Health needs assessment for congenital anomalies in middle-income countries: Examining the case for neural tube defects in Brazil

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Received: 29 March 2013 / Accepted: 9 August 2013 / Published online: 30 August 2013
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Abstract Recent economic improvement in Brazil has been reflected in better maternal–child health indicators, with decreases in infant and perinatal mortality. However, under-five mortality due to congenital disorders remained unchanged, and congenital disorders have become the second leading cause of infant mortality. In the present study, we used the PHG Foundation Health Needs Assessment (HNA) Toolkit with the objective of first assessing the burden of disease caused by neural tube defects (NTDs) in Brazil and the impact of interventions already put in place to address the burden, and second to evaluate and prioritize further interventions and policies required for its prevention and treatment. The results from these two components of the HNA process are described in this paper. The published literature was reviewed to identify studies of NTDs (prevalence; morbidity; prenatal, perinatal, and postnatal mortality; treatment or prevention). Data on indicators of maternal and child health

were obtained directly from the Brazilian Ministry of Health, through the online Live Births Information System (SINASC) and from the Mortality Information System (SIM). Descriptive analyses included reports of the rates of NTD in liveborns, fetal, and infant deaths. Differences between folic acid flour pre-fortification (2001–2004) and post-fortification (2006–2010) periods were expressed as prevalence rate ratios. Around 20 % of fetal deaths were related to congenital disorders with approximately 5 % of those being NTDs. For infant mortality, congenital disorders were notified in approximately 15 % of cases, with NTDs present in 10 % of the malformed children. Although statistically significant, the prevalence rate ratio (PRR) for spina bifida in live births was only 0.937 (95 % confidence interval (CI) 0.884–0.994), a decrease of 6.3 % when comparing the pre and post-fortification periods. The impact of fortification seemed to be more visible in fetal deaths due to anencephaly (PRR=0.727, 95 % CI 0.681–0.777) and for spina bifida (PRR=0.700, 95 % CI 0.507–0.967) with associated decreases of 27.3 and 30 %. The lower impact of folic acid fortification in Brazil, compared to other Latin-American countries, can be due to differences in dietary habits, concentration of folic acid in flour, as well as characteristic population ethnic composition. The HNA led to the identification of the needs to be addressed in Brazil, including the improvement of reporting congenital disorders within the nationwide birth certification system, and revision of the policy of flour folic acid fortification.

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Keywords Neural tube defects · Folic acid fortification ·
Brazil · Health Needs Assessment

Introduction

In recent years, Brazil has become an emerging international economy, being part of the so-called BRICS countries (Vercueil

2010). This economic change has been reflected in improved maternal–child health indicators, with an impressive impact on infant and perinatal mortality, which has decreased by 47 % from 1990 to 2007 (Victora et al. 2011). However, under-five mortality due to congenital disorders remained unchanged, contributing to approximately five deaths per thousand (Victora et al. 2011). As a result, congenital disorders have become the second leading cause of infant mortality, superseded only by perinatal causes (Brazil 2012a). Moreover, it is also likely that among perinatal causes of death, there are undiagnosed congenital disorders, for example cardiac defects, aneuploidies, and inborn errors of metabolism (Christianson et al. 2006). To understand if congenital disorders should be considered a priority for health policies in middle-income countries like Brazil, it is essential that we estimate the true magnitude of their contribution.

Neural tube defects (NTDs) are a group of congenital disorders that have a significant impact on perinatal mortality (mostly due to anencephaly). Encephalocele and spina bifida (SB) may be associated with fetal and/or infant death, but also with other central nervous system complications such as hydrocephalus and lifelong disabilities such as sensory and motor impairments, learning disabilities, epilepsy, orthopedic contractures and deformities, and bladder and bowel incontinence. Prevalence at birth in Brazil is estimated to be around 1/1,000 births for anencephaly; 1.5/1,000 for spina bifida; and 0.5/1,000 cephalocele (Castilla and Orioli 2004; López-Camelo et al. 2010).

