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ROSTOCKER ZENTRUM – DISKUSSIONSPAPIER  
ROSTOCK CENTER – DISCUSSION PAPER

No. 32

**Parkinson's Disease in Germany: Prevalence, Incidence and  
Mortality Based on Health Claims Data**

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Juni 2015

# **Parkinson's Disease in Germany: Prevalence, Incidence and Mortality Based on Health Claims Data**

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Accepted by the ,editorial board‘\*

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## **Abstract**

**Background:** In Germany, epidemiological information on Parkinson's Disease (PD) is rare and outdated, exclusively conducted as door-to-door surveys. Considering aging populations, current measures about this age-related disease would be important for adequate public health planning.

**Objectives:** To assess the latest data on prevalences, incidences and mortality of PD, we used newly available health claims data from the largest German health insurer. We developed validation strategies to deal with shortcomings of this data type and to detect reliable PD diagnoses.

**Methods:** We used two longitudinal data sets dating 2004-2007 and 2007-2010 with an analysis population in the base years of 491,038 persons aged 50 years and above. Quarter-specific information about ICD-10 diagnoses and PD-drug prescriptions from the inpatient and outpatient sectors were used to validate PD cases.

**Results:** Depending on the validation strategy, crude prevalences (50+) vary with a range from 1,423/100,000 considering all diagnoses to 335/100,000 using tighter restrictions. Based on one final strategy, the crude period prevalence was 1,140/100,000 persons showing an age-specific increase up to category 85-89 and a slightly decline thereafter. Crude incidence was 257/100,000 person-years with a similar age-specific shape. Prevalences and incidences were higher for men compared to women in regard to age. After the 4-year follow-up, 35.7% of persons with PD and 12.7% without PD had died, showing significant differences in mortality.

**Conclusions:** After performing validation strategies, health claims data are found to be suitable for PD assessment. Case ascertainment based on PD drug prescriptions underestimates PD, particularly for the oldest old.

## **Introduction**

Idiopathic Parkinson's disease (PD) is the second most common neurodegenerative disorder at higher ages (>50), causing disability and care dependency with increasing duration.<sup>1</sup> With ageing populations, the number of individuals affected by this incurable disease will grow in the future. Bach et al. (2011) expect a 92% increase in PD patients for Europe (EU27), USA, and Canada combined from 2010 to 2050.<sup>2</sup> PD lowers life expectancy<sup>3-6</sup>, reduces quality of life for patients and relatives<sup>7, 8</sup>, and leads to substantial social and economic burdens.<sup>9, 10</sup> Taking these developments into account, data on prevalence, incidence, and mortality of PD is an important prerequisite for adequate public health planning and for investigating hypotheses about risk factors and mechanisms of PD. German data on prevalence and incidence are rare, outdated, and had been designed primarily as door-to-door surveys.<sup>1</sup> Therefore, the aim of this study is to provide current epidemiological information for Germany using newly available population based health claims data. Because health claims data are prone to shortcomings in accuracy and completeness,<sup>11</sup> we examine different validation strategies for detecting reliable PD diagnoses and discuss their impact on the estimated prevalence of the disease. Based on one of the validation criteria, we present estimates of the prevalence and incidence of PD, as well as of the mortality with PD.

## **Background**

PD is characterized by a loss of dopaminergic neurons in the substantia nigra and protein deposits in the cytoplasm of neurons (Lewy bodies). All primary symptoms are related to motor dysfunctions and affect bradykinesia, resting tremor, rigidity, and postural instability.<sup>12</sup> PD develops insidiously with slow progression and a preclinical phase without these cardinal symptoms. Usually signs occur approximately 4.5 to 6 years after the onset of PD.<sup>13, 14</sup> In addition to these motor-symptoms, patients often develop comorbidities and non-motor symptoms such as dementia, depression, psychosis, and sleeping disorders which are the main cause of care dependency, disability, and reduction in quality of life.<sup>15</sup>

To date, several studies have investigated epidemiological rates regarding PD. Due to methodological differences in the study design, conclusions of prevalence and incidence rates should be drawn carefully, as differences in study designs and diagnostic criteria lead to various results. Most of these studies rely on door-to-door surveys and engage neuropsychiatrists to identify PD. For Germany, the German Society of Neurology assumes a crude prevalence (65+ population) of 1,800/100,000 persons.<sup>16</sup> PD is rare before age 60 (0.07 to 0.13%), increases in subsequent age groups, and can reach a maximum of 9% among people of age 80-84. In higher ages (85-89), prevalences decline and vary from 0.9% to 2.9%.<sup>17-25</sup>

Incidence rates are also low for those aged 50-59 and increase sharply afterwards. Age-specific peaks differ between studies, however, ranging from 80.4 to 678 new cases/100,000 person-years.<sup>26-33</sup>

Studies of mortality refer to increased hazard ratios in patients with PD. They range from 1.58 to 2.7, with a median duration from disease onset to death of 4.8 to 10.3 years.<sup>34</sup>

## Data and Methods

### Data

We performed PD analyses using routine claims data of the largest German statutory health insurance, the “Allgemeine Ortskrankenkasse” (AOK). In Germany, about 70 million people are covered through statutory programs, one third of whom are members of the AOK. As many as half of this group belong to the population of higher ages.<sup>35</sup> Routine claims data provide quarter-specific information about diagnoses by ICD-10 and treatment in the inpatient and outpatient sectors. We used two longitudinal data sets from the years 2004-2007 and 2007-2010, each containing a sample size in the base years of 250,000 persons aged 50 years and above, which was about 2% of all persons insured in the AOK. After combining the datasets, data cleaning, and validation processes, we arrived at an analysis sample for the base years of 491,038 individuals.

