Treating Obesity in Primary Care

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CERTIFIED DIPLOMATE

- I have no financial disclosures or conflicts of interest
- This session will include discussion of unapproved or investigational uses of products or devices.

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Outline

- Metabolic Adaptation
- AHA/ACC/TOS Guidelines
  - Evaluation
  - Diet
  - Behavioral Lifestyle Intervention
  - Very Low Calorie Diets
  - Surgery
- The Endocrine Society Guidelines
  - Prescription Medications
- AACE/ACE Guideline
  - Exercise
- Summary

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Learning Objectives

- 1) Understand the evaluation and risk/comorbidity discussion for patients with obesity
- 2) Have complete knowledge of the evidence-based and expert guidelines for obesity treatment algorithms
- 3) Obtain knowledge and confidence to safely and appropriately prescribe diet and exercise interventions, prescribe obesity medications, and refer to bariatric surgery

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Speaker's Viewpoint

- ***"Obesity is a chronic disease, as much as hypertension and hyperlipidemia are chronic diseases. Treat it like a chronic disease, and treat it early."***
  - ***-David Rometo***

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Why is Weight Loss and Maintenance So Hard?

Metabolic Adaptation

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Metabolic Slowing with Massive Weight Loss despite Preservation of Fat-Free Mass

Darcy L. Johannsen,* Nicolas D. Knuth,* Robert Huizenga, Jennifer C. Rood, Eric Ravussin, and Kevin D. Hall

- At NIH
  - Body composition: DXA
  - RMR: indirect calorimetry: fasting VO_2 and VCO_2 at rest
  - TEE: Doubly-labeled water: drink $^2H_20$ and $H_2{}^{18}0$, sample urine for 14 days
  - Physical Activity EE: calculated from TEE – RMR minus estimated thermic effect of food (0.1xTEE, or $0.1xTEE_{BL}$-180), all divided by current body weight
- Predicted RMR was calculated according to the following equation developed using baseline data:
  - RMR (kilocalories per day) = 1241 kcal/d + 19.2 (FFM) + 1.8 (FM) – 9.8 (age) + 404 (for males)

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J Clin Endocrinol Metab, July 2012, 97(7):2489–2496

TABLE 2. Biochemical and blood pressure measurements (n = 16)

	Baseline	Wk 30	*P* value
Glucose (mg/dl)	95 ± 15	76 ± 6	<0.001
Insulin (μU/ml)	9.8 ± 8.0	5.1 ± 4.3	0.07
C-peptide (ng/ml)	2.8 ± 1.3	1.4 ± 0.9	0.004
HOMA-IR[a]	2.3 ± 2.1	0.9 ± 0.8	0.03
TAG (mg/dl)	119 ± 77	55 ± 24	0.003
Cholesterol (mg/dl)	168 ± 40	192 ± 48	0.07
LDL (mg/dl)	105 ± 29	126 ± 45	0.07
HDL (mg/dl)	43 ± 17	55 ± 14	0.002
Adiponectin (μg/ml)	2.6 ± 1.2	4.7 ± 1.9	<0.001
Leptin (ng/ml)	42.9 ± 17.8	2.7 ± 2.4	<0.001
Thyroid profile			
T_3 (ng/dl)	94 ± 27	53 ± 15	0.0002
T_4 (μg/dl)	7.3 ± 1.5	6.9 ± 1.4	0.35
TSH (μIU/ml)	1.5 ± 1.2	1.3 ± 0.8	0.6

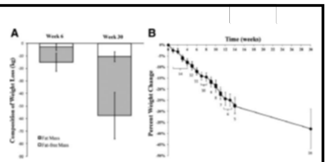

FIG. 1. A, Loss of FFM and FM at wk 6 (n = 11) and wk 30 (n = 16) of the weight-loss competition. The FFM did not decrease significantly from baseline to wk 6 ($P > 0.05$). All other decreases were significant at $P < 0.01$. B, The progression of weight loss over the 30-wk competition. The *numbers below each data point* indicate the number of participants who had their body weight measured at that time and comprise the measurement. At week 13.4, 5 participants were weighed prior to all leaving the ranch; however, only 4 remained in contention and were considered finalists.

- Once in the competition, participants were housed together at an isolated ranch outside Los Angeles.
  - The exercise component of the competition consisted of **90 min/d (6 d/wk)** of directly supervised vigorous circuit training and/or aerobic training. Subjects were encouraged to exercise up to **an additional 3 h/d (9-30 hrs/week).**
  - Dietary intake was not monitored; however, subjects were advised to consume a calorie-restricted diet greater than 70% of their baseline energy requirements as calculated by the following: 21.6 kcal/kg*d x FFM (kilograms) + 370 kcal/d (**2000 kcal/day** for average contestant).
  - Every 7–10 d, a participant was voted out of the competition and returned home to continue their exercise and diet program unsupervised at home. Four participants remained at the ranch by wk 13, at which time they all returned home. At wk 30 (7 months), all the participants returned to Los Angeles for testing, coincident with the live television broadcast.

