

Things We Do for No Reason™: Prescribing Appetite Stimulants to Hospitalized Older Adults With Unintentional Weight Loss

Lindsey Gay, MD^{1,2}, Shaila Sheth, PharmD^{1,2}, Molly J Horstman, MD, MS^{1,3,4*}

¹Michael E DeBakey VA Medical Center, Houston, Texas; ²Section of General Internal Medicine, Department of Medicine, Baylor College of Medicine, Houston, Texas; ³Section of Health Services Research, Department of Medicine, Baylor College of Medicine, Houston, Texas; ⁴Center for Innovations in Quality, Effectiveness and Safety (IQUES), Michael E DeBakey VA Medical Center, Houston, Texas.

Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent clear-cut conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

An 87-year-old hospitalized man has lost 7% of his body weight in the past year. His family and the inpatient nutritionist ask about a prescription appetite stimulant.

WHY YOU MIGHT THINK PRESCRIBING APPETITE STIMULANTS FOR UNINTENTIONAL WEIGHT LOSS IN OLDER ADULTS IS HELPFUL

Unintentional weight loss—the loss of more than 10 lb or 5% of usual body weight over 6 to 12 months—affects up to 27% of older adults in the community and 50% to 60% of older adults in nursing homes.^{1,2} Patients who report weight loss on hospital admission have an almost four times greater risk of death in the 12 months following discharge.³ To address unintentional weight loss, clinicians may prescribe appetite stimulants.

Megestrol acetate is approved by the US Food and Drug Administration (FDA) for the treatment of weight loss in patients with AIDS.⁴ Megestrol acetate promotes weight gain through inhibition of cytokines, interleukin-6, and tumor necrosis factor-alpha, which are increased in older adults. In a randomized, placebo-controlled trial of 69 nursing home residents with ≥6 months' life expectancy and Karnofsky score of ≥40%, patients treated with megestrol acetate for 12 weeks reported increased appetite and well-being. They achieved significant weight gain (>1.82 kg), but not until 3 months after therapy ended.⁵ No significant adverse events were reported; however, adverse event monitoring continued only for the 12-week treatment period. This follow-up duration may have

been insufficient to identify some adverse events, such as venous thromboembolism.

Mirtazapine, an antidepressant and serotonin receptor antagonist, reduces levels of serotonin, a neurotransmitter that promotes early satiety.⁶ In a meta-analysis of 11 trials comparing mirtazapine to selective serotonin reuptake inhibitors for depression, patients treated with mirtazapine demonstrated an increase in the composite secondary outcome of weight gain or increased appetite.⁷ The amount of weight gain was not specified. Weight gain is more common with low-dose mirtazapine, potentially due to increased antihistamine activity at lower doses.⁸ Overall, mirtazapine is well-tolerated and efficacious in the treatment of depression and may benefit older adults with concomitant weight loss.⁶

Cyproheptadine is a first-generation antihistamine with appetite-stimulating effects. It has been found to increase weight or appetite in various disease states, particularly in the pediatric population,⁹ including cystic fibrosis¹⁰ and malignancy.¹¹ Given this evidence, there has been interest in its use in the geriatric population with unintentional weight loss.

Dronabinol is an orally active cannabinoid approved for anorexia-associated weight loss in patients with AIDS.¹² In a randomized, placebo-controlled trial in patients with AIDS-related anorexia and weight loss, participants receiving dronabinol had a statistically significant increase in appetite but no change in weight. Participants receiving dronabinol also experienced more nervous system-related adverse events, including dizziness, thinking abnormalities, and somnolence.¹³

WHY PRESCRIBING APPETITE STIMULANTS FOR UNINTENTIONAL WEIGHT LOSS IN OLDER ADULTS IS NOT HELPFUL

Weight gain may not improve clinically meaningful outcomes. The absence of consistent evidence that prescription appetite stimulants improve patient-centered outcomes, such as quality of life or functional status, and the potential morbidity and mortality of these medications make prescribing appetite stimulants in older adults concerning.

Megestrol Acetate

A 2018 systematic review of randomized controlled trials studying megestrol acetate for treatment of anorexia-cachexia, primarily in adults with AIDS and cancer, found that treatment resulted in a 2.25-kg weight gain, with no improvement in quality of life and an increased risk of adverse events.¹⁴

*Corresponding Author: Molly J Horstman, MD, MS;
Email: molly.horstman@bcm.edu; Telephone: 713-791-8601;
Twitter: @mhorstman.

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TABLE. **Contributing Factors to Unintentional Weight Loss and Possible Hospital Interventions**

Contributing factors	Hospital interventions
Acute and chronic medical disease	Medical treatment Bowel regimen for constipation
Restricted diets	Registered dietitian consultation Reduce or stop dietary restrictions Provide snack foods or finger foods Oral nutritional supplements Limiting NPO orders
Functional limitations (upper extremity function, decreased mobility)	Occupational and physical therapy consultations Use of eating and drinking aids Discuss options for assisted feeding with unit nurses
Cognitive impairment, delirium	Meal supervision Discuss options for supervised or assisted feeding with unit nurses
Chewing problems	Oral care Referral for outpatient dental evaluation Texture-modified diet Oral nutrition supplements
Swallowing problems	Speech-language pathologist consultation Swallowing training Texture-modified diet Goals of care discussion with patient and family if enteral tube feeding is recommended
Depression, mood disorders	Medical treatment Communication with outpatient primary care provider and/or referral to outpatient mental health
Poverty, limited food access	Social work consultation for community support programs (eg, Meals on Wheels)
Medication side effects (eg, dry mouth, gastrointestinal upset, constipation)	Reduce, replace, or stop medications, if possible Change the timing of medication administration to limit side effects, if possible

Data were derived from Bouras et al,¹ McMinn et al,² and Volkert et al.²⁷

Abbreviation: NPO, nothing by mouth.