NTDs are of multi-factorial etiology with an empirical recurrence risk of 3–5 % for first-degree relatives and in 95 % of the cases, it is the first occurrence in a kinship (Blencowe et al. 2010). Known risk factors include both genetic and environmental, but the exact biological mechanism leading to the failure of the neural tube to close are still not known. Many candidate genes have been investigated in the published literature, with most of the studies concentrating on the folate metabolism pathway (Beaudin and Stover 2007; Greene et al. 2009). Maternal folic acid deficiency is the leading environmental risk factor for NTDs. Folic acid supplementation and fortification of food have been proven to have a significant protective effect for primary prevention (for a review, see: Czeizel et al. 2011). However, many other environmental factors have also been implicated in the etiology of NTDs, like low socio-economic status, maternal obesity, hyperthermia, diabetes, use of folate antagonist medications during pregnancy, and parental occupation (Au et al. 2010).

In most high-income countries, prevention of NTDs includes folic acid supplementation programs, food fortification, and/or prenatal screening with the possibility of terminating the pregnancy (Blencowe et al. 2010). However, in many low- and middle-income regions, including Brazil and many other South-American countries, food fortification has already started, but termination of pregnancy (TOP) is not a legal option (Cook et al. 2008).

In 2009, the PHG Foundation in Cambridge, UK, began a program to help low- and middle-income countries tackle the problem of congenital disorders. It included the development of a “toolkit” to assist users in conducting a health needs assessment (HNA) for congenital disorders. The aim of using the Toolkit is to enable a wide range of stakeholders to undertake such assessments and to prioritize actions appropriate to the local context (Nacul et al. 2013; Groisman et al. 2013). The program responds to the World Health Assembly resolution 2010 that calls on member states to “*prevent birth defects wherever possible, to implement screening programmes, and to provide ongoing support and care to children with birth defects and their families* (World Health 2010).”

In the present study, we used the PHG Foundation HNA Toolkit with the objective of (1) assessing the burden of disease caused by NTDs in Brazil and the impact of interventions already put in place to address the burden and (2) to evaluate and prioritize further interventions and policies required for prevention and treatment of NTDs in this country. The results from these two components of the health needs assessment process are described in this paper.

Methods

HNA protocol we used the HNA Toolkit developed by the PHG Foundation available at <http://toolkit.phgfoundation.org/>. The toolkit is a multi-stage guide that enables users to undertake a HNA in relation to congenital disorders. It comprises a structure for demographic and epidemiological data collection; assessment of current policies, programs, and services; and a comparison between the current situation and the desired situation in terms of availability, quality, coverage, and effectiveness of the policies, programs, and services. The next stage is the identification of interventions to meet the needs indicated by the HNA along with a quantitative or qualitative assessment of the potential impact of the interventions and finally, action planning and review. The toolkit can be used to assess one or more of a range of congenital disorders and also services aimed at prevention, treatment, and ongoing care of those affected. For NTDs, the package within the Toolkit contains a background document (introducing information on risk factors and estimated global data on the burden of NTDs), and the NTD HNA tool and calculator, which allows the user to evaluate existing services and interventions in a qualitative and quantitative manner including a situation assessment through a Strengths, Weaknesses, Opportunities, and Threats (SWOT) analysis in relation to the policies and services identified through needs assessment for NTDs in Brazil. The calculator also contained pre-populated modeled data specific to Brazil that can be supplemented further by locally available data (including demographic, socio-economic, and epidemiological data specific to NTDs). Further details on the methodology can

be found both at the website homepage (<http://toolkit.phgfoundation.org>) and within the user guide (<http://toolkit.phgfoundation.org/guide.pdf>).

