Differences in methylphenidate use between immigrants and Spaniards in the child population of Aragon, Spain: a retrospective study

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WORD COUNT: 2277 words.

Abstract

The aim of this research is to study the differences in methylphenidate use in children from different ethnic groups in the region of Aragon, Spain. Differences in the use of methylphenidate between both group of children, immigrants and Spanish nationals, were assessed based on the total number of methylphenidate prescriptions made out for all children in Aragon in 2008 (N=98,837). We have used Defined Daily Doses and the Defined Daily Doses per 1000 inhabitants per Day. Defined Daily Doses per 1000 inhabitants per Day of methylphenidate use was 18.49 in Spanish boys compared with 2.70 in immigrant boys, and 5.48 in Spanish girls vs. 0.83 in immigrant girls. All differences between groups were statistically significant (p<0.001). This study confirms that methylphenidate use is higher in a local population than an immigrant population. Western European and North American children show the highest use, followed by Latin Americans and Eastern Europeans.

Keywords:

Immigration, methylphenidate, Attention Deficit/Hyperactivity Disorder

Introduction

Attention Deficit/Hyperactivity Disorder is the most common chronic behavioural disorder in children and adolescents[1]. This condition is the origin of many disturbances in the social, emotional and cognitive development of the child[2], which cause important morbidity and disability both in the patient and the family[3]. Attention Deficit/Hyperactivity Disorder is not limited to childhood; many symptoms remain up to adult life[1, 2, 4-6] and can produce important limitations in everyday life that are also associated with other psychiatric disorders over an individual's lifetime[1]. The prevalence of Attention Deficit/Hyperactivity Disorder is calculated at about 5% with an enormous geographical heterogeneity[7, 8]. In Spain, prevalence of Attention Deficit/Hyperactivity Disorder ranges between 1.2 and 8% [9]. The reasons for this heterogeneity are unknown[1, 2, 4, 10-13]. In a recent meta-analysis studying differences in prevalence according to place of birth, prevalence of Attention Deficit/Hyperactivity Disorder in European and American children was similar and significantly higher than the prevalence in African and Middle Eastern children. Differences in prevalence can be the result of methodological differences in published studies[7] or due to discrepancies in diagnostic criteria[14].

Owing to the increasing number of diagnosed and treated cases of Attention Deficit/Hyperactivity Disorder [15], some authors warn of the possible overdiagnosis and overtreatment of this disorder, while others even doubt its very existence. This condition has been included within the concept of "disease mongering", a term that refers to conditions not considered to be disorders until recently, and which were believed to have been invented by the pharmaceutical industry seeking economic gain[16-18]. The diagnosis and treatment of Attention Deficit/Hyperactivity Disorder seems to be influenced by cultural factors. A disorder is not only a biological phenomenon, but also the experience of a patient and his/her family influenced by the culture and the society in which the condition develops[19-21].

Some studies show that 56% of children diagnosed with Attention Deficit/Hyperactivity Disorder receive some sort of drug treatment [10]. The use of methylphenidate, the most common treatment for Attention Deficit/Hyperactivity Disorder [12], in different ethnic groups can be both an indirect marker of the prevalence of the disorder in each group and the expression of cultural differences in its management. Disorder. The aim of this research is to study the differences in methylphenidate use in children from different ethnic groups in the region of Aragon, Spain.

Methods

Design

This is a retrospective, observational study on the prescription-based use of methylphenidate, stratified by age and gender, comparing two populations of children residing in Aragon: immigrants and Spanish nationals.

Setting and study sample

Aragon is one of the 17 autonomous regions into which Spain is divided, with a population of 1,300,000 inhabitants. The population studied in this research includes the child population of Aragon, aged 6-14 years, entitled to health care provided by the Aragonese Health Service. This entitlement is demonstrated by a Health Identification Card. The threshold of 6 years was chosen because this is the minimum age limit used by clinical guides to accept the diagnosis of Attention Deficit/Hyperactivity Disorder and to recommend drug treatment. In order to give an operational definition of immigrant, we have used the legal category of foreign national. Although both terms may be used interchangeably in this context [(22)], "immigrant" is used throughout the text defined as any person of any nationality other than Spanish. Immigration is a recent phenomenon in Spain and most of the immigrants residing in Spain, now making up 15% of the population, have arrived during the last decade[(23)].

