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Epidemiology of Huntington's Disease in the United States Medicare and Medicaid Populations

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Abstract
Introduction: Huntington's disease (HD) is a rare, genetic, and ultimately fatal neurodegenerative disease, with a devastating impact on individuals and families across generations. Few estimates of HD epidemiology in the United States (US) exist. ***Methods:*** This study employed a retrospective cross-sectional design to examine the epidemiology of HD in the US Medicare and Medicaid beneficiary populations using 2016-2017 claims data from the Medicare 100% Research Identifiable Files (RIFs) and 2014 claims data from the Medicaid Analytic eXtract (MAX) files for 17 states. Medicare beneficiaries ≥65 years with a diagnosis of HD (≥1 claim with ICD-10-CM code G10) in 2017 and Medicaid beneficiaries <65 years with a diagnosis of HD (≥1 claim with ICD-9-CM code 333.4) in 2014 were identified. The study outcomes included the 2017 prevalence proportion and incidence rate of HD in the Medicare population and the 2014 prevalence proportion of HD in the Medicaid population. ***Results:*** In the Medicare population, 1,941 prevalent and 819 incident cases of HD were identified in 2017, corresponding to a prevalence proportion of 13.1 per 100,000 persons and incidence rate of 6.1 per 100,000 person-years. In the Medicaid population, 353 prevalent cases of HD were identified in 2014, corresponding to a prevalence proportion of 15.2 per 100,000 persons. ***Conclusion:*** This study suggests that prevalence and incidence of HD in the US may be higher than previously estimated. This has important implications in raising awareness of HD among providers and payers and ensuring availability of and access to services for HD patients and care partners in the Medicare and Medicaid populations.

Introduction

Huntington's disease (HD) is a rare, genetic, and ultimately fatal neurodegenerative disease, with a devastating impact on individuals and families across generations [1, 2]. HD, which has an equal risk of inheritance by males and females, is characterized by a triad of cognitive, behavioral, and motor symptoms, which include cognitive decline, psychiatric problems, and progressive motor impairment. The onset of HD typically occurs in the prime of life between the ages of 30–50 years [2]; however, symptoms can manifest from before age 5 to as late as age 80 and beyond. Mean and median survival of individuals with HD is 15 years [3].

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Estimates of the prevalence and incidence of HD vary widely, both globally and in the United States (US), due in part to differences in study populations or methodologies [4]. These past studies have relied on administrative claims data, medical chart review, clinical assessment by a health professional, or genetic testing to estimate epidemiological rates [4–7]. Nevertheless, investigation of HD prevalence and incidence in the US is limited. A recent analysis estimated the true HD prevalence in the US to be 12.7 per 100,000 persons, applying estimates for a province in Canada to 2018 US Census data [8]. Other studies in the US have focused on commercially insured populations and, using older data sources, a representative population for a single US state [5, 6]. No estimates of HD prevalence or incidence currently exist for the Medicare and Medicaid beneficiary populations in the US. The objective of the current study was to provide comprehensive estimates of overall and age- and sex-specific HD prevalence and incidence in the US Medicare population and HD prevalence in the US Medicaid population using the most recent available data.

Materials and Methods

Study Design and Setting Overview

This study employed a retrospective cross-sectional design to examine the epidemiology of HD in the US Medicare and Medicaid beneficiary populations. The Medicare program provides health insurance coverage to more than 55 million US citizens who are at least 65 years old, or who are less than 65 years old but have received Social Security Disability Insurance for 24 months or have other qualifying circumstances [9]. Medicaid is a US federal-state public insurance program that provides healthcare coverage to more than 64 million low-income, qualified pregnant women and children, and individuals with qualified medical needs, as defined by individual states [10]. This study received approval for full waiver of Health Insurance Portability and Accountability Act (HIPAA) authorization from the Western Institutional Review Board.

Medicare Analysis

Medicare Research Identifiable Files (RIFs) from 2016 to 2017 (100%) were used to identify Medicare beneficiaries with HD. The RIF database is the most comprehensive Medicare database covering 100% of Medicare beneficiaries from all census regions and includes patient-level information on demographics, enrollment, and administrative claims data. We identified Medicare beneficiaries, including enrollees with dual eligibility for Medicaid, who were 65 years and older and who had a diagnosis of HD (cases), based on the presence of at least one medical claim with a diagnosis code for HD (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]: G10) in 2017.

