Overcoming Obstacles in Obesity Management: New Tools, Techniques, and Treatment Strategies

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- During the panel discussion, please use the Question Cards located on each table.
- Complete and return a CME Evaluation Form at the conclusion of the symposium.

Opening Remarks and Introductions

Louis J. Aronne, MD
Sanford I. Weill Professor of Metabolic Research
Medical Director
Center for Weight Management & Metabolic Clinical Research
Weill-Cornell Medical College
New York, NY

Obesity Treatment Update: Where Are We Now?

Harold Bays, MD, FTOS, FACC, FACE, FNLA
Medical Director/President
Louisville Metabolic and Atherosclerosis Research Center
Louisville, KY

Topics

- Obesity as a treatable disease
- Adopting a weight-centric approach to cardiometabolic disease prevention and management
- Obesity and its adverse consequences (“comorbidities”)
- Updated clinical practice guidelines in the management of overweight/obese
- Overview of current pharmacologic therapies
- Utilizing a multidisciplinary team approach to manage obesity

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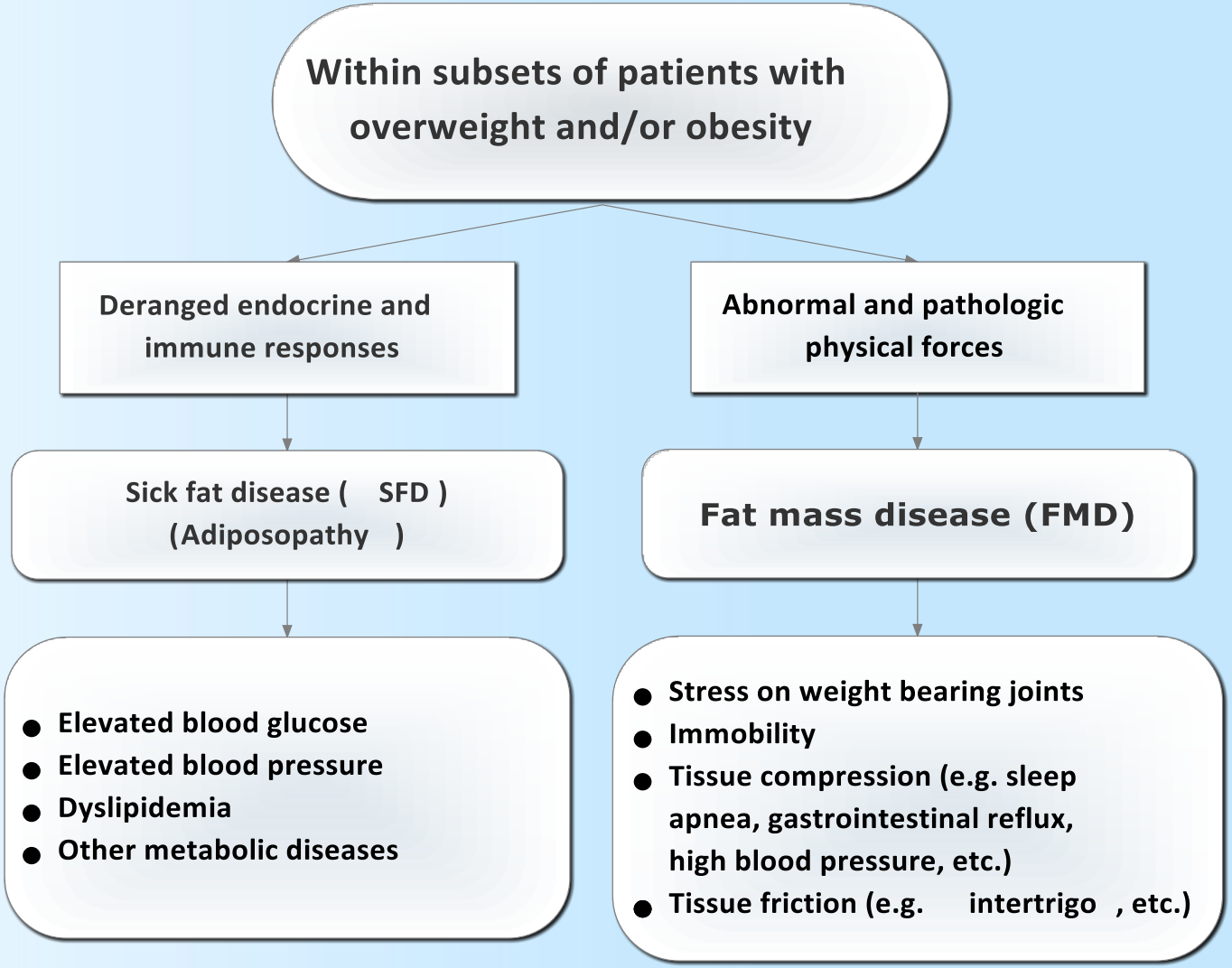
Obesity as a disease



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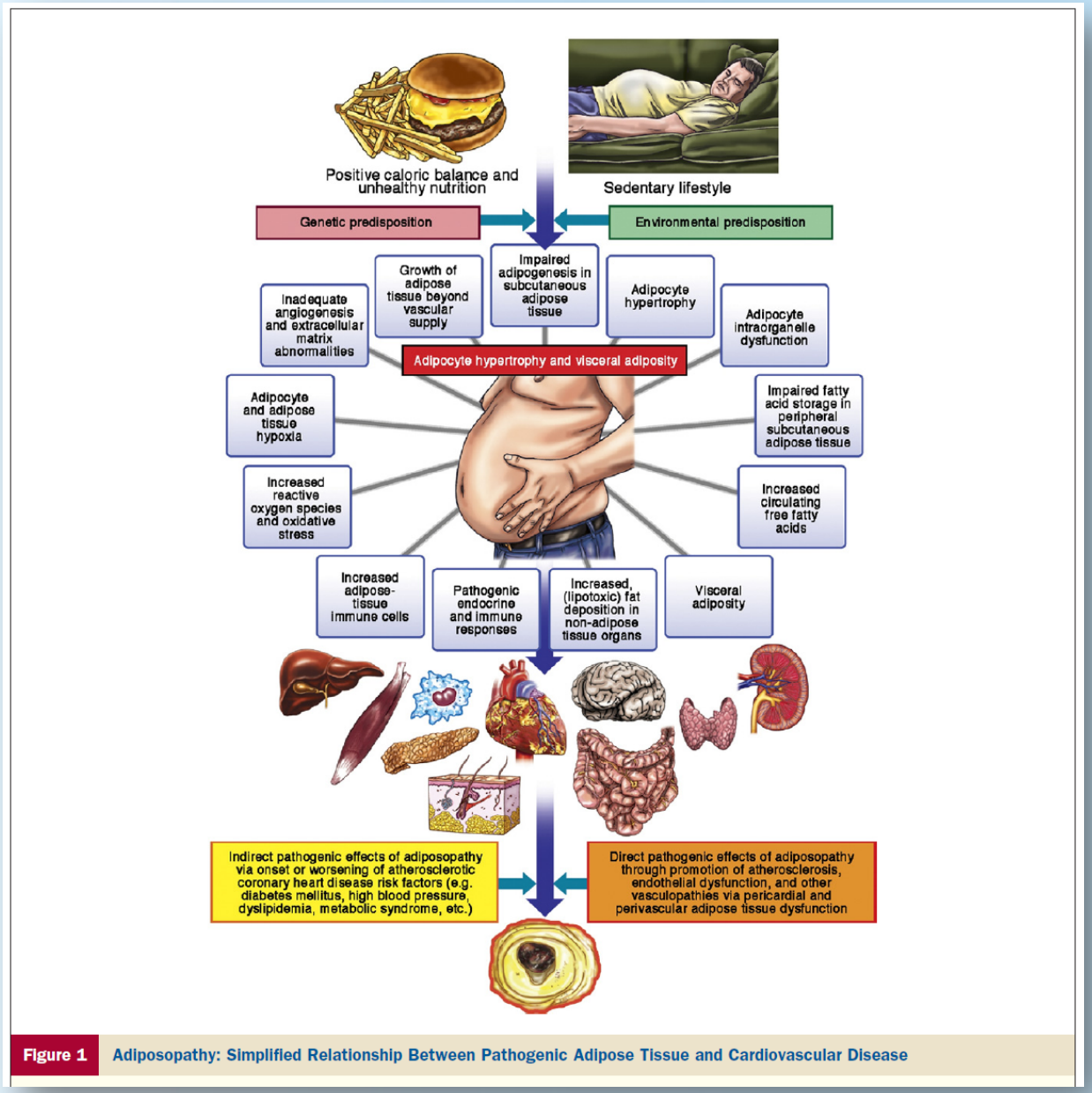

Figure 1 Adiposopathy: Simplified Relationship Between Pathogenic Adipose Tissue and Cardiovascular Disease

Bays. Adiposopathy: is sick fat a cardiovascular disease? JACC 2011;57:2461-73.

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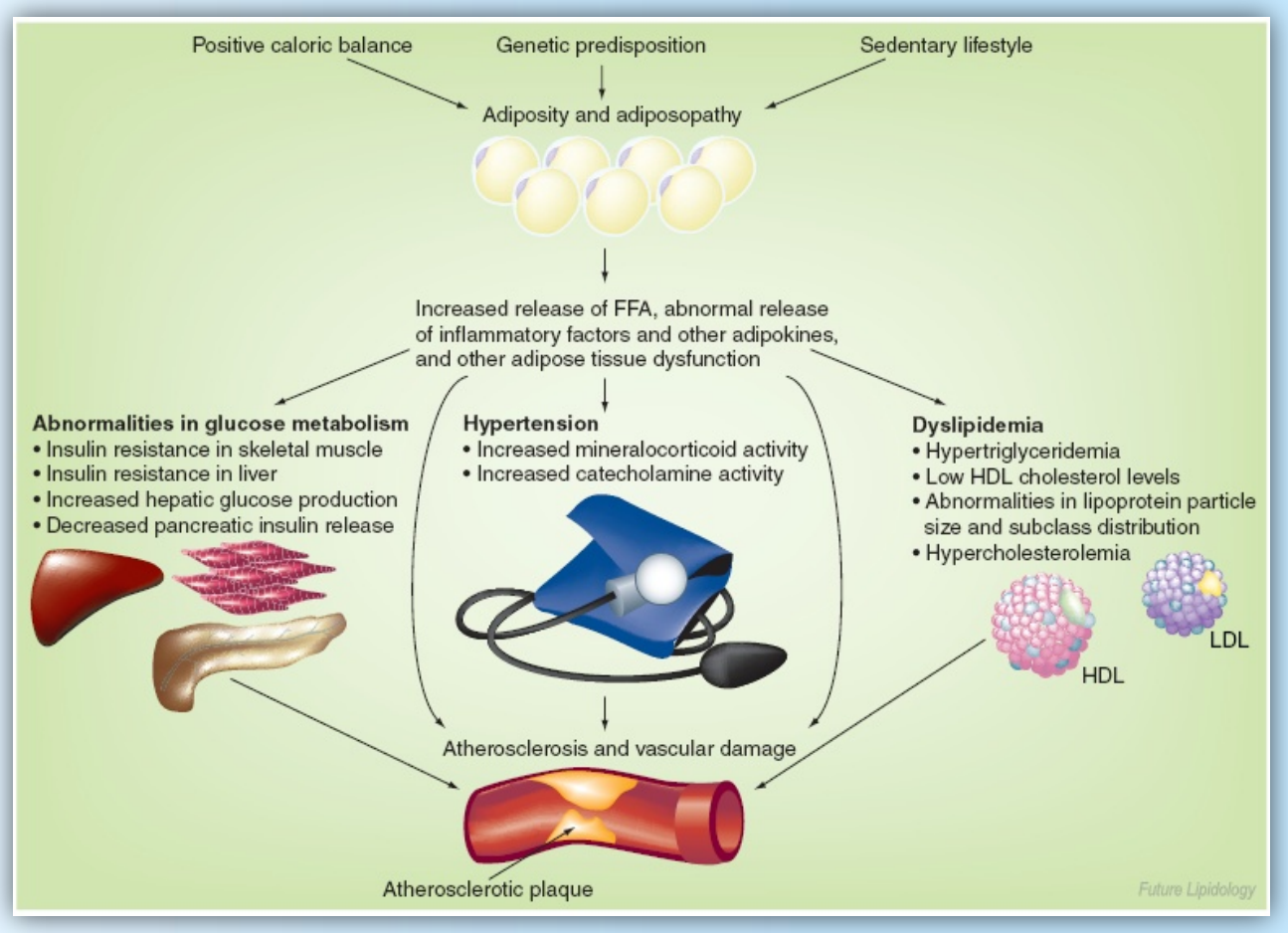
Adiposopathy and Cardiovascular Disease Risk



Bays et al. Future Lipidology. 2006;1:389-420.
Kalant et al. Can J Diabetes. 2003;27:154-71.
Pausova. Curr Opin Nephrol Hypertens. 2006;15:173-78.
Landsberg . Cell Mol Neurobiol. 2006;26:497-508.
Yu et al. Circ Res. 2005;96:1042-52.

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Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity
Report of the American College of Cardiology/American Heart Association Tas
Practice Guidelines and The Obesity Society

Michael D. Jensen, Donna H. Ryan, Caroline M. Apovian, Jamy D. Ard, Anthony G
Karen A. Donato, Frank B. Hu, Van S. Hubbard, John M. Jakicic, Robert F. Kushner,
Loria, Barbara E. Millen, Cathy A. Nonas, F. Xavier Pi-Sunyer, June Stevens, Victo
Thomas A. Wadden, Bruce M. Wolfe and Susan Z. Yanovski

Circulation. published online November 12, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, T

Print ISSN: 0009-7322. Online ISSN: 1524-4539

American Society of Bariatric Physicians (ASBP)

Obesity Algorithm™

Citation:

Seger JC, Horn DB, Westman EC, Lindquist R, Scinta W, Richardson LA, Primack C, Bryman DA, McCarthy W, Hendricks E, Sabowitz BN, Schmidt SL, Bays HE. Obesity Algorithm, presented by the American Society of Bariatric Physicians. www.obesityalgorithm.org (Accessed = [insert date])

Position Paper

Obesity-Related Hypertension: Pathogenesis, Cardiovascular Risk, and Treatment—A Position Paper of the *The Obesity Society* and the *American Society of Hypertension*

Lewis Landsberg, MD[1], Louis J. Aronne, MD[2], Lawrence J. Beilin, MB, BS, M
Leon I. Igel, MD[2], Donald Lloyd-Jones, MD, ScM[1] and James Sowers, MD[4]

Complications-Centric Model for Care of the Overweight/Obese Patient

Obesity, adiposity, and dyslipidemia: A consensus statement from the National Lipid Association

Harold E. Bays, MD, FNLA, Chair*, Peter P. Toth, MD, PhD, FNLA, Co-Chair,
Penny M. Kris-Etherton, PhD, RD, FNLA, Co-Chair, Nicola Abate, MD, Louis J. Aronne, MD,
W. Virgil Brown, MD, FNLA, J. Michael Gonzalez-Campoy, MD, PhD,
Steven R. Jones, MD, FNLA, Rekha Kumar, MD, Ralph La Forge, MSc, FNLA,
Varman T. Samuel, MD, PhD