### Methods

In order to increase the number of PD cases in our analysis sample, we combined the two time periods. All calculations are performed for valid PD cases only (see validation process and PD diagnosis below), for five-year age groups, and for the two sexes separately. We present crude prevalence and rates which cover all ages as well as age-specific information.

Period prevalence was estimated by dividing all PD cases in the base-years 2004 and 2007 by the total number of insured persons of the two years. It is expressed as PD cases per 100,000 persons.

$$Prevalence_{x,04,07} = \frac{PD\ cases_{x,04,07}}{total\ number\ of\ persons_{x,04,07}} \quad (1)$$

For estimating incidence rates, we used the longitudinal data sets of the years 2004-2007 and 2007-2010 combined. New cases of PD included all subjects who had a diagnosis-free period of at least six months but developed PD during the follow-up. Incidence rates are expressed as new PD cases per 100,000 person-years.

$$Incidence\ rate_{x,04-07,07-10} = \frac{new\ PD\ cases_{x,04-07,07-10}}{total\ number\ of\ person-years\ at\ risk_{x,04-07,07-10}} \quad (2)$$

Finally, we conducted mortality analyses with Kaplan-Meier survival curves to describe the impact of PD on mortality. We used the combined longitudinal dataset and calculated the median survival time for persons with and without PD. For estimating death rates with PD, we divided the number of deaths among PD cases by the number of person-years with PD. Death rates without PD are estimated by dividing the number of deaths among those without PD by the number of person-years without PD.

$$Death\ rate\ PD_{x,04-07,07-10} = \frac{dead\ PD\ cases_{x,04-07,07-10}}{total\ number\ of\ person-years\ with\ PD_{x,04-07,07-10}} \quad (3)$$

$$Death\ rate\ w/o\ PD_{x,04-07,07-10} = \frac{dead\ persons\ w/o\ PD_{x,04-07,07-10}}{total\ number\ of\ person-years\ w/o\ PD_{x,04-07,07-10}} \quad (4)$$

### Validation process and PD diagnosis

PD was identified based on the ICD-10 codes G20.0, G20.1, G20.2 and G20.9. Because a definite diagnosis of PD can only be made post-mortem, we developed internal validation strategies to rule out false positive diagnoses and increase the accuracy of our PD measure. These validation strategies were based on the type of physician, repeated diagnoses, and medication. In the outpatient sector we distinguished between physicians who were “neurologists/psychiatrists” (NP) and those who were not (“others”). The condition “Two quarters” requires a confirmative diagnosis in at least one further quarter of the base year or a second diagnosis by another physician in the same quarter. The condition “Medication” uses a PD-drug prescription during the complete follow-up (ATC-Code N04B).

For all strategies, the first step of the validation process included only those diagnoses internally marked as “verified” in the outpatient sector and as “discharge diagnosis” or “secondary diagnosis” in the inpatient sector. In some cases of PD, atypical parkinsonism<sup>1</sup> was coded in the same quarter or afterwards. In a second step, we excluded these persons from our prevalent or incident cases in case the last diagnosis in our longitudinal data was atypical parkinsonism. Finally, we developed eight validation strategies by combining diagnoses from different medical sectors with both conditions (Table 1).

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<sup>1</sup> Atypical parkinsonism summarizes ICD-10 codes G21, G23, G25.

Table 1 Eight validation strategies for measuring PD in health claims data

Strategy	Label	Medical Care			Condition		Crude Prevalence	
		Outpatient		Inpatient	2 Quarters	Medication	50+	65+
		NP	Other					
S I	All	x	x	x			1,423	2,191
S Ia	All + 2 quarters	x	x	x	x		1,140	1,759
S Ib	All + medication	x	x	x		x	582	871
S Ic	All + 2 quarters + medication	x	x	x	x	x	520	781
S II	NP / inpatient	x		x			778	1,192
S IIa	NP / inpatient + 2 quarters	x		x	x		515	782
S IIb	NP / inpatient + medication	x		x		x	428	639
S IIc	NP / inpatient + 2 quarters + medication	x		x	x	x	335	501

