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Androgen Therapy and Rehospitalization in Older Men with Testosterone Deficiency

Jacques Baillargeon, PhD, Rachel R. Deer, PhD, Yong-Fang Kuo, PhD, Dong Zhang, PhD, James S. Goodwin, MD, and Elena Volpi, MD, PhD

Department of Preventive Medicine and Community Health (Baillargeon, Kuo, Goodwin), Department of Internal Medicine (Baillargeon, Kuo, Zhang, Goodwin, Volpi) and Sealy Center on Aging (JB, YFK, RD, DZ, JSG, EV) University of Texas Medical Branch, Galveston, TX

Abstract

Objective—To assess whether the receipt of androgen therapy was associated with a reduced 30-day rehospitalization rate among older men with testosterone deficiency.

Patients and Methods—We conducted a retrospective cohort study using a 5% national sample of Medicare beneficiaries. We identified 6,372 nonsurgical hospitalizations between January 1, 2007 and December 31, 2012 for male patients, aged ≥66 years, with a prior diagnosis of testosterone deficiency. Patients who died or lost coverage in the 30 days following hospital discharge, or who were discharged to another inpatient setting, were excluded from the analysis. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of 30-day hospital readmissions associated with receipt of androgen therapy.

Results—In older men with testosterone deficiency, receipt of androgen therapy was associated with a reduced risk of rehospitalization (9.8% versus 13.0%; odds ratio [OR]=0.73, 95% CI, 0.58, 0.92) in the 30 days following hospital discharge. In a logistic regression analysis adjusting for multiple demographic, clinical and health service variables, the OR was similar (OR=0.75, 95% CI=0.59, 0.95). The adjusted OR for unplanned 30-day hospital readmissions was 0.62 (95% CI=0.47, 0.83). Each of these findings persisted across a range of propensity score analyses—including adjustment, stratification, inverse probability treatment weighting—and several sensitivity analyses.

Conclusion—Androgen therapy may reduce the risk of rehospitalization in older men with testosterone deficiency. Given the high rates of early hospital readmission among older adults, further exploration of this intervention holds broad clinical and public health relevance.

Keywords

Androgen; Testosterone replacement therapy; hospital readmission

Correspondence: Address to Jacques Baillargeon PhD, Department of Preventive Medicine and Community Health, University of Texas Medical Branch, 301 University Blvd, Mail Route 1007, Galveston TX 77555 (jbaillar@utmb.edu).

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Hospitalization often causes substantial declines in physical function, and the inability to regain physical function following a hospital stay strongly predicts the risk of rehospitalization and mortality in older adults.^{1–4} Such hospital-related functional decline represents a growing healthcare concern, particularly as our aging population continues to expand.^{1–3} Hospitalized older adults frequently experience inactivity,^{5–7} malnutrition,^{8–10} and disease burden, which collectively contribute to the acceleration of sarcopenia.^{11,12} Older men with low testosterone are particularly susceptible to these adverse events, given that testosterone deficiency is independently associated with sarcopenia and overall functional health decline.^{13–15} Because testosterone deficiency occurs in a high percentage of older men with chronic disease—including heart failure (HF), chronic obstructive pulmonary disease (COPD), diabetes, and chronic kidney disease^{16,17}—examining the outcomes of hospitalization in this population is important. It is possible that androgen therapy—which is reported to improve physical strength, exercise capacity and functional health—will help reduce such adverse hospital outcomes.^{18–21} To date, no large-scale studies have examined the effectiveness of this treatment in hospital settings. We therefore conducted a cohort study using a 5% national sample of Medicare beneficiaries to examine whether androgen therapy was associated with a reduced risk of 30-day hospital readmissions in older men with testosterone deficiency.