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TABLE 1. Anthropometrics and energy expenditure

	Entire sample (n = 16)		Wk 6 completers only (n = 11)		
	Baseline	Wk 30	Baseline	Wk 6	Wk 30
Anthropometry					
Body weight (kg)	149.2 (38.0)	91.6 (22.9)[a]	144.9 (39.4)	129.9 (35.2)[a]	86.8 (24.0)[a,b]
BMI (kg/m²)	49.4 (9.4)	30.4 (6.3)[a]	48.7 (10.1)	43.6 (9.1)[a]	29.3 (6.9)[a,b]
Weight change (%)		37.9% (9.1%)		10.3% (1.6%)	39.4% (9.5%)
FFM (kg)	75.7 (20.2)	65.2 (15.5)[a]	73.6 (20.8)	70.7 (19.6)[ns]	62.4 (14.8)[a,b]
FM (kg)	73.5 (21.1)	26.4 (13.8)[a]	71.3 (22.7)	59.1 (19.1)[a]	24.5 (14.0)[a,b]
Body fat (%)	49% (5%)	28% (10%)[a]	49% (6%)	46% (6%)[a]	27% (9%)[a,b]
Weight loss proportion					
FFM (%)		17.4% (7.8%)		17.1% (16.5%)	18.4% (8.4%)
FM (%)		82.6% (7.8%)		82.9% (16.5%)	81.6% (8.4%)
Energy expenditure					
RMR measured (kcal/d)	2679 (624)	1890 (423)[a]	2614 (690)	2258 (441)[a]	1763 (344)[a,b]
RMR predicted (kcal/d)		2393 (466)		2502 (548)	2279 (429)
Metabolic adaptation (kcal/d)		−504 (171)[c] (n = 14)		−244 (231)[c] (n = 9)	−516 (185)[c,d]
TEE (kcal/d)	3900 (957)	3114 (571)[a]	3727 (1035)	4531 (1041)[a]	2906 (540)[a,b]

Data were mean (SD). Metabolic adaptation refers to the change in energy expenditure not explained by changes in FFM and FM, i.e. the difference between actual and predicted values. Predicted values were calculated on the basis of the equation for RMR generated at baseline. ns, Not significant.

[a] $P < 0.05$ compared with baseline.

[b] $P < 0.05$ compared with wk 6.

[c] $P < 0.05$ adaptation different from baseline (zero).

[d] $P < 0.05$ adaptation different from wk 6.

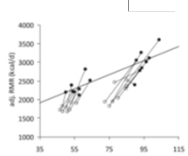

FIG. 2. RMR adjusted for sex, age, and FM (adjusted RMR, kilocalories per day) at baseline (●) and wk 30 (○) of the weight-loss competition (n = 16). The regression line was derived from RMR measurements at baseline in all 16 participants. The deviation from the regression line at wk 30 suggests that RMR per kilogram of FFM was reduced, indicative of metabolic adaptation.

- RMR per kilogram of FFM fell to 29.2 kcal/kg*d after weight loss at wk 30 from a baseline of 36 +/- 4 kcal/kg*d (*P* 0.0001), thereby demonstrating the presence of a substantial "metabolic adaptation" or "adaptive thermogenesis"

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Persistent Metabolic Adaptation 6 Years After "The Biggest Loser" Competition

Erin Fothergill[1], Juen Guo[1], Lilian Howard[1], Jennifer C. Kerns[2], Nicolas D. Knuth[3], Robert Brychta[1], Kong Y. Chen[1], Monica C. Skarulis[1], Mary Walter[1], Peter J. Walter[1], and Kevin D. Hall[1]

	Baseline	End of competition at 30 weeks	Follow-up at 6 years	*P* Baseline vs. 30 weeks	*P* Baseline vs. 6 years	*P* 30 weeks vs. 6 years
Age (years)	34.9 ± 10.3	35.4 ± 10.3	41.3 ± 10.3	<0.0001	<0.0001	<0.0001
Weight (kg)	148.9 ± 40.5	90.6 ± 24.5	131.6 ± 45.3	<0.0001	0.0294	0.0002
BMI (kg/m²)	49.5 ± 10.1	30.2 ± 6.7	43.8 ± 13.4	<0.0001	0.0243	0.0002
% Body fat	49.3 ± 5.2	28.1 ± 8.9	44.7 ± 10	<0.0001	0.0894	0.0003
FM (kg)	73.4 ± 22.6	26.2 ± 13.6	61.4 ± 30	<0.0001	0.0448	0.0001
FFM (kg)	75.5 ± 21.1	64.4 ± 15.5	70.2 ± 18.3	<0.0001	0.0354	0.0101
RQ	0.77 ± 0.05	0.75 ± 0.03	0.81 ± 0.02	0.272	0.0312	<0.0001
RMR measured (kcal/d)	2,607 ± 649	1,996 ± 358	1,903 ± 466	0.0004	<0.0001	0.3481
RMR predicted (kcal/d)	2,577 ± 574	2,272 ± 435	2,403 ± 507	<0.0001	0.0058	0.0168
Metabolic adaptation (kcal/d)	29 ± 206	−275 ± 207	−499 ± 207	0.0061	<0.0001	0.0075
TEE (kcal/d)	3,804 ± 926	3,002 ± 573	3,429 ± 581	0.0014	0.0189	0.0034
Physical activity (kcal/kg/d)	5.6 ± 1.8	10.0 ± 4.6	10.1 ± 4.0	0.0027	0.001	0.8219

- 39% weight loss in 30 weeks
- Gained back 70% of lost weight in 6 years
- Estimates that subjects must be now eating at least 3429 kcal/day,
  - burning 1903 kcal/day RMR, calculated 1329.16 kcal/day from physical activity, and 197 kcal/day from thermic effect of food (0.057xTEE, or $0.1xTEE_{BL}$-184)

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2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Nutrition, American Society for Parenteral and Enteral Nutrition, American Society for Preventive Cardiology, American Society of Hypertension, Association of Black Cardiologists, National Lipid Association, Preventive Cardiovascular Nurses Association, The Endocrine Society, and WomenHeart: The National Coalition for Women With Heart Disease

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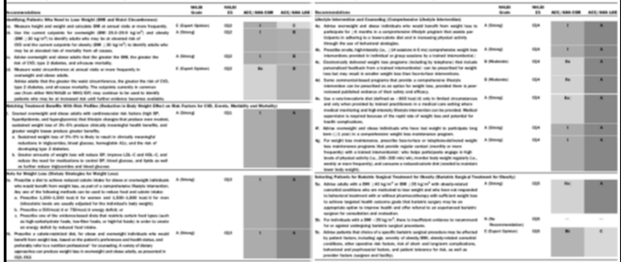

