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Richard T. James Jr. M.D.

Editor/Publisher.

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9-1 ASSESSMENT AND LIFESTYLE MANAGEMENT OF PATIENTS WITH OBESITY:

Clinical Recommendations from Systematic Reviews

The goal of *Guidelines for Managing Overweight and Obesity in Adults (2013)* was to help clinicians (physician, nurse practitioner) in the primary care setting to manage obesity more effectively. In addition to the 2013 guideline, this article relied on other guidelines.

Obesity often remains undiagnosed and undertreated.

SCREENING RECOMMENDATIONS:

Because of the burden of obesity and the benefits of treatment, the USPSTF recommends screening all adults for obesity. Patients with a body mass index (BMI) of 30 and over should receive intensive behavioral intervention, either in the primary care office or by referral.

Height and weight should be measured and BMI calculated annually, or more frequently depending on a patient's risk factors. The Centers for Medicare and Medicaid Services has mandated that electronic medical records calculate BMI as part of Core Measurements of Vital Signs. This record is capable of tracking weight trajectory so that intervention can occur at an earlier time to prevent further weight gain.

TAKING AN OBESITY-FOCUSED HISTORY;

Issues that affect treatment decisions should be incorporated into the history. This "obesity-focused" history allows physicians to develop tailored treatment recommendations that are consistent with the needs and goals of the individual.

One approach is to identify bio-social determinants of weight gain. Patients may complete a lifestyle events-body weight graph. For many patients, weight gain initially occurs or is accelerated due to smoking cessation, a change in life events such as marital status, or occupation or an illness. Risk times for women are menopause and pregnancy. Stressful life events often result in a change in eating habits and physical activity.

A dietary and physical activity history should be taken. Assessment of psychological health should be obtained routinely. Asking about mood disorders is important because they occur in high rates in obese persons. Major depression in the presence of an eating disorder should trigger referral to a psychological counselor. Drug induced weight gain should be considered, including some neuroleptics, anti-depressants, anti-convulsants, anti-diabetic drugs, anti-histamines, beta- and alpha adrenergic, blockers, and steroid hormones. Substitution with weight neutral drugs should be considered.

Determining the patient's readiness to make lifestyle changes is an important part of the initial evaluation. Is the patient ready and willing to undertake the measures necessary to succeed at weight loss? Many patients are ambivalent about changing long-standing lifestyle behaviors.

PHYSICIAN EXAMINATION OF OBESE PATIENTS:

Guidelines recommend measuring waist circumference. (WC)

Using BMI cut points to define healthy weight (18.5-24), overweight (25-29) and obesity (30 and above) is useful for screening and treatment decisions. However, BMI alone underestimates CVD risk and all-cause mortality. In addition to BMI, complications of overweight and obesity are independently associated with excess abdominal fat and fitness level. WC, measured at the level of the iliac crest, should be obtained and used to identify patients who may be at increased risk of CVD. Guidelines (2013) treat WC as a risk factor. When BMI is 25-29, an elevated WC is considered a risk justifying medical intervention for weight loss.

Population studies show that people with large WCs halve elevated obesity-related health risks compared to those with normal WC despite having similar BMI. Cut points for WC greater than 88 cm (>35 inches) for women and greater than 102 cm (>40 inches) for men are recommended for North American populations.

Cardio-respiratory fitness as measured by maximum treadmill exercise is an important indicator of all-cause mortality, independent of BMI. Fit obese men and women have a lower risk of all-cause mortality than unfit lean persons. Consequently, fitness assessment is an important component of clinical evaluation of obese persons. For most patients, obtaining at least 150 minutes a week of moderate-intensity or 75 minutes of vigorous-intensity aerobic exercise performed in episodes of at least 10 minutes is a reasonable goal.

Determining glucose levels and a lipid profile are consistent with current guidelines.

IDENTIFYING HIGH-RISK OBESE PATIENTS:

With the high prevalence of obesity, identifying which patient to treat is an important clinical decision.