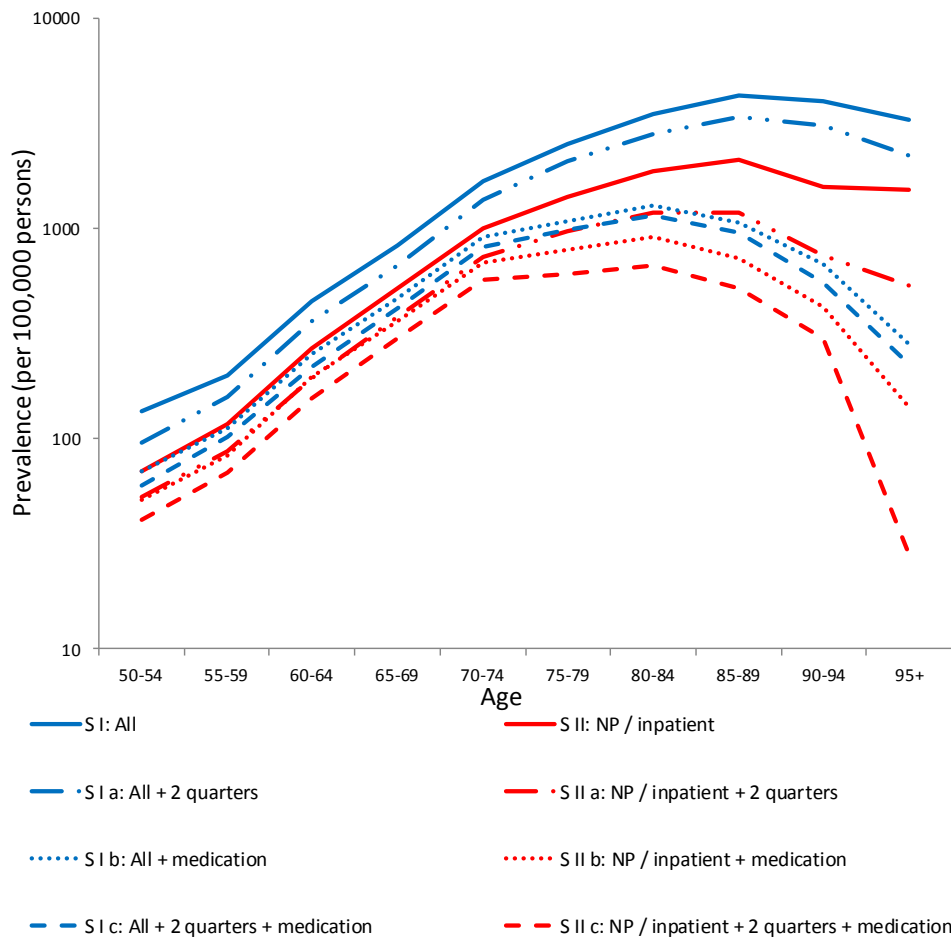
The validation strategies depicted in Table 1 fall into the two broad groups I and II and become more restrictive transitioning from (a) to (c). Strategy group S I uses all PD diagnoses irrespective of the type of physician, group S II use NP and inpatient diagnoses only. In strategy S I, all PD diagnoses in the inpatient and outpatient sector were considered valid. In strategy S Ia, valid PD diagnoses are all diagnoses in the inpatient or outpatient sector which were confirmed in at least one further quarter or in the same quarter by a second physician. Strategy S Ib includes valid PD diagnoses in case of any diagnoses, inpatient or outpatient, followed by a PD drug prescription. Valid PD cases in accordance with strategy S Ic require a PD diagnosis in another quarter or a confirmative diagnosis by a second physician in the same quarter. Additionally, PD drugs have to have been prescribed. In strategy S II valid PD was diagnosed by an NP or in the inpatient sector. S IIa in addition applies the 2 Quarter-criterion. In strategy S IIb, all PD diagnoses by an NP or in inpatient sector were considered valid in case PD drugs were prescribed. In strategy S IIc, valid PD cases are diagnosed by NPs or in the inpatient sector if they were repeated in at least one further quarter within a year or confirmed in the same quarter by a second NP or inpatient diagnosis. A PD drug prescription is required as well.

Table 1 also presents the crude PD prevalences over all age groups combined by validation strategy, and Figure 1 displays the corresponding age-specific prevalences. Regardless of any strategy, the prevalence of PD increases up to age 80-84 and declines thereafter. Despite this similar shape, the strategies vary considerably in their resulting prevalence. The strategies result into two groups of prevalence estimates: those containing the highest crude prevalences (S I, S I a, S II) with a range from 778 to 1,423 per 100,000 persons, and the remaining strategies (S I b, S I c, S II b, S II c) showing total numbers from 335 to 582 per 100,000 persons. Diagnoses in the first group use either all PD cases, are conditioned by a confirmative diagnosis within the same year, or by an NP/ inpatient diagnosis. They are all characterized by a moderate decline in prevalence at the highest ages. The second group includes the more restrictive strategies and the differences are most evident in the higher age groups. Prevalence falls rapidly for those



aged 85 and above, most apparently for the strategy conditioning on medical treatment. This suggests that at advanced ages PD patients may be prescribed PD medication to a lesser extent than at younger ages, probably due to negative side effects or adverse interactions.<sup>36</sup> It also suggests that validation strategies based on PD medication may be unsuitable for detecting valid PD cases and may lead to severe underestimation at old age. In consequence, our final validation strategy relies on diagnoses from the inpatient and outpatient sector confirmed in at least one further quarter within a year or on a secondary diagnosis by another physician in the same quarter (S Ia).

