

# Costs of illness and care in Parkinson's Disease: An evaluation in six countries

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## Abstract

We investigated the costs of Parkinson's Disease (PD) in 486 patients based on a survey conducted in six countries. Economic data were collected over a 6-month period and presented from the societal perspective. The total mean costs per patient ranged from EUR 2620 to EUR 9820. Direct costs totalled about 60% to 70% and indirect costs about 30% to 40% of total costs. The proportions of costs components of PD vary notably; variations were due to differences in country-specific health system characteristics, macro economic conditions, as well as frequencies of resource use

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and price differences. However, inpatient care, long-term care and medication were identified as the major expenditures in the investigated countries.

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## 1. Introduction

Parkinson's Disease (PD) is among the most common neurodegenerative diseases. PD is characterized by bradykinesia, tremor, rigidity and postural instability. Comorbidities such as mental disorders, autonomic dysfunction, difficulties in swallowing and speech as well as sleep impairment may occur during the course of the disease. PD primarily affects the elderly and thus due to population aging has become a rapidly growing area of concern. In Europe, the prevalence of PD is approximately 160 per 100,000 among those aged 65 and older and this number will considerably increase in the coming years (Dorsey et al., 2007; von Campenhausen et al., 2005).

Care for PD patients consumes a considerable amount of health care resources, as current data on costs of PD indicate (Findley et al., 2003; Hagell et al., 2002; Schrag et al., 2000; Spottke et al., 2005). Only limited data on PD costs are available. In Eastern Europe, Austria and Portugal, data on the economic burden of PD are lacking (Lindgren et al., 2005).

The aim of this study was to evaluate the direct and indirect costs of PD using the same methodological approach in order to increase the comparability of the results from different countries. No such comparative studies exist for PD in Europe.

## 2. Experimental procedures

### 2.1. Study design and patient recruitment

This health-economic study was one project undertaken by the "EuroPa network on Parkinson's Disease" and was funded by the Fifth European Framework program ([www.EuroParkinson.net](http://www.EuroParkinson.net)). As such, participants were recruited from the EuroPa registry, founded by the EuroPa study group as a patient pool for clinical trials and research on PD. The EuroPa registry consisted of 1821 patients with PD, randomized between June 1, 2003 and December 31, 2005 from study sites in ten European countries. Five member countries took part in the health-economic substudy: Austria, Czech Republic, Germany, Portugal and Italy (von Campenhausen et al., 2009; Winter et al., 2010a; Reese et al., 2010). Russia, although not a member of the EuroPa study group, participated as well (Winter et al., 2009). A total of 600 consecutive PD patients were recruited. The study was approved by the local ethics committees. All patients gave written informed consent.

### 2.2. Data collection and management

The questionnaire assessed socioeconomic background information on age, gender, marital status, living situation, educational level, employment status and quality of life (QoL) (e.g. Appendix, Supplemental Fig. 1).

Clinical data were collected at baseline: all study participants underwent a complete medical and neurological examination that was performed by a movement disorder specialist. PD diagnosis was based on the UK PD Society Brain Bank clinical diagnostic criteria for

PD (Gibb and Lees, 1989). The clinical examination was performed in the clinical 'on' state. Clinical data were documented by the investigator and included time of symptom onset, date of first diagnosis, disease stage according to Hoehn and Yahr (H&Y) (Hoehn, 1967) and the Unified Parkinson's Disease Rating Scale (UPDRS II-IV) (Fahn and Elton, 1987) as well as complications of the disease (e.g. motor complications, dementia, depression).

Health-economic data were collected using a standardized questionnaire that was filled out by the patients at baseline with a 3 months recall period for resource use. Patients were asked to indicate their expenses, a sample of the questionnaire is presented as Supplemental Fig. 1. A follow-up questionnaire was completed 3 months after baseline by the patients. Thus, data for a 6-month period were obtained.

The questionnaire developed for the study was translated into the appropriate languages by native speakers. The questionnaire was adapted by local health economists after taking into account the country-specific regulations and organisation of the respective health care system.

### 2.3. Resource use and costs

The questionnaires provided information on resource consumption, costs and care related to PD. Costs were calculated per patient as the mean costs over the 6-month observation period.

The resource unit costs were obtained from several publicly available sources by health economists in each country. The data were recorded in local currency and converted into Euros (EUR) using purchasing power parity (PPP) (OECD, 2008), and adapted to 2008 Euros using the Medical Care Component of the Consumer Price Index (Czech Statistical Office, 2008; Istituto nazionale di statistica, 2009; Ministério do Trabalho e da Solidariedade Social (INE), 2005; Russian State Committee for Statistics, 2007; Statistik Austria, 2009; Statistisches Bundesamt Deutschland, 2008). The societal perspective, which is the most comprehensive perspective, was chosen providing direct health care costs, non-medical costs, informal care and indirect costs. Country-specific regulations were considered and are mentioned separately below. References for unit costs are presented in Table 1 ordered by country and cost category.

