

# Update in Obesity: the 10 Most Interesting Studies in 2009

DGIM Grand Rounds  
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Adam Gilden Tsai, MD, MSCE  
Assistant Professor of Medicine

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- Conflicts of Interest: none
- Slides
  - Frank Greenway, MD
  - Dan Bessesen, MD

# Outline

- Epidemiology
- Obesity Prevention
- Diet
- Pharmacotherapy
- Surgery
- Public Policy

# Outline

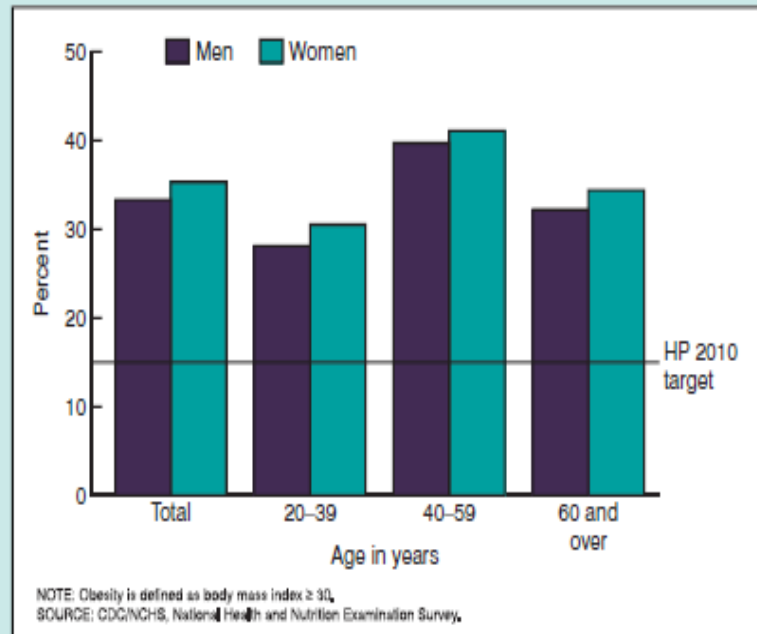
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# Obesity Rates Are Stabilizing

## How many adults in the United States are obese?

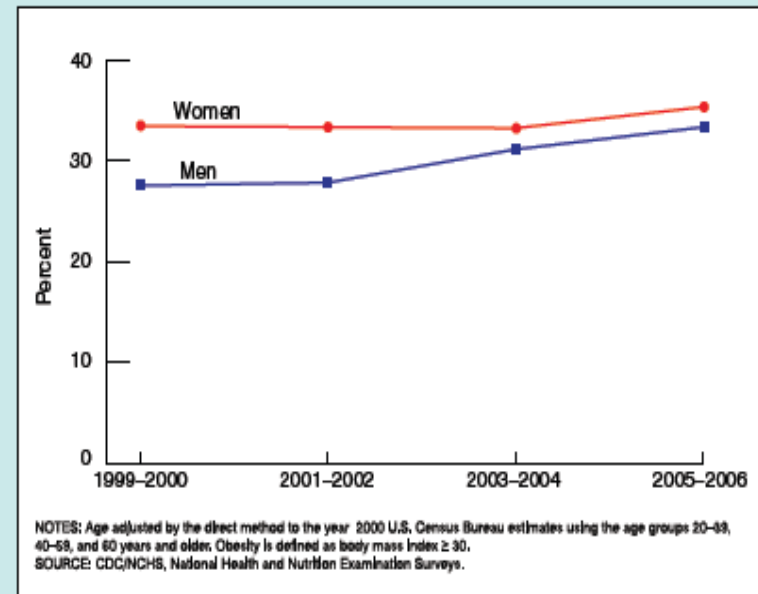
- More than one-third of adults, or over 72 million people, were obese in 2005–2006

Figure 1. Obesity prevalence, by age and sex, and the Healthy People (HP) 2010 obesity target, adults aged 20 years and older: United States, 2005–2006



There was no significant increase in the prevalence of obesity between 2003–2004 and 2005–2006 in the United States.

