Present and Future of Birth Defects Surveillance in the Americas

PAHO
Pan American Health Organization
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Acronyms

BD	birth defects
CA	congenital anomalies
CLAP/WR	Latin American Center for Perinatology, Women, and Reproductive Health, PAHO/WHO
CNS	central nervous system
CREC	*Centro de Registro de Malformaciones Congénitas* (Congenital Malformation Registry Center, Costa Rica)
ECLAMC	Latin American Collaborative Study of Congenital Malformations
FAF	folic acid fortification
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research
ICD	International Classification of Diseases
INCIENSA	*Instituto Costarricense de Investigación y Enseñanza en Nutrición y Salud* (Costa Rican Institute for Research and Teaching on Nutrition and Health)
LAC	Latin America and the Caribbean
MDGs	Millennium Development Goals
NTDs	neural tube defects
PAHO	Pan American Health Organization
PHEIC	Public Health Emergency of International Concern
PIS	Perinatal Information System
PPP	purchasing power parity
RCPCH	Royal College of Paediatrics and Child Health
RENAC	*Red Nacional de Anomalías Congénitas de Argentina* (National Congenital Anomalies Network of Argentina)
SDGs	Sustainable Development Goals
SIVIGILA	*Sistema Nacional de Vigilancia de Salud Pública* (National Public Health Surveillance System)
WHO	World Health Organization
ZIKV	Zika virus

Preface

Health conditions during gestation and childbirth are vitally important because of their implications throughout the life course. Reducing mortality from preventable causes and promoting the best conditions and care in this period continue to be major imperatives, because promoting these actions helps to improve human and social capital in our Region and in the world.

Childhood health has made great strides in recent decades. There have been significant decreases in health conditions that are highly prevalent during this period of life. Respiratory diseases, diarrheal diseases, and other infections, which years ago were responsible for a high burden of sickness and death, have decreased substantially.

However, other challenges concern us and this is where we must strengthen our actions.

One of these challenges is the concentration of mortality in the neonatal period. The mortality profile has changed and birth defects are now one of the leading causes of death in this period. For children, their families, the health services that must deal with birth defects, and society as a whole, this is a very important issue. Another challenge is to confront the considerable and overt inequalities and inequities surrounding us. To this end, we must strengthen advocacy and undertake action to solve these problems; timely, high-quality information is fundamental to achieving the imperative to "leave no one behind."

We have decided to focus on the important issue of birth defects to help strengthen the children's health agenda. The emergence of Zika and its impact on our Region has underscored the need for information that allows timely interventions. Different actions aimed primarily at strengthening birth defects surveillance systems have been carried out in the Americas, with the participation of multiple actors.

This publication summarizes the epidemiological situation, availability of resources, and strategies and actions implemented thus far. It underscores the crucial importance of preexisting resources and the actions already undertaken, as well as the concern and interest of the international community. But at the same time, this document attempts to show the persisting gaps and challenges, and it seeks to contribute to analyze and highlight the coordinated efforts among actors who are sensitive to an issue that is so important for children's health, their families, and society as a whole.

Everyone has a specific role—national authorities, United Nations system agencies, international agencies, scientific and academic societies, health teams, and civil society organizations. We hope that this publication helps continue and expand efforts in this area, in light of the Sustainable Health Agenda for the Americas and other international frameworks.

Dr. Jarbas Barbosa da Silva Jr.
Assistant Director, Pan American Health Organization

Introduction

In Latin America and the Caribbean (LAC), more than 15 million children are born every year. Approximately 15 of every thousand will be at risk of dying during their first year of life, and 10 of every thousand in the first month of life, according to estimates published in 2018 by the Inter-agency Group for Child Mortality Estimation. [1] Approximately one of every five deaths during the first 28 days of life is due to birth defects.

Reduction of child mortality is a priority on the public agenda. Its magnitude, characteristics, and determinants are changing significantly, while at the same time important challenges persist.

The established goals and targets, such as Goal 4 of the Millennium Development Goals (MDGs), have helped to orient this agenda by setting the target to reduce by two-thirds the under-5 mortality rate by 2015.

In this context, from 1990 to 2017 (1990 is the starting point to measure attainment of the MDGs), neonatal mortality in Latin America and the Caribbean decreased from 23 to 10 neonatal deaths per 1,000 live births, a 58% reduction.

However, inequalities in neonatal mortality must be emphasized: in 2008, estimated neonatal mortality in the region's countries[1] ranged from 3.8 to 24.6 per 1,000 live births. The difference is still not substantially smaller and this disparity means that countries with the highest neonatal mortality have rates six times greater than countries with the lowest rates.

At the same time, the under-5 mortality rate has declined in the same period for all age subgroups, but with significant differences among them. The reduction was greatest in the group aged 28 days to 1 year (4.83%), followed by the group aged 1 to 5 years (4.51%). The reduction was smallest in the neonatal (3.0%) and fetal (2.3%) periods, implying that the latter has increased its proportional contribution to infant and under-5 mortality. [2,3]

Specific international initiatives have reduced neonatal morbidity and mortality, and have improved integration of interventions and strategies for the health of women, mothers, and newborns.

The Sustainable Development Goals (SDGs)[4] were put forward to continue and expand the outcomes already attained. Goal 3 includes among its indicators the under-5 mortality rate, with a target of reaching a value at least as low as 25 per 1,000 live births and neonatal mortality at least as low as 12 per 1,000 live births.

High mortality from preventable causes and significant inequalities—not only in deaths but also in other health conditions and diseases—continues to be a challenge, requiring specific interventions in view of the current situation of different population groups. Also relevant are health conditions and their implications for the early years and their impact on the life course, and the environment in which children grow and develop, which jeopardize health and development and contribute to the burden of disease and disability, as well as affecting human capital and social capital.

There is abundant evidence concerning the impact of early conditions that (positively or negatively) can help or hinder the full development of human potential. In this regard, The Global Strategy for Women's, Children's and Adolescents' Health[5] proposes three core objectives:

> Survive: Put an end to preventable mortality
>
> Thrive: Achieve health and well-being
>
> Transform: Expand enabling environments

Birth defects are among the conditions that contribute to the burden of morbidity and mortality. In this regard, in recent years there has been growing interest in how they are addressed. The World Health Organization (WHO), in Resolution 63.17 of the 63rd World Health Assembly[6], encourages countries to prevent birth defects whenever possible, promoting new detection programs and providing ongoing support and attention, both to children with birth defects and to their families.

The resolution on birth defects asked all Member States to promote primary prevention and the health of children with birth defects through:

- development and strengthening of registry and surveillance systems;
- development of expertise and creation of capabilities;
- strengthening of research and studies on etiology, diagnosis, and prevention; and
- promotion of international cooperation.

The international community has made strides both in advocacy and in implementation of specific actions aimed at reducing the impact of birth defects using different approaches. An example of this has been the establishment of World Birth Defects Day, devoted to raising awareness and informing professionals and the public about actions to prevent disease and promote the health of newborns.

This process accelerated forcefully after the major impact of the Zika virus (ZIKV) outbreak and its association with birth defects initially described as first reported in late 2015 in Brazil and then spreading through the other 47 countries of the Region. This led WHO to declare a Public Health Emergency of International Concern (PHEIC) and recommend intensifying surveillance and investigation of the unusual increase in microcephaly and other birth defects.[7] Accordingly, actions were stepped up in the areas of prevention, surveillance, monitoring, and public health impact.

Birth defects contribute substantially to the burden of morbidity and mortality in the Region of the Americas. Numerous efforts exist to raise awareness of this problem and to implement surveillance in health and government sectors. However, there is still a long way to go.

In this regard, for several years, countries have been taking actions to coordinate efforts, while strengthening and establishing strategic alliances to achieve significant results. The extensive history of efforts aimed at responding to the situation of birth defects in the Region includes actions in health care, epidemiology, legislation, and investigation, with participation from the scientific and technical community, government, and civil society.

After taking into account all these aspects, the Pan American Health Organization/Latin American Center for Perinatology, Women, and Reproductive Health (PAHO/CLAP/WR), together with the World Bank, decided to create a document summarizing the regional situation of birth defects from an epidemiological and programmatic perspective, to analyze the challenges and offer countries guidance to address birth defects, their determinants, and consequences, with the ultimate goal of helping to "leave no one behind."

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Burden of morbidity and mortality associated with birth defects

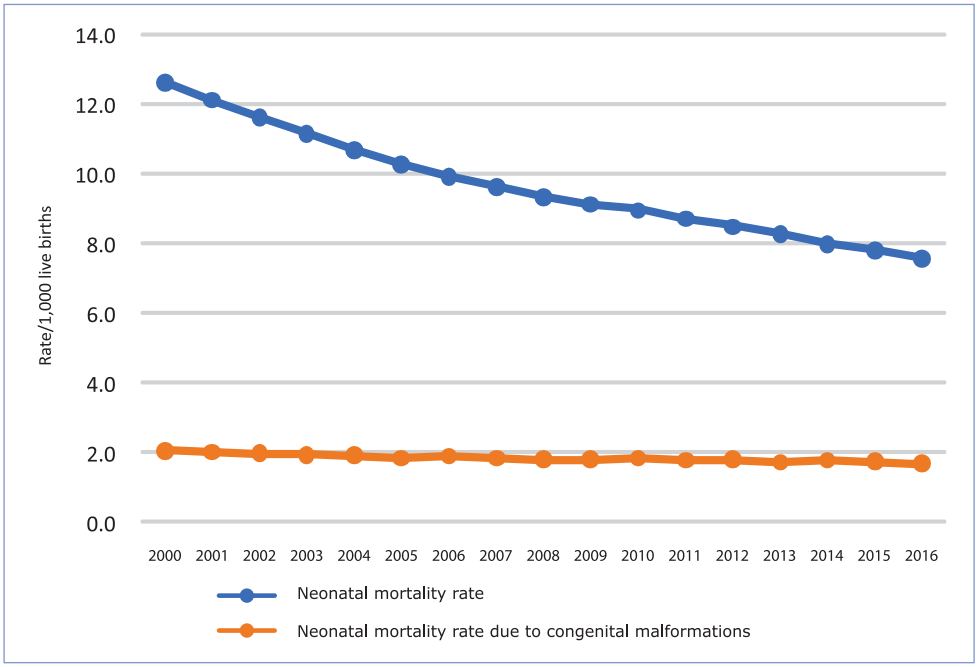
The burden of mortality associated with birth defects is relevant both globally and regionally. It was estimated that for 2016, worldwide prevalence of birth defects (in absolute numbers) was 82,890,000 cases, with an incidence of 14,922,120 cases. The most prevalent defects are circulatory system (15,377,000), musculoskeletal system (10,812,000), digestive system (9,711,000), urogenital (7,172,000), and neural tube (5,782,000) malformations.[1]

Every year, more than 15 million children are born in the Region of the Americas. In 2017, approximately 15 out of every thousand were at risk of dying before their first birthday and 10 out of every thousand during the first month of life.[2] Estimated neonatal deaths (103,000) in 2017 in Latin America and the Caribbean represented almost two-thirds (65.5%) of all deaths during the first year of life and 55% of all deaths of children under 5.[2]

One of every five deaths during the first 28 days of life is due to birth defects, which in absolute numbers represents almost 20,000 children. Along with the contribution of birth defects to neonatal mortality, their contribution to fetal mortality cannot be ignored.[3]

In view of achievements in reducing other causes of preventable death in this age group, the proportion of neonatal deaths due to birth defects increased from 16.2% to 22.3% from 2000 to 2016. In general, proportional mortality due to birth defects is increasing over time in most countries. However, a clear increase in neonatal mortality from this cause has not been observed, although neonatal mortality is generally declining, as shown in Figure 1.[4]