Figure 1 Age-specific prevalence of Parkinson's disease by validation strategies; logarithmic scale



Source: AOK claims data 2004, 2007

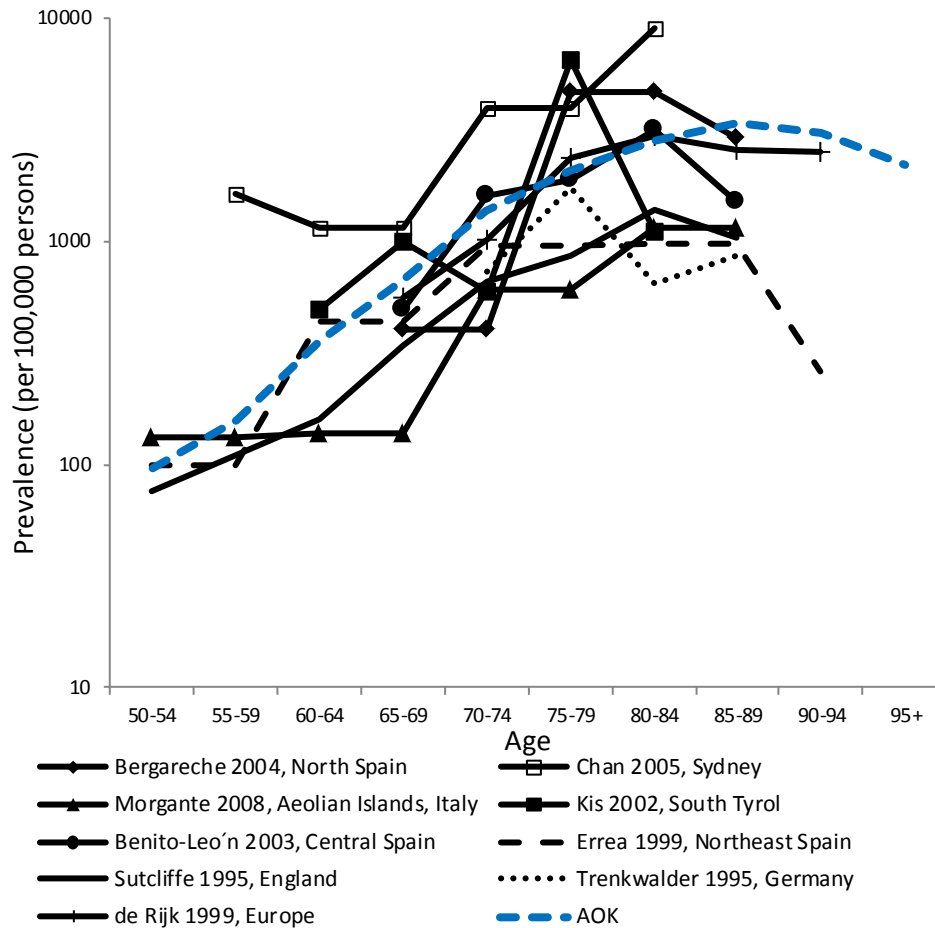
## Results

In the description of our results, we refer to the prevalence per 100,000 persons and to the incidence rate and death rate per 100,000 person-years. For the sake of brevity, however, we shall omit the latter qualifications.

## Prevalence

The analysis population of the two base years consisted of 491,038 persons with 5,598 valid PD cases, resulting in a crude prevalence of 1,140 for ages 50 and above and 1,759 cases for ages 65 and above. Figure 2 presents age-specific prevalences of PD from our data and previous studies. The level and the age profile are comparable to those of previous international studies. The only study for Germany, however, showed a lower prevalence compared to our calculations with a crude prevalence of 713 ( $\geq 65$  years).<sup>23</sup> Turning to the age-specific prevalences (Table 2), we estimated 96 cases at ages 50-54, which increased exponentially up to age 85-89. In comparison to the 361 cases in age group 60-64, the prevalence had nearly doubled in age group 65-69 (671 cases) and increased nine-fold for those aged 85-89 (3,378 cases). Then, the numbers declined and reached a level of 2,230 cases in the highest age category (95+). The crude prevalence was higher in women (1,175 cases) than in men (1,093 cases), but in regard to age prevalences were constantly higher in men (Table 2). Moreover, sex-specific differences increased constantly with age up to age group 80-84. Men reached their maximum at 90-94 years (4,207 cases) and women already peaked in age group 85-89 (3,291 cases).

