Prevalence and Cost of Care for Parkinson’s Disease in Luxembourg: An Analysis of National Healthcare Insurance Data

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Abstract

Background Parkinson’s disease (PD) is the second most common neurodegenerative disorder, with an increasing prevalence worldwide. Estimates of the economic burden associated with PD vary widely across existing studies due to differences in setting and study design. The prevalence and cost of care for PD in Luxembourg are currently unknown.

Objective The aims of this study were to estimate (1) the prevalence of PD in Luxembourg and (2) the cost of care for PD to the national healthcare insurance based on routinely collected healthcare data.

Methods This analysis was based on individual patient-level data collected by the national healthcare insurance in Luxembourg during 2007–2017, which covers over 95% of the resident population. People with PD were identified based on drug reimbursement profiles. Cost of care was estimated according to a comparative analysis of the healthcare resources consumed by people with PD compared with an age- and sex-matched control group.

Results We determined a PD prevalence of 928 per 100,000 individuals aged 50 years and older in 2016, higher in men (1032 per 100,000) than in women (831 per 100,000). The total mean cost of care for PD was estimated at €22,673 per patient per year in 2016, with the highest costs being associated with long-term care (69%).

Conclusion This was the first attempt to estimate the prevalence and cost of care of PD in Luxembourg. The work demonstrated the usefulness of routinely collected data in Luxembourg for such analyses. Our study confirms the significant burden of PD to the healthcare system, especially on long-term care.

Key Points for Decision Makers

The prevalence of Parkinson’s disease (PD) in Luxembourg was estimated at 1032 per 100,000 men and 831 per 100,000 women aged 50 years and older.

PD poses a significant burden to the healthcare system in Luxembourg, with the highest costs being associated with long-term care.

1 Introduction

Parkinson’s disease (PD) is the second most common neurodegenerative disorder, affecting around 0.3% of the entire population in Western countries. Prevalence increases with age, reaching 1% of the population aged 60 years and older [1], but factors beyond age need to be considered as the cause for the expected doubling of prevalence within the next 20 years [2]. PD is a progressive syndrome characterised by a combination of motor and non-motor symptoms of variable degree. Key motor symptoms include bradykinesia, rigidity and rest tremor [3]. Other common motor symptoms include flexed posture, freezing of gait, dystonia and falls; however, the clinical manifestation and progression rate of PD remains highly variable. Additionally, PD patients are affected by a number of non-motor symptoms ranging from sleep disturbance, dysphagia, constipation, apathy, depression and autonomic dysfunction with large impact on disease-related complications and quality of life. The impact of the disease depends highly on disease severity [4]. The
causes and risk factors for PD are not yet fully understood. Current research focuses mainly on stratification strategies and disease subtypes discovery, improving early diagnosis through identification of diagnostic biomarkers, and translational research with the goal of implementing personalised medicine [5].

Apart from the disease impact on patients and families, PD presents a significant economic burden to the healthcare system, society, and patients. The burden increases as the disease progresses and the effect is further intensified with an aging population. Several studies have investigated the economic burden of PD with diverse results [6–14]. A systematic review providing a comprehensive overview of cost studies highlights the heterogeneity in estimates and methods to derive costs associated with PD [15], with cost estimates per patient varying from under 1000 US$/year in developing countries [16, 17] to over 100,000 US$/year in a privately insured population in the US [18].

Most cost-of-illness studies take one of two approaches: some authors directly estimate the economic burden of PD based on resource use questionnaires on a sample of patients with PD, while other studies have used large administrative databases to estimate the burden of PD. The latter studies are usually based on much larger samples and costs are estimated by comparing the resources used by a sample of patients with PD and a matched control group [19].