Study outcomes included the prevalence proportion and incidence rate in 2017. Prevalence was calculated as the number of HD cases in 2017 divided by all beneficiaries in that year (reported per 100,000 persons). To be included in the numerator or denominator, beneficiaries needed to be continuously enrolled in Fee-for-Service (FFS) Medicare Parts A and B (coverage of inpatient and outpatient medical services, respectively) and Part D (prescription drug coverage) during the entire year. Incidence rate was calculated as the number of new HD cases in 2017 divided by total at-risk patient-years from January 1st until diagnosis (cases) or until end of FFS/Part D enrollment (noncases) in 2017 (reported per 100,000 person-years). The at-risk population was defined as beneficiaries who did not have a diagnosis of HD and were continuously enrolled in 2016. We defined new HD cases as beneficiaries who were diagnosed with HD in 2017 and who had continuous enrollment in Medicare FFS and Part D and lacked a diagnosis code for HD in 2016. The denominator for both the prevalence and incidence cohorts was derived from a separate 5% sample of all Medicare enrollees.

The estimates of prevalence and incidence were stratified by age, sex, and race and reported according to HD stage distribution. We measured the stage of HD (early, middle, late) using a published hierarchical algorithm that assigns stage based on the presence of disease markers (i.e., diagnoses or services) in claims during the calendar year [11]. Beneficiaries with late-stage HD were identified first based on the presence of any of the following markers: nursing home, feeding tube, incontinence, bedsore, hospice care, at least two falls within a 1-month period, and dysphagia. Among the remaining beneficiaries, those with any of the following markers were classified as having middle-stage disease: home assistance, physical therapy, dementia, gait disorder, dysarthria, speech therapy, and falls. Finally, beneficiaries without late- or middle-stage markers were defined as having early-stage disease.

Medicaid Analysis

Medicaid Analytic eXtract (MAX) data for 2014 from 17 states (CA, GA, ID, IA, LA, MI, MN, MS, MO, NJ, PA, SD, TN, UT, VT, WV, WY) were used to identify beneficiaries with HD; at the time of this study, complete 2014 MAX data were only available for these 17 states. MAX is a research-ready data source developed by the Centers for Medicare and Medicaid Services (CMS) that contains patient-level demographics, eligibility and enrollment, and administrative medical and pharmacy claims data from Medicaid FFS enrollees. We identified Medicaid beneficiaries who were less than 65 years old and who had a diagnosis of HD (cases), defined by the presence of at least one medical claim with a diagnosis for HD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code: 333.4) in 2014. Only nondual-eligible beneficiaries having FFS plans were included in the study because MAX data may be incomplete for the dual-eligible population.

The primary outcome of the Medicaid analysis was the prevalence proportion; the incidence rate was not calculated because study enrollment and Medicaid eligibility requirements did not allow us to identify a representative sample of new HD cases. The prevalence proportion was calculated as the number of HD cases in 2014 divided by all beneficiaries enrolled in 2014 (reported per 100,000 persons). Beneficiaries who were included in the numerator or denominator were continuously enrolled in Medicaid during the entire year. The denominator for the prevalence cohorts was derived from a separate, 100% sample of all Medicaid enrollees. As with the Medicare analysis, the prevalence estimates were stratified by age, sex, and race and distributed by HD stage, as defined above.

Sensitivity Analysis

Among the Medicare and Medicaid populations described above, we tested the sensitivity of the overall prevalence estimates to chang-

Table 1. Prevalence and incidence of Huntington's disease among Medicare beneficiaries in 2017

	Cases, *n* (%)	Annual membership	Prevalence per 100,000 persons			
			all (*n* = 1,941)	early stage (*n* = 455, 23.4%)	middle stage (*n* = 582, 30.0%)	late stage (*n* = 904, 46.6%)
All individuals	1,941 (100.0)	14,870,760	13.1	3.1	3.9	6.1
By age, in years						
65–74	1,104 (56.9)	8,092,740	13.6	3.8	4.2	5.7
75–84	652 (33.6)	4,803,540	13.6	2.7	4.1	6.8
85+	185 (9.5)	1,974,480	9.4	1.1	2.3	5.9
By sex						
Female	1,096 (56.5)	8,722,120	12.6	2.8	3.9	5.8
Male	845 (43.5)	6,148,640	13.7	3.4	3.9	6.4
By race						
White	1,742 (89.7)	13,386,260	13.0	3.1	3.9	6.0
Black	113 (5.8)	746,700	15.1	3.2	4.2	7.8
Other/Unknown[a]	86 (4.4)	737,800	11.7	1.9	3.4	6.4
	Cases, *n* (%)	Total at-risk person-years	Incidence per 100,000 person-years			
			all (*n* = 819)	early stage (*n* = 174, 21.2%)	middle stage (*n* = 244, 29.8%)	late stage (*n* = 401, 49.0%)
All individuals	819 (100.0)	13,446,030	6.1	1.3	1.8	3.0
By age, in years						
65–74	352 (43.0)	6,719,414	5.2	1.6	1.9	1.8
75–84	320 (39.1)	4,711,868	6.8	1.2	1.9	3.7
85+	147 (17.9)	2,014,749	7.3	0.7	1.4	5.3
By sex						
Female	466 (56.9)	7,915,232	5.9	1.2	1.8	2.9
Male	353 (43.1)	5,530,798	6.4	1.5	1.9	3.1
By race						
White	705 (86.1)	12,173,393	5.8	1.2	1.7	2.9
Black	78 (9.5)	659,857	11.8	3.0	3.2	5.6
Other/Unknown[a]	36 (4.4)	612,780	5.9	1.1	2.1	2.6

[a] Other/Unknown category includes Asian, Hispanic, North American Native, and Unknown.

es in the algorithm for identifying patients with HD. In the sensitivity analysis, the prevalence proportion was calculated among beneficiaries who had at least two medical claims with a diagnosis of HD.