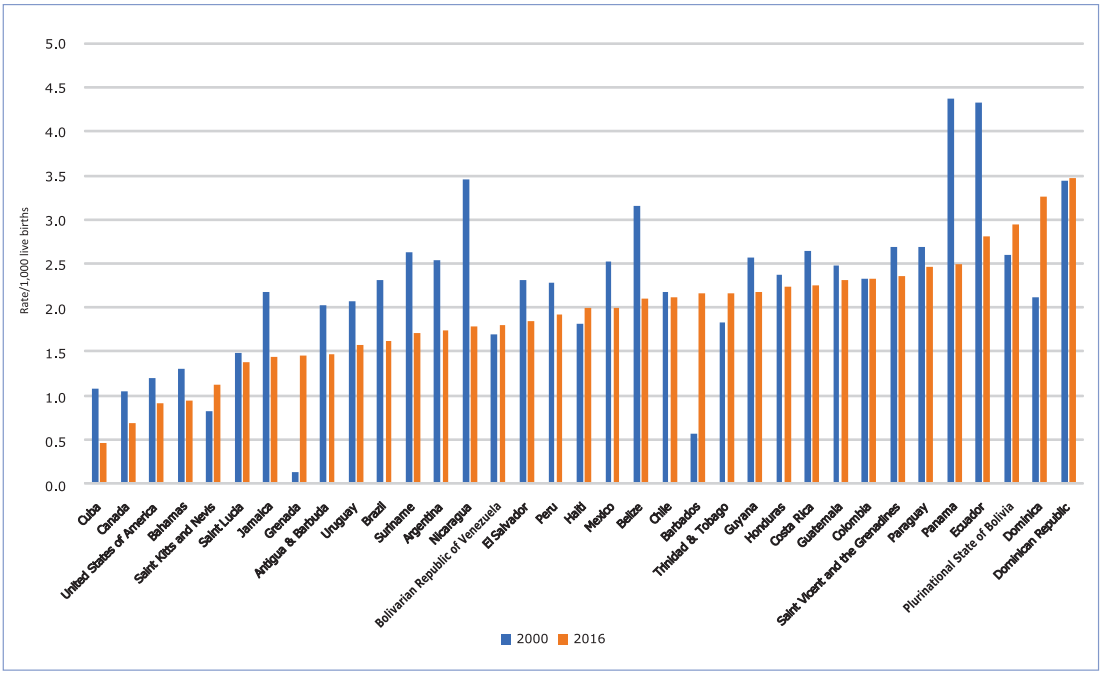
Figure 1. Neonatal mortality, total and from congenital malformations (Q00-Q99), the Americas, 2000-2016



The specific rate of neonatal mortality from birth defects varied little during the period analyzed, at close to 2 deaths per 1,000 live births per year.

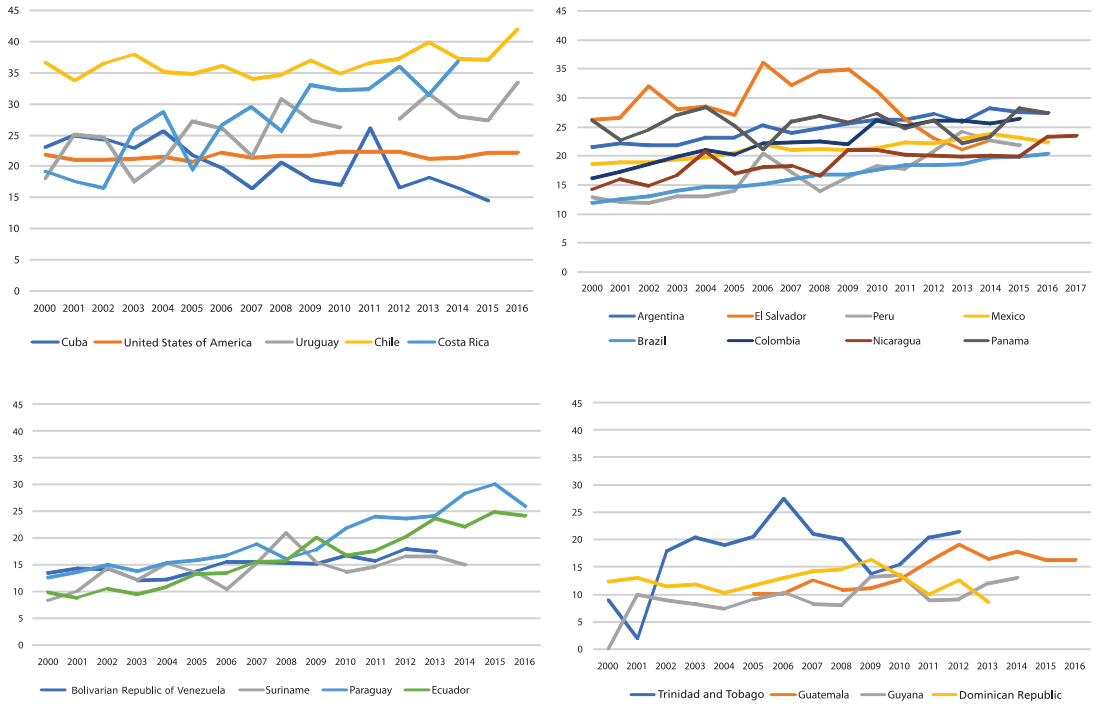
As mentioned above, birth defects account for a significant proportion of neonatal deaths in the Region of the Americas, and the trend is growing. However, both the trend and the contribution of this group of causes vary from country to country. This is due, among other factors, to the accuracy with which causes of death are recorded, access to prenatal diagnostic techniques for each population group, and the possibility of voluntary interruption of pregnancy. A comparison of rates for this group of causes (Figure 2) shows these differences.

Figure 2. Neonatal mortality from congenital malformations (Q00-Q99), per country, 2000 and 2016



In countries where mortality is under 6 deaths per 1,000 live births, deaths from birth defects account for 15-40% of neonatal deaths. In contrast, where neonatal mortality is higher than 12 per 1,000 live births, deaths from birth defects usually account for less than 15% of total deaths in that age group. In countries with a mortality rate of 6-12 per 1,000 live births, the behavior varies, with proportions that fluctuate from approximately 10% to 30% of neonatal mortality.

Figure 3. Proportion of neonatal deaths from congenital malformations, deformities, and chromosomal abnormalities (Q00-Q99) in the Region of the Americas, 2000-2016

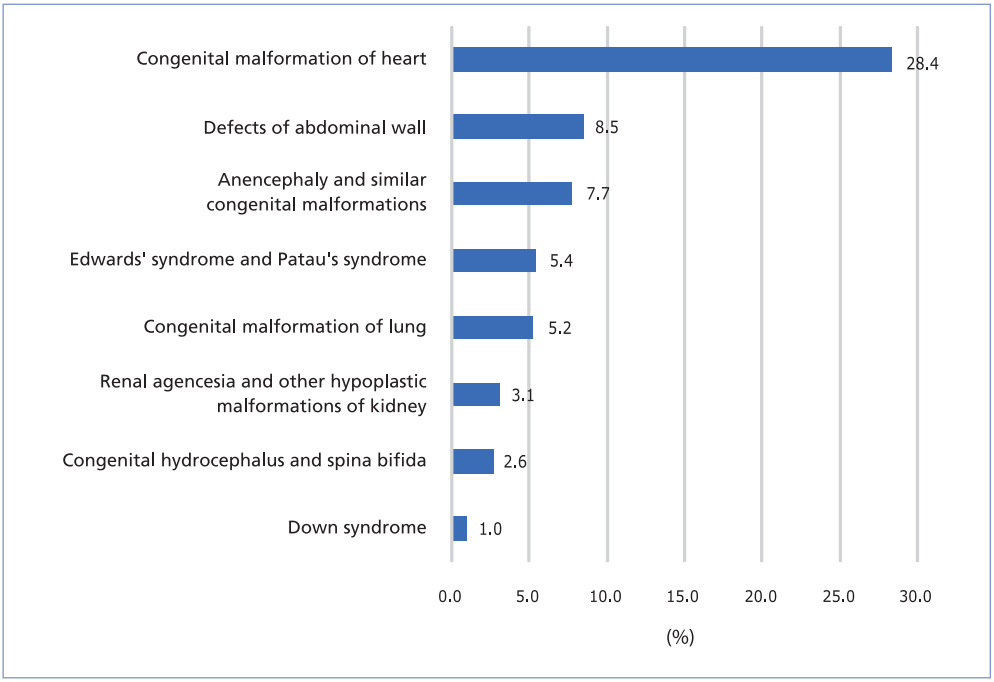


It is important to consider that mortality data reported by countries has also changed over time due to efforts to better record infant and neonatal deaths and to ensure correct classification of the underlying cause of death. It is not surprising that certifying physicians now have more information on the cause of death. Specifically, there is greater access to diagnosis of birth defects, an aspect that is changing quickly in the countries, added to the fact that the profile of causes of neonatal death is also changing due to the interventions that have been implemented.

In this regard, the proportional contribution of birth defects is growing as neonatal mortality declines, at the expense of reducing mortality secondary to other groups of causes.

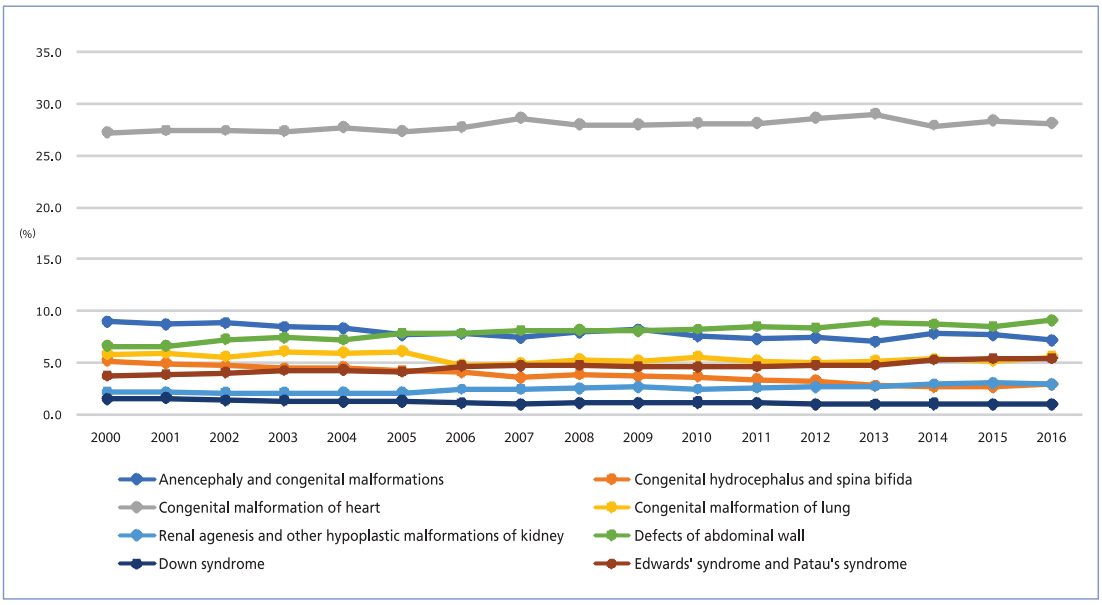
Of all deaths in the Region due to birth defects, one of every three is due to congenital malformations of the heart, which is the main cause of death in this group, maintaining a steady trend over time (Figures 4 and 5).