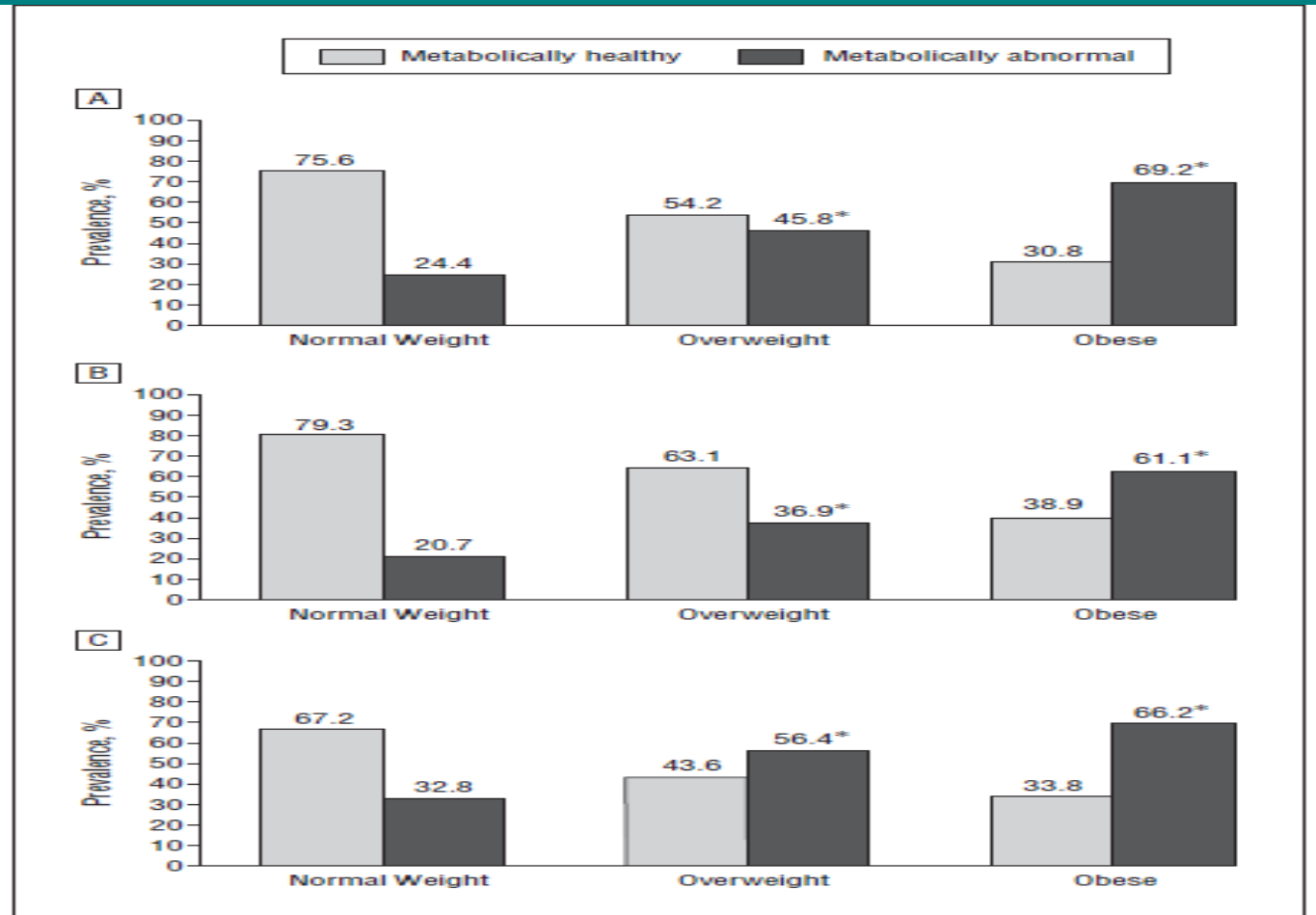
Figure 2. Trends in obesity by sex, adults aged 20 years and older: United States, 1999–2000 through 2005–2006.



# Obesity and Metabolic Risk

- NHANES 1999-2004
- N = 5440 aged 20 and older
- Metabolically abnormal (0-1 versus 2 or more)
  - BP ( $\geq 130/85$ )
  - TG ( $\geq 150$ )
  - hsCRP ( $\geq 0.1$  mg/L)
  - Fasting glucose ( $\geq 100$ )
  - HOMA (homeostasis model assessment)
  - HDL ( $<40$  men,  $<50$  women)

# Obesity and Metabolic Risk



A = Non-Hispanic whites; B = Non-Hispanic blacks; C = Mexican-Americans

# Take Home

- Patients with BMI  $\geq 25$  kg/m<sup>2</sup> should undergo routine testing of fasting glucose (or A1c) and lipids
  - But ... not everybody needs “treatment” for their weight

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# Obesity and Sleep Deprivation

- 10 healthy, overweight volunteers
- Two 14-day study periods, 3 months apart
- Randomized to 5.5 hours or 8.5 hours of sleep
  - Actual sleep: 5.25 and 7.5 hours
- Calorie intake of 90% of requirement
  - Balanced deficit diet

# Obesity and Sleep Deprivation

- Weight losses: 3.0 vs 2.9 kg; NS
- Lean tissue loss: 75% vs 49% ( $p < 0.01$ )
- Significantly increased hunger by VAS in sleep-restricted group (0.64 cm;  $p < 0.01$ )