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2013 AHA/ACC/TOS Guideline: Evaluation

Recommendations	NHLBI Grade
Identifying Patients Who Need to Lose Weight (BMI and Waist Circumference)	
1a. Measure height and weight and calculate BMI at annual visits or more frequently.	E (Expert Opinion)
1b. Use the current cutpoints for overweight (BMI 25.0–29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) to identify adults who may be at elevated risk of CVD and the current cutpoints for obesity (BMI ≥30 kg/m^2) to identify adults who may be at elevated risk of mortality from all causes.	A (Strong)
1c. Advise overweight and obese adults that the greater the BMI, the greater the risk of CVD, type 2 diabetes, and all-cause mortality.	A (Strong)
1d. Measure waist circumference at annual visits or more frequently in overweight and obese adults. Advise adults that the greater the waist circumference, the greater the risk of CVD, type 2 diabetes, and all-cause mortality. The cutpoints currently in common use (from either NIH/NHLBI or WHO/IDF) may continue to be used to identify patients who may be at increased risk until further evidence becomes available.	E (Expert Opinion)

- Identify and quantify overweight and obesity by BMI and waist circumference in your patients annually.
  - Discuss risk of CVD, DM, death.

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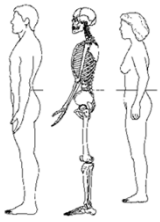
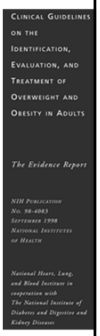
Waist Circumference



Disease Risk* Relative to Normal Weight and Waist Circumference

	BMI (kg/m^2)	Obesity Class	Men ≤ 102 cm (≤ 40 in.) Women ≤ 88 cm (≤ 35 in.)	Men >102 cm (>40 in.) Women >88 cm (>35 in.)
Underweight	18.5		-----	-----
Normal†	18.5 - 24.9		-----	-----
Overweight	25.0 - 29.9		Increased	High
Obesity	30.0 - 34.9	I	High	Very High
	35.0 - 39.9	II	Very High	Very High
Extreme Obesity	≥ 40	III	Extremely High	Extremely High



- Parallel to ground, between ribs and pelvis at mid axillary line
- Useful for risk stratification in patients with BMI 25-35

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2013 AHA/ACC/TOS Guideline: Risk

Matching Treatment Benefits With Risk Profiles (Reduction in Body Weight Effect on Risk Factors for CVD, Events, Morbidity and Mortality)			
2. Counsel overweight and obese adults with cardiovascular risk factors (high BP, hyperlipidemia, and hyperglycemia) that lifestyle changes that produce even modest, sustained weight loss of 3%–5% produce clinically meaningful health benefits, and greater weight losses produce greater benefits. a. Sustained weight loss of 3%–5% is likely to result in clinically meaningful reductions in triglycerides, blood glucose, hemoglobin A1c, and the risk of developing type 2 diabetes; b. Greater amounts of weight loss will reduce BP, improve LDL–C and HDL–C, and reduce the need for medications to control BP, blood glucose, and lipids as well as further reduce triglycerides and blood glucose.	A (Strong)	CQ1	I

- Discuss which conditions they have will improve with weight loss

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2013 AHA/ACC/TOS Guideline: Diet

Diets for Weight Loss (Dietary Strategies for Weight Loss)	
3a. Prescribe a diet to achieve reduced calorie intake for obese or overweight individuals who would benefit from weight loss, as part of a comprehensive lifestyle intervention. Any one of the following methods can be used to reduce food and calorie intake: a. Prescribe 1,200–1,500 kcal/d for women and 1,500–1,800 kcal/d for men (kilocalorie levels are usually adjusted for the individual's body weight); b. Prescribe a 500-kcal/d or 750-kcal/d energy deficit; or c. Prescribe one of the evidence-based diets that restricts certain food types (such as high-carbohydrate foods, low-fiber foods, or high-fat foods) in order to create an energy deficit by reduced food intake.	A (Strong)
3b. Prescribe a calorie-restricted diet, for obese and overweight individuals who would benefit from weight loss, based on the patient's preferences and health status, and preferably refer to a nutrition professional[‡] for counseling. A variety of dietary approaches can produce weight loss in overweight and obese adults, as presented in CQ3, ES2.	A (Strong)

- Whatever will work for that patient to eat significantly less calories, and maintain a diet of restricted calories
- Low-carb for specific metabolic conditions
- All these diets achieve on average 8 kg, or 5-10% weight loss

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2013 AHA/ACC/TOS Guideline: Lifestyle Program

Lifestyle Intervention and Counseling (Comprehensive Lifestyle Intervention)	
4a. Advise overweight and obese individuals who would benefit from weight loss to participate for ≥6 months in a comprehensive lifestyle program that assists participants in adhering to a lower-calorie diet and in increasing physical activity through the use of behavioral strategies.	A (Strong)
4b. Prescribe on-site, high-intensity (i.e., ≥14 sessions in 6 mo) comprehensive weight loss interventions provided in individual or group sessions by a trained interventionist.‡	A (Strong)
4c. Electronically delivered weight loss programs (including by telephone) that include personalized feedback from a trained interventionist‡ can be prescribed for weight loss but may result in smaller weight loss than face-to-face interventions.	B (Moderate)
4d. Some commercial-based programs that provide a comprehensive lifestyle intervention can be prescribed as an option for weight loss, provided there is peer-reviewed published evidence of their safety and efficacy.	B (Moderate)
4e. Use a very-low-calorie diet (defined as <800 kcal/d) only in limited circumstances and only when provided by trained practitioners in a medical care setting where medical monitoring and high-intensity lifestyle intervention can be provided. Medical supervision is required because of the rapid rate of weight loss and potential for health complications.	A (Strong)
4f. Advise overweight and obese individuals who have lost weight to participate long term (≥1 year) in a comprehensive weight loss maintenance program.	A (Strong)
4g. For weight loss maintenance, prescribe face-to-face or telephone-delivered weight loss maintenance programs that provide regular contact (monthly or more frequently) with a trained interventionist‡ who helps participants engage in high levels of physical activity (i.e., 200–300 min/wk), monitor body weight regularly (i.e., weekly or more frequently), and consume a reduced-calorie diet (needed to maintain lower body weight).	A (Strong)

- Recommend 6-month intense lifestyle intervention meeting guideline criteria:
  - 14 visits, achieve significant calorie restriction
- And 1 year maintenance program, monthly
  - 200-300 min/week exercise. Self-monitoring weight and calories.