Figure 4. Main congenital malformations and chromosomal abnormalities as cause of neonatal death. Region of the Americas, 2016



Congenital malformations of the circulatory system contribute the most to neonatal mortality (33.6%), representing one out of three deaths from birth defects.

Figure 5. Main congenital malformations and chromosomal abnormalities as cause of neonatal death, the Americas 2000-2016



It is important to consider that the regional panorama and the regional trend in the figures are influenced by their behavior at the country level, which in turn are affected by the subnational level. As a result, it is crucial to conduct a behavioral analysis of neonatal mortality from this group of causes at the subnational level, comparing the trend with causes from the group of certain disorders originating in the perinatal period whose distribution is declining due to interventions. Furthermore, it is important to measure and monitor the weight of social determinants and their inequalities on neonatal mortality among subnational levels. However, the remaining challenge is to identify areas where there are specific opportunities to contribute more and better, not only to attain SDG 3 but also to improve neonatal health. Different actions are aimed at improving access to and quality of care as well as at prevention of specific conditions and determinants associated with perinatal and neonatal mortality.

Although there is no estimate of the burden of secondary disease associated with birth defects in the Region of the Americas, its magnitude can be assessed based on available worldwide estimates that indicate that in 2016, birth defects accounted for 9,723,000 disability-adjusted life years. Although such values represent a decline of 1.5% compared to 2006, they continue to be high.

A recent study makes it possible to assess the contribution of selected birth defects in children under 5, based on analyses and estimates in 195 countries. Birth defects are the second leading cause of hearing loss (21.1%) following otitis media (57.1%). Birth defects (39.7%) and neonatal disorders—which include complications of preterm birth, infections, and birth asphyxia (21.0%)—were the leading known causes of intellectual disability, while idiopathic causes accounted for 29.0%.[5]

A recent study[2] based on data from 21 studies in 15 countries of the Americas shows that the Region has the least variability in reported estimates of prevalence of neural tube defects (NTDs). Among the analyses that included spina bifida and at least one other NTD, the lowest prevalence was 3.3 per 10,000 births. A Brazilian study that only considered spina bifida showed a prevalence of 1.4 per 10,000 births. In this Region, the highest prevalence was observed in Guatemala (27.9 per 10,000 births). Median prevalence was 11.5 per 10,000 births.[6]

In comparison to the persistence of birth defects as a group of causes that contributes both to mortality and to morbidity and disability, there are certain cases where concrete, effective actions have led to the elimination of specific causes. This is the case with congenital rubella syndrome: in April 2015, an international expert committee reviewed the epidemiological evidence presented by the PAHO/WHO Member Countries and determined that the Region had eliminated endemic transmission of rubella and congenital rubella.

These last two illnesses are the third and fourth diseases eliminated in the Americas, after smallpox in 1971 and polio in 1994. In the four cases, the Region was the first in the world to achieve their eradication. To maintain this status, PAHO/WHO and the International Expert Committees for Measles and Rubella Elimination recommend that all countries in the Americas strengthen active surveillance and maintain high immunity in the population through vaccination.

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Surveillance of birth defects

Data analysis, based primarily on vital records, provides essential input for the assessment of the mortality burden, trend analysis, and evaluation of the impact of specific interventions. However, while it is generally useful, assessing less common conditions or continuously analyzing the disease burden is more appropriate when based on surveillance systems for specific birth defects. This is the case for congenital rubella syndrome, where epidemiological surveillance has demonstrated its importance.

Public health surveillance is the systematic and ongoing collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of practices, closely integrated to the timely dissemination to those that need to know, to carry out public health actions.[1] The ultimate goal of public health surveillance is prevention.

The objectives of birth defects surveillance are:

- Monitoring prevalence of birth defects in a defined population.
- Detecting geographical and temporal clusters of birth defects.
- Referring those affected to appropriate health services at the right time.
- Informing families about available health resources for treatment of affected persons.
- Communicating results to relevant health organizations and actors.
- Informing health authorities of the estimated number of cases, for planning necessary treatment resources.
- Training health professionals on birth defects.
- Providing a basis for epidemiological investigation.
- Evaluating population-based interventions (e.g., fortification of staples with folic acid).

Public health surveillance includes consideration of several interconnected definitions and processes. For birth defects in particular, this includes case-finding; data collection; and the transmission, coding, classification, analysis, interpretation, and dissemination of information. This series of procedures can occur in systems of varying design (Table 1).

Table 1. Elements of birth defects surveillance[4]

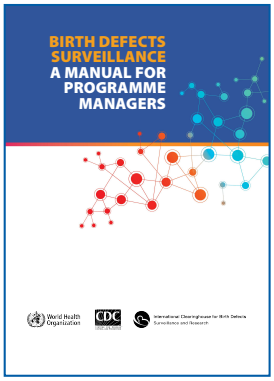
Element	Options
Coverage	Population- or hospital-based
Case-finding	Active, passive, or hybrid
Data sources	Single source or multiple sources
Case definition	All birth defects (external and internal) or only external ones; major or minor anomalies, or only major anomalies
Information on healthy children	Inclusion of controls or not
Description	Through an open field or checklist
Inclusion age	Up to discharge from the maternity service, 1 year, or later
Pregnancy outcomes	Live births; live births and stillbirths; live births, stillbirths, elective interruption of pregnancy due to fetal anomaly
Coding system	ICD-10[2] (with or without the adaptation by the Royal College of Paediatrics and Child Health (RCPCH[3])), or an internal adaptation
Coding process	Local or centralized
Means of reporting	Online, printed/physical, mixed

Several tools and instruments are available that contribute to establishing and strengthening surveillance of birth defects. One of them is the Birth Defects Surveillance Toolkit, which includes guidance on implementing and strengthening this process for monitoring at birth.[4]

The Toolkit is at an interactive online portal that can be accessed through the websites of the U.S. Centers for Disease Control and Prevention (CDC)[5], WHO, and the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR). Although there are printed publications of materials, the Toolkit was developed for the Internet so that countries can easily adapt it. Its main components are currently available in English, Spanish, and French.

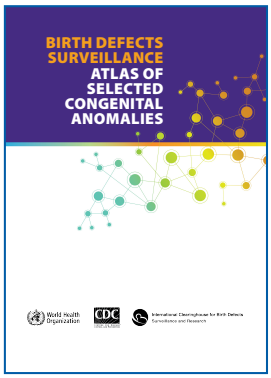
The Toolkit consists of a manual, a photographic atlas, and a facilitator's guide.

Manual



The document "Birth defects surveillance: a manual for programme managers"[6] has served not only as the basis for numerous international workshops, but also for the design of birth defects surveillance systems. This manual provides guidance, specific definitions of types of surveillance, diagnosis, coding of birth defects, and the use of criteria such as the International Classification of Diseases (ICD), and necessary qualifications of surveillance program personnel.

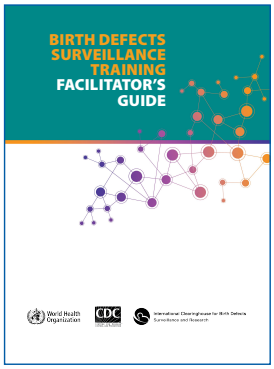
Atlas



A complement to the Manual for Programme Managers is "Birth defects surveillance: atlas of selected congenital anomalies,"[7] created as a contribution to the design, implementation, and strengthening of surveillance in countries.

It contains photographs of a selected set of birth defects, with their corresponding codes from the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), and its expansion, by the Royal College of Paediatrics and Child Health (RCPCH).

Training guide



This material is for personnel involved in training courses, with suggestions for the facilitator and graphics.[8] Its objective is to provide the instruments necessary to begin the development, implementation, and ongoing improvement of a birth defects surveillance program.

These tools have proven useful and are highly valued by the countries where they have been used, both in the Americas and in other regions, in the process of establishing and strengthening surveillance of birth defects.

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What is the current status of birth defects surveillance in Latin America and the Caribbean?

Birth defects surveillance systems in the region

The epidemiological situation presented above, together with the emergence of Zika and its consequences, as well as the availability of instruments and experience, prompted the planning and implementation of different activities aimed at strengthening birth defects surveillance systems in the Americas.

These activities included a situation assessment of the availability and characteristics of birth defects surveillance systems and registries. This task was coordinated by CLAP/PAHO and the World Bank, with technical support from the professional team of the National Congenital Anomalies Network of Argentina (RENAC).

Together with the results of the situation assessment, this report provides details on some of the surveillance systems in the region that have been involved in training programs on the implementation and improvement of new surveillance programs. The systems that are presented in greater detail are the Latin American Collaborative Study of Congenital Malformations (ECLAMC), RENAC, the Birth Defects Surveillance Programs of Cali and Bogotá (Colombia), and the Congenital Malformation Registry Center (CREC) of Costa Rica. All these systems are members of ICBDSR, a consortium of organizations that work on birth defects, whose experience is summarized later in this document.

Regional mapping of surveillance systems in Latin America

A key objective in the process of strengthening surveillance is to characterize the availability and characteristics of birth defects surveillance systems and registries in the region.

In order to learn about the availability and characteristics of birth defects surveillance systems in the countries of the Americas, a semi-structured, self-administered survey was set up on Survey Monkey (in English and Spanish), and sent to focal points responsible for newborn health in the ministries of health of all the countries of Latin America and the Caribbean. Data collection was carried out by the PAHO/WHO Representative Offices in each country, from July to November 2017.

The survey included questions on the availability of a birth defects surveillance system in the country and asked what authority the system is under, contact information, and the characteristics of its methodological design (Table 2). The dimensions assessed in the survey included the reference basis of the surveillance system, type of coverage, data sources, what authority the reporting facilities are under, and data collection method. Furthermore, there were questions on the coding system in use, the approximate number of births examined annually, pregnancy outcomes, age of inclusion, availability of an operations manual or other data collection support materials, and periodic reporting to disseminate information.

At present, 14 countries from Latin America and the Caribbean have a working system at the national level: Argentina, Bolivia (Plurinational State of), Brazil, Colombia, Costa Rica, Cuba, Dominican Republic, Guatemala, Honduras, Mexico, Panama, Paraguay, Uruguay, and Venezuela (Bolivarian

Republic of). In all cases, the surveillance systems are under the corresponding health ministry or secretariat. Those who responded to the survey indicated that the data collected through these registries are sent to a central national coordinating center. Table 3 summarizes the characteristics of 11 country surveillance systems.

The systems surveyed have heterogeneous features and for the most part they were started in the last 10 years; eight began in 2010 or later, while Cuba began in 1985, Costa Rica in 1987, and Mexico in 1999. The systems are both hospital- (6) and population-based (4). Of the former, five (Argentina, Cuba, Guatemala, Paraguay, and Venezuela (Bolivarian Republic of)) collect data only from maternity services, while the Dominican Republic includes maternity services and other facilities, and the latter include five countries with population-based systems (Brazil, Colombia, Costa Rica, Mexico, and Uruguay). For the most part, the systems provide national coverage.

The data collection method is largely hybrid, except for Colombia, Paraguay, and Venezuela (Bolivarian Republic of), where it is passive. Practically all countries code birth defects according to the International Classification of Diseases, 10th revision (ICD-10), although Argentina, Costa Rica, and Cuba also use the RCPCH adaptation.