Literature search The published literature was reviewed to identify studies of NTDs (prevalence; morbidity; prenatal, perinatal, and postnatal mortality; treatment or prevention), on 22 July 2012. MEDLINE, through PubMed, was searched, including publications in English, Portuguese, or Spanish. Snowball searching was used whereby literature referenced in key papers was included. Combinations of the following search terms were used as follows: “neural tube defect,” “spina bifida,” “meningocele,” “myelomeningocele,” “anencephaly,” “cephalocele,” “NTD,” “NTDs,” “folic acid,” “folate,” and “Brazil” both in English as well as their counterpart in Portuguese (“*defeitos de tubo neural*,” “*espinha bifida*,” “*meningocele*,” “*meningomielocoele*,” “*anencefalia*,” “*cefalocele*,” “*DTN*,” “*DTNs*,” “*acido folico*,” “*folato*,” and “*Brasil*”). We also performed a search on Literature in the Health Sciences in Latin America and the Caribbean (LILACS) and Scientific Electronic Library Online (SciELO) databases, through Virtual Health Library (VHL) (<http://regional.bvsalud.org/php/index.php?lang=en>). LILACS (in Portuguese) is considered as the most important and comprehensive index of scientific and technical literature of Latin America and the Caribbean (<http://lilacs.bvsalud.org/>). SciELO, developed in Brazil, provides access to Latin Americans, more specifically, Brazilian journals published in Portuguese, which are not necessarily on MEDLINE (<http://www.scielo.org/>). We also searched VHL for the terms “birth defects” and “Brazil” to evaluate health policies and facilities concerning birth defects in the country. A total of 170 papers were identified. The depuration process has eliminated articles not related to neural tube defects (neglected tropical diseases has the same acronym as neural tube defects—NTDs); clinical case reports; chromosomal or gene mutations associated with specific syndromes which include NTDs; description of surgical procedures; folic acid use for other clinical conditions not related to congenital anomalies e.g., anemia; nutrition after hyperbaric surgery; and nutrition in gastrointestinal disorders. We finally kept 71 pertinent publications.

Demographic and health indicators Data on indicators of maternal and child health were obtained directly from the Brazilian Ministry of Health (MoH), through the online Live Births Information System (SINASC) (Brazil 2012b), created in 1990. Mortality data were obtained from the Mortality Information System (SIM), also available at the same MoH website (Brazil 2012c). These web-based systems allow data retrieval at the level of the 27 states and 5,564 municipalities of Brazil. SIM provides information on the underlying cause of death and on demographic characteristics (age, sex, etc.). Demographic data were obtained from the last Brazilian

census (IBGE 2011). Maternal–child health information in Brazil is also well described by Victora et al. 2011 and Horovitz et al. 2012.

Statistical analysis Birth prevalence was calculated as the number of cases with a congenital disorder (e.g., spina bifida) in Brazil during a single calendar year (e.g., 2001) divided by the total number of live births in Brazil during the same calendar year and presented per 10,000 live births. The data were obtained as described above. Descriptive analyses included also the annual prevalence for NTDs per 1,000 fetal and infant deaths for each year between 2001 and 2010. Fetal deaths were defined as the spontaneous intrauterine death of a fetus at any time during pregnancy (from 22 weeks gestation or more or 500-g birth weight or more). Infant deaths were defined as the death of a child under the age of 1 year (Brazil 2012b and c).

In order to identify a specific period for when the prevalence may have changed in Brazil for NTDs, we have classified NTD cases into two time periods related to the implementation of folic acid fortification (FAF) of flour in Brazil. Exposure to folic acid fortification was classified by year of birth (or pregnancy completion). The birth years 2001 to 2004 were classified as “pre-fortification” where all conceptions were assumed to have occurred before fortification became mandatory in Brazil in June 2004. The years 2006 to 2010 were classified as “post-fortification” where all conceptions were assumed to have occurred after fortification became mandatory. Differences between these periods were expressed as prevalence rate ratios (PRRs) with corresponding 95 % confidence intervals (CIs) and chi-squared *p* value, which were calculated using EPI Info (Version 7, from CDC Atlanta, GA, USA). The prevalence rate ratio represents the change in birth prevalence of NTDs between the two time periods. The “pre-” and “post-fortification” groupings were also used to determine differences between these periods for fetal deaths and infant deaths.

Results

Demographic and health indicators (country profile)

Brazil has, presently, a population of about 190,000,000 with approximately 3,000,000 live births every year (IBGE 2011). Infant mortality was estimated in 2007 to be 19 deaths per 1,000 live births with newborn deaths accounting for 68 % of infant mortality. This represents a remarkable decrease when compared to 115 infant deaths per 1,000 live births in 1970. The stillbirth rate was 11 per 1,000 births in 2007 compared to more than 20 per 1,000 in 1979 (Brazil 2012a).

