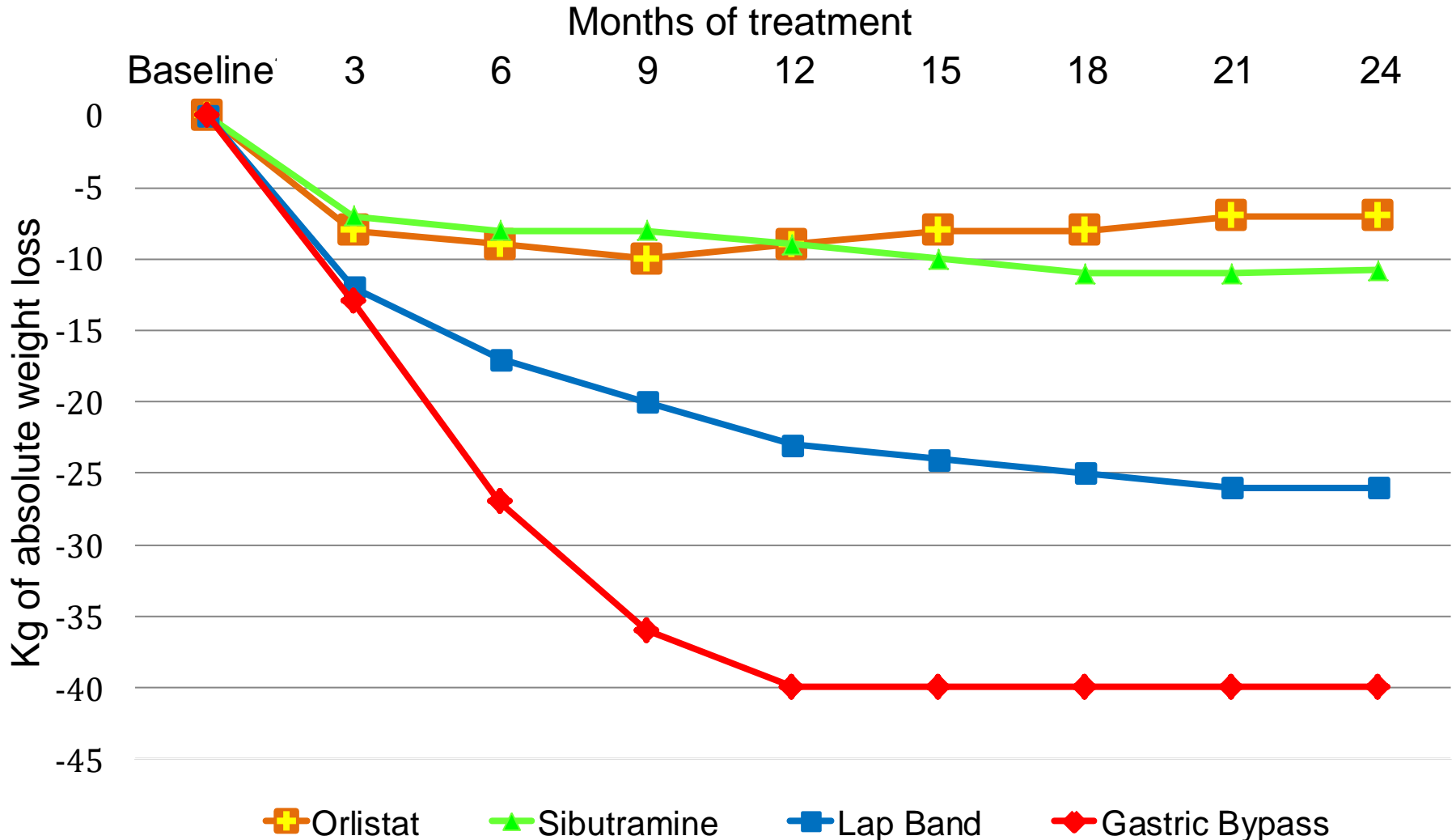
# Risks and Efficacy



- \* Endoluminal gastric sleeve, gastric balloon, and vagal stimulator
- VLCD = very low calorie diet.

