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Estimating the Burden of Disease for Autism Spectrum Disorders in Spain in 2003

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Abstract Autism Spectrum Disorders (ASD) are lifelong neurodevelopmental disabilities. Burden of Disease is an indicator that provides important information on health status and outcomes such as premature mortality and disability. In order to estimate the burden of disease of ASD in the Spanish population during 2003, we followed the procedures used in the WHO Global Burden of Disease Study. ASD generated 43,928 Disability Adjusted Life Years (DALY) in Spain in 2003, from which 33,797 were attributable to Autistic Disorder and 10,131 were caused by Asperger's Disorder and Pervasive Developmental Disorder-Not Otherwise Specified. DALY could be a useful tool for health policy makers for setting health service priorities, allocating available resources effectively and providing a comparable measure of output for early intervention.

Keywords Pervasive developmental disorders · Autistic spectrum disorders · Burden of disease · Disability adjusted life years · DALY · Epidemiology

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Autism Spectrum Disorders (ASD) are a group of neurodevelopmental conditions with a lifelong developmental disability (Volkmar, 1998). According to the most widely used classification, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 1994), the Pervasive Developmental Disorders (PDD) category includes five conditions: Autistic Disorder, PDD-Not Otherwise Specified (PDD-NOS), Asperger's Disorder, Rett's Disorder and Childhood Disintegrative Disorder. The aetiology of ASD is still unknown, although evidence from families and twin studies has consistently suggested a strong genetic influence (Cook, 1998) probably with multiple interacting both genetic and environmental factors in many cases (Hertz-Picciotto et al., 2006), except for Rett's Disorder, attributable to mutations in the gene encoding methyl-CpG-binding protein-2 (MECP2) in most affected individuals. ASD are characterized by a triad of impairments in social interaction, verbal and nonverbal communication and a lack of flexibility in thinking and behaviour (Roberts, 2003). Autism is not a learning disability, but people with autism often have a learning disability: 70% of the people with autistic disorder have some degree of learning disability and around 7% of the cases with PDD-NOS have from mild to moderate learning disability. People with Asperger's Disorder have an intellectual functioning within the normal range (Fombonne, 1999; Chakrabarti & Fombonne, 2001, 2005).

Autism diagnosis is made on the basis of observed behaviour and although diagnosis is not usually definitive until 5 years of age or more in the case of autistic disorder (Barbaresi, Katusic, Colligan, Weaver, & Jacobsen, 2005) and the Asperger's disorder diagnosis is not usually confirmed until 11 years (Howlin & Asgharian, 1999), first symptoms become visible since 18 months (Chakrabarti & Fombonne, 2005).

The natural history of autism can be modified with an early diagnosis and treatment, especially in those cases with better intelligence quotient and language abilities (Harris & Handleman, 2000; Bibby, Eikeseth, Martin, Mudford, & Reeves, 2001; Gabriels, Hill, Pierce, & Rogers, 2001; Eikeseth, Smith, Jahr, & Eldevik, 2002; Sallows & Graupner, 2005). Early treatment implies a better prognosis for the child and more optimistic expectations for parents. Although it is difficult to measure the outcomes, benefits of early identification and adequate intervention have been sufficiently demonstrated (Dawson & Osterling, 1997; Smith, 1999; Harris & Delmolino, 2002). There is an improvement in communication, language, social interaction and intelligence quotient. It also seems that better results are to be achieved when parents are involved in therapy (Hurth, Shaw, Izeman, Whaley, & Rogers, 1999), when the child is younger (intervention as early as possible) and when intervention is sufficiently intensive.

There are also some medical conditions associated to autism. An epidemiological survey conducted by Fombonne (2005), mentions epilepsy as the most frequent comorbid condition, followed by hearing or visual impairments, cerebral palsy, Down syndrome, tuberous sclerosis and fragile X syndrome, among others.