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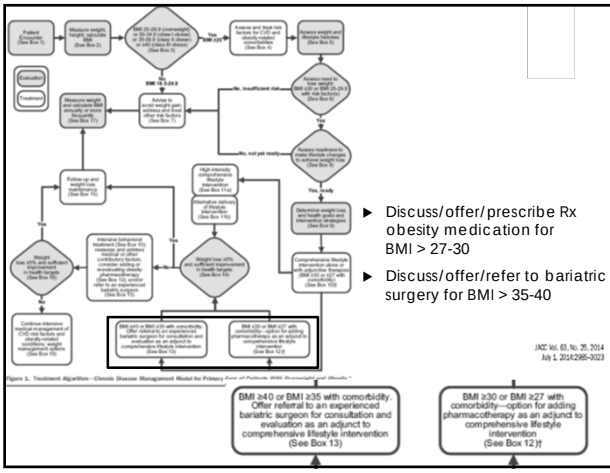

- Discuss/offer/prescribe Rx obesity medication for BMI > 27-30
- Discuss/offer/refer to bariatric surgery for BMI > 35-40

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2013 AHA/ACC/TOS Guideline: Surgery

Selecting Patients for Bariatric Surgical Treatment for Obesity (Bariatric Surgical Treatment for Obesity)	
5a. Advise adults with a BMI $\geq$40 kg/m^2 or BMI $\geq$35 kg/m^2 with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment with or without pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery may be an appropriate option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.	A (Strong)
5b. For individuals with a BMI <35 kg/m^2, there is insufficient evidence to recommend for or against undergoing bariatric surgical procedures.	N (No Recommendation)
5c. Advise patients that choice of a specific bariatric surgical procedure may be affected by patient factors, including age, severity of obesity/BMI, obesity-related comorbid conditions, other operative risk factors, risk of short- and long-term complications, behavioral and psychosocial factors, and patient tolerance for risk, as well as provider factors (surgeon and facility).	E (Expert Opinion)

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- Example: Patient loses 9% of their weight (BMI now 36), and still has T2DM requiring insulin and an A1C of 8. Patient wants diabetes remission (A1C < 6.5 off meds)
  - Discuss/refer to bariatric surgeon for gastric bypass (more remission vs sleeve or band)

2013 AHA/ACC/TOS Guideline: VLCD

Lifestyle Intervention and Counseling (Comprehensive Lifestyle Intervention)	
4e. Use a very-low-calorie diet (defined as <800 kcal/d) only in limited circumstances and only when provided by trained practitioners in a medical care setting where medical monitoring and high-intensity lifestyle intervention can be provided. Medical supervision is required because of the rapid rate of weight loss and potential for health complications.	A (Strong)

- Usually meal replacements (protein bars and shakes)
- Risks of gall stones, gout, electrolyte abnormalities, complications from not stopping/reducing BP and DM meds

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A Multicenter Evaluation of a Proprietary Weight Reduction Program for the Treatment of Marked Obesity

Thomas A. Wadden, PhD; Gary D. Foster, MS; Kathleen A. Letizia; Albert J. Stunkard, MD

- 517 patients in 18 clinics
  - weekly 60–75 min groups of 10–12 persons. 26 weeks of treatment
  - led by masters or doctoral-level counselors
- Week 1: 1200 -1500 kcal/day
- Week 2-13: 420-800 kcal/day
  - 70 g protein, <2-13 g fat, 30-100 g carb
  - Higher kcal for men and higher weights
- Week 14-19: refeed up to 1000 - 1200 kcal
- Week 20-26: 1200 -1800 kcal/day

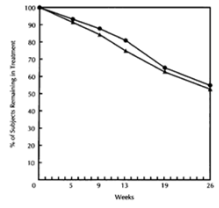
Table 1.—Baseline Characteristics of Women and Men Participating in the Study*

Variable	Women (N = 407)	Men (N = 110)
Age, y	40.9 ± 0.6	42.3 ± 1.0
Weight, kg	102.1 ± 0.9	128.7 ± 2.3†
Height, cm	164.6 ± 0.3	179.4 ± 0.7†
BMI, kg/m^2	37.6 ± 0.3	39.9 ± 0.7†

*BMI indicates body mass index.
†Difference between sexes are significant at $P<.0001$.

Arch Intern Med. 1992;152:961-966

OPTIFAST: Results



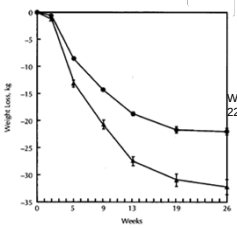


Table 2.—Mean Weight Losses and Number of Treatment Sessions Attended for Men and Women Who Completed and Did Not Complete Treatment*

Patient Group	N	Weight Loss, kg	No. of Visits
Women			
Total Sample	407	19.2 ± 0.5	17.8 ± 0.3
Completing treatment	226	22.0 ± 0.6	21.8 ± 0.4
Not completing treatment	181	14.3 ± 0.7†	11.7 ± 0.5†
Men			
Total Sample	110	27.0 ± 1.2	17.0 ± 0.7
Completing treatment	59	32.1 ± 1.4	21.6 ± 0.6
Not completing treatment	51	20.0 ± 1.6†	11.1 ± 0.8†

