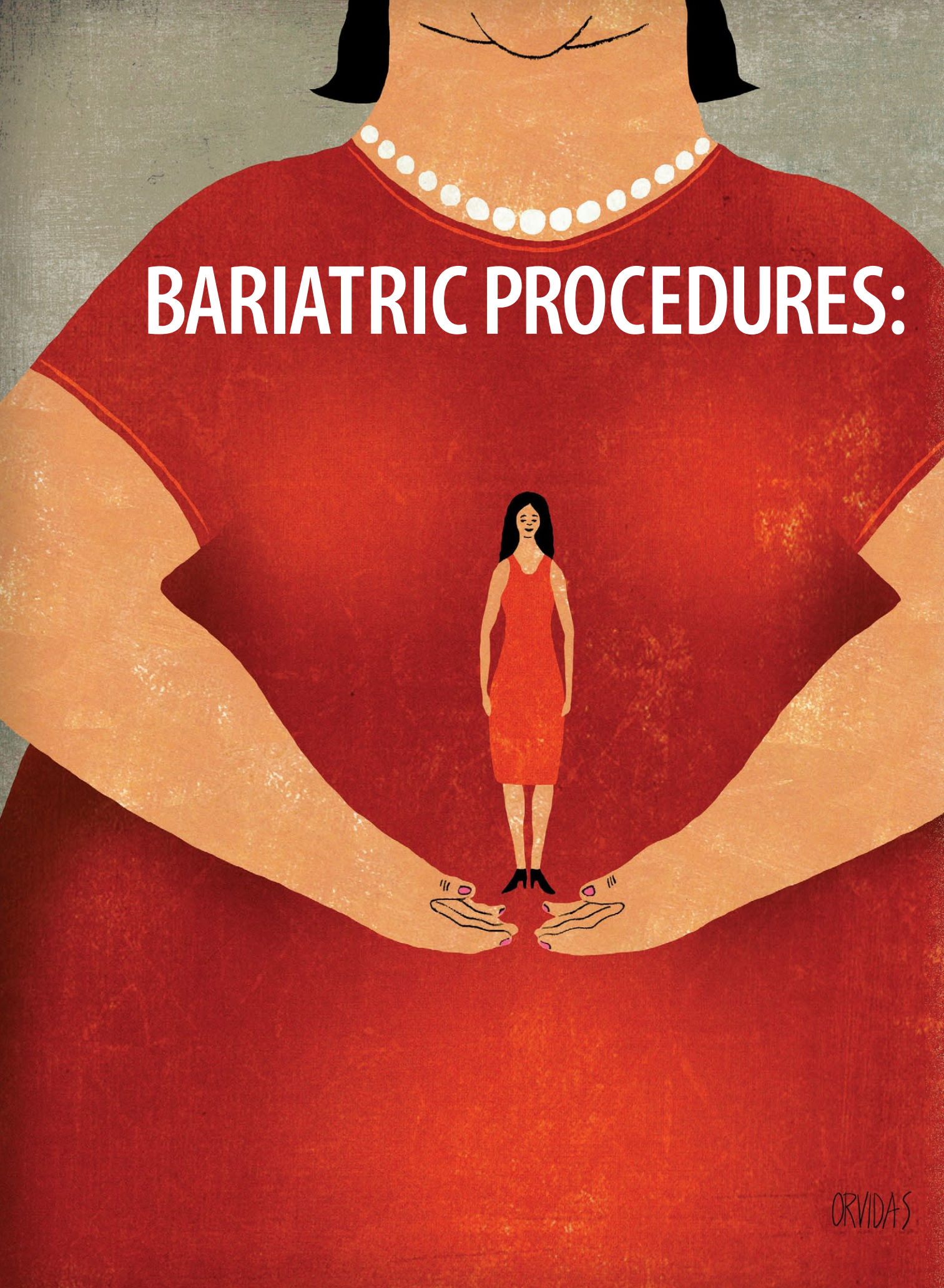
BARIATRIC PROCEDURES:



Web audio at CurrentPsychiatry.com
Dr. Sarwer: Patients' psychosocial concerns after bariatric surgery