Figure 2 Age-specific prevalences of Parkinson's disease by AOK claims and previous prevalence studies; logarithmic scale



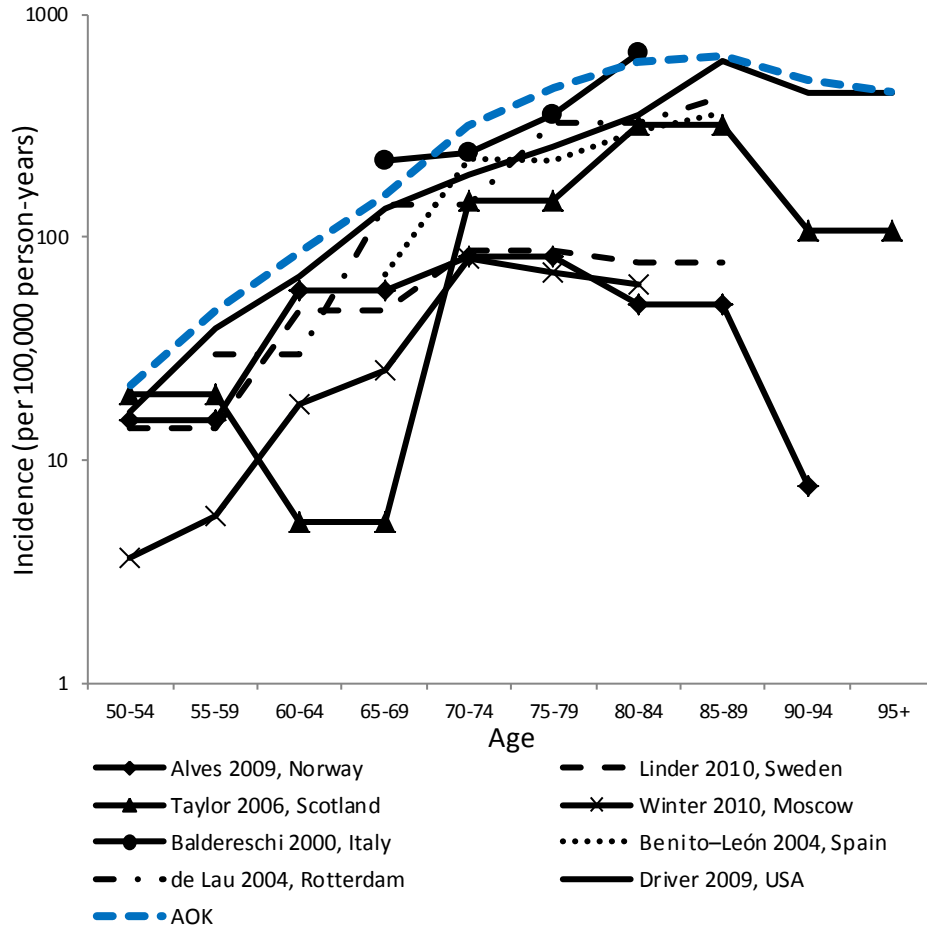
Source: AOK claims data 2007, 2010

## Incidence

Table 2 shows age- and sex-specific incidence rates of PD. A total of 3,948 new cases had their onset of PD during the follow-up, leading to a crude incidence rate of 257 new cases. The mean age of PD onset was 76.7 years (age range 50-101; sd 8.3 years). Figure 3 compares age-specific incidence rates of this study with previous studies. While incidences vary considerably between studies, our estimates are at the higher end. Turning to the age-specific rates, total incidence rates nearly doubled (age group 50-54: 22 new cases) every five years until age group 70-74 (316 new cases). Thereafter, the increase of new PD cases slowed down. The rate peaked for those aged 85-89 (657 new cases), and declined afterwards to 452 new cases in the highest age group. Men (260 new cases) had a slightly higher crude incidence rate than women (255 new cases), and this was also true for the age-specific rates. Both male and female

incidence rates peaked at ages 80-84 (men: 795 new cases; women: 619 new cases) and declined thereafter.

Figure 3 Age-specific incidence rates of Parkinson’s disease by AOK claims and previous incidence studies; logarithmic scale



