

Parkinson's disease in Germany: Prevalence and incidence based on health claims data

M. Nerius^{1,2,3} | A. Fink^{1,2} | G. Doblhammer^{1,2,3,4}

¹German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

²Rostock Center for the Study of Demographic Change, Rostock, Germany

³Institute for Sociology and Demography, University of Rostock, Rostock, Germany

⁴Max Planck Institute for Demographic Research, Rostock, Germany

Correspondence

M. Nerius, Institute for Sociology and Demography, University of Rostock, Rostock, Germany.

Email: nerius@demogr.mpg.de

Background: In Germany, epidemiological information on Parkinson's disease (PD) is rare and outdated. Considering aging populations, current prevalences and incidence rates about this age-related disease would be important for adequate public health planning.

Methods: We used newly available health claims data sets from the largest German health insurer dating 2004-2007 and 2007-2010 with an analysis population in the base years of 491 038 persons aged 50 and older. Quarter-specific information about ICD-10 diagnoses and PD drug prescriptions from the inpatient and outpatient sectors was used to validate PD cases. Estimations were presented for two validation strategies relying on repeated PD diagnoses (Sl_a) and on one PD diagnosis followed by at least one PD drug prescription (Sl_b).

Results: The standardized prevalence was 797 (Sl_b) to 961/100 000 persons (Sl_a), showing an age-specific increase up to category 85-89 and a decline thereafter. The standardized incidence rate was 192 to 229/100 000 person-years with a similar age-specific shape. Prevalences and incidences rates were higher for men compared to women in regard to age.

Conclusions: Health claims data are found to be suitable for PD assessment using the repeated diagnoses or PD drug prescriptions as necessary criteria.

KEYWORDS

health claims data, incidence, Parkinson's disease, prevalence

1 | 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.¹ With aging populations, the number of individuals affected by this incurable disease will almost double in Europe, USA, and Canada combined by 2050.² Generally, PD is rare before age 60 (0.13%-1.6%), increases with age, and can reach a maximum of 9% among people aged 80-84. Thereafter (85-89), prevalences decline and vary from 0.87% to 3.6%.³⁻¹⁰ Incidence rates are also low for those aged 50-59 and increase sharply afterward. Age-specific peaks differ between studies, however, ranging from 80.4 to 678 new cases/100 000 person-years.¹¹⁻¹⁹ German data on prevalence and

incidence are rare, outdated, and had been designed primarily as door-to-door surveys.¹ The German Society of Neurology (GSN) assumes a crude prevalence (65+ population) of 1800/100 000 persons.²⁰

The aim of this study was to provide current epidemiological information for Germany using newly available population-based health claims data. Because these data allow for a wide range of estimations depending on the choice of criteria, we present results from two selected estimation strategies.

1.1 | Data

We performed PD analyses using routine claims data from the years 2004-2007 and 2007-2010 of the largest German statutory health

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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. The AOK covers more than 50% of the population of higher ages.²¹ We drew two exclusive randomized samples in the first quarters of the years 2004 and 2007, each containing a size of 250 000 persons aged 50 and older, which was about 2% of all persons insured in the AOK. The AOK sample is almost representative in terms of sex, but does not represent the German population with regard to age because persons from the sample are older (Table S3). AOK-insured persons as a whole are less educated and probably sicker than the German population.²² We will consider this aspect more closely in the discussion part. After combining the data sets, data cleaning, and validation processes, we arrived at an analysis sample for the first quarter of the base years of 491 038 individuals.

The data provide diagnoses by ICD-10 and treatment in the inpatient and outpatient sector which are relevant for the documentation of billing. This information is reported quarterly and covers every insured person regardless of actual utilization. Information on medical treatment contains filled-in drug prescriptions in the outpatient sector. PD medication is based on the Anatomical Therapeutic Chemical (ATC) Classification System and defined by code N04B.

2 | METHODS

To increase the number of PD cases in our analysis sample, we combined the two time periods. All calculations refer to persons aged 50 and older and are performed for valid PD cases only, for 5-year-age groups x and for the two sexes separately.

