

# A Retrospective Study of the Association Between Megestrol Acetate Administration and Mortality Among Nursing Home Residents with Clinically Significant Weight Loss

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## ABSTRACT

**Background:** Megestrol acetate (MA) is a progestin widely used to treat weight loss and cachexia in patients suffering from AIDS or cancer. Although MA is also frequently prescribed for similarly malnourished elderly individuals, the efficacy and morbidity of MA treatment in this patient population remain unclear.

**Objective:** The goal of this study was to examine the effects of MA therapy on weight and overall mortality in elderly nursing home residents.

**Methods:** This was a case-control cohort study of 17,328 nursing home residents admitted to a Beverly Healthcare nursing home between January 1, 2000, and December 31, 2003, who had lost either 5% of total body weight within 3 months or 10% of total body weight within 6 months. Residents within this weight loss group who received MA therapy—within 30 days of their weight loss documentation—were matched (1:2) with non-MA-treated residents with respect to age, sex, race, weight, and first notation of weight loss. Residents were further matched by propensity score for activities of daily living, cognitive functioning, number of medications taken during the 7 days before data entry, clinical condition (unstable, acute episode of a recurrent problem, end-stage disease), cancer diagnosis, and human immunodeficiency virus diagnosis.

**Results:** A total of 709 patients (mean [SD] age, 84.1 [9.7] years; 70.9% female) who received MA therapy were matched with 1418 non-MA-treated patients (mean [SD] age, 84.2 [9.0] years; 70.9% female). Of the 709 MA patients, 281 (39.6%) were alive and in the nursing home at last follow-up, 149 (21.0%) were alive and discharged to another facility or to home, and 279 (39.4%) died in the nursing home. For the controls, 651 (45.9%) were alive and in the nursing home, 308 (21.7%) were discharged to another facility or to home, and 459 (32.4%) died in the nursing home. The median survival of MA-treated residents (23.9 months; 95% CI, 20.2–27.5) was significantly less than untreated residents (31.2 months; 95% CI, 27.8–35.9) ( $P < 0.001$ ). Median weight and median of weight differences were unchanged after 6 months of treatment with MA compared with matched controls.

**Conclusions:** MA treatment of elderly nursing home residents with significant weight loss was associated with a significant increase in all-cause mortality without a significant increase in weight. Randomized, prospective studies of the use of MA in elderly nursing home residents are necessary to more fully evaluate morbidity and mortality associated with this therapy. (*Am J Geriatr Pharmacother.* 2007;5:137–146) Copyright © 2007 Excerpta Medica, Inc.

**Key words:** megestrol acetate, aged, nursing home, elderly.

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## INTRODUCTION

The prevention and treatment of weight loss in nursing home residents have become major goals among providers under the assumption that this practice prolongs life. Nursing homes are also under intense scrutiny to prevent unintentional weight loss under the federal regulations set forth by the federal Nursing Home Reform Act under the Omnibus Budget Reconciliation Act of 1987.<sup>1</sup> Low body mass index or poor nutritional status are clearly associated with increased mortality<sup>1</sup>; however, there are few data that demonstrate improved survival with refeeding of this patient population. To complicate the issue, treatment of weight loss is not an easy matter in these patients. Oral dietary supplementation is effective but difficult to execute, and tube feedings entail invasive procedures with ethical and possibly legal consequences.

Megestrol acetate (MA) is a progesterone-like hormone that has been utilized as a birth control agent,<sup>2,3</sup> chemotherapeutic drug, and, more recently, to induce appetite and weight gain in patients malnourished as a result of cancer, chemotherapy, cystic fibrosis, AIDS, or dementia.<sup>4-15</sup> Although only approved to combat weight loss associated with AIDS,<sup>16</sup> MA is frequently prescribed for long periods of time to prevent or reverse weight loss in frail nursing home residents and in elderly patients with serious illnesses in the community. Of the monies spent on medication in the Beverly Healthcare nursing home system in 2002, MA ranked eighth, at an expense of approximately \$1.25 million annually (T. Hughes, BS, personal oral communication, June 2003). However, few data are available to support this practice. Moreover, MA treatment is associated with real and potential adverse effects. Among its many properties, MA acts as a partial glucocorticoid agonist. Both long-term and short-term use of MA has been reported to cause adrenal suppression.<sup>17-28</sup> In men, MA markedly decreases testosterone levels and results in substantial loss of lean muscle mass.<sup>29</sup> MA is also associated with an increased risk of deep venous thrombosis.<sup>30</sup> There are reports that MA therapy may be associated with increased mortality in patients with AIDS<sup>31</sup> and cancer.<sup>32</sup>