Among US adults 51% of overweight adults and 32% of obese adults are metabolically healthy, defined having 0 or 1 cardiovascular abnormalities (high BP, triglyceride, and glucose; insulin resistance, decreased HDL-cholesterol, and high C-reactive protein [systemic inflammation]); 17% of obese men and women have 0 metabolic abnormalities. Guidelines (2013) recommend weight loss treatment for obese individuals with or without co-morbidities, and for overweight

individuals with 1 or more indicators of increased CVD (diabetes, pre-diabetes, hypertension, dyslipidemia, elevated WC).

Although BMI and WC are useful to identify potential risk, they do not accurately reflect the presence or severity of health risks.

TREATMENT

Guidelines for Primary Care Settings:

The 2013 guidelines provide evidence-based recommendations for achieving and maintaining weight loss. Based on systematic review, the guidelines recommend 3 treatment modes for achieving weight loss: diet, comprehensive lifestyle change, and bariatric surgery.

SELECT RECOMMENDATIONS (2013)

1) Advise patients that the greater the BMI and the WC, the greater the risk of CVD, diabetes, and all-cause death.

2) Matching treatment benefits with risk profiles: counsel those with CVD risk factors (hypertension, hyperlipidemia, and hyperglycemia) that lifestyle changes producing even modest, sustained, weight loss of 3% to 5% result in clinically meaningful health benefits, and greater loss produces greater benefits.

3) Diets: Any one of the following methods can be used.

A. 1200-1500 kcal for women and 1500-1800 for men. Calorie intakes are usually adjusted for individual body weight.

B. Prescribe a 500-750 kcal energy deficient diet or

C. Any one of the evidence-based diets that restrict certain food types (low carbohydrate or low fat).

THE BEST DIET FOR WEIGHT LOSS:

The recent Guidelines found no superiority for any of the 17 diets reviewed. Clinicians in primary care should prescribe a diet with negative energy balance that considers the patient's health status as well as the patient's personal preferences about food choices. Referral to a dietician is recommended.

LIFESTYLE INTERVENTION AND COUNSELING:

- 1) Advise participation for 6 or more months in a comprehensive lifestyle program that assists the patient in adhering to a low calorie diet and increasing physical activity.**
- 2) Prescribe on-site high-intensity (14 or more sessions in 6 months) comprehensive weight loss interventions that provide individual or group sessions by a trained interventionist.**
- 3) May prescribe some commercial-based programs that provide comprehensive lifestyle interventions as an option provided there is peer-reviewed published evidence of safety and efficacy.**
- 4) Advise participation in a long-term (1 year or longer) comprehensive weight maintenance program.**
- 5) For weight-loss maintenance, prescribe a face-to-face weight loss maintenance program that provides monthly or more frequent contacts with a trained interventionist who helps patients participate in high levels of physical activity (200--300 minutes per week), monitor weight regularly, and consume a reduced-calorie diet dedicated to maintain lower weight.**

SELECT PATIENTS FOR BARIATRIC SURGERY:

Advise patients with BMI 40 and above or patients with BMM 35 and above with obesity-related co-morbid conditions who are motivated to lose weight and who have not responded to behavioral treatments (with or without drug treatment) with sufficient weight loss to achieve targeted goals, that bariatric surgery may be an appropriate option. Offer referral to an experienced surgeon for consultation and evaluation.

BENEFITS OF TREATMENT:

It is not necessary for patients to get to a BMI less than 25 to have a significant health benefit. There is strong evidence that modest to moderate weight loss (5%-15%) can reduce risk of obesity-related complications even if the patient remains in the obese or overweight category.

Sustained weight loss as little as 3% to 5% is likely to result in clinically relevant reductions in triglycerides, blood glucose, glycated hemoglobin and the risk of developing type-2 diabetes. Greater losses reduce BP, improve LDL and HDL-cholesterol and lower the need for drugs to reduce these factors.

The effectiveness of modest weight loss on reduction of cardiovascular disease remains unresolved.

Modest weight loss produces improvement in symptoms of sleep apnea, though it usually requires loss of 10% or more. Urinary stress incontinence in women may improve, and sexual function in both sexes may also improve. The large look AHEAD study reported a potentially significant reduction in symptoms of depression after 1 year with lifestyle interventions.

Depression is not a reason to avoid weight loss.

