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Prevalence of Nonmetastatic Prostate Cancer Patients on Continuous Androgen Deprivation Therapy in the United States

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BACKGROUND

- Although androgen deprivation therapy (ADT) is the cornerstone treatment of metastatic prostate cancer (PC), its role in the nonmetastatic setting is more controversial, particularly in cases of low-risk, localized tumors where ADT has an unproven benefit.[1]
- During the 1990s, ADT use in the United States (US) markedly increased across all stages and grades of disease.[1]
- More recent research has demonstrated substantial declines in incident primary or adjuvant use among men diagnosed with localized tumors from 2003 to 2005, which is thought to be linked to reductions in Medicare reimbursement for ADT in PC in 2004 and 2005.[2]
- Monitoring trends in ADT use in earlier stages of disease is important, primarily because of the growing evidence around unintended adverse effects linked to ADT.[3]
- This is the first comprehensive assessment of the prevalence of primary ADT exposure (defined here as continuous ADT for ≥ 6 months) in the nonmetastatic PC setting at the national level.

STUDY OBJECTIVE

- To estimate the prevalence of nonmetastatic PC patients actively receiving continuous ADT for a duration of at least 6 months in the US.

METHODS

- Data sources and study cohort formation
  - Two point-prevalent cohorts on 12/31/2008 with continuous coverage in 2008 were assembled:
    - Men aged 18–64 years enrolled in fee-for-service (FFS) commercial health plans (Thomson Reuters MarketScan® Commercial Claims and Encounters Database)
    - Men aged ≥ 67 years (to ensure adequate look-back for ADT exposure) enrolled in FFS Medicare (Parts A and B) (The Centers for Medicare and Medicaid Services 5% Medicare database)
  - The cohorts were restricted to men without evidence of metastases (except to lymph nodes) using up to a 5-year look-back period (01/01/2004–12/31/2008).
    - Metastasis defined as 2 outpatient claims (on different days within any 12-month interval) or as 1 inpatient claim with ICD-9-CM diagnosis codes for metastasis to a given specific system or site
      - The ICD-9-CM diagnosis code for bone metastasis was augmented with HCPCS codes for bisphosphonate therapy (zoledronic acid and pamidronate).
- ADT types examined
  - Bilateral orchiectomy: ICD-9-CM procedure codes 62.41 and 62.42
  - Gonadotropin-releasing hormone (GnRH) agonists: leuprolide acetate (J1950, J9217, J9218, J9219); histrelin implant (J9225); goserelin acetate implant (J9202); triptorelin pamoate injection (J3315)
- Selection of prevalent ADT users with active and adequate (≥ 6 months) continuous exposure on the point-prevalence date
  - Receipt of bilateral orchiectomy at least 6 months prior to 12/31/2008
  - Continuous exposure to GnRH agonists during at least the 6 months immediately prior to 12/31/2008

METHODS (Continued)

- We made allowances for gaps in calendar time during treatment to reflect real-world use (FDA label-recommended GnRH agonist regimens may not be administered on a strictly regular schedule, testosterone recovery may be used as a trigger to treat):
  - In Medicare, up to 3 months for ≤ 6-month regimens and up to 6 months for 12-month regimens could elapse from the end date of the active dose period (ie, the number of months of the intended regimen) of the most recent qualifying GnRH agonist claim to 12/31/2008 (to satisfy the "active" requirement) and in between end and start dates of active dose periods of separate consecutive GnRH agonist claims (to satisfy the "adequate" requirement).
  - In MarketScan®, information on the intended regimen for those ≤ 6 months is not reliable. GnRH agonist claims that were not for 12-month regimens were assumed to be 1-month regimens, and up to 6 months (for all claims) could elapse from the end date of the active dose period of the most recent qualifying GnRH agonist claim to 12/31/2008 (to satisfy the "active requirement") and in between end and start dates of active dose periods of separate consecutive GnRH agonist claims (to satisfy the "adequate" requirement). This approach was deemed appropriate based on sensitivity analyses conducted in the Medicare database.
- Estimation of number of prevalent ADT users in the national commercially insured population and FFS Medicare population
  - Prevalence in the national commercially insured population aged 45–64 years was extrapolated with person-level weights derived from the Medical Expenditure Panel Survey and provided by the data vendor.
    - National estimates for the group aged 18–44 years were not calculated given the extremely low frequency of prevalent ADT users of this age in the study cohort (n = 8).
  - Prevalence in the national FFS Medicare population aged ≥ 65 years was extrapolated with person-level weights calculated by comparing the size of the age groups in the study cohort (67–74, 75–84, ≥ 85) with the size of the corresponding age groups in the total FFS Medicare population (65–74, 75–84, ≥ 85).
- Estimation of number of prevalent ADT users in the entire US male population aged ≥ 45 years
  - To account for men not represented in the commercially insured or Medicare populations, prevalence measured in the two data sources was extrapolated to the entire US male population by applying age-specific prevalence estimates (45–64, 65–74, 75–84, ≥ 85) to the US population on 12/31/2008 (the average of the mid-2008 and mid-2009 US Census).