In some studies,<sup>33,34</sup> MA has been shown to successfully treat anorexia and weight loss in frail elders (ie, those aged >65 years); however, its impact on mortality in this patient population is unknown. To examine this issue, we retrospectively identified elderly nursing home residents who had experienced significant weight loss and examined the effect of MA treatment on weight and overall mortality.

## MATERIALS AND METHODS

### Study Design and Population

Beverly Healthcare is one of the largest nursing home providers in the United States, operating in 32 states. The patient records in these facilities are largely computerized and accessible. One aspect of the computerized patient record is the minimum data set (MDS) assessment, a tool that is required by Medicare and Medicaid to be completed for each resident on admission to the nursing home facility, quarterly, and at any time point when there is a change in physical or mental status. The MDS assessment evaluates cognitive, behavioral, and physical functioning.

The protocol was approved by the University of Arkansas for Medical Sciences Human Research Advisory Committee. Using this database, residents admitted to a Beverly Healthcare nursing home between January 1, 2000, and December 31, 2003, and who had experienced a 5% loss of total body weight in a 3-month period, or a 10% loss in a 6-month period, were identified for further study (N = 17,328). With mortality as the primary end point, it was important to choose an index—or start—date that was common for all residents to ensure as uniform a follow-up period as possible. Admission to the nursing home could have been used as the index date for follow-up, but it had no apparent relationship to the development of weight loss or the initiation of MA. Thus, for consistency, the index date was defined as the first MDS report of weight loss using the above criteria. Residents were therefore excluded if they had no recorded index weight (n = 276), if the index date was the same as the last follow-up date (n = 428), or if the resident was comatose (n = 30) (Figure 1). Of the remaining 16,594 residents with significant weight loss, 2466 had received MA at some time during their stay. MA-treated residents were excluded if they received <7 days of MA (n = 239), were followed up for <30 days after the index date (n = 89), or MA was initiated >30 days from the index date (n = 1429). The remaining 709 residents in the MA group were matched in a ratio (1:2) with non-MA-treated residents alive within 30 days of their index event (Table I). Residents were individually matched for age ( $\pm 10$  years), sex, race (white, black, or other), index date ( $\pm 90$  days), and index weight ( $\pm 20$  pounds).

We also wanted to match the non-MA-treated residents to the MA-treated residents with respect to other factors found in the MDS, specifically activities of daily living, cognitive functioning, unstable condition, acute episode of a recurrent problem, end-stage disease, number of medications taken during the 7 days before