Source: AOK claims data 2004-2007, 2007-2010

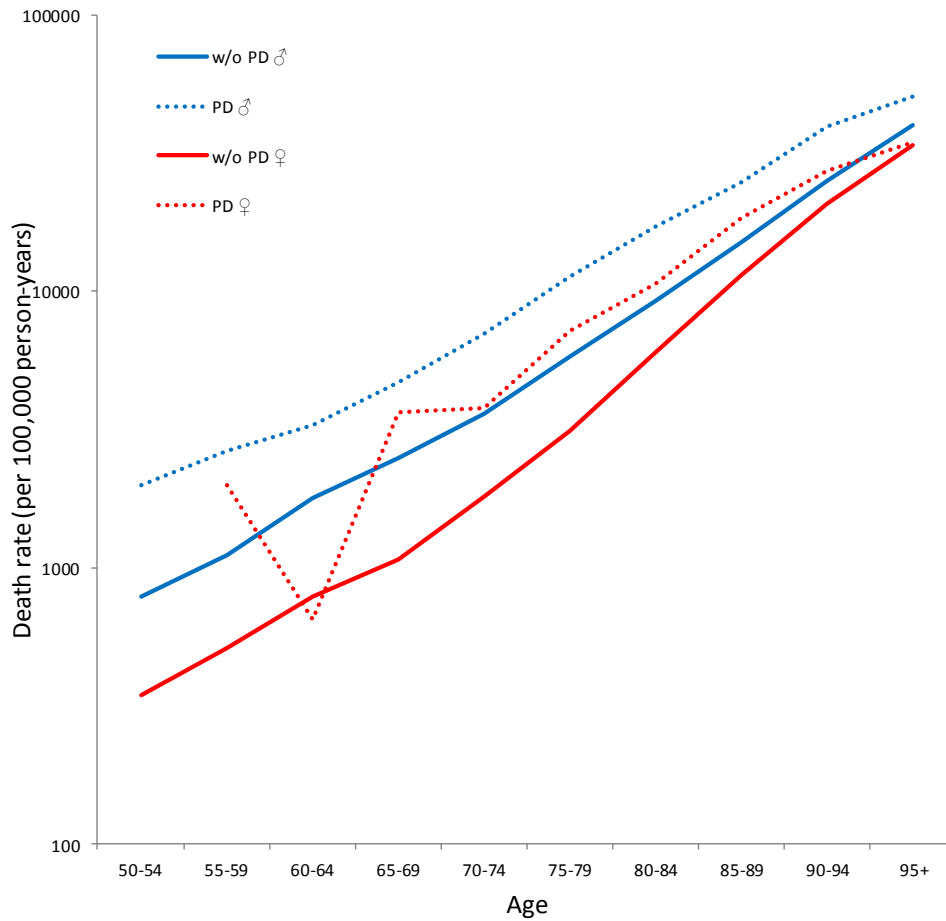
### Mortality

After four years of follow-up, 59,961 individuals without PD (12.7%) and 2,827 individuals with PD (35.7%) had died, thus revealing significant differences in the survival of the two groups (Wilcoxon test  $p \leq 0.001$ ). The median survival time could not be computed because fewer than half of those with and without PD had died after 4 years. Women had slightly higher survival chances than men (not shown).

Death rates for PD cases increase exponentially with age and were generally higher compared to persons without PD, showing crude death rates of 11,203 deaths (PD) and 3,879 deaths (w/o PD) (Figure 4).

Among male PD cases, excess mortality was 2.5 times as high in the youngest age group (50-54) and 1.5 times as high among the cases in age group 90-94. The rate increased from 1,987 deaths at ages 50-54 to 50,802 deaths at age 95 and above. Among women, the excess mortality of PD cases was inconsistent at young ages, most probably due to the low number of cases. It was nearly four times as high at age 55-59 and 1.3 times as high at age group 90-94. The maximum in females PD cases also occurred in group 95+ with a rate of 34,724 deaths.

Figure 4 Age- and gender-specific death rates of persons with and without PD; logarithmic scale