Regarding autism epidemiology, a possible increase in time trend prevalence has been described. There are differences in the reported incidence and prevalence of the disorder which range from less than 4 per 10,000 in the initial estimate to more than 30 per 10,000 (Centers for Disease Control and Prevention, 2000; Bertrand et al., 2001; Barbaresi et al., 2005; National Autistic Society, 2006). The estimated incidence of ASD in the review by Rutter (2005) is likely to be within the range of 30–60 cases per 10,000. The US Department of Developmental Services reported an important increase in the autism prevalence from 1991 to 1997 (Stokstad, 2001). The reasons for these differences have been postulated to be the inclusion of less restricted criteria for ASD diagnosis—changes in diagnostic criteria and development of the wider concept of the autistic *spectrum*—the different methods used in epidemiological studies; an increasing awareness among physicians and parents of ASD symptoms and the availability of services, rather than possible unidentified new environmental influences or risk factors. In spite of it all, the possibility of a real prevalence increase cannot be ruled out.

Burden of Disease (BoD) is a summary measurement of a population's state of health estimated by Disability-Adjusted Life Years or DALY. This is a health measure that combines the concept of potential years of life lost due to a premature death and the time lived in state of poor health or disability. One DALY represents the loss of one year of equivalent full health and the burden of disease as a measurement of the gap between current health status and an ideal situation where everyone would live into old age free of diseases and disability. Thus, for a disease or a health condition, DALY are calculated as the sum of the years of life lost due to premature mortality (YLL) in the population and the years lived with disability (YLD) for incident cases of that health condition (World Health Organization, 2006).

For instance, if there were 10 deaths of males at age 20, and the life expectancy in the general population at that age was 60 years, then the YLL = 10 deaths * 60 lost years/death = 600 years.

In the same line, one person living to age 100 but totally disabled for all 100 years represents 100 DALY, as does two people living in perfect health, but only to age 30 when 80 was expected.

The utility of these kind of indicators has been well established: analysing the benefits of health interventions; monitoring of changes in a population's state of health; assessment of the relative contribution of different diseases to the total burden of disease in a population; comparisons of health state between different populations, etc; their ability to engage in debate on social value orientations, as well as their application in summary measures, have also been documented in a published book (Murray, Salomon, & Mathers, 2000; Murray, Salomon, Mathers, & Lopez, 2002).

Disability Adjusted Life Years estimates have never been applied before to autism in Spain and we believe it could be a useful tool to approach this disorder. BoD depends on the frequency (incidence) and on the mortality and disability—physical or mental—it entails.

Although a higher mortality risk has been observed in autism compared with the general population, there are no deaths caused directly by the condition. Elevated death rates are due to several causes, including seizures, accidents and respiratory diseases among people with severe learning disability (Shavelle & Strauss, 1998; Shavelle, Strauss, & Pickett, 2001; Shavelle, Strauss, & Day, 2003; Pickett, Paculdo, Shavelle, & Strauss, 2006).

Our aim in this study has been to estimate BoD for ASD, describing its quantitative importance in the Spanish state of health and thus providing a reference for future studies.

Methods

In order to estimate the burden of disease of ASD in the Spanish population we have followed the methods used in the Global Burden of Disease Study (GBD) described by Murray and López (1996) in order to ensure comparability with other studies using the same methodology.

Disability Adjusted Life Years (DALY) are obtained from the addition of two components: years of life lost (YLL) and years lived with disability (YLD). [DALY = YLL + YLD].

According to the available bibliography and the DSM-IV-TR classification, we have focussed our study on Autistic Disorder, Asperger's disorder and PDD-NOS. Rett's Disorder and Childhood Disintegrative Disorder have been excluded from the study due to their low prevalence.

Participants

The Spanish population between 0 and 14 years old in 2003 included in this study was 6,043,479 people (14.5% of the total population), from which 3,105,283 were men (14.7% of the total male population) and 2,938,196 were women (13.6% of the female population). The population distribution by age groups was obtained from the Instituto Nacional de Estadística (INE, Spanish National Statistics Institute, 2006).