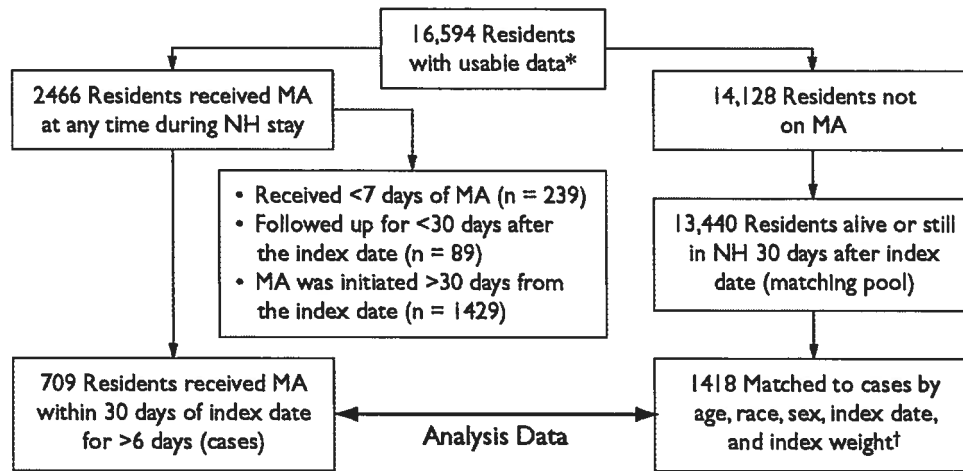


Figure 1. Data set derivation from nursing home (NH) residents with 5% loss of body weight at 3 months or 10% loss at 6 months. MA = megestrol acetate. \*Residents were excluded if they had no recorded index weight ( $n = 276$ ), if the index date was the same as the last follow-up date ( $n = 428$ ), or if the resident was comatose ( $n = 30$ ). †Scores derived from data in the Minimal Data Set (MDS) were also adjusted for by using propensity score methodology (number in parenthesis refers to item number in the MDS). These include activities of daily living score, cognitive functioning, number of medications (O1), unstable condition (J5a), acute episode of a recurrent problem (J5b), and end-stage disease (J5c).

data entry, diagnosis of cancer, and diagnosis of HIV. Because individual matching using these MDS factors quickly became impractical, we used propensity score methods to match the non-MA-treated patients to MA-treated patients. Briefly, propensity scores were calculated using a logistic regression model in which the MA exposure status was modeled as the dependent variable, and the additional matching features were included as independent variables. Using this model, a score was calculated for each patient in the MA-exposed cohort and for each patient in the control pool. This score effectively summarized information from several variables into one value, which was then used as the matching criterion.

Matching was performed using an optimization algorithm described by Rosenbaum.<sup>35</sup> The algorithm was implemented using the %dist SAS macro written by Bergstralh and Kosanke.<sup>36</sup>

### Statistical Analysis

Baseline information from the study cohorts were summarized using mean (SDs) for continuous variables, and percentages and counts for categorical variables. The Student 2-sample  $t$  tests and Pearson  $\chi^2$  tests were used to compare the cohorts with respect to baseline variables. Wilcoxon rank sum tests were

used to compare the weights of the groups at 3 and 6 months, while Wilcoxon signed rank tests were used to compare changes in weight at 3 and 6 months within groups. The primary goal of this study was to determine whether exposure to MA was associated with an increase in mortality in nursing home residents experiencing clinically significant weight loss. As a consequence of the definition of MA exposure, overall survival in this analysis was defined as the time from 30 days past the index date to last follow-up or death. The Kaplan-Meier method was used to estimate survival distributions of the cohorts, and log-rank tests were used to compare the distributions. A Cox proportional hazards (CPH) model was used to adjust the MA effect for potential confounders. Specifically, all of the matching variables were included in the model, as well as those variables that were used in the calculation of propensity scores. Restricted cubic splines were used to account for potential nonlinear associations between the continuous variables and mortality. All 2-way interactions involving MA exposure were evaluated and remained in the final model if they were significant at the 0.10 level. Hazard ratios (HRs) and 95% CIs were calculated for each variable in the final model. One of the assumptions of the CPH model is that the effect of a variable in the model is constant

**Table I. Summary of demographic and disease status variables for the megestrol acetate and control cohorts of elderly nursing home residents with clinically significant weight loss.**

Variable	Megestrol Acetate (n = 709)	Control (n = 1418)	P
Index weight, lb*	122.6 (28.9)	123.9 (27.8)	0.334†
Age, y*	84.1 (9.7)	84.2 (9.0)	0.804†
Index date, days*‡	985.3 (311.2)	984.5 (311.2)	0.951†
Female, %	70.9	70.9	–
Race, %			
White	79.7	79.7	–
Black	13.5	13.5	–
Other	6.8	6.8	–
ADL score*§	2.9 (1.0)	2.9 (1.0)	0.975†
Cognitive functioning score*	3.0 (1.6)	3.0 (1.7)	0.235†
No. of medications*	10.0 (4.2)	9.4 (4.0)	<0.001†
Unstable condition, %	54.9	53.4	0.529¶
Acute episode of a recurrent problem, %	23.3	24.7	0.478¶
End-stage disease, %	1.4	1.1	0.578¶
Cancer diagnosis, %	9.3	8.7	0.631¶
HIV diagnosis, %	0.3	0.1	0.259¶

ADL = activities of daily living.