PATIENTS AND METHODS

Study Design and Data Source

We conducted a retrospective cohort study using enrollment and claims data for a 5% national sample of Medicare beneficiaries. The Centers for Medicare and Medicaid Services selected these beneficiaries based on the eighth and ninth digits (05, 20, 45, 70, 95) of their health insurance claim number. Data files were constructed to include the patient's demographic and enrollment information (denominator file), claims for hospital stays (Medicare Provider Analysis and Review file), outpatient visits (Outpatient Standard Analytic file), Prescription Drug Event (PDE) records and physician services (Medicare carrier claim file). The methodology used in this analysis was consistent with those used in previous studies of hospital readmission using national Medicare claims data.^{22–24} This study was reviewed and approved by the University of Texas Medical Branch Institutional Review Board.

Study Cohort

We identified male Medicare beneficiaries who were hospitalized at least once between January 1, 2007 and December 31, 2012. To be included in the study, patients were required to have met each of the following criteria: aged ≥66 years at hospital admission, a non-surgical diagnosis-related group, a diagnosis of hypogonadism (International Classification of Diseases, Ninth Revision, Clinical Modification, [ICD-9-CM] code=257.xx) in the 12 months prior to admission, continuous enrollment in Medicare parts A, B, and D in the 12 months prior to hospital admission, and no healthcare maintenance organization enrollment in the prior 12 months.

To be classified as an androgen user, the patient was required to have filled a prescription for androgen therapy or received an androgen injection that extended at least until the patient's index hospitalization date. We included, in this definition, pharmacy fill dates of 30, 60, or 90 days before the index hospital admission date. For each of these the drug supply duration was required to match the look-back period. All injections of androgen therapy were treated as the equivalent of a 30-day supply of a prescription androgen. We included all doses and formulations of androgen therapy in our analyses, using National Drug Code (NDC) numbers for topical gel, transdermal patch, subcutaneous pellets, and oral formulations (see Supplemental Table) and Healthcare Common Procedure Coding System (HCPCS) codes for injectable formulations (see Supplemental Table).

Covariates

Sociodemographic characteristics, including age at index hospitalization, race and ethnicity (white, black, Hispanic, or other) were obtained from the Medicare database. Two zip-code level variables, median income of neighborhood and proportion of persons aged 25 years in neighborhood with at least a high school education, were obtained from Medicare data linked to 2011 American Community Survey estimates from the United States Census Bureau. Additionally, we examined and adjusted for all conditions included in the Elixhauser comorbidity index.²⁵

Outcome Assessment

We examined all readmissions to an acute care hospital that occurred within 30 days following discharge for the patient's index hospitalization. We also assessed unplanned readmissions defined as an admission type code of 'emergency' or 'urgent.' For the primary analyses, we excluded patients who were discharged to another inpatient care setting, including a rehabilitation facility, a skilled nursing facility, or a psychiatric hospital. For patients hospitalized multiple times during the study period, we randomly selected one hospitalization per calendar year to include in the analysis.

Statistical analysis

We used logistic regression models to estimate the association of androgen therapy with all 30-day hospital readmissions and unplanned 30-day hospital readmissions. Multivariable analyses were adjusted for all demographic, clinical, and health services variables listed in Table 1. We also used three types of propensity score analyses: adjustment, stratification, and inverse probability treatment weighting (IPTW).^{26–28} We estimated the propensity score using a logistic regression model with receipt of androgen therapy as the binary outcome variable in the 6,372 hospitalizations of men with testosterone deficiency. The propensity score model included all demographic, clinical, and health services variables listed in Table 1 with the exception of duration of index hospital visit and presence/absence of ICU stay in index visit. These factors were not included in the propensity score models because they did not temporally precede the models' dependent variable (receipt of androgen therapy). Patients with propensity scores in the overlap region (99.7% of the cohort) were included in the final models.