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Managing patients after surgery

Changes in the gastrointestinal tract and body weight can alter drug absorption

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Bariatric surgery is the most effective treatment for obesity (defined as a body mass index [BMI] ≥30 kg/m^2) and is recommended for extremely obese individuals (BMI ≥40 kg/m^2) age ≥18.[1,2] Most patients experience significant weight loss accompanied by improvements in mood, physical comorbidities, and quality of life (***Box, page 20***).[3-8] Despite these favorable outcomes, several aspects of postoperative care—such as management of mental health issues—remain unclear. Bariatric surgery candidates show high rates of preoperative psychopathology, particularly depression and dysphoria. Little is known about how bariatric surgery affects absorption of psychiatric medications, leaving prescribing clinicians with minimal guidance when a postoperative patient reports changes in mood symptoms.

This article discusses the psychosocial status of bariatric surgery candidates and presents a rationale for increased medication monitoring after surgery.

Surgical treatment of obesity

The most common surgical procedures for weight loss are adjustable gastric banding (AGB) and Roux-en-Y gastric bypass (RYGB); each can be performed laparoscopically. With both procedures, food intake is restricted by creating a gastric pouch at the base of the esophagus. RYGB (***Figure, page 27***)[9,10] also is thought to induce weight loss through selective malabsorption and favorable effects on gut peptides[11,12] and currently is the procedure of choice in the United States.[13]

Bariatric surgery patients typically lose 25% to 35% of their initial body weight within 12 to 18 months of surgery.[3,4] However, 20% to

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Bariatric surgery

Clinical Point

Rapid reduction in body weight and fat mass may impact the efficacy and tolerability of antidepressants

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Box

Outcomes after bariatric surgery: Physical and psychological improvements

Weight loss after bariatric surgery is associated with significant improvements in obesity-related comorbidities, including diabetes and cardiovascular disease, and decreased mortality.[3,4]

Many patients are able to reduce or discontinue many of their nonpsychiatric preoperative medications as their comorbid conditions improve.[5] Symptoms of depression and anxiety, health-related quality of life, self-esteem, and body image often improve dramatically in the first year after surgery and endure for several years.[6,7]

Psychosocial improvements, however, may not translate into changes in psychotropic use. In a sample of 114 bariatric surgery patients, 43% were taking a selective serotonin reuptake inhibitor before surgery, 40% at 12 months postsurgery, and 31% at 24 months.[8] These percentages do not account for patients who were taking other types of antidepressants.

30% of patients fail to achieve typical postoperative weight loss or regain large amounts of weight within a few years.[14-16] Suboptimal results have been attributed to multiple factors, including problematic dietary intake, disordered eating, low levels of physical activity, preoperative psychopathology, and poor follow-up.[6,17,18]

Preop psychopathology

Twenty percent to 60% of extremely obese persons who pursue bariatric surgery have a psychiatric illness.[6,7] In a study of 288 bariatric surgery candidates assessed with the Structured Clinical Interview for DSM-IV, 38% received a current axis I diagnosis and 66% were given a lifetime diagnosis.[19] In a separate study of 174 individuals seeking bariatric surgery, 24% met criteria for a current axis I or axis II disorder and 37% were found to have ≥1 lifetime diagnoses.[20] The most common lifetime diagnoses were affective disorders (22%), anxiety disorders (16%), and eating disorders (14%).[20]

Psychopathology could negatively impact postoperative outcome. In an observational study, patients with a lifetime diagnosis of any axis I disorder—particularly mood and anxiety disorders—experienced less weight loss 6 months after RYGB compared with those who never received an axis I diagnosis.[21] Bariatric surgery patients with ≥2 psychiatric diagnoses were more likely to stop losing weight or regain weight after 1 year compared with those with 1 or no diagnosis.[22] Psychiatric illness also appears to impact longer term weight loss.[23]

Most bariatric surgery programs in the United States require a mental health evaluation as part of the patient selection process.[24] These assessments may include evaluating a patient's behavior patterns, motivation, expectations, and cognitive and emotional functioning, and performing psychological testing (see ***Related Resources, page 29***). Psychiatric problems such as substance abuse, active psychosis, bulimia nervosa, and severe, uncontrolled depression[1,9,25] are widely considered contraindications to bariatric surgery.[24,26]