Economic growth in Brazil has been partially reflected in improvements in social determinants and general health indicators including lower poverty, increase in women's education, higher levels of urbanization, and access to sanitation and treated water. A unified nationwide health system (Sistema Unico de Saude—SUS) with special emphasis on primary care was implemented in the late 1980s. The Millennium Developmental Goal (MDG) 1 (a reduction in the number of underweight children by half between 1990 and 2015) has already been attained ahead of schedule and it has been estimated that MDG 4 (a two third reduction in the mortality rate of children younger than 5 years between 1990 and 2015) will probably be achieved before 2014 (Victora et al. 2011).

Fertility rates have also substantially decreased with a mean of 1.8 children per woman and in 2010, 20 % of children were born to mothers under 20 years of age and 9 % to mothers over 35 years (Brazil 2012b).

Since 1989, public health delivery of services in Brazil has been based on SUS, which allows every Brazilian citizen access to free health care at primary, secondary, and tertiary levels. Implementation of SUS was accompanied by an increase in access to primary health care through the Family Health Strategy (Victora et al. 2011).

However, these improvements in economic, demographic, and health indicators are not uniformly distributed in Brazil. There are large socio-economic disparities (Victora et al. 2011), and in the North and Northeast regions, a greater proportion of the population is poor and has less access to health services.

Epidemiology of congenital disorders and NTDs in Brazil

We found two main sources of information on congenital disorders and NTDs prevalence in Brazil. One source originated from the nationwide live birth certificates (SINASC) (Brazil 2012b), as well as fetal deaths and infant death notifications (SIM) (Brazil 2012c). The second source is from hospital-based studies found in the published literature (Castilla and Orioli 2004; López-Camelo et al. 2010).

Table 1 shows information available at SINASC and SIM. There is a low prevalence of spina bifida (*ICD 10-Q05*) notifications in live births (SINASC), ranging from 1.6 to 2.1 per 10,000 live births over the 10 years of data presented. When we examined the death notifications (SIM), NTDs notified as a cause of death are considerably more frequent, ranging from 93.9 to 156.0 for fetal deaths and 142.4 to 178.7 for infant deaths, per 10,000. As expected, anencephaly is the most frequent NTD contributing to both fetal and infant deaths (Table 2). Around 20 % of fetal deaths were related to congenital disorders with approximately 5 % of those being NTDs. For infant mortality, congenital disorders were also notified in approximately 15 % of cases, with NTDs present

in approximately 10 % of the malformed children. These rates are in line with the SINASC data.

The gold standard program for detection of congenital disorders in South America is the hospital-based surveillance system Latin American Study of Congenital Malformations (ECLAMC) (Castilla and Orioli 2004). ECLAMC has published data on NTDs surveillance from 19 Brazilian hospitals, showing a total birth prevalence of NTDs of 31.4/10,000 (live births and stillbirths) in the pre-fortification triennium (2003–2005) and 24.3/10,000 in the post-fortification period (López-Camelo et al. 2010). This is much higher than the data from the SINASC registry. If we sum the live births and fetal deaths, the prevalence of NTDs in 2010 would be 3.1/10,000 (887 NTDs/2,892,797 total births) according to SINASC and SIM or approximately 10 % of that estimated from the surveillance of the 19 ECLAMC hospitals.

Primary prevention

Folic acid fortification and supplementation

Flour FAF in Brazil was made mandatory by law in June 2004 (Santos and Pereira 2007), and “fortified births” must have therefore occurred approximately from June 2005 onward. The 12-month period from the beginning of maternal fortification to the birth of the first “fortified” children includes a 3-month period for the implementation of flour fortification plus 9 months of pregnancy.

To evaluate the impact of flour folic acid fortification policy in Brazil, we analyzed the data from SINASC and SIM and divided it into two periods as described in the methods: before fortification (2001–2004) and after fortification (2006–2010) (Table 3). Although statistically significant, the PRR for spina bifida in live births was only 0.937 (95 % CI 0.884–0.994), a decrease of 6.3 %. There was also a significant reduction of fetal deaths due to anencephaly (PRR=0.727, 95 % CI 0.681–0.777) and for spina bifida (PRR=0.700, 95 % CI 0.507–0.967) with associated decreases of 27.3 and 30 %, respectively. A small decrease was observed in fetal deaths for cephalocele (PRR=0.961, 95 % 0.673–1.373) although this was not statistically significant.