Calculations based on counts of fewer than 11 beneficiaries were not reported in accordance with the CMS cell-size suppression policy [12]. All data analyses were performed using SAS® version 9.4.

Results

Medicare Analysis

Among Medicare beneficiaries 65 years and older, we identified 1,941 prevalent and 819 incident HD cases in 2017 who met the study criteria and were included in the analysis. Overall and demographic-specific estimates of prevalence and incidence are shown in Table 1 and Figures 1 and 2.

In 2017, the prevalence proportion of HD in the Medicare population was 13.1 per 100,000 persons. The mean (standard deviation, SD) age of prevalent cases was 74.5 (6.8) years, while the majority (56.9%) of beneficiaries with HD were between 65 and 74 years of age. The age-specific prevalence proportions (per 100,000) were highest among beneficiaries who were 65–74 years of age (13.6) and 75–84 years (13.6), followed by 85+ years (9.4). HD prevalence was higher among males (13.7 per 100,000) than females (12.6 per 100,000). Prevalence (per 100,000) was also higher among Black (15.1) compared to White (13.0) or Other/Unknown (11.7) beneficiaries. The distribution of disease stage (early, middle, late) among preva-

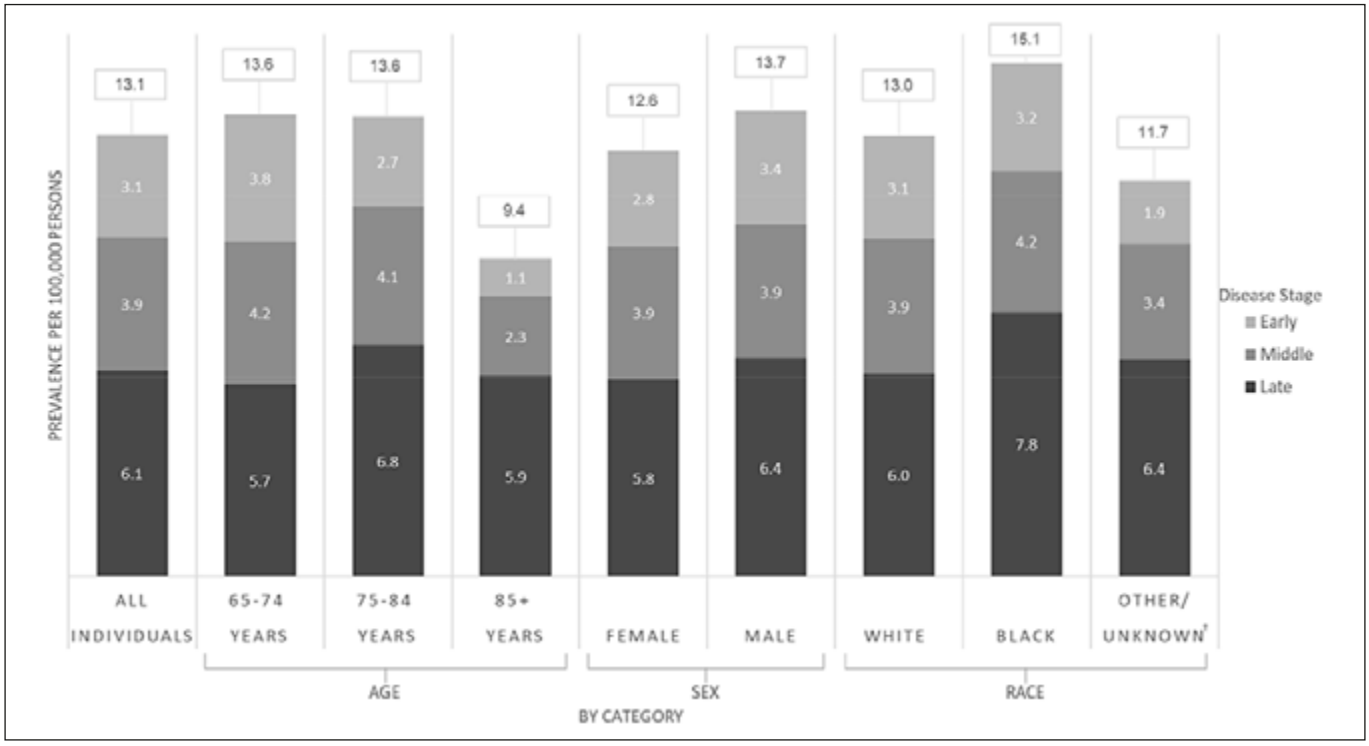

Fig. 1. †Other/Unknown category includes Asian, Hispanic, North American Native, and Unknown.