Procedures

a) The general calculation formula for YLL is:

$$YLL = \sum_{0}^{L} Di * Ei$$

where (D_i) is the number of dead autistic people at age (i), (E_i) is the remaining life expectancy at each year of age for the general population, and L is the life expectancy obtained from a model life table, namely the Princeton Model Life Table with the ''New West'' model, level 26 (Coale & Guo, 1989), that has been used in the Global Burden of Diseases Study (Murray & López, 1996).

According to the International Statistical Classification of Diseases, 10th Revision (World Health Organization, 1993) and following the INE, there were no deaths in 2003 in Spain caused by Childhood Autism, Atypical autism, Asperger's syndrome or PDD-NOS (F84.0, F84.1, F84.5 and F84.9) as primary cause of death. For this reason, we decided to adapt the standardized mortality rate from the California Developmental Disability System (Pickett et al., 2006) to the Spanish population distribution by age groups.

The interpolated life expectancy for the different age groups was estimated from the observed mean age at death in each age interval and the life expectancy at the different intervals. The initial life expectancy figures at birth for the first interval (0–4 years old) would be 82.5 years for women and 80 years for men and 80.93 for both sexes.

b) The general formula to quantify YLD is

$$YLD = \sum_{0}^{L} Ni * Ii * Ti * d$$

where (N_i) is the population at risk for ASD at each age (i); (I_i) is ASD incidence referred to some population unit (per 10,000 in our case) in each age group (i) (N_i * I_i = total number of cases); (T_i) is the average remaining duration of the condition for each age (i) and (d) is the level of disability (condition severity). In most of the diseases, (d) takes an unique value for the whole disease. Thus, in order to calculate YLD the following data were needed:

1. ASD (I_i) incidence by age group: Taking into account that there is not a population registry of this condition in Spain—nor specific accurate bibliography—due to difficulties in defining cases and diagnosing (Posada-De la Paz, Ferrari-Arroyo, Touriño, & Boada, 2005), incidence data have been collected from the Western Australia Register for Autism Spectrum Disorders (Glasson, 2002; Williams et al., 2005) after a comprehensive literature revision of the studies on autism epidemiology (Fombonne, 1999; Powell et al., 2000; Chakrabarti & Fombonne, 2001; Wing & Potter, 2002; Barbaresi et al., 2005; Chakrabarti & Fombonne, 2005; Fombonne, 2005; Posada et al., 2005; Rutter, 2005; Jick, Beach, & Kaye, 2006). The incidence rate offered by the Australian study was adapted to our population. Given that the Australian study provided data by age groups but not by sex, we had to join both sexes in one category to make our calculations. There are few studies on the incidence of ASD (Wing & Potter, 2002; Fombonne, 2005), but we preferred to obtain incidence data directly from former studies rather than to make an estimate based on prevalence rates, since differences in prevalence rates vary greatly in the literature. The epidemiological study carried out by Williams et al. (2005) in several Australian regions checked up on new diagnoses of autistic disorder and PDD-NOS or Asperger's Disorder according to DSM-IV criteria in children younger than 14 by age groups. In one of the regions, data was obtained from a prospective registry and in the other two by active surveillance. Since some differences regarding findings were stated between both methods, likely caused by different epidemiological approaches, we preferred to use data from the registry in Western Australia. Acknowledging the higher ASD incidence of this latter registry, we also valued its methodological qualities in obtaining and managing data. Since January 1999, the Western Australia Registry for ASD has gathered all new diagnosed cases in that region using DSM-IV criteria

as case definition. All diagnoses were carried out by specialized teams of experts from the private and public clinic practice working in an informal network. The Australian study accounts for all cases detected between July 1999 and December 2000.