Age- and sex-specific prevalences were estimated by dividing all PD cases in the base years 2004 and 2007 by the total number of insured persons of the 2 years at age x . It is expressed as PD cases per 100 000 persons (Equation 1). 95% confidence intervals (CI) for prevalences were calculated by assuming a normal distribution.

$$\text{Prevalence}_{x,04,07} = \text{PD cases}_{x,04,07} / \text{total number of persons}_{x,04,07}. \quad (1)$$

For calculating the standardized prevalence, we used the average age distribution for both sexes combined of 2004 and 2007 in Germany. The total number of PD cases in Germany aged 50 and older was calculated by applying the age- and sex-specific prevalences to the average age and sex distribution of 2004 and 2007 in Germany.²³

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 6 months, but developed PD during the follow-up. Because of our internal PD validation strategies, we include only the person-times at risk before the last quarter. Incidence rates are expressed as new PD cases per 100 000 person-years (Equation 2). 95% CI for incidence rates were calculated by assuming a Poisson distribution. For calculating the standardized incidence rate, we used the average age distribution for both sexes combined of 2004 and 2007 in Germany.

$$\text{Incidence rate}_{x,04-07,07-10} = \frac{\text{new PD cases}_{x,04-07,07-10}}{\text{total number of person-years at risk}_{x,04-07,07-10}} \quad (2)$$

Data access was legally approved by the Scientific Institute of the AOK (WIdO). The study is based on anonymized administrative claims data that never involved patients directly. Individual patients cannot be identified, and the analyses presented do not affect patients whose anonymized records were used.

2.1 | PD diagnosis

PD was identified based on the ICD-10 codes G20.0, G20.1, G20.2, and G20.9. We developed internal validation strategies to rule out false-positive diagnoses (Table 1, Appendix S1, Figure S1). These validation strategies were based on the type of physician, repeated

TABLE 1 Eight validation strategies for measuring PD and the corresponding prevalences

Strategy	Label	Medical care			Criterion		Prevalence	
		Outpatient		Inpatient	2 Quarters	Medication	50+	65+
		NP	Other					
S I	All	x	x	x			1167	2061
S Ia	All+2 quarters	x	x	x	x		961	1704
S Ib	All+medication	x	x	x		x	797	1411
S Ic	All+2 quarters+medication	x	x	x	x	x	689	1221
S II	NP inpatient	x		x			648	1137
S IIa	NP/inpatient+2 quarters	x		x	x		454	790
S IIb	NP/inpatient+medication	x		x		x	541	950
S IIc	NP/inpatient+2 quarters+medication	x		x	x	x	402	699

"NP"=neurologists or psychiatrists; prevalences are given per 100 000 persons and standardized by the average German population in 2004 and 2007; Source: AOK claims data 2004, 2007.

diagnoses, and medication. In the outpatient sector, we distinguished between physicians who were “neurologists/psychiatrists” (NP) and those who were not (“others”).

For all strategies, first we included only those diagnoses internally marked as “verified” in the outpatient sector and as “discharge diagnosis” or “secondary diagnosis” in the inpatient sector. Secondly, we excluded 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 using the following criteria: “2 Quarters” requires a confirmative diagnosis in at least one further quarter or a second diagnosis by another physician in the same quarter. “Medication” uses at least one PD drug prescription during the complete follow-up (ATC N04B). In accordance with the guidelines of the GSN, physicians are recommended to call their patients with PD no later than every 6 months for follow-up examinations and to start the medical treatment as soon as possible.²⁰ Therefore, we present the results of two final validation strategies based on at least two PD diagnoses (Sl_a) and on at least one PD diagnosis followed by a PD drug prescription (Sl_b; for an in-depth discussion of all strategies, see Appendix S2).

3 | RESULTS

In the description of our results, we refer to the prevalence per 100 000 persons and to the incidence rate per 100 000 person-years at age 50 and older. For the sake of brevity, however, we shall omit the latter qualification.

