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Multiple sclerosis epidemiology in Finland: regional differences and high incidence

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Abstract

Objectives: Studies on the east-west gradient of multiple sclerosis (MS) are scarce. In Finland, epidemiological differences have been only partially elucidated, but the MS risk is high, and it has been claimed that the occurrence follows a longitudinal gradient. In this register-based study,

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we updated the MS epidemiology in southwest Finland (SwF) and compared it to the easternmost hospital district, North Karelia (NK), for which no previous data exist.

Material and methods: Patients with ICD-10 code G35 were identified from hospital district administrative data. Patient records were reviewed to include only cases with a definitive diagnosis. Incidence period covered 5 years (2012–2016) and the prevalence date was December 31, 2016. Results were standardized using the direct method.

Results: 1184 persons had MS in SwF and 253 persons in NK at the end of 2016. The prevalence was 280/100,000 (95% Cl 264-296) in SwF and 168/100,000 (95% Cl 148-190) in NK (age-standardized for the European standard population 2013). During the incidence period, 211 new MS diagnoses were made in SwF and 49 in NK. The annual age-standardized (ESP 2013) incidence was 12.1/100,000 person-years (95% Cl 10.5–13.8) in SwF and 8.6/100,000 person-years (95% Cl 6.4-11.2) in NK in the age group 10-69 years.

Conclusions: There are regional differences in MS epidemiology in Finland, possibly related to demographic, social and genetic circumstances but the retrospective nature and limited sample size of this study might introduce some uncertainty to the calculations. SwF is a region with a globally very high risk for MS.

Keywords: epidemiology, Finland, incidence, multiple sclerosis, prevalence

Introduction

Although the epidemiology of multiple sclerosis (MS) varies considerably among regions and populations, the prevalence and incidence of MS are almost universally increasing (1, 2). The more distant the location from the equator, the higher the prevalence and incidence figures tend to be (3,

4), but this latitude gradient has been questioned, especially in Europe and North America (1). The very high prevalence and incidence rates in the Nordic countries do suggest, however, that latitude may be associated with the occurrence of MS. In 2008, the incidence of MS in Sweden was 11.1/100,000 person-years and the prevalence 189/100,000 (5, 6). In Norway, the nationwide prevalence of MS in 2013 was even higher, 208/100,000 (7). An east-west (longitudinal) gradient describing the prevalence of MS has also been reported in some studies, but the results have been inconsistent (8-11). A slightly lower prevalence of 167/100,000 in 2007 has been recently reported for Iceland (12).

Finland is a high-risk MS region, like the other Nordic countries. There are, however, no nationwide statistics on the prevalence and incidence of MS, and there is no epidemiological data on the eastern part of the country. The regional prevalence of MS in southwest Finland was recently reported; it was even higher (213/100,000) than what has been reported as the nationwide rates in Sweden and Norway (13). The incidence in southwest Finland is unknown. Interestingly, significant interregional differences in the occurrence of MS have been observed in Finland since 1964 (14) and the areas with the highest prevalence are located in the western and southwestern parts of the country (15-18). The causes for these interregional differences are unknown, but there are well-known and marked genetic differences between eastern and western Finns (19, 20). Previous studies have also shown a rising trend in the incidence of MS over the past decades similar to what has been reported from the other Nordic countries (6, 7). In the 1990's the prevalence of MS in Finland varied by region between 100 and 200/100,000 and incidence between 5 and 12/100,000 person-years (16, 21). In 2010, the incidence of MS in the western regions of Finland was 6.7–12.5/100,000 person-years and had increased over 30 years (1981–2010), especially in the region of Ostrobothnia, which had a high incidence at the outset (22). During these three decades, the incidence had risen especially among females and the female-to-male ratio had increased (23).

The objective of this study was to evaluate the regional differences in the epidemiology of MS in Finland. We updated the epidemiology of MS in southwest Finland and compared it with the easternmost hospital district of Finland, the North Karelia Hospital District.

Material and methods

We obtained population data from Statistics Finland (24). The total population of Finland in 2016 was 5.5 million of which 4.9 million were aged 10 years or older. During the study period (1 January 2012 to 31 December 2016, the population (aged ≥ 10 years) of southwest Finland (SwF) increased by 2.0 % to 430,064 and that of North Karelia (NK) decreased by 1.1 % to 151,707. The population density in Finland is unevenly distributed (variation from 2 to 178 inhabitants per square kilometer) and the mean population density is 18 inhabitants per square kilometer. The catchment area of our study has population densities of 45 (SwF) and 25 (NK) inhabitants per square kilometer. In SwF, 85.0% of the population lived in urban areas while in NK this proportion was 72.2%.