2. Disease Model (Autism average duration and age of onset for the different age groups and disability weight): We have formulated autism natural history through the current bibliography and the experts' opinion. Autism has been modelled as a lifelong condition, with an age of onset of 1.5 years old and a duration equal to the average life expectancy: 80.93 years at birth for the 0–4 age-group. For the rest of the age intervals, and since we are dealing with incident cases, the initial age of the interval was used as initial starting point of the disease for that age group and the condition duration was calculated as the remaining years until life expectancy for each age group was fulfilled. In order to determine the severity of disabilities related to each form of ASD, we used the stage-weighting from the Victorian Burden of Disease Study: Morbidity (1999). To estimate disability weights a group of experts ranged the severity of several disabling conditions from 0 (equal to perfect health) to 1 (equal to death) using a person trade-off methodology (Salomon & Murray, 2004). Based on the Victorian Burden of Disease Study, Autistic Disorder disability coefficient was 0.55 and Asperger's Disorder implies a disability coefficient of 0.25. Since Western Australia incidence data collects all the information regarding Asperger's Disorder and PDD-NOS together, we have made an estimate of the disability weight for Asperger/PDD-NOS using the experts' opinion, with a result of 0.35. For Autistic Disorder we took the same disability weight used in the Victorian Burden of Disease Study.

The DALY measure expresses the sum of YLL and YLD, reflecting the future stream of healthy years of life lost as a result of each incident case of disease or injury. It is thus an incidence-based measure rather than a prevalence-based measure. To calculate DALY, we applied the same age-weighting and discounting factors used in the WHO Global Burden of Disease study (Murray & López, 1996). A 3% discount rate and an age-weighting modulation factor of k = 1. Discounting of future benefits is a standard practice in economic analysis (Murray & Acharya, 1997). Including a discount rate in the model, we avoid giving excessive weight to deaths at younger ages.

Without age weighting and discounting, a male death at birth results in 44% more YLL than a male death at age 25 and 97% more than a death at 40 years old. Applying a discount rate of 3%, an infant death results in only 12% and 29% more YLL than a death at age 25 and 40 years respectively. When we include age weighting and a discount rate in the general formula, the calculation of YLL and YLD becomes more complex:

$$\text{Age} - \text{weighting function} = Cxe^{-\beta x}$$

Where: C is a constant = 0.16243; β is a constant = 0.04; x = age; e is a constant = 2.71

$$\text{Discounting function} = e^{-r(x-a)}$$

Where: r is the discount rate, fixed at 0.03; a = onset of disease year; x = age; e is a constant = 2.71; L = Years of life left at age a;

Thus, the full formulas are as follow:

$$YLL = K\,Ce^{(ra)}/(\beta + r)^2\,[e^{-(\beta+r)(L+a)}[-(\beta + r)(L + a) - 1] - e^{-(\beta+r)a}[-(\beta + r)a - 1]] + [(1 - K)/r)(1 - e^{-rL})]$$

and

$$YLD = D\{K\,Ce^{(ra)}/(\beta + r)^2\,[e^{-(\beta+r)(L+a)}[-(\beta + r)(L+a) - 1] - e^{-(\beta+r)a}[-(\beta + r)a - 1]] + [(1 - K)/r)(1 - e^{-rL})]\}$$

Where: D = Disability weight (ranging from 1—death to 0—perfect health).

A sensitivity analysis was carried out showing different total DALY values with and without including discount rate and age-weighting functions. We also show the DALY value using a disability coefficient of 0.25 for the Asperger and PDD-NOS group as the Australian Burden of Diseases Study did.

Analyses were performed using GesMor (2003), a computer software tool developed by the International Health Department of the Spanish Health Institute specifically to calculate DALY.

Results

Assuming that the ASD incidence in Spain is the same as that seen in the Western Australia Study, the total number of estimated incident ASD cases in Spain in the age interval 0–14 years old in 2003 was 2,513 (1,692 cases with autistic disorder and 821 with Asperger's Disorder or PDD-NOS) (Table 1).