3.1 | Prevalence

The analysis population of the two base years consisted of 491 038 persons with 5751 valid PD cases for the Sl_a strategy (2 Quarters) and 4736 valid PD cases for the Sl_b strategy (medication), resulting in an standardized prevalence of 961 (Sl_a: CI 957-964) and 797 (Sl_b: CI 794-800). 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. Figure 1 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. Turning to the age- and sex-specific prevalences (Figure 2, Table S1), the numbers of both validation strategies increased exponentially up to age 80-84 (Sl_a: 3533; CI 3284-3781; Sl_b: 2669; CI 2456-2882). Then, they declined mildly and reached a level of 2456 (Sl_a: CI 1940-2972) and 1552 (Sl_b: CI 1145-1959). The Sl_a strategy resulted in a higher standardized prevalence for men (964; CI 959-969) than for women (961; CI 953-962), and with regard to age, prevalences were constantly higher in men (Figure 2, Table S1). This is also true for the Sl_b strategy (Figure 2, Table S1) which resulted in a standardized prevalence of 820 (CI 815-824) for men and of 779 (CI 774-783) for women.

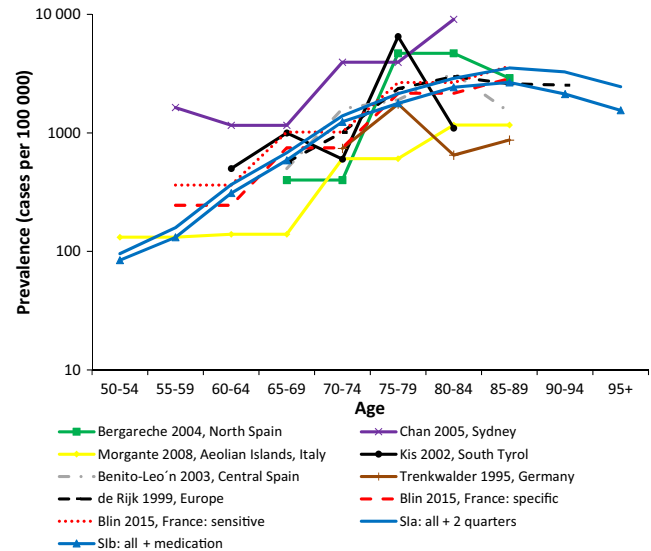


FIGURE 1 Age-specific prevalences of Parkinson's disease by AOK claims and previous prevalence studies; logarithmic scale. Source: AOK claims data 2004, 2007

3.2 | Incidence

A total of 3994 (Sl_a) and 3623 (Sl_b) new cases had their onset of PD during the follow-up, leading to an standardized incidence rate of 229 (Sl_a; CI 223-236) and 192 (Sl_b; CI 186-198) new cases (Table S2). The mean age of PD onset was 76.8 years according to the Sl_a strategy and 76.9 with regard to the Sl_b strategy. Figure 3 compares age-specific incidence rates of this study with previous studies. While incidence rates vary considerably between studies, our estimates are at the higher end. Turning to the age- and sex-specific rates, incidence rates nearly doubled every 5 years from age 50-54 until age 70-74 (Figure 4, Table S2), reaching 344 (Sl_a: CI 321-369) and 281 (Sl_b: CI 261-303). Thereafter, the increase in new PD cases slowed down. The rate reached a maximum for those aged 85-89 with 722 (Sl_a: CI 661-788) and declined thereafter to 521 (CI 391-696) in age group 95+. Using the Sl_b strategy, the rate peaked for those aged 85-89 (630; CI 575-689) and declined afterward to 434 (CI 321-588) in the highest age group. Regarding sex, men had a higher standardized incidence rate (Sl_a: 242; CI 232-253; Sl_b: 203; CI 193-213) than women (Sl_a: 224; CI 215-233; Sl_b: 187; CI 179-195), and this was also true for the age-specific rates.