All the systems include live births and stillbirths, except for Venezuela (Bolivarian Republic of), which only considers live births; Cuba, Mexico, and Uruguay also include elective termination of pregnancy. Three countries (Argentina, Cuba, and the Dominican Republic) register birth defects until newborns are discharged from the maternity service or until one month of life (Guatemala); four detect congenital anomalies (CA) until the first birthday (Colombia, Costa Rica, Mexico, and Paraguay), and two, until the sixth birthday (Uruguay and Venezuela (Bolivarian Republic of)).

For the most part, surveillance systems include cases with major and minor anomalies (i.e., which involve significant damage to the health or do not represent an important health problem or have consequences), except for Argentina, Colombia, and Guatemala, which only include major anomalies. Only four of the systems produce periodic reports and scientific publications using surveillance system data (Argentina, Colombia, Costa Rica, and Uruguay). Argentina and Costa Rica have an operations manual; Colombia has a protocol. Only Argentina has an atlas for professionals who report data.

The first conclusion that emerges from the assessment is that a significant number of countries do not have birth defects registries or surveillance systems. Second, characteristics differ among the countries that do have surveillance systems (well consolidated or still in development).

We also see that only certain systems (in Argentina, Chile, Colombia, Cuba, Mexico, and South America) regularly share data with global consortia such as the ICBDSR. At present, only a few national systems publish or share their data, so there is limited opportunity to compare information from these registries in the region with reports in the literature.

Table 2. Variables used in the "Survey of congenital anomalies surveillance systems in the Americas," July to November 2017

Variables	Categories
Type of surveillance	Hospital-based: Information is collected in selected maternity services and coverage corresponds to the births that occur in them. Population-based: coverage encompasses all deliveries by women living in a specific area, regardless of where the birth takes place.
Data source	Maternity services Maternity services and other facilities
Coverage	National, provincial, public, social security, private facilities
Case collection method	Passive: participating facilities report information, without review from a central coordinating body. Active: personnel from the central coordinating body visit participating facilities and collect information on affected cases. Hybrid: participating facilities report information to the central coordinating body, which reviews cases.
Coding	ICD-10 ICD-10 with the RCPCH/BPA (British Paediatric Association) modification Internal system Other
Number of live births per year	Number of live births per year in the system Number of live births per year in the country
Pregnancy outcomes	Live births, stillbirths Elective termination of pregnancy due to fetal anomalies
Definition of cases entered into the system	Major or minor anomalies Only major anomalies Other (specify)
Registry cut-off point	Discharge from maternity service 1 week of life 1 month of life 6 months of life 1 year of life 6 years of life
Source of denominator	Births in participating hospitals Vital statistics Other
Operations manual	Yes No
Type of form used by the system	Paper Electronic format
Data transmission method	By postal mail By email through webpage Other
Where data are sent	To a central national coordinating body To intermediate nodes
Is there a coordinating team at the central level?	Yes No
Are periodic reports prepared?	Yes No
Do they have a photographic atlas?	Yes No

Table 3. Characteristics of surveyed surveillance systems

Country	Name of program	Year established	Basis	Data sources	Coverage	Reporting facilities	Method	Coding
Argentina	National Congenital Anomalies Network of Argentina (RENAC)	2010	Hospital	Only maternity services	National	Public, private, and social security facilities	Hybrid	ICD-10 with RCPCH/BPA modification
Colombia	National Birth Defects Surveillance System (SIVIGILA)	2010	Population	Maternity services and other facilities	National	Public and private facilities	Passive	ICD-10
Costa Rica	Congenital Malformation Registry Center (CREC)	1987	Population	Maternity services and other facilities	National	Public and private facilities	Hybrid	ICD-10 with RCPCH/BPA modification
Cuba	Cuban Congenital Malformation Registry (RECUMAC)	1985	Hospital	Only maternity services	National	NS	Hybrid	ICD-10 with RCPCH/BPA modification
Dominican Republic	National Epidemiological Surveillance System	2016	Hospital	Maternity services and other facilities	National	NS	Hybrid	ICD-10
Guatemala	Congenital Anomalies Surveillance Protocol	2017	Hospital	Only maternity services	NS	Public facilities	Hybrid	ICD-10
Mexico	Epidemiological Surveillance System for Neural Tube Defects and Craniofacial Defects	1999	Population	Maternity services and other facilities	National	NS	Hybrid	ICD-10
Panama	Neural Tube Malformation Detection System	2013	NS	NS	NS	NS	NS	NS
Paraguay	National Birth Defects Registry	2016	Hospital	Only maternity services	National	Public facilities	Passive	ICD-10
Uruguay	National Registry of Birth Defects and Rare Diseases (RNDCER)	2011	Population	Maternity services and other facilities	National	NS	Hybrid	ICD-10
Venezuela (Bolivarian Republic of)	Registry of Patients with Diseases of Inborn Errors of Metabolism	2017	Hospital	Only maternity services	NS	Public facilities	Passive	NS

NS: not specified.

Table 3. Characteristics of surveyed surveillance systems (continuation)

Country	No. of births covered per year	Total births per year	Included outcomes	Inclusion age	Source of denominator	Inclusion criteria	Operations manual	Periodic report	Atlas
Argentina	300,000	770,000	Live births and stillbirths	Discharge from maternity service	Births in participating hospitals	Only major anomalies	Yes	Yes	Yes
Colombia	660,999	660,999	Live births and stillbirths	1 year of life	Vital statistics	Only major anomalies	Yes	Yes	No
Costa Rica	70,000	70,000	Live births and stillbirths	1 year of life	Vital statistics	Major or minor anomalies	Yes	Yes	No
Cuba	120,000	120,000	Live births, stillbirths, and elective terminations	Discharge from maternity service	Births in participating hospitals	Major or minor anomalies	No	No	No
Dominican Republic	193,000	193,000	Live births and stillbirths	Discharge from maternity service	Estimates from the National Statistics Office	Major or minor anomalies	No	No	No
Guatemala	155,000	391,425	Live births and stillbirths	1 month of life	Births in participating hospitals	Only major anomalies	No	No	No
Mexico	1,404	2,080,253	Live births, stillbirths, and elective terminations	1 year of life	Vital statistics	Major or minor anomalies	No	No	No
Panama	NS	NS	NS	NS	NS	NS	No	No	No
Paraguay	80,000	114,000	Live births and stillbirths	1 year of life	Births in participating hospitals	Major or minor anomalies	No	No	No
Uruguay	28,000	48,000	Live births, stillbirths, and elective terminations	6 years of life	Vital statistics	Major or minor anomalies	Yes	Yes	No
Venezuela (Bolivarian Republic of)	NS	399,068	Live births	6 years of life	Vital statistics	Major or minor anomalies	No	No	No

NS: not specified.

Review of selected registries

International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

Characteristics	
Year established	1974
Participating programs	42 programs in 36 countries
Births evaluated	More than 4 million per year
Website	www.icbdsr.org

History

ICBDSR is a voluntary international nonprofit organization affiliated with WHO. It brings together birth defects surveillance and research programs from around the world. Currently, 42 programs from 36 countries participate in this organization (some with more than one subnational program), and it has a coverage of over 4 million births per year. The mission of ICBDSR is public health surveillance and research on the occurrence and possible causes of birth defects. Its main objective is to prevent birth defects and reduce their impact on the health of the population.

This organization was created as a response to the threat of unrecognized teratogens. After the epidemic of birth defects caused by thalidomide in the late 1950s and early 1960s, coordinators of birth defects registries in the Americas and Europe agreed to jointly and continuously share and evaluate data on birth defects to prevent similar epidemics.

Since then, ICBDSR has evolved in size and scope. Its headquarters, the International Clearinghouse for Birth Defects (ICBD), is funded by nongovernmental and governmental organizations and it has official relations with several related international organizations, including other birth defects networks, such as EUROCAT, the European Surveillance of Congenital Anomalies Association.

Structure

Since 1974, ICBDSR holds an annual meeting, with scientific sessions and discussion of collaborative research projects. The ICBDSR business meeting also takes place there, which designates three members of the Executive Committee for the following year, votes on the inclusion of new programs, and discusses operational aspects of the organization.

Surveillance systems interested in joining ICBDSR submit an application (available on the website) and make a commitment to contribute to the systematic collection and analysis of data for birth defects surveillance, provide baseline data for at least two years using the same surveillance methodology, and maintain the capacity to provide data annually to ICBDSR.

Activities

- Cooperates in investigations of changes in the frequency of birth defects.
- Carries out epidemiological studies on the causes of birth defects.
- Strengthens the surveillance capacity of its member programs and encourages the development of new programs, surveillance training, and investigation of birth defects.
- Promotes standards and definitions for birth defects surveillance.
- Coordinates research activities with its members and other collaborators.

There are numerous examples of collaborative studies conducted as part of the ICBDSR network:

- Determining the frequency of different birth defects subject to routine surveillance.[1]
- Study of the frequency of specific birth defects in the different programs, e.g., holoprosencephaly.[2]
- Specific study of the epidemiology of certain birth defects, e.g., hypospadias.[3]
- Study of the epidemiology of certain very rare birth defects, taking advantage of ICBDSR's high coverage of births around the world.[4-11]
- Analysis of specific clusters of some birth defects.[12]
- Surveillance of adverse fetal effects of medications.[13] Confirmation of teratogenicity of specific agents[14], after prior suspicion by another researcher in the group.[15]
- Assessment of the impact of specific measures at the international level, such as supplementation with folic acid and enrichment.[16]

All these collaboration activities by ICBDSR are based on systematic data collection by the participating programs. This enables their use for implementation of public health actions such as comparison of prevalence rates; advocacy; policy-making; epidemiological studies of causes and clinical outcomes of cases affected by birth defects; evaluation of preventive and therapeutic interventions; and interaction with the population, research institutions, and government.

ICBDSR helps implement and improve surveillance systems through training carried out in collaboration between its members and other organizations, such as PAHO/WHO, CDC, March of Dimes Foundation, and the Task Force for Global Health. These training programs generally consist of an online resource on the ICBDSR platform, followed by an in-person workshop to address the needs of each country. Furthermore, these activities are complemented by the preparation of educational materials and useful guides for professionals dedicated to birth defects surveillance.[17,18] Training has been provided using this method in the Americas, Africa, Europe, and Southeast Asia.

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Latin American Collaborative Study of Congenital Malformations (ECLAMC)

Characteristics	
Year established	1967
Admission to ICBDSR	1974
Coverage	Hospital-based, multinational
Maximum age at diagnosis	Until discharge from birth hospital
Pregnancy outcomes included	Live birth
Case definition	Stillbirths >500 grams
Controls	Major and minor structural anomalies
Information on risk factors	Yes
Website	www.eclamc.org

History

ECLAMC is a clinical and epidemiological research program on birth defects in Latin American hospital births. The initiative began in 1967 as an investigation limited to the city of Buenos Aires. However, in a short time it began expanding and, two years later, included hospitals in different cities of Argentina, Chile, and Uruguay. In 1973, ECLAMC also expanded to Brazil, Ecuador, Peru, and Venezuela (Bolivarian Republic of). Seventeen years later, it comprised all the countries of South America, Costa Rica, and the Dominican Republic.

As it grew, it essentially maintained its original experimental design from 1967, although some changes were introduced as the result of the experience gained in ECLAMC, as well as general advances in knowledge.

More than 200 maternity services in Latin America have been part of the program. In 1999, ECLAMC began DNA sampling for research on the contribution of specific genetic factors to the etiology of birth defects, producing a repository used by a large number of research studies.