There are 2 systems that regulate food intake, the homeostatic system and the reward system. The reward system can override the homeostatic system to encourage food intake and is particularly susceptible to stress. Thus, resisting high-palatability foods may be difficult in times of stress. Therapy will include strategies for sleep hygiene, time management, and stress management.

WEIGHT LOSS MAINTENANCE:

Guidelines recommend face-to-face or telephone-delivered weight loss management programs for at least 1 year.

Regular contact with a trained interventionalist at least monthly is advised to help the patient to engage in high levels of physical activity (200-300 minutes a week) to monitor weight at least weekly, and consume a reduced calorie diet.

SETTING EXPECTATIONS:

Obesity is a chronic disease. Relapses and recurrences are expected and should be anticipated. Adaptations to weight loss produce increased appetite, and reduce resting energy expenditure—physiological responses that promote weight gain. Patients must recognize that weight loss does not cure obesity and that it remains a constant threat requiring maintaining lifestyle changes long-term. Patients who are unsuccessful in maintaining loss can reinstitute behaviors that produce success again.

PATIENTS WHO STRUGGLE

Adjunctive therapies may be needed. Bariatric surgery is a possibility. Drugs for weight loss should be considered when comprehensive lifestyle interventions have failed. Drugs should be considered for patient with BMI 30 and above and for those with BMI 27 or higher with obesity-related co-morbidity. Drug therapy has made progress in the past few years with addition of 2 new medications (lorcaserin and phentermind/topiramate extended release). Others are under regulatory review.

Because of the challenges of producing and sustaining weight loss with low intensity counseling typically provided by primary care clinicians, drugs can be useful adjuncts to help patients achieve their lifestyle goals. Medications for obesity treatment must be viewed through the lens of long-term use when evaluating their safety and efficacy. The only drug approved for long-term use prior to 2012 is orlistat. When used as adjuncts to lifestyle counseling, the drugs currently approved for long-term use produce greater odds of meaningful weight loss compared with lifestyle counseling as a control. For lorcaserin the proportion of patients achieving a loss of 5% (when added to counseling in a typical office) is 37% with type-2 diabetes, to 47% in those without diabetes, and 67% for those taking phentermind/topiramate extended-release. For orlistat proportion ranges from 3% to 73%.

Three drugs provide useful options for patients who struggle with weight loss and maintenance. But their long-term effects on mortality and CV events are unknown.

CONCLUSIONS:

Providing care for patients who are overweight and obese is both a challenge and an opportunity for primary care clinicians. The opportunity is to address obesity, the underlying driver of many co-morbidities, and to have a major effect on health status with modest weight loss.

The challenge for primary care clinicians is learning how to translate the behavioral interventions into the office setting.

JAMA September 3, 2014;312:943-52 First author Robert F Kushner, Northwestern University Feinberg School of Medicine, Chicago, Ill.

This is the longest and one of the most important abstracts I have written in 29 years. I thank the authors for a timely article about a disease of overabundance and affluence that is common, deadly, and neglected.

Many patients consult the primary care clinician (PCP) about complications of obesity (hypertension, dyslipidemia, cardiovascular disease, and osteoarthritis) not for obesity itself. And the clinician may focus on these disorders without addressing the obesity.

Treating obesity is time consuming for both clinician and patient. Both must devote time and effort to the enterprise, and the patient must bear the expense. Simply giving the patient a diet list accomplishes nothing. The PCP must develop a cadre of associates (dieticians, physical exercise experts, psychotherapists) who are readily available and willing to help.

The patient, at the onset, must understand the seriousness of the disease, and be willing to undergo the difficult treatment path. If obese patients are not convinced that the effort, time, and expense of treatment are worthwhile, there is little to be gained pursuing treatment. Are you concerned about your weight? Are you ready to accept the expense, effort and time required to control your weight?

The physician must be dedicated to the task. The busier the PCP is, the more difficult the task. I believe few are experts in cognitive-behavioral therapy and relatively few will be willing to spend the time to guide long-term treatment. Certainly, multiple visits will be required. Many PCPs may simply write a prescription for a weight-control drug, or refer the patients to an expert consultant.

One approach, which I believe will appeal to the younger adults, is to stress the importance of undergoing a physical fitness program. Obese patients may be told that attaining a high degree of fitness reduces the complications of obesity, even if little weight is lost. And that losing a small percentage of weight is beneficial.