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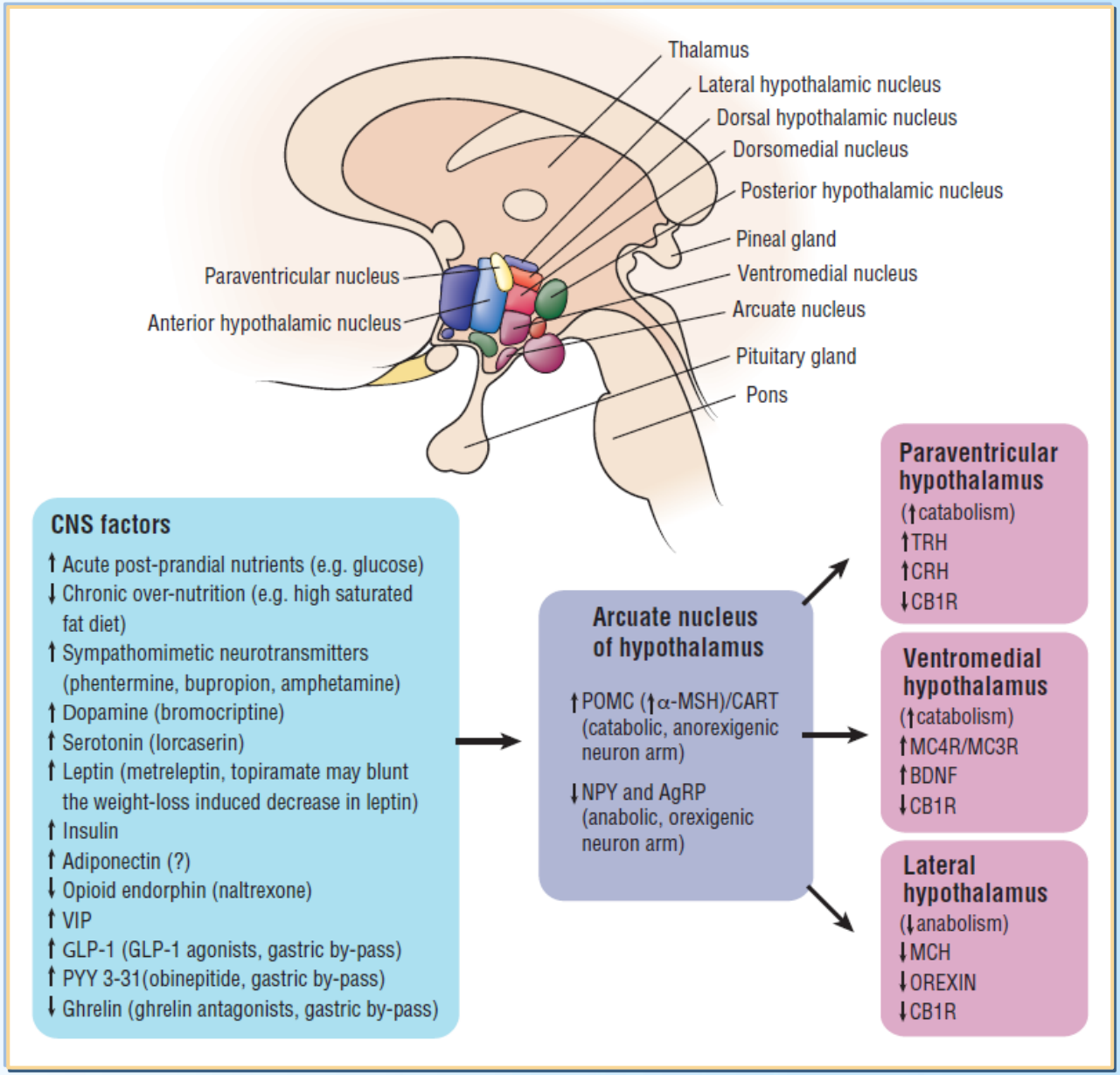
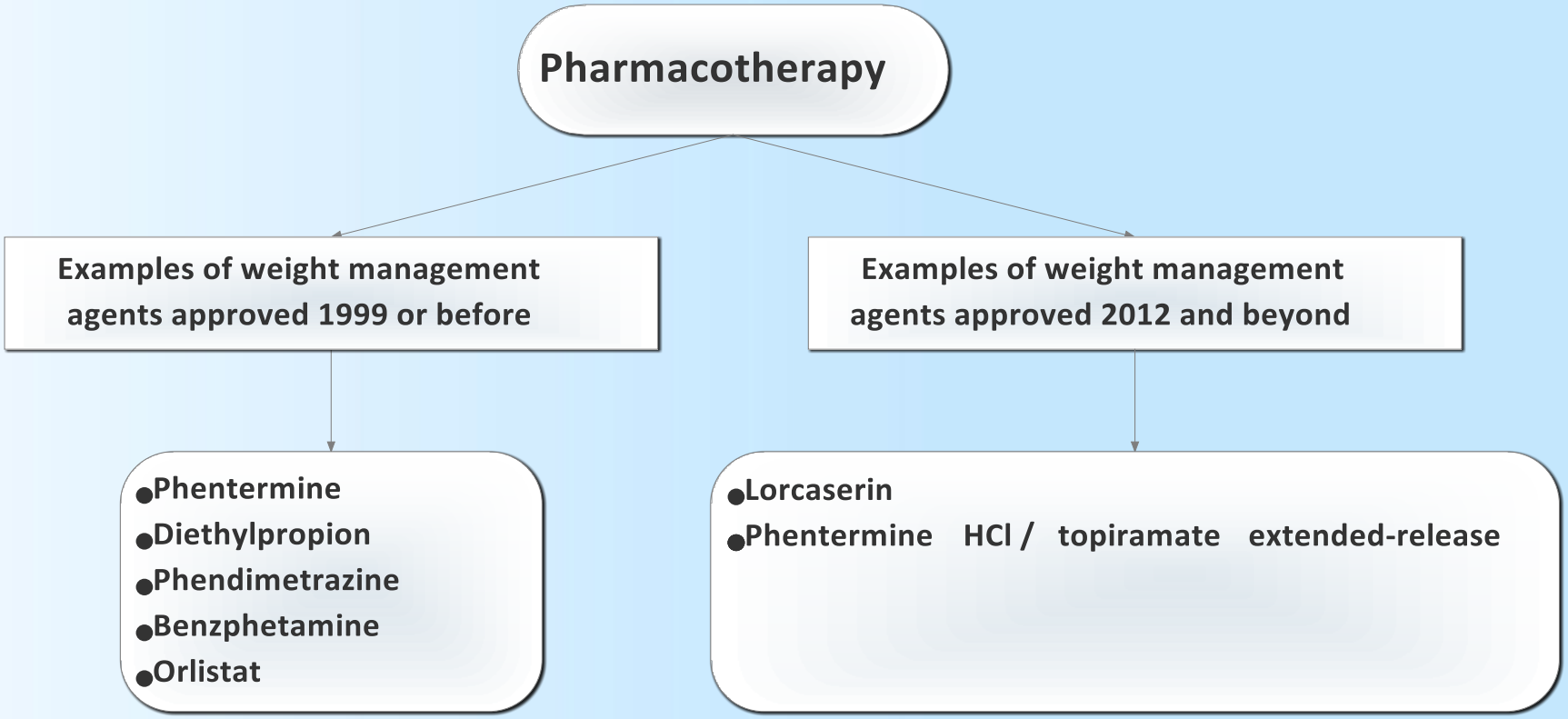


- AgRP = agouti-related protein;
- α-MSH = α-melanocyte-stimulating hormone;
- BDNF = brain-derived neurotrophic factor;
- CART =cocaine and amphetamine-regulated transcript;
- CB1R = cannabinoid receptor type 1;
- CNS = central nervous system;
- CRH = corticotropin-releasing hormone;
- GLP-1 = glucagon-like peptide-1;
- MC3R = melanocortin-3 receptor;
- MC4R = melanocortin-4 receptor;
- CH = melanin-concentrating hormone;
- NPY = neuropeptide Y;
- POMC = proopiomelanocortin;
- TRH = thyrotropin-releasing hormone;
- VIP = vasoactive intestinal peptide.

Bays. Am J Cardiol.2012;doi: 10.1016/j.amjcard.2012.08.029.

Treatment



Treatment

Pharmacotherapy

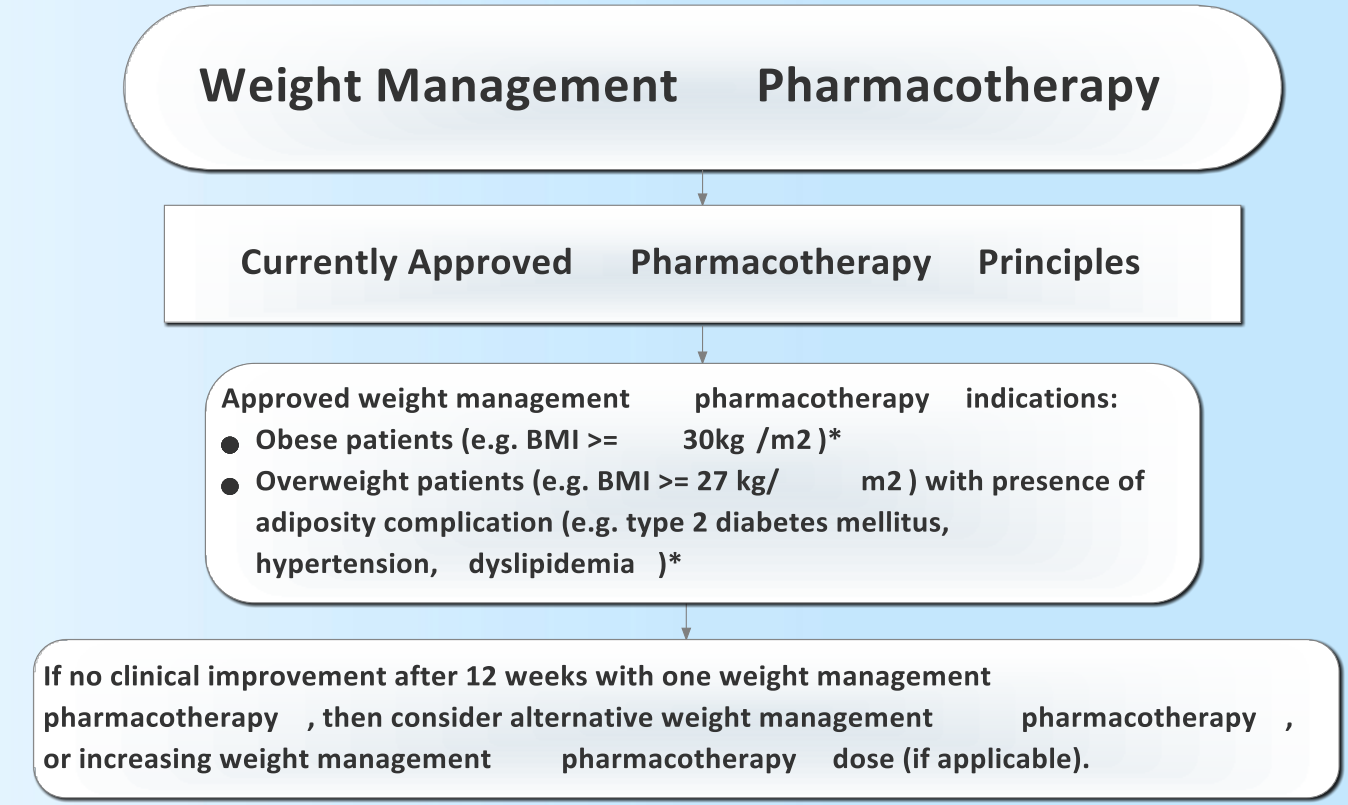
Sympathomimetic amines

- Examples: Phentermine , diethylpropion , phendimetrazine , benzphetamine
- Increases satiety
- Drug Enforcement Agency Schedule weight management agents
  - DEA IV for phentermine and diethylpropion
  - DEA III for phendimetrazine and benzphetamine
- Potential adverse experiences include palpitation, tachycardia , increased blood pressure, overstimulation , tremor, dizziness, insomnia, dysphoria ,headache, dryness of mouth, dysgeusia , diarrhea, constipation
- Pregnancy category X

Gastrointestinal lipase inhibitors

- Example: Orlistat
- Impairs gastrointestinal energy absorption
- Potential adverse experiences include oily discharge from the rectum, flatus with discharge, increased defecation, fecal incontinence, may increase risk of cholelithiasis , may increase risk of urinary oxalate, rare postmarketing reports of severe liver injury, m ay decrease fat-soluble vitamin absorption (e.g. vitamins A, D, E, K, and beta carotene)
- Pregnancy category X

Treatment



*** While BMI (body mass index) is the only measure listed in the prescribing information for weight management pharmacotherapy , BMI may have limitations; in some circumstances, obesity and overweight are more accurately assessed by other measures**

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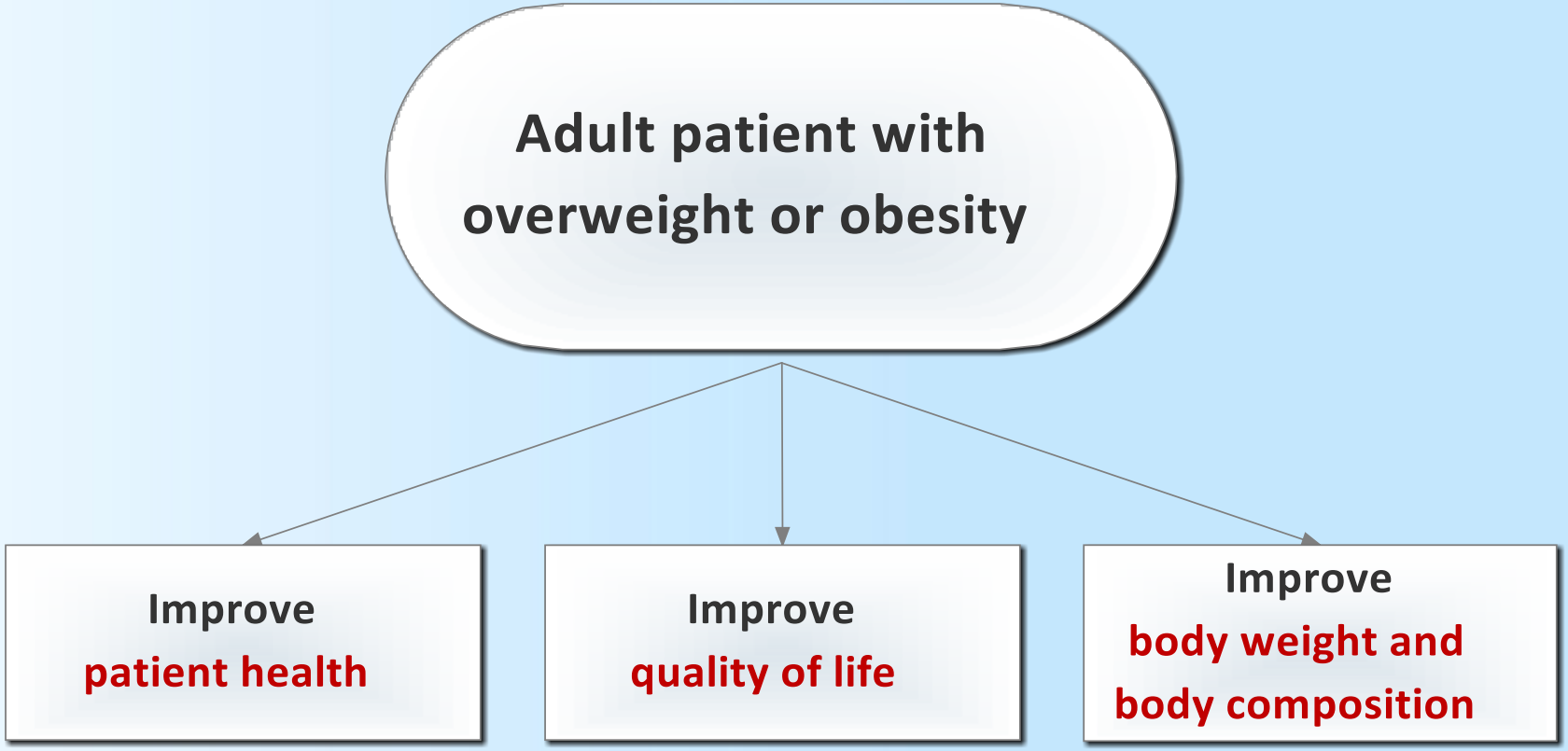
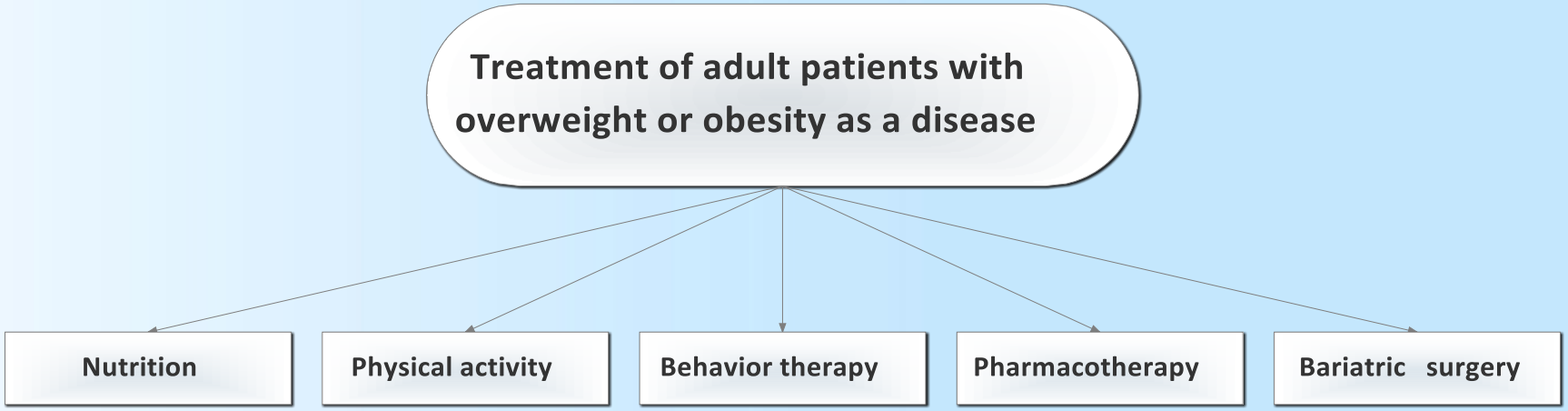
Overall Management Goals



Treatment



Neurobiological Approaches to Appetite Regulation and Therapeutic Advances in Weight Loss

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Professor of Medicine
Boston University School of Medicine
Boston Medical Center
Boston, Massachusetts