ECLAMC is made up of a coordination structure and hospitals (maternity services) where information is recorded and reported. Institutionally, the program has been located in various centers in Argentina and Brazil, and linked administratively to public and private research agencies. The coordinating team works in ECLAMC headquarters facilities: the Center for Medical Education and Clinical Research (CEMIC) in Buenos Aires; the Congenital Malformations Epidemiology Laboratory of the Osvaldo Cruz Institute (FIOC-FIOCRUZ); and the Congenital Malformations Laboratory of the Department of Genetics, Rio de Janeiro Federal University.

Its activities focus on voluntary cooperation among its members, which operate according to a set of operational standards that ensure the uniformity of criteria necessary for comparing data recorded at different hospitals.

At present, 25 hospitals from eight South American countries are participating. In the maternity services that are part of ECLAMC, all major and minor anomalies diagnosed at birth are registered, following a procedures manual. They are also documented with photos and x-rays, whenever possible.

ECLAMC follows a case-control methodology: after the birth of a patient with birth defects (case), the next non-malformed newborn of the same sex born in the same hospital is registered (control). For both cases and controls, 50 variables on risk factors are recorded. Information is collected by a pediatrician during the puerperium directly from the mother. Using 10 variables, ECLAMC collects information on all births in participating hospitals.

One of its primary activities is scientific output. ECLAMC is a research program on risk factors for birth defects that follows a case-control methodology. To date, this group has published more than 300 research studies in indexed journals, other publications, and books, as well as more than 50 doctoral theses.[1]

ECLAMC has served as the model for and has promoted the creation of several birth defects registries, such as the Spanish Collaborative Study of Congenital Malformations (ECEMC), created in 1976; the Mexican Registry and Epidemiological Surveillance of External Congenital Malformations (RYVEMCE), begun in 1978; the Cuban Congenital Malformation Registry (1985); the Congenital Malformations Registry Center (CREC), in Costa Rica (1986); the Regional Congenital Malformations Registry of the Maule Health Service, in Chile, (2001); the Congenital Malformations Surveillance Program of the city of Bogotá (2005); the National Congenital Anomalies Network (RENAC), of Argentina (2009); and the National Registry of Birth Defects and Rare Diseases of Uruguay (2011).

It has contributed to epidemiological surveillance, evaluating fluctuations in frequencies of different anomalies and their geographical distribution. It has also provided information on the impact of public policies on birth defects, such as policies on folic acid fortification in some countries in the region.[2]

It has investigated possible clusters or geographical aggregates of several anomalies, such as microtia[3], oral clefts[4], sirenomelia[5], and microcephaly[6], among others. Through "rumor" methodology, it has also evaluated possible CA epidemics in the region.[7] In 2009, it created the National Census of Isolates (CENISO)[8] in Brazil, a system for the registry of population-based genetic isolates, usually clusters of genetic disorders, based on the search for rumors. Another of its activities has been to promote the creation of services providing information on teratogenic agents, which became a tool for primary prevention of this type of birth defect.

It has promoted sensitization and training activities on the prevention of birth defects both for health workers and in the community, focused mainly on primary, preconception, and tertiary prevention. One of the proposed actions has been the publication of "The ten commandments for primary prevention," which lists widely disseminated primary prevention measures for birth defects, as well as a book ("Primary prevention of birth defects") aimed at health providers specializing in birth defects.[9]

It produced an orientation program for parents, consisting of informative material on the main birth defects (folders) and a directory with more than 500 patients/parents from organizations in South America, to improve sharing among family members and professionals.

It has participated in multiple training activities on birth defects, in undergraduate and graduate-level programs.

In Brazil, ECLAMC spearheaded the creation of the National Institute of Science and Technology for Medical Population Genetics, a new medical specialty that brings together medical genetics, genetic epidemiology, population genetics, and community or health genetics for the care of sick populations, from genetic, environmental, or mixed causes. The detection and study of these populations is part of the movement to increase epidemiological surveillance in the Region.

With the increase in birth defects from the Zika virus epidemic in 2015, ECLAMC participated in the effort to promote increased epidemiological surveillance in Latin America, submitting a proposal (now in implementation) to share birth defects frequencies with other regional or national registries on an electronic platform in the Latin American Congenital Malformations Network (RELAMC).

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National Congenital Anomalies Network of Argentina (RENAC)

Characteristics	
Year established	2009
Admission to ICBDSR	2012
Coverage	Hospital-based
Maximum age at diagnosis	Until discharge from maternity service
Pregnancy outcomes included	Live births Stillbirths ≥500 grams
Case definition	Major structural anomalies
Controls	No
Information on risk factors	No
Website	http://www.anlis.gov.ar/cenagem/?page_id=33

History

The National Congenital Anomalies Network of Argentina (RENAC) arose from a study conducted together with ECLAMC[1] in 2009, coordinated by the National Medical Genetics Center of the National Administration of Laboratories and Institutes of Health of the Ministry of Health. This Argentine network began with four hospitals in the country's northwest region. In 2015, it was renamed from "register" to "Congenital Anomalies Network."

Structure

RENAC is made up of a central coordinating body and a network of approximately 150 maternity services. Each one has two professionals as focal points involved with the care of newborns (neonatologists, pediatricians, nurses), reporting monthly to the coordinating body on cases with birth defects and the total number of births in the maternity service. Live births and stillbirths (≥500 grams) are included. Simplicity was prioritized in the design of the system, which does not routinely collect risk factors, but which has broad coverage and high diagnostic quality, a result of the detailed description of birth defects and coding by geneticists in the coordinating body. For special research projects, specific risk factors are surveyed, depending on the objectives of each project.

RENAC follows standards set in an operations manual and an atlas for case detection and description of birth defects. Monthly data are collected and sent to the coordinating body, where the quality of the descriptions is reviewed, anomalies are coded, and information is analyzed and disseminated through periodic reports and other publications. Data are transmitted through a website that includes a communication system involving online forums. Among other activities, this permits exchange of information to discuss clinical cases, clear up doubts, learn about new developments, send cases every month, send photographs and other documentation, discuss clinical cases, and disseminate new academic developments.[2]

Activities

- Periodically monitor the prevalence of birth defects: seven categories of grouped anomalies are monitored annually (NTDs, severe heart disease, oral clefts, clubfoot, abdominal wall defects, limb reduction defects, chromosomal disorders); 48 specific anomalies selected according to their frequency, clinical importance, and comparability with other registries in the world; eight syndromes: thanatophoric dysplasia, short ribs-polydactyly, achondroplasia, imperfect osteogenesis, campomelic dysplasia, trisomy 13, trisomy 18, and Down syndrome. Seven very rare CAs are also monitored: cloacal estrophy, bladder estrophy, amelia, phocomelia, cyclopia, sirenomelia, and conjoined twins. The annual reports can be found on the webpage of the National Medical Genetics Center—National Administration of Laboratories and Institutes of Health of Argentina.[3] As a result of monitoring, the increased frequency of sirenomelia from 2009 to 2014[4] has been studied, as well as the existence of geographic clusters[5].

- Specific analyses of the implications of birth defects: RENAC studies and analyses have provided input for decision-making on public health issues: e.g., estimates of the impact of the main anomalies for evaluation of needs for resources[6]; analysis of newborn survival in a set of cases with isolated anomalies, selected for their high impact on morbidity and mortality, prevalence, and amenability to medical-surgical interventions, such as encephalocele, spina bifida, gastroschisis, omphalocele, diaphragmatic hernia, esophageal atresia, intestinal atresia, and anal-rectal malformation[7]; and impact assessment of population-based interventions.[8,9]

- Routinely connect affected patients to the health system through the online forum. RENAC links families of affected neonates with local geneticists for diagnosis and technical assistance. In 2015, a network was developed to provide care for newborns with oral clefts, clubfoot, and developmental dysplasia of the hip.[10]

- For human resources education, RENAC uses three strategies:

    1. Training based on reported cases, in which the coordinating body advises maternity service practitioners on initial management and possible diagnoses.

    2. Blended learning courses, designed to be given online with in-person evaluations, addressing the problem of birth defects from the perspective of public health, epidemiology, dysmorphology, and etiology.

    3. Annual meeting of the RENAC membership: annual report is presented, updates are given on topics of interest, and operational improvements are made.

The expansion of RENAC's objectives and its networked activities favor its sustainability and quality of information, while enabling it to carry out actions in the country's 24 jurisdictions aimed at timely care for those affected. RENAC provides its members with training, processed data, and support for initial case management, diagnosis, and monitoring of affected newborns. The surveillance system is based on the ongoing commitment of the people involved, not only for the systematic production of epidemiological information, but also for direct improvement of the health of those affected. When the surveillance system was developed, the priority was to make it useful for public health practice and for the clinical practice of those who report cases to the system.

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Malformation surveillance programs in Colombia (Bogotá and Cali)

Características	
Year established	2001 (Bogotá) 2010 (Cali)
Admission to ICBDSR	2006
Coverage	Hospital-based
Maximum diagnosis age	Until discharge from maternity service
Pregnancy outcomes included	Live births Stillbirths >500 grams Elective interruption of pregnancy due to fetal anomaly
Case definition	Major and minor structural anomalies
Controls	Yes
Information on risk factors	Yes
Website	http://www.anomaliascongenitas.org/

History

The Birth Defects Surveillance Programs of Bogotá and Cali were designed by researchers from the Pontificia Universidad Javeriana, in association with Bogotá's Secretariat of Health and Cali's Municipal Secretariat of Public Health, and structured on the ECLAMC model. The program in Bogotá began in 2001 with surveillance in one hospital and now includes 56 hospitals, while the Cali program began in 2010 and includes 3 hospitals using a case-control method and the 20 hospitals in the city that have maternity wards.

The rapid growth of both programs led to 100% coverage of births in both cities, made possible by collaboration with the National Public Health Surveillance System (SIVIGILA) and Ministries of Health (MOHs), institutions that receive detailed information on live births and cases with birth defects.[1]

Structure

The Birth Defects Surveillance Programs of Bogotá and Cali receive data from two sources: SIVIGILA, using National Institute of Health methodology; and case-control studies.

The database enables epidemiological research on prevalence, risk factors, and the location of clusters of birth defects. Both programs also carry out telephone and clinical monitoring of patients with birth defects at high risk of disability.

With respect to the case-control method, Postgraduate Medical Doctors in the program receive specific training on conducting systematic and detailed physical examinations to identify and diagnose birth defects. The training includes provision of written guidelines, and evaluating

participants using a recorded practical test in a simulation center. Physicians also receive a manual that ECLAMC designed to guide the process of describing birth defects.

Each participating physician is responsible for surveillance in one or more hospitals and is required to see patients daily, evaluating liveborn and stillborn children. When cases are found, photographs are taken and a case report form is completed that includes information on the mother and the newborn, history of problems of pregnancy, and a detailed description of the defects.

The form completed by physicians participating in the case-control system includes different variables linked to birth defects: immunizations; acute illnesses during pregnancy; chronic illnesses; physical factors, such as x-rays, surgery, radiation therapy, etc.; medications; smoking; use of recreational drugs or alcohol; parents' educational level; and place of residence during periconceptional period. With respect to controls, the next healthy newborn at the facility is included, using the same form.

Both programs include stillbirths weighing >500 g, in which case no additional controls are added. Data are stored, respecting security and confidentiality agreements. Information is compiled and photos are taken only if the mother provides her informed consent. Within the first 10 days of every month, a meeting is held at the coordinating center office at which the physicians in the program share data compiled during the previous month. The coordinator loads, corrects, and codes data. All the information is sent to a central server, together with a report to the city health authorities of Bogotá and Cali.

