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Nationwide prevalence of primary dystonia, progressive ataxia and hereditary spastic paraplegia

Clara Hellberg[a], Erik Alinder[a], Daniel Jaraj[a,b], Andreas Puschmann[a,*]

[a] Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Neurology, Lund, Sweden
[b] Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

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ABSTRACT

Objective: To determine the nationwide prevalence of primary dystonia, ataxia and hereditary spastic paraplegia (HSP) in Sweden.
Methods: We extracted data on all patients who were registered in The National Patient Register (NPR) in Sweden (population 9.64 million) at least twice during five consecutive years with a diagnosis of primary dystonia, ataxia or HSP. We excluded patients with an additional diagnosis possibly indicating secondary causes, and determined the proportion of wrongly diagnosed patients at our own tertiary center by patient examination or chart review. We analyzed patients' age and disorder subtypes, geographical distribution of patients within Sweden and the country of birth of all patients.
Results: Nationwide, we identified 4239 patients (31.6% male) with a diagnosis of primary dystonia. Of 347 patients with dystonia at our center, 20.2% may have had a different final diagnosis. Extrapolation of this uncertainty rate to the national population resulted in a prevalence for primary dystonia of 35.1/100,000. There were 672 patients (49.6% male) with ataxia in NPR, and the diagnostic uncertainty rate among 81 patients in our center was 13.6% (prevalence 6.0/100,000). HSP was diagnosed in 235 patients nationwide (52.3% male, prevalence 2.4/100,000). Patients were distributed relatively evenly throughout the country. The proportions of patients with these diagnoses who were born outside of Sweden were lower (8.0–12.7%) than the proportion of all Swedish residents born abroad (15.9%).
Conclusions: In this large, nationwide study, the prevalence of dystonia was high compared to previous studies, which partly may be explained by the high coverage of NPR.

1. Introduction

Primary dystonia, progressive ataxia and hereditary spastic paraplegia (HSP) are relatively rare neurological syndromes in most populations. They often cause severe impairment and disability, and patients may require intensive contact with a neurology service. Patients with these disorders have in common that they are frequently seen by neurologists specializing in movement disorders, often necessitating extensive clinical workup to establish a diagnosis. Also, some of the syndromes manifesting as primary dystonia, progressive ataxia or HSP may be closely related in terms of underlying pathogenesis [1,2].

Previous studies on the prevalence of primary dystonia, progressive ataxia, or HSP have mainly used selected populations and yielded variable results [3–10]. There have been few nationwide population-based studies, making it difficult to use the results for the dimensioning of health services for these patients. Two recent reviews and meta-analyses commented that the various studies on the prevalence of these disorders had methodological differences and limitations [11,12].

We performed a nationwide assessment of the prevalence of primary dystonia, progressive ataxia and HSP. The entire Swedish population (9.64 million) was sampled using data from the Swedish National Patient Register (NPR) in order to calculate prevalence estimates. In addition, we examined geographical distribution and possible associations with country of birth.

2. Methods

2.1. Nationwide data

NPR is a validated national health care register that completely covers all inpatient and outpatient visits to doctors in specialized medical care of all specialties within the Swedish public health service,

* Corresponding author. Department of Neurology, Skåne University Hospital, Getingevägen 4, 221 85, Lund, Sweden.
E-mail address: Andreas.Puschmann@med.lu.se (A. Puschmann).

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and contains additional data from private caregivers [13,14]. The majority of the country's health service is public and 86% of neurologists in Sweden work within the public health service. Through two separate searches in NPR, data were compiled on all individuals who had received a diagnosis of non-drug-induced dystonia (ICD-10 G24.1–9), chronic progressive ataxia (ICD-10 G11.1–3, 11.8–9) or HSP (ICD-10 G11.4) during visits to a doctor during the years 2009–2013. To ensure high specificity, we then only counted those patients who had received their diagnosis at least twice during the 5 years. We extracted data on the exact subtype diagnoses (ICD-10), sex, age at registration, Swedish municipality and county of residence, and country of birth. We excluded individuals who also had ICD-10 diagnoses of Parkinson disease, Parkinsonism, Huntington disease, Wilson disease, cerebral palsy, and multiple sclerosis, or codes for external causes of morbidity attributed to the diagnosis of dystonia, ataxia or HSP; from the ataxia group we additionally excluded any patient who also had received a diagnosis of any alcohol-related disorder. We considered it possible that these patients may have non-primary forms of dystonia, ataxia or HSP. Patients who were deceased by Dec 31, 2013, were excluded. Data on the entire Swedish population was retrieved from the online database of Statistics Sweden (http://www.scb.se/en_/).