4 | DISCUSSION

Using a data sample from the largest German public health insurance, we present age-specific figures of prevalence and incidence rates of 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. Depending on the validation strategy, the total number

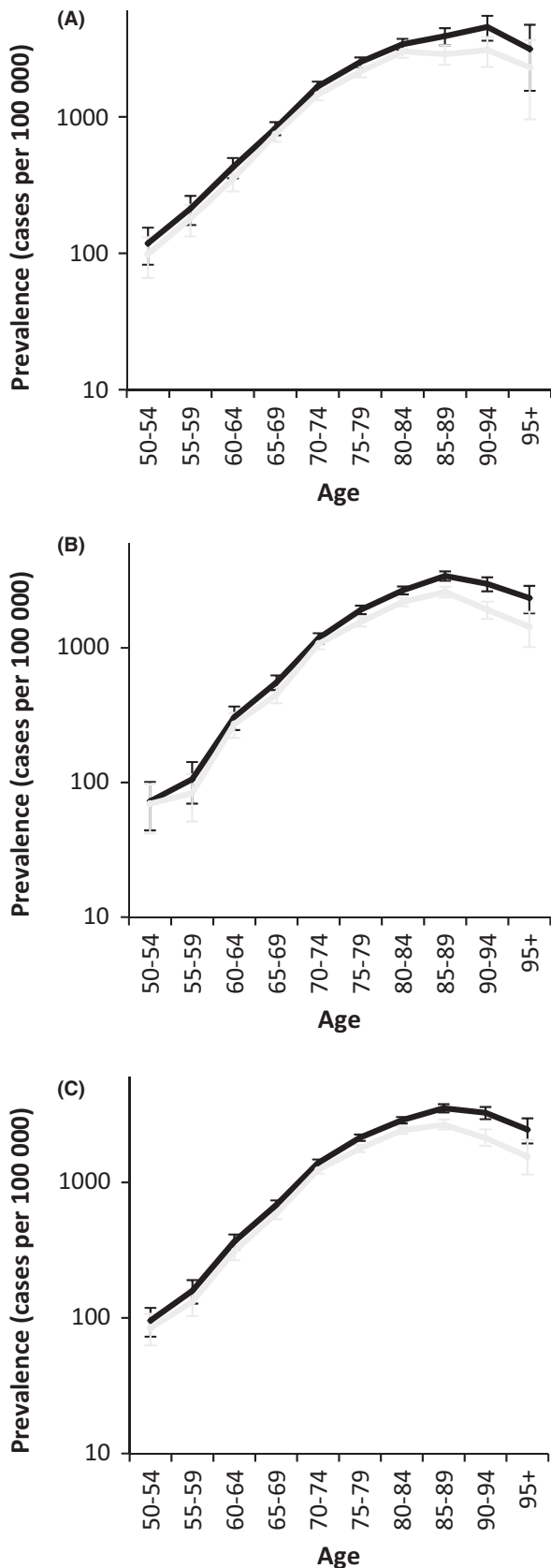


FIGURE 2 Age-specific prevalences according to the Sla (black) and Slb (gray) validation strategies for men (A), women (B), and both sexes (C) displayed in a logarithmic plot. 95% confidence intervals are shown as error bars. AOK claims data 2004, 2007

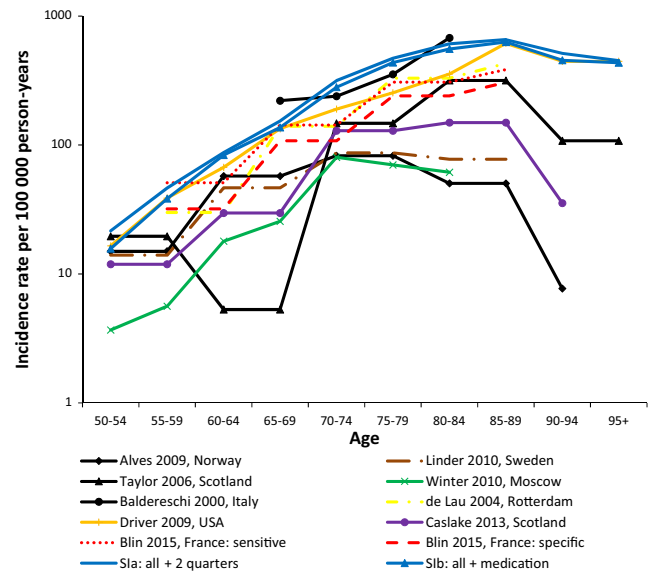


FIGURE 3 Age-specific incidence rates of Parkinson's disease by AOK claims and previous incidence studies; logarithmic scale. Source: AOK claims data 2004-2007, 2007-2010

of patients with PD in Germany aged 50 and older lies between 245 912 and 296 248.