For supplementation, there is no specific policy in Brazil. One study published in 2007 (Mezzomo et al. 2007) interviewed 1,450 women who gave birth in five hospitals in Pelotas, in South Brazil. Only 4.3 % had taken folic acid in the periconceptional period. Factors positively associated with supplementation were, among others, white skin color, higher schooling, higher economic status, and a planned pregnancy.

Secondary and tertiary prevention

Prenatal care reaches more than 89 % of all pregnant women in Brazil, and around 83 % of women start it during the first

Table 1 Yearly prevalence of spina bifida in live births and in fetal and infant deaths in Brazil

Year	Live births	SB	/10,000	Fetal deaths	NTD	/10,000	Infant deaths	NTD	/10,000
2010	2,861,868	545	1.9	30,929	342	110.6	39,870	693	173.8
2009	2,881,581	461	1.6	32,147	302	93.9	42,462	759	178.7
2008	2,938,424	449	1.5	32,065	351	109.5	44,100	764	173.2
2007	2,891,328	438	1.5	32,175	314	97.6	45,370	756	166.6
2006	2,944,928	393	1.3	33,434	347	103.8	48,332	748	154.8
2005	3,035,096	465	1.5	34,233	371	108.4	51,544	734	142.4
2004	3,026,548	634	2.1	36,214	565	156.0	54,183	886	163.5
2003	3,938,251	566	1.4	37,103	488	131.5	57,540	899	156.2
2002	3,059,402	502	1.6	37,417	519	138.7	58,916	920	156.1
2001	3,115,474	505	1.6	38,759	529	136.5	61,943	916	147.9

SB spina bifida (ICD-10 Q05); NTD anencephaly; Cephalocele; Spina Bifida (ICD-10 Q00; Q01; Q05)

Livebirths: SINASC/DATASUS (<http://www2.datasus.gov.br/DATASUS/index.php?area=0205&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinasc/cnv/nv>) Accessed 12 Dec 2012

Fetal Deaths: SIM/DATASUS <http://www2.datasus.gov.br/DATASUS/index.php?area=0205&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/fet10> Accessed 12 Dec 2012

Infant Deaths: SIM/DATASUS <http://www2.datasus.gov.br/DATASUS/index.php?area=0205&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/inf10> Accessed 12 Dec 2012

trimester of pregnancy (Victoria et al. 2011). However, morphological ultrasound is not routinely performed. Elective abortion is illegal, even for congenital disorders. The only exception is anencephaly, where termination of pregnancy with an anencephalic baby was made legal in 2012, without the need of a special judicial authorization (Diniz 2007; Fonseca 2011; Diniz et al. 2009).

Despite free access to primary, secondary, and tertiary health services through SUS (Unified Health System), the quality of child health services is not consistent and equitably distributed throughout the country. Tertiary public hospitals

and genetics clinics are concentrated in the South and South-east regions, and are usually overcrowded. In the North region, genetics services are almost non-existent. Special care facilities for treatment of patients affected by NTDs, such as social services, rehabilitation, and education, are very limited. Most are non-profit, charity-funded clinics (Horovitz et al. 2012). However, in Brazil, there are a few policies to support people with disabilities: monthly minimum wage, free public transport including one accompanying person, and if the parents are working, they have one extra day's leave per month (Elias et al 2008).