Jensen MD, J Am Coll Cardiol. 2013;pii:S0735-1097(13) 06030-0.  
<http://formularyjournal.modernmedicine.com/print/368664>.

# Pharmacotherapy vs Surgery for Obesity (kg of absolute wt loss)





# Principles of Bariatric Endocrinology (8)

- ❄️ Failure of monotherapy to achieve effective weight loss should not lead to discontinuation of treatment, but rather the institution of combination therapy



# Case Study #1



Before, BMI = 42,  
Weight = 313 lbs



After, BMI = 32,  
Weight = 235 lbs

**Down 78 pounds**





# Case Study #2



Before, BMI = 57,  
Weight = 315 lbs



After, BMI = 40,  
Weight = 222 lbs

**Down 93 pounds**



# Case Study #3



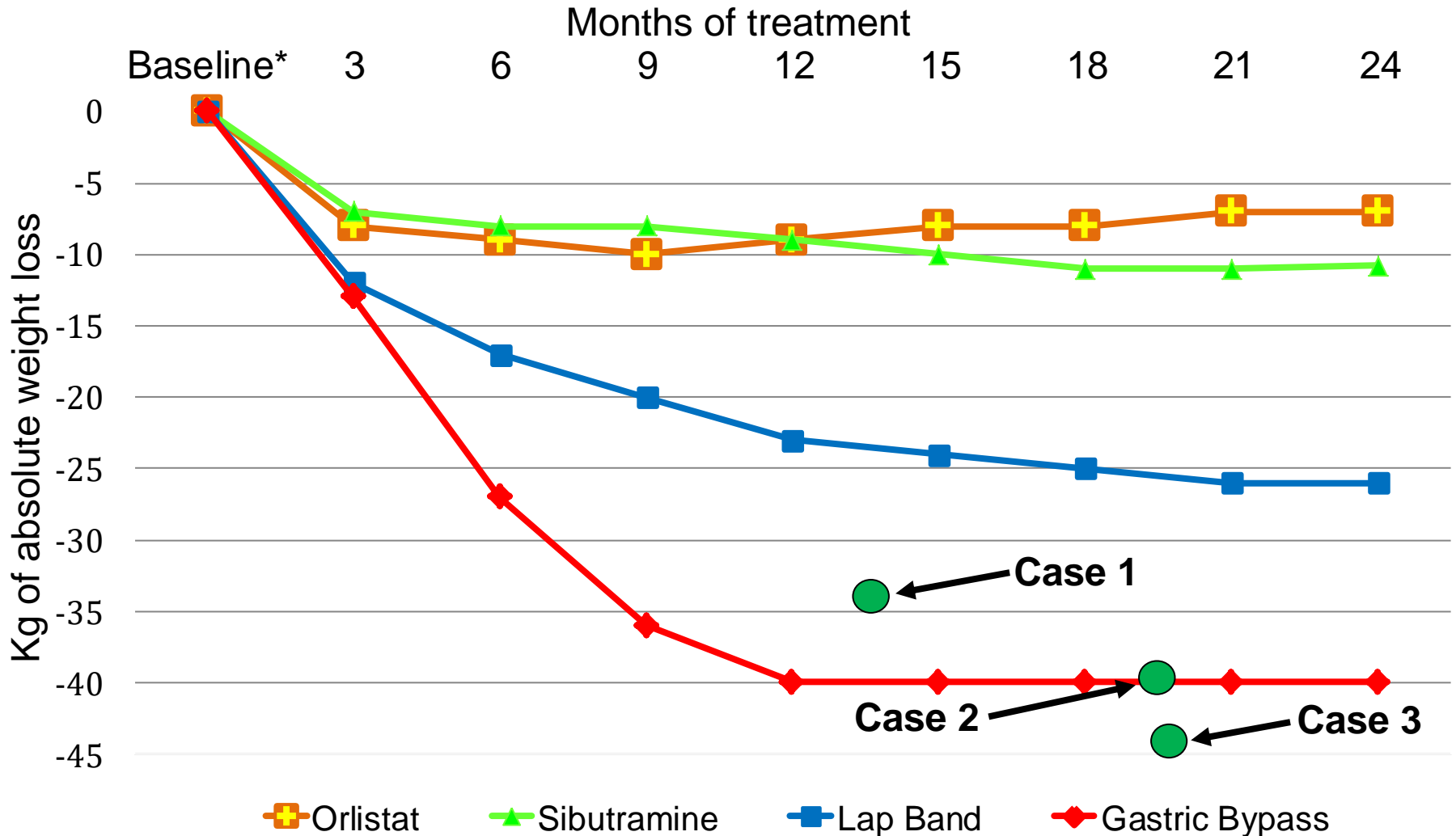
Before, BMI = 43,  
Weight = 279 lbs



After, BMI = 27,  
Weight = 176 lbs

**Down 103 pounds**

# Pharmacotherapy vs Surgery for Obesity (kg of absolute wt loss)





# How does MNCOME do with extreme obesity?



July 10, 2004:  