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RESULTS

- Prevalence of ADT use in the study cohorts is summarized in Table 1
  - In the MarketScan® point-prevalent study cohort (n = 7,222,421), a total of 1,720 men aged 18–64 years were identified as nonmetastatic PC patients actively receiving continuous ADT for a duration of at least 6 months. Less than 0.5% of these cases were in men aged 18–44 years.
  - In the FFS Medicare point-prevalent study cohort (n = 465,720), a total of 5,469 men aged ≥ 67 years were identified as nonmetastatic PC patients actively receiving continuous ADT for a duration of at least 6 months.

Table 1. Measured Estimates: Age-Specific Patient Counts for Men With Nonmetastatic PC Actively Receiving Continuous (≥ 6 Months) ADT in the Study Cohorts

	Total	Prevalence of ADT use	
	N	N	%
Commercially insured cohort			
18–44 years	3,583,579	8	< 0.001%
45–64 years	3,638,842	1,712	0.047%
Total (18–64 years)	7,222,421	1,720	0.024%
Medicare 5% sample cohort			
67–74 years	224,623	1,165	0.519%
75–84 years	181,444	2,537	1.398%
≥ 85 years	59,653	1,767	2.962%
Total (≥ 67 years)	465,720	5,469	1.174%

- Prevalence of ADT use in the national commercially insured population and FFS Medicare population is summarized in Table 2
  - Among 26.7 million commercially insured males aged 45–64 years in the US, an estimated 11,935 (95% confidence interval [CI]: 11,310–12,561) or 0.045% represented nonmetastatic PC patients actively receiving continuous ADT for ≥ 6 months on 12/31/2008.
  - Among the 10.9 million FFS Medicare male enrollees in the US, an estimated 115,468 (95% CI: 112,304–118,633) or 1.055% represented nonmetastatic PC patients actively receiving continuous ADT for ≥ 6 months on 12/31/2008.

Table 2. Extrapolated Estimates: Prevalence of Men With Nonmetastatic PC Actively Receiving Continuous (≥ 6 Months) ADT in the National Commercially Insured and FFS Medicare Populations

	Total	Prevalence of ADT use			
	N	N	95% CI	%	95% CI
US commercially insured					
45–64 years	26,686,875	11,935	11,310–12,561	0.045%	0.042–0.047
US FFS Medicare					
65–74 years	6,043,760	28,087	26,272–29,902	0.465%	0.435–0.495
75–84 years	3,686,380	51,541	49,549– 53,532	1.398%	1.344–1.452
≥ 85 years	1,210,060	35,841	34,195–37,487	2.962%	2.826–3.098
Total (≥ 65 years)	10,940,200	115,468	112,304–118,633	1.055%	1.026–1.084

- Prevalence of ADT use in the US male population aged ≥ 45 years is summarized in Table 3
  - Applying the age-specific prevalence estimates to the corresponding population counts from the US Census, among 55 million males aged ≥ 45 years in the US, a total of 188,916 (95% CI: 184,104–193,727) men with nonmetastatic PC were actively receiving continuous ADT for ≥ 6 months on 12/31/2008.

Table 3. Extrapolated Estimates: Prevalence of Men With Nonmetastatic PC Actively Receiving Continuous (≥ 6 Months) ADT in the US Population

	US Male Population	Prevalence of ADT use	
	N	N	95% CI
45–64 years	38,376,000	17,163	16,264–18,062
65–74 years	9,436,000	43,851	41,017–46,686
75–84 years	5,447,000	76,157	73,214–79,100
≥ 85 years	1,747,000	51,745	49,368–54,121
Total	**55,006,000**	**188,916**	**184,104–193,727**

CONCLUSIONS

- At the end of 2008, nearly 190,000 US males aged ≥ 45 years (~0.34% of the entire male population in this age group) were actively receiving continuous ADT for ≥ 6 months in the nonmetastatic setting, and the vast majority (91%) of these men were aged ≥ 65 years.
- It is difficult to directly compare our work with previously published analyses on trends in ADT use in the US, primarily because of the uniqueness of our measure of interest (point-prevalent patient counts) and the specific type of ADT examined (continuous exposure for ≥ 6 months).
- Nonetheless, given that the 5-year prevalence of PC (all stages) in the US was estimated to be roughly 1 million on 01/01/2009,[4] our study suggests that a substantial number of men in the nonmetastatic setting are managed with continuous ADT during the course of their disease.
- A major strength of this study is its use of large population-based databases that are representative of two important segments of the US adult population – the commercially insured population aged 18–64 years and the FFS Medicare population aged ≥ 65 years.
- A main limitation is the assumption that the prevalence of ADT use measured in the commercially insured and FFS Medicare populations is generalizable to the remaining adult male population (men with private insurance, uninsured men, Medicaid beneficiaries without Medicare coverage, Medicare Advantage participants, and military forces).
- Despite this possible limitation, we provide a recent snapshot of the number of US men with nonmetastatic disease actively being exposed to continuous ADT for a duration of at least 6 months.

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