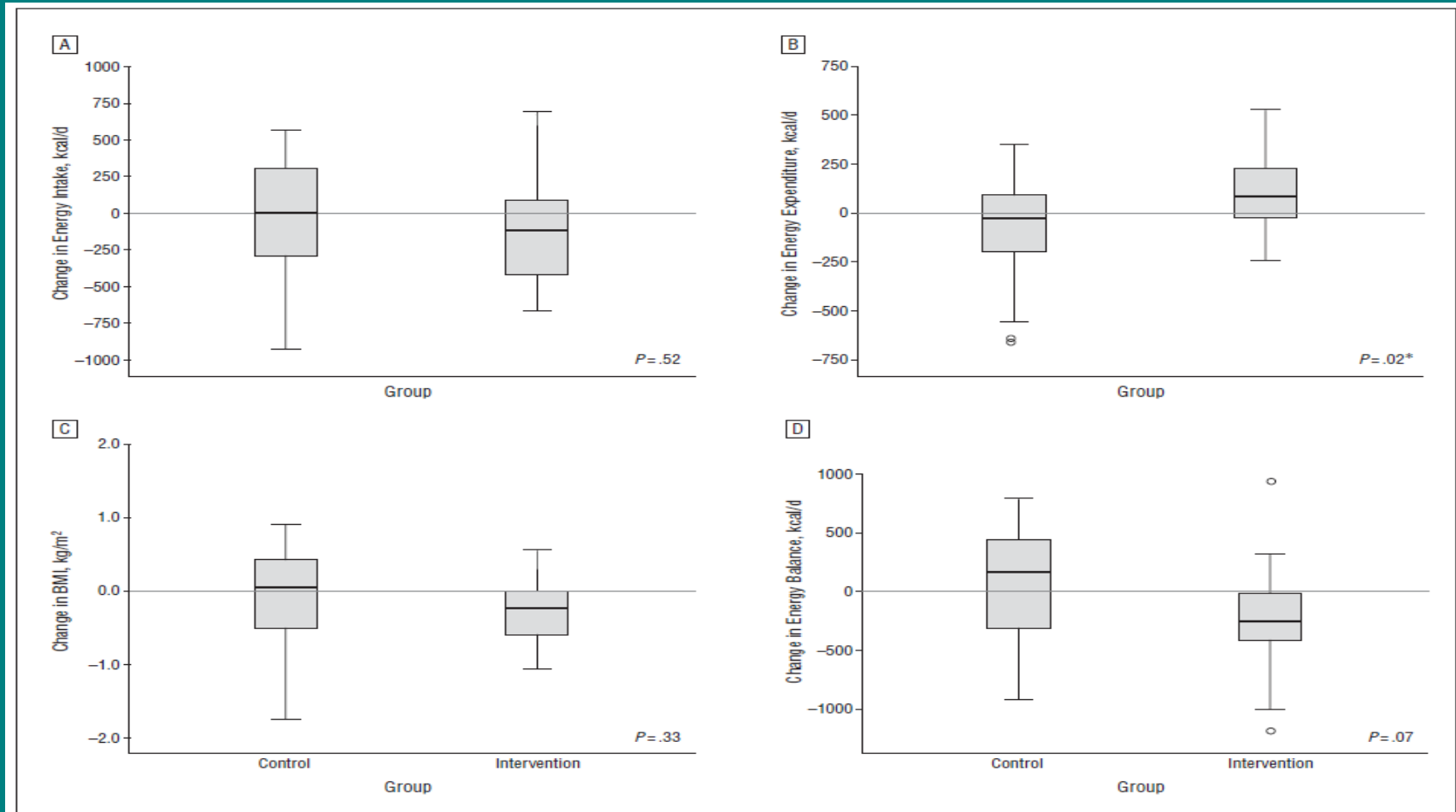
# Obesity and Television Viewing

- TV viewing is associated with obesity and with weight gain
  - Lower metabolic rate than any other sedentary activity
- The average American watches 4 hours of TV per day (#3 after work and sleep)

# Obesity and Television Viewing

- Randomized trial, n = 36
- 3 week observation period to estimate TV watching
  - Average was 4.8/5.3 hours per day
- Randomized to control condition versus block on TV after 50% of baseline viewing time

# Obesity and Television Viewing



# Take Home

- \*8-5-3-2-1-almost none
- **8 (HOURS OF SLEEP)**
- 5 (fruits and veggies per day)
- 3 servings of dairy (low-fat)
- **2 (MAX HOURS SCREEN TIME)**
- 1 (hours or more of physical activity)
- Almost none (sugar-sweetened beverages)

\*Christy Boling, MD, MHS (UT Southwestern/Houston VA)

# Obesity and Secondary Prevention

- Health and Retirement Survey (RAND)
  - Individuals < 75 yo, BMI  $\geq$  25 kg/m<sup>2</sup>
- Regression analysis controlled for:
  - Age
  - Sex
  - Race/ethnicity
  - Educational status
  - baseline BMI and health status
  - Marital status
  - Weight status of spouse
  - Smoking status
  - Employment status
  - Health insurance status
  - Income

# Obesity and Secondary Prevention

- New dx of heart disease or diabetes
  - Gain of 0.04 BMI units over 2 years for entire sample
  - Decrease of 0.35 BMI units for 1 dx (2.5 lbs for a 220 lb, 5 foot 8 person)
  - Decrease of 0.64 BMI units for 2 dx (4 lbs for a 220 lb, 5 foot 8 inch person)

# Take Home

- Use new diagnoses as an opportunity to counsel patients about their weight
  - Use metabolic syndrome in the same way