Measurements

Differences in the use of methylphenidate between both group of children, immigrants and Spaniards, were assessed based on the total number of methylphenidate prescriptions made out for all children in Aragon in 2008. Data were obtained from Aragonese Health Service Pharmacy Service data. All prescriptions delivered by this service that were totally or partially subsidized by the Spanish National Health System were included.

We have used the variables of Defined Daily Doses, which is the average maintenance daily dosage for a specific drug used for its main indication, and Doses per 1000 inhabitants per Day, which is defined as the number of Defined Daily Doses per 1000 inhabitants and per day. The latter gives an idea of what proportion of the population is treated daily with the usual dosage of a specific drug.

Procedure

As described in a previous paper[24], pharmaceutical expense was analysed from the Aragonese Health Service Pharmacy Service pharmaceutical billing database statistics for 2008 covering all publicly-subsidized prescription drugs dispensed by pharmacies. These do not include drugs prescribed by private practices or those dispensed without prescription. Nor do they include drugs utilized in hospitals or dispensed there to outpatients (very specific treatments for particular diseases and conditions). Drugs corresponding to immunization campaigns were also excluded from this study. The data collected are cross-sectional. Long-term drug utilization patterns were not studied.

In order for their bills to be settled by the Pharmacy Service, pharmacists must use the computerized data-collection system to record the details of the prescribed drug (national drug formulary code), those of the prescribing doctor (health area identification code and registration number) and those of the patient for whom the drug is prescribed (personal identification code), among others. By matching the personal identification code with the information from a health identification card, which provides details of the cardholder's age, sex, country of birth and status (Spanish or foreign national), data can be obtained on prescription-drug utilization by age and sex of the local Spanish and immigrant population. By matching the drug code with the drug formulary database, Digitalis, information can be obtained regarding the active ingredient, Anatomical Therapeutic Chemical classification therapeutic main group and subgroup, the content in Defined Daily Doses in each package needed to calculate the Defined Daily Doses per 1000 inhabitants per Day and on whether a generic drug has been dispensed.

We associated patients' identification data with their Health Identification Card in order to obtain information on their age, gender, country of birth and prescribed drug use. We related the drug code with the drug database in order to know its active principle and treatment subgroup according to the Anatomical Therapeutic Chemical Classification[24], and the Defined Daily Doses from each drug dosage form to calculate the Defined Daily Doses per 1000 inhabitants per Day. The study was carried out between January and December 2008. It was approved by the Ethical Committee of Aragon.

Statistical analysis

The sample included in the study consists of all children aged 6-14 years living in the autonomous region of Aragon. Mean use by groups, immigrants and Spanish nationals, stratified by gender and age, was compared using Student-*t* test for independent samples. Frequency rates for primary care visits were calculated adjusting for age and sex of the immigrant and Spanish national populations. Rates were also standardized by direct method, taking the Spanish population as a benchmark, according to data from the Spanish National Institute of Statistics (www.ine.es) on 1 January 2008, in order to prevent differences from appearing that are caused by population distribution (gender and age). Differences in methylphenidate use between immigrants and Spanish nationals were analysed by means of *t*-tests for independent samples weighted by sample size.

Results

The total sample studied included 98,837 children, 15,516 (16%) of whom were immigrants. The distribution of the population by place of birth, gender and age is summarized in Table 1. A total of 23,331 prescriptions of methylphenidate for patients aged 6-14 years were analysed.