- 118 were followed for 1 year after end of 26 week treatment.
- They had lost 24.8 kg during treatment, and gained back 9.5 kg in the next 13 months (net 15.3 kg loss at 1.5 years)
  - 21% maintained initial weight loss
  - **59% maintained > 10 kg loss**
    - **>10% weight loss for 102.1 kg women**
  - 11% regained all or more weight lost

***Arch Intern Med.* 1992;152:961-966**

Primary care-led weight management for remission of type diabetes (DiRECT): an open-label, cluster-randomised trial

Michael E J Lean*, Wilma S Leslie, Alison C Barnes, Naomi Brosnahan, George Thom, Louise McCombie, Carl Peters, Svastiana Zhyzhneuskaya, Ahmad Al-Mrabeh, Kieren G Hollingsworth, Angela M Rodgers, Lucia Rehackova, Ashley J Adamson, Falko F Sniehotta, John C Mathers, Hazel M Ross, Yvonne McIlvenna, Renae Stefanetti, Michael Trimble, Paul Welsh, Sharon Kean, Ian Ford, Alex McConnachie, Naveed Sattar, Roy Taylor

- Aim for at least 15 kg loss
- 825-853 kcal/day
  - 59% carbohydrate, 13% fat, 26% protein (53-56 g), 2% fibre
  - ALL meds for DM and BP were stopped on day 1. Reintroduced as needed per protocol
  - Visit after 1st week, then every 2 weeks
- For 3 months, up to 5 months at participant request
  - No increase in activity during this phase
- 2-8 weeks food reintroduction: 50/35/15 C/P/F
  - Given step counters, aim for sustainable maximum up to 15,000/day
  - Visit every 2 weeks
- Monthly weight maintenance visits
  - Up to 2 years
  - 1 meal replacement included.

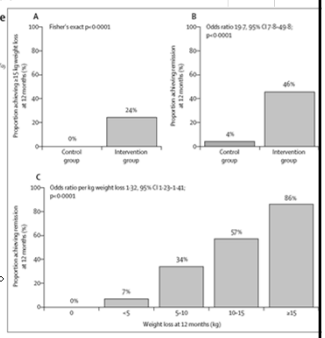
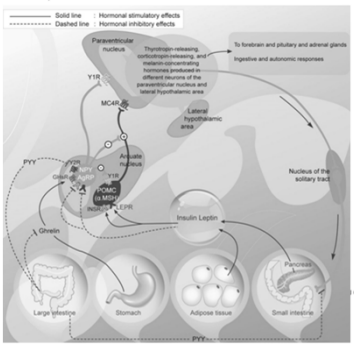


Figure 2: **Primary outcomes and remission of diabetes in relation to weight loss at 12 months**
(A) First co-primary outcome: achievement of at least 15 kg weight loss at 12 months. (B) Second co-primary outcome: remission of diabetes (glycated haemoglobin <6·5% [48 mmol/mol], off antidiabetic medication for 2 months). (C) Remission of diabetes, in relation to weight loss achieved at 12 months (both groups combined).

Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline

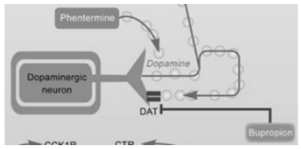
Caroline M. Apovian, Louis J. Aronne, Daniel H. Bessesen, Marie E. McDonnell, M. Hassan Murad, Uberto Pagotto, Donna H. Ryan, and Christopher D. Still



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

Endocrine Society Guideline:

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Phentermine resin	Adipex-P (37.5 mg), 37.5 mg/d Ionamin (30 mg), 30–37.5 mg/d	Norepinephrine-releasing agent	3.6 kg (7.9 lb); 2–24 wk	Approved in 1960s for short-term use (3 mo)	Headache, elevated BP, elevated HR, insomnia, dry mouth, constipation, anxiety Cardiovascular: palpitation, tachycardia, elevated BP, ischemic events Central nervous system: overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache, psychosis Gastrointestinal: dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances Allergic: urticaria Endocrine: impotence, changes in libido	Anxiety disorders (agitated states), history of heart disease, uncontrolled hypertension, seizure, MAO inhibitors, pregnancy and breastfeeding, hyperthyroidism, glaucoma, history of drug abuse, sympathomimetic amines

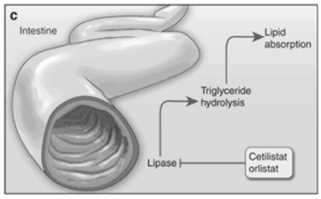


J Clin Endocrinol Metab, February 2015, 100(2):342–362

02HERD

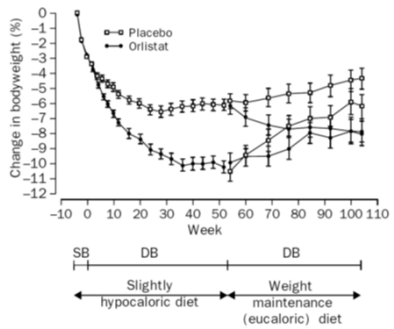
Endocrine Society Guideline: Orlistat

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Orlistat, prescription (120 mg)	120 mg TID	Pancreatic and gastric lipase inhibitor	2.9–3.4 kg (6.4–7.5 lb), 2.9–3.4%; 1 y	FDA approved in 1999 for chronic weight management	Decreased absorption of fat-soluble vitamins, steatorrhea, oily spotting, flatulence with discharge, fecal urgency, oily evacuation, increased defecation, fecal incontinence	Cyclosporine (taken 2 h before or after orlistat dose), chronic malabsorption syndrome, pregnancy and breastfeeding, cholestasis, levothyroxine, warfarin, antiepileptic drugs