Weight = 629 pounds  
BMI = 91.65



August 24, 2012:  
Weight = 464 pounds  
BMI = 69.7

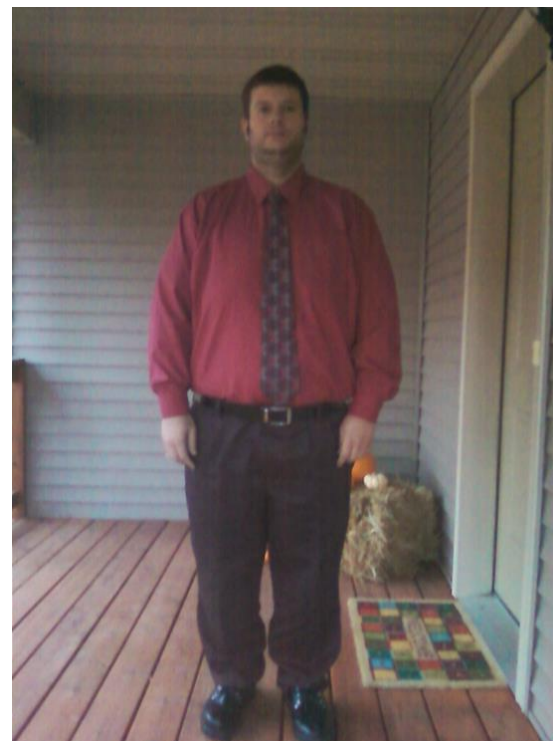
**Down 165 pounds in 8 years**



# Will extreme obesity respond to medical management?



September 13, 2006:  
Weight = 513 pounds  
BMI = 71.62

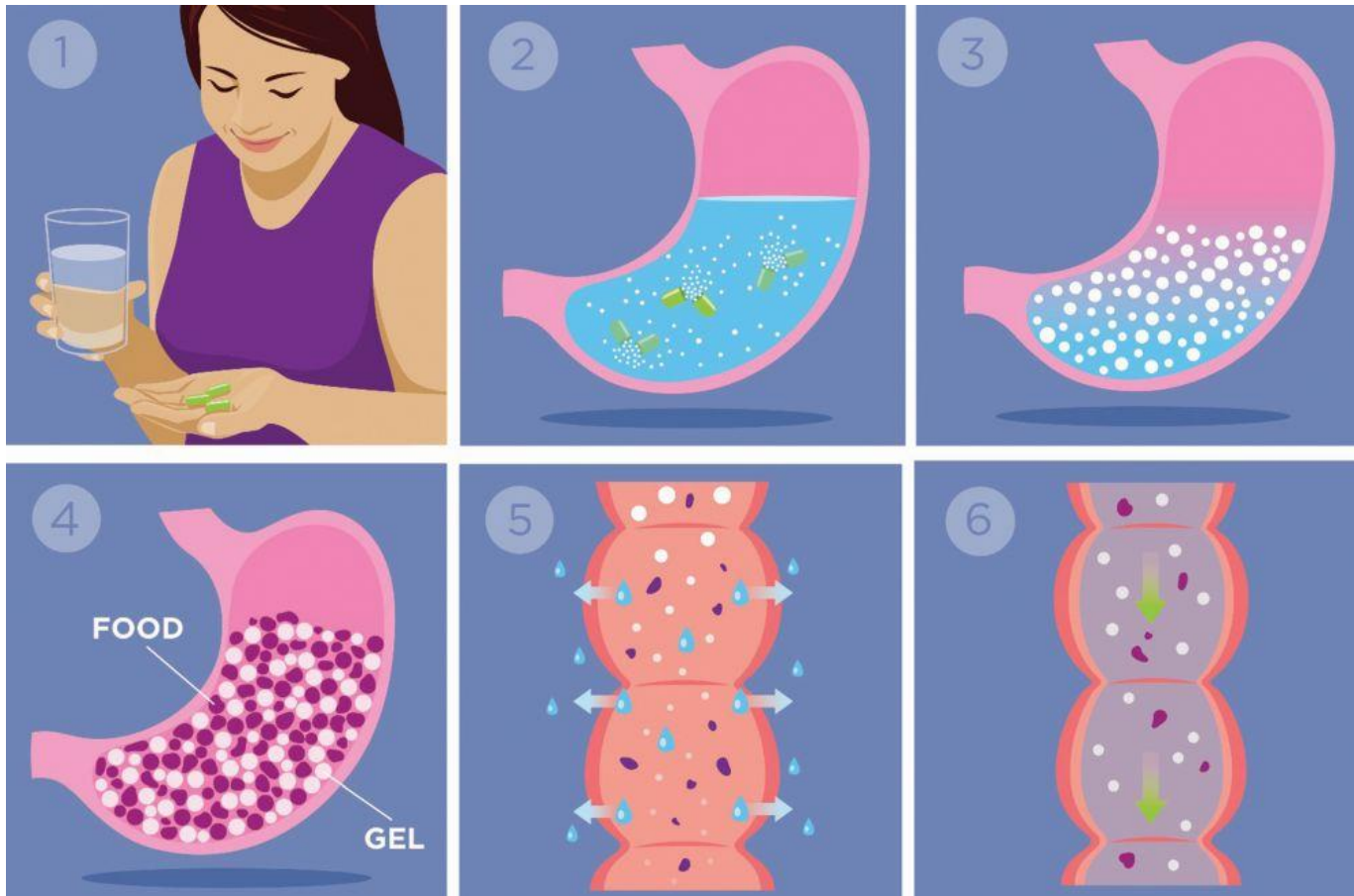


July 21, 2012:  
Weight = 248 pounds  
BMI = 34.6