After deriving the propensity score, we examined its distribution in the study cohort and checked the balance of each covariate according to receipt of androgen therapy, before and after adjustment of propensity score quintile as a covariate.^{27,28} We then fitted the regression models adjusting for quintile of propensity score and for covariates that remained statistically significant after inclusion of the propensity score quintile. Next, we conducted an analysis stratified on propensity score quintile. In this model, the strata specific odds ratio (OR) for androgen therapy with 30-day readmission was estimated and then weighted by the proportion of patients at each strata to generate an overall OR. Finally, we conducted an IPTW analysis, in which the inverse of the propensity score was used to weight each patient in the androgen therapy group, and the inverse of one minus the propensity score was used to weight each patient in the non-androgen group.

Eighty-two percent of the study cohort had only one hospitalization. The remaining 18 percent had 2 or more hospitalizations. To account for patients with multiple events, we conducted a General Estimating Equation (GEE) analysis with a binomial logit link with repeated measurement to adjust for clustering effects within patient.

To assess the robustness of our findings, we conducted sensitivity analyses. We ran a logistic regression model that included men who were discharged to inpatient facilities and another model that included men who died within 30 days of readmission with deaths classified as readmission. We also ran a series of logistic regression models in which we iteratively removed patients with each of the 7 diagnoses—anemia, depression, electrolyte disorders, metastatic cancer, paralysis, peripheral vascular disease, and tumor without metastasis—that were elevated in the non-androgen group. All analyses were two-sided and performed using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

The baseline characteristics of androgen therapy users and nonusers are presented in Table 1. Androgen users and nonusers had comparable distributions of education, household income, and likelihood of having an ICU stay during their index hospitalization. Androgen users were younger, had a shorter duration of index hospitalization, had fewer outpatient visits and had fewer hospital admissions in the previous 12 months. In addition, androgen users had a lower prevalence than non-users of anemia, depression, electrolyte disorders, peripheral vascular disease, and metastatic and non-metastatic cancer. After adjustment for propensity score quintile, only one of the variables (duration of index hospitalization) remained significantly different (4.6 versus 5.6 days, $P<.001$) among androgen users.

Table 2 presents the distribution of major diagnostic categories for the index hospitalization for androgen users and non-users. For both groups, over 50 percent of hospitalizations were attributable to conditions of the respiratory, circulatory and digestive systems. The rate of all 30-day hospital readmissions was 9.8% for androgen users and 13.0% for non-users (OR=0.73, 95% CI=0.58, 0.92). Likewise, the rate of unplanned 30-day readmissions was 6.2% for androgen users and 10.0% for non-users (OR=0.60, 95% CI=0.45, 0.78). Table 3 presents the results of the multivariable logistic regression analyses, conducted using a range of propensity score and sensitivity analyses. After adjusting for demographic, clinical and

health services covariates, androgen therapy was associated with a decreased risk of 30-day rehospitalization (OR=0.75, 95% CI, 0.59, 0.95) and an even stronger decreased risk of unplanned 30-day readmission (OR=0.62, 95% CI 0.47, 0.83). Androgen use was not associated with planned 30-day readmissions (OR=1.21, 95% CI=0.82, 1.68). In addition, the results of the multivariable GEE analyses, to adjust for clustering within patients, were comparable (all readmissions: 0.75, 95% CI=0.58, 0.95; unplanned readmissions, 0.62, 95% CI 0.46, 0.84) to the logistic regression findings. Results based on each of the three propensity score methods—adjustment, stratification, and IPTW—yielded similar results. In addition, we conducted sensitivity analyses consisting of logistic regression models that included men who were discharged to inpatient facilities and men who died within 30 days of readmission (with deaths classified as readmission). These analyses yielded results that were comparable to the original analyses. Finally, we ran a series of multivariable logistic regression models in which we iteratively removed patients with each of the 7 conditions that were more prevalent in the non-androgen group. We also ran a single model in which we removed all patients with any of the 7 conditions. For the primary outcome (unplanned hospital readmissions), all 8 of the models yielded ORs and 95% CIs for androgen use that were comparable with the original model. The ORs ranged from 0.58 to 0.63, and the 95% CIs all excluded 1.00.