#### 2.3.1. Direct costs

**2.3.1.1. Inpatient care (hospital and rehabilitation).** Patients documented their inpatient stays. Cost calculations were generally based on admissions using diagnosis-related groups (DRG). When this was not possible like in the Czech Republic, per diem costs were obtained from official tariff lists or from the hospital or rehabilitation center to which the patient was admitted. Costs of rehabilitation centres were based on costs per day (Appendix, Supplemental Table 1).

**2.3.1.2. Outpatient care.** Outpatient cost was based on cost per visit. Unit costs for visits to the physician were taken from the local official tariff lists for outpatient care and based on costs per visit by speciality, multiplied by the number of visits. For ancillary treatment such as physiotherapy, the costs per session were calculated according to the official tariff lists. Costs not covered by third party payers were included in the patient costs (Appendix, Supplemental Table 1).

**Table 1** Selected unit costs adjusted to 2008 prices per country. References per country.

	Type of costs (per drug package/per visit)	Austria		Czech Republic		Germany		Italy		Portugal		Russia	
		€	Reference	€	Reference	€	Reference	€	Reference	€	Reference	€	Reference
Medication	Levodopa/ benserazide 250 mg	40	AMI- Arzneimittelin- formation (2005)	58	General Health Insurance Fund of the Czech Republic (GHIF CR) (2004)	80	Bundesverband der pharmazeutischen Industrie (2006)	18	L 'Informatore farmaceutico Medicinali (2004)	7	Infarmed (2008)	40	Ministry of Public Health and Social Development of Russian Federation (2005a)
	Dopamine- agonist (Pramipexole 0.7 mg)	240	AMI- Arzneimittelin- formation (2005)	292	General Health Insurance Fund of the Czech Republic (GHIF CR) (2004)	356	Bundesverband der pharmazeutischen Industrie (2006)	66	L 'Informatore farmaceutico Medicinali (2004)	168	Infarmed (2008)	72	Ministry of Public Health and Social Development of Russian Federation (2005a)
Inpatient care	Rehabilitation (daily charge)	253	Pensionsversich erungsanstalt Österreich (2006)	10	Charles University in Prague and General Hospital in Prague (2006)	172	Bundesministerium der Justiz (2003); Deutsche Rentenversicherung (2006)	496	Ministero della Salute (2006)	268	Portuguese Ministry of Health (2007)	410 (21 days)	Ministry of Public Health and Social Development of Russian Federation (2005b)
	Hospitalization	298	Bundesministerium für Gesundheit und Frauen (2005)	70	Charles University in Prague and General Hospital in Prague (2006)	441	Bundesministerium der Justiz (2003); Institut für das Entgeltssystem im Krankenhaus (InEK) (2006)	3773 (max 48 days)	Ministero della Salute (2003)	638	Portuguese Ministry of Health (2007)	410 (21 days)	Ministry of Public Health and Social Development of Russian Federation (2005b)

Outpatient care	General practitioner	12	Ärztammer für Tirol (2005)	7	The Czech Medical Chamber (2002)	18	Krauth et al. (2005)	19	Ministero della Salute (2004)	152	Portuguese Ministry of Health (2008)	5	Ministry of Public Health and Social Development of Russian Federation (2005b)
	Neurologist	14	Ärztammer für Tirol (2005)	12	The Czech Medical Chamber (2002)	28	Ehret et al. (2009)	19	Ministero della Salute (2004)	215	Portuguese Ministry of Health (2008)	6	Ministry of Public Health and Social Development of Russian Federation (2005b)
	Physiotherapy	6	Tiroler Gebietskrankenkasse (2006)	10	The Czech Medical Chamber (2002)	31	Verband der Angestelltenkrankenkassen und Arbeiter-Ersatzkassenverband (2006)	10	Ministero della Salute (2004)	8	Portuguese Ministry of Health (2007)	3	Ministry of Public Health and Social Development of Russian Federation (2005b)
	Speech therapy	6	Tiroler Gebietskrankenkasse (2006)	7	The Czech Medical Chamber (2002)	22	Verband der Angestelltenkrankenkassen und Arbeiter-Ersatzkassenverband (2006)	6	Ministero della Salute (2004)	9	Portuguese Ministry of Health (2007)	3	Ministry of Public Health and Social Development of Russian Federation (2005b)
Special home equipment	Wheelchair	370	Catalogue of company Danner (2006)	710	Catalogue of company Setrans (2004)	194	Catalogue of company Kaphingst (2005)	338	Catalogue of the company Crom Ortopedia (2009)	194	Catalogue of the medical goods company Bastos Viegas (2008)	210	Catalogue of company "SIMS-2" (2005), Catalogue of company Med-Magazin (2005)

**2.3.1.3. Antiparkinsonian drugs.** The package size, dosage, and dose per day were documented in the patients' questionnaire. Average costs per day were calculated using the average costs across package sizes and dosage (when dosage and package size were unknown). Costs for prescription medication were based on local official price lists (public prices) from each country. However, not all medication prescribed is covered by the health insurance system. Medication not listed on the official reimbursement list and over-the-counter drugs (OTC) were added to the patient expenditures (Appendix, Supplemental Table 1).