**Down 265 pounds in 6 years**



# Superabsorbent Hydrogel Particles in Capsules



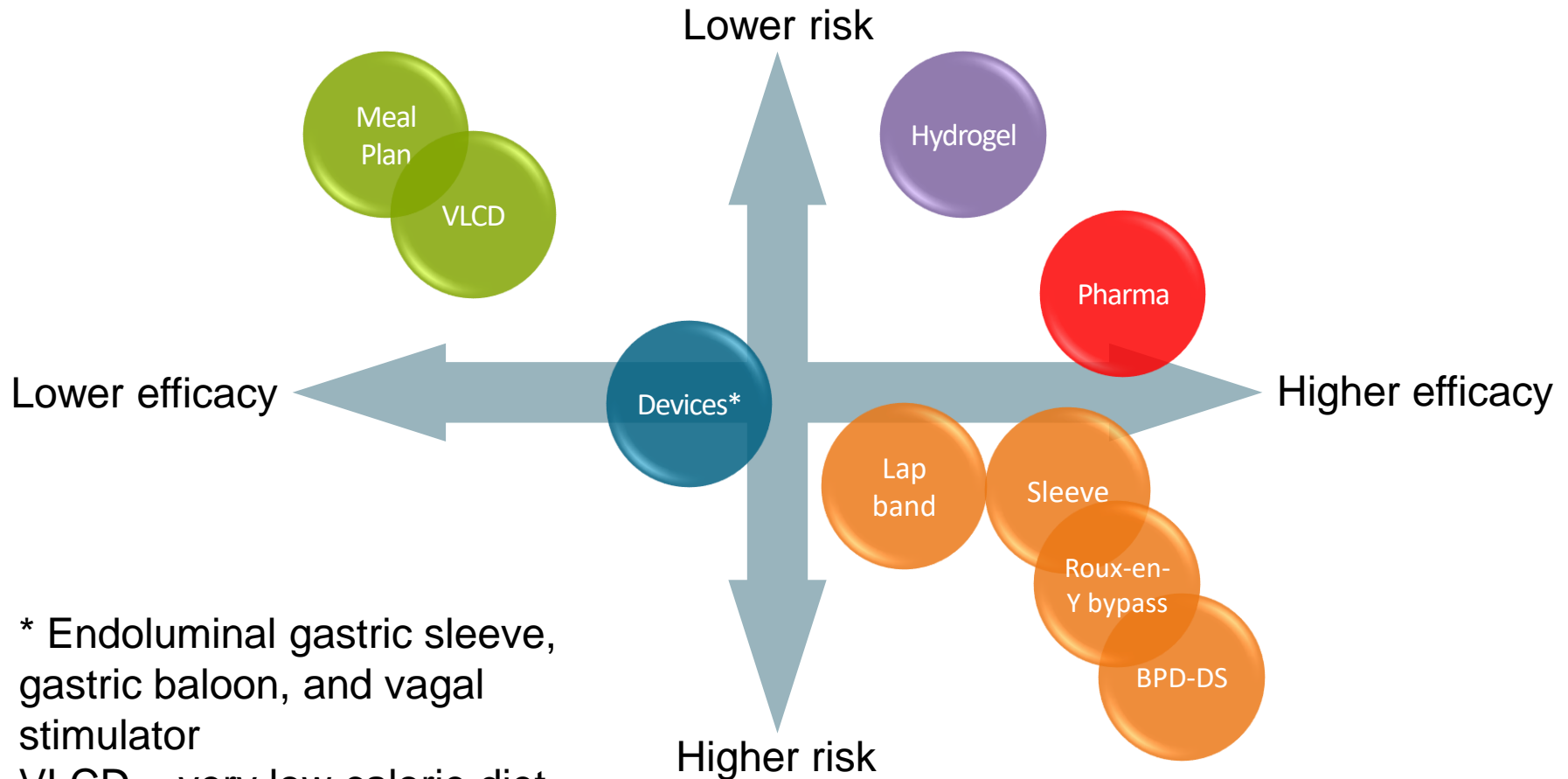


# Superabsorbent Hydrogel Particles in Capsules

- ❄️ ~6 out of 10 adults treated with superabsorbent hydrogel particles achieved  $\geq 5\%$  weight loss (an average weight loss of 10% or ~22 pounds).
- ❄️ 1 in 4 adults treated with superabsorbent hydrogel particles achieved  $\geq 10\%$  weight loss (an average weight loss of 14% or ~30 pounds)