Table 2 Yearly prevalence of anencephaly, cephalocele, and spina in fetal and infant deaths in Brazil

Year	Fetal deaths	Q00	/1,000	Q01 + Q05	/1000	Infant deaths	Q00	/1,000	Q0 + Q05	/1000
2010	30,929	317	10.2	13+12	0.8	39,870	543	13.6	56+94	3.8
2009	32,147	278	8.6	12+12	0.7	42,462	578	13.6	70+111	4.3
2008	32,065	323	10.1	14+14	0.9	44,100	590	13.4	67+107	3.9
2007	32,175	293	9.1	12+9	0.6	45,370	566	12.5	80+110	4.2
2006	33,434	320	9.6	10+17	0.8	48,332	591	12.2	50+107	3.2
2005	34,233	346	10.1	5+20	0.7	51,544	539	10.4	63+132	3.8
2004	36,214	533	14.7	12+20	0.9	54,183	623	11.5	80+183	4.8
2003	37,103	454	12.2	17+17	0.9	57,540	640	11.1	94+165	4.5
2002	37,417	480	12.8	15+24	1.0	58,916	626	10.6	86+208	5.0
2001	38,759	490	12.6	15+24	1.0	61,943	637	10.3	66+213	4.5

Anencephaly ICD-10 Q00; Cephalocele ICD-10 Q01; Spina Bifida ICD-10 Q05

Fetal Deaths: SIM/DATASUS <http://www2.datasus.gov.br/DATASUS/index.php?area=0205&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/fet10> Accessed 12 Dec 2012

Infant Deaths: SIM/DATASUS <http://www2.datasus.gov.br/DATASUS/index.php?area=0205&VObj=http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/inf10> Accessed 12 Dec 2012

Table 3 Impact of folic acid supplementation in neural tube defects in Brazil

NTD	Pre-fortification 2001–2004 (/10,000)	Post-fortification 2006–2010 (/10,000)	Prevalence rate ratio	Lower 95 % CI	Upper 95 % CI	<i>p</i> Value
LB SB	1.679	1.574	0.937	0.884	0.994	0.03
FD AN	130.909	95.241	0.727	0.681	0.777	<0.0001
FD CE	3.947	3.795	0.961	0.673	1.373	0.83
FD SB	3.686	3.981	0.700	0.507	0.967	0.03

LB live births, FD fetal deaths, SB spina bifida, AN anencephaly, CE cephalocele

Discussion

Underreporting at SINASC of congenital disorders notifications is recognized in Brazil. One study observed that the sensitivity for notification of birth defects ranged from 11.4 to 96.8 % in different hospitals in Brazil (Luquetti and Koiffman 2010) and showed wide discrepancies among different regions. The Southeast region, which includes the more developed states in Brazil, has the greatest sensitivity in reporting major congenital disorders. Specificity was 99 % or higher in all hospitals, meaning that very few false-positive diagnoses were being made. Underreporting of neural tube defect births limits the use of this information for both surveillance and decision-making processes by policy makers. However, continued improvement in the ability to correctly diagnose congenital anomalies and due to its nationwide coverage, SINASC is still a very useful tool to study changes in rates of congenital disorders.

Effect of folic acid fortification on spina bifida birth prevalence rates

Surprisingly, we observed a low impact of FAF on rates of spina bifida births, with a reduction of less than 10 % in the live birth prevalence. Orioli et al. (2011) compared data from SINASC for SB prevalence in live births for 2004 (pre-fortification period) and 2006 (post-fortification period) in Brazil. They observed a reduction in SB birth prevalence in 2006 of 39 % (95 % CI, 33 to 45 %; O/E 50.61; 95 % CI, 0.55–0.67), compared to 2004. However, they noted marked differences between different states, with some states having no statistical reduction in SB prevalence. The difference between reduction percentages found by Orioli et al. (2011) and our present data can be explained by the fact that those authors have analyzed the data only from the years 2004 and 2006, and here, we took data from the whole decade comparing pre-fortification rates between 2001 and 2004 and post-fortification rates between 2006 and 2010. From the data available from the 19 ECLAMC reporting hospitals in Brazil, including both live births and fetal deaths (López-Camelo et al. 2010) a PRR of 0.57 for

anencephaly ($p < 0.001$); 0.99 for spina bifida ($p = 0.973$), and 0.59 for cephalocele ($p = 0.091$) was observed, using the triennium before and after fortification for comparison. A meta-analysis of eight population-based observational studies from Chile (1), South Africa (1), Argentina (1), USA (1), and Canada (4), performed by Blencowe et al. (2010) gave an estimated reduction in NTD incidence of 46 % (95 % CI: 37–54 %).