Methylphenidate use by gender, age and immigrant status is showed in Figure 1. Defined Daily Doses per 1000 inhabitants per Day of methylphenidate in Spanish boys was 18.49 compared with 2.70 in immigrant boys, while Defined Daily Doses per 1000 inhabitants per Day in Spanish girls was 5.48 vs. 0.83 in immigrant girls. All differences between groups were statistically significant ($p<0.001$ for both boys and girls). Rates of metylphenidate use in Spanish boys were 6.8 times higher than in immigrant boys and 6.8 times higher in Spanish girls than in immigrant girls. Metylphenidate use by Spanish girls is twice that of immigrant boys. Defined Daily Doses per 1000 inhabitants per Day of non-steroidal anti-inflammatory drugs in Spanish children was 11.05 compared with 7.24 in immigrants (a difference of only 53%).

Rates of metylphenidate use in immigrants by geographical origin are summarized in Figure 2. It can be seen that all immigrant groups show lower Defined Daily Doses per 1000 inhabitants per Day than Spanish children ($p<0.001$). By origin, Western European and North American children show the highest use followed by Latin Americans and Eastern Europeans. Lower rates are found in children born to immigrants in Spain and in Africans. Finally, metylphenidate use by Asians is irrelevant.

Discussion

This is the first study in Spain and one of the few studies worldwide[25] that assesses differences in the psychopharmacological treatment for Attention Deficit/Hyperactivity Disorder between inhabitants of a Western country and immigrant children. Some strengths of the research are the large population studied (N=98,800 children) and the high reliability of the database used. In addition, Spain is a very suitable country for this kind of study owing to the fact that immigration is a recent phenomenon, and that these immigrants, mostly first-generation, have largely not yet assimilated Spanish culture. There are two main limitations to the study: 1.- Only methylphenidate prescriptions were studied. There is another approved treatment for Attention Deficit/Hyperactivity Disorder in Spain, atomoxetine. However, methylphenidate accounts for more than 99% of the total prescriptions for this indication in the Aragonese Health Service. 2.- Our data do not include prescriptions delivered by private practice/hospitals. In Spain, private pharmaceutical consumption makes up 25% of the total[26]. In Aragon, this percentage is probably much lower owing to the comparatively low availability of private health care providers and the use made of them. In any case, if private pharmaceutical consumption is taken into account, differences between immigrants and Spanish nationals would be even higher, given the fact that most users of private health care providers are from the latter group.

Our data show that methylphenidate use is significantly higher in Spanish children than in immigrant children: 6.8 times higher than in boys and in girls. These findings are similar to those described in the other study carried out in the Netherlands, where first-generation immigrants showed higher risk of receiving antidepressant and antipsychotic drug prescriptions but lower risk of receiving Attention Deficit/Hyperactivity Disorder medicationption[25]. Other studies focusing on disorder prevalence rather than prescription drug use confirm that immigrant adolescents in Belgium are more at risk of traumatic events, peer problems and avoidance symptoms, while Spanish adolescents suffer from more anxiety, externalizing problems and hyperactivity [27].

By ethnic origin, Western European and North American children show the highest rates of use followed by Latin Americans and Eastern Europeans. Lower rates are found in Africans and in the children born to immigrants in Spain. Finally, methylphenidate use by Asians is insignificant. As can be seen, ethnic

groups whose cultures have greater similarities to that of Spaniards show higher methylphenidate prescriptions. These differences in prescriptions[28] and even in Attention Deficit/Hyperactivity Disorder prevalence[29-31] depending on ethnic origin have been previously reported. Some authors have interpreted these relevant differences in worldwide prevalence to mean that Attention Deficit/Hyperactivity Disorder is a cultural condition mainly limited to Western countries[16]. This could explain higher prevalence in ethnic groups with or closer to Western culture such as Western Europeans and Eastern Europeans, North Americans and Latin Americans. However, ethnic groups with more divergent cultures, such as Africans and Asians, show lower rates of use. It has been previously demonstrated that Asians have lower rates of use of any type of mental health-related service than the general population[32], probably owing to their reluctance to use Western medicine instead of their own traditional treatments. Other possible explanations would be that Attention Deficit/Hyperactivity Disorder is a chronic disorder and immigrants are more used to seeking treatment only for acute disorders. Prevention and adherence to long-term treatments is more difficult in immigrant populations; therefore, treatment withdrawal over time would be significantly higher than in the Spanish population[23, 33].