# Risks and Efficacy

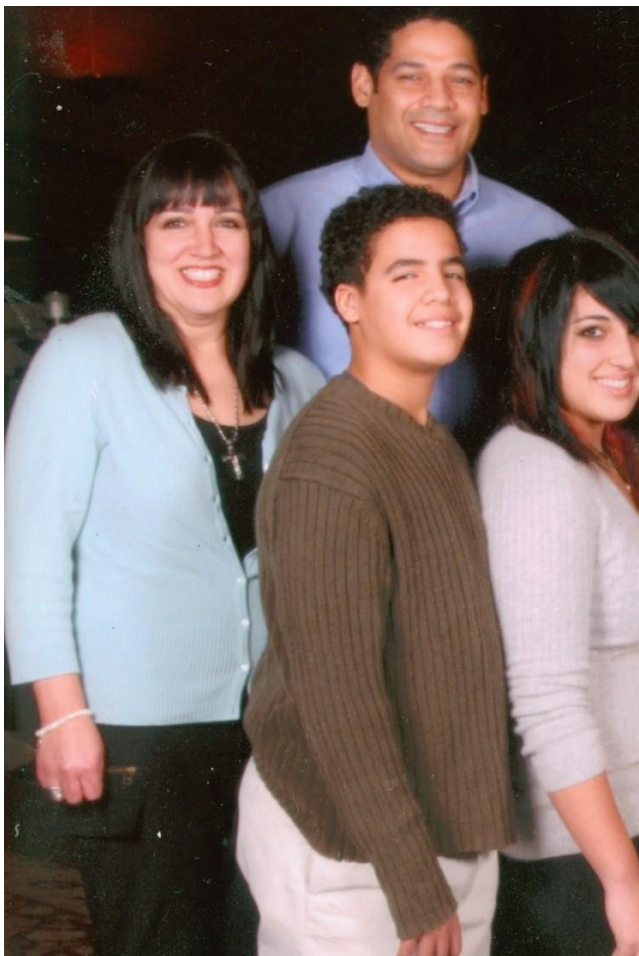


- \* Endoluminal gastric sleeve, gastric balloon, and vagal stimulator
- VLCD = very low calorie diet.

Jensen MD, J Am Coll Cardiol. 2013;pii:S0735-1097(13) 06030-0.  
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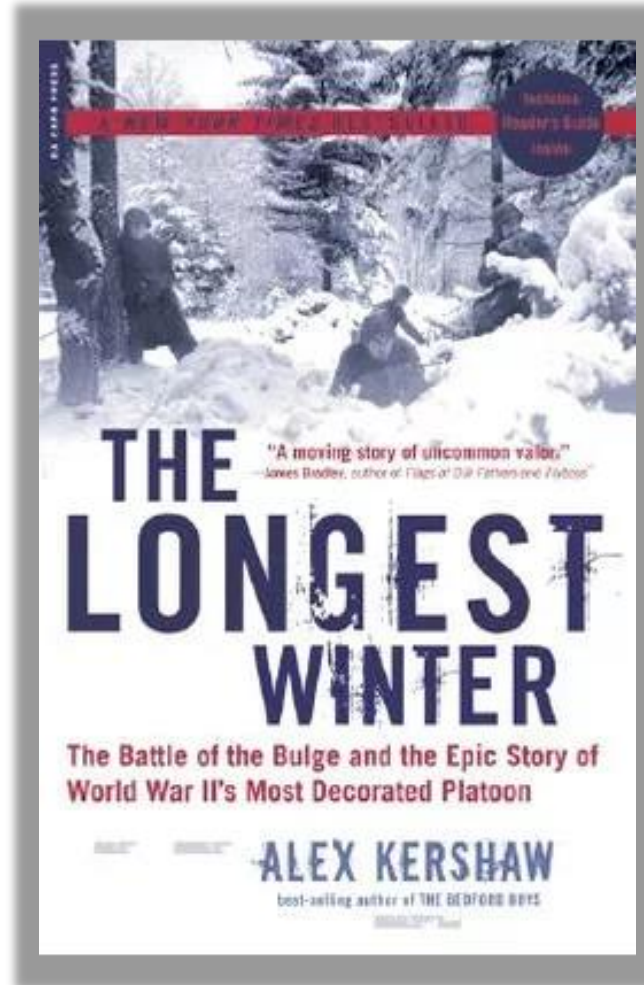
# How Does MNCOME do with BMI 30-35?



Down from 167 to 134  
pounds with maintenance  
of weight loss over 5 years  
-- EASY!!!!