Secular changes in the birth prevalence of neural tube defects are well known and our analysis was based on the assumption of a stable prevalence before introduction of folic acid fortification. López-Camelo et al. (2010) addressed this issue in the discussion section of their paper. They estimated secular trends before fortification for 52 anomaly types (data not shown—available from the corresponding author). Interestingly, in Brazil, they observed significantly rising secular trends ($p < 0.0001$) for spina bifida (cephalic, caudal, and total). No significant decreasing trend was observed for any anomaly type, meaning that anencephaly had a stable prevalence before introduction of FAF.

Effect of folic acid fortification on fetal and neonatal deaths

In contrast to the effect of FAF on rates of NTDs among live births, in the present study, we observed a greater impact of FAF on NTDs observed in fetal and neonatal deaths of around 30 %. Blencowe et al. (2010) estimated that 13 % of neonatal deaths could be prevented by reductions in NTDs if FAF were implemented in low-income countries, as NTDs account for 30 % of deaths in children with a visible congenital anomaly in those countries.

The low impact of FAF on NTDs compared to that observed in other Latin-American countries (Lopez-Camelo et al. 2005, López-Camelo et al. 2010) could be due to a number of reasons. The immediate explanation would be that the fortification policy in Brazil, although similar to that employed in USA for cereals, differs from those in Chile and Argentina. In Brazil, the folic acid flour fortification concentration (1.5 mg/kg) is lower than that of Chile and Argentina (2.2 mg/kg). In addition, there is a much lower estimated consumption of wheat-flour bread in Brazil than in

the other two countries. The estimated per capita daily intake of flour in Chile is 227 g (Calvo and Biglieri 2008); in Argentina is 221 g (Zabala et al. 2008); and in Brazil, only 176 g (Ferreira and Giugliani 2008). As a result of differences in fortification levels and flour consumption, the estimated daily dose of folic acid is 499 mcg in Chile, 486 mcg in Argentina, and 264 mcg in Brazil (Ferreira and Giugliani, 2008; López-Camelo et al. 2010).

It should also be taken into consideration that actual FAF levels in flour may be different from those mandated by regulatory agencies. Agência Nacional de Vigilância Sanitária (ANVISA) is the national regulatory agency responsible for periodic measurements of actual folic acid concentration in flour. A search at ANVISA's website (<http://portal.anvisa.gov.br/wps/content/Anvisa+Portal/Anvisa/Inicio/Laboratorios>, last accessed on 16 June 2013) shows that certified laboratories perform routine folic acid and iron measurements in flour brands commercialized in Brazil.

However, other factors can also play a role such as genetic factors. This may be because Brazil has had a unique colonization process and has a very different ethnic profile compared to other countries in South America. Greene et al. (2009) reviewed studies on candidate genes for NTDs and there are at least 200 different genes with some role in the etiology of NTDs worldwide. Williams et al. (2002) in USA reported a reduced effect of folic acid fortification in black Americans compared to white Americans. In Australia, the 30 % reduction in the incidence of NTDs seen following the promotion of folic

acid supplementation and voluntary food fortification was limited to the white population, with no changes in the NTD rates amongst the aboriginal populations (Bower et al. 2004).

TOP in Brazil has been legal in cases of anencephaly after special authorization from a judge; so we cannot rule out that the observed decrease in prevalence rate for anencephaly may be due to increases in the numbers of termination of pregnancies following detection of anencephaly. A survey conducted in Brazilian obstetricians (Diniz et al. 2009) has shown that 37 % of women who came to them with a pregnancy of an anencephalic fetus had successfully obtained authorization for legal abortion.