We explored different validation strategies to deal with the shortcomings of claims data, particularly false-positive diagnoses, such as atypical parkinsonism. Wermuth, Lassen²⁴ evaluated PD diagnoses from Danish medical records and found that 17.4% did not meet the definition of PD. However, our validation procedures cannot deal with false-negative diagnoses: The stricter the strategy (see strategy SlIc in Figure S1), the more patients we exclude from our analysis and consequently the lower the prevalence became, particularly for the oldest old. Our two final strategies result in comparatively similar age-specific prevalences and incidence rates; however, the gap increases with age. One may argue that at advanced ages patients with PD may be prescribed PD medication to a lesser extent than at younger ages, probably due to negative side effects or adverse interactions.²⁵

Age-specific prevalences and particularly incidence rates in this study were somewhat higher than those of the latest German study by Trenkwalder, Schwarz.⁸ The GSN assumes prevalences close to ours; however, it should be noted that they use data from a collaborative European study rather than German data.¹⁰ The age profile of nearly all studies consistently showed an increase in prevalences and incidence rates with age up to group 85-89 and a decline beyond this age. Compared to the other studies, our higher incidence rates may be explained by¹ the inclusion of the institutionalized population, which is missing in most other studies. In our study, 20% of all patients with PD were living in nursing homes, allowing us to analyze PD up to the highest ages;² the over-representation of less educated and chronically ill persons in the AOK.²² To quantify this overrepresentation of sick persons, we calculated death rates as an indicator of morbidity and compared them with death rates of the German population. As a result, age-specific death rates are higher