Since no deaths were directly attributable to any of the conditions included in the ICD-10 code for PDD in the Spanish Mortality Registry in 2003, we estimated the

Table 1 Estimation of autistic disorder and Asperger-PDD-NOS incident cases

		Age Groups (years)			Total (all age groups)
		0–4	5–9	10–14	0–14
Population Size, Spain 2003[a]	Males & females *N* (%)	1,901,859 (31.4)	1,967,866 (32.6)	2,173,754 (36.0)	6,043,479 (100%)
Population Size, Western Australia 2000[b]	Males & females *N* (%)	126,589 (31.8)	132,981 (33.4)	138,261 (34.7)	397,831 (100%)
Autistic disorder	Incidence Rate × 10,000 (IC 95%)[c]	5.5 (4.5–6.7)	2.4 (1.8–3.2)	0.8 (0.0–1.3)	NA
	Estimated Number of Incident Cases (IC 95%)	1,046 (856–1,274)	472 (354–630)	174 (0–283)	1,692 (1,210–2187)
Asperger's Syndrome & PDD-NOS	Incidence Rate × 10,000 (IC 95%)[c]	2.5 (1.8–3.3)	1.1 (0.0–1.7)	0.6 (0.0–1.1)	NA
	Estimated Number of Incident Cases (IC 95%)	475 (342–628)	216 (0–335)	130 (0–239)	821 (342–1,202)
Totals (Autism & Asperger) by age groups	Incidence Rate × 10,000 (IC 95%)[c]	8.0 (6.8–9.3)	3.5 (2.8–4.4)	1.4 (0.0–2.0)	NA
	Estimated Number of Incident Cases (IC 95%)	1,521 (1,198–1,902)	688 (354–965)	304 (0–522)	2,513 (1,552–3,389)

[a] Source, Spanish National Institute of Statistics (http://www.ine.es)

[b] Australia Institute Bureau (http://www.abs.gov.au/)

c Source, Williams, 2005

NA: Data not available

number of deaths due to other related causes using the mortality rate for ASD of the California Developmental Disability System (DDS). When we adjusted this rate to our population, it resulted in 29 cases (2 in the age interval 0–4; 6 in the interval 5–9 and 21 in the interval 10–14), yielding a total YLL of 1,080.04.

Intermediate calculations needed for the final YLD estimation are shown in Table 2 by age groups. Applying a disability coefficient of 0.55 for the Autistic Disorder, the YLD per case ranges from 18.92 to 20.2. For the Asperger/PDD-NOS group, the 0.35 disability coefficient results in a range of YLD from 12.04 to 12.86. These figures have taken into account the standard BoD method, that is: a discount of 3% and a weighted age.

Total DALYs for our ASD population in that year would amount to 43,928 (33,797 for autistic disorder and 10,131 for Asperger's syndrome and/or PDD-NOS) (Table 3). We also show the possible DALY variation using the range that would have been obtained if we had applied the confidence interval of the incident cases: DALYs would have ranged from 28,453 for 1,552 cases (lower limit for the mean of incident cases) and 58,347 for 3,389 (upper limit for the mean of incident cases).

Since YLD is the only measure altered when BoD standard conditions change, a sensitivity analysis was carried out for this parameter. Results are shown in a standardized way: YLD per 1,000 ASD cases (Fig. 1).