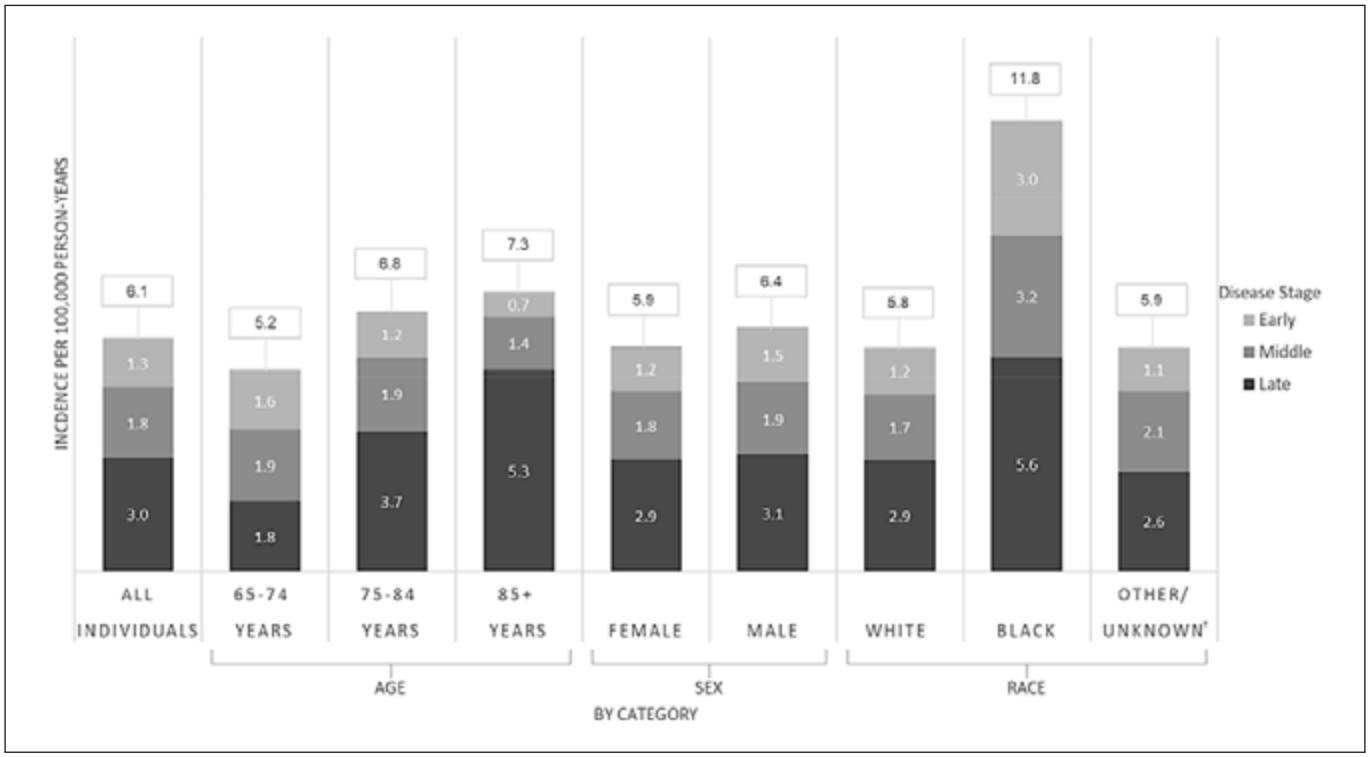

Fig. 2. †Other/Unknown category includes Asian, Hispanic, North American Native, and Unknown.

Table 2. Prevalence of Huntington's disease among Medicaid beneficiaries in 2014

	Cases, *n* (%)	Annual membership	Prevalence per 100,000 persons			
			all (*n* = 353)	early stage (*n* = 80, 22.7%)	middle stage (*n* = 50, 14.2%)	late stage (*n* = 223, 63.2%)
All individuals	353	2,318,525	15.2	3.5	2.2	9.6
By age						
≤17	17 (4.8)	1,491,242	1.1	–[a]	–[a]	–[a]
18–34	49 (13.9)	399,945	12.3	–[a]	–[a]	5.0
35–44	66 (18.7)	130,481	50.6	–[a]	–[a]	26.1
45–54	96 (27.2)	147,423	65.1	13.6	8.1	43.4
55–64	125 (35.4)	149,434	83.7	8.7	10.0	64.9
By sex						
Female	234 (66.3)	1,191,904	19.6	4.5	2.5	12.7
Male	119 (33.7)	1,126,621	10.6	2.4	1.8	6.4
By race						
White	228 (64.6)	1,053,393	21.6	4.8	2.9	14.1
Black	49 (13.9)	605,387	8.1	1.8	1.2	5.1
Other/Unknown[b]	76 (21.5)	659,745	11.5	2.9	2.0	6.7

[a] Data not displayed in accordance with CMS cell-size suppression policy. [b] Other/Unknown category includes American Indian or Alaskan Native, Asian, Native Hawaiian or Other Pacific Islander, Hispanic or Latino, Hispanic or Latino and one or more races, more than one race, and Unknown.

lent cases was 23.4%, 30.0%, 46.6%, respectively, which was similarly reflected in the distribution of the prevalence proportion by stage (3.1, 3.9, 6.1; all per 100,000).