\*Mean (SD).

†P value was obtained using a Student 2-sample t test.

‡The number of days from January 1, 2000, to each patient's index date was calculated.

§Scored based on a scale of 0 to 4.

||Scored based on a scale of 0 to 6.

¶P value was obtained using a Pearson  $\chi^2$  test.

over time (the proportional hazards assumption). Scaled Schoenfeld residuals were used to evaluate the proportional hazards assumption for each variable in the model.

The survival analyses were performed using PROC LIFETEST and PROC PHREG in SAS version 9.1 (SAS Institute Inc., Cary, North Carolina) and the Hmisc and Design libraries in S-Plus 6.1 (Insightful Corporation, Seattle, Washington).

**RESULTS**

A total of 1418 controls (mean [SD] age, 84.2 [9.0] years; 70.9% female) were successfully matched to the 709 MA-treated residents (mean [SD] age, 84.1 [9.7] years; 70.9% female). The MA and control cohorts were well matched with respect to demographic variables (Table I). Only the number of medications differed significantly between the 2 groups, with the

MA group receiving a mean of 10.0 medications compared with 9.4 medications for the control group ( $P < 0.001$ ). However, this discrepancy is explained by the inclusion of MA in the treated group.

Of the 709 MA patients, 281 (39.6%) were alive and in the nursing home at last follow-up, 149 (21.0%) were alive and discharged to another facility or to home, and 279 (39.4%) died in the nursing home. For the controls, 651 (45.9%) were alive and in the nursing home, 308 (21.7%) were discharged to another facility or to home, and 459 (32.4%) died in the nursing home. Those patients who were discharged to another facility or to home were censored at the time of their discharge. The median survival of the control cohort was estimated to be 31.2 months (95% CI, 27.8–35.9), compared with the median survival of 23.9 months (95% CI, 20.2–27.5) estimated for the MA cohort, representing a 23.4% decrease in median survival

(Figure 2). The log-rank test comparing these distributions was significant ( $P < 0.001$ ). After adjusting for demographic, medical, and quality-of-life variables, the CPH estimates (Figure 3) demonstrated that the MA exposure effect was still highly significant (HR, 1.37; 95% CI, 1.17–1.59). Older age (HR, 1.44; 95% CI, 1.16–1.75) was significantly associated with increased mortality, and female sex correlated with decreased mortality (HR, 0.65; 95% CI, 0.54–0.77).

The median dose of MA was 486 mg (range, 20–2400 mg), with a median duration of administration of 90 days (range, 7–934 days). Patients treated with MA were separated into 3 groups based on initial and mean dosages: <200 mg/d, 200 to 400 mg/d, and >400 mg/d. A total of 214 patients were initially given doses <200 mg/d, of whom 64 had their dosages increased (30 to between 200 and 400 mg/d, and 24 to >400 mg/d). Similarly, 181 patients were initially dosed at between 200 and 400 mg/d, and 30 of these subsequently had their dosage increased to >400 mg/d. Thus, the mean dose was higher than the initial dose in 94 patients and lower than the initial dose in 12, indicating dose titration. Forty-seven percent of patients received a mean dose <400 mg/d of MA and 22% received a mean dose <200 mg/d. Demographic, physical, and cognitive variables were not significant-

ly different between the groups except for race: the <200-mg/d group comprised significantly more whites than the other 2 dosage groups ( $P < 0.032$ ).

The relationship between MA dosage and mortality was also examined. The median survival times in the <200-mg/d group (24.0 months; 95% CI, 18.1–27.8), the 200- to 400-mg/d group (20.5 months; 95% CI, 14.5–27.9) and the >400-mg/d group (25.5 months; 95% CI, 20.2–33.5) were not significantly different. The HR of the 200- to 400-mg/d group compared with the <200-mg/d group was 1.15 (95% CI, 0.848–1.58; NS) and the >400-mg/d group compared with the <200-mg/d group was 1.056 (95% CI, 0.8–1.39; NS).