With respect to collaboration with SIVIGILA, hospitals report monthly to the Secretary of Health in each city on cases of birth defects using the reporting form that describes birth defects and compiles basic information on cases and their mothers. In cases with birth defects, the physician completes the reporting form and then the epidemiology chief corroborates the data and sends them to the Program platform. These data are integrated into the surveillance program and are used to produce periodic reports.

The Congenital Malformations Surveillance Programs of Bogotá and Cali not only record and analyze information, they also monitor the patient to ensure an accurate prognosis. The International Classification of Functioning, Disability, and Health is used to code and classify the probability of disability. Children who may have a disability as a result of their disorder enter a monitoring program that consists of telephone interviews. The interviewer determines if the patient needs an additional evaluation through clinical consultation, also ensuring that the respective insurance company will provide the necessary care. During the clinical consultation, a social worker evaluates the child using the Bayley Scale of Infant Development and the abbreviated neurological development scale. If potential developmental problems are detected, a geneticist can evaluate the case by scheduling a free consultation at the Genetics Institute of the Pontificia Universidad Javeriana in Bogotá or the Simulated Hospital at the Pontificia Universidad Javeriana in Cali.[1]

Activities

- Both programs periodically monitor the frequency of CA and publish monthly and quarterly online newsletters[2] that report birth defect frequencies by group and specifically, and classify them according to risk of disability. Furthermore, an atlas has been developed of congenital malformations and their ICD-10 codes, which is also available on the same web page. The website also offers training courses for health professionals at public and private hospitals, emphasizing the importance of mandatory reporting of birth defects.

- Trainings and workshops for health workers at regional and national levels.

- With data from the programs, descriptive epidemiology of congenital heart diseases[3], hypospadias[4,5,6], and birth defects in general have been investigated.[7] Ultrasound detection of birth defects in the cities of Bogotá and Cali has also been described.[8] With regard to the Zika virus epidemic in Colombia, these programs were used to identify and describe the increase in microcephaly associated with the infection.[9]

- Risk factors for urological birth defects[10], microtia[11], craniofacial malformations[12], hypospadias[4,5], and anomalies of surgical interest[13] have been studied. Regarding protection factors, program data have been useful in the study of prenatal vitamin use and the prevention of genitourinary anomalies.[14]

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Congenital Malformation Registry Center (CREC) of Costa Rica

Characteristics	
Year established	1985
Admission to ICBDSR	2003
Coverage	Population-based
Maximum diagnosis age	Until first birthday (since 2008)
Pregnancy outcomes included	Live births Stillbirths >500 grams
Case definition	Major and minor structural anomalies
Controls	No
Information on risk factors	No
Website	http://www.inciensa.sa.cr/inciensa/unidades_especializadas/unidad_enfermedades_congenitas.aspx

History

The Congenital Disease Registry Center (CREC) grew out of a nationwide epidemiological investigation of birth defects, after which, and with technical assistance from ECLAMC, it became the national birth defects surveillance system in 1985, through Executive Decree No. 16488-S. Initially, the registry only operated in maternity services where patients had been born and birth defects detected in the first 7 days of life were registered, before hospital discharge. However, in 2008, after an epidemiological investigation of congenital heart disease conducted together with the National Children's Hospital demonstrated nearly 70% underreporting of these defects, reporting was expanded from birth to the first year of life through Executive Decree No. 34398-S. This made it possible to include unrecorded cases, diagnosed in other health centers after discharge from the maternity service, and to expand the search for anomalies. This decreased underreporting and improved the quality of collected data. Since then, CREC has shared its information with the National Children's Hospital (national referral center for children with birth defects) and collaborated with it on several research projects. Currently, it covers over 98% of births in all the country's public and private maternity services.

CREC monitors birth defects, investigates their determinants, and proposes prevention measures; it also evaluates their impact on morbidity and mortality and provides input for decision-making.

Structure

CREC has a central coordinating group located at the Costa Rican Institute for Research and Teaching on Nutrition and Health (INCIENSA), which is part of the Ministry of Health. It is also comprised of professionals in pediatrics and epidemiology, and it has an administrative assistant. Its network includes 32 public (28) and private (4) health centers with maternity services, covering over 98% of births in the country. In addition, primary and secondary health centers with pediatrics services

became birth defects reporting entities in 2008, together with the National Children's Hospital (the country's only pediatric hospital and national referral center for birth defects). Data are collected from all health facilities where major and minor birth anomalies are detected in children under 1 and in stillbirths weighing >500 g.

Since it began, the registry has had a technical manual to standardize information collection, and since 2018 it has had an online reporting system. A Protocol for Birth Defects Surveillance in Coast Rica[1] includes a description of the most frequent birth defects. Coding (ICD-10 with the RCPCH/BPA modification) and data analysis is done centrally. The online reporting system, linked to the national registry of births and deaths, permits real-time and simultaneous reporting by several users, and allows each reporting entity to access the data.[2]

Activities

CREC focuses on public health research, epidemiological surveillance, and education on subjects related to birth defects. Its activities include the following:

- To systematically and promptly detect and monitor newborns with birth defects, to analyze their epidemiological behavior in the country and contribute reliable and timely information to the health authorities for appropriate treatment and prevention. Both major and minor birth defects are monitored. Analysis is done according to: categories (groups) of birth defects, a single group of major birth defects, the most frequent (prevalent) ones, and those with greatest impact (morbidity/mortality) in the country, as well as birth defects that are monitored internationally regardless of their severity. Quarterly reports are produced for the country's health authorities and members of the network, along with annual reports and maps, tables, and graphics of interest, which are available on the INCIENSA Web page (http://www.inciensa.sa.cr/vigilancia_epidemiologica/estadisticas.aspx)

- Training for the network of reporting health centers and the country's health professionals (pediatricians, neonatologists, residents, nurses, and other health professionals). Every year there are new and refresher training for network members. Every 2 years there is a round of training and motivational visits to the central and regional centers in the network. Finally, for the last 5 years CREC has been participating as facilitator for training initiatives in the Region, in coordination with PAHO.

- As part of its epidemiological research activities, it has analyzed the prevalence of patients with multiple birth defects[3], as well as the impact of birth defects on infant mortality in Coast Rica.[4] The registry has also evaluated the prevalence of congenital heart disease and, in particular, changes in frequency, by extending the detection of anomalies to 1 year of age.[5] CREC has conducted studies of survival at 1 year and 5 years of age for this pathology.[6] It has conducted a study on the impact on the prevalence of NTDs following folic acid fortification of certain foods, which Costa Rica began in 1997.[7,8] In 2009, it began compiling information on exposure to the rubella vaccine to support surveillance of congenital rubella syndrome and contribute evidence on its eradication in the country through retrospective case-finding[9]. It has been involved in active investigation of the birth defects and updates to the surveillance protocol. In addition, it has conducted a study on the presence of epilepsy in pediatric tuberous sclerosis patients.[10] Finally, it has performed analyses of abdominal wall defects, given their high impact on mortality from birth defects in the country.[11]

- In recent years, because of the Zika epidemic, the registry has worked actively, together with other institutions in Costa Rica's Ministry of Health, to detect embryopathy from this virus.

From the onset of the Zika epidemic in the country, in January 2016, it was charged with the task of creating a sub-registry for surveillance of birth defects associated with Zika in the country, and it developed the "Protocol for surveillance of microcephaly and congenital Zika syndrome in Costa Rica."[12]

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What progress has been made in recent years?

Strengthening birth defects surveillance in Latin America and the Caribbean

The need to respond to international resolutions and agreements, to the epidemiological situation, and, more recently, to the Zika emergency, motivated planning and implementation of different activities aimed at strengthening birth defects surveillance in the Region.

One of the main actions was the design and implementation of an education and training program on birth defects surveillance. PAHO/WHO, CDC, ICBDSR, RENAC, CREC, the Pontifical Xavierian University of Bogotá and of Cali, and the Neonatal Alliance for Latin America and the Caribbean all participated in the initiative.

The main purpose of the activity was to identify and train leaders in the countries[1] who could help to implement birth defects surveillance systems, strengthen those already in existence, improve specific surveillance processes for birth defects, and promote collaborative networking among the different countries of the Region. In this regard, the instruments mentioned in the chapter on birth defects surveillance were essential inputs for the trainings.

Regional training programs

The health authorities in each country designated representatives for this training on the basis of professional profiles and national priorities. A total of 90 students from 18 Latin America and Caribbean countries attended (Table 4 and Figure 6). Trainings aimed at promoting leaders in the countries of the Region were held in 2015 and 2016. After this initial phase, a specific per-country approach was chosen, starting in 2017.

Table 4. Distribution of participants by country in the regional training programs held in Costa Rica (2015) and Colombia (2016)

Participants' country of origin	Number of course participants in Costa Rica N (%)	Number of course participants in Colombia N (%)	Total participants N (%)
1. Argentina	0 (0)	4 (7)	4 (4)
2. Bolivia	3 (10)	9 (15)	12 (13)
3. Brazil	2 (6)	12 (20)	14 (15)
4. Chile	1 (3)	1 (2)	2 (2)
5. Colombia	4 (13)	9 (15)	13 (14)
6. Costa Rica	4 (13)	2 (3)	6 (7)
7. Cuba	1 (3)	8 (14)	9 (10)
8. Dominican Republic	0 (0)	2 (3)	2 (2)
9. Ecuador	1 (3)	1 (2)	2 (2)
10. El Salvador	2 (6)	1 (2)	3 (3)
11. Guatemala	3 (10)	1 (2)	4 (4)
12. Honduras	0 (0)	2 (3)	2 (2)
13. Nicaragua	1 (3)	0 (0)	1 (1)
14. Panama	3 (10)	0 (0)	3 (3)
15. Paraguay	1 (3)	2 (3)	3 (3)
16. Peru	3 (10)	1 (2)	4 (4)
17. Uruguay	2 (6)	1 (2)	3 (3)
18. Venezuela	0 (0)	3 (5)	3 (3)
Total	31 (100)	59 (100)	90 (100)

Figure 6. Map of countries that sent students to the regional training programs in Costa Rica (2015) and Colombia (2016)

Note: In the map, countries that already had national or subnational birth defects surveillance systems before the trainings are marked with white dots. Countries without national or subnational birth defects surveillance systems before the trainings are marked with yellow dots. Box: Territories with confirmed Zika virus (ZIKV) cases in 2016.

Figure 7. In-person workshops for the regional training programs, 2015 (Costa Rica) and 2016 (Colombia) cohorts

The programs used a blended learning methodology that consisted of a one-month online pre-course (e-learning) located on the ICBDSR platform, and a 5-day in-person workshop in the cities of San José (Costa Rica) in 2015, and Bogotá (Colombia) in 2016 (Figure 7).

Both groups (2015 and 2016) were mainly focused on professionals who could plan and coordinate a surveillance system in countries that lacked them at that time (Table 5) or whose systems required strengthening. The main contents of the training programs were prevention, etiology, and impact of birth defects; premature births in the spectrum of adverse events related to birth defects; basic principles and designs of CA surveillance systems; designs for epidemiological studies for etiological investigation; anomaly coding and case classification; principal characteristics of the most frequent defects; indicators of frequency at birth and introduction to epidemiological analysis using Epi Info; and principal aspects of prevention, surveillance, and care of the syndrome associated with ZIKV infection.

During the in-person days, the following teaching resources, among other materials, were distributed and used: WHO-CDC-ICBDRS manual, 2015, entitled "Birth defects surveillance: a manual for programme managers"; reports on specific surveillance systems (RENAC for 2014 and 2015, ICBDSR Annual Report for 2013 and 2014); an identifier of congenital anomalies and malformations, the ECLAMC Atlas; adaptation of a case study on planning and design of a surveillance system in a hypothetical country; the ICD-10 coding system with RCPCH adaptation in Spanish; and examples of reporting forms from RENAC, SIVIGILA Colombia, and ECLAMC.