Both patient and the clinician need a lot of help addressing this disorder, which requires a lifetime of attention. Good luck!

9-2 COMPARISON OF WEIGHT LOSS AMONG NAMED DIET PROGRAMS IN OVERWEIGHT AND OBESE ADULTS: A Network Meta-analysis

Named or branded (trade marked) weight loss programs are broadly available. They provide structured dietary and lifestyle recommendations via popular books and on-line behavioral support, accompanied by advertising claims.

Debate continues about the relative merits of the diets. Which is superior?

Recent reviews suggest that most diets are equally effective.

Network meta-analysis facilitates comparisons of different diets, using all available randomized controlled trial data. In the absence of published head-to-head clinical trials of each diet against each other diet, network meta-analysis uses both direct and indirect clinical trial evidence to estimate relative effectiveness in weight loss.

STUDY

- 1. This study included randomized, controlled trials that assigned overweight (BMI 25-29) and obese (BMI 30 and above) adults to a popular brand name diet vs no diet.**
- 2. Included diet programs with recommended macronutrient, caloric intake, or both for 12 weeks of more, with or without exercise or behavioral support. Those including pharmacological**

agents were excluded.

3. The primary outcome was weight loss at 6 month and 12 month follow-up.
4. Secondary outcomes included BMI and adverse events.
5. Defined caloric restrictions as less than 1800 kcal/d.
6. Dietary classes based on macronutrient composition (approximate %):

	kcal carb	kcal protein	kcal fat
Low carbohydrate—Atkins, South Beach, and Zone;	40	30	30-50
Low fat—Ornish, Rosemary Conley;	60	10-15	<20
Moderate macronutrients—Biggest Loss, Jenny Craig, Volumetric, Weight Watchers;	55-60	15	21-30

RESULTS

1. Identified 889 potential articles relevant for full review. A total of 59 articles reported 48 RCTs (named diet vs no diet).
2. The 48 trials included 7286 individuals: median age 48, median weight 94 kg; and median BMI 33.
3. The median duration of the diet intervention was 24 weeks.
4. Weight loss and BMI change were considered the main outcomes.
5. At 6 months:
All diets were superior to no diet.
Compared with no diet, low carb diets had median difference in weight loss of 8.7 kg, the low fat diets had a loss of 7.9 kg, and the moderate diets 6.8 kg.
6. At 12 months:
The estimated average weight loss of all diet classes, compared with no diet, was approximately 1 to 2 kg less than after the first 6 months. (ie, participants began to regain some weight.)
7. Mean weight loss (named diet vs no diet) at 12 months (kg):

Moderate macronutrients	5.7
Low carb	7.25
Low fat	7.25
9. Due to the lower number of studies reporting BMI, the analysis was not trustworthy.
10. Adverse effects (reported in only 5 RCTs): constipation, headache, halitosis, muscle cramps, diarrhea, and general weakness occurred more frequently in the low carb group.

DISCUSSION

- 1. Among 48 original RCTs, evidence of low to moderate quality showed that both low carb and low fat diets were associated with an estimated 8 kg loss at 6 months compared with no diet. Approximately 1 to 2 kg of this loss was regained by 12 month follow-up.**
- 2. Most caloric-reducing diets result in clinically important weight loss as long as the diet is maintained.**
- 3. Although there were statistically significant differences between some of the named diets, these differences were small and are likely to be unimportant to many seeking to lose weight.**
- 4. Limitations of the study: 1) there was substantial heterogeneity between studies. 2) 19 of 48 trials were at high risk of bias mostly as a result of missing participant outcome data. 3) although patients were randomized to various diets or no diet, details of the actual adherence to the dietary program and daily caloric intake, macronutrient composition, and length and intensity of exercise were not accounted for in the analysis.**
- 5. Similar reviews (e.g., the Obesity Society) have come to the same conclusion that popular diets are roughly equally effective.**
- 6. Some weight was regained between 6 and 12 months. Future trials should focus on maintenance on weight loss over a longer period.**
- 7. There is no need for a one-size-fits-all approach to dieting because many different diets appear to offer comparable weight benefits. This is important because many patients have difficulty adhering to strict diets that may be particularly associated with craving (the low-carb diet) or be culturally challenging.**
- 8. Patients may choose the diet that gives them the least challenge with adherence.**

CONCLUSION

Low-carbohydrate and low-fat dietary programs were associated with more weight loss than no diet over a 12-month period. Behavioral support and exercise enhanced weight loss.