Median weights at baseline, 3 months, and 6 months are presented in Table II for both groups. The median weight of the control group at the index event (122 pounds) was maintained at 3 months and increased slightly by 6 months (124 pounds). The median weight of patients treated with MA decreased 2 pounds after 3 months of therapy (119 pounds) but was only 1 pound less than the initial weight after 6 months (120 pounds). The median of the differences in patient weight at 3 and 6 months are also shown in Table II. These differences were also not significant between the control and the MA-treated patients. The minimum and maximum differences noted between the 2 groups were

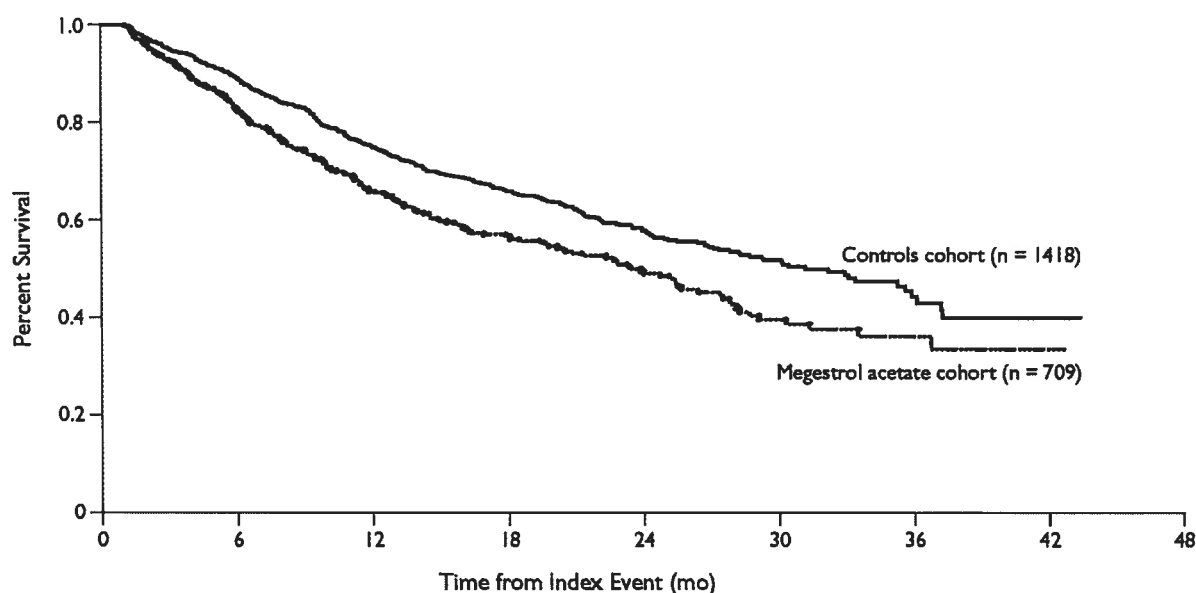


Figure 2. Kaplan-Meier survival curves of untreated (upper curve) and megestrol acetate-treated (lower curve) nursing home residents. Median survival: control cohort, 31.2 months (95% CI, 27.8–35.9); megestrol acetate cohort, 23.9 months (95% CI, 20.2–27.5). The log-rank test comparing these distributions was significant ( $P < 0.001$ ).