2.2. Local data and estimated diagnostic uncertainty rate

We compared local data from our center at Skåne University Hospital with data from the NPR in order to estimate the diagnostic uncertainty rate of primary dystonia and progressive ataxia (Fig. 1). Skåne University Hospital is the only public primary neurological caregiver for 640,000 inhabitants in the health care districts of Lund and Malmö, where there were 1–2 private neurologists during the study period, and also serves as a tertiary referral center for the Southern Swedish Healthcare district with 1.77 million inhabitants.

All patients residing in this area, who had received an ICD-10 diagnosis of primary dystonia during 2011–2014 were contacted by mail, and invited to participate in a then ongoing research study that included a study visit for clinical re-evaluation by a movement disorder neurologist, where a diagnosis of dystonia was made or rejected based on consensus criteria [15]. Available medical records of all remaining patients with primary dystonia were reviewed with the aim of determining whether the diagnosis was correct and certain. Criteria for a true diagnosis of primary dystonia at this review were: repeated visits to a neurologist with dystonia as main diagnosis and no additional neurological diagnoses that could explain the patient's dystonia, or a diagnosis of dystonia combined with treatment with botulinum toxin as registered by procedure codes for reimbursement. All patients with a diagnosis of ataxia or HSP were re-evaluated by a review of medical records. Those who had young onset ataxia (age at onset under 26 years) were also invited for renewed clinical examination. The rate of uncertain or erroneous diagnoses, as defined above, of primary dystonia or ataxia was determined for our center, and was extrapolated on the nationwide data from NPR. Written informed consent was obtained from all patients who were re-examined within research studies; these were approved by the regional ethical review board in Lund, Sweden. Review of medical records in our department was performed within a clinical audit.

2.3. Statistical analysis

Crude prevalence of primary dystonia, progressive ataxia and HSP was calculated using binomial proportions based on the number of diagnoses in the NPR and Swedish population data. We estimated the diagnostic uncertainty rate for primary dystonia and progressive ataxia in the NPR using local data from our center. We used the estimated diagnostic uncertainty rate to adjust the crude prevalence. We used the Wald method to calculate 95% confidence intervals for crude and adjusted prevalence estimates. Prevalence is reported as patients per 100.000 population. Statistical analyses were performed using R statistical software environment (https://www.r-project.org/).

3. Results

3.1. Prevalence of primary dystonia

The crude prevalence of primary dystonia in Sweden, according to the NPR, was 44.0/100.000. Adjusting for the estimated rate of misdiagnosis, the prevalence of primary dystonia was 35.1/100.000 (95% CI: 34–36/100.000).

From 2009 to 2013, 4312 individuals received a diagnosis of primary dystonia in the NPR at least twice; of these, 73 were excluded as they also had an additional diagnosis possibly indicating a secondary cause. Of the remaining 4239 patients, 31.6% were male (Table 1). Supplementary Table 1 shows the age distribution of all patients nationwide. The total number of ICD-10 codes identified in the 4239 patients was 4974; a proportion of patients had received more than one