In our study, the rate of methylphenidate use was found to be higher in boys than in girls, both in immigrants and Spaniards: The finding was 18.49 in Spanish boys vs 5.48 in Spanish girls, while for immigrants it was 2.70 in boys vs 0.83 in girls. This expected finding has been consistently described in medical research[3, 34, 35], with a boy/girl ratio of 4: 1[1, 5], quite similar to what we have found in our study. Most authors think that this difference is due to boys showing a more externalizing and disruptive symptomatology and producing more consultations, whereas Attention Deficit/Hyperactivity Disorder in girls is expressed as attention deficit [36, 37]. It should be pointed that our lower rate of metylphenidate use in immigrants in Spain is not caused by lower use of health services. For instance, Defined Daily Doses per 1000 inhabitants per Day of non-steroidal anti-inflammatory drugs in Spanish children was 11.05 compared with 7.24 in immigrants, which implies a difference of only 53%. In a previous paper [24], we reported that general prescription-drug use among Spanish children is only 72% higher than that of immigrants.

In conclusion, this is the first study in medical research that confirms that methylphenidate use is higher in the Spanish population than in immigrants in Spain. Lower use of health resources and prescription-

drug based treatment has been repeatedly described in immigrants, and more so in recent ones[38]. In addition to cultural reasons for this behaviour, it seems that an overtreatment of Attention Deficit/Hyperactivity Disorder in Western countries may be an additional explanation. New research studies for the specific purpose of studying this fact would be necessary.

Acknowledgments

This work has beeen possible thanks to the Red de Investigación en Actividades de prevención y Promoción de la salud (REDIAPP-06/018), nodo de Aragón, from Instituto de Salud Carlos III, Madrid, Spain.

Authors contribution/roles

RMMC: conceived of the study, and participated in its design and coordination section.

JGC: participated in the design and prepared the manuscript.

LLGF: participated in the design of the study and performed the statistical analysis.

RMB: participated in design and prepared the manuscript.

JAG: participated in data analysis.

All authors read and approved the final manuscript.

Declaration of conflicting interests

The authors declare that they have no competing interests.

Financial disclosure/funding

This study was funded by the "Programa de uso Racional del Medicamento" (2007), from Aragon Health Sciences Institute (PIURM07/04).

Ethical approval

This research has been aproved by Ethic Committe of Clinic Research of Aragón (November 5, 2008) : Acta nº CP05/11/2008.

References

1. Houshian S, Poulsen S, Riegels-Nielsen P. Bone and joint tuberculosis in Denmark: increase due to immigration. *Acta Orthop Scand*. 2000;71(3):312-5.

2. Cardo E, Servera M. Trastorno por deficit de atencion/hiperactividad: estado de la cuestion y futuras lineas de investigacion. *Rev Neurol*. 2008 Mar 16-31;46(6):365-72.

3. Huss M, Holling H, Kurth BM, et al. How often are German children and adolescents diagnosed with ADHD? Prevalence based on the judgment of health care professionals: results of the German health and examination survey (KiGGS). *Eur Child Adolesc Psychiatry*. 2008 Dec;17 Suppl 1:52-8.

4. Biederman J, Faraone SV. Attention-deficit hyperactivity disorder. *Lancet*. 2005 Jul 16-22;366(9481):237-48.

5. Cornejo JW, Osio O, Sanchez Y, et al. Prevalencia del trastorno por deficit de atencion-hiperactividad en ninos y adolescentes colombianos. *Rev Neurol*. 2005 Jun 16-30;40(12):716-22.

6. Wilens TE, Dodson W. A clinical perspective of attention-deficit/hyperactivity disorder into adulthood. *J Clin Psychiatry*. 2004 Oct;65(10):1301-13.

7. Polanczyk G, de Lima MS, Horta BL, et al. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry*. 2007 Jun;164(6):942-8.