# Outline

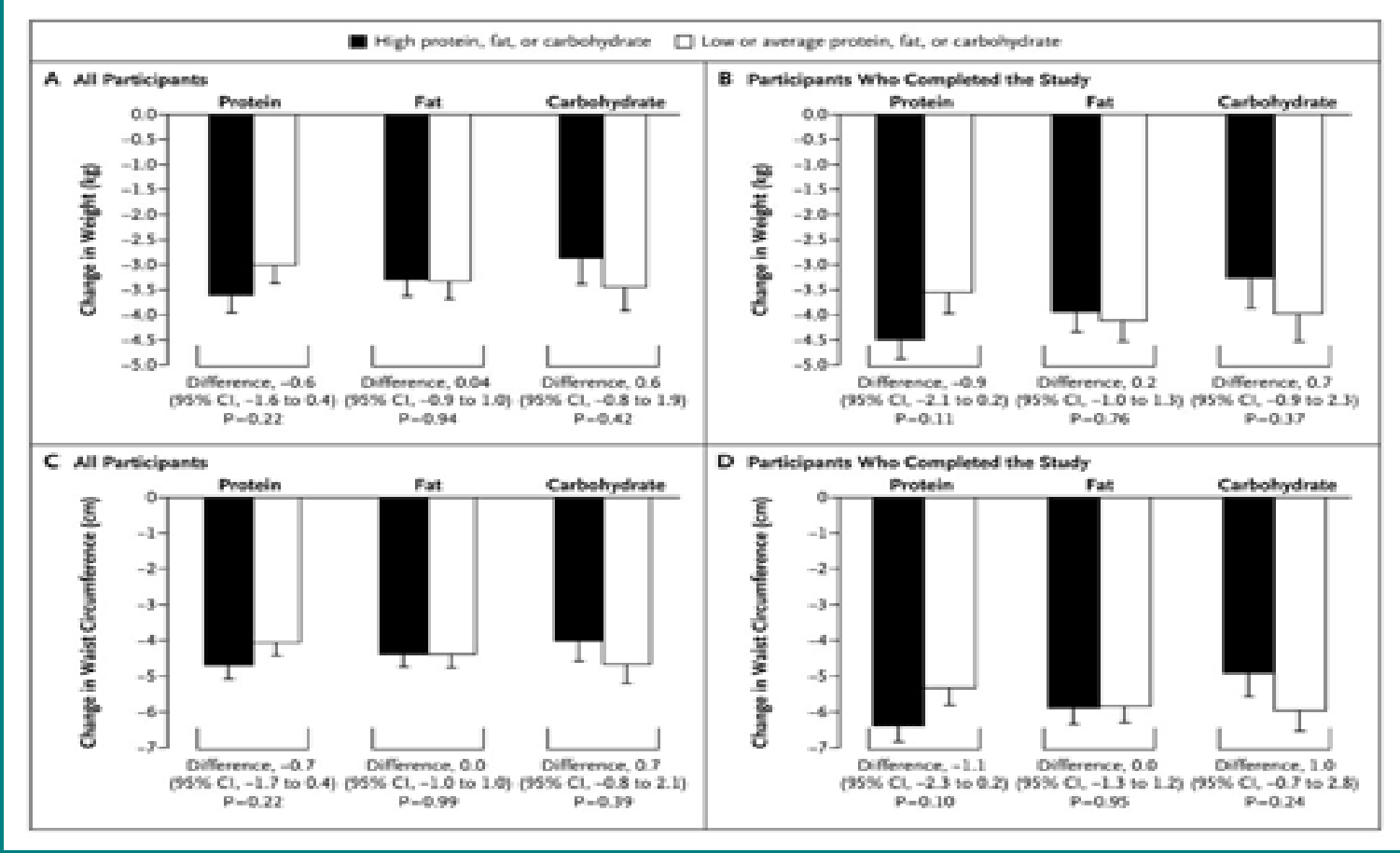
- Epidemiology
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# How important is macronutrient content?

- N = 811 individuals followed for 2 years
- Individual and group counseling

Carbohydrate	Fat	Protein
65%	20%	15%
55%	20%	25%
45%	40%	15%
35%	40%	25%

# Macronutrient Content of Diet Did Not Affect Weight Loss at 2 Years



# Take Home

- Caloric restriction and self-monitoring are more important than macronutrient content for the average patient

# Outline

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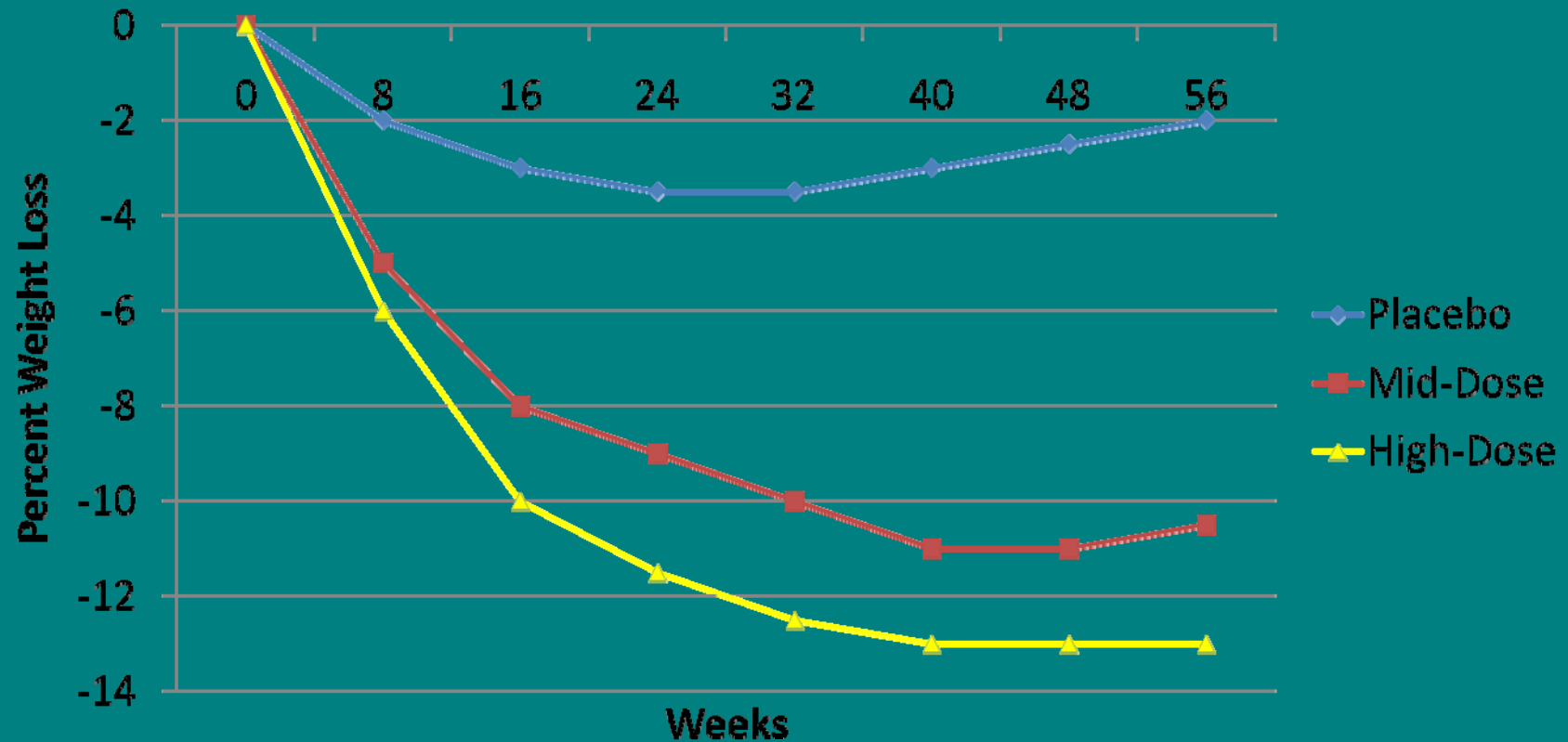
# Qnexa