**2.3.1.4. Care.** We have distinguished between formal care and informal care.

*Formal care;* hourly costs for domestic help were calculated according to the official tariff lists for home care provided by professional services or according to the regulations on nursing allowance. Since a standardized methodology for calculation of costs of care does not exist, the respective third party payers in the various countries apply different rules. In this study, no distinction was made between health care insurance and long-term care insurance.

*Informal care;* is unpaid help provided by family members or other relations, and can be seen as either a direct or indirect cost. In this study, we decided to calculate informal care as a component of direct costs. In Austria, Germany and Portugal calculation was based on the nursing allowance ("Pflegegeld") provided in these countries. In the other countries, it was calculated using the net income after taxes and social contributions (lost of leisure time) (Appendix, Supplemental Table 1).

**2.1.3.5. Patient co-payments.** Patients documented their PD-related expenses during the study period. Co-payments for drugs, outpatient care, hospitalization, specialists' fees, house renovations and special equipment expenses were calculated as part of the burden of the patient (Appendix, Supplemental Fig. 1).

**2.1.3.6. Special equipment.** Costs per unit were taken from the official price lists for medical devices (Appendix, Supplemental Table 1). If products were not listed as medical equipment, market prices were used. Patients' records of expenses were used when no price was available (e.g. disease-related modifications in the patient's home). Depending on country-specific regulations, in some cases only part of the expenditure is covered by the health insurance system. In these instances, the remaining costs were then added to the patient's costs.

**2.1.3.7. Costs for transportation.** These costs were not taken into consideration as former studies have shown low costs in this field (Spottke et al., 2005).

## 2.3.2. Indirect costs

**2.3.2.1. Productivity loss (sick leave/early retirement).** Productivity losses were calculated using the human capital approach. The average national gross income was used and the official age of retirement in the different countries was taken into consideration. For the calculation of the loss of productivity due to early retirement, calendar days remaining in the study period prior to the age of official retirement were divided by 30.44 (mean calendar days per month) and multiplied by the mean gross monthly wage per country as provided by the National Institutes of Statistics (Czech Statistical Office, 2008; Istituto nazionale di statistica, 2009; Ministério do Trabalho e da Solidariedade Social (INE), 2005; Russian State Committee for Statistics, 2007; Statistik Austria, 2009; Statistisches Bundesamt Deutschland, 2008). Productivity loss caused by premature retirement was calculated only for persons below the official retirement age. In case of sick leave, the

respective number of days was divided by 30.44 (mean calendar days per month) and multiplied by the mean gross wage. Productivity loss by the patients and their caregivers was taken into consideration (Appendix, Supplemental Table 1).

## 2.4. Statistics

Primary data were entered into a Microsoft Access database (2003). For statistical analyses, SPSS Version 15.0 (SPSS Inc., Chicago, Illinois) and STATA10IC (StataCorp LP Inc., College Station, Texas) were used. Cost data were presented as arithmetic means with 95% confidence intervals, minimum and maximum values, or percentages as appropriate. As most cost variables are right-skewed, traditional statistical methods are inappropriate for analyzing differences in mean costs (Barber and Thompson, 2000; Efron and Tibshirani, 1993). Confidence limits 95% CI for the estimates were calculated using a nonparametric bootstrap algorithm that could accommodate potential skewness in the cost data. We used B=2000 bootstrap replications with 95% confidence intervals calculated by means of the bias corrected and accelerated method. Differences in mean costs between groups were tested using a bootstrap *t*-test.

## 3. Results

A total of 600 patients participated in the study. 114 patients were excluded because of incomplete clinical records or discontinued study participation. Finally, data from 486 patients were used in the analyses. The mean age of patients was  $65.6 \pm 9.6$  years. The mean age at onset of symptoms ranged from  $55.3 \pm 10.0$  years to  $62.6 \pm 7.3$  years and the mean duration of the disease at baseline was between  $5.7 \pm 5.0$  and  $10.1 \pm 7.0$  years. Patients in the advanced stages of the disease H&Y IV/V were under-represented in this study, especially in the Czech Republic and Italy, as only 3% and 4% of the study sample were in H&Y stages IV/V, respectively. Characteristics of the study population are presented in Table 2.

### 3.1. Resource use and costs

In our study, total costs from a societal perspective were lower in Eastern European countries (Russia: EUR 2620, Czech Republic EUR 5510) as compared to most Western European countries as expected (Austria EUR 9820, Germany EUR 8610, Italy EUR 8340). However, total costs in Portugal (EUR 3000) are similar to total costs in Russia (EUR 2620) (Appendix, Supplemental Table 2).

In all countries, total direct costs were higher than indirect costs by approximately 20-40%. Direct costs as a percentage of total costs were as follows: Germany and Italy 70%, Portugal 69%, Russia 67%, and 60% in Austria and Czech Republic (Fig. 1). Direct costs reimbursed by the national health insurance were lower in Eastern Europe (49% in the Czech Republic, 47% in Russia) as compared to a reimbursement rate of 59%-89% in Western European countries. Costs increased with disease severity in all countries, except Portugal where costs in the higher disease stages decreased. Total costs by disease severity (H&Y stage) are presented in Fig. 2.