Identified needs

In addition to reviewing epidemiological data on specific congenital disorders, the health needs assessment process as advocated by the toolkit, enables users to examine the specific context of the country in relation to the congenital disorder being considered. This process allowed the identification of SWOT for the development of policies and services to manage NTDs in Brazil. The summary results of the SWOT analysis that we undertook is presented in Fig. 1 and provides suggestions for how policies and services could be improved in order to decrease the burden of disease arising from NTDs in Brazil. The HNA led to the identification of the following needs to be addressed in Brazil:

Fig. 1 SWOT analysis for NTDs management in Brazil

Internal environment	External environment
<p>Strengths</p> <ul style="list-style-type: none"> ➤ There are medical geneticists and other professionals trained and capable to provide counseling, treatment and rehabilitation ➤ FAF is already established countrywide. ➤ A nationwide birth defects registry, integrated to birth certificates system and to mortality reports is already established and easily accessible by anyone through internet. ➤ Parents associations for rare diseases are very active in Brazil ➤ People with disabilities receive governmental attention and support 	<p>Opportunities</p> <ul style="list-style-type: none"> ➤ The Brazilian Unified Health System (SUS) provides universal access to health to all citizens. ➤ Maternal-child health is a priority in government policies ➤ Care for disabled people is in the agenda of present government ➤ Emergent economy ➤ Recent ToP decriminalization for anencephalic fetus
<p>Weakness</p> <ul style="list-style-type: none"> ➤ Inequities in the access to secondary and tertiary health facilities: geographically, and socially. ➤ In general, knowledge and education about birth defects is deficient in average health professionals. ➤ FAF policy in Brazil is not sufficient for a reduction in the birth prevalence of NTDs. ➤ There is under-registration of birth defects. ➤ Lack of preconception care policies and programs 	<p>Threats</p> <ul style="list-style-type: none"> ➤ Illegal status of ToP for other conditions. ➤ Health policies and priorities can be discontinued following government and political changes.

- Increase the sensitivity of reporting congenital disorders within nationwide birth certification systems
- Further studies to understand the low effectiveness of FAF in the primary prevention of NTDs in Brazil
- Revision of the policy of flour folic acid fortification to improve the primary prevention of NTDs
- Improve professional education through courses and publications
- Implementation of prenatal screening based on first trimester ultrasound scan
- Decriminalization of termination of pregnancy
- Implement preconception care policies and programs in relation to NTD prevention
- Public education: creation of information sheets for parents of children with congenital disorders and awareness, raising on the importance of folic acid for NTDs prevention for the general population
- Specific attention to underserved health regions—North, Center, East being the most deficient in infra-structure regarding services for the prevention and management of congenital disorders

Toolkit use in other South-American countries

The decision to use the toolkit reflects the fact that it was designed to facilitate the aggregation and interpretation of not only epidemiological data, but also other relevant information, such as health services and social, economic, and demographic indicators. This enables the recognition of needs and directs the setting of priorities and planning of services, allowing non-epidemiologists to perform health needs assessment.

Recently, Groisman et al. (2013) published a paper describing the utilization of the toolkit in Argentina. It is interesting to observe some similar conclusions of identified needs; for example, to improve congenital disorders registries, to enhance public education regarding congenital disorders, and to improve professional education, the need to modify present laws that consider TOP as a crime, and the need to acknowledge social and geographic inequalities. The main difference was, as observed above, the fact that FAF is more effective for primary prevention of NTDs in Argentina, compared to Brazil.

However, the similarities in the conclusions reached by the two countries can lead to interesting conclusions: (1) the validation of the toolkit as a useful instrument for HNA in congenital disorders; (2) the identification of similar challenges in both countries can be used as a driver for scientific and political collaboration between South-American countries to tackle the problem of congenital disorders.

In conclusion, our findings from the HNA show that Brazil presents a clear example of why congenital disorders should

be considered a priority for health policies in countries with middle-income economies such as Brazil, where steps can be taken to tackle the burden of disease and mortality. Although much progress has been made in the health system in this country, the lack of specific policies for congenital disorders increases the gap in health experiences between social groups. In the case of NTDs, poorer individuals have both a higher risk of having an affected child due to less access to primary and secondary prevention, and at the same time, are more affected by the burden of child disability due to the lack of tertiary prevention and ongoing social care and support services.

Considering specifically NTDs, the HNA has highlighted the need for an in-depth review of policies for the folic acid fortification program in Brazil, particularly, in light of the present low impact of fortification on the primary prevention of neural tube defects.

Ethical standards

The research complies with the current Brazilian ethics Guidelines. The study did not include any individual-level data.

Conflict of interest The authors declare that they have no conflict of interest.

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