For patients hospitalized multiple times during the study period, we randomly selected one hospitalization per calendar year to include in the analysis. Our analyses showed that 5.2% of the randomly selected index hospitalizations occurred within 30 days after another hospitalization. To ensure that the inclusion of such index hospitalizations did not bias our results, we assessed the distribution of these findings across the two study groups. The percentage of such index hospitalizations was comparable in androgen (5.1%) and non-androgen (5.8%) subgroups. In addition, we ran the multivariable logistic regression model after excluding all persons with an index hospitalization that was also a 30-day readmission. This model yielded an OR for androgen therapy predicting unplanned 30-day hospital readmissions (OR=0.59, 95% CI=0.44, 0.80) that was comparable to the original model.

DISCUSSION

In this nationally representative cohort study of testosterone deficient older men, the use of androgen therapy was associated with lower 30-day hospital readmission after adjustment for multiple demographic, clinical, and health services variables, and across several propensity score approaches and sensitivity analyses. This decline was stronger for unplanned or emergency readmissions. Our investigation represents the first large-scale population-based study examining the association of androgen therapy with hospital readmission. Reducing avoidable hospital readmissions is a national health priority and a major focus of health care reform in the United States.^{23,24,29}

Hospitalization can have adverse effects on the physical function and independence of older adults, resulting in early rehospitalization.¹⁻⁴ Several studies have reported that sarcopenia—the age-associated loss of muscle mass and strength—is accelerated by hospitalization and leads to functional dependence, institutionalization, and mortality.^{11,30} During hospitalization, disease burden, inactivity, and malnutrition each contribute to muscle

dysfunction, increased falls, and loss of independence in older patients.^{1,5–10} Such deconditioning resulting from hospitalization, termed “post-hospital syndrome,” is considered a risk factor for disability, rehospitalization, and mortality.^{1,2,31,32}

Because testosterone deficiency is independently associated with sarcopenia and overall functional health decline,^{13–15} older men with low testosterone may be particularly susceptible to such adverse effects of hospitalization. Androgen therapy—which increases muscle mass and strength by stimulation of protein anabolism^{33,34}—is reported to have broad therapeutic effects on muscle mass, strength and function in older hypogonadal men. Specifically, androgen therapy has been reported to improve timed walking,³⁵ grip strength,²¹ exercise capacity,²⁰ leg-press strength, chest-press strength and stair climbing.¹⁸ It is possible that our findings of decreased hospitalization among male Medicare beneficiaries who received androgen therapy are reflective of the improved functional health, strength, and exercise capacity observed in these previous studies. It will be important for future clinical studies to examine the specific pathways that underlie this observed association.

Recent reports of increased cardiovascular events associated with androgen therapy^{18,36,37} have raised the public’s concern about the overall safety of androgens. Although we did not focus on cardiovascular outcomes, our findings are consistent a large body of research—including the recently published NIH-funded multisite randomized clinical trial of older men³⁸—that have shown no short term increased risk of adverse events associated with androgen therapy.^{39–43} Some investigators have suggested that androgen therapy may even improve cardiovascular health by way of decreasing fat mass, insulin sensitivity and lipid profile.^{44–46} Given the chronicity of hypogonadism and its treatment, it will be important for future studies to examine the full range of risks and benefits of androgen therapy over a sufficient period of time. Such studies—especially those that include assessment of health care utilization and associated costs—will hold particular public health relevance.⁴⁷

Our study has several limitations. First, information on both outcomes and risk factors came from diagnosis codes included in charges for outpatient and hospitalization services. Such diagnoses are not always accurate or complete.⁴⁸ For example, we were unable to determine whether diagnoses of hypogonadism met the established serum and symptom criteria for this condition or whether men who received androgen therapy reached an appropriate serum testosterone level. Second, given the observational nature of this study, it is possible that undetected selection bias may have affected the findings. For example, older men who used androgen therapy may have been more likely than their peers to have engaged in positive health behaviors (e.g., healthful diet, exercise). Alternatively, testosterone deficient men who use androgen therapy may have had more severe hypogonadism than those who did not use such treatment. However, the latter scenario would have likely biased our findings in the direction of the null hypothesis. In addition, our database lacked information on several important health behaviors such as smoking status, exercise, and diet. In this regard, it is somewhat reassuring that the addition of measured potential confounders had little effect on the association of androgen therapy with readmission. The unadjusted odds ratio was 0.73 and was 0.75 after the addition of all measured potential confounders to the model. This makes it somewhat less likely than an unmeasured confounder would have a major effect.