## Topiramate and Phentermine

- Topiramate stimulates GABA and is approved for migraines and epilepsy
- Phentermine releases norepinephrine and is approved for short-term (3 months) obesity treatment
- Controlled release combination, taken daily, 4-week titration period in trials
- T/P: High-dose = 92/15mg, Mid-dose = 46/7.5mg and Low-dose = 23/3.37mg

# Qnexa Phase III Conquer Trial

N = 2,487



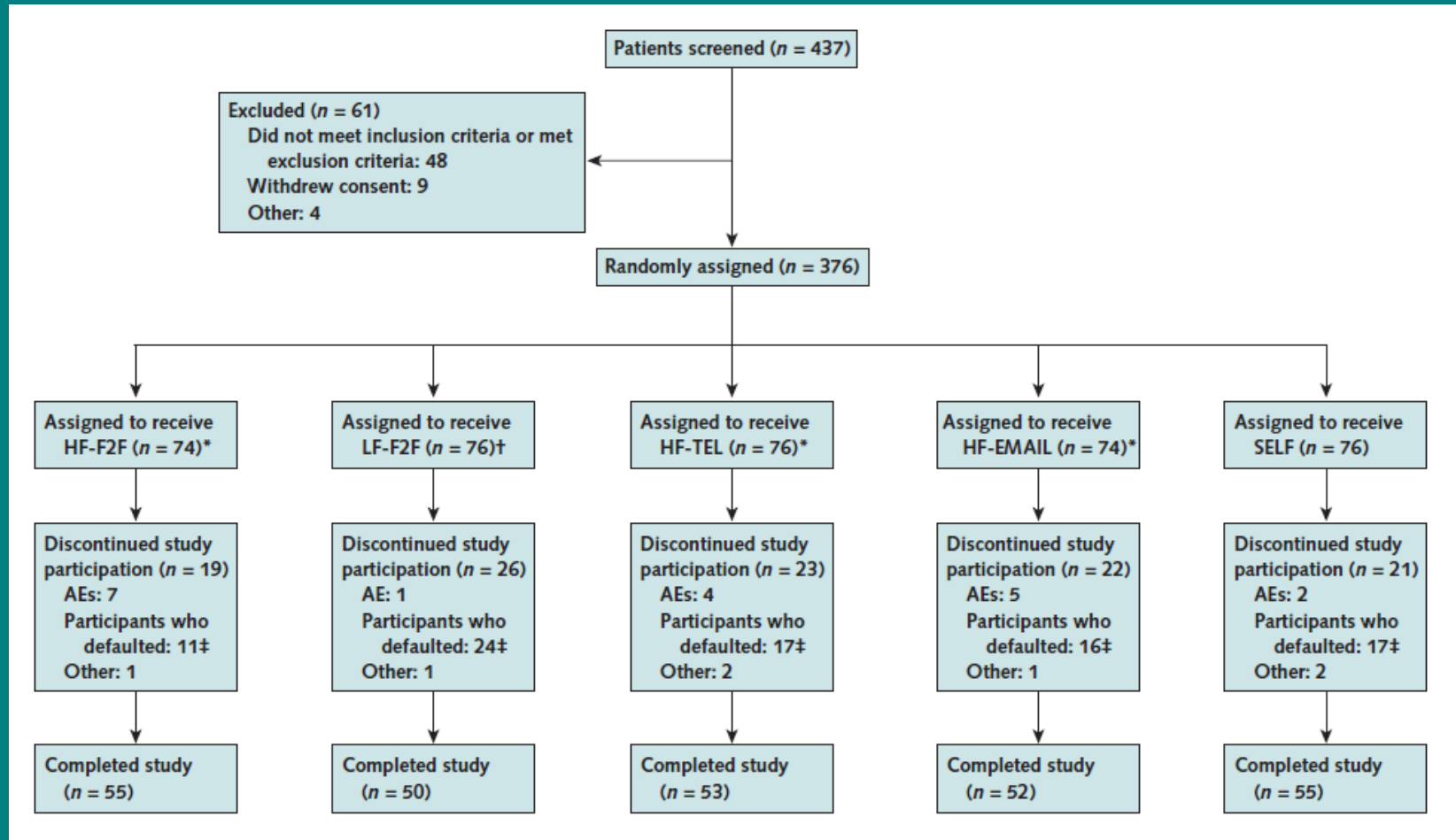
# Adverse Events in Qnexa Trial

	Qnexa	Topir	Phent	Placebo
Alt. Taste	16%	2%	2%	2%
Paresth.	38%	22%	4%	2%
Ur. Freq.	14%	2%	2%	6%
Headach	10%	8%	14%	2%
Memory	8%	4%	0%	12%
Insomnia	2%	4%	2%	12%