8. García Campayo J, Santed Germán MA, Cerdán Lanero C, et al. Tratamiento del trastorno por déficit de atención. *Aten Primaria*. 2007;39:669-72.

9. Rodriguez Molinero L, Lopez Villalobos JA, Garrido Redondo M, et al. Estudio psicométrico-clínico de prevalencia y comorbilidad del trastorno por déficit de atención con hiperactividad en Castilla y León (España). *Rev Pediatr Aten Primaria*. 2009;11:251-70.

10. Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder--United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2005 Sep 2;54(34):842-7.

11. Faraone SV, Sergeant J, Gillberg C, et al. The worldwide prevalence of ADHD: is it an American condition? *World Psychiatry*. 2003 Jun;2(2):104-13.

12. Miller AR, Lalonde CE, McGrail KM, et al. Prescription of methylphenidate to children and youth, 1990-1996. *CMAJ*. 2001 Nov 27;165(11):1489-94.

13. Perilla JL, Wilson AH, Wold JL, et al. Listening to migrant voices: focus groups on health issues in south Georgia. *J Community Health Nurs*. 1998;15(4):251-63.

14. Sciutto MJ, Eisenberg M. Evaluating the evidence for and against the overdiagnosis of ADHD. *J Atten Disord*. 2007 Sep;11(2):106-13.

15. Criado Alvarez JJ, Romo Barrientos C. Variabilidad y tendencias en el consumo de metilfenidato en España. Estimación de la prevalencia del transtorno por déficit de atención con hiperactividad. *Rev Neurol*. 2003 Nov 1-15;37(9):806-10.

16. Moynihan R, Doran E, Henry D. Disease mongering is now part of the global health debate. *PLoS Med*. 2008 May 27;5(5):e106.

17. Lacasse JR, Leo J. Questionable advertising of psychotropic medications and disease mongering. *PLoS Med*. 2006 Jul;3(7):e321.

18. Mintzes B. Disease mongering in drug promotion: do governments have a regulatory role? *PLoS Med*. 2006 Apr;3(4):e198.

19. Bengi-Arslan L, Verhulst FC, van der Ende J, et al. Understanding childhood (problem) behaviors from a cultural perspective: comparison of problem behaviors and competencies in Turkish immigrant, Turkish and Dutch children. *Soc Psychiatry Psychiatr Epidemiol*. 1997 Nov;32(8):477-84.

20. Davies MM, Bath PA. The maternity information concerns of Somali women in the United Kingdom. *J Adv Nurs*. 2001;36(2):237-45.

21. Munroe-Blum H, Boyle MH, Offord DR, et al. Immigrant children: psychiatric disorder, school performance, and service utilization. *Am J Orthopsychiatry*. 1989 Oct;59(4):510-9.

22. Malmusi D, Jansa JM, del Vallado L. Recomendaciones para la investigacion e informacion en salud sobre definiciones y variables para el estudio de la poblacion inmigrante de origen extranjero. *Rev Esp Salud Publica*. 2007 Jul-Aug;81(4):399-409.

23. García-Campayo J, C. SC. Salud mental en inmigrantes: el nuevo desafío. *Med Clin(Barc).* 2002;118:187-91.

24. Pen L. Patologías prevalentes en pacientes de etnia china. *Medifam*. 2001;11(7):390-8.

25. Wittkampf LC, Smeets HM, Knol MJ, et al. Differences in psychotropic drug prescriptions among ethnic groups in the Netherlands. *Soc Psychiatry Psychiatr Epidemiol*. 2010 Aug;45(8):819-26.

26. Medicamentos y Farmacia en cifras 07. *Farmacéuticos*. 2008;337:49-57.

27. Derluyn I, Broekaert E, Schuyten G. Emotional and behavioural problems in migrant adolescents in Belgium. *Eur Child Adolesc Psychiatry*. 2008 Feb;17(1):54-62.

28. Hahn BA. Children's health: racial and ethnic differences in the use of prescription medications. *Pediatrics*. 1995 May;95(5):727-32.