The weight loss differences between named diets were small.

This supports the practice of recommending any diet the patient will adhere to.

JAM September 3, 2014; 312: 923-32 Meta-analysis , first author Bradley C Johnston, Hospital for Sick Children, Ontario, Canada.

For me and many others, the low carb would be the most difficult diet to follow because of the frequent desire to indulge in a sweet.

In the journals I review, a decade ago, there were a number of articles touting special diets. I have seen none recently.

9-3. LOW CARBOHYDRATE DIETS: Commentary

Low carbohydrate, high fat (LCHF) diets continue to attract attention. LCHF diets invariably involve radical restriction of total carbohydrate (typically 12% of energy intake). Recent publications suggest benefit.

Recent evidence, however, confirms the established cornerstones of dietary advice—reductions in saturated fat, free sugars, and sodium, and increases in whole grain cereals and fiber—although additional data has necessitated some changes in emphasis.

One change has been the acceptance of a wider range of macronutrients than previously recommended for the prevention and treatment of obesity and associated chronic diseases. The change has enabled the transformation of nutritional recommendations for the prevention and treatment of obesity and associated chronic diseases to dietary patterns such as the Mediterranean diet, which includes up to 40% of energy intake from fat mainly derived from unsaturated vegetable oils.

Whatever the total fat intake, evidence supports lowering saturated fat. Reducing saturated fat lowers blood cholesterol. Increases in cholesterol occur in parallel with increase in saturated fat.

However, at 12 months duration, LCHF diets show that compliance with energy restriction is the main determinant of sustained weight loss, with no clear merit of LCHF diets over diets with different macronutrient composition.

Systematic reviews and meta-analyses commissioned by the WHO have confirmed the importance of free (added) sugars and total fat intake when consumed ad libitum in contributing to excess body fat.

These findings have led to the strong recommendation from the WHO that free sugars should be radically reduced from present levels of intake.

Recent recommendations have extended the acceptable upper limit of total fat to 35-40% of total energy.

Although fairly high intakes of total fat from nuts, seeds, and unsaturated vegetable oils can reduce cardiovascular risk, lowering fat intake to 30% of total energy might help to prevent weight gain in populations with high rates of obesity and diabetes.

Other than the need to restrict consumption of free sugars, limited attention has been paid to type of dietary carbohydrate.

In many countries, grains are heavily processed and white rice and potatoes provide a high proportion of total carbohydrate calories. Such carbohydrates are rapidly digested, absorbed, and metabolized, and have predominated in many studies that purport to show adverse effects when high and low carbohydrate intakes have been compared. By contrast, diets rich in fiber from whole grains, pulses, fruit and vegetables have been shown to be protective against type-2 diabetes, colon cancer, and cardiovascular diseases. Randomized trials have shown that diets high in such carbohydrates substantially reduce risk of progression to pre-diabetes and cardiovascular disease.

Thus, consumption of appropriate carbohydrate sources is recommended, rather than carbohydrate restriction. Carbohydrate should principally be derived from vegetables, fruit, and whole grains. Intake of dietary fiber should increase to 30 grams per day, and the population should derive about half of total calories from carbohydrates.

Public health initiatives to promote health and reduce risk of chronic disease will be advanced by the recognition that a range of dietary patterns, supported by strong, evidence-based research on nutrients and foods, are acceptable.

This does not include a LCHF diet.

Several features are common to recommended dietary patterns: consumption of fruits, vegetables, nuts, legumes, fish, unsaturated oils, and low-fat dairy. Cereal-based foods should be predominantly whole, minimally processed grains. Restrictions of saturated fat and sodium continue to be advised.

Fad diets often arise from the publication of a few studies that seem to contradict conventional wisdom. They can harm public health.

Lancet October 25, 2014; 384: 1478-80 First author Jim Marn, University of Otago, New Zealand.