# Take Home

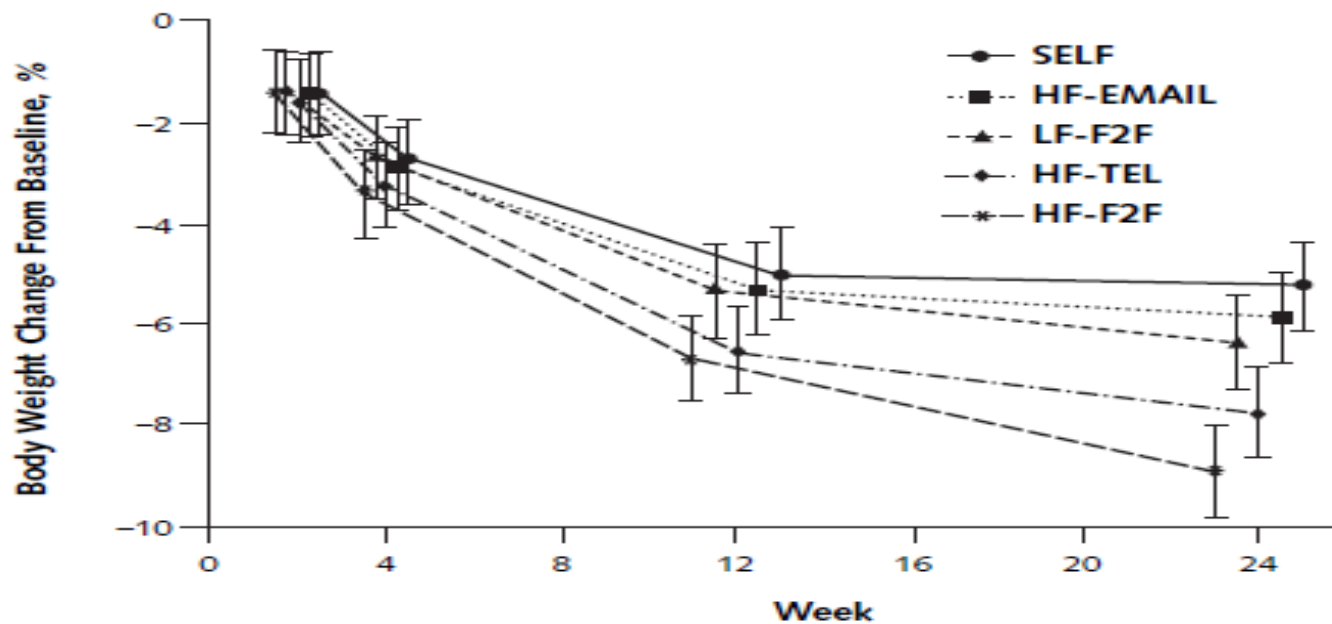
- New drugs are coming
  - Contrave (Bupropion-Naltrexone)
  - Empatic (Bupropion-Zonisamide)
  - Lorcaserin (5HT2 agonist)
  - Tesofensine (norepinephrine, dopamine, serotonin reuptake inhibitor)
- Likely to be combination agents
- Cost will be prohibitive for many patients

# Sibutramine + Counseling



# Sibutramine + Counseling

Figure 2. Mean percentage change in body weight with 95% CIs (mixed-model repeated-measures analysis).



# Take Home

- Weight loss medication and high-intensity weight loss counseling are additive
  - Caveat: recent FDA alert about increased risk of CV events for patients taking Meridia in the SCOUT (Sibutramine Cardiovascular Outcome Trial) in Europe

# Outline

- Epidemiology
- Obesity Prevention
- Diet
- Pharmacotherapy
- **Surgery**
- Public Policy

# Bariatric Surgery Getting Safer

- 4776 patients undergoing first-time surgery
  - Mean ( $\pm$ SD) age 44.5  $\pm$ 11.5 years; 21% men
  - Median BMI 46.5
  - 82.1% of the patients had at least one condition, 53.9% had two or more, and 26.5% had three or more
  - Hypertension (55.1%), obstructive sleep apnea (48.9%), diabetes (33.2%), asthma (23.1%); CAD (4.4%), venous edema with ulcerations (4.0%), a history of deep-vein thrombosis or venous thromboembolism (3.5%), dependence on supplemental oxygen (3.5%), congestive heart failure (2.2%), an inability to walk 200 ft (1.8%), and pulmonary hypertension (1.2%).

# Bariatric Surgery Getting Safer

- Surgery Type
  - Bypass 3412 (71.4%), of which 87.2% laparoscopic
  - Laparoscopic banding 1198 patients (25.1%)
  - Other 166 patients (3.5%) – not included for outcomes
- Outcomes: 30-day rate of death for banding or bypass = 0.3%
  - 0% of banding patients
  - 0.2% of laparoscopic bypass
  - 2.1% of open bypass
  - No difference in mortality after adjustment for patient or center characteristics banding
- 4.3% of patients had at least one major adverse outcome: death; venous thromboembolism; percutaneous, endoscopic, or operative reintervention; failure to be discharged from the hospital)

# Bariatric Surgery Getting Safer

**Table 2.** Adverse Outcomes within 30 Days after Surgery, According to Surgical Procedure.

Outcome	Total (N=4610)*	Laparoscopic Adjustable Gastric Banding (N=1198)	Laparoscopic Roux-en-Y Gastric Bypass (N=2975)	Open Roux-en-Y Gastric Bypass (N=437)	P Value†‡
		<i>number (percent)</i>			
Death	15 (0.3)	0	6 (0.2)	9 (2.1)	<0.001
Deep-vein thrombosis or venous thromboembolism	20 (0.4)	3 (0.3)	12 (0.4)	5 (1.1)	0.05
Tracheal reintubation	20 (0.4)	2 (0.2)	12 (0.4)	6 (1.4)	0.004
Endoscopy	51 (1.1)	1 (0.1)	45 (1.5)	5 (1.1)	<0.001
Operation					
Tracheostomy	11 (0.2)	0	6 (0.2)	5 (1.1)	0.001
Placement of percutaneous drain	16 (0.3)	0	13 (0.4)	3 (0.7)	0.48
Abdominal operation	118 (2.6)	9 (0.8)	94 (3.2)	15 (3.4)	<0.001
Failure to be discharged by day 30	17 (0.4)	0	13 (0.4)	4 (0.9)	0.02
Composite end point‡	189 (4.1)	12 (1.0)	143 (4.8)	34 (7.8)	<0.0001

\* The total excludes 166 procedures, including 117 sleeve gastrectomies, 47 biliopancreatic diversions with or without a duodenal switch, 1 vertical banded gastroplasty, and 1 open adjustable gastric banding.