The diagnosis of MS patients is centralized to Turku University Hospital in SwF region and to North Karelia Central Hospital in NK region. All patient records with an ICD-10 (International Statistical Classification of Diseases and Related Health Problems – Tenth Revision) diagnostic code of MS (ICD-10: G35) were identified by searching the hospital administrative data in SwF as described previously (13). In NK the hospital discharge registry was searched, leading to identification of persons who had visited the hospital either as inpatients or outpatients with the diagnostic code of MS during 2012–2016. Case ascertainment was performed by review of the medical records by A.-L.P. and M.S.-H. in SwF and by J.S. in NK. The incidence and prevalence calculations were based on the cases with a definitive diagnosis. The diagnosis of MS in each case in the incidence cohort had been established by a neurologist or a pediatric neurologist (for patients aged 10–16 years) according to the McDonald 2010 criteria (25).

All patients with a clinically definitive diagnosis of MS were included in the prevalence cohort. Total prevalence, gender-specific, 10-year age-specific and age-adjusted prevalences were calculated per 100,000 population (aged ≥ 10 years) at the end of 2016. Incidence figures were calculated per 100,000 person-years in age group 10–69 years. All new MS cases identified over the five-year study period were included in the incidence cohort. We also identified an 83-year-old male patient with a new diagnosis of primary-progressive multiple sclerosis (PPMS) during the study period. He was not included in the incidence cohort. The total incidence of MS and the gender-specific, 10-year age-specific and age-adjusted incidences of MS were calculated. The diagnostic delay was reported in years. Mann-Whitney's U-test was used to compare the duration of the diagnostic delay between the genders. Incidence and prevalence rates were standardized for age by a direct method. The standard population is the European standard population (ESP) and the World Health Organization (WHO) standard population.

According to Finnish law, ethics committee approval was not needed since the study was based on administrative register data and did not involve any contact with patients. The study was approved by the Turku University Hospital Clinical Research Services and North Karelia Central Hospital Research Administration. The data processing practices followed the EU Data Protection Directive rules (permissions numbers T16/2017 for SwF and 1716/13.00.01.01/2017 for NK). This manuscript adheres to the applicable STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.

Results

Prevalence

At the end of 2016, there were 1,184 persons (70.4% females) with an ICD-10 diagnosis code of MS in SwF and 253 persons (67.2% females) in NK. The overall crude prevalence in the population aged ≥ 10 years was 275/100,000 (95% CI 260–291) in SwF and 167/100,000 (95% CI 146–187) in NK. The prevalence of MS among males was 168/100,000 (95% CI 150–186) in SwF and 110/100,000 (95% CI 86–134) in NK and among females 377/100,000 (95% CI 351–402) in SwF and 233/100,000 (95% CI 191–259) in NK. The combined crude prevalence of SwF and NK was 247/100,000 (95% CI 234–260); 153/100,000 (95% CI 138-167) among males and 337/100,000 (95% CI 316–358) among females. The European standardized prevalence was 280/100,000 (95% Cl 264-296) in SwF and 168/100,000 (95% Cl 148-190) in NK. Prevalence was highest among people aged 40-49 years (Figure 2). The WHO standardized prevalence rate was 247/100,000 (95% Cl 232-262) in SwF and 150/100,000 (95% Cl 131-171) in NK.

Incidence

During the study period (1 January 2012 through 31 December 2016), 211 new MS diagnoses were made in SwF. The mean age of the patients was 37.0 years (range 15–69 years). Relapsing-remitting multiple sclerosis (RRMS) was diagnosed in 186 patients (88.2%), PPMS in 24 (11.4%) and secondary-progressive multiple sclerosis (SPMS) in 1 (0.5%). A total of 59 of the patients were male (mean age at diagnosis 38.3 years, SD 11.6) and 152 were female (mean age 36.5 years, SD 11.6). The female/male ratio in SwF was 2.58. In NK, there was no gender difference (F/M ratio 0.96); 25 male (mean age 35.5 years, SD 11.5) and 24 female (mean age 41.2 years, SD 13.2) patients were diagnosed during the study period. Of these, 42 (86%) had RRMS, 5 (10%) PPMS and 2 (4%) SPMS. The overall annual MS incidence in SwF was 11.7/100,000 person-years (95% CI 10.2–13.3) and in NK 7.8/100,000 person-years (95% CI 5.6–9.9) in the age group 10–69 years. The incidence of MS