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

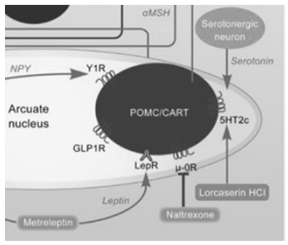
Orlistat



THE LANCET • Vol 352 • July 18, 1998

Endocrine Society Guideline: Lorcaserin

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Lorcaserin (10 mg)	10 mg BID	5HT2c receptor agonist	3.6 kg (7.9 lb), 3.6%; 1 y	FDA approved in 2012 for chronic weight management	Headache, nausea, dry mouth, dizziness, fatigue, constipation	Pregnancy and breastfeeding **Use with caution:** SSRI, SNRI/MAOI, St John's wort, triptans, bupropion, dextromethorphan



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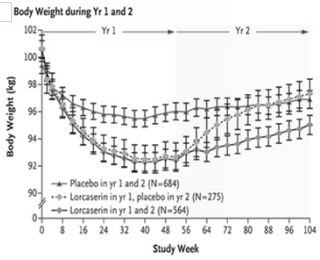
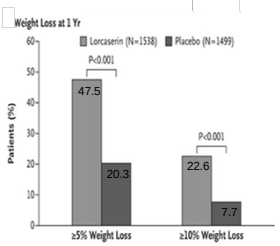
Lorcaserin



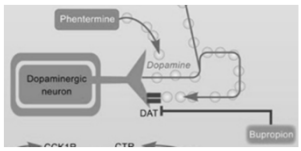


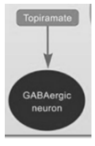
NEJM, Smith et al, July 2010

02HERD

Endocrine Society Guideline: Phentermine/Topiramate

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Phentermine (P)/ topiramate (T)	3.75 mg P/23 mg T ER QD (starting dose) 7.5 mg P/46 mg T ER daily 15 mg P/92 mg P/T ER daily (high dose)	GABA receptor modulation (T) plus norepinephrine-releasing agent (P)	6.6 kg (14.5 lb) (recommended dose), 6.6% 8.6 kg (18.9 lb) (high dose), 8.6%; 1 y	FDA approved in 2012 for chronic weight management	Insomnia, dry mouth, constipation, paraesthesia, dizziness, dysgeusia	Pregnancy and breastfeeding, hyperthyroidism, glaucoma, MAO inhibitor, sympathomimetic amines

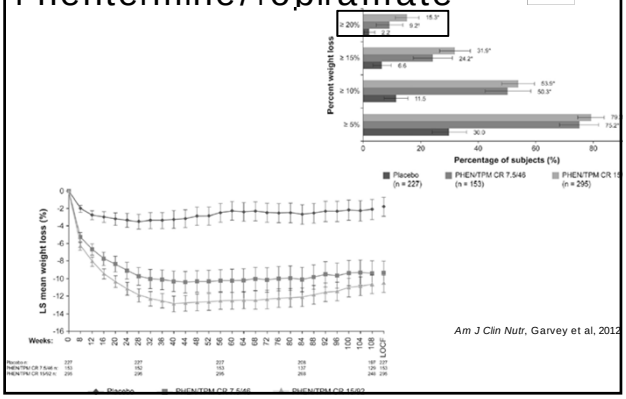




J Clin Endocrinol Metab, February 2015, 100(2):342–362

02HERD

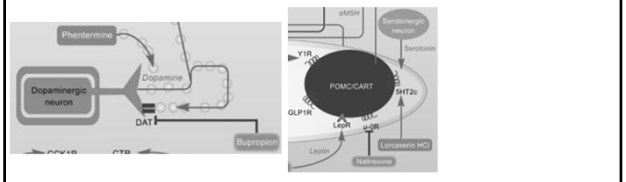
Phentermine/Topiramate



Am J Clin Nutr, Garvey et al, 2012

Endocrine Society Guideline: Naltrexone/Bupropion

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Naltrexone/ bupropion	32 mg/360 mg 2 tablets QID (high dose)	Reuptake inhibitor of dopamine and norepinephrine (bupropion) and opioid antagonist (naltrexone)	4.8%; 1y (Ref. 79)	FDA approved in 2014 for chronic weight management	Nausea, constipation, headache, vomiting, dizziness	Uncontrolled hypertension, seizure disorders, anorexia nervosa or bulimia, drug or alcohol withdrawal, MAO inhibitors



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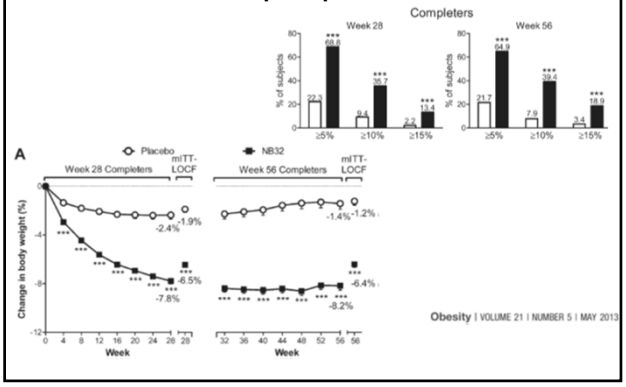
J Clin Endocrinol Metab, February 2015, 100(2):342–362

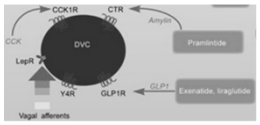
Naltrexone/Bupropion

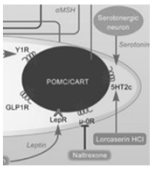


Obesity | VOLUME 21 | NUMBER 5 | MAY 2013

Endocrine Society Guideline: Liraglutide

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg[a]; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Liraglutide	3.0 mg injectable	GLP-1 agonist	5.8 kg; 1 y (Ref. 30, 31)	FDA approved in 2014 for chronic weight management	Nausea, vomiting, pancreatitis	Medullary thyroid cancer history, multiple endocrine neoplasia type 2 history