† P values are for the comparison between treatment groups. Values were calculated with the use of the chi-square test.

‡ This end point is a composite of death; deep-vein thrombosis or venous thromboembolism; reintervention with the use of a percutaneous, endoscopic, or operative technique; or failure to be discharged from the hospital within 30 days after surgery.

# Take Home

- Refer patients that meet criteria for surgery
  - BMI  $\geq 40$  kg/m<sup>2</sup> or  $\geq 35$  kg/m<sup>2</sup> with comorbidity
    - Patients with diabetes

# Outline

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- **Public Policy**

# A Natural Experiment

- Does calorie labeling reduce calorie intake?
- 11 fast food chains in NYC
  - Subway posted point-of purchase calorie information prior to NYC law on labeling
- N = 7,318 (receipts analyzed)

# Public Policy – Calorie Posting

- Average = 827 calories consumed
- Subway customers more likely
  - to see calorie information (32% vs 4%)
  - To consume fewer calories if they saw calorie information (714 vs 766 calories)
- Subway customers less likely
  - To purchase high calorie meals ( $\geq 1000$  calories): 17% vs. 23%
- Calorie posting at Subway described as “not prominent”

# Take Home

- Aggressive public policy measures are likely to be needed to make changes at the population level
  - Not all will agree

# SUMMARY

- 8-5-3-2-1-almost none
- Caloric restriction, not macronutrient content
- Watch for new medications
- Combine medication and lifestyle modification
- Refer for surgery in selected patients
- Policy change

# THANK YOU

- Questions?
- Comments?

# Public Policy

- Calorie intake from beverages increased by 222 calories per person from 1965 to 2002, mostly from sweetened drinks<sup>1</sup>
- Calorie intake from sweetened beverages increased from 70 to 190 kcal per person from 1977 to 2001<sup>2</sup>
- 42 Starbucks and 73 Dunkin' Donuts stores during the spring of 2007
- 1,127 beverage purchases at Starbucks and 1,830 at Dunkin' Donuts

Duffey KJ, Popkin BM. Obesity 2007;15(11):2739-47.

Nielsen SJ, Popkin BM. Am J Prev Med 2004;27(3):205-10.

Huang C et al. Prev Chronic Dis 2009;6(4):1-8.

# Calories from Coffee Purchases

**Table 1. Beverage Purchases and Mean Calories per Customer, Starbucks and Dunkin' Donuts, New York City, 2007**

Type of Beverage	n (%)	Mean (SD) Calories, kcal	% of Purchases in Calorie Ranges, kcal <sup>a</sup>				
			<100	100-199	200-299	300-399	≥400
<b>Both chains</b>	2,957 (100)	132 (184)	56	21	11	8	4
Brewed coffee/tea	1,799 (61)	63 (57)	87	13	0	0	0
Blended beverage	1,158 (39)	239 (167)	9	33	29	20	10
<b>Starbucks</b>	1,127 (100)	156 (153)	40	27	19	10	5
Brewed coffee/tea	377 (34)	38 (30)	97	3	0	0	0
Blended beverage	750 (66)	215 (115)	10	39	28	14	8
<b>Dunkin' Donuts</b>	1,830 (100)	117 (149)	67	17	7	6	3
Brewed coffee/tea	1,422 (78)	69 (36)	84	16	0	0	0
Blended beverage	408 (22)	284 (131)	5	23	30	29	14

# Obesity Treatment in Primary Care

**Table 1. Studies of Primary Care Provider (PCP) Counseling and PCP Counseling Plus Pharmacotherapy**

Study	N	Interventions	Number of visits	Weight change (kg)	Attrition (%)*
Brief PCP counseling					
Martin <sup>30</sup>	144	(1) Usual care + monthly PCP visits	6	-0.5	44
		(2) Usual care	0	0.1	23
Christian <sup>32</sup>	310	(1) Quarterly PCP visits; lifestyle change goal sheets	4	-0.1	9
		(2) Quarterly PCP visits	4	0.6	15
Ockene <sup>34†</sup>	1,162	(1) PCP training + office support	3.6	-2.3	37
		(2) PCP training	3.1	-1.0	42
		(3) Usual care	3.4	0.0	42
Cohen <sup>31</sup>	30	(1) Usual care + additional PCP visit	12	-0.9	Not stated
		(2) Usual care	0	1.3	
Brief PCP counseling + pharmacotherapy					
Hauptman <sup>33</sup>	796	(1) Counseling + orlistat, 120 mg tid	10	-5.0	46
		(2) Counseling + orlistat, 60 mg tid	10	-4.5	44
		(3) Counseling	10	-1.7	57
Poston <sup>29</sup>	250	(1) RD/RN counseling + orlistat, 120 mg tid	13	-1.7	34
		(2) Orlistat, 120 mg tid	13	-1.7	35
		(3) RD/RN counseling	13	1.7	67
Wadden <sup>35‡</sup>	106	(1) PCP counseling + sibutramine, 15 mg/day	8	-7.5	19
		(2) Sibutramine, 15 mg/day	8	-5.0	18