The 2017 incidence rate of HD among Medicare beneficiaries was 6.1 per 100,000 person-years. The mean (SD) age of incident cases was 77.1 (7.4) years, with most beneficiaries newly diagnosed between the age of 65–74 years (43.0%) and 75–84 years (39.1%). The age-specific incidence rate (per 100,000 person-years) was highest among beneficiaries who were 85+ years (7.3), followed by 75–84 years (6.8), and 65–74 years of age (5.2). Incidence was higher among males (6.4 per 100,000 person-years) than females (5.9 per 100,000 person-years). Incidence (per 100,000 person-years) was also higher among beneficiaries who were Black (11.8) versus White (5.8) or Other/Unknown (5.9). Incident cases represented mostly middle to late stages of disease (21.2% early, 29.8% middle, 49.0% late), with the following distribution of incidence by stage: 1.3, 1.8, 3.0, all per 100,000 person-years.

Medicaid Analysis

Among Medicaid beneficiaries under 65 years of age from 17 states, we identified 353 prevalent cases of HD in 2014 who met the diagnostic criteria and were included in the analysis. Overall and demographic-specific estimates of prevalence are shown in Table 2 and Figure 3.

The 2014 prevalence proportion of HD in the Medicaid population was 15.2 per 100,000 persons. The mean (SD) age of prevalent cases was 46.4 (13.4) years, while the highest percentage of beneficiaries with HD were between 55 and 64 years of age (35.4%). The prevalence proportions (per 100,000) increased by age stratum: 1.1 (≤17 years), 12.3 (18–34 years), 50.6 (35–44 years), 65.1 (45–54 years), 83.7 (55–64 years). The prevalence of HD was higher among females (19.6 per 100,000) than males (10.6 per 100,000). Prevalence (per 100,000) was also higher among White (21.6) compared to Black (8.1) or Other/Unknown (11.5) beneficiaries. Most beneficiaries with HD were in the late stage of disease: early (22.6%), middle (14.1%), late (63.1%), corresponding to the following distribution of prevalence by stage (per 100,000): 3.5, 2.2, 9.6.

Sensitivity Analysis

In the sensitivity analysis in which at least two medical claims with an HD diagnosis were required for patient identification, we identified 1,310 prevalent cases of HD in 2017 among Medicare beneficiaries 65 years and older; this translated to 8.8 cases per 100,000 persons. Among Medicaid beneficiaries under 65 years of age, we identified 302 prevalent cases of HD in 2014, corresponding to a prevalence proportion of 13.0 cases per 100,000 persons.