We must continue to consider the quality of fat and carbohydrate while lowering calorie content.

9-4 EFFECTS OF LOW-CARBOHYDRATE AND LOW-FAT DIETS: A Randomized Trial

According to the latest estimates, more than 1/3 of American adults have at least one form of cardiovascular disease, and 1/3 of total deaths are due to CVD.

Low-carbohydrate diets have become a popular strategy for weight loss and weight management in recent years. However, their cardiovascular effects are unknown. Prospective cohort studies have reported conflicting results.

The present study is a randomized, parallel group trial of the effects of a low-carbohydrate diet compared with a low-fat diet on body weight and CVD risk factors in a diverse population.

STUDY

- 1. Men and women aged 22 to 75 with a body mass index (BM) of 30 to 45 were recruited from the general public. None had self-reported clinical CVD, type-2 diabetes, or kidney disease, or use of drugs for weight loss.**
- 2. The cohort consisted of 148 participants—mean age 47; 88% female; 51% black. Study period lasted from 2008 to 2011.**
- 3. Allocated participants to 1 of 2 diets—low-fat or low-carb.**
- 4. Participants in the low-carb diet were instructed to maintain an intake of digestible carbohydrate (total carb minus total fiber) of less than 30% of daily caloric intake. Those assigned to the low-fat diet were instructed to maintain less than 30% of daily energy from total fat (<7% saturated fat) and 55% from carbohydrate, based on National Cholesterol Education Program.**
- 5. Neither diet indicated a specific caloric goal. Participants were asked to refrain from changing their physical activity levels.**
- 6. Individual counseling sessions were held frequently. Both groups received the same information on dietary fiber (recommended intake 25 grams per day) and types of dietary fat. Trans fats were eliminated.**

RESULTS

- 1. Observation for each participant ended at 1 year. A total of 82% low-fat group completed a 12-month trial and 79% of the low-carb group completed the trial.**
- 2. Baseline characteristics were similar between groups: Mean levels of body weight, body mass index, lipids, plasma glucose, and BP; also use of anti-hypertension medicine and lipid-lowering drugs.**

3. Daily dietary compositions

	Baseline		12 months	
	Low fat	Low carb	Low fat	Low carb
Energy kcal	2034	1998	1527	1446
Carbohydrate grams	242	242	198	127
Total fat grams	80	75	52	69

(Note: At 12 months, subjects in the low carb diet were consuming considerably less energy than those in the low fat group. Total fat intake actually decreased slightly in the low-carb diet.)

4. Physical activity remained similar.

5. At 12 months, the low-carb diet had several advantages:

More weight loss (- 5.2 kg vs -1.8 kg—statistically significant)

Greater reduction in 10-year Framingham risk score (-1.0% vs +0.4%)

More fat loss and greater proportional gain in lean body mass

Greater rise in HDL-cholesterol (significant)

Greater decrease in triglycerides (significant)

6. No serious adverse effects were reported.

DISCUSSION

1. The low-carb diet induced greater weight loss and reductions in cardiovascular risk factors than the low-fat diet. It resulted in greater improvements in body composition, HDL-c, triglycerides, and estimated 10-year CHD risk.
2. This trial may offer new evidence for recommending a low-carb diet to obese persons in addition to other non-pharmacological approaches for weight loss and reduction in CVD risk factors.
3. Typical low-carb diets for weight loss contain 20% of energy intake from carbohydrates. This trial contained 30%.
4. This study suggests that loss of fat mass accounts for most of the loss of body weight on the low-carb diet.
5. A recent study indicated that a low-carb diet may have a more favorable effect on resting energy expenditure and total energy expenditure.
6. The study also observed moderate reductions in BP, plasma glucose, serum insulin, and serum creatinine that did not differ significantly between groups.

CONCLUSION

Over 12 months, a low carbohydrate diet resulted in greater weight loss than a low-fat diet. Reducing carbohydrate may be an option for weight loss, and reducing cardiovascular risk factors.

Annals Internal Medicine September 2, 2014; 161: 309-18 Original investigation, first author Lydia A Bazzano, Tulane University School of Public Health, New Orleans, Louisiana.

Funded by the National Institutes of Health.