Third, prescription claims data do not capture information on pharmaceutical agents purchased outside the plan. Given the perceived social stigma associated with receiving androgen therapy, some men may have chosen to seek treatment outside their usual health care setting, such as specialty hormone clinics. Finally, we assumed that patients adhered to their prescribed medication regimen. It is possible, however, that some patients did not take all or any of their prescribed medication.

Despite these limitations, we believe this study has important strengths including a large sample size, representation of all US geographic regions, and inclusion of a socioeconomically diverse cohort. Androgen therapy has a number of reported toxicities—including increased hematocrit, sleep apnea, fluid retention, and prostate growth^{40–42,49}—and is possibly overprescribed.⁵⁰ However, androgens may be beneficial in selected populations, such as men with testosterone deficiency.^{18–21,35} Our findings suggest that one of the benefits of androgen therapy might be a quicker recovery from hospitalization and lower readmission rates.

CONCLUSION

Androgen therapy may reduce the risk of rehospitalization in older men with testosterone deficiency. This finding persisted across a range of propensity score and sensitivity analyses. Given the importance of reducing avoidable hospital readmissions among older adults, further exploration of this intervention holds broad clinical and public health relevance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and Acronyms

OR	odds ratio
CI	confidence interval
COPD	chronic obstructive pulmonary disease
ICD-9-CM	International Classification of Diseases, ninth revision, clinical modification
CV	cardiovascular

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Table 1

Baseline Demographic and Clinical Characteristics for Androgen Users and Nonusers

Characteristic ^a	Androgen <i>n</i> (%) or mean (st.dev)	No Androgen <i>n</i> (%) or mean (st.dev)	<i>P</i> -value	
			Before PS ^b adjustment	After PS ^b Adjustment
All	929 (100)	5,443 (100)		
Age (years) at index hospitalization (Mean)	74.3 (6.3)	75.6 (6.2)	<i>P</i> <.001	<i>P</i> =.77
Age (years) at index hospitalization				
66–69	243 (26.1)	1,207 (22.1)		
70–74	272 (29.3)	1,446 (26.6)		
75–79	204 (22.0)	1,209 (22.2)		
80	210 (22.6)	1,581 (29.1)	<i>P</i> <.001	<i>P</i> =.78
Race				
White	858 (92.3)	4,890 (89.8)		
Black	40 (4.3)	353 (6.5)		
Hispanic	10 (1.1)	76 (1.4)		
Other	21 (2.3)	124 (2.3)	<i>P</i> =.13	<i>P</i> =.15
Education (% high school education) ^c				
Q1:.	227 (24.4)	1,321 (24.3)		
Q2:	220 (23.6)	1,337 (24.5)		
Q3:	239 (25.7)	1,316 (24.2)		
Q4:	225 (24.2)	1,354 (24.9)		
Unknown	18 (1.9)	115 (2.1)	<i>P</i> =.91	<i>P</i> =.63
Household Income ^d				
Q1:	241 (25.9)	1,302 (23.9)		
Q2:	231 (24.9)	1,328 (24.4)		
Q3:	232 (25.0)	1,309 (24.1)		
Q4:	206 (22.2)	1,387 (25.5)		
Unknown	19 (2.0)	117 (2.2)	<i>P</i> =.08	<i>P</i> =.13
ICU stay during index hospitalization (%) ^e	1,187 (21.8)	222 (23.9)	<i>P</i> =.15	<i>P</i> =.19
Duration of index hospitalization (Mean) ^e	4.3 (4.8)	5.6 (8.8)	<i>P</i> <.001	<i>P</i> <.001
Number, visits, prior 12 months (Mean)	0.5 (0.8)	0.6 (0.9)	<i>P</i> <.001	<i>P</i> =.85
Number, hosp adm, prior 12 months (Mean)	0.5 (1.5)	0.9 (1.5)	<i>P</i> =.04	<i>P</i> =.92