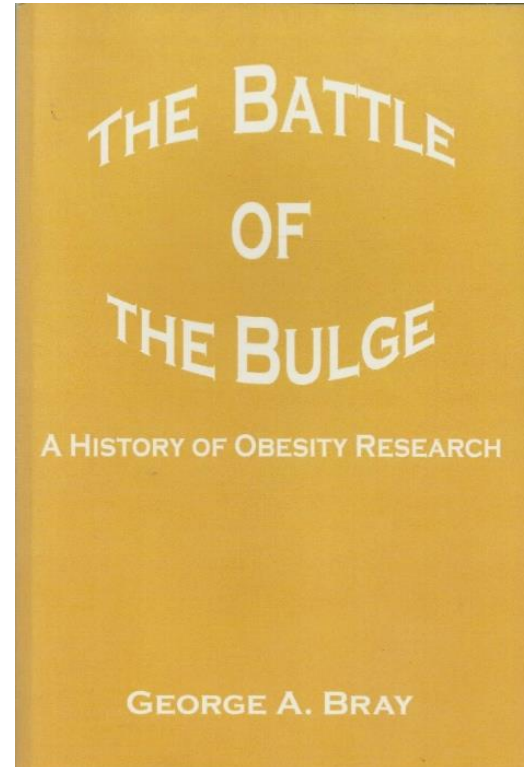
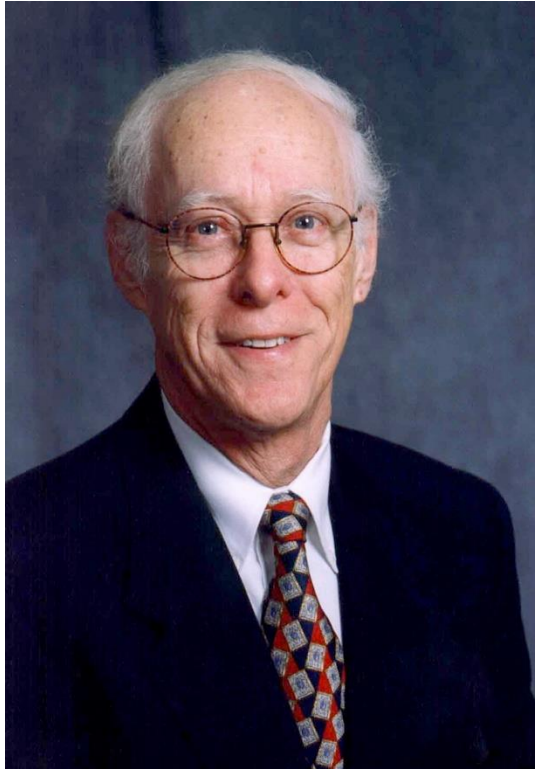
# The Battle of the Bulge



Dec 16, 1944 – Jan 25, 1945



# The Battle of the Bulge



George A Bray



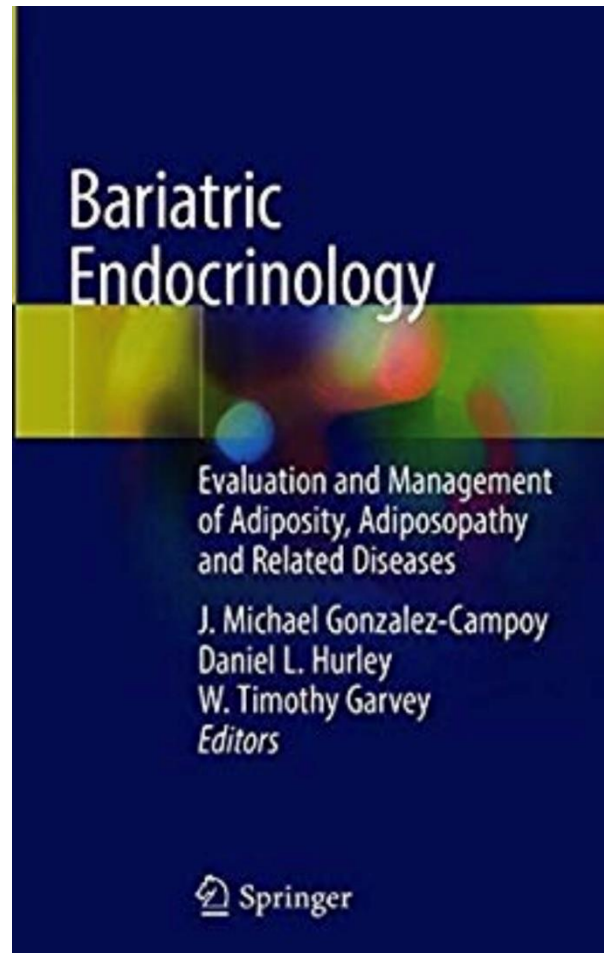
# Bariatric Endocrinology



J. Michael Gonzalez-Campoy  
drmike@mncome.com



# Bariatric Endocrinology





# Summary

- ❄️ Patients with overweight or obesity should have a thorough initial evaluation, and periodic risk re-stratification.
- ❄️ Comorbidities and obesity complications, including adiposopathy, should be identified and treated.
- ❄️ Treatment plans should be individualized, and designed according to severity of comorbidities and complications, as well as body mass index