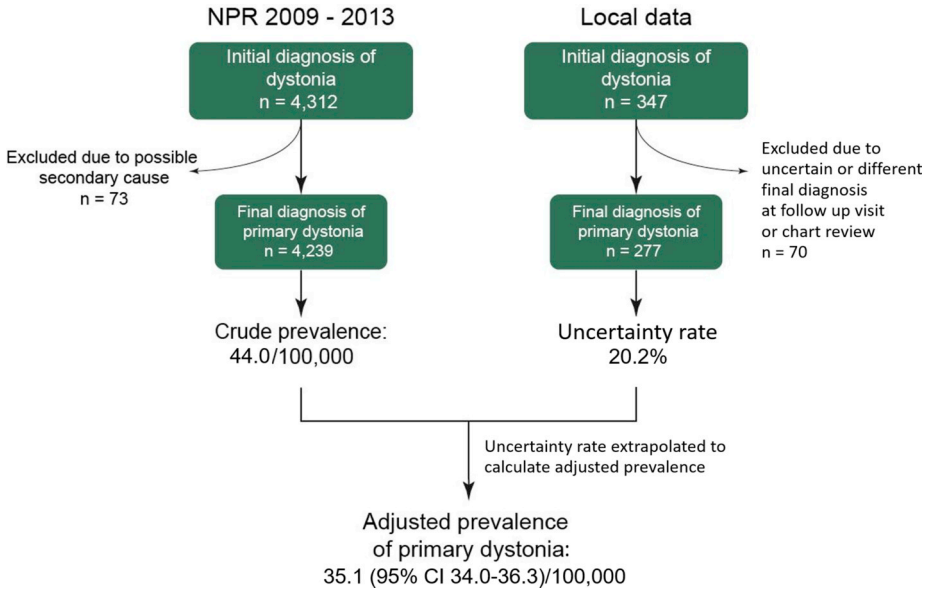

Fig. 1. Study outline.

Table 1
Prevalence of primary dystonia, progressive ataxia and hereditary spastic paraplegia.

	Primary dystonia	Progressive ataxia	Hereditary spastic paraplegia
Number of patients diagnosed *at least once* during 5 years	5810	1085	334
Crude prevalence (at least one visit)	60.2	11.2	3.5
Number of patients diagnosed *at least twice* during 5 years	4239	672	235
Crude prevalence (at least two visits)	44.0	7.0	2.4
Diagnostic uncertainty rate at our center	20.2%	13.6%	*NA*
Adjusted prevalence	35.1	6.0	*NA*
95% Confidence interval	34.0–36.3	5.5–6.5	*NA*

Prevalence is stated per 100,000 inhabitants. NA, not applicable, see main text. Individuals who also had other diagnoses that may indicate an underlying cause for a secondary form of the neurological disorder have been excluded.

Table 2
Subtypes of primary dystonia and progressive ataxia.

ICD-10 code	Number of diagnoses
G24.1 Idiopathic familial dystonia	126 (2.5%)
G24.2 Idiopathic nonfamilial dystonia	61 (1.2%)
G24.3 Spasmodic torticollis	1742 (35.0%)
G24.4 Idiopathic orofacial dystonia	140 (2.8%)
G24.5 Blepharospasm	1133 (22.8%)
G24.8 Other dystonia	951 (19.1%)
G24.9 Dystonia, unspecified	821 (16.5%)
Total number of dystonia diagnoses	**4974**
G11.1 Early-onset cerebellar ataxia	209 (25.4%)
G11.2 Late-onset cerebellar ataxia	295 (35.9%)
G11.3 Cerebellar ataxia with defective DNA repair	26 (3.2%)
G11.8 Other hereditary ataxias	81 (9.9%)
G11.9 Hereditary ataxia, unspecified	211 (25.7%)
Total number of progressive ataxia diagnoses	**822**

ICD-10 code for dystonia during the five-year period examined (Table 2). Codes for “Other dystonia” and “Dystonia, unspecified” together made up 35.6% of diagnoses.

At our department, 347 patients were diagnosed with primary dystonia, and our department's records were congruent with the data retrieved from NPR. Of these, 122 were re-examined within our research study, of whom 11 (9.0%) had other disorders. Review of medical records of the remaining 225 individuals revealed that the diagnosis remained uncertain or was considered erroneous in 59 (25.4%). Altogether, 20.2% of the 347 patients who had been diagnosed with an ICD-10 code for primary dystonia may have had any of a variety of different diagnosis. Extrapolation of this uncertainty rate to the NPR figures resulted in the adjusted prevalence rate of 35.1/100.000 (95% CI: 34–36/100.000).

3.2. Progressive ataxia

The crude prevalence of progressive ataxia in Sweden, according to the NPR, was 7.0/100.000. Adjusting for the estimated rate of misdiagnosis, the prevalence of progressive ataxia was 6.0/100.000 (95% CI: 5.5–6.5/100.000).

There were 673 patients who had been diagnosed at least twice with ataxia in NPR. One was excluded due to a concurrent diagnosis suggesting a possible secondary cause. Of the remaining 672 individuals, 49,6% were male. The 672 individuals received a total of 822 ataxia diagnoses (Table 2). We identified 81 patients who were diagnosed with ataxia in our department. Eleven were not considered to have chronic progressive ataxia in our review of medical records; there either were no signs of ataxia at follow-up examinations, or they subsequently developed other disorders, which included motor neuron disease, polyneuropathy without cerebellar degeneration, multiple sclerosis, multiple systems atrophy or paraneoplastic cerebellar degeneration. Thus, 70 of 81 patients had true progressive ataxia and the diagnostic uncertainty rate was 13.6%. Extrapolation of this uncertainty rate to the national population resulted in a prevalence for ataxia of 6.0/100,000 (95% CI: 5.5–6.5/100.000). Of 70 patients with a final diagnosis of progressive ataxia at our center, medical records contained information that four were relatives to other patients.