among males was 6.6/100,000 person-years (95% Cl 5.0-8.5) in SwF and 7.7/100,000 person-years (95% Cl 5.0-11.3) in NK and among females 16.9/100,000 person-years (95% Cl 14.3-19.8) in SwF and 7.8/100,000 person-years (95% Cl 5.0.117) in NK. The combined crude incidence of SwF and NK was 10.7/100,000 person-years (95% CI 9.4–12.0), 6.9/100,000 person-years (95% CI 5.4–8.3) for male and 14.6/100,000 person-years (95% CI 12.4–16.8) for female patients. Age- and gender-specific incidence rates are shown in Table 1 and Figure 3. The European age-standardized incidence was 12.1/100,000 (95% Cl 10.5–13.8) in SwF and 8.6/100,000 (95% Cl 6.4–11.2) in NK. The WHO standardized rates were 12.6/100,000 (95% Cl 11.0–14.4) (SwF) and 8.8/100,000 (95% Cl 6.6–11.4) (NK).

The diagnostic delay from the onset of symptoms was 2.8 years (range 0–27 years, SD 4.4) in SwF and 4.3 years (range 0–28, SD 4.7) in NK. The duration of the diagnostic delay was similar for both genders in SwF (p=0.246) and in NK (p=0.437, Mann-Whitney's U-test).

Discussion

This study confirms that there are regional differences in MS prevalence and MS incidence in Finland with the southwest showing rates a third higher than the easternmost parts. However, incidence rates differed only in the age group 20-39 years and there were differences in the gender distribution between the regions, suggesting demographic and social explanations. Our results also confirm that Finland is a country of very high MS risk even when areas with probably the smallest risk within the country are included in the analysis.

Finland has been known to be a country of high MS risk and our results support this. The 280/100,000 age-standardized (ESP) prevalence of MS in SwF is among the highest in the world and has increased significantly during the past four years (13). Furthermore, the crude incidence rate of 11.7/100,000 is similar to other high-risk regions in Finland confirming that southwest Finland is a hotspot of multiple sclerosis in Finland. Also, the combined crude prevalence of SwF and NK was surprisingly high (247/100,000) considering that data thus far suggest that MS is not as prevalent in the central parts of Finland as in the southern and western parts (15). The rate was clearly higher than the reported nationwide prevalence rates in Sweden and Norway (5, 7), but lacking standardized Swedish nor Norwegian figures, comparisons will be incomplete. The study from Iceland reported a crude and standardized prevalence of 167/100,000 (12), although they had used the US 2000 population for standardization weighing the younger age groups slightly more than ESP 2013. Nevertheless, the prevalence in Iceland seems to be on the same level as in NK, representing the lower end of the Nordic prevalence range.

The WHO standardization puts more weight on younger age groups and yielded higher incidence rates, while the European standardized prevalence rate was higher implying that population age profiles must be given consideration when rates are compared globally. Innate population-specific differences are nevertheless suggested by the much lower prevalence rates among Asian populations that have similar age structure and economic status (26) compared to European results. Notably, even our crude incidence rates were high compared to those reported, for example, in Latin America (27) and further increased when standardized. Epidemiological comparisons are hampered by a lack of population-standardized data, as reported by a recent review (2). Epidemiologic comparisons could have important scientific implications for the pathogenesis, clinical work and health care planning of MS and we therefore strongly encourage the reporting of standardized epidemiological results.

In this first epidemiological study to cover any part of eastern Finland, we found that, compared to other parts, the easternmost part of the country has a medium-to-low risk of MS. This may, at least partly, be explained by demographic factors since the population of NK is declining and showed a net loss of 4% of its working-aged population from 2001-2012, mainly to southern urban centers. Nearly a half of the loss consisted of well-educated people among whom women were overrepresented. The male population cohort aged 20-39 is 10% larger than that of women, whereas in SwF the difference is only 2%. This is certain to lower the overall figures in NK. Interestingly, the age-specific incidence for women aged 20-39 were quite low in NK, especially compared to SwF, but there was no regional difference for men. Migration and urbanization have affected MS epidemiology on Crete by increasing the impact of many predisposing factors; the effect was especially strong among females who had translocated from the countryside. This led also to a smaller gender ratio in non-urban areas (28). This suggests that the women who move out of NK (to more urban areas such as SwF) are or become more susceptible to MS compared to those who stay and warrants further studies.