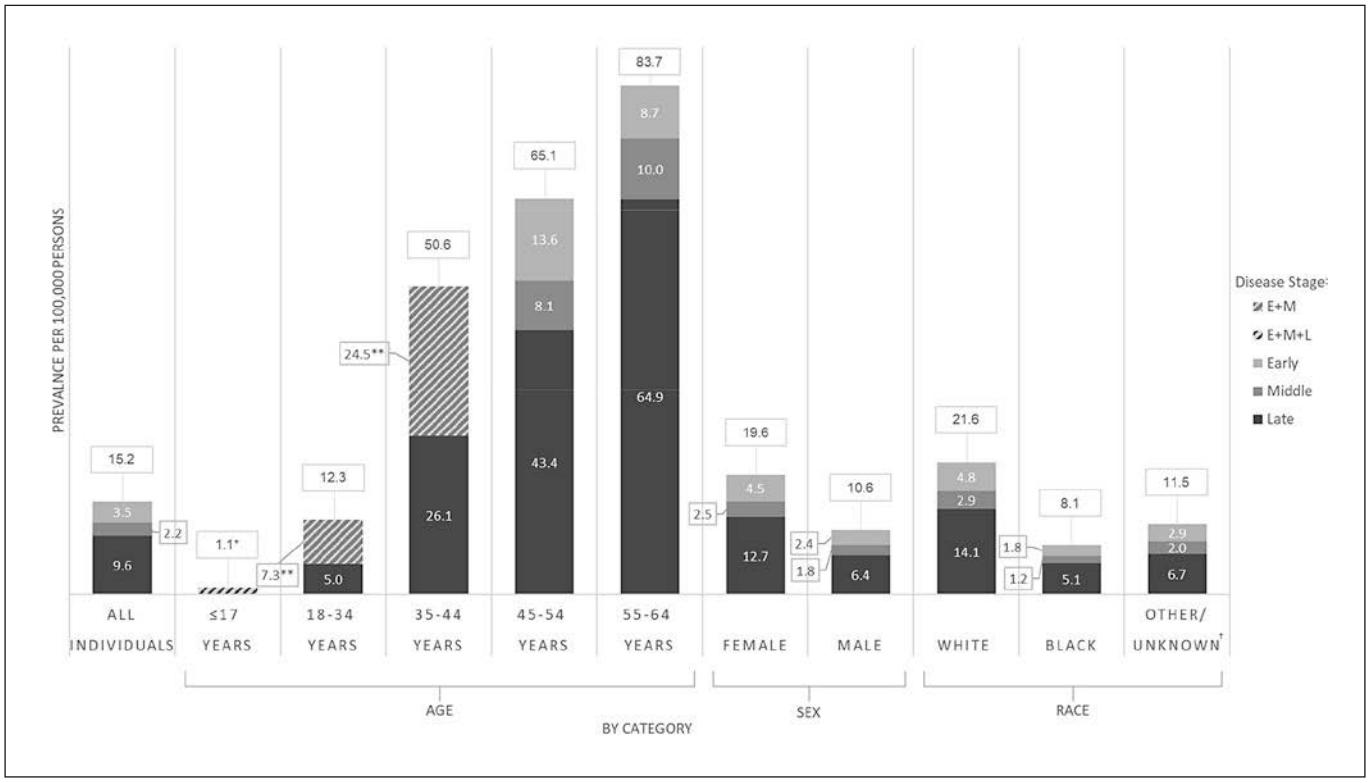

Fig. 3. †Other/Unknown category includes American Indian or Alaskan Native, Asian, Native Hawaiian or Other Pacific Islander, Hispanic or Latino, Hispanic or Latino and one or more races, more than one race, and Unknown. ‡E, early stage; M, middle stage; L, late stage. * All three disease stages combined to adhere to CMS cell-size suppression policy. ** Early and middle disease stages combined to adhere to CMS cell-size suppression policy.

Discussion

This epidemiological observational study of HD among Medicare and Medicaid beneficiaries is the first of its kind. We found that among Medicare beneficiaries 65 years and older, the prevalence of HD was 13.1 HD cases per 100,000 persons in 2017, while the incidence rate of HD was 6.1 cases per 100,000 person-years. For Medicaid beneficiaries under 65 years of age, the prevalence of HD was 15.2 cases per 100,000 in 2014. Both Medicare and Medicaid beneficiaries were predominantly in the late stage of HD.

These findings of the prevalence and incidence of HD in US Medicare and Medicaid populations are meaningful for a few reasons. First, this is the first study to our knowledge to examine the epidemiology of HD among Medicare and Medicaid beneficiaries, populations which represent a sizeable proportion (34%) of insured individuals in the USA, yet have not been previously studied [13]. Furthermore, the Medicare RIF and Medicaid MAX data used in this study are advantageous for studying the epidemiology of rare diseases such as HD in these populations because they are the most comprehensive data sources for Medicare and Medicaid beneficiaries compared to commercial databases which consist of a small subset of these beneficiaries. Second, our estimates of HD prevalence and incidence among Medicare and Medicaid beneficiaries are higher than those previously reported in other patient populations in the US and in other countries [4]. These differences may reflect a myriad of factors, including increased detection over time, variations in measurement across studies, or the heterogeneity of the populations studied. However, they may also indicate that the prevalence and incidence of HD in the US is higher than previously understood [8]. Third, most Medicare beneficiaries who were newly diagnosed with HD were in the middle or late stage of disease (78.8%); this finding points to an opportunity for earlier clinical recognition and di-

agnosis of HD, which may improve access to care and services within this population.

Few other studies have investigated HD epidemiology in US populations. A 1994 study of a population in Olmsted County, Minnesota, using clinical chart, administrative, and nursing home record data from 1950 to 1989, estimated prevalence and incidence to be 1.9 per 100,000 persons and 0.3 per 100,000 person-years, respectively [5]. A more recent analysis of 2003–2016 administrative claims data for privately insured enrollees in the US found a cumulative prevalence and incidence of 6.52 per 100,000 persons and 1.22 per 100,000 person-years, respectively, which remained relatively stable over the time period [6]. Although the study examined a similar time frame as ours, its estimates were lower than those generated in our analysis of Medicare and Medicaid beneficiaries. However, these disparate study populations were composed of commercial versus government-insured enrollees, and may have underlying characteristic differences that, in conjunction with different HD case identification criteria, accounted for the variation in estimates.