### 3.2. Inpatient care/rehabilitation

The mean length of inpatient stay in hospitals ranged from 8 days in Austria to 19 days in Germany during the 6-month observation

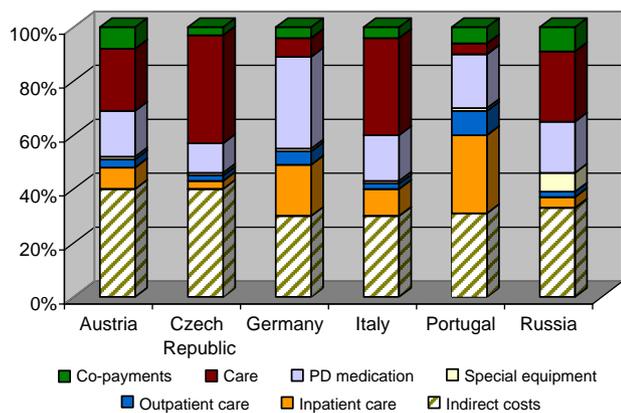
**Table 2** Sociodemographic and clinical characteristics of the study population in different countries.

	Austria	Czech Republic	Germany	Italy	Portugal	Russia
Sample size (n)	81	100	86	70	49	100
Gender						
Female	32 (40%)	40 (40%)	27 (31%)	29 (41%)	22 (45%)	62 (62%)
Male	49 (60%)	60 (60%)	59 (69%)	41 (59%)	27 (55%)	38 (38%)
Age distribution						
Mean age	69.3±9.8	63.6±9.4	63.1±9.9	65.0±8.5	68.4±11.8	68.9±7.0
≤60 years	13 (16%)	36 (36%)	30 (35%)	18 (26%)	9 (18%)	16 (16%)
61-70 years	26 (32%)	38 (38%)	37 (43%)	33 (47%)	14 (29%)	43 (43%)
>70 years	42 (52%)	26 (26%)	19 (22%)	19 (27%)	26 (53%)	41 (41%)
Marital status						
Married/living in relationship	59 (73%)	80 (80%)	69 (80%)	55 (79%)	35 (71%)	62 (62%)
Clinical data						
Mean age at first symptom onset	57.3±11.6	55.3±10.0	57.4±10.9	57.3±8.6	58.4±13.8	62.6±7.3
Disease duration (years)	10.1±7.0	7.9±6.3	5.7±5.0	7.8±5.5	9.5±6.4	6.7±5.1
H&Y I	7 (9%)	13 (13%)	32 (37%)	23 (33%)	2 (4%)	24 (24%)
H&Y II	38 (47%)	42 (42%)	38 (44%)	35 (50%)	29 (59%)	33 (33%)
H&Y III	23 (28%)	42 (42%)	11 (13%)	9 (13%)	14 (29%)	20 (20%)
H&Y IV	10 (12%)	2 (2%)	4 (5%)	3 (4%)	4 (8%)	19 (19%)
H&Y V	3 (4%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	4 (4%)

period (mean of the entire group was 14 days). The admission rate ranged from 6% to 21% of patients, with highest rates found in Austria. Costs for inpatient days (hospitalization and rehabilitation) ranged from EUR 100 (95% CI: 50-150) to EUR 1600 (95% CI: 890-3020) in our study. Across countries, the highest costs were found in Germany. In Portugal, inpatient costs represented a major cost component of the direct costs and consisted of EUR 770 (95% CI: 230-1940) for hospitalization and EUR 90 (95% CI: 6-430) for rehabilitation. The lowest inpatient costs were found in Eastern European countries where they comprised 5% of the total direct costs as compared to 13%-42% in Western European countries (Fig. 1).

### 3.3. Outpatient care

89% of study patients were treated by a neurologist. On average, patients had one to three visits with their neurologist



**Figure 1** Costs presented as total costs per patient in percentage per country from the societal perspective (Euro 2008) (absolute values are presented in Supplemental Table 2).

during the 6-month study period. In addition, an average of zero to six general practitioner visits was reported by the patients (Fig. 3), lowest numbers of visits were found in Portugal.

The costs of outpatient treatment included consultations at office-based physicians and outpatient clinics. Mean costs per patient for outpatient care during the observation period ranged from EUR 60 (95% CI: 50-80) to EUR 460 (95% CI: 350-590), thus constituting 3% to 13% of direct costs. The lowest costs were calculated for Russia and the highest expenses were found in Germany. Ancillary treatment such as physiotherapy, massage, speech therapy and occupational therapy were prescribed in all participating countries. Physiotherapy was the most frequently prescribed form of non-medical therapy.

### 3.4. Antiparkinson medication

Only antiparkinson medication was taken into consideration in our study. In all participating countries, levodopa or a combination of levodopa and a decarboxylase inhibitor were the primary medication prescribed for PD therapy, followed by dopamine agonists though the prescription pattern varied in each of the countries. Apomorphine was only used in Western European countries, where 2.7% of study patients reported having used it. The details on prescription patterns are summarized in Fig. 4.