Factors Related to CNS Systems and Peripheral Signals

CNS Systems

Recent research suggests that alterations in certain CNS pathways are associated with obesity

- **Homeostatic system[1,2]**
- **Reward system[3,4]**

Peripheral Signals

Some evidence suggests that certain peripheral signals (hormones / gastrointestinal peptides) are altered in obese individuals; some examples include

- **Insulin[5]**
- **Leptin[5]**
- **Ghrelin[5]**
- **PYY[5]**

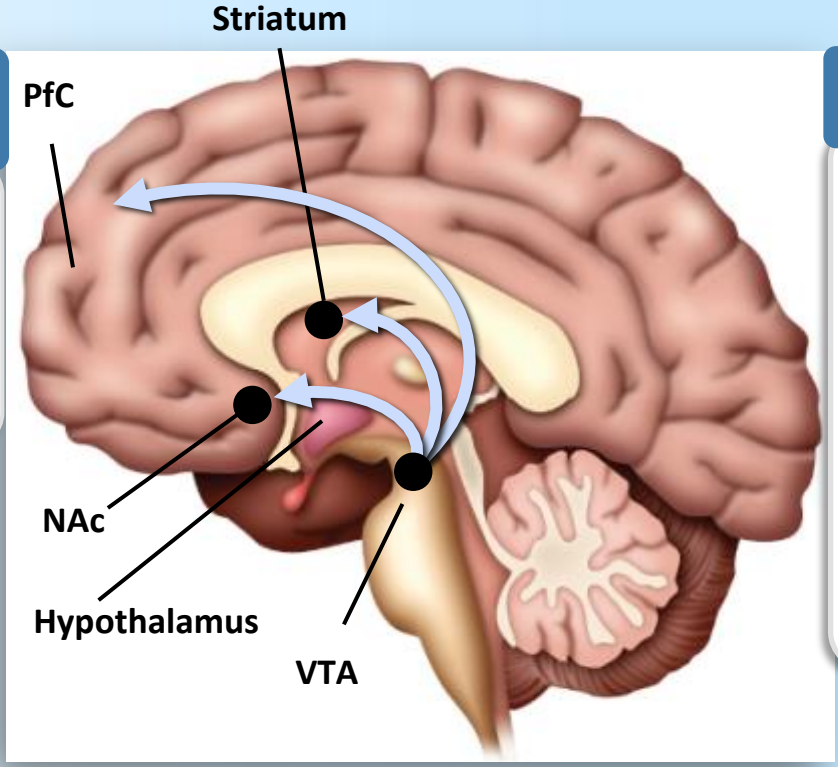
CNS, central nervous system
PYY, peptide YY

1. Morton et al. Nature. 2006;443:289-95.
2. Goldstone. Prog Brain Res. 2006;153:57-73.
3. Stoeckel et al. NeuroImage. 2008;41:636-47.
4. Wang et al. Lancet. 2001;357:354-57.
5. Yu et al. Diabetes Metab J. 2012;36:391-98.

CNS Systems Regulate Appetite, Energy Expenditure, and Reward in Response to Eating

Homeostatic Control System[1,2]

- Based in the hypothalamus
- Regulates appetite and energy balance



Reward System

- Involves activity of dopamine (VTA projections to NAc, striatum, PfC)[2]
- Modulates rewarding aspects and behavioral responses of activities needed for survival (eg, food and fluid intake, reproductive behaviors)[3]

- Homeostatic control and reward systems bidirectionally interact to affect food intake[2]
- Reward system regulation can override the homeostatic pathway during periods of relative energy abundance by increasing the desire to consume foods that are highly palatable[4,5]

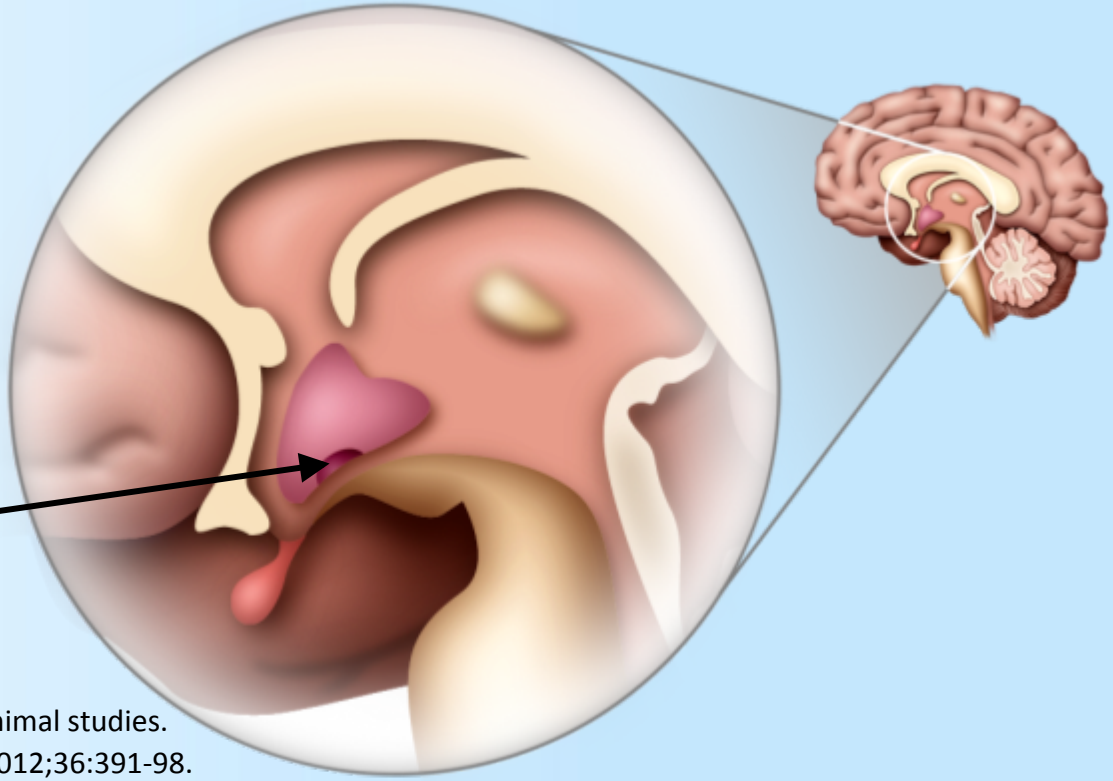
Primarily based on data from animal studies.

CNS, central nervous system; PfC, prefrontal cortex; NAc, nucleus accumbens; VTA, ventral tegmental area.

1.Yu et al. Diabetes Metab J. 2012;36:391-98. 2. Morton et al. Nature. 2006;443:289-95. 3. Stahl. In: Stahl's Essential Psychopharmacology. 4th ed. New York, NY: Cambridge University Press; 2013:537-75. 4. Lutter et al. J Nutr. 2009;139:629-32. 5. Volkow et al. Obes Rev. 2013;14:2-18.

Hypothalamus is a Regulation Center of Appetite and Energy Expenditure

- Integrates peripheral and CNS signals that collectively modulate feeding behavior and energy balance[1-3]
- A primary regulation center is the ARC[1]



CNS, central nervous system
ARC, arcuate nucleus

Primarily based on data from animal studies.

1. Yu et al. Diabetes Metab J. 2012;36:391-98.
2. Morton et al. Nature. 2006;443:289-95.
3. Cone. Nat Neurosci. 2005;8:571-78.
4. NetterImages. http://www.netterimages.com/image/4742.htm.

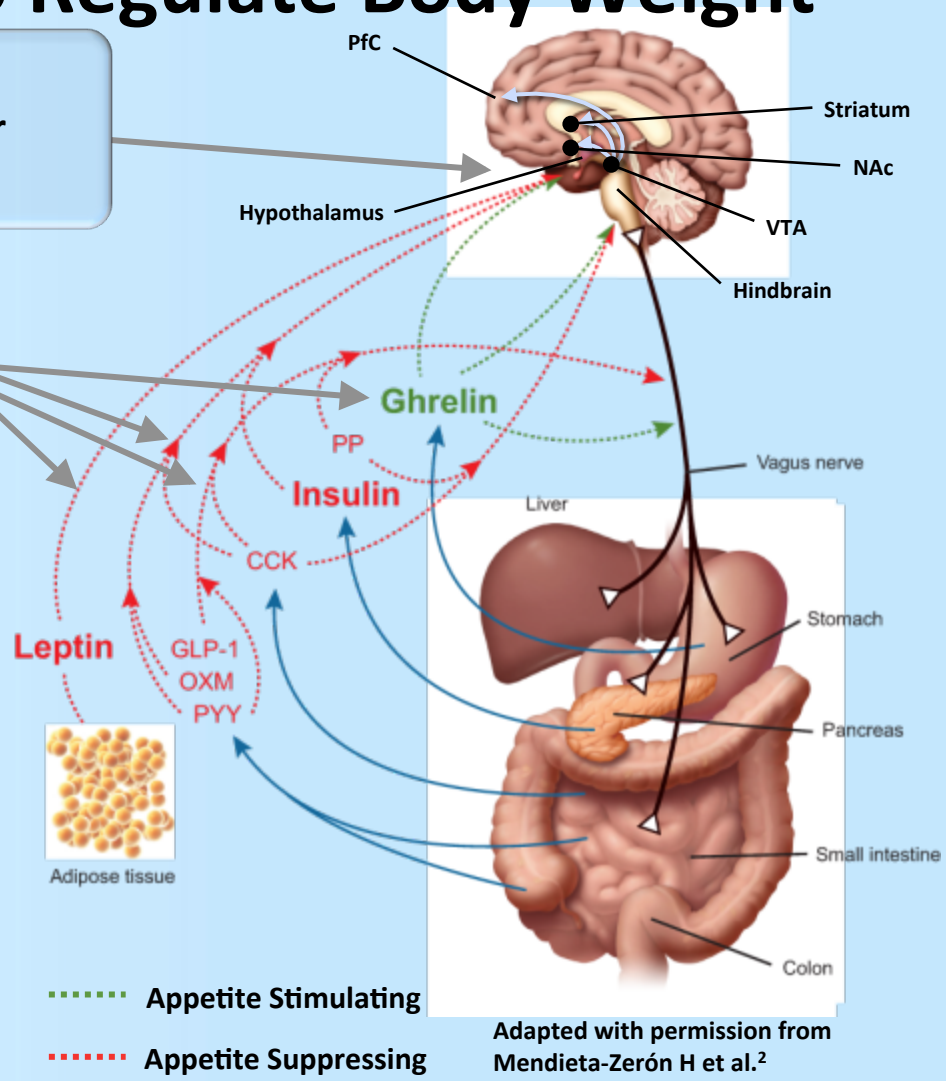
Complex Peripheral Signals are Integrated into CNS Systems to Regulate Body Weight

Brain systems (homeostatic and reward) receive and integrate peripheral and other CNS signals (eg, dopamine, serotonin)[1,2]

Peripheral signals are released by pancreas, gastrointestinal system, and adipose tissue[1,2]

Peripheral signals are relayed to brain systems via blood and vagus nerve[1,2]

Leptin, insulin, and ghrelin are integrated directly into hypothalamus



Adapted with permission from Mendieta-Zerón H et al.[2]

CNS, central nervous system
PfC, prefrontal cortex
NAc, nucleus accumbens
VTA, ventral tegmental area
PP, pancreatic polypeptide
CCK, cholecystokinin;
GLP-1, glucagon-like peptide 1
OXM, oxyntomodulin
PYY, peptide YY.
Primarily based on data from animal studies.

1. Yu et al. Diabetes Metab J. 2012;36:391-98.
2. Mendieta-Zerón et al. Gen Comp Endocrinol. 2008;155:481-95.

Overview

Gut Hormones

- Modulated by acute food ingestion

Suppresses Appetite

- Peptide YY
- Pancreatic Polypeptide
- Glucagon-like Peptide-1
- Oxyntomodulin

Increases Appetite

- Ghrelin

Adiposity Signals

- Short and long-term energy homeostasis
  - Leptin
  - Insulin

Summary of Main Gut Hormones and Adiposity Signals that Influence Food Intake

	Feeding	Receptor	Major secretion site	Other actions
Gut hormones				
PYY (3-36)	↓	Y2	L cells in gut	Delays gastric emptying
PP	↓	Y4, Y5	PP cells in pancreas	
GLP-1	↓	GLP-1	L cells in gut	Incretin, decreases blood glucose, delays gastric emptying, neurotrophic effect
GLP-2	-	GLP-2	L cells in gut	Intestinal trophic effect
OXM	↓	GLP-1	L cells in gut	
Glucagon	↓	GCGR	Pancreatic α cells	Increases blood glucose levels and insulin secretion
CCK	↓	CCK 1, 2	I cell of small intestine	Gall bladder contraction, relaxation of sphincter of Oddi, pancreatic enzyme secretion
Ghrelin	↑	GHS	stomach	Growth hormone secretion
Amylin	↓	AMY1-3	pancreatic β cells	Decreases blood glucose levels
Adiposity signals				
Insulin	↓	Insulin	pancreatic β cells	Decreases blood glucose levels, stimulates glycogen synthesis
Leptin	↓	Leptin (Ob-R)	adipocyte	Regulation of energy metabolism

PYY, peptide YY; PP, pancreatic polypeptide; GLP-1, glucagon-like peptide-1; GLP-2, glucagon-like peptide-2; OXM, oxyntomodulin; CCK, cholecystokinin; GCGR, glucagon receptor.

Suzuki et al. Endocr J. 2010;57:359-72.

Current and Emerging Obesity Therapies

Drug	Brand name (developer)	Stage of development	Frequency and route of administration	Mechanism of action	Efficacy*	Safety and tolerability concerns	Notes
Phentermine + topiramate *fixed dose combination*	Qsymia (Vivus)	Approved July 2012	Once-daily oral	Noradrenergic agent, antiepileptic drug	9–10%	Birth defect risk, minor elevation in heart rate	FDA has requested ten post-marketing studies and a cardiovascular outcomes trial
Lorcaserin	Belviq (Arena and Eisai)	Approved June 2012	Twice-daily oral	Selective serotonin receptor agonist	3–4%	Possible risk of valvulopathy in obese type 2 diabetics	FDA has requested six post-marketing studies and a cardiovascular outcomes trial
Bupropion + naltrexone *fixed dose combination*	Contrave (Orexigen and Takeda)	Approved September 2014	Twice-daily oral	Dopamine and norepinephrine reuptake inhibitor, opioid receptor antagonist	4–5%	Minor increase in heart rate and blood pressure	Undergoing 10,000 patient FDA-mandated pre-marketing cardiovascular outcomes trial;
Liraglutide*	Victoza‡ (Novo Nordisk)	Phase III¶	Once-daily injectable	Glucagon-like peptide 1 analogue	5–6%	Nausea, hypoglycemia, risk for pancreatitis	A lower dose formulation is on the market for type 2 diabetes *Recommended for FDA Approval September 2014*

*Mean placebo-adjusted weight loss demonstrated in clinical studies. ‡Liraglutide is marketed as Victoza for type 2 diabetes. ¶Liraglutide was approved in Europe and in the United States in 2009 and 2010, respectively, as a treatment for type 2 diabetes. Recommended for FDA Approval September 2014.

Wong et al. Nat Rev Drug Discov. 2012;11:669-70.

Overview
Impact of Weight-Loss Medications on Cardiometabolic Comorbidities

Phentermine/Topiramate ER Improves Risk Factors and Manifestations of Cardiometabolic Disease CONQUER Study

Changes from baseline to week 56 in secondary endpoints

Variable		Phentermine 7.5mg/ Topiramate 46 mg ER	Placebo	*P* value
Waist circumference (cm)	↓	-7.6	-2.4	<0.0001
Systolic BP (mm Hg)	↓	-4.7	-2.4	0.0008
Diastolic BP (mm Hg)		-3.4	-2.7	0.1281
Triglycerides (%)	↓	-8.6	4.7	<0.0001
LDL–C (%)		-3.7	-4.1	0.7391
HDL–C (%)	↑	5.2	1.2	<0.0001
CRP (mg/L)	↓	-2.49	-0.79	<0.0001
Adiponectin (µg/mL)	↑	1.40	0.33	<0.0001

Gadde et al. Lancet. 2011;377:1341-52.