Since 2015, the national funding agency in Luxembourg (Fond National de la recherché [FNR]) has supported the National Centre for Excellence in Research in PD (NCER-PD; http://www.parkinson.lu). The joint effort from several national research institutions together with international partners focuses on improving (earlier) diagnosis, treatment and stratification of PD by combining detailed clinical and molecular patient data to develop novel biomarkers for stratification of patients. A national cohort of individuals with PD and other forms of parkinsonism and a healthy control group form a key aspect of the centre [5]. There is no estimate of the prevalence or cost of care for PD in Luxembourg to date. Therefore, within the framework of the NCER-PD research programme, this study aims to estimate (1) the prevalence of PD in Luxembourg, and (2) the associated cost of care to the national healthcare payer.

Establishing estimates of prevalence and baseline costs of illness in the country are important steps towards assessing the impact of future changes to care. Luxembourg has a comprehensive national health insurance (Caisse Nationale de Santé [CNS]) covering over 95% of the resident population and also recording information on the long-term care insurance (l’Assurance Dépendance). We used routinely collected data by the CNS to estimate the cost of care associated with PD to the national healthcare payer. This is the first study analysing CNS data for the purpose of estimating the prevalence and economic burden of PD.

2 Methods

2.1 Data Source

This analysis was based on data routinely collected by the CNS. The CNS covers over 95% of the resident population in Luxembourg and collects information on inpatient, outpatient, general practitioner and specialist care, as well as dispensed medication and home and nursing home care. For healthcare visits, the database records details on the healthcare provider, the date and the associated costs of the visit. Details on medication include date of prescription, prescriber information, date of dispensed medication, package size and dose per unit as well as cost details. Outpatient visits and prescriptions do not include diagnoses. Diagnoses are recorded for hospital stays, however there are a lot of missing data in this regard.

We had access to individual patient-level data collected during the years 2007 to 2017. Insured individuals have up to 2 years to claim reimbursements, resulting in a 2-year time lag for a year to provide complete data. At the time of data extraction (September 2019), the most recent year providing complete data was 2017.

2.2 Data Analysis

2.2.1 Prevalence

Since the CNS database does not record information on diagnosis, we identified subjects with PD indirectly based on their individual drug reimbursement profiles. Regression algorithms for this purpose have been developed elsewhere [20]. However, differences in population and care habits across countries impair the direct translation of such models across countries, where no information on diagnosis is available to adapt to national needs. Therefore, we developed a national algorithm based on the definition of drug treatment profiles indicating diseases other than PD among patients prescribed anti-parkinsonian drugs, as has been done elsewhere [21].

We defined the at-risk population in any year as individuals in the CNS database, aged 50 years or older, alive and a resident of Luxembourg with active CNS cover on 1 January. Furthermore, individuals with insufficient data to detect drug-induced parkinsonism (DIP) were excluded from the analysis. Sufficient data were defined as a minimum of 300
days as a resident with CNS cover during the 12 months prior to the index date.

We restricted our analysis to individuals aged 50 years and older in order to reduce the risk of including false positive subjects in a younger population, where the prevalence of PD is generally low [22]. Luxembourg has a large proportion of cross-border workers, i.e. individuals employed in Luxembourg, but resident in neighbouring countries, mostly Belgium, France and Germany. Cross-border workers are also covered under the national healthcare system. However, we restricted our analysis to individuals resident in Luxembourg for two reasons: (1) for the estimation of national prevalence, only the resident population is relevant; and (2) cross-border workers have access to healthcare in Luxembourg, however may also avail of healthcare in their country of residence. Detailed information on healthcare use is only available for care provided in Luxembourg, resulting in unreliable resource use information for cross-border workers within the database.

Figure 1 provides a flowchart representing the algorithm applied to identify individuals with PD among the at-risk population.