In all countries except Russia, dopamine agonists were the main cost driver in the context of antiparkinsonian medications, representing 35%-74% of the total PD medication costs. In Russia, expenses for levodopa were the main cost factor and constituted 68% of medical costs.

Average costs for antiparkinsonian medication varied from 490 Euro (95% CI: 440-550) in Russia to 2960 (95% CI: 2390-3660) in Germany and constituted 18%-49% of total direct costs across countries. Costs of medication were the most expensive cost factor among direct costs in Germany (Fig. 1 and Appendix, Supplemental Table 2).

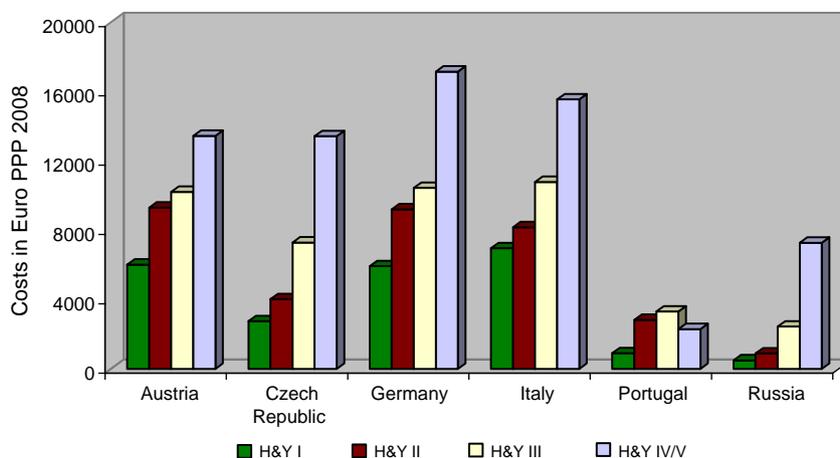


Figure 2 Total costs (Euro 2008) stratified by disease stage and country.

### 3.5. Care

*Formal care* is defined as the hours of professional care utilized per day as documented by the patient. The mean number of hours of professional care ranged from 1 h to 73 h per week. In Portugal and Austria approximately 14% and 12% of study patients obtained professional care as compared to less than 8% in the Czech Republic, Italy, Russia and Germany. Costs ranged from EUR 60 (95% CI: 20-110) in Portugal to EUR 1060 (95% CI: 330-3580) in Italy over the observation period.

*Informal care* is unpaid care that proved to be the most common source of home care in all participating countries. 76% to over 90% of patients in need of care were cared for by family members or volunteers (Fig. 5). In our study, informal care was much more common than professional care. The number of hours of informal care ranged from 10 h to 56 h per week. The costs of informal care ranged from EUR 60 (95% CI: 30-80) in Portugal to EUR 1960 (95% CI: 1320-2860) in Italy during the

observation period. Interestingly, we calculated relatively low costs (EUR 520 (95% CI: 330-750)) of informal care in Germany. In the Czech Republic, Italy and Russia, the costs of informal care were the highest single direct costs and in Eastern European countries these were more than six times higher than the respective inpatient costs. Costs for (informal and formal) care represented the major cost driver for direct costs in Austria, the Czech Republic, Italy and Russia. Women were much more likely than men to be involved in care. The mean age of the caretaker ranged from 55 years to 64 years. 57% of caretakers suffered from diseases themselves.

### 3.6. Special equipment

Costs for special equipment varied, especially costs for adapting patients' homes. The mean costs per patient varied between EUR 50 (95% CI: 20-160) in Portugal and EUR 190 (95% CI: 140-270) in Russia. In our study, the expenses for special equipment in Russia were high compared to other countries, and higher than both inpatient costs (EUR 100) and outpatient costs (EUR 60) (Appendix, Supplemental Table 2).

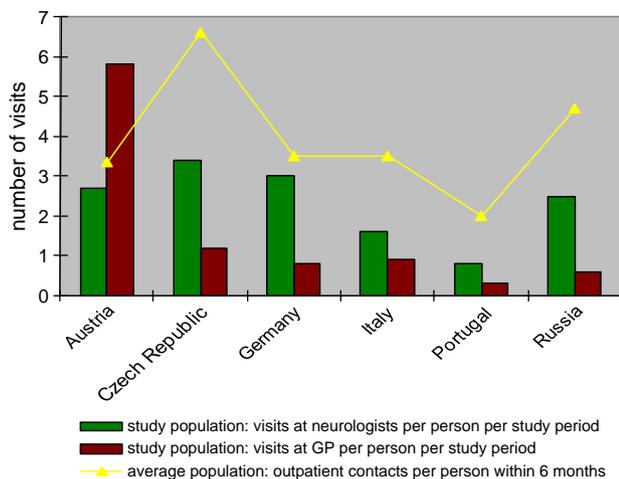


Figure 3 Consultations per PD patient during the study period. Curve of average population includes all outpatient contacts (from: OECD, 2007). Contacts for PD patient represent only visits at neurologists and GPs.