Three prospective trials studied the effect of megestrol acetate in older adults (Appendix Table). One trial randomized 47 patients receiving skilled nursing services following an admission for acute illness to megestrol acetate vs placebo. While the investigators noted increases in appetite at higher doses of megestrol acetate, there was no change in weight or clinically relevant outcomes.¹⁵ In a second randomized controlled trial, 29 patients with illness-induced functional decline were enrolled in a strength training program in addition to being assigned to megestrol acetate or placebo. While patients receiving megestrol acetate with the exercise program had significant increases in weight and nutritional intake, they suffered a deterioration in physical function.¹⁶ In a pilot study, 17 nursing home residents who consistently ate less than 75% of their meals received megestrol acetate plus standard or optimal feeding assistance. The percentage of meals consumed increased only when patients received optimal feeding assistance in conjunction with megestrol acetate.¹⁷

The largest case-control study examining megestrol acetate for unintentional weight loss in older adults compared 709 residents in a multistate nursing home system treated with mege-

strol acetate to matched untreated controls. After 6 months of treatment, the median weight and change in weight did not differ significantly. Patients receiving megestrol acetate had a significant increase in mortality, surviving an average of 23.9 months, compared to 31.2 months for controls ($P < .001$).¹⁸

Additionally, two retrospective reviews of nursing home patients who were prescribed megestrol acetate showed incidences of venous thrombosis of 5% and 32%.^{19,20} Other potentially significant adverse effects include adrenal insufficiency and fluid retention.⁶ In 2019, the American Geriatrics Society's Beers Criteria included megestrol acetate as a medication to avoid given its "minimal effect on weight; increases [in] risk of thrombotic events and possibly death in older adults."²¹

Mirtazapine

No studies have evaluated mirtazapine for weight gain without concomitant depression. In older adults with depression, mirtazapine has minimal impact on promoting weight gain compared to other antidepressants. In two retrospective studies of older patients with depression and weight loss, researchers found no difference in weight gain in those treated with

mirtazapine vs sertraline or other nontricyclic antidepressants, excluding fluoxetine.^{22,23}

Cyproheptadine

There have been no controlled trials evaluating the use of cyproheptadine in older adults, in part due to anticholinergic side effects. In a trial of cancer patients, sedation and dizziness were common adverse effects.¹¹ The 2019 American Geriatrics Society's Beers Criteria include cyproheptadine as a medication to avoid based upon the "risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity."²¹

Dronabinol

In a retrospective cohort study of 28 long-term care residents with anorexia and weight loss, participants receiving dronabinol for 12 weeks had no statistically significant weight gain.²⁴ The FDA cautions against prescribing dronabinol for older adults due to neurological side effects.¹² A systematic review of randomized controlled trials found that cannabinoid-based medications in patients older than 50 years were associated with a significant increase in dizziness or lightheadedness and thinking or perception disorder.²⁵

WHAT YOU SHOULD DO INSTEAD

In the *Choosing Wisely*[®] initiative, the American Geriatrics Society recommends avoiding prescription appetite stimulants for patients with anorexia or cachexia.²⁶ Instead, hospitalists should evaluate older patients for causes of unintentional weight loss, including malignancy, nonmalignant gastrointestinal disorders, depression, and dementia. Hospitalists can identify most causes based on the history, physical exam, and laboratory studies and initiate treatment for modifiable causes, such as constipation and depression.²

Hospitalists should work with an interprofessional team to develop an individualized plan to optimize caloric intake in the hospital (Table).²⁷ One in five hospitalized older adults has insufficient caloric intake during admission, which is associated with increased risk for in-hospital and 90-day mortality.²⁸ Removing dietary restrictions, increasing the variety of foods offered, and assisted eating may increase food intake.^{27,29} Hospitalists should also consider discontinuing or changing medications with gastrointestinal side effects, such as metformin, cholinesterase inhibitors, bisphosphonates, and oral iron supplements. Dietitians may recommend oral nutrition supplements; if started, patients should be offered supplements after discharge.^{27,29} For patients with limited access to food, social workers can help optimize social supports and identify community resources following discharge. Finally, hospitalists should coordinate with outpatient providers to monitor weight long-term.

RECOMMENDATIONS

- Recognize and address unintentional weight loss in older adults in the hospital.
- Do not prescribe appetite stimulants for unintentional weight loss in hospitalized older adults as they have no proven benefit for improving long-term outcomes and, in

the case of megestrol acetate, may increase mortality.

- Work with an interprofessional team to address factors contributing to unintentional weight loss using nonpharmacologic options for improving food intake.

CONCLUSION

After discussing the lack of evidence supporting prescription appetite stimulants and the potential risks, we shifted the focus to optimizing oral intake. The team worked with the patient and the patient's family to optimize nutrition following discharge and communicated the need for ongoing monitoring to the primary care provider.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason™"? Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason™" topics by emailing TWDFNR@hospitalmedicine.org

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