**Table 2. Studies of Collaborative Obesity Treatment**

Study	N	Interventions	Number of visits	Weight change (kg)	Attrition (%)*
Ashley <sup>26</sup>	113	(1) Registered dietitian (RD) counseling	26	-3.4	38
		(2) RD counseling + meal replacements	26	-7.7	32
		(3) MD/RN counseling + meal replacements	26	-3.5	34
Ely <sup>27</sup>	101	(1) Patient and PCP education + telephone calls + treatment recommendations given to PCP	8	-4.3	48
		(2) Patient and PCP education	0	-1.0	52
Logue <sup>28</sup>	665	(1) Brief in-person counseling + telephone calls	28	-0.4	31
		(2) Brief in-person counseling	4	-0.2	38

# Obesity Treatment in Primary Care

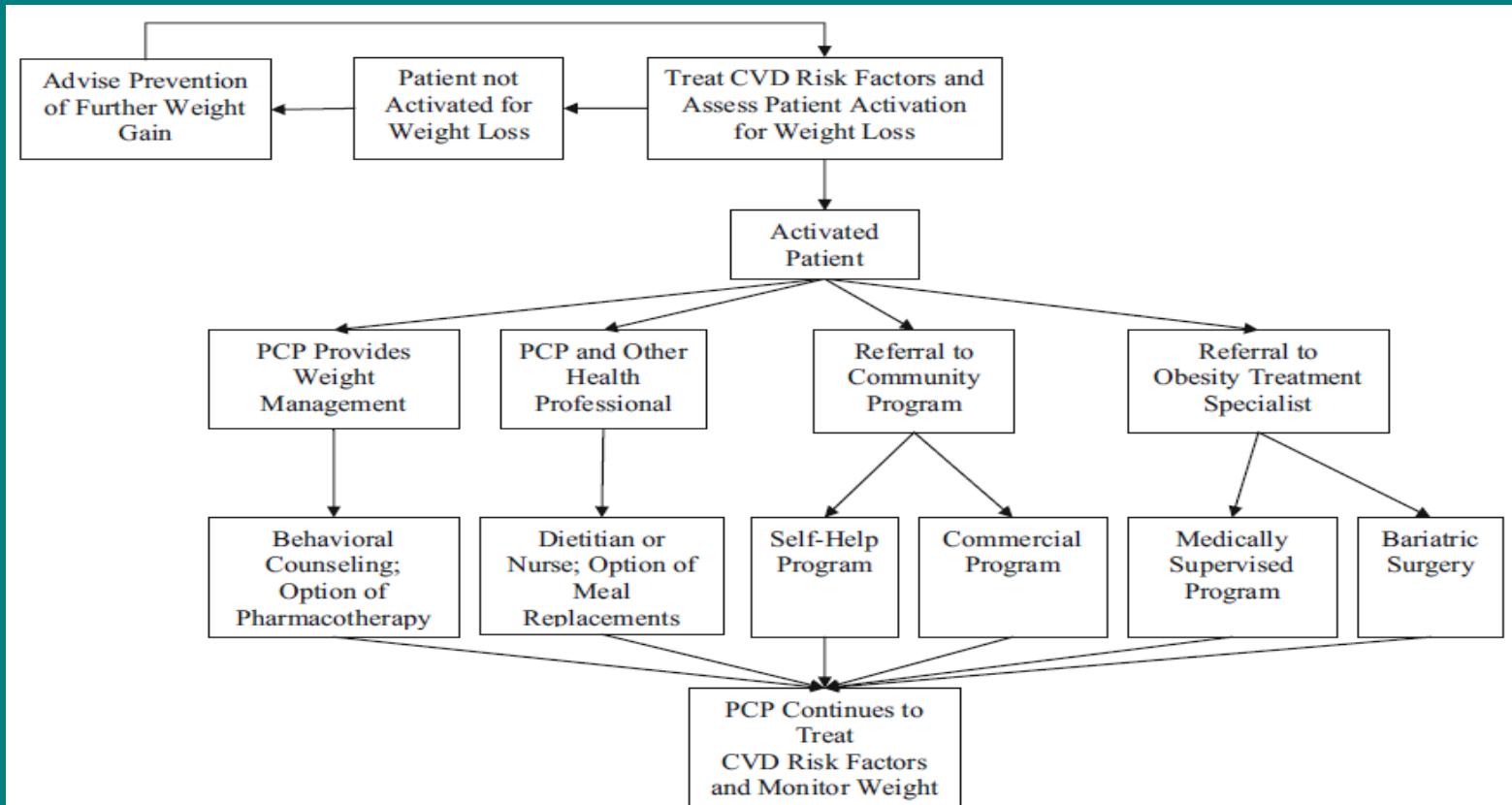


Figure 2. An algorithm for identifying an appropriate weight loss option. After treating cardiovascular disease (CVD) risk factors and assessing patients' activation for weight loss, primary care providers (PCPs) may elect to offer behavioral counseling themselves (with or without pharmacotherapy) or to provide counseling in collaboration with other practice staff. Alternatively, PCPs may refer patients to community programs (e.g., Weight Watchers) or to obesity treatment specialists (e.g., medically supervised programs, bariatric surgery).

# USPSTF recs

- The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians screen all adult patients for obesity and offer intensive counseling and behavioral interventions to promote sustained weight loss for obese adults.
- This is a **grade B recommendation**.

# USPSTF recs

- It is advisable to refer obese patients to programs that offer intensive counseling and behavioral interventions for optimal weight loss
  - High intensity = >1 person-to-person session per month for the first 3 months
  - Medium intensity = monthly
  - Low intensity intervention = < monthly