Genetic factors may also be at play as there is a substantial genetic difference between Finns living in the eastern and western parts of the country (19), possibly due to long-term genetic drift (20). There may also be regional differences in lifestyle and environmental factors known to influence MS risk such as those affecting vitamin D levels and UV-radiation exposure (29, 30) and EBV-infection rates (31). Unfortunately, there is no data available on these. Smoking is a risk for MS and females aged 20–34 years are more often smokers in eastern and northern Finland than in western or southern Finland (no difference for males) (32), counterintuitively to the east-west MS gradient we observed.

In Finland, MS is exclusively diagnosed and mostly treated by neurologists working in public healthcare, which is why we believe that in this study there is full coverage of the MS patients who fulfill the diagnostic criteria. All MS diagnoses in the incidence cohort were made by a neurologist or pediatric neurologist (age group 10–16 years) according to the revised McDonald criteria, which have been validated also for children and adolescents, particularly for those older than 11 years (33, 34). We also scrutinized all the patient records in the prevalence and incidence cohort to confirm the diagnoses. Compared to adult-onset MS, pediatric MS is more difficult to diagnose, especially in early childhood (35) and children and adolescents may be underdiagnosed. However, a recent study from Ontario found crude incidence and prevalence rates of adolescent MS very similar to our data although the lack of widely used standard population in the Canadian study makes the comparison tentative (34).

Within Finland, there are regional differences in availability of and accessibility to health care services, especially of the private sector. This may affect the east-west gradient we have observed in this study. This may also explain reported difference in diagnostic delay. It is possible that the presence of a well-developed private sector, a university hospital and neurologists specifically specialized in MS may result in higher incidence and prevalence figures in SwF compared to NK with a central hospital clinic staffed with less than 10 general neurologists and little private sector neurology services available. However, considering the chronic nature of the disease, these factors are more likely to affect the disease status when the diagnosis is made than the epidemiologic figures.

The search methods differed slightly in the two regions. In NK, most PPMS patients and those RRMS patients who have chosen not to initiate disease-modifying treatment are followed up in municipal health centers after diagnosis. These patients are not identified by a time-limited search of hospital records and therefore the MS prevalence figures in NK represent a minimum estimate. However, this slight difference between the search methods does not affect the incidence rates, and the

reported difference between the incidence rates, along with our clinical experience, suggests that any error in the NK prevalence rate would be minute. Our study includes only two hospital districts in Finland, comprising over 11% of the country's population. Our study is by population and geography the most comprehensive epidemiological MS investigation made in Finland for 25 years (16) but a further nationwide study is needed. Our study is retrospective, and the duration of follow-up was rather short for condition like MS, only 5 years. However, it does show an increasing prevalence of MS compared to the result of the previous study in SwF from 2012 (13).

To conclude, our study shows that there is a clear difference between southwestern and eastern parts of Finland regarding the prevalence and incidence of MS which may result from demographic differences. There is a very high prevalence and incidence of MS, especially in the high-risk region of southwest Finland.

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Conflicts of interest

Anna-Leena Pirttisalo: has received congress fee covering by Sanofi Genzyme.

Jussi O.T. Sipilä: has received honoraria (Pfizer, Merck, Sanofi Genzyme), travel grants and congress fee covering (Orion Corporation, Abbvie, Lundbeck, Merck Serono, Sanquin, NordicInfucare) and holds shares (Orion Corporation).

Merja Soilu-Hänninen: has received congress fee covering, investigator fees and honoraria for lectures or advisory boards (Biogen, Merck, Novartis, Roche, Sanofi- Genzyme, Teva).