Postsurgery considerations

At the time of bariatric surgery 16% to 40% of patients are receiving mental health treatment, which often includes antidepressants.[27-29] Unfortunately, little is known about how medications interact with these surgical procedures. Dramatic changes in medication absorption may occur because of reduced gastrointestinal (GI) surface area. Rapid reduction in body weight and fat mass and postoperative complications also may impact the efficacy and tolerability of antidepressants.

Pharmacokinetics. Anatomic and physiologic changes with bariatric surgery may lead to changes in the pharmacokinetic (PK) parameters of certain medications, particularly after RYGB. PK studies typically are conducted by collecting a series of plasma samples at predetermined intervals after a patient takes a medication. The blood levels of the medication and its active metabolites are used to compute multiple PK parameters that illustrate drug absorption, distribution, and metabolism. Theoretically, a bariatric surgery patient

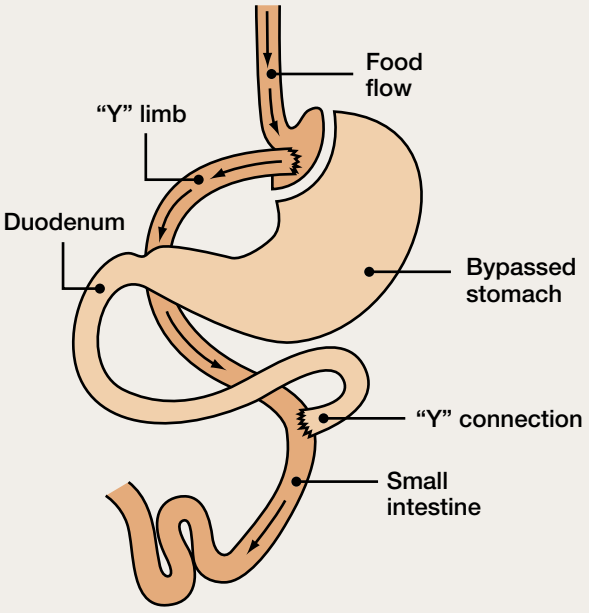
continued on page 27

continued from page 20

Figure

Roux-en-Y: Bariatric procedure of choice

Roux-en-Y gastric bypass typically involves creating a small, proximal gastric pouch with a capacity of 15 to 25 ml, which is then attached to the jejunum via a 12 mm in diameter gastrojejunostomy, leaving a Roux limb that ranges in length from 60 to 250 cm. The minimum amount of the gastrointestinal tract bypassed includes the distal stomach, the duodenum, and approximately 40 cm of the proximal jejunum.



Source: References 9,10

may experience changes in the rate and/or extent of:

- medication absorption from the GI tract into systemic circulation
- distribution throughout the body as fat mass and total body water change after surgery
- drug metabolism.

The effects of bariatric surgery on medication PK appears to be drug-specific.[30-33]

The bypassed portion of the GI tract is the primary absorption site for most medications; therefore, the length of the Roux limb may affect the extent of drug absorption impairment. However, the duodenum wall is one of many locations of the cytochrome P450 (CYP) isoenzymes CYP3A4 and CYP3A5,[34] which are the primary metabolic enzymes for drugs such as atorvastatin. Eliminating this portion of the bowel could increase rather than decrease bioavailability.[35] Alterations in drug absorption also may result from changes in gastric emptying rate, reduced exposure to absorptive mucosal surfaces, and alterations in gastric pH that can impair drug dissolution and solubility.[30] These changes could reduce medication bioavailability.[33]

The impact of such changes may differ according to the characteristics of the specific drug. It has been theorized that drugs that are intrinsically poorly absorbed, are highly lipophilic, and undergo enterohepatic circulation carry the highest risk of malabsorption.[30] Antidepressants vary in the extent to which they demonstrate these characteristics. Progressive changes in the volume of distribution as weight is lost also could affect the blood levels of some antidepressants.