COR-I and COR-II: Improvements in Markers of Cardiometabolic Risk: High Risk Subgroups

Bupropion + naltrexone *fixed dose combination*

	COR-I		COR-II	
	Placebo	NB32	Placebo	NB32
Waist circumference, males >102, females >88 cm **Baseline 110-111 cm**	**-2.8 ± 0.5** (n=282)	**-7.1 ± 0.5*** (n=279)	**-2.2 ± 0.5** (n=254)	**-7.3 ± 0.4*** (n=410)
Fasting triglycerides, ≥150 mg/dL **Baseline 200-222 mg/dL**	**-32.0 ± 10.4** (n=82)	**-66.3 ± 10.1*** (n=87)	**-13.9 ± 10.3** (n=69)	**-51.2 ± 6.8*** (n=135)
Fasting HDL, males <40, females <50 mg/dL **Baseline 40-41mg/dL**	**+1.3 ± 0.7** (n=122)	**+5.0 ± 0.7*** (n=121)	**+1.3 ± 0.7** (n=117)	**+6.2 ± 0.6*** (n=184)
Fasting LDL, ≥160 mg/dL **Baseline 175-185 mg/dL**	**-22.5 ± 6.8** (n=29)	**-12.8 ± 6.5** (n=31)	**-8.0 ± 8.0** (n=26)	**-27.3 ± 5.5** (n=44)
hsCRP, >3 mg/L **Baseline 8-9 mg/L**	**-0.7 ± 0.7** (n=163)	**-2.9 ± 0.7*** (n=177)	**-1.1 ± 0.9** (n=144)	**-1.6 ± 0.6*** (n=261)

*P<0.05 vs. placebo. P-values for triglycerides and hsCRP are based on log transformed data. Data is for Completers in high-risk subgroups. High risk subgroups defined by NHLBI NCEP ATPIII Guidelines, 2002, and Pearson et al., *Circulation,* 2003;107;499-511.

Baseline data are means. Change from baseline to Week 56 endpoint data are LS mean±SE. COR-II: Week 56 data from subjects re-randomized to NB32 is double-weighted to account for the pre-specified exclusion of subjects re-randomized to NB48. Data on file at Orexigen Therapeutics, Inc.

Improvement in Risk Factors with Use of Naltrexone SR/Bupropion SR

Measure	Week 28 Placebo *N* = 456	Week 28 NB32 *N* = 825	Week 28 *P*-value	Week 56 Placebo *N* = 456	Week 56 NB32 *N* = 702	Week 56 *P*-value
Waist circumference, cm						
Baseline	108.9 ± 11.7	109.3 ± 11.9		108.6 ± 11.8	109.0 ± 11.8	
Change	−2.7 ± 0.4	−6.2 ± 0.3	<0.001	−2.1 ± 0.5	−6.7 ± 0.3	<0.001
Triglycerides, mg/dL						
Baseline	113.4 ± 1.6	119.0 ± 1.6		112.8 ± 1.6	118.9 ± 1.6	
Percent change (95% CI)	−1.4% (−5.0%, +2.4%)	−7.3% (−9.8%, −4.8%)	0.007	−0.5% (−4.5%, +3.7%)	−9.8% (−12.4%, −7.1%)	<0.001
HDL-cholesterol, mg/dL						
Baseline	51.4 ± 13.1	51.4 ± 13.3		51.6 ± 12.9	51.8 ± 13.6	
Change	−1.4 ± 0.4	+1.2 ± 0.3	<0.001	−0.9 ± 0.5	+3.6 ± 0.4	<0.001
LDL-cholesterol, mg/dL						
Baseline	117.1 ± 32.6	119.8 ± 30.2		116.8 ± 32.9	120.5 ± 30.2	
Change	0.0 ± 1.3	−4.4 ± 0.9	0.004	−2.1 ± 1.3	−6.2 ± 0.9	0.008

Apovian et al. Obesity. 2013 May;21:935-43.

Lorcaserin – BLOOM Study: Key Secondary Endpoints

Endpoint		Lorcaserin	Placebo	*P* value
Waist circumference (cm)	↓	−6.8	−3.9	<0.001
SBP/DBP (mm Hg)	↓	−1.4 / −1.1	−0.8 / −0.6	0.04/0.01
Cholesterol (% Δ)				
Total	↓	−0.90	0.57	0.001
LDL	↓	2.87	4.03	0.049
HDL		0.05	−0.21	0.72
Triglycerides (%)	↓	−6.15	−0.14	<0.001
Safety				
HR (beats/min)	↓	−2.0	−1.6	0.049
Beck depression II		−1.1	−0.9	0.26

Intention-to-Treat Analysis with LOCF Imputation

Smith et al. NEJM. 2010;363:245-56.

Liraglutide* and Cardiometabolic Risk Factors

Risk factor	Exenatide 10 mcg twice daily (3.5 years)[39]	Liraglutide 1.2 mg once daily (26 weeks)[95]	Exenatide LAR 2.0 mg once weekly (1 year)[96]
Systolic BP (mm Hg)	-3.5*	-6.7†	-6.2*
Diastolic BP (mm Hg)	-3.3*	-2.3	-2.8*
Total cholesterol (mg/dL)	-10.8*	-8.1	7.9*
LDL cholesterol (mg/dL)	-11.8*	-10.8†	-2.2
HDL cholesterol (mg/dL)	8.5*	-1.2	NR
Triglycerides (mg/dL)	-44.4*	-14.7†	-40.0*
Free fatty acids (mmol/L)	NR	-1.2†	NR

LAR = long-acting release; NR = not reported

*$P < .05$ vs baseline; † $P < .05$ vs placebo

*Not FDA Approved. Recommended for FDA Approval September 2014

1. Klonoff et al. Curr Med Res Opin. 2008;24:275-86. (Exenatide 3.5 yrs)
2. Zinman et al. Diabetes Care. 2009;32:1224-30. (LEAD-4 Met+TZD)
3. Bergenstal et al. Presented at: American Diabetes Association 69th Scientific Sessions; June 5-9, 2009; New Orleans, LA. Abstract 165-OR. (Exenatide)

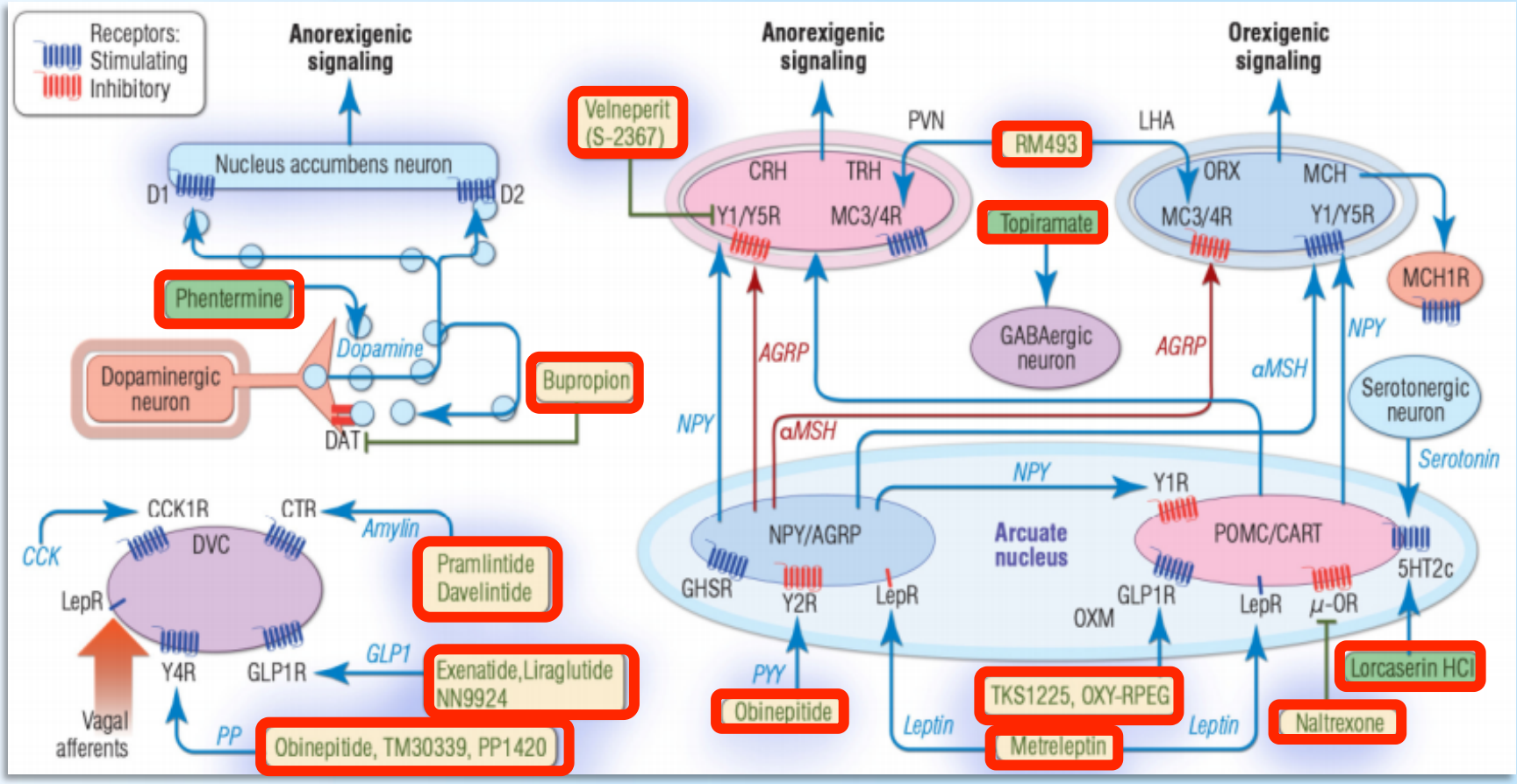
Expected Weight Loss with Newly Approved and Investigational Anti-Obesity Medications

Agent	Brand Name	Drug (kg)	Placebo (kg)	Net Weight Loss (kg)	Duration	FDA Approval
Topiramate/ phentermine	Qsymia	10.5	1.8	8.7	104 weeks	July 2012
Lorcaserin	Belviq	8.2	3.4	4.8	52 weeks	June 2012
Bupropion/ naltrexone	Contrave	8.2	1.9	6.2	48 weeks	Sept. 2014
Liraglutide* 3.0 mg	Victoza	10.3	4.1	6.2	104 weeks	**Pending** Recommended for Approval September 2014

*Not FDA Approved. Recommended for FDA Approval September 2014

Powell et al. Clin Pharmacol Ther. 2011;90:40-51.

Molecular Targets for Anti-Obesity Pharmacotherapeutics



Kim et al. Clin Pharmacol Ther. doi: 10.1038/clpt.2013.204.

Obesity and Addiction: Neurobiological Overlaps

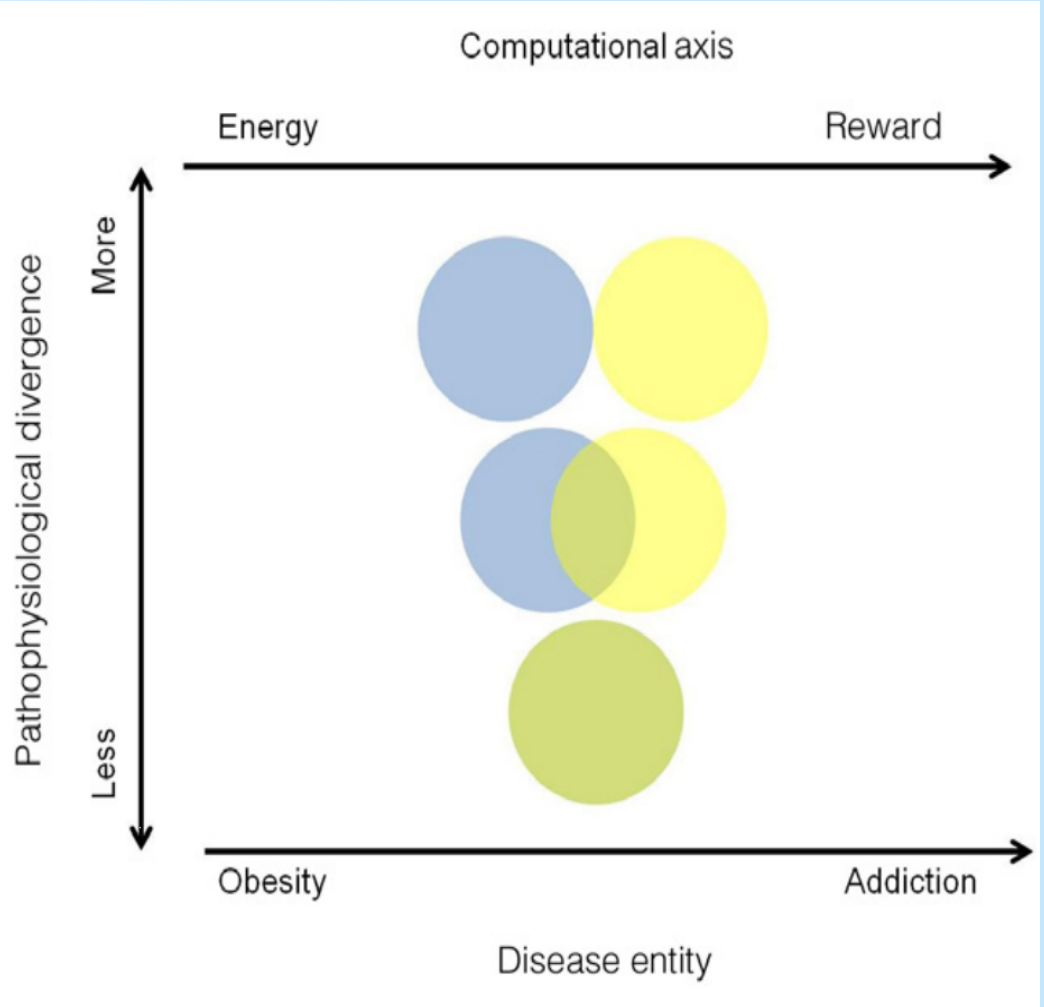
- **Inability to resist urge to use a drug or eat past point of satiety is based on:**
  - Improper functioning of neuronal circuits, and
  - Conditioned responses that trigger desire to ingest food or drug
- **Obesity, similar to drug addiction, appears to result from imbalanced processing in a range of regions implicated in:**
  - Reward/saliency
  - Motivation/drive
  - Emotion/stress
  - Reactivity
  - Memory/conditioning
  - Executive function/self-control and interoception
  - Possible imbalances in homeostatic regulation of food intake

Volkow et al. Obes Rev. 2013 Jan;14:2-18.

Obesity and Addiction: Neurobiological Overlaps

Obesity and addiction:

- Complex bio-behavioral disorders
- Exist along various etiological, pathological and physiological dimensions
- Likely to display some similarities as well as differences

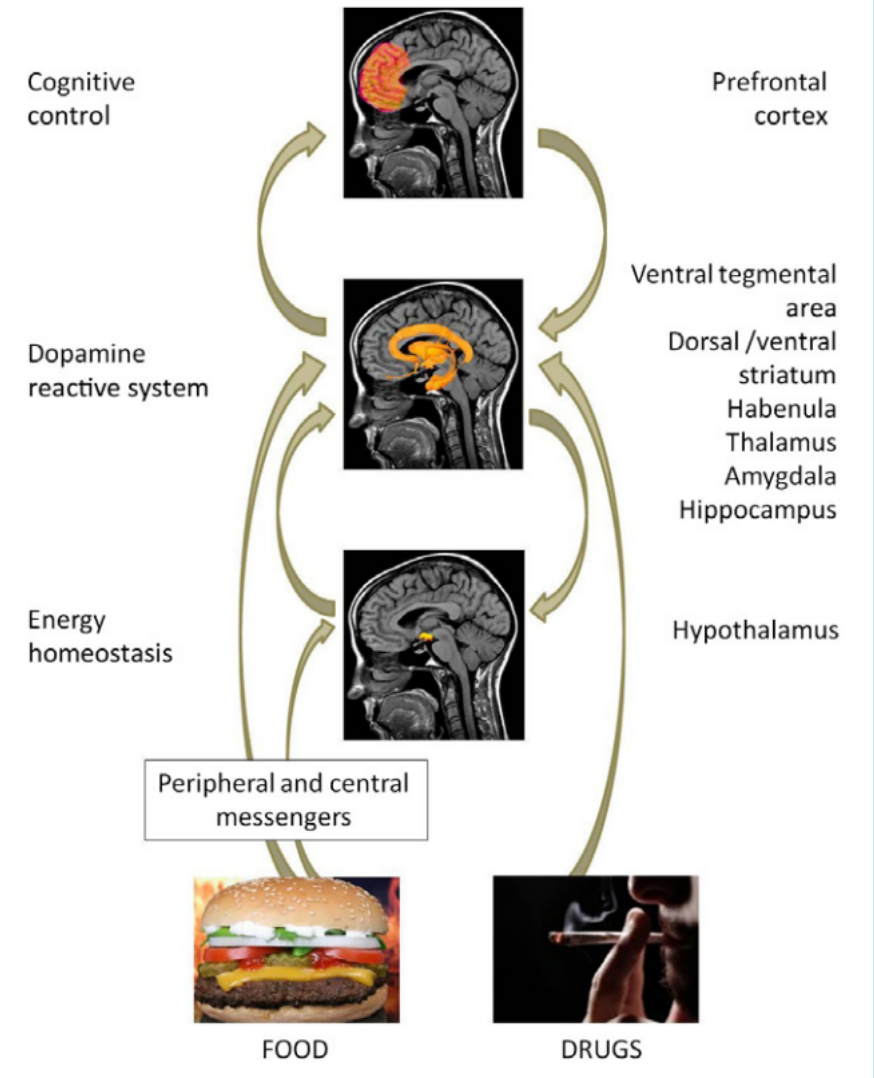


Volkow et al. Obes Rev. 2013 Jan;14:2-18.