This is an interesting, but not a strong study. It lasted only one year and did not include clinical benefits.

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9-5 TWO DRUGS FOR WEIGHT LOSS: From the Medical Letter for Drugs and Therapeutics.

In 2012, the FDA approved one new drug and a new combination of 2 old drugs to add to lifestyle changes for chronic weight management.

These new drugs are approved for use in obese patients (BMI 30 and above), and for overweight patients (BMI 27 and above) who have one weight-related risk factor such as hypertension, dyslipidemia, or type-2 diabetes.

1) Lorcaserin (*Belviq*) is a schedule IV controlled substance. It is a serotonin receptor agonist acting mainly in the CNS, suppressing appetite. It is unlikely to cause hallucinations, cardiac-valvulopathy, or pulmonary hypertension, which have been associated with other serotonin agonists.

Lorcaserin approval was based on 3 trials of obese and overweight adults. After 1 year, in one trial, participants lost 5.8 kg compared with 2.2 kg for placebo. Those taking lorcaserin were then randomized for 1 year to 1) continued drug or 2) placebo. Those continuing lorcaserin regained 25% of their initial weight loss. Those in the placebo group regained more weight, losing only 1.2 kg more than those who had taken placebo for 2 years. In a second trial of patients with type-2 diabetes, the HbA1c in those taking lorcaserin was lowered by 1% vs 0.4% for the placebo group

Adverse effects of lorcaserin: headache, dizziness, nausea. Withdrawal rate was as high as 50%.

2) *Qsymia* is a fixed dose combination of 2 drugs: the weight loss drug phentermine and an extended-release form of topiramate.

Phentermine is a sympathetic amine that has been available for many years. It was used for short term treatment of obesity. When combined with fenfluramine (phen-fen), it was associated with heart valve abnormalities, and it was withdrawn from the market. There have been rare reports of valvular disease in patients taking phentermine alone.

Topiramate is a carbonic anhydrase inhibitor. It has produced significant weight loss in some trials. The mechanism is unknown.

Approval of *Qsymia* was based on several trials. In one trial, at one year weight loss was 8 to 10 kg compared with placebo loss of 1.4 kg. When continued for a second year, the weight loss remained at 9 to 10 kg.

Adverse effects: In 5% of patients: dry mouth, parenthesis, constipation, and with higher doses, insomnia. Cognitive difficulties, attention, concentration, and memory difficulties have been reported. Discontinuation rate at one year was 40%.

Metabolic acidosis and kidney stones can occur. Adverse effects may occur when combined with some other drugs. It has been associated with increased risk of oral cleft when taken in the first trimester of pregnancy.

Orlistat, an older drug for weight loss (a lipase inhibitor) is modestly effective. Patients have lost 2.5-3.5 kg more than placebo over 1-4 years. But it causes unpleasant adverse effects such as flatulence with discharge, oily spotting, and fecal urgency.

The sympatho-minetics (eg, methamphetamine), which are approved for short term use to initiate weight loss may have a high abuse potential and adverse cardiovascular and CNS effects. They are best not used.

CONCLUSION

Both *Belviq* and *Qsymia*, taken as adjuncts to diet and exercise may be beneficial in increasing weight loss in the first year. But less weight is lost in the second year.

Both drugs can cause troublesome adverse effects.

JAMA September 3, 2014;312: 955-57 From the Medical Letter for Drugs and Therapeutics.

I would not prescribe these drugs. I would leave them to clinicians who have special interests in obesity treatment and are familiar with the drugs.

Note the high withdrawal rate.

9-6 COMPARATIVE EFFECTS OF GENERIC STATINS AND BRAND NAME STATINS ON PATIENT OUTCOMES: A Cohort Study

Statins are the most frequently prescribed drugs in the U.S. They reduce the relative risk of major cardiovascular events by 21% for each 39 mg/dL (1 mmol/L) reduction in LDL-cholesterol levels in patients at low risk for vascular disease. Patients assigned to statins in trials tend to achieve reductions in LDL-c of 70 mg/dL with doses used regularly in practice.

However, in practice, patients assigned to statins do not fully adhere to statins and may not receive full benefits. Approximately half of patients in ambulatory care discontinue statin therapy within 1 year of initiation.