We considered all drugs with an Anatomical Therapeutic Chemical (ATC) code starting with N04B (all drugs classified as dopaminergic agents) to identify subjects potentially suffering from PD. Based on the discussion of a panel of national neurologists, individuals prescribed anticholinergic agents only, with no co-prescription of a dopaminergic agent, were not considered for the PD group, as this treatment pattern points towards individuals with tremor rather than PD disease. A starting cohort of candidates was identified within the CNS database as those subjects who have received at least one delivery of an N04B medication during the years 2008–2016 while aged 50+ years on 1 January in the year of delivery. We called the date of an individual’s first delivery of an N04B drug the ‘index date’. In a stepwise fashion, we excluded subjects with a profile indicating a disease other than PD explaining the use of N04B medication. These steps aimed at excluding individuals with DIP, restless leg syndrome (RLS) or hyperprolactinaemia (HYP) [see the Info box in Fig. 1].

We deemed individuals to suffer from DIP rather than PD if they had received medication known to induce parkinsonian symptoms during the 12 months prior to their index date. These included neuroleptics (except quetiapine and clozapine, which are agreed among movement disorder specialists for the treatment of hallucinations in patients with PD), metoclopramide, cinnarizine and flunarizine.

Furthermore, we deemed individuals to suffer from RLS rather than PD if they had received low doses of ropinirole, pramipexole, rotigotine or levodopa and no other N04B medication during the 12 months following the index date. We estimated an average daily dose based on the number of deliveries, the dose per delivery and assuming a coverage of 3 months per delivery, as was deemed most probable during discussions with a national expert panel. An estimated daily dose of < 4 mg/day for ropinirole, < 0.5 mg/day for pramipexole, < 3 mg/day for rotigotine and < 200 mg/day for levodopa were used as cut-offs to point towards RLS rather than PD.

Finally, we deemed individuals treated exclusively with bromocriptine or lisuride to suffer from HYP rather than PD.

We excluded individuals not receiving a second delivery of N04B medication during the 12 months following the index date, to avoid including individuals due to administrative or diagnostic errors.

Subjects identified as individuals suspected of having PD were included in the prevalence estimation; we estimated the annual prevalence from 2008 to 2016. Data from 2007 were used to evaluate DIP in subjects identified in 2008, while data from 2017 were used to evaluate RLS and HYP for individuals identified in 2016.

Individuals were considered prevalent in each year including and following the index date if (1) they were resident in Luxembourg with active CNS cover on 1 January, and (2) alive on 1 January of that year. Annual prevalence is defined as the ratio of the number of individuals suspected of having PD and the number of individuals at risk.

2.2.2 Cost Analysis

We estimated the cost of care for PD to the national healthcare payer as the difference in the cost of resource consumption among individuals with PD and an age- and sex-matched control group.

We selected a control group twice the size of the prevalent population using an exact matching approach, separately for each year. Age- and sex-matched controls were selected at random from the at-risk population, excluding candidate individuals, i.e. individuals who had been prescribed a dopaminergic agent between 2008 and 2016.

All costs were inflated to 2020 prices. We inflated costs using the national consumer price index for health published by the Institut National de la Statistique et des Études Économiques du Grand-Duché (https://statistiques.public.lu/en/index.html), and applied the methodology recommended by the Health Information and Quality Authority in Ireland (https://www.hiqa.ie/sites/default/files/2020-09/HTA-Economic-Guidelines-2020.pdf).

We calculated the cost per patient for the years 2008–2016, and present total costs as well as costs divided into eight categories.

(1) Long-term care: Costs related to resources associated with long-term care provision and palliative care
(including institutionalised care and day care as well as care at home and technical aids and changes to the home, depending on the level of care required by the patient).

(2) Hospital: Costs related to resources associated with hospital stays, including all resources except for clinician costs.

(3) Medication and medical devices: Medication costs and costs related to medical devices (only including prescribed items).

(4) Clinicians: Covering the costs of inpatient and outpatient services provided by clinicians.

(5) Specialist services: Cost of outpatient services provided by specialists, including opticians, orthopaedists, speech therapists, dieticians, masseurs and physiotherapists, psychometricians, podiatrists and midwives.

(6) Nurses: Costs related to the outpatient services provided by nurses.