Interconnected System Affects Intake of Food and Drugs

In contrast to drugs whose effects are exerted directly at the level of the brain reward dopamine pathway, food affects first multiple peripheral and central mechanisms that directly and indirectly convey information to the brain's DA reward pathway

Hypothalamus plays a particularly prominent role and is also strongly implicated in drug reward



Volkow et al. Obes Rev. 2013 Jan;14:2-18.

“Bow Tie” Layered Architecture

Complex systems allow for input of a wide range of elements:

(a) nutrients, or

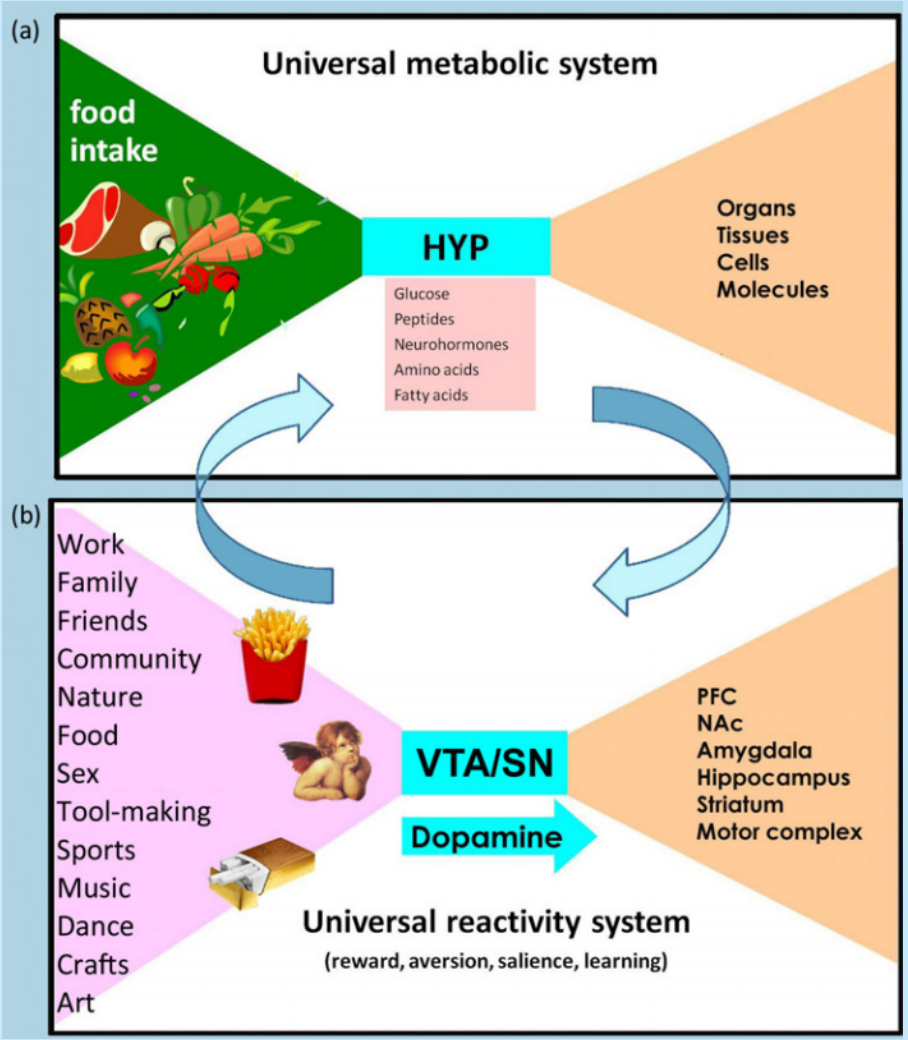
(b) rewarding stimuli

Produce large variety of:

(a) products/ macromolecules, or

(b) goal-directed behaviors

using common orexigenic/ anorexigenic signals and dopamine



Volkow et al. Obes Rev. 2013 Jan;14:2-18.

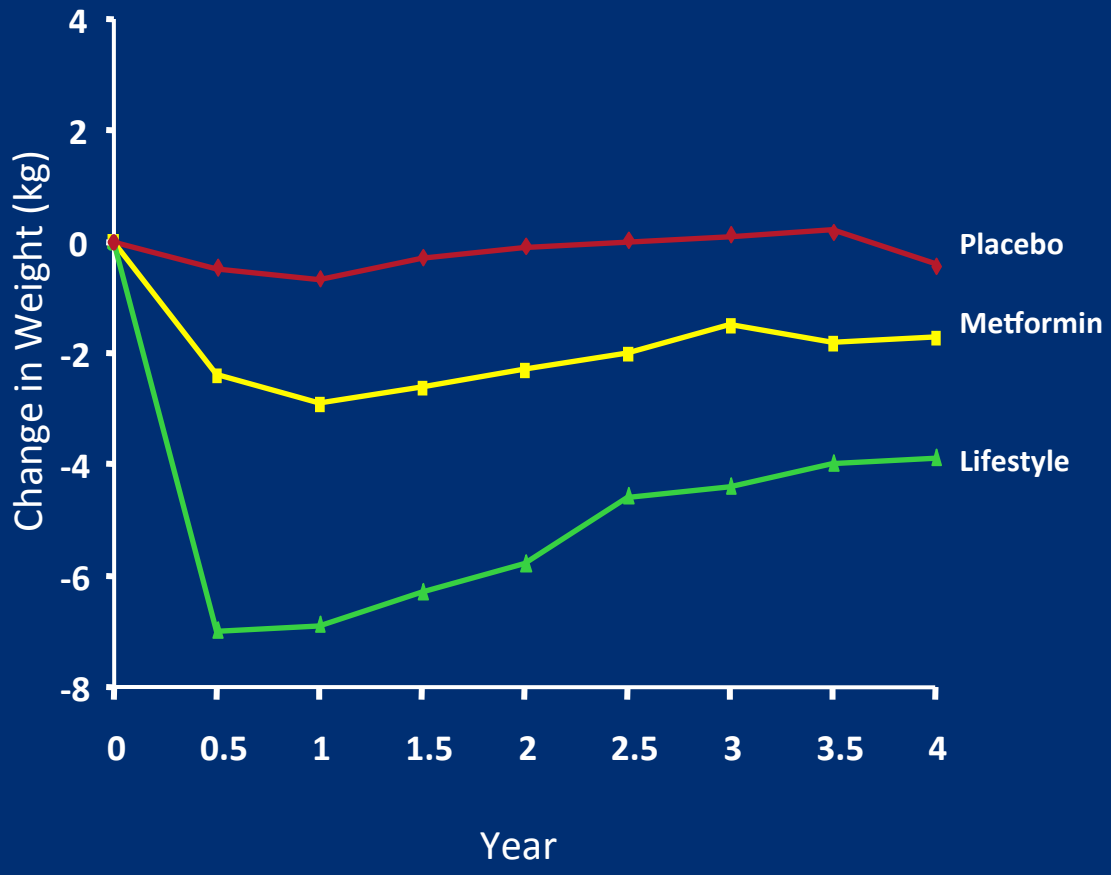
Summary

- CNS systems regulate appetite, energy expenditure, and response to eating
- Complex peripheral and central signals are integrated in the CNS to regulate body weight
- Hypothalamus is a primary regulation center of appetite and energy expenditure
- Homeostatic control system and reward system bidirectionally interact to affect food intake
- Gut hormones act peripherally to modulate digestion and absorption of nutrients; act as neurotransmitters within the central nervous system to control food intake
- New anti-obesity medications show promise
- Drug addiction and obesity share several properties

Breaking Down Clinician and Patient Barriers in the Treatment of Obesity

Thomas A. Wadden, PhD
Albert J. Stunkard Professor in Psychiatry
Center for Weight and Eating Disorders
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

DPP: Treatment Interventions and Weight Loss



Diabetes Prevention Program Research Group. N Engl J Med 2002;346:393-403.

COMPREHENSIVE LIFESTYLE MODIFICATION PROGRAM

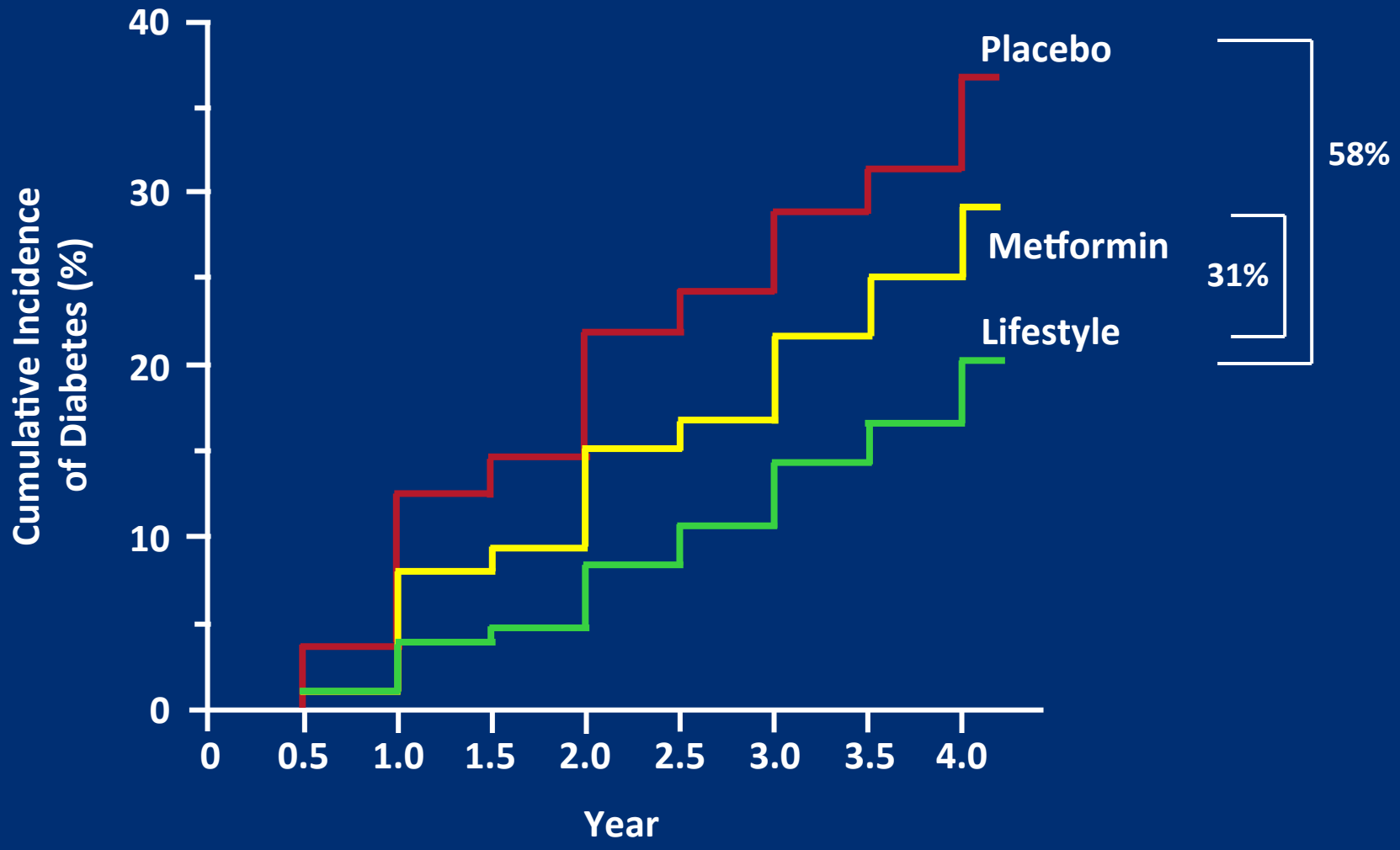
Weight Loss Induction:
16 individual visits over 6 months

Diet: Low-fat diet, conventional foods (1200-1800 kcal/d)

Activity: ≥ 150 minutes/week of moderate intensity exercise

Weight Maintenance: Individual visits at least every 2 months.
- -Three group classes/year for 4-6 weeks (campaigns)
- -Toolbox

Diabetes Prevention Program



Diabetes Prevention Program Research Group. N Engl J Med 2002;346:393-403.

Is Your Patient Ready to Lose Weight? Initiating a Discussion

- "You need to lose weight or your health will get even worse."
- "You are about 20 kg overweight. Losing as little as 5 kg could improve your health."
- "We have not discussed your weight recently. What are your thoughts about your weight and health at this time?"

Wadden, 2003

Broaching the Subject: Words to Use

- “Are you concerned about your weight?”
- “What is hard about managing your weight?”
- “How does being overweight affect you?”
- “What can’t you do now that you would like to do if you weighed less?”
- “What kind of help do you need to manage your weight?”

Courtesy of Dr. R. Kushner

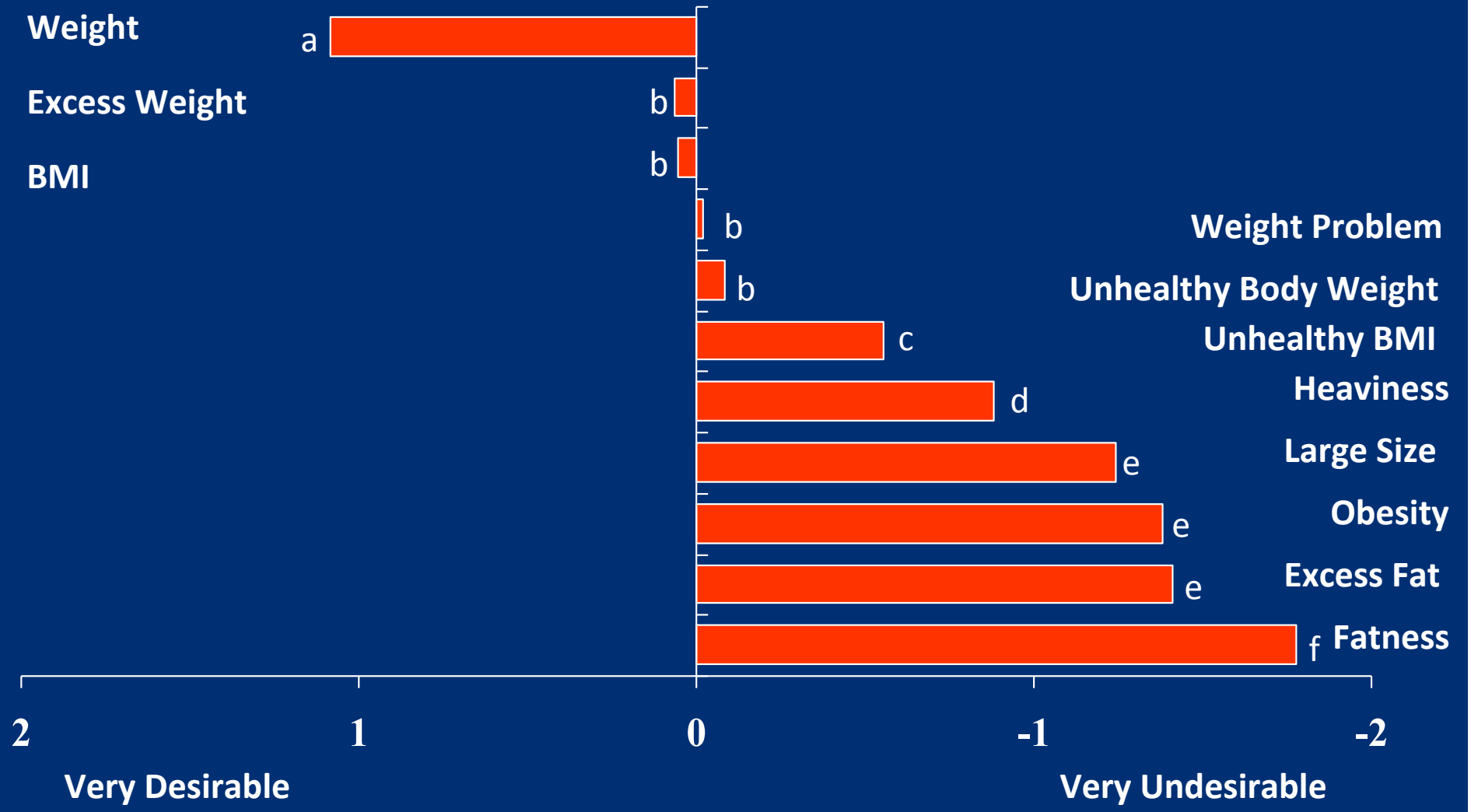
Patients' Preferred Terms for Describing Their Obesity

- "Imagine you are visiting your doctor for a check up. The nurse has measured your weight and found that you are at least 50 pounds over your recommended weight."
- "Please indicate how 'desirable' or 'undesirable' you would find each of the following terms if your doctor used it to describe your weight."