References

1. Koch-Henriksen N, Sørensen PS. The changing demographic pattern of multiple sclerosis epidemiology. Lancet Neurol 2010;9(5):520-532.
2. Kingwell E, Marriott JJ, Jetté N et al. Incidence and prevalence of multiple sclerosis in Europe: A systematic review. BMC Neurol 2013;13.
3. Alonso A, Hernan MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. Neurology 2008;71(2):129-135.
4. Simpson S, Blizzard L, Otahal P, Van Der Mei I, Taylor B. Latitude is significantly associated with the prevalence of multiple sclerosis: A meta-analysis. J Neurol Neurosurg Psychiatry 2011;82(10):1132-1141.
5. Ahlgren C, Odén A, Lycke J. High nationwide prevalence of multiple sclerosis in Sweden. Mult Scler J 2011;17(8):901-908.
6. Ahlgren C, Odén A, Lycke J. High nationwide incidence of multiple sclerosis in Sweden. PLoS One 2014;9(9).
7. Grytten N, Torkildsen Ø, Myhr K-M. Time trends in the incidence and prevalence of multiple sclerosis in Norway during eight decades. Acta Neurol Scand 2015;132:29-36.
8. Vukusic S, Van Bockstael V, Gosselin S, Confavreux C. Regional variations in the prevalence of multiple sclerosis in French farmers. J Neurol Neurosurg Psychiatry 2007;78(7):707-709.
9. Petersen G, Wittmann R, Arndt V, Göpffarth D. Epidemiology of multiple sclerosis in Germany: Regional differences and drug prescription in the claims data of the statutory health insurance. Nervenarzt 2014;85(8):990-998.
10. Bulman DE, Ebers GC. The geography of MS reflects genetic susceptibility. J Trop Geogr Neurol 1992;2(2):66-72.
11. Dilokthornsakul P, Valuck RJ, Nair KV et al. Multiple sclerosis prevalence in the United States commercially insured population. Neurology 2016;86(11):1014-1021.

12. Elíasdóttir Ó, Kjartansson Ó, Olafsson E. Prevalence of Multiple Sclerosis in Iceland. Neuroepidemiology 2018;51(1-2):50-56.

13. Åivo J, Kurki S, Sumelahti ML, Hänninen K, Ruutiainen J, Soilu-Hänninen M. Risk of osteoporotic fractures in multiple sclerosis patients in southwest Finland. Acta Neurol Scand 2017;135(5):516-521.

14. Kinnunen E. Multiple sclerosis in Finland: evidence of increasing frequency and uneven geographic distribution. Neurology 1984;34(4):457–461.

15. Sarasoja T, Wikström J, Paltamaa J, Hakama M, Sumelahti ML. Occurrence of multiple sclerosis in central Finland: A regional and temporal comparison during 30 years. Acta Neurol Scand 2004;110(5):331-336.

16. Sumelahti ML, Tienari PJ, Wikstrom J, Palo J, Hakama M. Increasing prevalence of multiple sclerosis in Finland. Acta Neurol Scand 2001;103(3):153-158.

17. Sumelahti ML, Tienari PJ, Hakama M, Wikström J. Multiple sclerosis in Finland: Incidence trends and differences in relapsing remitting and primary progressive disease courses. J Neurol Neurosurg Psychiatry 2003;74(1):25-28.

18. Krökki O, Bloigu R, Reunanen M, Remes AM. Increasing incidence of multiple sclerosis in women in Northern Finland. Mult Scler 2011;17(2):133-138.

19. Salmela E, Lappalainen T, Fransson I et al. Genome-wide analysis of single nucleotide polymorphisms uncovers population structure in Northern Europe. PLoS One 2008;3(10).

20. Palo JU, Ulmanen I, Lukka M, Ellonen P, Sajantila A. Genetic markers and population history: Finland revisited. Eur J Hum Genet 2009;17(10):1336-1346.

21. Sumelahti ML, Tienari PJ, Wikström J, Palo J, Hakama M. Regional and temporal variation in the incidence of multiple sclerosis in Finland 1979-1993. Neuroepidemiology 2000;19(2):67-75.

22. Holmberg M, Murtonen A, Elovaara I, Sumelahti ML. Increased Female MS Incidence and Differences in Gender-Specific Risk in Medium- and High-Risk Regions in Finland from 1981-2010. Mult Scler Int 2013;2013:182516.

23. Sumelahti ML, Holmberg MHA, Murtonen A, Huhtala H, Elovaara I. Increasing Incidence in Relapsing-Remitting MS and High Rates among Young Women in Finland: A Thirty-Year Follow-Up. Mult Scler Int 2014;2014:1-8.

24. Statistics Finland. http://www.stat.fi/org/index_en.html. Accessed August 27, 2018.

25. Polman CH, Reingold SC, Banwell B et al. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. Ann Neurol 2011;69(2):292-302.

26. Eskandarieh S, Heydarpour P, Minagar A, Pourmand S, Sahraian MA. Multiple Sclerosis Epidemiology in East Asia, South East Asia and South Asia: A Systematic Review. Neuroepidemiology 2016;46(3):209-221.