(7) Laboratory tests: Costs of medical analyses and clinical biology tests conducted in laboratories (outside of the hospital).

(8) Other: Cost of rehabilitation stays and other various items.

The cost of individual items within each category are published in the nomenclatures on the CNS website (https://cns.public.lu/en/legislations.html?r=f%2Faem_legislation_type%2Ftags_type_legislation%3Anomenclature).

Despite the typical skewness of cost data, the mean provides the most informative measure for policy decision making as it allows for budget calculations; on the other hand, the median cost can be used to describe the typical cost of an individual [23]. We followed the recommendation by Thomson and Barber and summarised cost data as means, and differences between groups as mean differences, as well as confidence intervals and p-values obtained from a standard t-test [23]. While this approach is not without limitations, considerable differences are unlikely due to the large sample size. Nevertheless, we present median values in addition to mean values to show the cost of a typical patient. Since we tested for differences between groups in eight categories as well as overall, we adjusted for multiple testing using a Bonferroni adjustment of the p-value: 0.05/9 = 0.005.

The cost of care for PD highly depends on the severity of the disease, increasing with the level of dependency. In the absence of information on disease severity, we used years since the first prescription of an anti-PD drug as a surrogate measure. We evaluated the annual mean total cost for patients prevalent in 2016, grouped by years since...
the first prescription of an anti-PD drug (0–4, 5–9, 10–14 and 15+ years).

3 Results

3.1 Prevalence

Within the database, we identified 9158 individuals who received a dopaminergic agent and who were aged 50 years or older while residing in Luxembourg, with CNS cover during the years 2008–2016. In order to appropriately assess DIP, we excluded 104 individuals with insufficient data during the 12 months prior to their index date. From the remaining individuals, we excluded 1989 individuals suspected of having DIP, due to the delivery of a drug known to induce parkinsonism during the 12 months prior to their index date. We further excluded 3826 individuals receiving low doses of drugs used for RLS and no additional dopaminergic agents. One individual was excluded due to HYP. Finally, we excluded 544 individuals who did not receive a second delivery of any dopaminergic agent within 12 months of their first delivery. Based on this algorithm, we thereby identified a total of 2694 individuals with PD, for the years 2008–2016. A flowchart of the exclusion process is presented in Fig. 1.

The number of prevalent individuals increased from 1248 in 2008 to 1632 in 2016. The mean age of the prevalent population remained steady between 76 and 77 years, and the proportion of males ranged between 49% and 54% over the years (see Table 1).

The number of individuals at risk (i.e., resident individuals with active CNS cover, alive and aged 50+ years on 1 January) increased from 140,630 individuals in 2008 to 175,898 individuals in 2016, an increase in line with population growth as reported by the National Institute for Statistics (Institut National de la Statistique et des Études Économiques du Grand-Duché de Luxembourg, https://statistiques.public.lu). There were more females in the population at-risk, representing between 52% and 53% every year (see Fig. 2).

Taking into account the population at risk of PD, we estimated an annual prevalence of 887–981 per 100,000 individuals aged 50 years and older in Luxembourg. Prevalence was higher for males than for females, ranging from 937 to 1054 per 100,000 for males and from 831 to 916 per 100,000 for females (see Fig. 2 for the annual prevalence).

3.2 Cost

We received details on 12,866,632 resource items consumed by individuals in the PD or control groups for the years 2008 to 2016. Individuals in the PD groups accounted for 50% of the claims, despite the fact that control individuals cover twice as many person years.

The mean annual cost per patient to the CNS in the control group varied from €14,683 to €16,018, while median annual costs were much lower, varying from €3430 to €4161. The mean annual cost per patient in the PD group varied from €35,858 to €40,842, with a median from €17,635 to €21,932. We observed no trend over time. This resulted in a mean difference between groups varying from €20,331 (2011) to €25,076 (2010), representing the additional annual cost per patient to the healthcare payer in the PD group. T-tests indicate a significant difference between groups in all years. Details are shown in Table 2.