3.3. HSP

The crude prevalence of HSP, nationwide, was 2.4/100.000. HSP was diagnosed at least twice in 237 patients nationwide, of whom two were excluded because of a different neurological disorder that may have been an underlying cause for spastic paraparesis. Of the remaining 235 individuals, 52,3% were male. The nationwide prevalence of HSP was 2.4/100,000. There is only one ICD-10 code for HSP. At our center, 16 patients had received this diagnosis during the study period, and record review could confirm this diagnosis in 15 of these; the remaining was a child of a confirmed HSP4 patient for whom it is not certain if clinical disease signs were seen or not. All but two patients had pure slowly progressive paraparesis, only 2 had complicated disease form. We considered numbers too low to calculate and extrapolate a diagnostic uncertainty rate.

For all these three diagnoses, the number of newly identified patients was highest during the first year but then remained constant during year 2–5, suggesting there were no major changes in disease awareness or diagnostic practice during the study period.

3.4. Geographical distribution within Sweden

The 4239 patients with dystonia retrieved from NPR resided in 288 of Sweden's 290 municipalities, and in each of the country's 21 counties. As a measurement for geographical distribution, we calculated a crude prevalence for each county and the mean and standard deviations of these 21 values (Supplementary Table 2 and Supplementary diagrams). Mean crude prevalence rate was 44.0 (SD 12.98)/100,000. The 672 ataxia patients resided in 184 municipalities in all counties; crude prevalence was 7.0 (SD 2.58)/100,000. The 235 HSP patients resided in 20 of 21 counties, crude prevalence was 2.4 (SD 1.41)/100,000. For none of the three groups of disorders was there any clear correlation of county means with the geographical location of the counties within the country.

3.5. Patients’ countries of birth

Information on the country of birth was available on all residents of Sweden and thus all patients investigated. We found that 12,7% of dystonia patients, 11,2% of ataxia patients and 8,0% of HSP patients were born outside of Sweden. This calculation is based on the patients who had received their diagnosis at least twice during the study period. This compares to 15.9% of all Swedish residents who were born outside of Sweden. As the disorders investigated usually manifest in adult age, we also determined the proportion of Swedish residents born abroad 30 years or older; this was 17.9%. The data suggest that individuals who were born outside of Sweden were less likely to have had contact with the health services with a diagnosis of dystonia, ataxia, or HSP than

Table 3
Countries of birth.

Country of birth	Primary dystonia patients	Progressive ataxia patients	HSP patients	All residents of Sweden	All residents of Sweden ≥30 years
Sweden	3701	597	216	8,112,301	5,061,901
Finland	187	11	3	161,129	154,630
Yugoslavia	30	4		68,554	56,962
Denmark	29	2	1	43,198	35,806
Norway	29	8	1	42,523	34,811
Iraq	27	8	3	128,946	77,927
Poland	21	4		78,175	58,937
Iran	20	3	2	67,211	54,586
Germany	15	4		48,987	39,302
Bosnia-Hercegovina	14	4		56,804	44,882
Somalia		6		54,221	22,112
Chile			2	28,241	24,955
Turkey			2	45,676	36,117
Other countries[a]	166	21	5	708,898	599,840
Total	**4239**	**672**	**235**	**9,644,864**	**6,163,601**
Sweden	87.3%	88.8%	92,0%	84.1%	82.1%
Neighboring countries[b]	6.6%	4.3%	2.1%	3.9%	5.3%
Non-neighboring countries	6.1%	6.9%	5.9%	12.0%	12.6%

This table lists the ten countries where most patients in each group (primary dystonia, progressive ataxia, HSP) were born, as well as figures from neighboring countries. For HSP, only 7 countries were countries of birth for more than one patient.

[a] Primary dystonia patients were born in 59 additional countries, progressive ataxia patients in 19 and HSP patients in 5. Below the total numbers, percentages are given for the number of patients in each category who were born in Sweden, in its neighboring countries.