27. Cristiano E, Rojas JI. Multiple sclerosis epidemiology in Latin America: An updated survey. Mult Scler J – Exp Transl Clin 2017;3(2):205521731771505.

28. Kotzamani D, Panou T, Mastorodemos V et al. Rising incidence of multiple sclerosis in females associated with urbanization. Neurology 2012;78(22):1728-1735.

29. Bjørnevik K, Riise T, Casetta I et al. Sun exposure and multiple sclerosis risk in Norway and Italy: The EnvIMS study. Mult Scler J 2014;20(8):1042-1049.

30. Ascherio A, Munger KL, Simon KC. Vitamin D and multiple sclerosis. Lancet Neurol 2010;9(6):599-612.

31. Olsson T, Barcellos LF, Alfredsson L. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. Nat Rev Neurol 2016;13(1):26-36.

32. Shemeikka R, Rinne H, Saares A, Murto J, Kaikkonen R. Alueelliset erot nuorten aikuisten terveydessä ja elintavoissa Suomessa 2012–2013. National Institute for Health and Welfare 2014. http://www.julkari.fi/handle/10024/116074. Accessed April 1, 2018.

33. Waldman A, Ghezzi A, Bar-Or A, Mikaeloff Y, Tardieu M, Banwell B. Multiple sclerosis in children: an update on clinical diagnosis, therapeutic strategies, and research. Lancet Neurol 2014;13(9):936-948.

34. Marrie RA, O'Mahony J, Maxwell C et al. Incidence and prevalence of MS in children: A population-based study in Ontario, Canada. Neurology 2018;91(17):1579-1590.

35. Yeshokumar AK, Narula S, Banwell B. Pediatric multiple sclerosis. Curr Opin Neurol 2017;30(3):216-221.

Figure legends:

Figure 1. Map of Finland showing the hospital districts involved in the study. 1. Southwest Finland 2. North Karelia.

Figure 2. Age-specific crude prevalence rates and standardized (ESP) rates of MS by region on December 31, 2016. ESP, European standard population.

Figure 3. Age-specific crude incidence rates and standardized (ESP) rates of MS by region in 2012–2016. ESP, European standard population.

Table 1. Age- and gender-specific crude incidence rates and standardized (ESP) rates of MS in Southwest Finland and North Karelia in 2012-2016. CI, confidence interval; ESP, European standard population.

		Southwest Finland			North Karelia		
Age group		Diagnoses	Population	Crude incidence (95% CI)	Diagnoses	Population	Crude incidence (95% CI)
10-19	all	4	254379	1.6 (0.4-4.0)	1	89121	1.1 (0-6.3)
	male	0	130366	0 (0-2.8)	0	45524	0 (0-8.1)
	female	4	124013	3.2 (0.9-8.3)	1	43597	2.3 (0.1-12.8)
20-29	all	56	301425	18.6 (14.0-24.1)	14	100971	13.9 (7.6-23.3)
	male	15	151613	9.9 (5.5.16.3)	9	53103	16.9 (7.7-32.2)
	female	41	149812	27.4 (19.6-37.1)	5	47868	10.4 (3.4-24.4)
30-39	all	78	297312	26.2 (20.7-32.7)	12	88196	13.6 (7.0-23.8)
	male	22	150259	14.6 (9.2-22.2)	8	46388	17.2 (7.4-34.1)
	female	56	147053	38.1 (28.8-49.5)	4	41808	9.6 (2.6-24.5)
40-49	all	40	296810	13.5 (9.6-18.4)	12	90745	13.2 (6.8-23.1)
	male	11	150135	7.3 (3.7-13.1)	4	45992	8.7 (2.4-22.3)
	female	29	146675	19.8 (13.2-28.4)	8	44753	17.9 (7.7-35.2)
50-59	all	24	315085	7.6 (4.9-11.3)	8	129523	6.2 (2.7-12.2)
	male	8	156167	5.1 (2.2-10.1)	4	65670	6.1 (1.7-15.6)
	female	16	158918	10.1 (5.8-16.3)	4	63853	6.3 (1.7-16.0)
60-69	all	9	331887	2.7 (1.2-5.1)	2	133149	1.5 (0.2-5.4)
	male	3	159580	1.9 (0.4-5.5)	0	68677	0 (0-5.4)
	female	6	172307	3.5 (1.3-7.6)	2	64472	3.1 (0.4-11.2)
Standardized (ESP)	all	12.1 (10.5-13.8)			8.6 (6.4-11.2)