Additional investigations of HD epidemiology in the literature have centered on populations in other countries. A 2013 study by Fisher and Hayden [7] that examined HD epidemiology in the Canadian population estimated the prevalence to be 13.7 per 100,000 persons in 2012. This estimate, like ours, was well above other published estimates [4]; however, Fisher and Hayden [7] employed a more conservative methodology requiring genetic testing confirmation of HD diagnoses, lending support to both findings. Additionally, a 2013 analysis by Evans et al. [14] investigated the prevalence of HD from 1990 to 2010 using electronic medical records in the UK. The study found the prevalence (per 100,000 persons) of HD in the UK rose from 5.4 in 1990 to 12.3 in 2010, similarly reflecting estimates that were higher than previously reported. Further, the highest prevalence was observed among patients 51–60 years (15.8), followed by 61–65 years (15.3) and 66–70 years (14.6). A 2012 multicountry systematic review compiled incidence and prevalence evidence from prior HD studies in populations from the US, Asia, Europe, and Australia from 1988 to 2007 [4]. The results from these studies were highly variable, with prevalence ranging from 0.25 to 12.8 per 100,000 persons and incidence ranging from 0.046 to 0.8 per 100,000 person-years, which may be explained by the variety of analytic approaches and of populations studied.

As a secondary finding in our study, we observed multiple age-related patterns in HD prevalence and incidence. For Medicare beneficiaries, HD incidence increased with age while prevalence did not. This relationship may be due to the Medicare age qualification as it captures both beneficiaries with common-onset HD (i.e., onset of HD between 30 and 50 years old) reaching the end-of-life and those with less typical late-onset HD (i.e., onset of HD after 65 years of age in this database) who are receiving their initial diagnoses of HD. For the Medicaid population, prevalence increased sharply with each age category, particularly for beneficiaries 35–64 years of age, which spans the period of the typical onset age for HD; Medicaid beneficiaries aged 55–64 years had the highest HD prevalence (83.7 per 100,000 persons). Past studies of other populations have reported a similar increase in prevalence by age from 35 to 59 years, however, of lower overall magnitude [7].

In addition, we observed that HD prevalence and incidence in Medicare was higher among Black beneficiaries than among White or Other/Unknown beneficiaries, which was counterintuitive based on what is known about underlying risk of HD according to race [15]. While such differences are difficult to explain, particularly as the ≥65-year-old Medicare population is nationally representative of the US population in this age category, Bruzelius et al. [6] found that diagnostic frequency among those who identified as Black/African American was not significantly different from those who identified as White. Bruzelius et al. [6] further state that although rare, HD-like illness is more common in populations of African ancestry and lacks differentiation in diagnostic coding from HD. However, potential limitations of the administrative race data in Medicare could contribute in part to this difference [16]. Among Medicaid beneficiaries, HD prevalence was much higher among White beneficiaries compared to Black or Other/Unknown beneficiaries, as expected.

Several limitations are worth noting. First, we did not examine certain patient populations within Medicare (i.e., beneficiaries less than 65 years of age or enrolled in non-FFS programs) and Medicaid (i.e., beneficiaries 65 years and older, beneficiaries with Medicare dual-eligibility or in non-FFS programs); thus, our results may not be generalizable to these groups. Moreover, our estimation of HD prevalence in Medicaid may not extend to Medicaid beneficiaries residing in the other 33 states for which we could not obtain complete MAX data and thus excluded from the analysis. Additionally, in the Medicaid analysis, our chosen age stratum for pre-adult patients (i.e., patients less than 18 years of age) does not reflect the clinical classification of Juvenile HD (defined as less than 20 years of age). Second, our calculation of HD incidence