We observed an increased mean cost in the PD group for all eight categories across all years. A statistically significant difference between groups based on the adjusted p-value was observed almost throughout, with the only exception being a difference in category 8 (‘Other’) in 2008. Details can be found in the electronic supplementary material.

Looking at the total cost of PD in 2016, more than two-thirds were accounted for by long-term care costs (69%). Hospital expenses accounted for 13% of the additional costs, while all other categories accounted for 5% or less

Table 1 Cohort description of individuals with Parkinson’s disease and the control group

| Year | PD N | Male (%) | Mean age, years | CG N | Male (%) | Mean age, years |
|------|------|----------|----------------|------|----------|----------------|
| 2008 | 1248 | 49       | 76.6           | 2496 | 49       | 76.6           |
| 2009 | 1369 | 50       | 76.7           | 2738 | 50       | 76.7           |
| 2010 | 1431 | 51       | 76.8           | 2862 | 51       | 76.8           |
| 2011 | 1492 | 51       | 76.8           | 2984 | 51       | 76.8           |
| 2012 | 1503 | 51       | 76.6           | 3006 | 51       | 76.6           |
| 2013 | 1564 | 52       | 76.5           | 3128 | 52       | 76.5           |
| 2014 | 1596 | 52       | 76.4           | 3192 | 52       | 76.4           |
| 2015 | 1620 | 53       | 76.6           | 3240 | 53       | 76.6           |
| 2016 | 1632 | 54       | 76.7           | 3264 | 54       | 76.7           |

PD Parkinson’s disease, CG control group, N number of individuals

△ Adis
of the additional costs (see Fig. 3a). The proportion of
costs in the different categories remained stable over the
years (data not shown).

We analysed costs accrued by individuals prevalent in
2016 by years since the first prescription of an anti-PD
drug. Figure 3b shows the total cost in each group. We
observed an increase in total mean costs with an increas-
ing number of years since the first prescription. Indeed,
the mean cost per individual rose from €33.7K in indi-
viduals with 0–4 years since the first prescription to
€53.2K in individuals with 15 years or more since the first

4 Discussion

Based on the available data from the CNS database, our
study estimated the prevalence of PD in Luxembourg as well
as the cost of care to the national healthcare payer for the
years 2008–2016. Our study estimates a prevalence of, on
average, 949 per 100,000 residents aged 50 years and older,
i.e. 0.95%. This rate remained relatively stable over the
evaluated years. In line with previous studies, we observed a higher prevalence in males (1029 per 100,000 in males vs. 877 per 100,000 in females). We estimated an additional mean cost of €22,346 per person per year for the care of patients with PD, with the majority of expenses spent on long-term care.

To our knowledge, this is the first study to use the database for this purpose and the first attempt to estimate national prevalence and cost of care for PD in Luxembourg.

The prevalence estimates in our study lie within the reported rates from the literature. A systematic review by Pringsheim et al. [24] found prevalence estimates in Europe, North America and Australia varied with age, increasing from 113 per 100,000 in 50- to 59-year-olds to 2953 per 100,000 in individuals aged 80+ years. Considering the age distribution in Luxembourg, this equates to around 840 cases per 100,000 individuals aged 50+ years. They also found a higher prevalence in males compared with females. The authors explained these findings by the fact that PD onset is slightly later in women and more commonly presents with a slower progression in females compared with males. Another systematic review by von Campenhausen et al. [25] summarised evidence on the prevalence of PD in Europe. The authors found highly variable results, with high-quality studies in older age groups (> 60 years) presenting rates of 1280–1500 per 100,000. A recent study by Marras et al. [26] estimated a prevalence of 572 per 100,000 inhabitants in the US in a population aged 45 years and older.