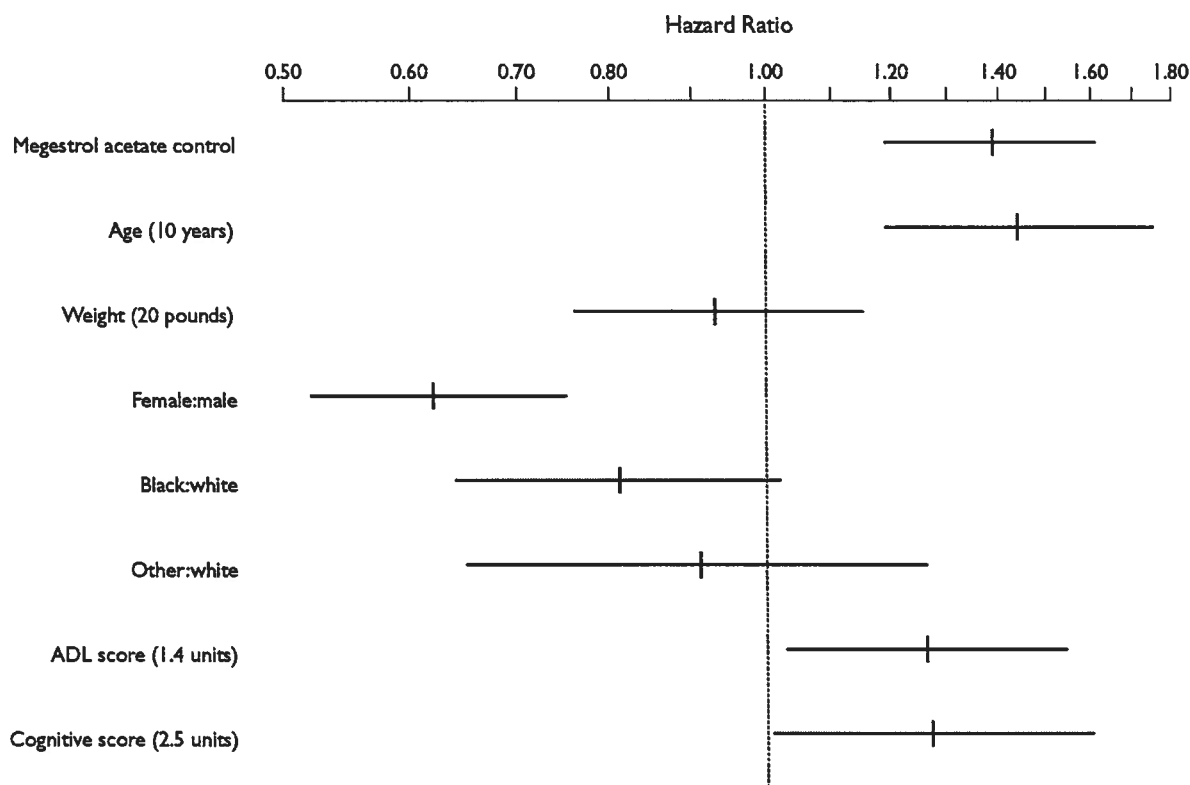


Figure 3. Hazard ratios and 95% CIs of the variables included in the final Cox proportional hazards model of nursing home residents. For continuous variables, numbers in parentheses represent the change in the value on which a hazard ratio is based. ADL = activities of daily living.

Table II. Effect of megestrol acetate on weight after treatment for 3 and 6 months in elderly nursing home residents with clinically significant weight loss.

	Time, mo	Megestrol Acetate Cohort			Control Cohort		
		No.	Median, lb	IQR, lb	No.	Median, lb	IQR, lb
Weight	0	709	121.0	103 to 137	1418	122.0	104 to 138
	3	493	119.0	102 to 137	1069	122.0	106 to 139
	6	339	120.0	104 to 139	793	124.0	106 to 141
Change from baseline	3	493	0*†	-7 to 6	1069	1.0*‡	-4 to 6
	6	339	1.0†§	-8 to 10	793	2.0‡§	-4 to 9

IQR = interquartile range.

\* $P = 0.001$ , Wilcoxon rank sum test used to compare groups.

† $P > 0.20$ , Wilcoxon signed rank test used to compare change within the megestrol acetate group.

‡ $P < 0.001$ , Wilcoxon signed rank test used to compare changes within the control group.

§ $P = 0.089$ , Wilcoxon rank sum test used to compare groups.

also similar. An identical analysis of patients surviving for the entire 6 months showed a 2-pound increase in the control group (122 to 124 pounds) and no change in the MA-treated group (even at 120 pounds).

A total of 369 patients were treated with doses of MA >400 mg/d. The median weight for these patients at baseline, 3 months, and 6 months was 120 (interquartile range [IQR], 104–136;  $n = 369$ ), 120 (IQR, 104–135;  $n = 267$ ), and 122 (IQR, 107–137;  $n = 175$ ) pounds, respectively. These patients experienced increases of 1 pound (IQR, –6 to 7; NS) at 3 months and 2 pounds (IQR, –6 to 11.5;  $P = 0.019$ ) at 6 months. These changes were not statistically significant from those experienced by the control group at 3 and 6 months.