### 3.7. Patients' co-payments

The economic burden on patients and their families due to PD included co-payments for medication, special equipment etc. Co-payments comprised up to 5% of the total direct costs in the Czech Republic, 6% in Germany and Italy, 8% in Portugal, and 14% in Austria and Russia. After taking the average net income per country into consideration, the relative economic burden of PD was highest in Russia (Fig. 1).

### 3.8. Indirect costs

Indirect costs associated with PD ranged from EUR 860 (95% CI: 630-1090) in Russia to EUR 3910 (95% CI: 2510-6140) in Austria and amounted to 30%-40% of the total costs (Fig. 1 and Appendix, Supplemental Table 2). One main cost-driving factor across countries was the premature retirement of PD patients.

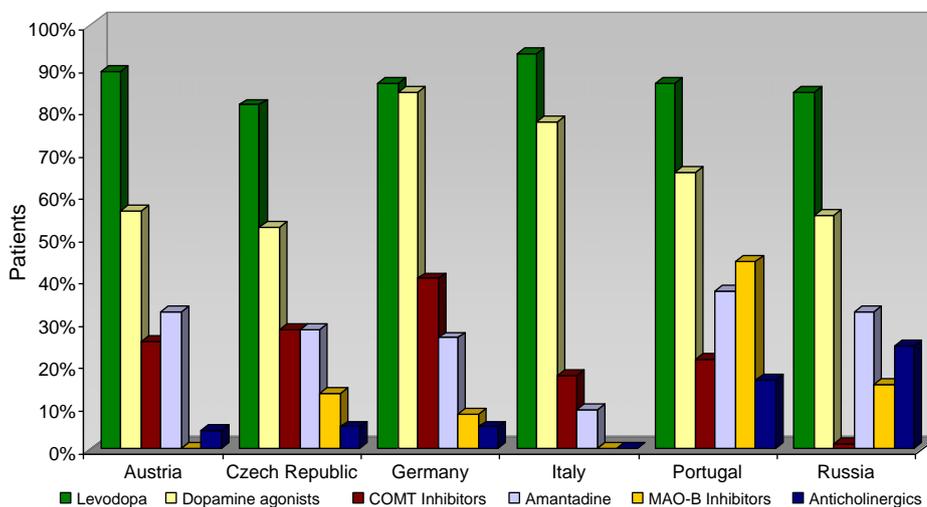


Figure 4 Treatment patterns for antiparkinson medication by different countries.

### 4. Discussion

We present here the results of a large multicenter cost-of-illness study (COI) on PD performed in six European countries, including Russia. As expected, resource consumption and costs varied between countries: unit costs, quantity of resources used and the study sample can all be regarded as important factors underlying this variation. Typically, the methodological approach is a primary concern when comparing data between studies from different countries; however, in our study we used a standardized methodology across the participating countries in order to minimize variation. This study provides insight into the resource use and the relevant cost components across different countries.

Total semi-annual costs per patient ranged from EUR 2620 (95% CI: 2050-3200) in Russia to EUR 9820 (95% CI: 7840-12,680) in Austria.

Costs of inpatient stays (hospitalization and rehabilitation) comprised 5% to 42% of direct costs across countries. In Portugal, hospitalization was the main driver of direct costs (42%). This is consistent with the findings of LePen and Keränen who also described hospitalization as the major cost factor in their studies, comprising 39% and 41% of direct costs, respectively (Keränen et al., 2003; LePen et al., 1999). Differences in hospital costs may also be due to

country-specific hospital beds available and admission rates and the length of stay (LOS). Country-data on macroeconomics and health system are provided in Table 3. Within the European Union, it is generally reported that Austria has the shortest LOS and the highest rate of hospital admissions (Hofmarcher and Rack, 2006), a fact that we also confirmed here. Interestingly, the longest LOS in our study was found to be in Germany (19 days). Traditionally for Russia an over-provision of inpatient facilities is reported. According to the OECD the number of acute beds in Russia and the average duration of stay are the highest reported among participating countries (Table 3). Reasons for these trends include the lack of social care provision and the use of beds for chronically ill patients (Tragakos and Lessof, 2003).

Unit costs for outpatient visits vary due to differences in personnel costs, among other factors (Table 1). Costs per contacts peaked in Portugal, followed by Germany, Italy and Austria. Outpatient contact costs were lowest in Russia. Generally, the costs for outpatient visits in our study were likely to be underestimated because the costs of diagnostics were excluded, as in other COI studies (Findley et al., 2003; Keränen et al., 2003; LePen et al., 1999). In addition, the costs for outpatient treatment comprised 3% (Czech Republic, Italy, Russia) to 13% (Portugal) of direct costs. As published by the Organisation for Economic Cooperation and Development, the number of consultations per capita differs across countries, with the highest number of consultations taking place in the Czech Republic and the lowest number in Portugal (Barros and de Almeida Simoes, 2007; Rokosova et al., 2005). Our study results confirm this fact as well. Cultural factors may play an important role as well as differences in co-payments and physician density. In the Czech Republic, the number of neurologists per 100,000 persons is high (13.2) as compared to Germany (3.3) or Portugal (3.2) (OECD, 2007). Cost per physician contact was 18-22 times higher in Portugal as in the Czech Republic (Tables 1 and 3).