Weight	Obesity	Body Mass Index
Excess Weight	Excess Fat	Unhealthy BMI
Large Size	Weight Problem	Unhealthy Body Weight
Heaviness	Fatness	

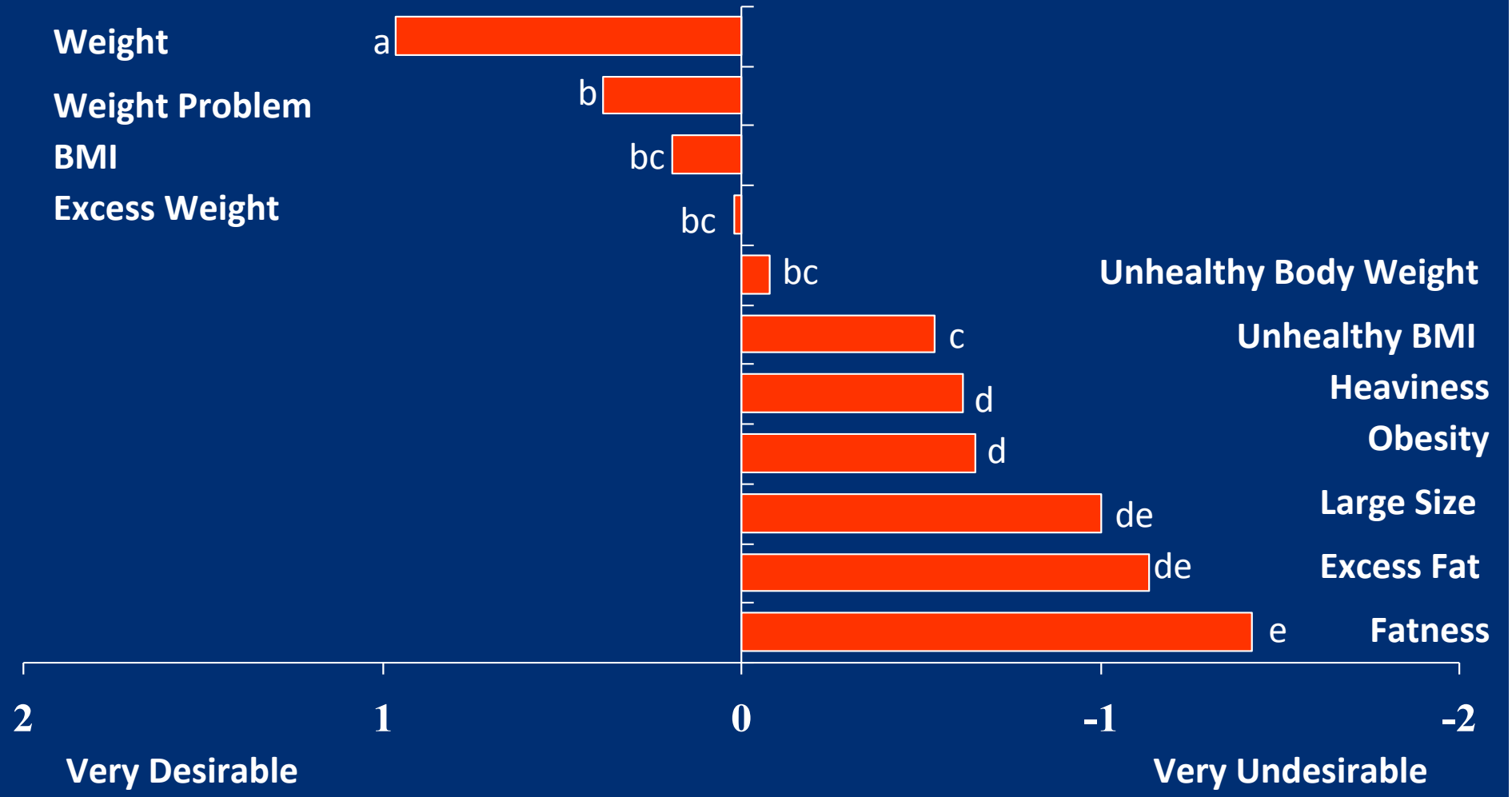
Wadden & Didie. Obes Res 2003;11:1140-46.

Obese Women's (N=167) Ratings of Terms to Describe Their Obesity



Wadden & Didie. Obes Res 2003;11:1140-46.

Severely Obese Women's (N=105) Ratings of Terms to Describe Their Obesity



Wadden & Didie. Obes Res 2003;11:1140-46.

Principles of Motivational Interviewing

- **Express Empathy**
  - See world through patients' eyes.
- **Support Self-Efficacy**
  - Individual has inner strength to change.
- **Develop Discrepancy**
  - Uncover mismatch between where the patient is and wants to be.
- Have the patient, rather than the clinician, be the advocate for change.

Miller & Rollnick. Behav Cogn Psychother. 2009;37:129-40.

How important is it to you to lose weight?

How confident are you that you can lose weight?

Miller & Rollnick. Behav Cogn Psychother. 2009;37:129-40.

Motivational Interviewing

"…a collaborative, person-centered form of guiding to elicit and strengthen motivation for change."

- Collaboration vs. Confrontation
- Evocation vs. Imposing Ideas
- Autonomy vs. Authority

Miller & Rollnick. Behav Cogn Psychother. 2009;37:129-40.

"Timing" of Weight Loss

- Stress level

  (Crises w/work, finances, family, etc.)

- Motivation

  (Patient initiates weight loss)

- Time

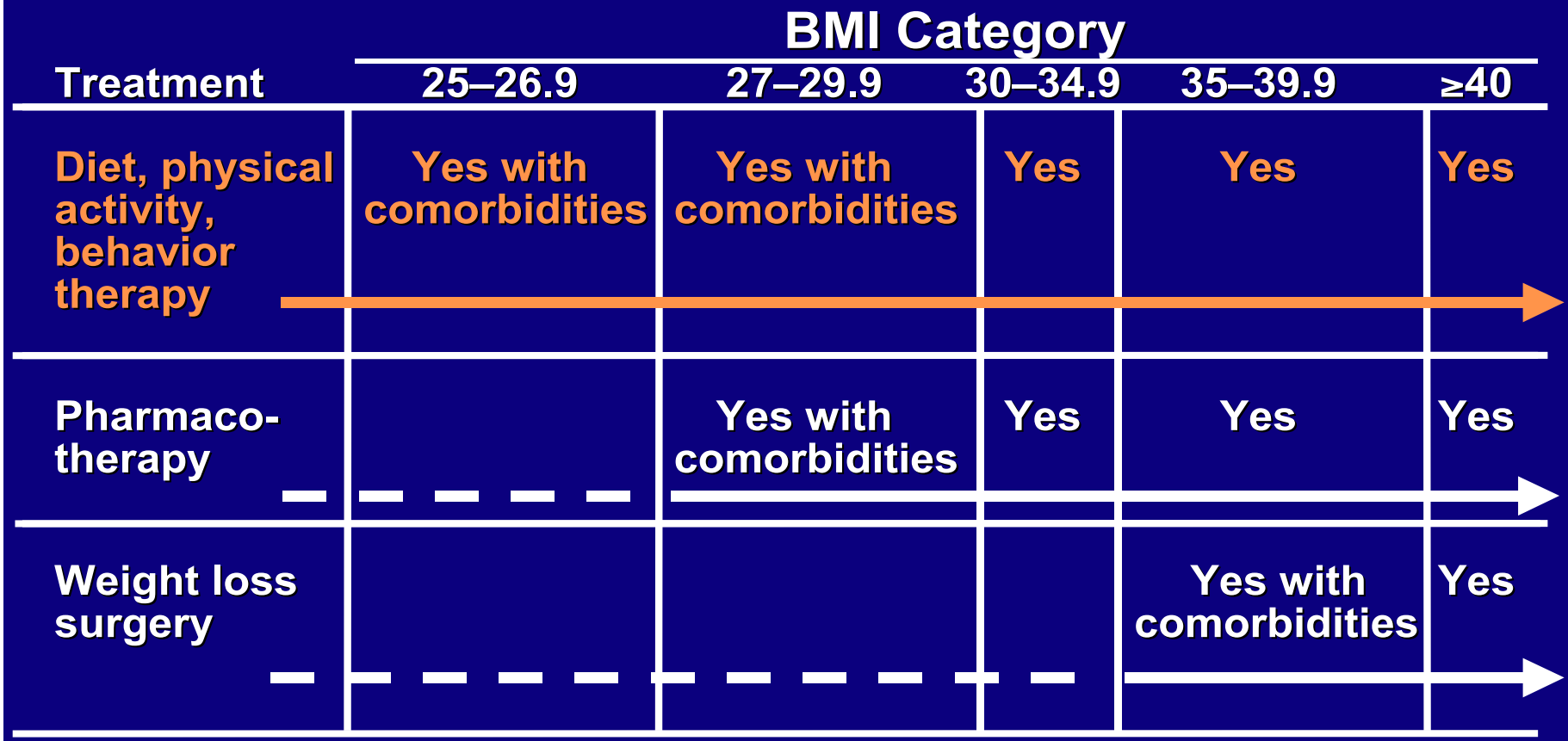
  (Can devote 15-30 min/day)

- Realistic expectations

  (Understands initial 10% goal)

Wadden T. Handbook of Obesity Treatment, 2004

A Guide to Selecting Treatment: NIH Guidelines*



**Yes* alone indicates that the treatment is indicated regardless of the presence or absence of comorbidities. The solid arrow signifies the point at which therapy is initiated.

The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. NIH/NHLBI/NAASO; October 2000. NIH publication No. 00-4084.

Preparing Patients for Treatment: The Initial Interview

- Describe the course of treatment
- Discuss expected results
- Assess patient's perceived ability to meet treatment demands
- Discuss barriers to treatment

Wadden T. Handbook of Obesity Treatment, 2004

Preparing Patients for Treatment

- Have patients articulate expectations and treatment goals:
  - Health/fitness
  - Appearance
  - Psychosocial
  - Weight loss

Wadden T. Handbook of Obesity Treatment, 2004

U.S. Preventive Services Task Force (USPSTF)

- "The USPSTF recommends screening all adults for obesity. Clinicians should offer or refer patients with a body mass index (BMI) of 30 kg/m^2 or higher to intensive, multicomponent interventions."
  - Moderate intensity = monthly contact
  - High intensity = more frequent
  - Low intensity = less frequent
- This is a grade B recommendation.

*There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate or substantial.

Moyer et al. Ann Intern Med 2012;157:373-79.

Recommendations for Lifestyle Modification

- Advise overweight/obese individuals 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 behavioral strategies. (Recommendation: A)

- Reduced calorie diet: ≥ 500 kcal/d deficit
- Physical activity: typically aerobic, ≥ 150 min/week
- Behavior therapy: structured behavior change program that includes regular monitoring food intake, activity, and weight, with personalized feedback from a trained interventionist

Jensen et al. Obesity. 2014;22(S2):S1-S410.

Recommendation for Losing 5-10% of Initial Weight

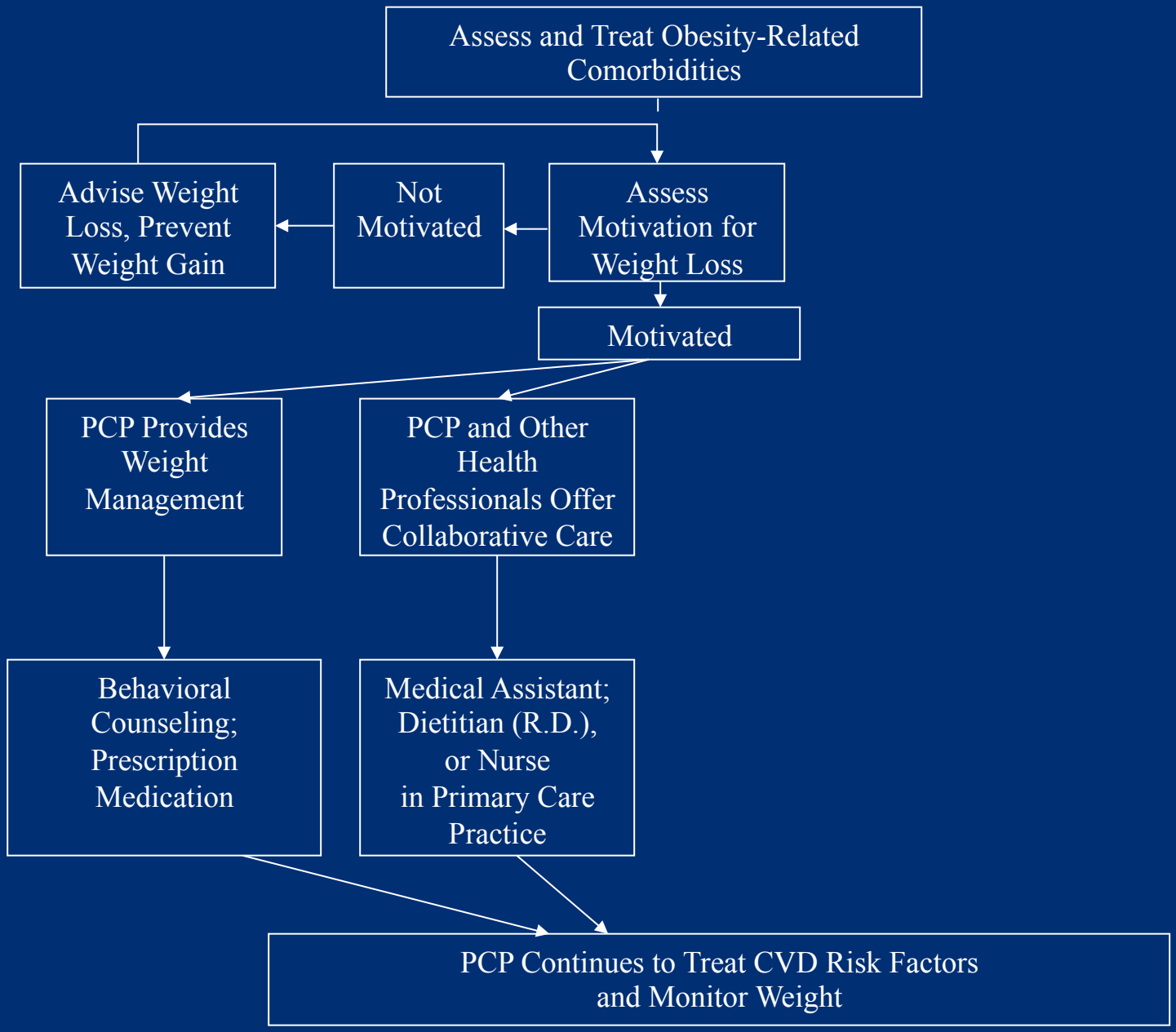
- "Advise overweight and obese individuals…to participate for ≥ 6 months in a comprehensive lifestyle program…"
  (Recommendation: A)

- "Prescribe on-site, high intensity (i.e., ≥ 14 sessions in 6 months) comprehensive weight loss interventions provided in individual or group sessions by a trained interventionist."
  (Recommendation: A)

- Comprehensive interventions "… produce average weight losses of up to 8 kg in 6 months of frequent (initially weekly) on-site treatment provided by a trained interventionist…"
  (Strength of Evidence: High)

Jensen et al. Obesity. 2014;22(S2):S1-S410.

Primary Care Practitioners' (PCP) Options for Managing Obesity and Its Complications



Tsai & Wadden. J Gen Intern Med 2009;24:1073-9.