[b] (Finland, Norway, Denmark, Germany or Poland), or in other countries. This is compared with the birthplaces of the entire Swedish population, and for all residents 30 years and older on Dec 31, 2013.

individuals born in Sweden. Details are provided in Table 3. We noted a higher crude prevalence of dystonia (116.1/100,000) and ataxia (6.8/100,000) among Swedish residents born in Finland, but due to immigration from Finland to Sweden in connection with World War II, the mean age of Swedish residents born in Finland is 61.4 years, compared to the mean age of all Swedish residents (41.2 years). As NPR does not release individual level data or data describing small groups with limited numbers of individuals, we were unable to directly compare the age distribution of patients born abroad with those born in Sweden.

3.6. Number of patients who had received their diagnosis only at least once

There were 5691 patients with one or more diagnoses of primary dystonia, 1085 patients with progressive ataxia, and 334 patients with HSP.

4. Discussion

This study used data from the NPR, a national register in Sweden (population 9.46 million) of patient visits to the health services, to determine the prevalence of primary dystonia, progressive ataxia and HSP. Prevalence rates were adjusted for the proportion of wrongly diagnosed patients in our own center. Key findings are a corrected prevalence for primary dystonia of 35.1 and for progressive ataxia of 6.0, as well as a prevalence for HSP of 2.4/100,000 inhabitants. To our knowledge, the prevalence of primary dystonia and HSP has never previously been assessed in a systematic nationwide register based on such a large population. Patients with these disorders resided all over the country with no evidence for geographical accumulation in any particular part of the country, which we interpret as an indication that differences in the access to and diagnostic praxis of neurologists throughout the country for patients with these diagnoses. These diagnoses were made more frequently among individuals born in Sweden than in first-generation immigrants.

The prevalence of primary dystonia in our study compares to previous estimations of between 1.17 and 60.2/100,000 inhabitants [3–5,12]. A meta-analysis of 12 service-based studies from European countries and Japan found a mean prevalence of 16.4/100,000 [12]; our results from this large nationwide study clearly indicates a markedly higher prevalence. Higher prevalence of primary dystonia has mainly been reported in service-based studies from Northern Europe [4,16,17]. In Iceland, primary dystonia prevalence was 37.1/100,000 [16]; in the Oslo region of Norway, prevalence for focal or segmental dystonia was 25.5 [18], and on the Faroe Islands, primary focal dystonia prevalence was 60.2/100,000 [4]. These three studies also have in common that they were performed relatively recently (2003–2015), in countries with a majority of Western Scandinavian inhabitants, and in settings where expensive treatment options such as botulinum toxin or deep brain stimulation are financed publicly. Primary dystonia most often occurs in mid-life and rarely remits, why it may be expected to be more prevalent in populations with long life expectancy. We found that 53.6% of primary dystonia patients are 60 years or older (Supplementary Table 1).

The prevalence of progressive ataxias in our study was similar to that in previous reports, but there are few population-based studies. In Japan, national register data reported a 5.3/100,000 prevalence of hereditary cerebellar ataxia [19]. In relatively rare disease, a founder effect of one or a few particular disease subtypes can markedly increase prevalence: A higher ataxia prevalence of 8.9/100,000 inhabitants was found in a systematic population-based survey of general practitioners and other health care providers in Portugal, but 3.1/100,000 were ascribed to SCA3 alone that is very frequent in certain geographical areas of Portugal [6]. Also in Japan, certain dominant disease forms occur more frequently due to a founder effect [19]. In Norway, a study on patients from a health service district with a population of 2.36 million revealed a prevalence of 6.5/100,000 for progressive ataxia [20], and in Northern England the prevalence was 5.8/100,000 [21].

The prevalence of HSP was previously found to be between 0.1 and 12/100,000 individuals [9,11,19], and was 7.4/100,000 in Norway, where HSP interestingly was more common than ataxia [20]. We noted a very low proportion of complicated HSP cases among our center's HSP patients, and hypothesize that the lower prevalence in our study compared to neighboring Norway might be explained by a tendency at our center not to make this diagnosis in atypical or complicated presentations.