Long-term care is the largest cost category in our analysis, which, depending on the level of disability, covers costly items such as daycare, home improvements and technical aids, as well as institutionalised or home care. Luxembourg has comprehensive long-term care coverage and it is not surprising to find a large expense for patients with PD, whose reliance on daily care increases as the disease becomes more severe.

Luxembourg has the highest per capita spending in health care in the European Union [34]. This aligns with our results, which are in line but are on the higher side compared with other studies. Several studies have estimated the cost of care for PD in Europe. Two of these studies, conducted in Sweden and Denmark, estimated a cost of care for PD of €9.3K and €7.7K, respectively, in 2011–2012; however, these studies did not include the cost of long-term care [27, 28]. Similar estimates to our work were obtained in cohort studies estimating direct and indirect costs conducted in Italy (€17.3K) and Germany (€18K–€35K, depending on severity) in 2010 [29–31]. Lower costs were estimated in the UK (€15K including informal care in 2007) and Spain (€13.7K) [32, 33] (which did not include the cost of long-term care as covered by the d’assurance dependance in Luxembourg). However,
another UK study published in 2018 estimated the costs of PD to be higher (£29k [€35k]) [41].

While previous publications forecast a significant increase in the burden of PD with time [2], our study did not confirm this.

The cost estimates are subject to a large standard deviation, among PD patients as well as in the control group. This was expected as individual patient needs are highly variable, partly due to their PD severity, but also due to their individual health profiles, which may include any number of diseases or chronic conditions. Nevertheless, we found significant differences in spending between the groups across all categories. Our analysis showed a much larger mean cost compared with median cost, in both groups, which is typical for cost data. The median cost represents the resources needed for a typical patient, while the mean cost is skewed by a number of individuals requiring a large amount of resources.

5 Limitations

In the absence of diagnosis information within the database, patients were identified based on individual treatment profiles. The classification algorithm was developed based on previous studies and the input of national and international experts in PD care, epidemiology and statistics; however, we were unable to check its accuracy and misclassification of subjects remained possible. Furthermore, the approach only detected cases who received treatment. Very mild or early cases not requiring any treatment, or those refusing treatment, could not be detected, leading to a possible underestimation of total cases. On the other hand, our algorithm is unlikely to distinguish between PD and other types of neurodegenerative parkinsonism, which may have led to an overestimation in cases. However, given the low prevalence of atypical parkinsonism compared with PD, this is unlikely to have a large impact on the cost analysis [35–37].

The at-risk population within the CNS database covers over 95% of the resident population aged 50 years and older. Individuals not included in the study are most likely individuals working for EU institutions or cross-border workers resident in Luxembourg but working abroad. We restricted our analysis to individuals aged 50 years and older—younger individuals are not captured. For these reasons, the real total number of prevalent cases in Luxembourg may be slightly higher. Nevertheless, we consider the large coverage in the database to provide a representative sample of the total PD population in terms of age, sex and severity of disease.

This comparative cost comparison assumes a similarity of both groups, except for their PD status. Both groups may suffer from a variety of additional comorbidities. In essence, we estimate the cost of people living with PD and other comorbidities, compared with people without PD but with other comorbidities. Comorbidities have been shown to be highly prevalent not only in individuals with PD [38] but also in the general population aged 65 years and older [39].

The total costs to the payer were somewhat underestimated by the fact that we restricted our analysis to residents. This was necessary to determine appropriate costs per patient, since details on costs accrued by non-residents are likely to be incomplete. Patients living abroad can make use of the local healthcare system with a contract in place for Luxembourg to cover the incurred costs. Individuals included in either the control group or the PD group in a given year had to be resident and alive with valid insurance cover on 1 January. Our analysis did not adjust for status changes during the year, which may lead to an underestimation of annual costs for individuals changing their residence or insurance cover status or those who die during the year; however, this only applies to a small number of individuals in both groups.