Developing leaders and establishing surveillance systems in the countries

The second phase in the process of developing birth defects surveillance systems was to promote in-country discussion and planning on these issues. Within the framework of World Birth Defects Day 2017, the goal was for every country to analyze the situation around birth defects and design a work plan. In this context, key actors, such as the MOH and neonatal alliances (in countries that have them), different scientific and academic agencies and entities, and professionals who attended the training courses, were invited to participate in a day of discussion and planning, facilitated by the PAHO/WHO Representative Offices in the countries.

Countries carried out different activities, such as work plans for the design and implementation of birth defects surveillance systems, and actions to improve the quality of existing specific systems. The work plans produced concrete proposals and training needs that were addressed primarily with the leadership of members of CLAP/WR-PAHO/WHO and RENAC's technical team. Among the training activities in different countries, those in El Salvador and Panama stand out, along with advocacy activities and technical cooperation for the design of surveillance systems in the Dominican Republic, Ecuador, Honduras, and Peru. In Trinidad and Tobago, a subregional meeting was held for the countries of the English-speaking Caribbean.

In the second phase, the country-specific training activities were also conducted in a blended learning format, with a virtual module or online pre-course (one month) followed by an in-person module (from 3 to 5 days duration in the capitals of every country). However, unlike the first phase aimed at developing leaders, on this occasion the courses were focused on each country's own needs and characteristics.

Along these lines, professionals working with neonatal/pediatric, epidemiology, and information systems were encouraged to participate, and efforts were made for all national and subnational institutions and administrative sections to be represented. Organizational and management aspects of each country's systems were addressed, and work was done to optimize the detection, description, and coding of specific birth defects. In quality improvement activities, participants were asked to prepare intra- and interinstitutional flow charts of the movement of information, identify the causes of delays and problems using root-cause diagrams, and make proposals for short- and medium-term action plans. Each intra-country in-person workshop was jointly coordinated with the health authorities and local PAHO offices. A comparison among regional and intra-country trainings is described in Table 5.

In addition to these trainings, video conferences were held periodically with the health authorities and representatives from the country coordination bodies. Technical cooperation activities and recommendations on and supervision of good practices were also carried out, mainly for the design of operations manuals, coding processes, and analysis of the frequency of birth defects; e.g., correcting possible coding errors, structuring frequency analyses, and producing annual reports on the frequency of birth defects. Work was done in the field, visiting the places where the coordinating body of the incipient surveillance systems operate, and remotely, through remote communications. Figure 8 lists participants' comments on how training has contributed in their local context, two years on.

Figure 8. Participants' comments on how training has contributed in their local context, two years on

"To mark World Birth Defects Day, the Program for the Prevention of Birth Defects was presented, which provided the framework for the formation of the Birth Defects Registry in Paraguay." (participant from Paraguay)

"It was fundamental, because it made it possible for me, in the first place, to raise awareness in the national health authorities about the importance of implementing a birth defects surveillance system in the country. Furthermore, it provided the opportunity to design a project to explain to different health professionals and the authorities about the importance of it being approved. After authorization of the system, they worked on implementation, with the preparation of regulatory technical documents. Furthermore, assistance was requested from RENAC for a mass training at the national level, both virtual and in-person, and the intent is to begin with the surveillance system in September 2018." (participant from Bolivia)

"The knowledge that I acquired in the course made it possible for me to strengthen processes and procedures related to public health surveillance of birth defects in the city of Bogotá, from planning up to monitoring and evaluation." (participant from Colombia)

"In my country, there are no surveillance systems for neonatal events. We were able to apply what we learned both to neonatal mortality and birth anomalies." (participant from Guatemala)

"Participating in this workshop helped me make a lot of progress with the development of the surveillance system for congenital anomalies of my country. Based on the knowledge and the experience of the different actors and professionals, we managed to modify and introduce some aspects and substantially improve our surveillance system. We still have to apply research studies to our system." (participant from Nicaragua)

"This experience made me feel more secure when participating in the annual planning of the National Registry of Birth Defects and Rare Diseases and I have been able to contribute new ideas to our everyday work and, above all, to understand why I do what I do under the coordination of Dr. Larrandaburu." (participant from Uruguay)

"El Salvador started its congenital anomalies registry system in the Ministry of Health in 2012. In 2016, it was implemented in the Salvadoran Social Security Institute, when the training was provided. In 2017, the integrated online system for both institutions started up." (participant from El Salvador)

Explain briefly whether after the training you could apply what you learned to planning and/or implementation of a congenital anomalies surveillance system in your country; explain how, and whether having taken this training program facilitated this work or not.

Table 5. Comparison among regional and intra-country trainings

Type of training strategy	Regional program Costa Rica 2015	Regional program Colombia 2016	Intra-country training El Salvador 2017	Intra-country training Panama 2017
Method	Blended learning	Blended learning	Blended learning	Blended learning
Recipients	Future CA surveillance system manager and coordinators	Future CA surveillance system manager and coordinators	Futures focal points in charge of detection, case reporting, and coding of birth defects from the different nodes in a national surveillance system	Futures focal points in charge of detection, case reporting, and coding of birth defects from the different nodes in a national surveillance system
Focus	Planning a specific CA surveillance system	Planning a specific CA surveillance system	Implementation of detection, description, and coding	Implementation of detection, description, and coding
Number of participants	31	59	48	44
Number of participating countries	14	16	1	1

Lessons learned

Obtaining commitment from the health authorities from the beginning of the training process was fundamental for both the invitation and the selection of participants. This will reinforce the importance of the topic on the health agenda and the relevance of direct inclusion of students in the coordinating bodies of incipient surveillance systems.

During the activities, it was useful to for the teaching team to be experts in active surveillance systems in Latin America, with experience in implementation and troubleshooting in local contexts. This facilitated similar languages, modes, strategies, and solutions in response to common problems. Furthermore, it favored the creation of networks among countries. Educators and participants remained linked formally and informally (discussion groups and forums through cellular technology) to share information and carry out consultations.

Providing an online pre-course strategically maximized the time available for discussion and integration in the in-person workshops. The pre-course enabled participants to get to know each other, link up in a joint project, and learn the conceptual basics to attain a standardized basic level with the necessary minimum subject matter, so that on-site activities could focus directly on how to design and/or strengthen their surveillance systems. Experiences on this topic in Africa obtained similar results.

Birth defects surveillance as a public health instrument

Neural tube defects and fortification of food

In the chapter on "Surveillance of birth defects," we are reminded that the goal of public health surveillance is prevention. Among its most important objectives are monitoring the prevalence of birth defects in populations, and evaluating population-based interventions (e.g., fortification of staple foods with folic acid).

Although it is not feasible to identify specific causal factors in a variable proportion of birth defects, it is often possible to detect and modify them with specific interventions. There are examples of primary prevention measures to prevent a birth defect, secondary early detection and intervention to reduce its harm or progression, and tertiary treatment and rehabilitation that prevent progression or worsening of different birth defects.

There are success stories, as well as lessons learned, around the value of birth defects surveillance in terms of identifying problems, implementing interventions, and measuring their results.

Immunization, as in the case of congenital rubella syndrome, fortification of food with folic acid, preconception care, prevention of habits associated with the development of birth defects, and prenatal or postnatal surgical interventions are examples of measures that can significantly reduce the impact of birth defects.

As an example, we will briefly analyze several milestones related to neural tube defects (NTDs).

NTDs are the most common birth defects of the central nervous system (CNS). In 2006, a global report on birth defects estimated that in 2001, the number of live births with NTDs worldwide was 324,000 patients (2.4/1,000 live births), contributing more than 2.3 million disability-adjusted life years.[1] Estimated global prevalence was 1.86 per 1,000 live births, with a range of 0.75 to 3.12 among the different regions of the world.[2]

Benefits of folic acid fortification to prevent the occurrence of NTDs were rapidly observed in several populations.[3-7]

In 2015, WHO recommended promoting actions to achieve optimal concentrations of folate in women of childbearing age and a threshold population-wide concentration of folate in erythrocytes above 400 ng/ml (906 nmol/l) to achieve the greatest reductions in the prevalence of NTDs.[8] Countries with policies for compulsory folic acid fortification (FAF) reduced the prevalence of NTDs to nearly 0.6 per 1,000 total births. In countries without fortification, average prevalence is approximately 2.5 per 1,000 live births, in some cases reaching frequencies as high as 10-20 per 1,000 live births. [6,9,10]

Several systematic reviews analyzed the data available in the literature on the prevalence of NTDs in different populations, monitoring of secular trends, and the impact of primary prevention through FAF.[11-14]

The limited development of birth defects surveillance systems and the limited and fragmented information available in Latin America hinder the ability to adequately determine the prevalence of NTDs in more than 11 million births per year.[6] Practically all countries in the region now have FAF legislation and programs designed to decrease conditions related to deficiencies of folic acid and

other micronutrients. However, few countries have established monitoring and evaluation of the impact of their prevention programs, and, to an even lesser extent have identified trends over time before and after FAF.

ECLAMC[15] was the first to observe the reduction in NTD prevalence following FAF of wheat flour in Chile[16], ruling out that the reduction was part of an ongoing trend; they found an average decrease of 51% in prevalence of spina bifida and of 42% for anencephaly. Subsequently, ECLAMC evaluated outcomes of FAF in three countries (Chile, Argentina, and Brazil)[17] on the basis of 3,347,559 births in 77 hospitals from 1982 to 2007. They detected significant reductions in NTD prevalence, with the greatest reduction in thoracic spina bifida, followed by lumbosacral spina bifida, anencephaly, and encephalocele.

Recently, Rosenthal et al.[12] did a literature review of institutional studies and reports published from 1990 to 2010 on prevalence of NTDs in Latin America, with data from 15 countries and one subregion. Following that systematization, other publications analyzed prevalence, secular trend, and impact of folic acid fortification of foods for several Latin American countries.

As Czeizel et al.[18] reported in 2011, there have been several important milestones in NTD prevention. Prior to the 1970s, most children born with these defects would have died, but in that decade they began to benefit from medical-surgical treatments, significantly reducing sequelae and disability. In the 1990s, primary prevention of NTDs began, based on preconceptional folic acid intake through vitamin supplementation or FAF. In the 2000s, intrauterine intervention became possible for spina bifida patients, with promising results.

Although NTDs, which have a substantial impact on child morbidity and mortality, can be prevented with folic acid fortification, this is a highly cost-effective measure. Furthermore, these conditions continue to be a health problem in Latin America, one that is still not clearly apparent due to limitations in surveillance systems and only partial detection of affected pregnancies, which keep these birth defects somewhat invisible.

Integrated surveillance of all adverse outcomes is needed to improve estimates of global NTD prevalence, evaluate effectiveness of prevention actions through FAF policies, and improve outcomes through care and rehabilitation.

In this regard, a "triple surveillance"[19] concept has been proposed, integrating surveillance of cause (e.g., folate deficiency), of disease occurrence (NTD prevalence), and of health outcomes (morbidity, mortality, and disability).

Consequently, although strengthening surveillance of disease occurrence is very important, from a public health perspective, much greater value and benefits could be attained if surveillance systems were implemented under the optics of "triple surveillance."