## DISCUSSION

This retrospective analysis reported that MA treatment of elderly nursing home residents was associated with a significant increase in mortality without a significant increase in weight. These results differ from those obtained in other patient populations where MA or other pharmacologic appetite stimulants may offer several advantages over labor-intensive methods of nutritional support.

MA is a progesterone-like compound that was first developed as an oral contraceptive agent.<sup>2,3</sup> MA was noted to profoundly reduce the level of circulating estrogen,<sup>37</sup> which led to its use as a chemotherapeutic agent in the treatment of hormone-dependent cancers of the endometrium<sup>38</sup> and breast.<sup>39</sup> Frequently observed adverse effects during these studies were increased appetite and weight gain.<sup>40,41</sup> Consequently, investigations were undertaken to evaluate MA as an appetite stimulant in anorexic patients. MA has predominantly been used in this regard to combat the malnutrition associated with AIDS<sup>4–8</sup> and cancer.<sup>9–15</sup> In contrast to the use of MA for cancer and AIDS cachexia, few studies have examined its use in the treatment of malnutrition in the elderly.<sup>33,34</sup> One of the few randomized trials involved 65 elderly nursing home patients treated for 12 weeks with 800 mg of MA.<sup>42</sup> At the end of the study period, the majority of patients reported increased appetite, enjoyment, and feelings of well-being; however, there was no significant change in body weight. Surprisingly, weight had increased by >4 pounds in 60% of patients 3 months after treatment had been stopped, suggesting that the effects of MA may last for long periods after discontinuation of the drug. A similar study randomized 47 individuals with a mean age of 83 years to placebo,

MA 200 mg, MA 400 mg, or MA 800 mg daily for 9 weeks.<sup>43</sup> Weight, appetite, and quality-of-life measures were similar in all groups. Prealbumin was the only nutritional marker that was significantly increased ( $P = 0.009$ ), and the changes occurred in the 400- and 800-mg groups. One explanation for the lack of efficacy in these studies may be that nursing home residents often need feeding assistance and cannot adequately express increased hunger. A very small pilot study of 17 nursing home residents attempted to evaluate this possibility.<sup>44</sup> Patients were given 400 mg/d of MA, and fluid and food intake were directly observed for 9 weeks, alternating between standard feeding and optimal feeding assistance. Only when residents were optimally fed was there a difference in intake from pre-MA levels.

Body composition analysis of patients who gained weight from MA treatment revealed an increase in adipose tissue and possibly an increase in body fluid but no change in fat-free mass.<sup>29</sup> Other research has determined that MA has a catabolic effect on muscle size and fat-free mass even when combined with testosterone replacement in male patients treated with MA.<sup>45</sup>

Little is known about the mechanism by which MA induces weight gain. Depression of cytokine production is one proposed mechanism. MA prevents the proliferation of murine thymocytes induced by interleukin (IL)-1<sup>46</sup> and down-regulates IL-6, tumor necrosis factor, and IL-1 levels in cancer-related cachexia.<sup>47</sup> A similar impact of MA on cytokine levels was noted in a follow-up study on previously published data involving 65 elderly patients treated for 12 weeks with 800 mg of MA.<sup>48</sup> However, this was not observed in the MA arms of a second study where 85 subjects were randomized to receive 800 mg of MA daily, 2.5 mg of dronabinol BID, or both for 1 month.<sup>49</sup> IL-6 levels were not different from baseline in either MA arm.