We also wanted to examine whether these diseases might be more common among portions of the immigrant population, hypothesizing that this might be an effect of higher rates of consanguineous marriages among immigrants from certain populations, or because migrants might be attracted by the country's relatively liberal access to publicly funded health care. However, we found no evidence for increased disease prevalence among individuals born outside of Sweden. Rather, the proportions of patients with these diagnoses who were born outside of Sweden were lower (8.0–12.7%) than the proportion of all Swedish residents born abroad (15.9%; over 30 year olds: 17.9%) in the population. A similar trend had been reported from Norway where dystonia was more often diagnosed among individuals of European descent than immigrants from Asia or Africa [18]. In our data, this difference was even more pronounced for progressive ataxias and HSP. Previous work has analyzed inequalities in the care and care-seeking behavior between immigrant and non-immigrant residents in Sweden and Norway [22–24] which might contribute to this difference.

Like all register-based studies, our study cannot claim to report the true occurrence of these disorders in the Swedish population. Also, disease definitions in the medical literature have varied over time and may differ from the criteria used by clinicians when selecting ICD-10

codes in clinical practice. Our study reports the number of individuals who received an ICD-10 code of one of these disorders and who had been in contact with a health service provider who registers in NPR during the five-year study period. The vast majority of neurologists in Sweden work in the public health service who is obliged to report to NPR and for which NPR coverage approaches 100%. The same datasets that are required for reimbursements are submitted to NPR. We see a strength in our study that the salary of doctors in the public health care sector does not depend on which diagnoses they make. Private neurologists are concentrated in major cities and are not obliged to report to NPR and coverage is uncertain, but are few in numbers.

In order to reach very high diagnostic certainty, we only counted patients who had received their diagnoses at least twice under the 5-year study period. However, 37–61% more patients received these diagnosis only once within the study period. We believe that the true prevalence lies between these figures and that our final results underestimate the prevalence. Patients with milder symptoms of any of the three disorders may not have had contact with the health services at all, or not twice during the 5-year period. On the other hand, our service based register figures reflect the number of patients with these diagnoses who required contact with health services, and thus are valuable for health service planning.

In our comparisons of different prevalence rates, we have been unable to directly standardize for factors such as age or sex, because NPR do not release data on single or small groups of individuals. Likely, different age and sex may explain part of the variation of prevalence between counties or countries of origin. Despite these limitations, to our knowledge this is the largest study assessing the prevalence of primary dystonia, and it shows that this disorder is more common than appreciated in many previous reports.

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Authors' contributions

Clara Hellberg: Study concept, analysis and interpretation of data, drafting and revising the manuscript.

Erik Alinder: Study concept, analysis and interpretation of data, drafting and revising the manuscript.

Daniel Jaraj: Analysis and interpretation of data, drafting and revising the manuscript; Statistical analysis.

Andreas Puschmann: Study concept, analysis or interpretation of data; revising the manuscript for content, statistical analysis, study supervision and coordination, obtaining funding

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.10.028.

This flowchart shows the general outline of the study part on the prevalence of primary dystonia. Assessment of the prevalence of progressive ataxia was conducted by an analogous outline. The reader is referred to the text for details.