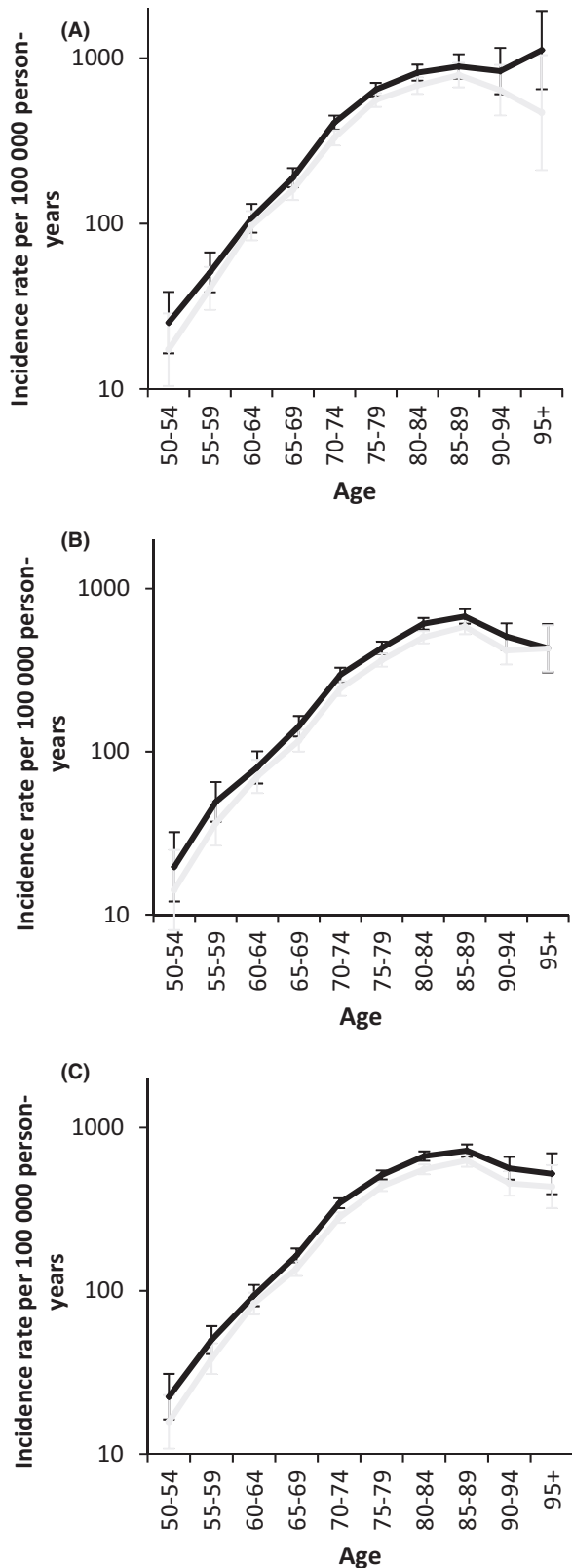


FIGURE 4 Age-specific incidence rates according to the Sla (black) and SlaB (gray) validation strategies for men (A), women (B), and both sexes (C) displayed in a logarithmic plot. 95% confidence intervals are shown as error bars. Source: AOK claims data 2004-2007, 2007-2010

but primarily for persons aged 50-64, and the differences are negligible at higher ages (Table S4). Thus, incidence rates of PD which start rising strongly at higher ages may only marginally be affected;³ the uncertainty of the diagnostic criteria of PD in claims data where more than half of all diagnoses were made by physicians who are not trained to detect PD.

Our incidence rates are higher than those of Blin, Dureau-Pourmin⁹ who also used claims data in France and different validation strategies based on ICD codes and drug prescriptions. In contrast to our approach, this French study required a PD diagnosis to be confirmed by two different physicians. Another definition of PD relies on at least three PD drug reimbursements over 1 year.

Age seems to be one of the main factors for the occurrence of PD. Some studies, including our investigation, found a decline in incidence rates for the oldest old,¹⁴⁻¹⁸ and others did not.¹¹⁻¹³ However, varying definitions and small sample sizes make comparisons difficult.¹ The highest age group in our study contains a substantial number of 3543 individuals with 55-87 prevalent cases at the base years and 42-46 incident cases during the follow-up, which makes analyses still reasonable.

The decline might be partly a consequence of diagnostic uncertainty. For instance, typical extrapyramidal signs of PD as tremors are often associated with Alzheimer's disease, leading to misdiagnoses.²⁵ In addition, affected people at older ages may never seek medical attention.²⁶ Finally, unobserved heterogeneity within a population leads to mortality selection and determines the proportion of PD and persons without PD in advanced ages in favor of the latter group.²⁷

We found sex differences in the occurrence of PD which are consistent with previous studies.^{11,12,15,28} Men may be at greater risk for PD because of their lifestyle, while female hormone estrogen may have neuroprotective effects.²⁹

This study has several limitations. AOK data display only a part of the German population resulting in a lack of representativeness. To give a more representative picture of PD in Germany, data from other insurances would be needed. Currently, 118 public health insurances cover about 70 million persons, whereby the AOK represents the largest part (25 million insured persons). The access to health claims data is very restricted because of the fact that the data are a sensible data source and have ethical restrictions imposed due to concerns regarding privacy. Furthermore, the comparison of death rates from the AOK and the German population indicates marginal differences (Table S4). Another limitation is that self-medication or treatments not covered by the AOK are not included. Routine claims data in general are primarily compiled for billing purposes in the healthcare sector and not for epidemiological analyses, meaning that coding errors are possible. We took this issue into account by performing internal validation procedures. Despite these procedures, wrong diagnoses may stem from the fact that some patients were diagnosed by general practitioners and not only by specialists. An external validation of diagnoses is not possible. Furthermore, financial incentives may lead to false diagnoses, resulting in excessive numbers in routine claims data.³⁰ Despite these incentives, intended false-negative diagnoses by physicians

are not very likely in the case of PD because these diagnoses would lead to far reaching consequences in terms of medical treatment, physiotherapy, speech therapy, etc.²⁰

One advantage of using AOK data is the large size of the study population on a national basis; a second is the inclusion of the institutionalized population. In our study, 20% of all patients with PD were living in nursing homes, allowing us to analyze PD up through the highest ages. Finally, because the routine documentation of diagnoses is provided by physicians, self-selection, non-response, or interviewer bias can be ruled out.³⁰

5 | 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 the 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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CONFLICT OF INTEREST

Mrs. Fink and Mr. Nerius have nothing to disclose. Dr. Doblhammer received honoraria for presentations at meetings of Novartis and Eli Lilly.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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