Characteristic ^d	Androgen <i>n</i> (%) or mean (st.dev)	No Androgen <i>n</i> (%) or mean (st.dev)	P-value	
			Before PS ^a adjustment	After PS ^a Adjustment
Comorbidity ^c				
AIDS/HIV	10 (1.1)	45 (0.8)	<i>P</i> =.57	<i>P</i> =.71
Alcohol Abuse	22 (2.4)	127 (2.3)	<i>P</i> =.94	<i>P</i> =.84
Anemia	389 (41.9)	2,560 (47.1)	<i>P</i> <.001	<i>P</i> =.28
Arthritis	99 (10.7)	555 (10.2)	<i>P</i> =.55	<i>P</i> =.40
Congestive Heart Failure	312 (33.6)	1,756 (32.3)	<i>P</i> =.49	<i>P</i> =.86
COPD	403 (43.4)	2,247 (41.3)	<i>P</i> =.27	<i>P</i> =.07
Coagulopathy	114 (12.3)	706 (12.9)	<i>P</i> =.59	<i>P</i> =.80
Depression	141 (15.2)	993 (18.1)	<i>P</i> =.03	<i>P</i> =.85
Diabetes without complications	450 (48.4)	2,664 (48.9)	<i>P</i> =.77	<i>P</i> =.61
Diabetes with complications	200 (21.5)	1,281 (23.5)	<i>P</i> =.18	<i>P</i> =.17
Drug abuse	26 (2.8)	121 (2.2)	<i>P</i> =.16	<i>P</i> =.27
End stage renal disease	4 (0.4)	47 (0.9)	<i>P</i> =.16	<i>P</i> =.17
Hypertension	810 (87.2)	4,836 (88.9)	<i>P</i> =.17	<i>P</i> =.39
Hypothyroidism	279 (30.0)	1,635 (30.0)	<i>P</i> =.99	<i>P</i> =.61
Liver Disease	44 (4.7)	264 (4.9)	<i>P</i> =.88	<i>P</i> =.97
Lymphoma	34 (3.7)	228 (4.2)	<i>P</i> =.45	<i>P</i> =.78
Electrolyte Disorders	237 (25.5)	1,640 (30.1)	<i>P</i> <.001	<i>P</i> =.19
Metastatic Cancer	26 (2.8)	321 (5.9)	<i>P</i> <.001	<i>P</i> =.05
Neurological Disorders	187 (20.1)	1,216 (22.3)	<i>P</i> =.13	<i>P</i> =.76
Obesity	116 (12.5)	667 (12.3)	<i>P</i> =.84	<i>P</i> =.63
Paralysis	23 (2.5)	195 (3.6)	<i>P</i> =.04	<i>P</i> =.22
Peripheral vascular disease	280 (30.1)	1,961 (36.0)	<i>P</i> <.001	<i>P</i> =.77
Psychosis	94 (10.1)	620 (11.4)	<i>P</i> =.24	<i>P</i> =.66
Renal failure	225 (24.2)	1,302 (23.9)	<i>P</i> =.84	<i>P</i> =.19
Tumor (no metastasis)	161 (17.3)	1,539 (28.3)	<i>P</i> <.001	<i>P</i> =.61
Peptic ulcer	4 (0.4)	36 (0.7)	<i>P</i> =.41	<i>P</i> =.59
Valvular disease	270 (29.1)	1,604 (29.5)	<i>P</i> =.80	<i>P</i> =.42

^a All percentages and frequencies are unadjusted

^b PS= propensity score

^c Percentage of persons (aged ≥ 25 years) in zip code with at least a high school education, presented by quartile

^d Median household income in zip code, presented by quartile

^e These factors were not included in the propensity score model because they temporally followed the propensity score model dependent variable (receipt of androgen therapy)

^a PS= propensity score

^c Comorbid conditions were measured using the factors that comprise the Elixhauser comorbidity index.