References

[1] M. Rossi, B. Balint, P. Millar Vernetti, K.P. Bhatia, M. Merello, Genetic dystonia-ataxia syndromes: clinical spectrum, diagnostic approach, and treatment options, Mov. Disord. Clin. Pract. 5 (2018) 373–382.
[2] M. Synofzik, R. Schule, Overcoming the divide between ataxias and spastic paraplegias: shared phenotypes, genes, and pathways, Mov. Disord. 32 (2017) 332–345.
[3] Epidemiological Study of Dystonia in Europe (ESDE) Collaborative Group, A prevalence study of primary dystonia in eight European countries, J. Neurol. 247 (2000) 787–792.
[4] P. Joensen, High prevalence of primary focal dystonia in the Faroe Islands, Acta Neurol. Scand. 133 (2016) 55–60.
[5] M.L. Evatt, A. Freeman, S. Factor, Adult-onset dystonia, Handb. Clin. Neurol. 100 (2011) 481–511.
[6] P. Coutinho, L. Ruano, J.L. Loureiro, V.T. Cruz, J. Barros, A. Tuna, C. Barbot, J. Guimaraes, I. Alonso, I. Silveira, J. Sequeiros, J. Marques Neves, P. Serrano, M.C. Silva, Hereditary ataxia and spastic paraplegia in Portugal: a population-based prevalence study, JAMA Neurol. 70 (2013) 746–755.
[7] H. Sasaki, I. Yabe, K. Tashiro, The hereditary spinocerebellar ataxias in Japan, Cytogenet. Genome Res. 100 (2003) 198–205.
[8] J. Sequeiros, S. Martins, I. Silveira, Epidemiology and population genetics of degenerative ataxias, Handb. Clin. Neurol. 103 (2012) 227–251.
[9] M. Braschinsky, S.M. Luus, K. Gross-Paju, S. Haldre, The prevalence of hereditary spastic paraplegia and the occurrence of SPG4 mutations in Estonia, Neuroepidemiology 32 (2009) 89–93.
[10] Y. Shimizu, K. Yoshida, T. Okano, S. Ohara, T. Hashimoto, Y. Fukushima, S. Ikeda, Regional features of autosomal-dominant cerebellar ataxia in Nagano: clinical and molecular genetic analysis of 86 families, J. Hum. Genet. 49 (2004) 610–616.
[11] L. Ruano, C. Melo, M.C. Silva, P. Coutinho, The global epidemiology of hereditary ataxia and spastic paraplegia: a systematic review of prevalence studies, Neuroepidemiology 42 (2014) 174–183.
[12] T.D. Steeves, L. Day, J. Dykeman, N. Jette, T. Pringsheim, The prevalence of primary dystonia: a systematic review and meta-analysis, Mov. Disord. 27 (2012) 1789–1796.
[13] J.F. Ludvigsson, E. Andersson, A. Ekbom, M. Feychting, J.L. Kim, C. Reuterwall, M. Heurgren, P.O. Olausson, External review and validation of the Swedish national inpatient register, BMC Public Health 11 (2011) 450.
[14] The Swedish National Board of Health and Welfare, In English – the national patient register, [online source], 2015. http://www.socialstyrelsen.se/register/halsodataregister/patientregistret/inenglish.
[15] A. Albanese, K. Bhatia, S.B. Bressman, M.R. Delong, S. Fahn, V.S. Fung, M. Hallett, J. Jankovic, H.A. Jinnah, C. Klein, A.E. Lang, J.W. Mink, J.K. Teller, Phenomenology and classification of dystonia: a consensus update, Mov. Disord. 28 (2013) 863–873.
[16] H. Asgeirsson, F. Jakobsson, H. Hjaltason, H. Jonsdottir, S. Sveinbjornsdottir, Prevalence study of primary dystonia in Iceland, Mov. Disord. 21 (2006) 293–298.
[17] A.G. Butler, P.O. Duffey, M.R. Hawthorne, M.P. Barnes, An epidemiologic survey of dystonia within the entire population of northeast England over the past nine years,

Adv. Neurol. 94 (2004) 95–99.
[18] K.D. Le, B. Nilsen, E. Dietrichs, Prevalence of primary focal and segmental dystonia in Oslo, Neurology 61 (2003) 1294–1296.
[19] S. Tsuji, O. Onodera, J. Goto, M. Nishizawa, D. Study, Group on Ataxic, Sporadic ataxias in Japan - a population-based epidemiological study, Cerebellum 7 (2008) 189–197.
[20] A.K. Erichsen, J. Koht, A. Stray-Pedersen, M. Abdelnoor, C.M. Tallaksen, Prevalence of hereditary ataxia and spastic paraplegia in southeast Norway: a population-based study, Brain 132 (2009) 1577–1588.
[21] D. Bargiela, P. Yu-Wai-Man, M. Keogh, R. Horvath, P.F. Chinnery, Prevalence of neurogenetic disorders in the North of England, Neurology 85 (2015) 1195–1201.
[22] G. Abdoli, M. Bottai, A. Sidorchuk, T. Moradi, Trends in mortality after cancer diagnosis: a nationwide cohort study over 45 years of follow-up in Sweden by country of birth, Cancer Epidemiol. 39 (2015) 633–640.
[23] K.S. Bakken, O.H. Skjeldal, B. Stray-Pedersen, Higher risk for adverse obstetric outcomes among immigrants of African and Asian descent: a comparison study at a low-risk maternity hospital in Norway, Birthkit 42 (2015) 132–140.
[24] A. Esscher, P. Binder-Finnema, B. Bodker, U. Hogberg, A. Mulic-Lutvica, B. Essen, Suboptimal care and maternal mortality among foreign-born women in Sweden: maternal death audit with application of the 'migration three delays' model, BMC Pregnancy Childbirth 14 (2014) 141.