29. Pastor PN, Reuben CA. Racial and ethnic differences in ADHD and LD in young school-age children: parental reports in the National Health Interview Survey. *Public Health Rep*. 2005 Jul-Aug;120(4):383-92.

30. Hillemeier MM, Foster EM, Heinrichs B, et al. Racial differences in parental reports of attention-deficit/hyperactivity disorder behaviors. *J Dev Behav Pediatr*. 2007 Oct;28(5):353-61.

31. Miller TW, Nigg JT, Miller RL. Attention deficit hyperactivity disorder in African American children: what can be concluded from the past ten years? *Clin Psychol Rev*. 2009 Feb;29(1):77-86.

32. Abe-Kim J, Takeuchi DT, Hong S, et al. Use of mental health-related services among immigrant and US-born Asian Americans: results from the National Latino and Asian American Study. *Am J Public Health*. 2007 Jan;97(1):91-8.

33. Flores G, Bauchner H, Feinstein AR, et al. The impact of ethnicity, family income, and parental education on children's health and use of health services. *Am J Public Health*. 1999 Jul;89(7):1066-71.

34. Baumgaertel A, Wolraich ML, Dietrich M. Comparison of diagnostic criteria for attention deficit disorders in a German elementary school sample. *J Am Acad Child Adolesc Psychiatry*. 1995 May;34(5):629-38.

35. Biederman J, Kwon A, Aleardi M, et al. Absence of gender effects on attention deficit hyperactivity disorder: findings in nonreferred subjects. *Am J Psychiatry*. 2005 Jun;162(6):1083-9.

36. Ramos Macías L, Poch Páez J, Pérez Arellano JL, et al. Infección parasitaria múltiple importada en una paciente pediátrica: patología del niño inmigrante. *Acta Pediátrica Española*. 2007;65(2):79-81.

37. Rucklidge JJ. Gender differences in ADHD: implications for psychosocial treatments. *Expert Rev Neurother*. 2008 Apr;8(4):643-55.

38. Muennig P, Fahs MC. Health status and hospital utilization of recent immigrants to New York City. *Prev Med*. 2002 Sep;35(3):225-31.

Table 1. Distribution of the sample by gender, age and place of birth

BOYS

Age	**Immigrants**	**Nationals**	**Total**
6	858	4,945	5,803
7	917	4,977	5,894
8	952	4,870	5,822
9	942	4,654	5,596
10	902	4,648	5,550
11	885	4,639	5,524
12	891	4,643	5,534
13	849	4,599	5,448
14	874	4,795	5,669
Total	**8,070**	**42,770**	**50,840**

GIRLS

6	825	4,797	5,622
7	873	4,623	5,496
8	861	4,485	5,346
9	883	4,338	5,221
10	849	4,339	5,188
11	768	4,481	5,249
12	810	4,397	5,207
13	794	4,468	5,262
14	783	4,623	5,406
Total	**7,446**	**40,551**	**47,997**

Fig 1 Methylphenidate use measured in DID by age, gender and immigrant status in children (6-14 years). Aragon. Spain. 2008