Source: AOK claims data 2004-2007, 2007-2010

Table 2 Age and sex-specific prevalences, incidences and death rates

Age	Prevalence			Incidence			Death rates							
	Cases	N	Cases per 100,000	Cases	Exposures	Cases per 100,000 person-years	with PD			without PD			Deaths per 100,000 person-years	
							Cases	Exposures	Deaths per 100,000 person-years	Cases	Exposures	Deaths per 100,000 person-years		
<b>Men</b>														
50-54	42	35,525	118.23	21	86,755.04	24.21	3	150.96	1,987.30	835	106,419.29	784.63		
55-59	65	31,084	209.11	50	106,102.63	47.12	8	304.25	2,629.42	1,337	121,223.87	1,102.92		
60-64	131	31,133	420.78	96	95,653.54	100.36	19	577.13	3,292.18	1,982	111,477.67	1,777.94		
65-69	312	38,579	808.73	212	120,394.42	176.09	62	1,331.00	4,658.15	3,462	139,384.92	2,483.77		
70-74	512	31,296	1,635.99	400	106,901.46	374.18	166	2,362.83	7,025.46	4,357	121,417.04	3,588.46		
75-79	546	22,189	2,460.68	436	73,448.13	593.62	292	2,581.50	11,311.25	4,859	83,442.29	5,823.19		
80-84	405	12,347	3,280.15	302	40,638.75	743.13	311	1,819.96	17,088.30	4,268	46,045.08	9,269.18		
85-89	179	4,858	3,684.64	130	16,359.54	794.64	218	877.00	24,857.47	2,754	18,272.25	15,072.04		
90-94	83	1,973	4,206.79	36	4,752.75	757.46	99	252.21	39,253.26	1,399	5,541.38	25,246.44		
95+	14	477	2,935.01	11	1,253.46	877.57	33	64.96	50,801.80	568	1,414.75	40,148.44		
<b>Total</b>	<b>2,289</b>	<b>209,461</b>	<b>1,092.80</b>	<b>1,694</b>	<b>652,259.71</b>	<b>259.71</b>	<b>1,211</b>	<b>10,321.79</b>	<b>11,732.46</b>	<b>25,821</b>	<b>754,638.54</b>	<b>3,421.64</b>		
<b>Women</b>														
50-54	25	34,479	72.51	16	84,651.00	18.90	0	105.00	0	359	103,889.04	345.56		
55-59	33	31,200	105.77	49	107,211.50	45.70	4	200.83	1991.70	628	122,373.92	513.18		
60-64	96	31,689	302.94	74	99,182.17	74.61	3	464.71	645.57	905	115,548.71	783.22		
65-69	242	43,945	550.69	183	136,926.50	133.65	39	1,070.96	3641.60	1,700	159,024.33	1,069.02		
70-74	483	41,492	1,164.08	384	141,424.79	271.52	84	2,230.33	3766.25	2,928	161,345.08	1,814.74		
75-79	711	37,713	1,885.29	491	122,909.42	399.48	230	3,183.08	7225.70	4,403	140,947.96	3,123.85		
80-84	832	31,750	2,620.47	557	100,314.08	555.26	396	3,716.75	10654.47	6,916	115,035.75	6,012.04		
85-89	564	17,137	3,291.12	359	58,019.42	618.76	495	2,680.79	18464.70	7,496	65,165.58	11,503.01		
90-94	258	9,106	2,833.30	109	23,426.67	465.28	262	962.75	27213.71	5,646	27,259.33	20,712.17		
95+	65	3,066	2,120.03	32	8,266.92	387.09	103	296.63	34723.98	3,159	9,383.46	33,665.63		
<b>Total</b>	<b>3,309</b>	<b>281,577</b>	<b>1,175.17</b>	<b>2,254</b>	<b>882,332.46</b>	<b>255.46</b>	<b>1,616</b>	<b>14,911.83</b>	<b>10,837.03</b>	<b>34,140</b>	<b>1,019,973.20</b>	<b>3,347.15</b>		
<b>Both Sexes</b>														
50-54	67	70,004	95.71	37	171,406.04	21.59	3	255.96	1,172.07	1,194	210,308.33	567.74		
55-59	98	62,284	157.34	99	213,314.13	46.41	12	505.08	2,375.85	1,965	243,597.79	806.66		
60-64	227	62,822	361.34	170	194,835.71	87.25	22	1,041.83	2,111.66	2,887	227,026.37	1,271.66		
65-69	554	82,524	671.32	395	257,320.92	153.51	101	2,401.96	4,204.90	5,162	298,409.25	1,729.84		
70-74	995	72,788	1,366.98	784	248,326.25	315.71	250	4,593.17	5,442.87	7,285	282,762.12	2,576.37		
75-79	1,257	59,902	2,098.43	927	196,357.54	472.10	522	5,764.58	9,055.30	9,262	224,390.25	4,127.63		
80-84	1,237	44,097	2,805.18	859	140,952.83	609.42	707	5,536.71	12,769.32	11,184	161,080.83	6,943.10		
85-89	743	21,995	3,378.04	489	74,378.96	657.44	713	3,557.79	20,040.52	10,250	83,437.83	12,284.60		
90-94	341	11,079	3,077.90	145	28,179.42	514.56	361	1,214.96	29,712.95	7,045	32,800.71	21,478.20		
95+	79	3,543	2,229.75	43	9,520.38	451.66	136	361.58	37,612.35	3,727	10,798.21	34,514.99		
<b>Total</b>	<b>5,598</b>	<b>491,038</b>	<b>1,140.03</b>	<b>3,948</b>	<b>1,534,592.20</b>	<b>257.27</b>	<b>2,827</b>	<b>25,233.63</b>	<b>11,203.31</b>	<b>59,961</b>	<b>1,774,611.70</b>	<b>3,378.82</b>		

Source: AOK claims data 2004-2007, 2007-2010

## Discussion

In this study, we examined the occurrence of PD based on one large data sample from the largest German public health insurance organization. It is the first study that presents age-specific figures of prevalence and incidence, and of mortality with PD for Germany. Until now, health claims data have not been widely used in the field of epidemiological research in Germany, and to our knowledge this is the first study that has investigated PD using this type of data. Our results suggest that there are approximately 293,364 PD patients in Germany.<sup>37</sup>

We explored different validation routines to deal with the shortcomings of claims data, particularly false positive diagnoses. Wermuth et al. (2012) evaluated 1,040 PD diagnoses from Danish medical records and found that 17.4% did not meet the definition of PD.<sup>38</sup> Due to validation strategies, we were able to avoid these false positive diagnoses (e.g. atypical parkinsonism) and improve the accuracy of PD measure. However, our validation procedures cannot deal with false negative diagnoses. As Figure 1 demonstrates, the stricter the strategy, the lower the crude prevalence and consequently the more patients we exclude from our analysis, particularly for the oldest old. We decided on the strategy “S Ia: All + 2 Quarters” because of the highly likely loss of valid PD diagnoses when using stricter strategies. We then used this strategy for the calculation of all measures presented.

Age-specific prevalences and particularly incidence rates in this study were somewhat higher than those of the latest German study by Trenkwalder et al. (1995).<sup>23</sup> The German Society of Neurology assumes prevalences similar to ours, however, it should be noted that they use data from a collaborative European study rather than German data.<sup>25</sup> Despite the differences, the age-profile of nearly all studies consistently showed an increase for prevalences and incidences with age up to group 85-89 and a decline beyond this age.