A series of small studies and case reports of PK changes in medications such as digoxin, oral contraceptives, cyclosporine, sulfisoxazole, and tacrolimus after jejunoileal bypass—an older, obsolete bariatric procedure—reveal variability in the surgery's effect on PK parameters, although most reported reduced absorption. Data specific to RYGB consist of small studies and case series that show reduced absorption after surgery with significant variability among agents (visit CurrentPsychiatry.com for a bibliography of studies describing PK changes in nonpsychiatric medications after bariatric surgery). In a systematic literature review, Padwal et al

Clinical Point

The effects of bariatric surgery on medication pharmacokinetic parameters appears to be drug-specific

Bariatric surgery

Clinical Point

There may be significant variability among antidepressants with regard to implications of an altered GI environment

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Visit this article at CurrentPsychiatry.com for a bibliography of studies of PK changes in nonpsychotropics

Table

Weights of dissolved portions of antidepressants before and after simulated RYGB

	Simulated pre-RYGB environment		Simulated post-RYGB environment		
Drug	Median weight of dissolved portion (mg)	Percentage*	Median weight of dissolved portion (mg)	Percentage*	*P*†
Amitriptyline, 75 mg/d	80	28%	60	21%	<.04
Fluoxetine, 20 mg/d	110	30%	40	11%	<.04
Paroxetine, 20 mg/d	30	9%	10	3%	<.04
Sertraline, 100 mg/d	50	16%	30	10%	<.04
Bupropion, 100 mg/d	320	52%	450	73%	<.05
Venlafaxine, 75 mg/d	180	59%	180	59%	Not significant
Citalopram, 20 mg/d	70	27%	80	31%	Not significant

*Relative to original pill weight
†Mann-Whitney U test
RYGB: Roux-en-Y gastric bypass
Source: Adapted from reference 37

found evidence for a decreased magnitude of absorption in 15 of 22 studies of jejunoileal bypass patients, 1 of 3 studies of gastric bypass/gastroplasty, and no studies examining biliopancreatic diversion.[30]

It is unclear if antidepressant absorption is impaired after RYGB because currently only 1 case report presents in-vivo data. Hamad et al describe an obese patient (BMI 46 kg/m^2) taking sertraline, 100 mg/d, for depression.[36] Researchers measured sertraline levels before and 1 month after RYGB, at which time the patient's depression worsened. After surgery, sertraline maximum concentration was lower (14.4 ng/ml vs 41.6 ng/ml), trough concentration was lower (11.1 ng/ml vs 17.5 ng/ml), and time to maximum concentration was shorter (240 vs 300 minutes). This suggests that a shift in sertraline absorption after surgery may have contributed to the patient's worsened mood symptoms.

An in-vitro study that simulated pre- and post-RYGB GI environments found that 12 of 22 psychotropic drugs tested dissolved differently between the models.[37] Whereas the dissolved fractions of amitriptyline, fluoxetine, paroxetine, and sertraline were significantly less in the post-RYGB environment, bupropion dissolved to a greater extent in the pre-RYGB environment, and venlafaxine and citalopram were not different between the 2 conditions (***Table***).[37] Although several limitations prevent translating these data into clinical recommendations, this study suggests that there may be significant variability among medications with regard to the implications of an altered GI environment.

Altering antidepressant doses

Current PK data are insufficient to make clinical recommendations regarding appropriate postsurgical adjustment of dose or alternate dosage formulations (liquid, extended-release, etc.). However, based on theoretical considerations, Miller and Smith suggest that patients avoid extended-release preparations whenever possible after bariatric surgery, citing the rationale that decreased intestinal length and sur-

face area leads to reduced absorption.[33] No data are available to advise clinicians regarding the appropriateness of switching patients from extended-release products to immediate-release or liquid preparations following surgery.

Presently, increased medication monitoring may be the most appropriate clinical approach. If appropriate doses have little or no effect, consider the possibility of decreased medication absorption.[33] Monitoring plasma levels of medications that have therapeutic ranges also is advisable.