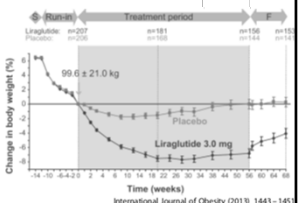


- Dorsal Vagal Complex

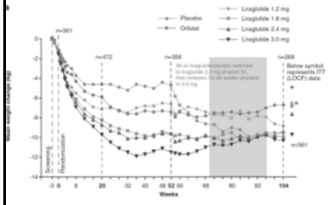
J Clin Endocrinol Metab, February 2015, 100(2):342–362

02HERD

Liraglutide



International Journal of Obesity (2013) 1443–1451

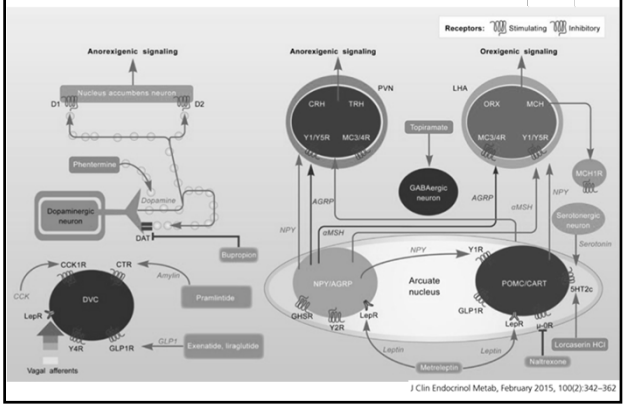


International Journal of Obesity (2012) 36, 843–854

02HERD

Off-Label Prescription

- Phentermine alone, long-term
  - Controlled substance, so paper script every 6 months
  - Neither I nor any obesity medicine physician I have ever met has concerns about addiction or abuse of this drug
- Generic phentermine + generic topiramate
  - Near equivalent of full dose Qsymia would be phentermine 15 mg PO daily, and topiramate 50 mg PO BID
- Generic bupropion + generic naltrexone
  - Near equivalent of full dose Contrave would be bupropion SR 150 mg BID, and naltrexone 12.5 mg (1/4 tab) BID-TID
  - Difficult to gradually titrate up naltrexone ¼ tabs to avoid nausea/vomiting and discontinuation
- Victoza at 3.0 mg/day with or without DM
  - 1.8 sc then 1.2 sc qAM, or BID
  - Affordability? Insurance denial?
- Generic bupropion alone
- Generic topiramate alone
- Generic metformin



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

Change Weight-Gain Drugs

2.0 Drugs that cause weight gain and some alternatives

A variety of prescription medications have been associated with weight gain. Drug-induced weight gain is a preventable cause of obesity. For all patients, and particularly for patients who have a BMI > 27 kg/m^2 with comorbidities or BMI > 30 kg/m^2, the desired level of clinical efficacy for a chosen therapy should be balanced against side effects, including the likelihood of weight gain. In cases where there are no acceptable therapeutic alternatives, the minimal dose required to produce clinical efficacy may prevent drug-induced weight gain. Patients' initial weight status, the presence of risk factors for cardiovascular disease, diabetes, and other obesity-related health complications, as well as the benefits of pharmacological therapies warrant careful consideration when prescribing a first-line therapy or change in medication.

2.1 We recommend weight-losing and weight-neutral medications as first- and second-line agents in the management of a patient with T2DM who is overweight or obese. (1|⊕⊕⊕○)

2.2 In obese patients with T2DM requiring insulin therapy, we suggest adding at least one of the following: metformin, pramlintide, or GLP-1 agonists to mitigate associated weight gain due to insulin. The first-line insulin for this type of patient should be basal insulin. This is preferable to using either insulin alone or insulin with a sulfonylurea. We also suggest that the insulin therapy strategy be considered a preferential trial of basal insulin prior to premixed insulins or combination insulin therapy. (2|⊕⊕⊕○)

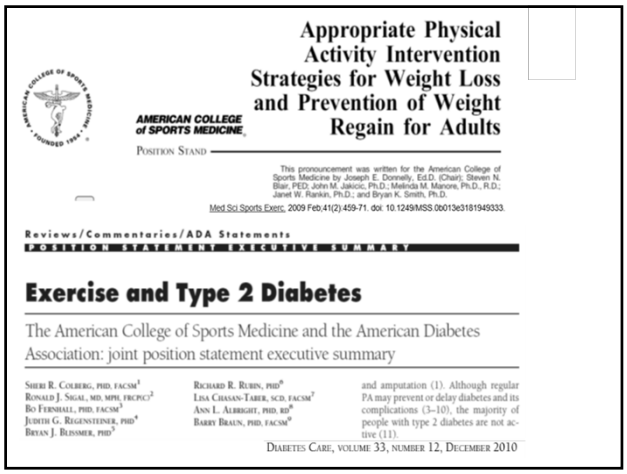
- Change current medications to favor weight loss

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

Change Weight-Gain Drugs

Class	Weight Loss	Weight Neutral	Weight Gain
Diabetes	Metformin GLP-1 agonists Pramlintide SGLT2-inhibitors	DPP4-inhibitors	Insulin Sulfonylureas TZDs
Hypertension		ACE-I/ARB CCBs	**Beta-Blockers**
Antidepressants	Bupropion (Wellbutrin) (Sertraline/Zoloft) (fluoxetine/Prozac)		Paroxetine (Paxil) Amitriptyline
Antipsychotics			aripiprazole (Abilify), lurasidone (Latuda), ziprasidone (Geodon) cause least clozapine (Clozaril) and olanzapine (Zyprexa) cause most
Antiepileptics	Felbamate **Topiramate** (migraine prophylaxis) zonisamide	Lamotrigine Levetiracetam phenytoin	gabapentin, pregabalin, valproic acid, vigabatrin, carbamazepine.