Medication non-adherence is a complex multi-factorial process. Drug costs may be one of the most modifiable determinants of non-compliance. Reducing patient spending for prescription drugs can improve adherence and, in some cases, improve clinical outcomes.

In small trials, generic drugs have been shown to be clinically equivalent to their counterparts, as required by the FDA. They are less expensive than brand-name drugs and have been associated with better adherence. However, no study has investigated whether the use of generics vs brand-name statins leads to improved health outcomes.

The study asked whether patients who were more adherent to therapy after initiating a generic statin versus a brand-name statin and whether this resulted in differences in health outcomes.

STUDY

- 1. This was an observational study (2006-2008) of Medicare beneficiaries age 65 and older who received a first prescriptions for a statin drug.**
- 2. Each filled prescription was linked to health care utilization and demographic data from Medicare files. The cohort included patients who initialed a statin (generic or brand-name lovastatin, pravastatin, or simvastatin).**
- 3. The primary composite clinical outcome was hospitalization for any acute coronary syndrome or stroke and all-cause mortality. Adherence was measured as the proportion of days covered by the index statin up to 1 year after the index**

prescription. The end of the study was 365 days after the index prescription.

RESULTS

1. 90 111 patients met the study eligibility criteria and initiated a statin during the study; 93% initiated a generic statin, mostly simvastatin.

	Generic	Brand name
Simvastatin	57 493	4629
Pravastatin	14 304	1720
Lovastatin	11 934	31

2. Mean age = 75.6. Generic drug users were more likely to be female, to be socially disadvantaged, and to be unemployed.

3. The average proportion of days covered by statin: 77% for generics; 71% for brand name.

4. Among 55 496 person-years of follow-up, 10 582 patients (12%) had at least 1 clinical outcome of interest. After adjusting for confounding, there was an 8% greater reduction in the rate of the primary composite outcome among generic users compared to brand-name users. The absolute difference was -1.53 events per 100 person-years.

5. Hazard ratios for outcomes (propensity score matched):

Outcome	Hazard ratio
Composite endpoint	0.92
Hospitalization for acute coronary syndrome	0.92
Hospitalization for stroke	0.96
Death from any cause	0.95

6. Adherence to therapy was the factor responsible for the primary findings in this study.

DISCUSSION

1. Patients initialing a generic statin were more likely than those initiating a brand-name statin to adhere to their prescribed treatment. Generic users had an 8% lower rate of a composite endpoint of cardiovascular disease and death.

2. Generics reduce patient out-of-pocket costs and payer spending. In this study, the mean payment for the index statin prescription was \$10 for the generic and \$48 for the brand name. It is not surprising that adherence is greater with generics.

3. The finding of an 8% reduction in the rate of the composite outcome among generics is commensurate with the expected effect based on the observed differences in adherence.
4. Given the observed proportion of days—77% for generic statins, and a 71% for brand name statins—the expected reduction in vascular events would be 32% and 29% respectively, an 8% reduction.
5. The study has limitations. Observational studies are subject to bias and confounding. Although propensity score methods were used to adjust for baseline differences in a large number of patient characteristics, there may be differences between the two groups in ways that could not be measured.
4. The results of the primary analysis were driven largely by acute coronary events, which is consistent with the pharmacology of statins.
5. Generic versions of atorvastatin and fluvastatin are now available. However, many patients still receive brand name drugs when a biologically equivalent generic is available.
6. This study was based on 3 statins which are generally considered to be low-intensity. It may not apply to high-intensity statins (atorvastatin and rosuvastatin).
7. The study was based on patients age 65 and older, it may not be generalizable of other populations.

CONCLUSION

Use of generic statins versus brand name statins was associated with lower out-of-pocket costs, improved adherence to therapy, and improved clinical outcomes.

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This article is important. It points out several applications which are important and generalizable to primary care:

1. Physicians should be mindful of the cost patients incur for their prescription drugs and procedures.

2. Physicians should know the socio-educational backgrounds of patients and gauge whether they can afford their medications and procedures. Help them if possible.

3. Prescribe generics most of the time, if available.

4. . Frequently ask patients if they are taking their medications as prescribed. Tell them, if they do not take them regularly they may not achieve full benefit.