Taken in their entirety, these studies<sup>42–44,48</sup> show that MA appears to increase appetite and feeling of well-being in most patients. The amount of actual weight gained is modest and highly variable between patients. Our results show an overall 1-pound weight loss from baseline to 6 months in MA-treated patients, but a modest 1-pound increase in weight from 3 to 6 months. The control group maintained their weight at 3 months and increased their weight by 2 pounds at 6 months. We also found no statistically significant weight increase in study patients treated with >400 mg/d of MA compared with untreated patients. These results differ from those obtained in a randomized trial of 800 mg/d of MA,<sup>42</sup> where little weight gain was noted at 3 months of treatment, but a signifi-

cant increase in weight was observed 3 months after discontinuation of MA ( $P < 0.05$ ). The discrepancy between the response to MA in patients with AIDS or cancer and nursing home residents is unclear. It may be that patients selected for treatment with MA are extremely ill, and the cachexia at that state is unresponsive to therapy. Alternatively, nursing home patients may differ in that they do not have free access to food, and caloric intake is restricted.

We observed a highly significant, 7.3-month difference in median survival between MA-treated and untreated nursing home residents. Although generally well tolerated, MA treatment is associated with several known and potential adverse effects that could have an impact on mortality. Deep venous thrombosis was identified in 4.9% of 246 nursing home residents treated with MA, representing a 6-fold higher incidence compared with untreated residents.<sup>30</sup> Adrenal suppression, with low cortisol and adrenocorticotropic hormone levels, is also associated with MA treatment,<sup>17-28</sup> but there are few data available that describe the recovery of the hypothalamic-pituitary-adrenal axis after discontinuation of MA. A single study by Loprinzi et al<sup>50</sup> measured serum cortisol levels in 3 patients after discontinuation of MA, and these levels reportedly returned to normal 5 weeks later. It is unknown whether clinically significant and potentially fatal adrenal insufficiency occurs during this time period after abrupt discontinuation of MA. In a small, randomized trial of 65 Veterans Affairs nursing home residents with a mean age of 85 years,<sup>51</sup> no significant difference in mortality was noted between MA-treated and untreated individuals, but the study was not powered to detect differences in mortality as an end point.

No dose-response effect on mortality was noted in our study. There was no statistically significant difference in median survival between residents treated with  $<200$  mg/d or  $>400$  mg/d of MA. These results suggest that the negative effects of MA are appreciated at doses lower than those associated with change in appetite and weight. Alternatively, there may be clinical attributes of the MA-treated group that are associated with increased mortality but undetected by the matching criteria employed. Also, any clinical improvement associated with MA treatment is predicated on adequate access to food and/or assistance in feeding. If the study population was sufficiently debilitated, a small increase in appetite induced by MA would have minimal effect on overall survival.

Approximately half of each group was alive at 2 years despite clinically significant weight loss. One explana-

tion for this finding would be that patients were identified by a percent loss of weight alone. The weight loss group was not based on initial weight. Thus, heavy patients with potentially fewer comorbidities would be included in the data set and may have experienced less mortality compared with lighter individuals.

There are several limitations to the current study. The data are derived from a historical cohort and are therefore subject to selection biases inherent in observational studies. This analysis attempted to minimize these biases by controlling for factors known to be associated with mortality through matching. These factors included demographic, quality-of-life, cognitive, and condition severity measures. However, they are limited by the data collected in the MDS form and cannot completely portray clinical severity.

The possibility exists, therefore, that the MA-treated residents were more ill despite comparable severity indices noted on the MDS. However, MDS weight loss quality indicators correlated strongly with the prevalence of weight loss between nursing homes<sup>52</sup> and has been used to identify the prevalence of obesity in nursing homes.<sup>53</sup> Activities of daily living and other demographic data abstracted from the MDS were very sensitive in identifying residents at high risk for hip fracture.<sup>54</sup> Similarly, an algorithm was constructed from MDS data that could accurately predict 1-year mortality.<sup>55</sup>

The practice patterns of specific nursing homes are also not noted in the MDS, and regional differences in MA-prescribing patterns may account for the increased mortality noted. Coprescribed medications are also unknown and may have biased overall mortality. One of the strengths of the study is that data were obtained from geographically diverse nursing homes, and this may minimize regional differences in delivery of care. Also, the large number of residents involved in the study adds to the precision of the survival estimates.

## CONCLUSION

MA administration was associated with an increase in mortality of elderly nursing home residents in this large, retrospective study. Randomized, prospective studies are needed to more fully understand the benefits and risks of MA treatment in the elderly.

## ACKNOWLEDGMENTS

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