POWER-UP Trial: 2-Year RCT of 390 Obese Participants in Primary Care

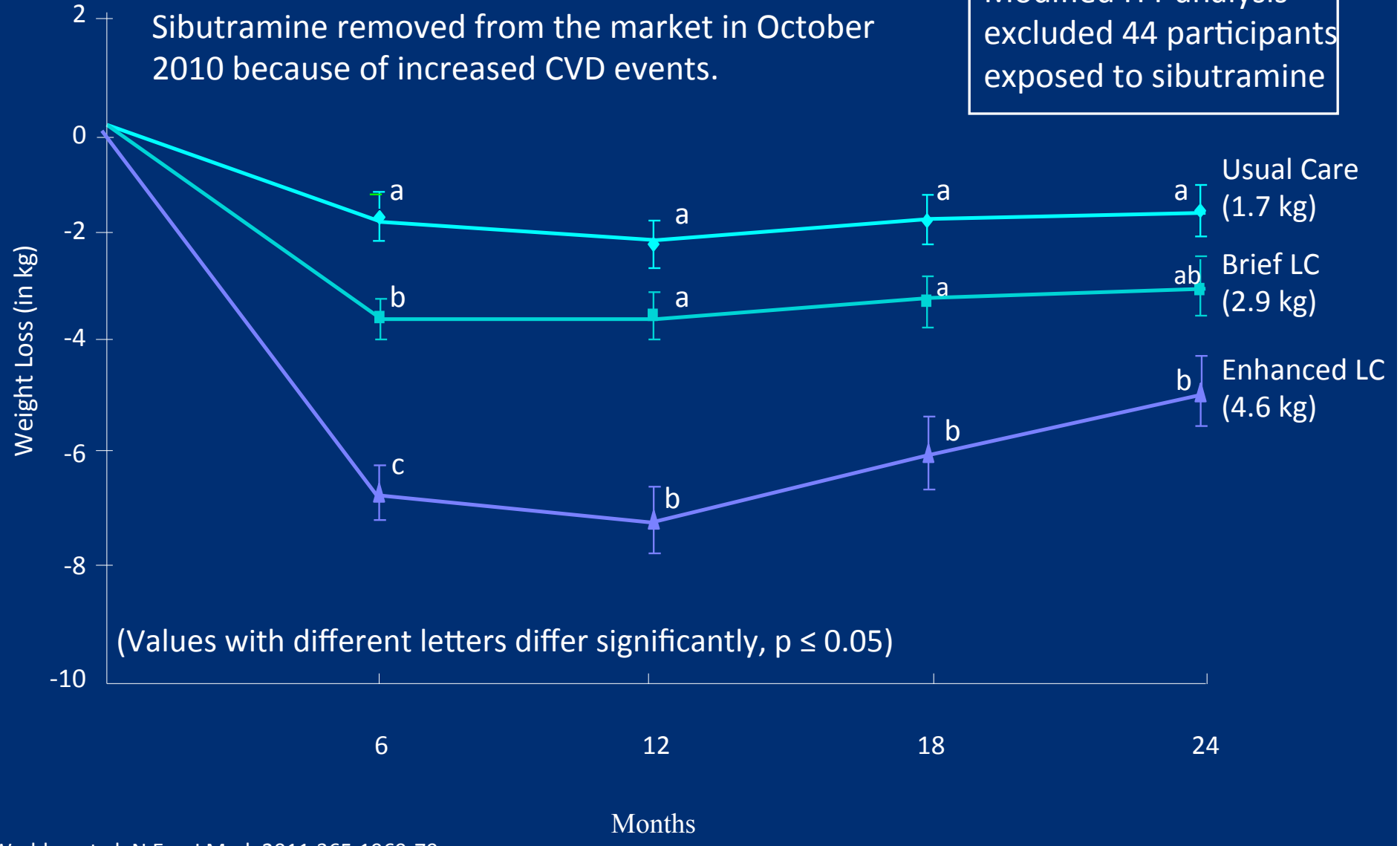
- **Usual care**: Quarterly PCP visits
- **Brief lifestyle counseling**: **Quarterly PCP visits** and approximately **monthly, brief visits** with **medical assistant who delivered adapted DPP protocol**
- **Enhanced lifestyle counseling**: PCP visits, same brief lifestyle counseling, and use of meal replacements or weight loss medications, sibutramine* or orlistat

Wadden et al. N Eng J Med. 2011;365:1969-79.

*Withdrawn from market

Weight Loss (in kg) in the ITT Population

Modified ITT analysis excluded 44 participants exposed to sibutramine



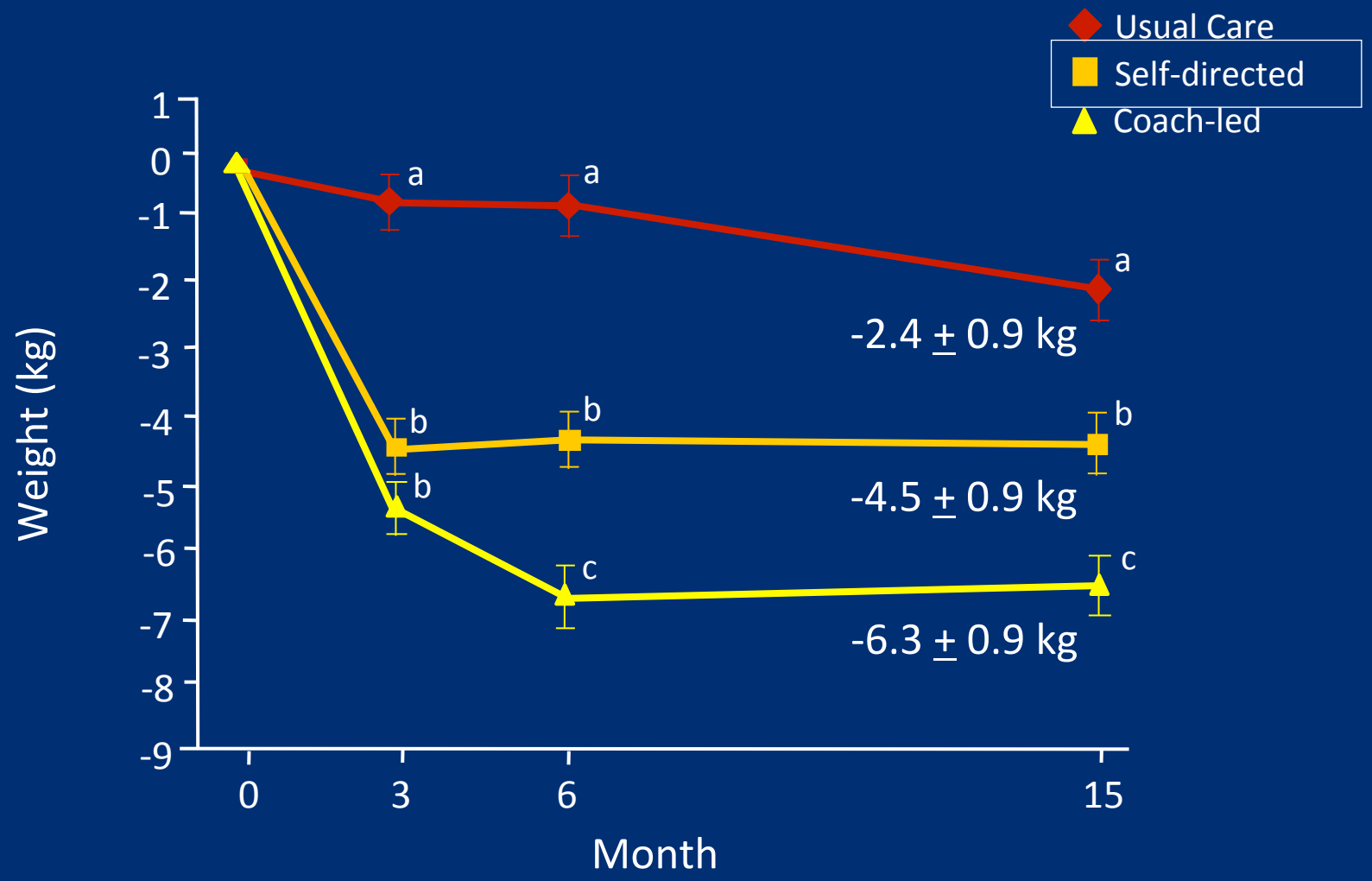
Wadden et al. N Eng J Med. 2011;365:1969-79.

E-LITE Trial: 15-Month RCT of DPP Interventions in Primary Care (*N*=241)

- Usual Care: No visits
- Self-directed - DVD:
  - Months 1-3: 12 sessions via DVD
  - Months 1-15: bi-weekly messages via email
  - **Total = 1 session (in person)**
- Coach-led Program (R.D., Exercise specialist):
  - Months 1-3: 12 weekly group sessions
  - Months 4-15: contact every 2-4 weeks by phone or email
  - **Total = 12 sessions (in person)**

Ma et al. JAMA Intern Med. 2013;173:113-21.

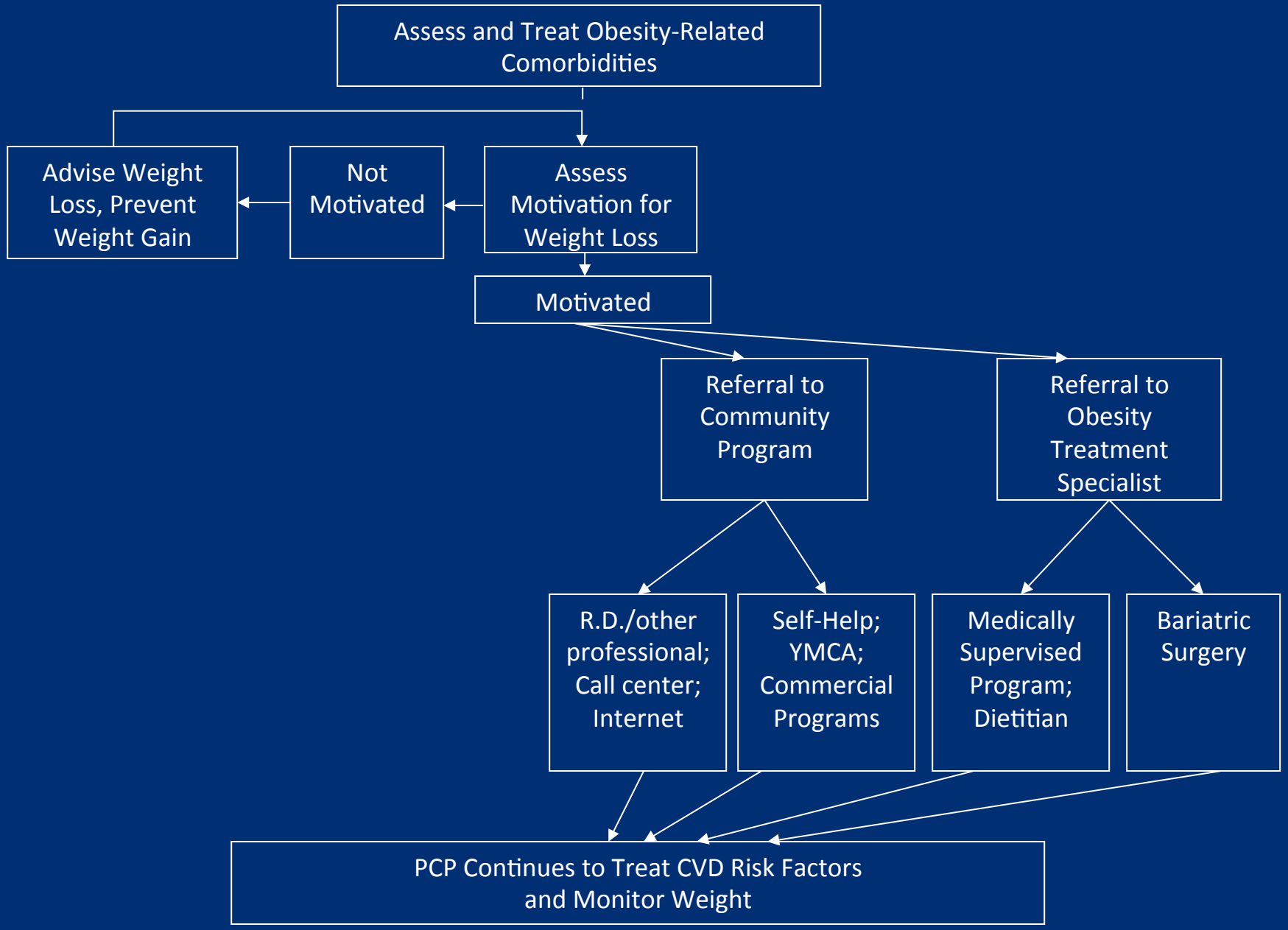
Weight Change Over a 15-Month Period



Ma et al. JAMA Intern Med. 2013;173:113-21.

Values with different letters differ significantly.

Primary Care Practitioners' (PCP) Options for Managing Obesity and Its Complications



Tsai & Wadden. J Gen Intern Med 2009;24:1073-9.

Electronically Delivered Intervention

- "Electronically delivered, comprehensive weight loss interventions developed in academic settings, which include frequent self-monitoring of weight, food intake, and physical activity – as well as personalized feedback from a trained interventionist – can produce weight loss of up to 5 kg at 6-12 months..."

  Strength of Evidence: Moderate

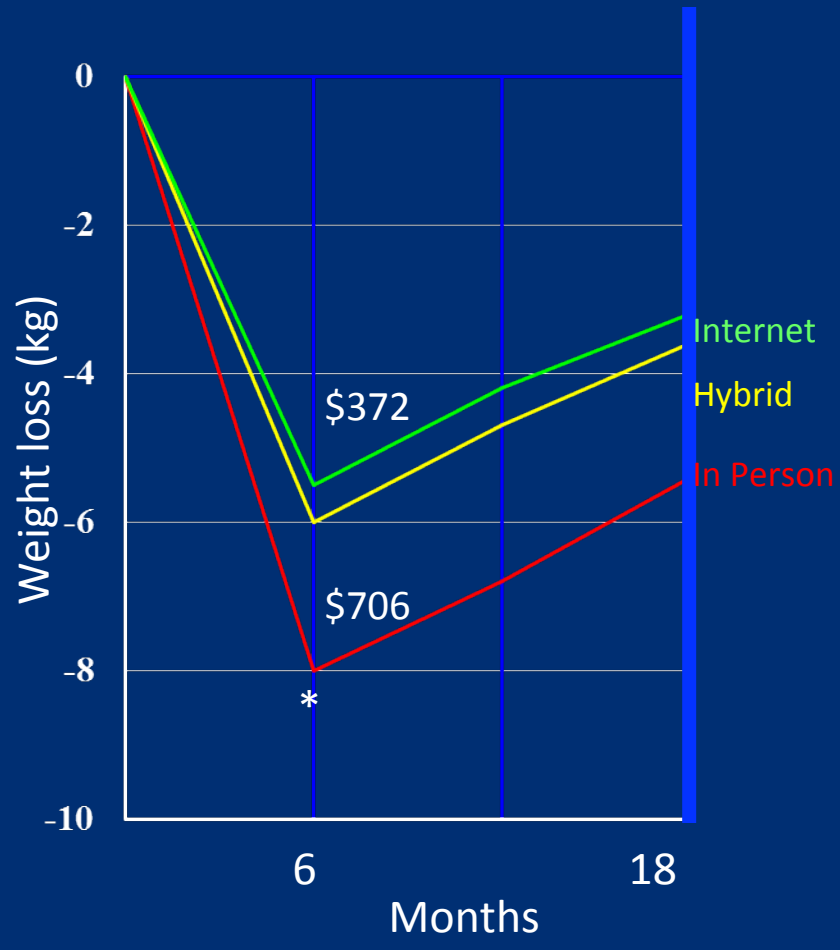
- Electronically delivered weight loss programs…can be prescribed for weight loss but may result in smaller weight loss than face-to-face intervention."

  Recommendation: B

Jensen et al. Obesity. 2014;22(S2):S1-S410.

Comparison of In-Person and Internet-Delivered Programs

- Treatment Conditions
  - In-person
  - Internet (synchronous chats)
  - Hybrid (1 in-person, 3 internet/mo)
- Weight Loss: months 1-6
  - Weekly group sessions
- Weight Maintenance: months 7-18
  - 1 session/mo



* $p \leq 0.05$ for In-person vs. Internet at month 6.

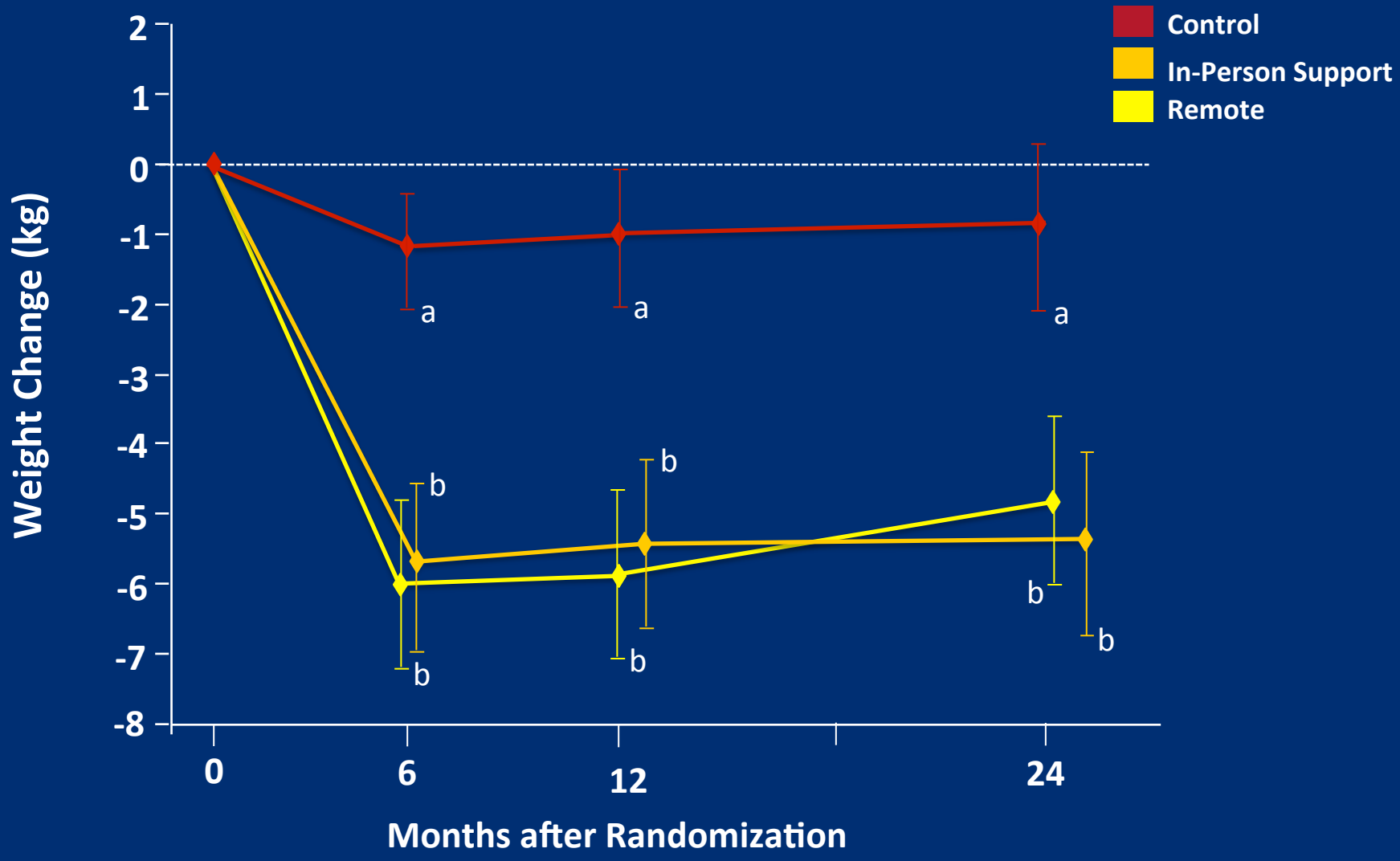
Harvey-Berino et al. Prev Med 2010;51:123-28.
Krukowski et al. Obesity 2011;19:1629-35.