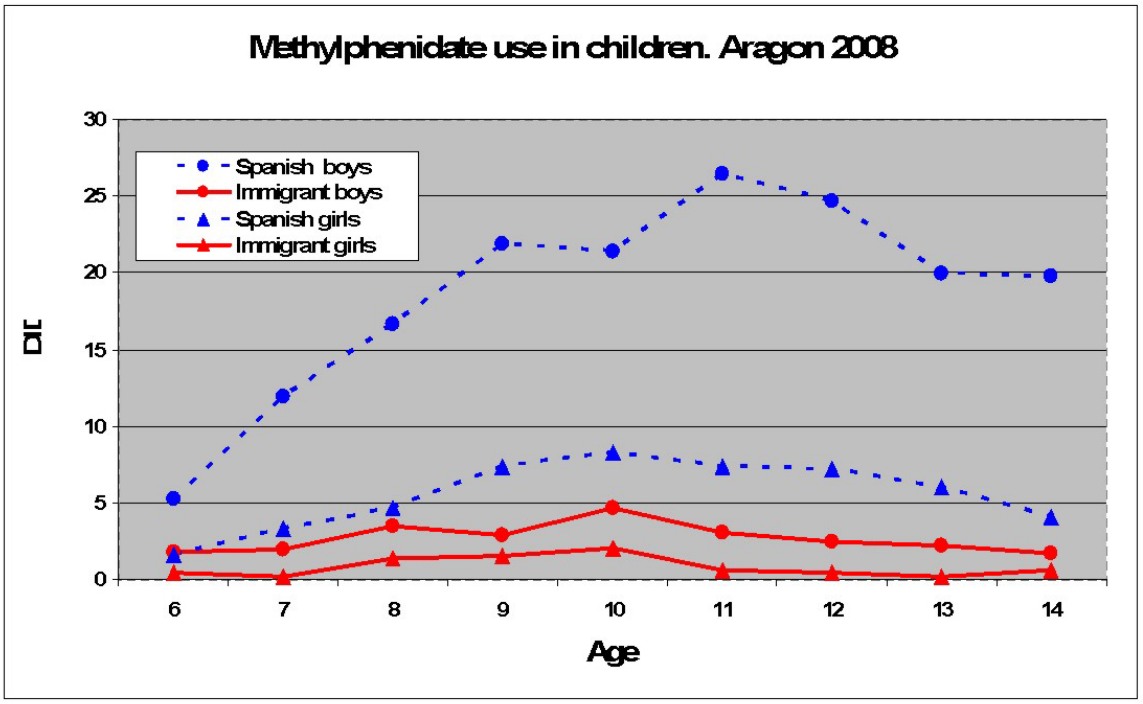
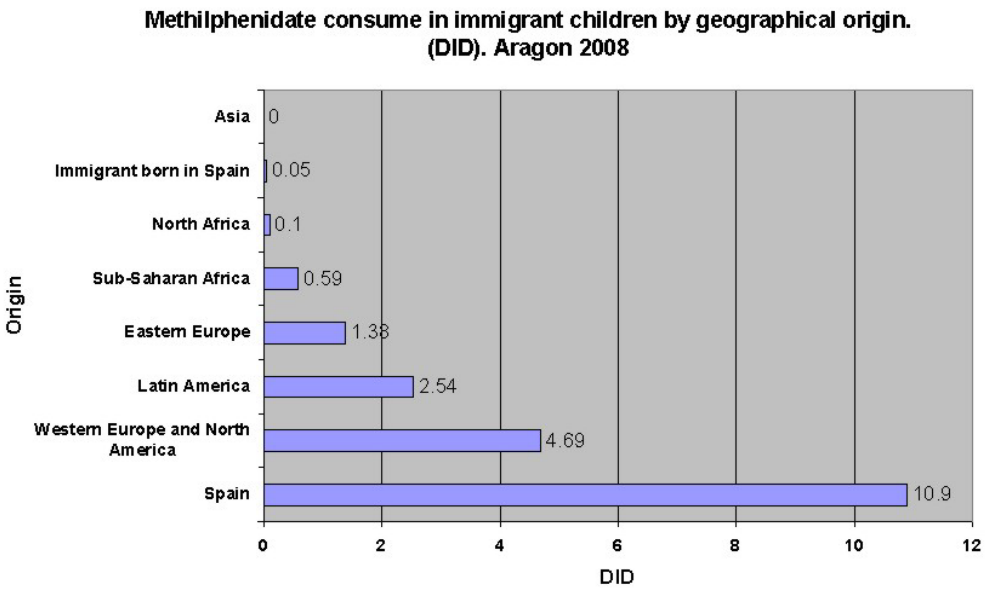


Fig 2 Methylphenidate use in immigrant children (6-14 years) by geographical origin. DID. Aragón, Spain. 2008



DID is defined as the number of DDD (Defined Daily Doses) per 1000 inhabitants and per day.