Areas for future research

Before specific clinical recommendations for managing antidepressants following RYGB can be proposed, the extent to which the absorption, volume of distribution, drug metabolism, and other measures change after surgery need to be quantified. It is also unclear whether changes in medication absorption are subject to inter-patient variability, whether predictive characteristics can be identified, and whether any observed changes remain stable over time. Similarly, the extent to which variability in surgical procedures (eg, surgeon preference regarding remnant intestinal length) affects medication absorption is unknown. Data regarding medication absorption following AGB and other bariatric procedures also will be needed.

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Related Resources

- American Society for Metabolic and Bariatric Surgery. Fact sheet: Metabolic and bariatric surgery. www.asbs.org/Newsite07/media/asmbs_fs_surgery.pdf.
- American Society for Metabolic and Bariatric Surgery. Suggestions for the pre-surgical psychological assessment of bariatric surgery candidates. www.asmbs.org/html/pdf/PsychPreSurgicalAssessment.pdf.

Drug Brand Names

Amitriptyline • Elavil
Atorvastatin • Lipitor
Bupropion • Wellbutrin
Citalopram • Celexa
Cyclosporine • Sandimmune
Digoxin • Lanoxin
Fluoxetine • Prozac
Paroxetine • Paxil
Sertraline • Zoloft
Sulfisoxazole • Truxazole
Tacrolimus • Prograf
Venlafaxine • Effexor

Disclosures

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Clinical Point

Presently, increased medication monitoring may be the most appropriate clinical approach

Bottom Line

Bariatric surgery candidates often present with psychopathology, particularly dysphoria and often DSM-IV-TR mood disorders. Most bariatric surgeons and third-party payers require presurgical psychological evaluation, in part because of the relationship between preoperative psychosocial functioning and postoperative outcomes. Bariatric surgeries could substantially change blood levels of psychiatric medications via alterations of the gastrointestinal tract. Dramatic changes in body weight and postoperative complications also can influence medication levels.

continued

This month's instant poll

For 2 years Ms. S, age 46, has been treated for depression with venlafaxine extended-release (XR), 75 mg/d, and has been doing well. Recently she underwent Roux-en-Y surgery and experienced substantial weight loss and improved overall quality of life. **How would you continue to treat her?**

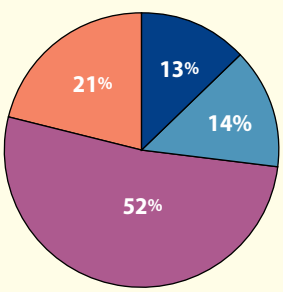
- ☐ Increase venlafaxine XR dosage
- ☐ Switch to an antidepressant from a different class
- ☐ Decrease venlafaxine XR dosage
- ☐ Make no change and carefully monitor for re-emergence of depressive symptoms
- ☐ Switch to an immediate-release formulation of venlafaxine

See **'Bariatric procedures: Managing patients after surgery'** *page 18-30*

Visit CurrentPsychiatry.com to answer the **Instant Poll** and see how your colleagues responded. ***Click on "Have more to say?"*** to comment.

NOVEMBER POLL RESULTS

For the last 8 years, Ms. U, age 68, has been taking paroxetine, 30 mg/d, for moderate anxiety and has had positive results. During her last visit, she mentions that her primary care physician recently prescribed a calcium channel blocker and aspirin for hypertension. She has no other medical comorbidities and is in good health. **Which strategy would you try first?**

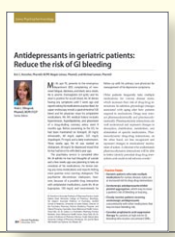


13% Begin prophylactic acid-suppressing treatment with an H2 antagonist to reduce her risk of internal bleeding

14% Consider a different antidepressant, such as bupropion

52% Do not change her medication regimen, but closely monitor Ms. U for signs of bleeding, such as black tarry stools or easy bruising

21% Suggest that Ms. U ask her primary care physician to prescribe a different medication to help lower her blood pressure


Antidepressants in geriatric patients: Reduce the risk of GI bleeding

▲ Data obtained via CurrentPsychiatry.com, November 2010

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PK: pharmacokinetic

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