Ancillary treatment is recommended in national treatment guidelines, but evidence for its benefit is still controversial (Keus et al., 2007). In our study physiotherapy was the most frequently prescribed therapy, similar to the findings of previous publications (Nijkraak et al., 2009).

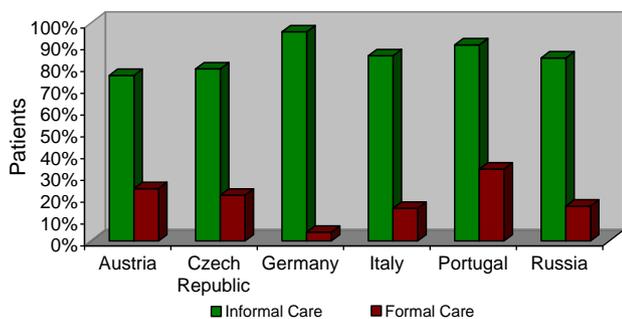


Figure 5 Caring patterns for patients in need of care by different countries.

**Table 3** Macro economic and health-system indicators ([www.oecd.org](http://www.oecd.org); <http://data.euro.who.int>).

Indicators	Austria	Czech Republic	Germany	Italy	Portugal	Russia
Population	8,281,948	10,266,646	82,437,992	58,941,500	10,584,344	142,487,264
Population 65+ (%)	16.7	14.2	19.7	19.6	17.3	14.0
Unemployment rate (%)	4.7	7.1	10.3	6.8	7.7	7.2
Gross domestic product, US\$ per capita	38,833	13,880	35,231	31,774	18,355	4042**
Physicians per 1000	3.7	3.6	3.5	3.7	3.4	4.3
General practitioners per 1000	1.5	0.7	1.5	0.9	1.7	0.3
Outpatient contacts per person per year	6.7	13.0	7.4	7.0	3.9	9.0
Hospital beds per 1000	7.6	7.4	8.3	4.0	3.5	9.7
Inpatient care admissions per 100	27.6	21.5	22.6	14.5	11.1	23.7
Average length of stay, all hospitals	6.9	10.8	10.1	7.7	8.6	13.6
Total health expenditure as % GDP	10.2	7.0	10.5	9.0	9.9	5.2*
Public sector health expenditure as % THE	75.9	86.7	76.8	76.8	71.5	62.0*
Total inpatient expenditure as % THE	39.7	33.6	35.1	44.9	20.8	-
Total outpatient expenditure as % THE	23.2	22.5	22.1	29.9	33.8	-
Total pharmaceutical expenditure as % THE	13.3	22.8	14.8	19.9	21.8	-
Private households' out-of-pocket payment on health as % THE	15.9	11.3	13.3	19.9	22.9	31.3*

GDP = gross domestic product; THE = total health expenditure; \*year=2005; \*\*year=2004.

An analysis of medical treatment showed that in each country most patients - at least 81% of the study population - received levodopa. Aside from levodopa, dopamine agonists were the most frequently prescribed drugs in our study. Costs varied depending on the preferential prescription of expensive dopamine agonists versus the proportion of prescriptions for cheaper anticholinergics. In this study, differences in treatment patterns were also found (Fig. 4) to partly explain variations in the costs of medication. Furthermore, there are substantial differences in unit costs and taxes across countries that at least partially explain differences in drug expenses. Germany has a 19% VAT as compared to only 10% in Italy and 5% in the Czech Republic and Portugal. Costs of drugs in Russia are lower than in most European countries, because generics are frequently offered. Generics play a key role in healthcare provision in the new EU member states and make up to 70% of all medicines prescribed in many Central and Eastern European countries (European Generic Medicines Association, 2004).

Annual costs for medication can be found for France EUR 1022 (1999) (LePen et al., 1999), Germany EUR 3511 (1995) (Dodel et al., 1998), and Sweden EUR 1411 (2002) (Hagell et al., 2002). We found higher costs in the participating Western European countries than were found in the studies above, though the ability to compare results is limited because these studies were conducted at least seven years ago. Changes in treatment patterns, medical progress and new medications have led to higher costs for PD medication today, e.g. rotigotine, stalevo and rasagiline received central marketing authorization in 2003 or later.

The care provided to patients is an important component of resource utilization when the costs of chronic diseases are estimated, especially since we have shown that the costs of care are the highest component of direct costs in four out of six countries. This was confirmed by Hagell et al. (2002) who also found that care was the greatest single direct cost component. In our study, costs for professional care in

Germany were low and totalled EUR 200 annually, which could be explained by the fact that only one patient in the German cohort received professional care.