Table 2

Distribution of Major Diagnostic Categories of Index Hospitalization

	AndrogenTherapy <i>n</i> (%)	No Androgen Therapy ^b <i>n</i> (%)
Major Diagnostic Category ^a		
Nervous system	55 (6.3)	416 (7.4)
Eye	8 (0.1)	7 (0.1)
Ear, Nose, Mouth, and Throat	10 (1.2)	81 (1.4)
Respiratory System	135 (15.6)	790 (14.1)
Circulatory System	237 (27.3)	1,342 (24.0)
Digestive System	120 (13.8)	633 (11.3)
Hepatobiliary System and Pancreas	15 (1.7)	139 (2.5)
Musculoskeletal, Connective Tissue	36 (4.3)	289 (5.2)
Skin, Subcut Tissue, Breast	25 (2.9)	158 (2.8)
Endocrine, Nutritional, Metabolic	23 (2.7)	195 (3.5)
Kidney and Urinary Tract	57 (6.6)	385 (6.8)
Male Reproductive System	6 (0.7)	33 (0.6)
Blood and Immunological Disorders	15 (1.7)	89 (1.6)
Myeloproliferative Dis.	6 (0.7)	52 (0.9)
Infectious Diseases	35 (4.1)	257 (4.6)
Mental Disorders	10 (1.2)	115 (2.1)
Alcohol/Drug Abuse	4 (0.5)	26 (0.5)
Injuries, Poison, Drug Toxicity	7 (0.8)	88 (1.6)
Burns	0 (0.0)	1 (0.2)
Factors influencing Health Status	60 (7.1)	484 (8.7)
Trauma	0 (0.0)	1 (0.0)
HIV	1 (0.1)	5 (0.9)

^aThe percentages of all presented major diagnostic categories are unadjusted

Table 3

Odds Ratios for 30-day rehospitalization associated with Androgen Therapy, Analyzed by Various Approaches

Analytic Method	All 30-day Readmissions OR (95% CI)	Unplanned 30-day Readmissions ^a OR (95% CI)
Unadjusted	0.73 (0.58, 0.92)	0.60 (0.45, 0.78)
Adjusted for all covariates using multivariable logistic regression ^b	0.75 (0.59, 0.95)	0.62 (0.47, 0.83)
Adjusted for all covariates using multivariable logistic regression, and including patients who were discharged to inpatient facilities	0.75 (0.59, 0.95)	0.62 (0.47, 0.83)
Adjusted for all covariates using multivariable logistic regression, and including deaths after discharge ^c	0.75 (0.59, 0.95)	0.62 (0.47, 0.83)
Adjusted for quintile of propensity score and additional covariates ^d using multivariable logistic regression	0.75 (0.59, 0.95)	0.62 (0.47, 0.83)
Stratified according to quintile of propensity score and adjusted for additional covariates	0.75 (0.60, 0.95)	0.63 (0.47, 0.83)
Adjusted using IPTW ^e	0.73 (0.65, 0.82)	0.62 (0.54, 0.71)

^a All 30-day hospital readmissions that were coded as 'elective' were classified as non-readmissions

^b Adjusted for all sociodemographic, health care utilization, and medical conditions included in Table 1.

^c For patients who died within 30 days of discharge, date of death was analyzed as date of readmission

^d Included the following covariates that were unbalanced after propensity score adjustment: household income, ICU stay during index hospitalization, duration of index hospitalization, and COPD

^e Inverse probability weighting score