POWER HOPKINS: Primary Care Weight Loss (N = 415) Delivered by Remote Support (Telephone) vs. In-person Support

- Control Group (Usual Care – 1 visit)
- Remote Support - Telephone
  - Months 1-3: weekly 20-minute calls
  - Months 4-24: monthly 20-minute calls
  - **Total = 33 individual calls**
  - Access to interactive Internet program
- In-Person Support – on-site visits
  - Months 1-3: weekly group (G) or individual (I) visits
  - Months 4-6: 3 monthly contacts (G, I)
  - Months 7-24: 2 monthly contacts (G, I)
  - **Total = 57 contacts**
  - Access to interactive Internet program

Appel et al. N Engl J Med 2011;365:1959-68

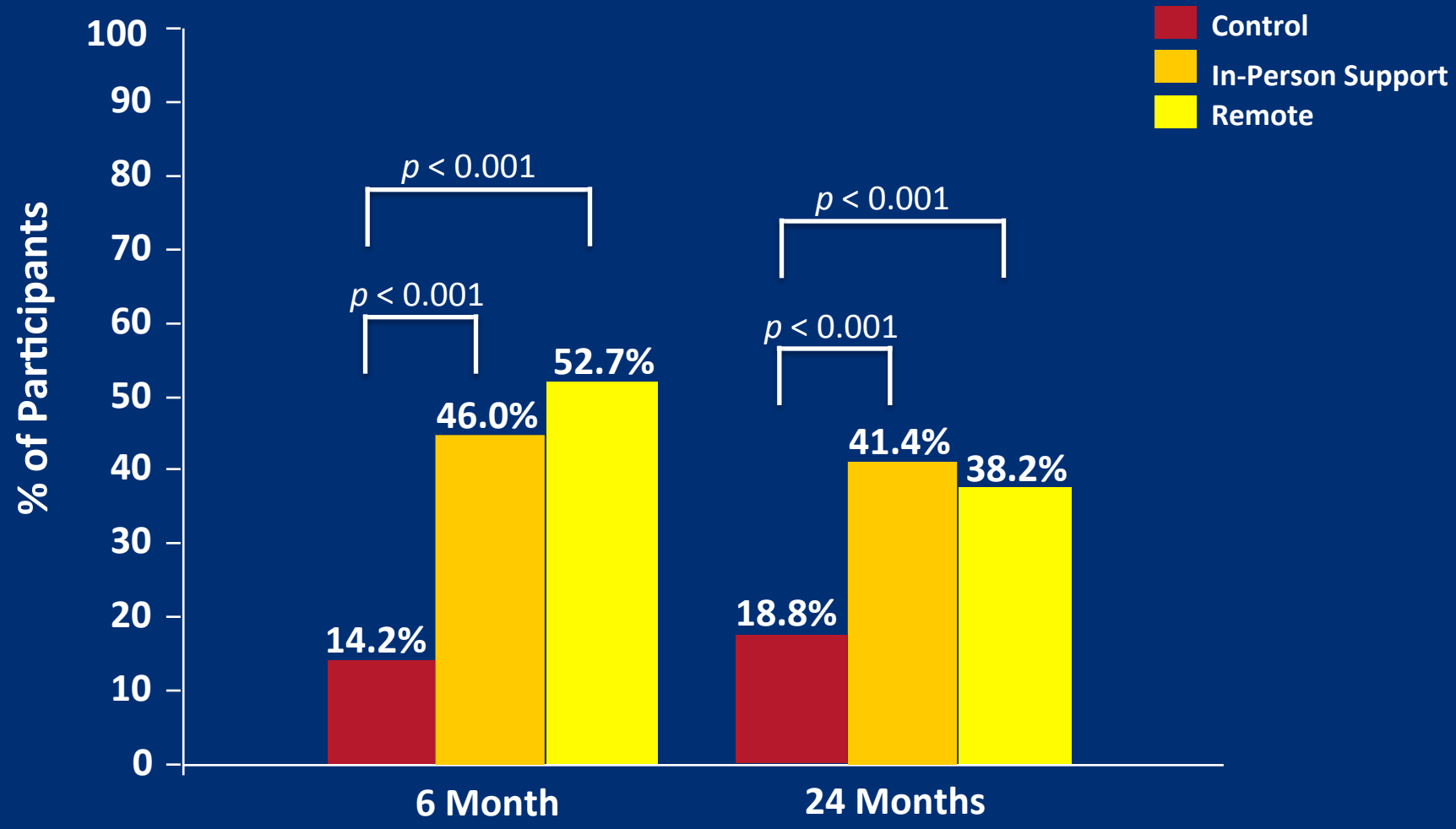
Mean Weight Change (kg) According to Randomized Group



Appel et al. N Engl J Med 2011;365:1959-68.

Values with different letters differ significantly.

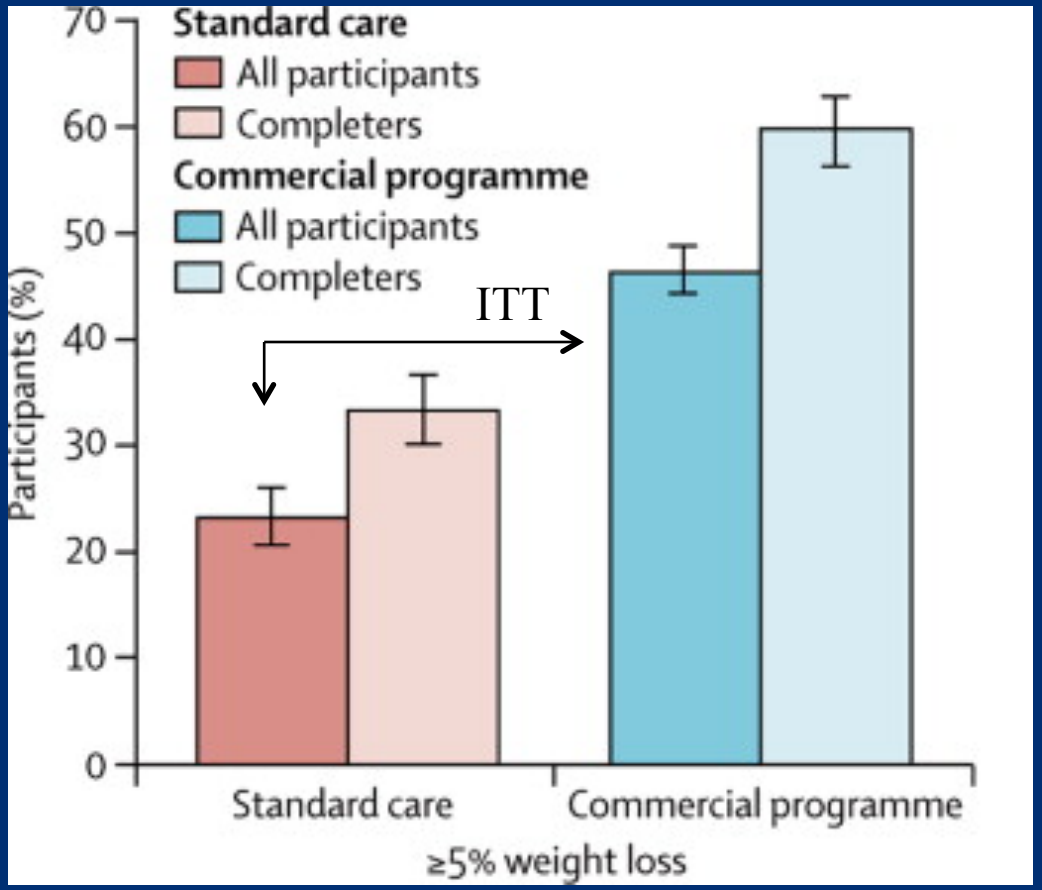
Percentage of Participants who Achieved ≥5% Weight Loss Goal



Appel et al. N Engl J Med 2011;365:1959-68.

Commercial Weight Loss Programs in Primary Care

- 772 patients recruited from primary care practices in 3 countries
- Randomly assigned to local Weight Watchers program or Usual Care
- Weekly meetings provided at no charge for 1 year
- Mean losses of 4.1 vs. 1.8 kg, respectively



Jebb et al. Lancet 2011;378:1485-92.

Conclusions

- Invite patients to discuss their weight – listen, empathize, and educate.
- Have patients advocate for weight loss, rather than the practitioner.
- Provide or refer motivated patients to a high-intensity, 6-mo program of lifestyle modification.
- Reinforce treatment attendance, weight loss, and improvements in health at follow-up medical visits.

Strategies to Optimize the Management of the Obese Patient and to Reduce Cardiometabolic Risk: Case Study Presentations, Panel Discussion, and Audience Q&A

Louis J. Aronne, MD
Caroline M. Apovian, MD
Harold E. Bays, MD
Thomas A. Wadden, PhD

Case Study 1

- A 50-year-old male with hypertension, type 2 DM, and osteoarthritis comes to your office for a visit.
- He is currently taking valsartan hydrochlorothiazide, naproxen, metformin, simvastatin, and glipizide. His blood pressure is 125/70 mmHg.
- His fasting blood glucose is 135mg/dL, and his HbA1c is 6.8%. He has gained 11 lbs over the last 3 months, and now has a BMI of 32.3kg/m^2.
- The patient's HDL is 28 mg/dL and his triglycerides are 630 mg/dL.

Case Study 2

- A 52-year-old female with a past medical history of major depressive disorder comes to your office with complaints of weight gain.
- Her fasting blood sugar is 166mg/dL, and her HbA1c is 7.2%. She states that her depression is well controlled and she has been taking paroxetine since last year. She is 5'5" tall and weighs 168lbs (BMI is 28 kg/m^2), up 10 lbs from last year.
- The patient also reports not feeling rested in the morning and her partner complains of her chronic snoring.
- The patient reports taking a "PM product" (diphenhydramine) to help her sleep.

Case Study 3

- A 61-year-old female detective with a history of severe rheumatoid arthritis, restless leg syndrome and fibromyalgia presents for an initial weight management consultation.
- She reported a high weight of 259 lbs. and engaged in previous weight loss attempts (no medication/commercial programs).
- She quit smoking 15 years ago, consumes 1-2 drinks/week, and is currently not exercising due to pain.
- Her prior surgical history includes R-ankle screw and fusion in April 2005 and hysterectomy at age 40 due to endometriosis.

Case Study 3, continued

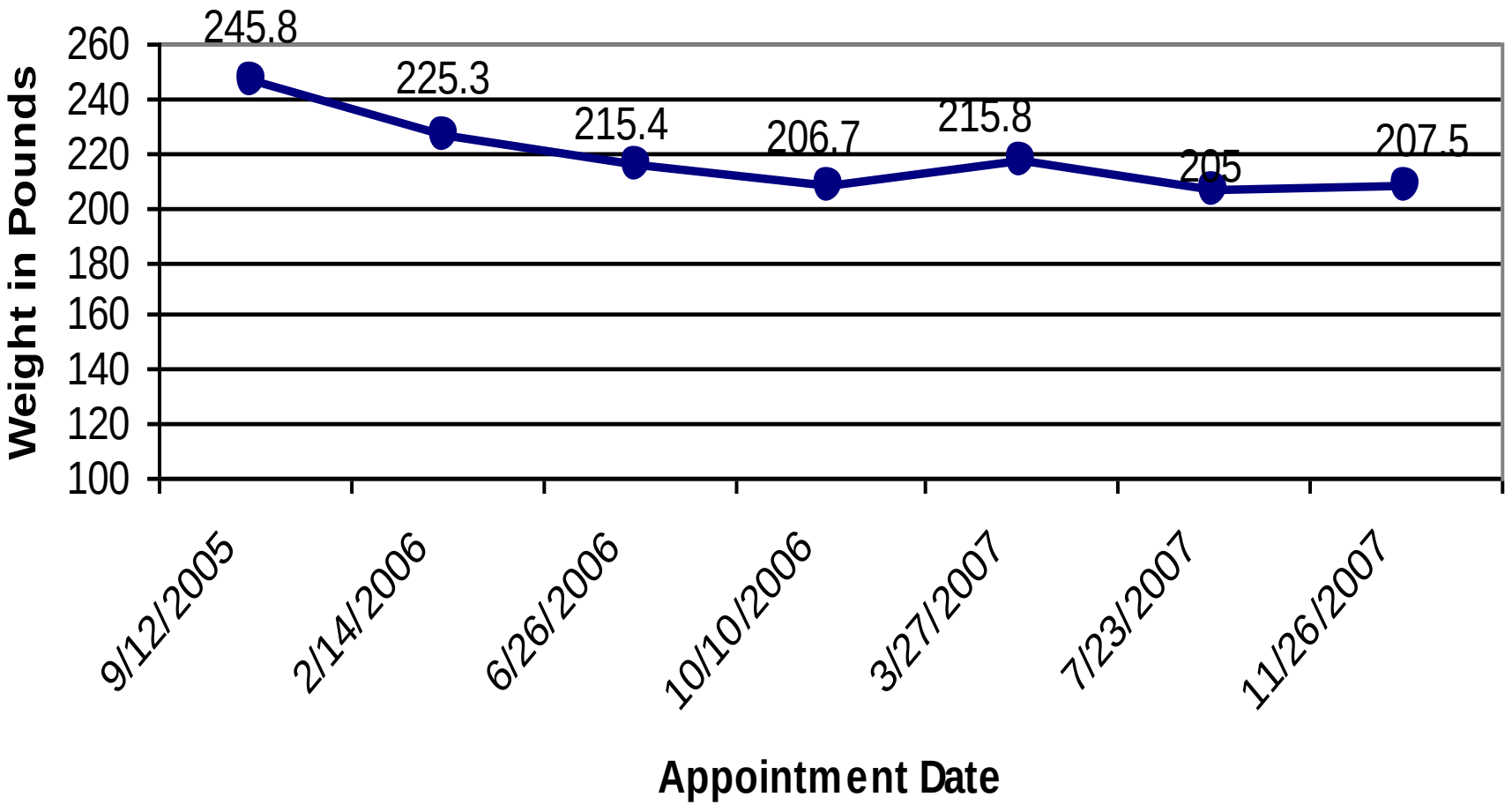
Meds: aspirin 81mg qd, adalimumab 40mg SQ every other week, leucovorin 5mg 3/wk, escitalopram oxalate 20mg qd, methotrexate Sodium 25mg/mL 1/wk, gabapentin 300mg 5/day, pravastatin 10mg qd, prednisone 1&5mg prn, budesonide 32mcg 2 spray/day, tramadol 50mg 8/day, trazadone 50mg tid, valacyclovir 1g 3/wk, enalapril 5mg qd

Lab Test Results:

- Glucose 93 mg/dL
- AST 29 unit/L
- ALT 35 unit/L
- RBC 3.45/pl
- MCV 103.2 fl
- MCH 36.5 pg

Exam: Weight 245.8 lbs, Height 67”, BMI 38.6 kg/m^2, BP 110/70, HR 72. Reviewed pt. history including severe RA on MTX and restless leg syndrome.

Weight Graph: Patient MW



Panel Discussion

ARS Question 1

Which of the following statements about obesity is correct?

1. Obesity results from eating too much.
2. There are many different causes of obesity, some of which are treatable.
3. There are many different causes of obesity, none of which are treatable.
4. Patients with obesity could lose weight if they tried hard enough.

ARS Question 2

The key hormone which tells the brain how much adipose tissue mass is stored is:

1. Ghrelin
2. PYY
3. Amylin
4. Leptin

ARS Question 3

Which of the following medication's mechanism of action is primarily at the serotonin 2c (5HT2c) receptor?

1. phentermine
2. topiramate
3. orlistat
4. lorcaserin
5. bupropion

Questions and Answers