It is difficult to assign appropriate cost estimates to informal care, i.e. the unpaid care provided by family members or volunteers and thus this can be seen as a direct cost or an indirect cost. We generally treated informal care as a direct cost. In our study, an average of 31% to 52% of patients needed help with activities of daily living, 76% to 96% of these patients were cared for by family members or volunteers. McCrone et al. described similar results; informal care provided by family members/volunteers accounted for approximately 80% of care (McCrone et al., 2007). Many families choose informal care instead of professional care, especially in those European countries where home care for the elderly is a tradition. Aside from these traditional factors, there is another factor that may explain differences in the management of care across countries: specifically, countries that offer less health services usually offer less professional or formal care, and family members/volunteers make up for the lack of such professional services. In Eastern European countries, institutional care was the dominant form of provision until the early 1990s (World Health Organisation, 2008). In the Czech Republic, the first professional services were not introduced before this time. The number of agencies increased from 27 in 1991 to 483 in 2002, but accessibility remained limited (Rokosova et al., 2005). Social services are also extremely limited in Russia as we found that only 8% of Russian patients utilized professional care. Previous studies have shown that women are the primary caregivers and this finding was confirmed in our study (Casado et al., 2007; World Health Organisation, 2008).

The burden of PD on patients and their families is complex and differs across countries. First, there may be a negative effect on the health status of family members; moreover, decreased health-related quality of life and a greater number of health issues among caregivers as compared to the general

population have been repeatedly reported in the literature (Martinez-Martin et al., 2007; Schrag et al., 2006). In our study, more than half of family members providing care suffered from health problems themselves.

Second, PD patients and their families have substantial expenses due to co-payments, as shown here (Fig. 1 and Appendix, Supplemental Table 2). Co-payments and reimbursement are regulated by the health care systems and thus are organized differently across countries. In Russia, for example, there exists a mandatory health insurance that covers basic medical services; however, only a few drugs are reimbursed. Differences in the financial burden across countries can at least partially be explained by the differences in the reimbursement systems. The average proportion of out-of-pocket expenses in the countries is presented in Table 3.

Indirect costs depend on how the labour market and the economy are structured in different countries. Although the human capital approach is commonly used to calculate the indirect cost-of-illness, it is criticized because it overestimates the indirect costs in times of high unemployment when open jobs are immediately taken and no productivity loss occurs (Koopmanschap et al., 1995). The difference in average income per country partially explains the differences in indirect costs among the participating countries. In our study, indirect costs represented between 30% and 40% of the total costs of PD. In three COI studies, indirect costs were found to be lower than direct costs (Hagell et al., 2002; Spottke et al., 2005; Winter et al., 2010b). In a Finnish study the loss of productivity exceeded the direct costs (Keränen et al., 2003).

Our study has several limitations. The "bottom up" approach used in this study provides detailed information on resource utilization but is both time and cost intensive. Therefore, we collected data using a hospital-based design instead of a population-based approach. Hospital-based settings were also used in a large number of other studies that employed a "bottom up" approach (Chrischilles et al., 1998; Hagell et al., 2002; Keranen et al., 2003; Spottke et al., 2005). Especially in Russia and Portugal, there are considerable differences between urban and rural areas with respect to economic status, infrastructure, and medical services, and these differences influence both care and PD outcomes. Moreover, all participating study centers were University hospitals, a fact that may bias the study sample and the estimates of resource consumption towards greater expenses. The number of patients who completed the study per country was probably too small to adequately reflect some cost components and the costs in different disease stages. A small sample size in these groups can lead to an underestimation or overestimation of costs. Because of different sample sizes and in particular, the small size of the Portuguese sample, group comparisons have to be interpreted very cautiously. Patients in severe disease stages were generally under-represented in this study and only a few nursing home residents were included. Due to comorbidities in older patients, it is difficult to precisely attribute costs to PD, and this fact may lead to an overestimation of costs of care. Furthermore, we did not include patients, who were treated with surgical treatment options such as deep brain stimulation, etc., which are costly and may have an impact on the cost distribution in the advanced stages of the

disease. Finally, we imputed missing values using a last-observation-carried-forward approach in order to overcome the reduced sample size due to loss to follow-up. However, it is important to note that this method may provide imprecise estimates, especially in subgroup estimations with small sample sizes. To allow reliable correlations of macro economic data with disease characteristics population-based sampling should be the basis of future research.

PD is the fourth most costly neurological disease after migraine, stroke and epilepsy and it remains among the most prevalent neurological diseases (Andlin-Sobocki et al., 2005). Our study, which is one of the first international studies of PD across European countries, has shown that PD places a considerable economic burden on European populations.

In addition, well-planned multicenter studies with large numbers of patients are needed as these will provide information for health policymakers that supports the increasing well-being of PD patients in EU countries. Policies that can guide planning and regulation of home care at a national level and inform resource allocation decisions are needed. Modern medicine becomes more complicated and specialized roles such as PD Nurse Specialists should play a more important part in the day to day management of PD. The steady increase in costs due to age-associated diseases in the coming years is a threat to the economic welfare of European countries (Dorsey et al., 2007). A multidisciplinary approach to the management of PD could help to deliver well-rounded care at manageable costs. Multidisciplinary teams currently do not exist in most European countries.

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- 2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
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## Conflict of interest

All authors declare that they have no conflict of interest.

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