Compared to the other studies, our slightly increased figures can be explained by differences in the case finding strategy, the diagnostic criteria and the response rate.<sup>39</sup> First, PD patients were identified from the largest German health insurance agency. In contrast to the widespread door-to-door survey previously conducted in this research field, our study also captures the institutionalized population, which contains a substantial position of all PD patients (see below). Another reason for the relatively high PD number is the socio-economic and the general health status of the population insured through the AOK. Less educated and chronically ill persons are historically over-represented in the AOK.<sup>40, 41</sup> The diagnostic criteria of PD vary widely in observational data such as claims data. This variation can lead both to over- and underrepresentation of PD patients. However, our validation procedure should take care of part of this problem by demanding a confirmatory PD diagnoses within a year. The response rate, an important topic

in door-to-door surveys or epidemiological surveys, is not an issue in medical claims data, which is also true for sample bias due to selection into the study.

Age seems to be one of the main factors for the occurrence of PD with the mitochondria in the nerve cells getting more vulnerable for toxins or other harmful factors.<sup>42</sup> However, several studies, including this investigation, found a decline of incidences for the oldest old<sup>29-33</sup>, others did not.<sup>26-28</sup> In general, the results of different studies of higher age groups should be interpreted with caution because varying definitions and small sample sizes makes comparisons difficult and might lead to distortions.<sup>1</sup> However, the highest age group in our study contains a substantial number of 3,543 individuals with 79 prevalent cases at the base year, and 43 incident cases and 3,863 deaths during the follow-up, which makes analyses in these ages still reasonable.

The alleged decline might be a consequence of diagnostic uncertainty. Due to comorbidity, age-related symptoms, and indicators which are similar to PD, it is difficult to distinguish PD from other diseases, resulting in false negative diagnoses.<sup>31</sup>

PD might also be underestimated for the oldest old because it is possible that affected people never seek medical attention in regard their symptoms.<sup>43</sup>

Finally, considerations about unobserved heterogeneity should also be taken into account. Individuals of a population differ in frailty, and mortality selection determines the proportion of PD and persons without PD in advanced ages in favor of the latter group.<sup>44</sup>

We found sex differences in the risk of PD which are consistent with previous studies<sup>26, 27, 30, 45</sup>. Considering both prevalences and incidence rates, in all but one age group men showed higher figures than women. From a behavioral view, one can argue that men are at greater risk for PD because of their lifestyle. Working in the agriculture sector with an increased toxicant exposure or the more frequent occurrence of head injuries may partly explain sex disparities. Furthermore, the female sexual hormone estrogen may show neuroprotective effects by providing higher dopamine levels and postponing the onset of the degenerative process.<sup>46, 47</sup>

Our mortality analysis produced results similar to preceding studies, showing the increased mortality risk of patients with PD compared to the reference population<sup>34</sup> and persons with and without PD differing in their survival rates.

This study has several limitations. Routine claims data are primarily compiled for billing purposes in the healthcare sector and not for epidemiological analyses, meaning that various coding errors are possible. We took this issue into account by performing internal validation procedures. Despite these validation procedures wrong diagnoses may stem from the fact that some patients were diagnosed by general practitioners and not only by specialists. In our data, 37.2% of all PD diagnoses were made by general practitioners, 25.6% by NPs, 20.7% by other specialists, and 16.5% in the inpatient sector. More than half



of all diagnoses were made by physicians who are not trained to detect PD. Furthermore, there might be over-coverage of PD patients due to remuneration. Thus, financial incentives may lead to false diagnoses, which ultimately result in excessive numbers in routine claims data.<sup>48</sup> Under-coverage also cannot be completely ruled out if affected people do not make use of medical services. Finally, analyses regarding mortality in PD were limited due to the follow-up time of only four years. Our analysis shows that survival time after initial PD diagnosis is considerable, as is evident by the fact that only 35.7% of those affected in our data set died within the course of four years. Longer time periods are needed in order to learn more about life expectancy of PD patients.

Although routine claims data have several limitations, which we tried to deal with, such data also provide many opportunities to investigate neurodegenerative diseases. The majority of previous PD studies were designed as door-to-door surveys conducted in local areas with small sample sizes. The advantages of our design are the large size of our study population (491,038 individuals) and the fact that it encompasses insured persons on a national basis. Another enormous benefit is the inclusion of the institutionalized population. One common weakness of door-to-door surveys is the lack of access to patients in nursing homes. As a result, these patients of higher ages and advanced stage of illness are often underrepresented, wherefore explanations about age effects cannot be made. In our study, 20% of all PD patients were living in nursing homes, allowing us to analyze PD up to the highest ages. In addition to the large number of patients, the quality of data after the validation procedure is also highly promising. Medical claims data are also independent of the research issue because they were collected by physicians in conjunction with routine documentation. Thus, self-selection, non-response, or interviewer bias can be ruled out.<sup>48</sup>

## **Conclusion**

Our results emphasize the present relevance of PD in Germany. Regarding aging populations worldwide, the consequences at the individual and society levels will be intensified. Thus, it is essential to be aware of recent and reliable epidemiological data of PD to obtain needs assessments and cost calculations, and to offer adequate care services. For a better understanding of PD in the future, it might be helpful to conduct investigations concerning potential risk factors and gather information about changes of PD over time.

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