This figure shows that the overall YLD change a lot depending on the model used. Thus, if we apply the discount but no age weighting is taken into account, YLD are 14,443. Applying a disability coefficient of 0.25 for Asperger and PDD-NOS (instead of a 0.35 coefficient), results in 15,898 YLD. If both weighting factors are applied (discount and age weighting) YLD are 17,050; without discount or age weighting, YLD are 36,550 and without applying any discount, YLD amounts to 40,627. Standard estimation—the one that implements a discount rate of 3% and age-weighting would be higher than the value obtained

Table 2 Estimation of the Years of Life with Disability (YLD) per each new case (both genders)

	Age group (years)	Age of autism onset[a]	Life expectancy	Disability coefficient	Years of Life with Disability per case
Autistic disorder	0–4	1.5	80.93	0.55	18.92
	5–9	5	76.67	0.55	19.93
	10–14	10	71.70	0.55	20.21
Asperger's Syndrome & PDD-NOS	0–4	1.5	80.93	0.35	12.04
	5–9	5	76.67	0.35	12.68
	10–14	10	71.70	0.35	12.86

[a] Estimations from the literature, taking into account autism's natural history and according to the expert opinions

Table 3 ASD DALYs in Spain in 2003 for incident cases. Standard estimation

Age group (years)	Autistic disorder DALY (IC 95%) Males & females	Asperger's Syndrome & PDD-NOS DALY (IC 95%) Males & females	Total DALYs by age group (IC 95%) Males & females
0–4	19,867 (16,271–24,181)	5,720 (4,119–7,563)	25,587 (20,390–31,744)
5–9	9,629 (7,278–12,778)	2,739 (0–4,248)	12,368 (7,278–17,026)
10–14	4,301 (785–6,504)	1,672 (0–3,073)	5,973 (785–9,577)
Total DALYs	33,797 (24,334–43,463)	10,131 (4,119–14,884)	43,928 (28,453–58,347)

3% of discount and age weighting were used in all these calculations

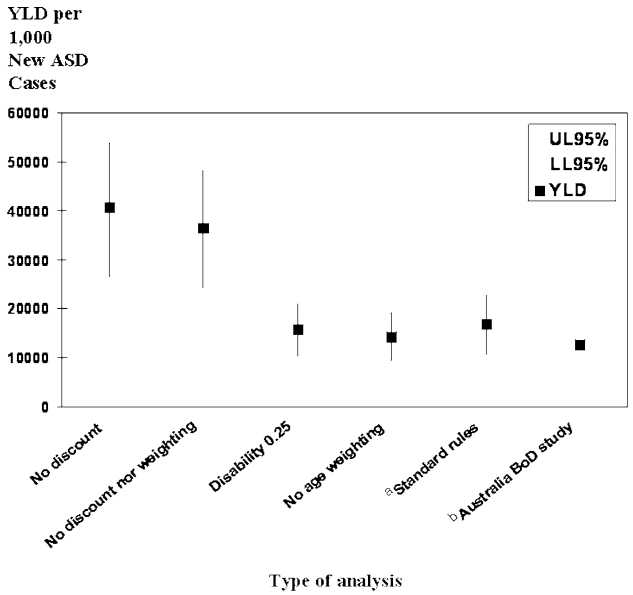

Fig. 1 Sensitivity Analysis: YLD per 1,000 New ASD Cases. Note: a. A 3% of discount and age weighting was used for the standard rules, b. DALY Limits were not provided by the authors in the Australia BoD study

with a lower disability coefficient, but lower than values obtained when standard rules for the BoD studies are not taken into account.

In the last column we also show the YLD per 1,000 new ASD cases obtained in the Australia BoD Study. As it can be seen, the result (12,648 YLD) is in the same interval of the rest of standardized measures used in our sensitivity study, but very far from results obtained with the other methods.

Discussion

Burden of Disease is an important measurement and a good health indicator that summarizes two important pieces on health information: premature mortality and life lived with disability, allowing the quantification of the lost health in the population and the comparison between different populations. The interest in this kind of indicators is clearly seen in the number and quality of studies such as the Global Burden of Disease by the WHO (2001) and World Health Organization (2006), the Australian Studies (Victorian Burden of Disease Study 1999, 2005) and others.