rate among Medicare beneficiaries may have overestimated the incidence due to our limited "at-risk" period for assessment; because our window for assessing prior HD diagnosis was restricted to 1 year (2016), we may have missed earlier diagnoses that occurred prior to this year. Third, we could not calculate the incidence rate of HD among Medicaid beneficiaries because the Medicaid eligibility and our study enrollment requirements did not yield a viable study population. Fourth, although the prevalence of HD was found to be higher among females compared to males in the Medicaid population, which is not expected given the equal risk of inheriting HD across sexes, we could not assess this comparison due to variability in Medicaid eligibility requirements across states. Furthermore, because Medicaid is a federal-state public insurance program, it allows states to establish unique "medically needy" eligibility criteria, thereby making comparisons across state populations difficult. Fifth, our algorithm for identifying patients with HD diagnosis in claims, which was based on other claims studies, has not been validated. Similar to two prior studies, we required only one HD diagnosis for study eligibility for our main analysis [6, 11]. We did not require a second confirmatory diagnosis for our main analysis because many people may not pursue care for HD until later in the course of disease, either due to social stigma or known family history, and thus would not have multiple HD claims. Despite a recent study finding similar estimates to ours using genetic confirmation to identify HD cases [7], we performed a sensitivity analysis due to concern that requiring only one HD diagnosis may lead to overestimation of the illness. As expected, the sensitivity results, which are based on a more restrictive algorithm, revealed a lower prevalence proportion than in the main analysis, from 13.1 to 8.8 cases per 100,000 Medicare beneficiaries and from 15.2 to 13.0 cases per 100,000 Medicaid beneficiaries. Notwithstanding these differences, both sets of prevalence estimates are considerably higher than those previously reported for other populations in the US [5, 6]. Sixth, while we used a previously published and validated algorithm to construct the disease stage variable in the absence of clinical data [11], this algorithm relies, in part, on healthcare utilization found in administrative claims data making interpretation of staging less direct. In exploratory analyses, we found that among Medicare beneficiaries, evidence of physical therapy, gait disorder, fall, and dementia were most common among patients with middle-stage HD, while those with late-stage HD were differentiated mainly by dysphagia, incontinence, and nursing home care; for Medicaid beneficiaries, dementia, gait disorder, and home assistance were most common, with late-stage beneficiaries, additionally experiencing nursing home care, dysphagia, hospice care, and feeding tube. Seventh, the diagnostic prevalence of HD may be lower than the true prevalence due to reliance on administrative claims, limiting our study sample to beneficiaries who received healthcare for HD. While our estimates of HD prevalence are higher than those previously published, the possibility remains that these estimates of prevalence and incidence are still underreported, particularly for early-stage disease. Research suggests there are more than 200,000 individuals at risk of inheriting HD with a 50% chance of developing symptoms [17]. Additionally, there is an avoidance of genetic testing among at-risk individuals due to associated social stigma, lack of effective HD treatments, inability to delay onset, and burden of knowledge [18]. Finally, the results in this study may not be generalizable to patients with other forms of insurance, including commercial health plans that may consist of patients with different demographic and clinical characteristics than Medicare and Medicaid beneficiaries in our study.

Conclusion

This study is the first to provide a comprehensive assessment of the prevalence and incidence of HD among US Medicare and Medicaid beneficiaries, a population for whom little was known about the disease. The estimates presented in this study suggest that incidence and prevalence of HD in the US may be higher than previously understood, which is consistent with other recent evidence; however, analytic limitations could not rule out overestimation. This has important implications in raising awareness of HD among providers and payers and ensuring availability of and access to treatments and services for HD patients and caregivers in the Medicare and Medicaid populations. The additional finding of this study that Medicare beneficiaries who are newly diagnosed with HD are predominantly in the middle or late stages of disease highlights an opportunity for earlier detection, diagnosis, and treatment of HD among beneficiaries.

Statement of Ethics

This study protocol was reviewed and approved by the Western Institutional Review Board (WIRB) and received a full waiver of HIPAA authorization. The study was determined to be exempt under 45 CFR § 46.104(d)(4) because the research involves retro-

spective data analysis, which contains identifiable private information that was recorded in a manner that the identity of the human subjects cannot be readily ascertained. Consent was not obtained nor required as this study employed a retrospective study design using administrative claims data and thus received a full waiver of HIPAA authorization.

Conflict of Interest Statement

Dr. Exuzides is an employee of Genentech, Inc., and shareholder of F. Hoffmann-La Roche Ltd. Dr. Reddy, Dr. Chang, and Mr. Paydar are employees of PHAR, LLC, which was paid by Genentech, Inc., to conduct this research, and reports other relevant financial activites with AbbVie, Amgen, AstraZeneca, BMS, Boston Scientific Corporation, Celgene, Eisai, Greenwich Biosciences, Jazz, Novartis, Otsuka, Prothena, Recordati, Regeneron, Sage, Sanofi US Services, Sunovion, and Takeda Pharmaceuticals USA outside the submitted work. Dr. Ta was an employee of Genentech, Inc., at the time of this study. Dr. Patel is an employee and shareholder of Genentech, Inc. Dr. Yohrling has no conflicts to disclose.

Funding Sources

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Author Contributions

Dr. Exuzides, Dr. Ta, Dr. Patel, and Dr. Yohrling contributed to the interpretation of data, revised work for important intellectual content, gave final approval of the version to be published, and provided agreement to be accountable for all aspects of the work. Dr. Reddy contributed to the acquisition, analysis, and interpretation of data, drafted and revised work for important intellectual content, gave final approval of the version to be published, and provided agreement to be accountable for all aspects of the work. Dr. Chang contributed to the analysis of data, revised work for important intellectual content, gave final approval of the version to be published, and provided agreement to be accountable for all aspects of the work. Mr. Paydar contributed to the acquisition and analysis of data, drafted and revised work for important intellectual content, gave final approval of the version to be published, and provided agreement to be accountable for all aspects of the work.

Data Availability Statement

The data in this study were obtained from the Centers for Medicare and Medicaid Services where restrictions apply. Such data may be requested from the Research Data Assistance Center (ResDAC) at www.resdac.org or .

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