The costs of the most relevant categories in this study, i.e. long-term care and hospital care, are fully covered with no cost to the patient, while there is a co-payment for outpatient visits and medication of up to 20% (up to 40% for some medications, but not including any anti-PD medication), which is not captured in this study. Our study only takes into account direct costs; indirect costs and the cost of over-the-counter medications are not considered. Nevertheless, the indirect costs of PD care are likely significant, especially as the disease advances. The indirect impact on costs and quality of life on patients and their caregivers was recently evaluated elsewhere [40]. An additional study exploring the indirect burden of PD in Luxembourg, including informal care, would be of interest but is not within the scope of this analysis.

Furthermore, the per-patient cost of PD is highly dependent on the severity of disease and we had no information on severity. In order to explain some of the variation, we performed a subgroup analysis, grouping individuals depending on the time since their first prescription of anti-PD medication. The analysis confirmed the increased cost with increasing time since the first prescription; however, a more detailed analysis based on accurate staging, including both motor and non-motor symptoms, is needed to provide more accurate insights.

6 Conclusion

To our knowledge, this is the first successful attempt to estimate the prevalence of PD and the associated cost of care in Luxembourg. We estimated the prevalence of PD in Luxembourg to be between 887 and 981 per 100,000 individuals aged 50+ years, and was higher for males compared
with females. This is in line with other estimates in developed countries. In 2016, PD patients accrued, on average, €22,863 more compared with those without PD; the cost of care increased with increasing time since the first prescription of an anti-PD drug. Expenditure on long-term care accounted for more than two-thirds of these expenses. Our results confirm the high economic burden of PD, especially as individuals become more reliant on daily care as the disease progresses.

We are convinced that this baseline analysis of costs is useful to direct and assess the impact of future changes in the care of PD in Luxembourg.

Our study has shown that data routinely collected by the CNS in Luxembourg can be used as a basis to conduct comparative cost-of-illness studies such as the one at hand. In the future, the database could be used to estimate the cost of care for other diseases, allowing for the comparison of PD costs with other non-neurological or neurological, equivalently debilitating medical illnesses.

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Declarations

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Conflicts of interest Susanne Schmitz received funding from the NCER-PD to conduct the work presented in this article. Christel Renoux is a recipient of a Chercheur-Boursier Salary Award from the Fonds de recherche du Québec – Santé. Rejko Krüger serves as an Editorial Board Member of the European Journal of Clinical Investigation, the Journal of Parkinsonism and Related Disorders, and the Journal of Neural Transmission, and has received research grants from Fonds National de Recherche de Luxembourg (FNR) as Coordinator of the NCER-PD and Coordinator of the Study on COVID-19 National survey for assessing Viral spread by Non-affected Carrières (CON-VINCE), as well as speaker’s honoraria and/or travel grants from Abbvie, Zambon and Medtronic. He also participated as Principal Investigator (PI) or site PI for industry-sponsored clinical trials without receiving honoraria. Robert L. Konsbruck, Pierre Hertz, Magali Perquin, Lukas Pavelka, Michel Vaillant, and Laetitia Huiart have no conflicts of interest to declare.

Availability of data and material The data the analysis is based on is not publicly available.

Code availability The code to conduct the analysis is specific to the data format provided and is not published with the manuscript.

Author contributions SS led the conception, organisation and execution of the research project, designed and executed the statistical analysis and wrote the first draft of the manuscript. MV guided the conception of the project and the design of the statistical analysis, and also reviewed and critiqued the draft document. CR provided guidance on the design and execution of the analysis. RLK provided guidance on the data and was involved in the execution of the data analysis. PH guided the design of the project and reviewed and critiqued the manuscript. MP and LP provided valuable input at the conception stage of the project and reviewed and critiqued the manuscript. RK guided the conception and organisation of the project, and reviewed and critiqued the manuscript. LH guided the conception and organisation of the project and provided guidance on the design and execution of the analysis.

Ethical approval This study received ethical approval from the CNER (Comité National d’Ethique de Recherche, Luxembourg).

Consent to participate Not applicable.

Consent for publication Not applicable.

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