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



Appropriate Physical Activity Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults

AMERICAN COLLEGE of SPORTS MEDICINE

POSITION STAND

This pronouncement was written for the American College of Sports Medicine by Joseph E. Donnelly, Ed.D. (Chair); Steven N. Blair, PED; John M. Jakicic, Ph.D.; Melinda M. Manore, Ph.D., R.D.; Janet W. Rankin, Ph.D.; and Bryan K. Smith, Ph.D.

Med Sci Sports Exerc. 2009 Feb;41(2):459-71. doi: 10.1249/MSS.0b013e3181949333.

Reviews/Commentaries/ADA Statements

POSITION STATEMENT EXECUTIVE SUMMARY

Exercise and Type 2 Diabetes

The American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary

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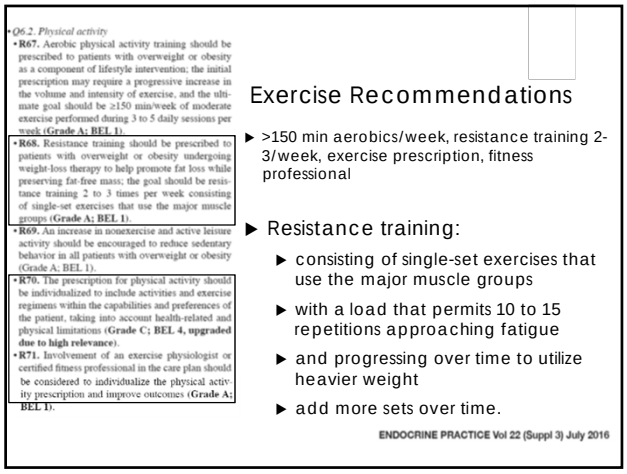
and amputation (1). Although regular PA may prevent or delay diabetes and its complications (3–10), the majority of people with type 2 diabetes are not active (11).

DIABETES CARE, VOLUME 33, NUMBER 12, DECEMBER 2010



• *Q6.2. Physical activity*

• **R67.** Aerobic physical activity training should be prescribed to patients with overweight or obesity as a component of lifestyle intervention; the initial prescription may require a progressive increase in the volume and intensity of exercise, and the ultimate goal should be ≥150 min/week of moderate exercise performed during 3 to 5 daily sessions per week **(Grade A; BEL 1)**.

• **R68.** Resistance training should be prescribed to patients with overweight or obesity undergoing weight-loss therapy to help promote fat loss while preserving fat-free mass; the goal should be resistance training 2 to 3 times per week consisting of single-set exercises that use the major muscle groups **(Grade A; BEL 1)**.

• **R69.** An increase in nonexercise and active leisure activity should be encouraged to reduce sedentary behavior in all patients with overweight or obesity (Grade A; BEL 1).

• **R70.** The prescription for physical activity should be individualized to include activities and exercise regimens within the capabilities and preferences of the patient, taking into account health-related and physical limitations **(Grade C; BEL 4, upgraded due to high relevance)**.

• **R71.** Involvement of an exercise physiologist or certified fitness professional in the care plan should be considered to individualize the physical activity prescription and improve outcomes **(Grade A; BEL 1)**.

Exercise Recommendations

- >150 min aerobics/week, resistance training 2-3/week, exercise prescription, fitness professional
- Resistance training:
  - consisting of single-set exercises that use the major muscle groups
  - with a load that permits 10 to 15 repetitions approaching fatigue
  - and progressing over time to utilize heavier weight
  - add more sets over time.

ENDOCRINE PRACTICE Vol 22 (Suppl 3) July 2016

In Summary

- Identify and quantify overweight and obesity by BMI and waist circumference in your patients annually.
  - Discuss risk of CVD, DM, death.
  - Discuss which conditions they have will improve with weight loss
- Change current medications to favor weight loss
- Recommend 6-month intense lifestyle intervention meeting guideline criteria:
  - 14 visits, achieve significant calorie restriction, >150 min aerobics/week, resistance training 2-3/week, exercise prescription, fitness professional
- 1 year maintenance program, monthly
  - 200-300 min/week exercise. Self-monitoring weight and calories.
- Discuss/offer/prescribe Rx obesity medication for BMI > 27-30
- Discuss/offer/refer to bariatric surgery for BMI > 35-40
- **Obesity is a chronic disease, as much as hypertension and hyperlipidemia are chronic diseases. Treat it like a chronic disease, and treat it early.**

Alternative Viewpoint

- **"Many chronic diseases are caused by 1) obesity, 2) the behaviors that result in obesity, and 3) the behaviors that result from obesity.**
- **Treatment for these diseases include weight loss and the behaviors that result in weight loss and weight loss maintenance.**
- **These diseases should be treated in primary care through prescribing interventions that result in these behaviors, weight loss and weight loss maintenance.**
  - ***-David Rometo***

Weight Loss Goals and Appropriate Prescriptions

- 5%:
  - Lifestyle program 1200-1500 or 1500-1800 kcal/day
- 10%:
  - Lifestyle program 1200-1500 kcal plus phentermine/topiramate or liraglutide
- 15-25%:
  - VLCD with meal replacements
- 30-50%:
  - Gastric bypass or Sleeve gastrectomy

Behavior/Habit Plan: In Order

- Eat low glycemic index foods.
- Replace 1-2 meals/day (Atkins meal replacement bar, shake, Quest bar, SlimFast Advanced Nutrition High Protein, Premier Protein shake)
- Get and wear pedometer or activity monitor (Fitbit, Jawbone, etc.).
- Keep steps and exercise log daily.
- Get 10,000 steps/day.
- Increase aerobic exercise to achieve 150-300 minutes per week. Can be 10-minute walks.
- Resistance training 2-3 days/week.
- Keep food/calorie log daily on MyFitnessPal app.
- Use measuring cup and food scale.
- Do not exceed 1500 calories per day.
- Weigh self daily, and keep log.
- Bring logs to all follow-up visits.

Questions?

02HERD