Life expectancy is losing ground to other non-fatal outcomes that have arisen more interest in the population as health indicator, such as health expectancy (instead of life expectancy) and quality of life. There has been an open debate for years about the use and utility of DALY, the indicator used in the burden of diseases studies. However, most part of the studies have been carried out in the general population considering large groups of diseases and, in some occasions, analyzing the influence of some risk factors in the aetiology of diseases. Indeed, this strategy has been used by the WHO to compare the relative weight of diverse diseases in different countries. In a few of these studies autism has been represented as one of the diseases included in the overall DALY for a certain country, but we do not know any particular study of BoD in Autism. That is why the current study could be one of the firsts in this field, contributing to the assessment of the impact of autism in our societies.

Autism Spectrum Disorders is an important cause of mental disability and for that reason we think DALY could be of use, since they are more the result of Years of Life lived with Disability than of Years of Life Lost. In our first analysis no YLL was considered, because we found no deaths in the Spanish Mortality Registry for our year of study caused by any of the ICD-10 codes for autism. However, we decided to adjust mortality rates of the California Developmental Disability System to our population to attempt to show the weight of both DALY components: YLL and YLD.

The first approach (without taking into account YLL) gave us a total of 41,959 DALY, and when we included YLL in the model, DALY raised to 43,928. In other words, YLL caused by comorbid conditions related to ASD represent 2,000 DALY (4.6% of the total DALY). In the Victorian Burden of Disease Study (2005), no Years of Life Lost are considered, because in this kind of

overall approaches all mortality causes are attributable only to one disease, the direct cause of death. Our study breaks in some way the general method because we do not estimate DALY for other diseases that are commonly comorbid to autistic conditions. However, if YLL are not to be considered, ASD DALY would be the 0.6% of the total DALY in Spain in 2003 (Álvarez and Morant, International Health Department, Instituto de Salud Carlos III, Spain, unpublished data), being the major causes of DALY for women dementias (13.1% of the total DALY for ASD in Spain in 2003), depression (11.7%) and osteomuscular disorders (6.3%). The DALY distribution for men was different: alcohol abuse (6% of the total DALY for ASD), followed by cardiac ischemia (5.9%), and dementia (5.9%).

Moreover, the only available information in Spain that offered stratified data by ages in the 0–14 age interval was carried out in 1999. Our study is based on data from 2003 but if incidence and total DALY in Spain have not changed between 1999 and 2003, our data will account for the 15.6% of the total DALY in the 0–14 interval for that year (Genova-Maleras, Alvarez-Martín, & Morant-Ginestar, 2005).

The most critical calculation in BoD is the YLD because either prevalence or incidence data are needed and a specific coefficient must be assigned to the disability. As we do not have an autism epidemiological registry in Spain and there are few studies about incidence (Fombonne, 2005), we had to obtain these data from the Western Australia Study for 2000 (Williams et al., 2005), since we consider this article as the most recent and accurate work for our purposes.

To reduce the potential bias, we applied the incident data after adjusting it with respect to our population size. There is a certain level of agreement that both autism prevalence rates and age of diagnosis are similar in Western countries. We decided to use data from the above mentioned study rather than collecting partial and probably inaccurate data from the national literature or reports, because we thought this latter approach would have supposed a higher bias.

The Western Australia Study (Williams et al., 2005) offers the incidence estimate for PDD-NOS and Asperger's Disorder on aggregate, and that represents another difficulty for the analysis. Moreover, we suspect that in all incidence studies Asperger's Disorder frequency (sometimes diagnosed at adulthood) is underestimated. If that would be the case, incidence and burden of disease would be biased and the real figures could be higher. Moreover, as ASD frequency is different in boys and girls, another limitation of the original data is that no differences between boys and girls were shown in previous studies, and we have had to join data regarding both sexes together in all our calculations. The bias theoretically produced by this limitation on the original information could not lead us to get different DALY estimates for the entire ASD spectrum, because no differential prognosis between sexes has been stated. In the future, it would be interesting to make incidence studies stratified by age and sex.

Finally, another strong point of the Western Australia Study is that it presents all data within a confidence interval and that allows us to make DALY estimates in a more reliable way, since it states the uncertainty somehow.

All our tables show a central estimate together with confidence intervals taken from the confidence intervals of incident cases. This is the first time that the DALY measurement is shown with a confidence interval, filling the gap left by imprecise epidemiological data traditionally used for this calculation. In the traditional method for calculating DALY there are no confidence intervals and we see this new strategy as a contribution to a better understanding of the type of information provided by this kind of measurements.

Another complex aspect in BoD studies is the assignment of a disability weight or coefficient (Murray et al., 2000). There is no consensus about the best procedure to establish a severity scale for different states of health and the equivalence in life lost because of a premature death or the disability.

Considering the main phenotypes, the prevalence of each disorder and their impact on the global disability, an average disability weight of 0.35 for Asperger's Disorder and PDD-NOS is assumed. This value has been calculated by national autism experts and later on consulted with experts on the BoD estimate for other diseases. This coefficient was used only for the Asperger and PDD-NOS group, since for Autistic Disorder we took the estimate stated in the Australian Burden of Disease Study, namely 0.5. In that study a disability coefficient of 0.25 was used for the Asperger group, and PDD-NOS cases were not considered. However, we have also estimated the total DALY considering both possibilities and although there were some differences between the central-point estimates, no substantial differences were observed between their confidence intervals (Fig. 1). We hope that the present work will be followed soon by other studies that will solve some of the limitations of the current epidemiological information.

The sensitivity analysis carried out shows the range of possible DALY results when the disability coefficient is changed and with and without an age-weighted coefficient and discount rate, and all possible DALY results show similar confidence intervals and also central-estimates similar to those of the Australia Burden of Disease Study. The only significant difference appears when discount rate is not implemented, in which case total DALY result is

much higher. However, the concept of discount rate is a common rule in studies where life is considered along a series of years and only results obtained following the general rules prescribed for BoD studies should be taken into consideration.

An important aspect in our study is the DALY's ability to detect changes after health interventions. An early diagnosis and treatment, especially in cases with a better intelligence quotient (around 33% of cases with Autistic Disorder and 88% of cases diagnosed with PDD-NOS have a normal intellectual functioning) (Chakrabarti, 2005), imply a better prognosis for the child. This means that early diagnosis and treatment could change the natural history of the disease, resulting in a lower disability level. When estimating DALY after an early adequate treatment, supposing, according to the experts, a reduction to a disability weight of 0.4 in the group with autistic disorder and a global disability weight of 0.25 in the Asperger and PDD-NOS group, DALY supposed 32,111 years (24,874 for autistic disorder and 7,237 for PDD-NOS and Asperger), which means a reduction of 11,817 years (26.95%). The estimated improvement in quality of life when an early intensive and adequate treatment is implemented is high, being also an efficient way to reduce distress among children, their families and the whole population. Besides, the absence of an early adequate treatment can imply not only the lack of improvement, but also the worsening of many clinical problems.

Another benefit of early intervention is the positive impact in the family. Early intervention reduces stress by providing a better understanding of the condition, and involves the whole family in supporting the child's development. When children and families receive support, family stress is often reduced with the result that families are better able to envision a more positive and optimistic future for their children. Therefore, the real benefit of an early adequate intervention would be much higher than the sole DALY reduction.

Despite the limitations of this study, which are mostly the same ones found in other BoD studies, we think it represents a relevant approach of the lost of health caused by autism in Spain. In the absent of appropriated incidence data in our country, this approach can be valid if the limitations are assumed and declared. DALY's ability to synthesize frequencies and lethal and non-fatal health outcomes of diseases provides information that could be used as effective measurements for interventional studies. These indicators have also a big potential as a policy tool as the quality of the data used to generate the YLD component of the DALY improves.

Results confirm as well the necessity of a rising awareness from both society and policy makers of autism, its early diagnosis and its adequate treatment.

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