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Birth defects surveillance systems in Latin American and Caribbean countries: present and future

This report details experiences and interventions concerning surveillance and management of birth defects in Latin America and the Caribbean as a public health issue. The development of surveillance systems is a crucial aspect enabling countries to have their own data, making it possible to assess the magnitude of CAs, evaluate their impact from different perspectives, and at the same time, evaluate the effect of interventions.

The heavy burden of secondary morbidity and mortality due to birth defects affects health, quality of life, and the human and social capital of our populations.

Different tools to address birth defects, including surveillance, have been studied. Along these lines, the availability of surveillance systems and registries in the Region's countries are an essential element for continued progress.

It is both desirable and essential for countries to have a birth defects surveillance system.

This report seeks to make a relevant contribution to raising the visibility of birth defects and the implementation of specific actions. Future actions should aim to reduce morbidity and mortality associated with birth defects and, finally, to contribute to the global objectives of promoting survival, improving health conditions, and timely interventions that make it possible to offer better quality care and leave no one behind. In those countries that still do not have registries or surveillance systems, it will be necessary to continue awareness-raising and training aimed at understanding the impact of birth defects and prematurity as adverse reproductive events that share common risk factors. The goal will be to help to identify the objectives of birth defects surveillance systems, design the registries they need, and plan their implementation.

Furthermore, in countries that need to strengthen incipient registries, training should be aimed at improving the system through analyzing surveillance processes, developing operations manuals, improving the quality of clinical description and coding of birth defects, while developing local capacity for data analysis, producing annual reports, and evaluating information quality attributes.

These formative activities will be accompanied by technical cooperation for professionals in each country, with specific content aligned with local characteristics. Furthermore, depending on the case, involvement will be sought from managers and coordinators of birth defects surveillance systems and/or members of the health team that make up the data collection nodes in countries' surveillance systems.

The development of surveillance systems in the region can also be strengthened by a regional network following the model of other surveillance consortia, such as ICBDSR at the international level.

CLAP/WR is collaborating in the construction of a regional registry that includes the following elements: a common data collection platform, a manual of standardized surveillance processes, a model annual report for the presentation and interpretation of data, in addition to trainings and technical cooperation that may be necessary. This regional network could produce standardized practices, always respecting the form most appropriate to the context of the country.

Based on available experience, the time is ripe in the Region of the Americas to establish a regional birth defects registry based on reports from country surveillance systems.

With a view to strengthening birth defects surveillance in the Region of the Americas, three linchpins are proposed as primary areas for technical cooperation:

1. Strengthening training and technical cooperation to contribute to the availability of birth defects surveillance systems in the Region's countries.

2. Establishing a regional birth defects registry in the Region of the Americas.

3. Facilitating access to tools that help to implement systems.

Training and technical cooperation activities will continue, based on countries' characteristics and needs.

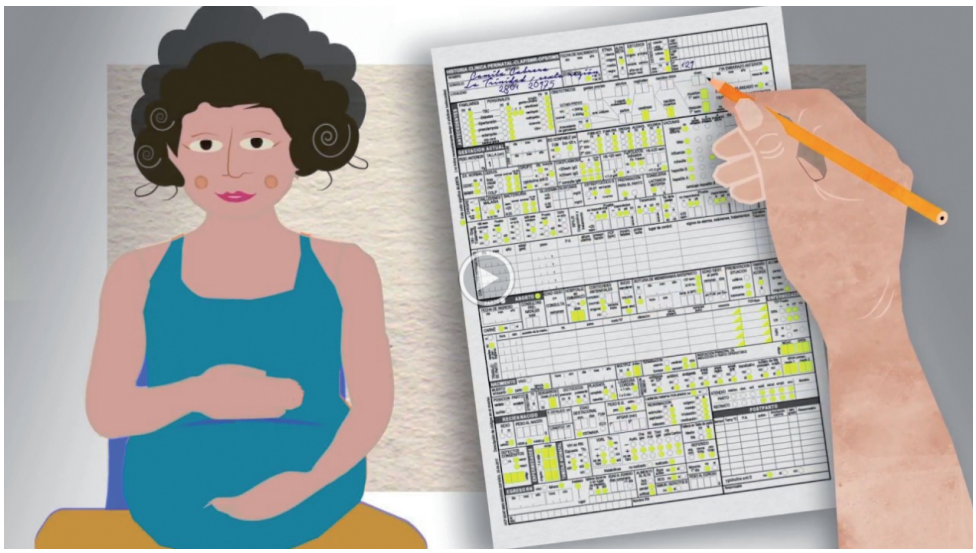
From the survey and regional map of the availability and characteristics of existing surveillance systems, standard operating procedures were developed and a pilot study was done to establish a regional registry. Based on the results, this registry will be formalized to consolidate the results and learn about the regional situation of birth defects.

The tools to implement this type of surveillance, mentioned in the chapter on birth defects surveillance, are essential elements for carrying out these activities. Along with them, other instruments contribute to this process.

Perinatal Information System

The Perinatal Information System (SIP) and its new Plus version are essential tools for the registry of birth defects, their determinants, and associated conditions (Figure 9).

Figure 9. Illustration of an informative video about the SIP



(This video can be watched at the following website: https://www.youtube.com/watch?v=N9wB2xzKY3o)

The Perinatal Information System consists of a set of instruments originally designed for use in OB/GYN and neonatology services: Specifically, the Perinatal Clinical History, the perinatal card, and specific forms for neonatal hospitalization, neonatal nursing, and birth defects, together with local data capture and processing programs; these are all important tools aimed at improving quality of care and contributing to surveillance.

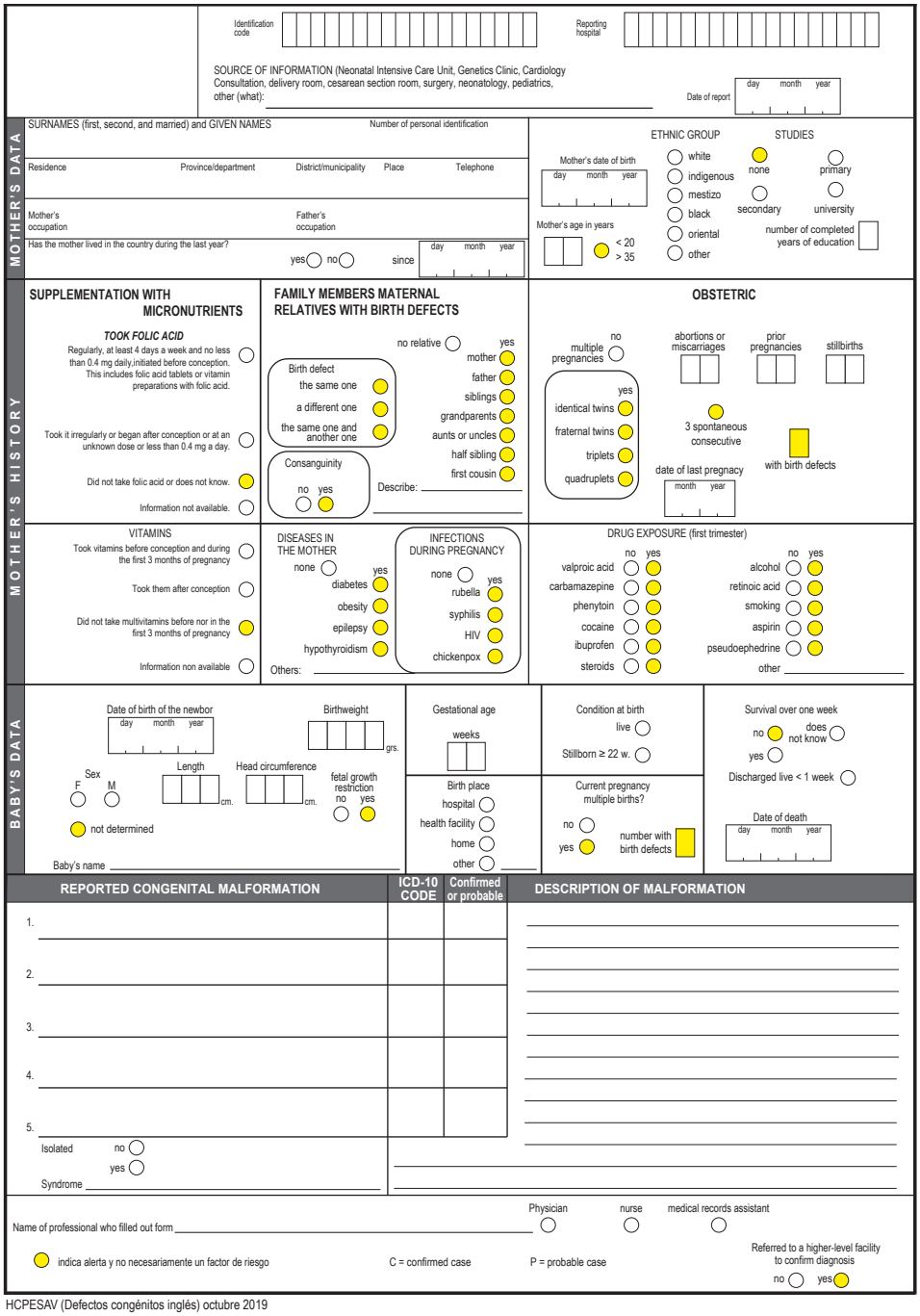
The objectives of the SIP are to:

- serve as the basis for planning care;
- confirm and follow implementation of evidence-based practices;
- unify data collection, adopting standards;
- facilitate communication among different levels;
- obtain reliable statistics locally;
- encourage compliance with standards;
- facilitate health-worker training;
- record data of legal interest;
- facilitate auditing;
- characterize the population receiving care;
- evaluate quality of care; and
- conduct epidemiological operations research.

Through the SIP, data from the Perinatal Clinical History can be entered into a database in the maternity service itself, created with the SIP program, and thus produce local reports. At the country or regional level, databases can be consolidated and analyzed to describe the situation of various indicators over time, by geographical areas, or other specific demographic characteristics. At the central level, it is a useful instrument for surveillance of maternal and neonatal events and for evaluation of national and regional programs.

In addition to the perinatal form that records information on the mother and her preconception and prenatal history, including different conditions associated with the development of birth defects, there is a new form linked to the previous one to capture additional data and information to characterize and register birth defects.

Figure 10. SIP Perinatal Clinical History



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The availability of a SIP and, above all, its use in a network, is valuable when establishing birth defects surveillance systems.

Tools are available to assist in the design and implementation of birth defects surveillance systems. Establishing networks within and between countries is crucial for aligned and timely information.

Coordination among different surveillance systems helps to simplify these systems and make them more efficient. Countries have multiple systems and they are not always linked. However, many of them recognize similar entry points. An example of this is the link between birth defects and infrequent diseases, and those included in neonatal screening programs.

Linked surveillance can greatly facilitate the implementation of the various components and thus contribute efficiently and rapidly to providing quality information.

Strategies recognized by experts to maximize surveillance, prevention, and treatment of birth defects in the Region include: addressing surveillance of birth defects, together with reduction of risks for their development; effective prevention actions, such as food fortification, prevention and treatment of infections, and neonatal screening; specialized care and services for children with birth defects; moving the research agenda forward; and involvement of policy/program managers, civil society, and cooperation agencies.[1]

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The financial impact of Zika virus on Latin America and the Caribbean*

Zika virus was first identified in Uganda in 1947 in monkeys.[1] Starting in 2015, it spread at an alarming rate throughout Latin America and the Caribbean, and, in 2016, arrived in the United States. Because the Zika virus has a high capacity to infect nerve cells, it can also cause Guillain-Barré syndrome (a disease that affects the nerves and causes muscle weakness and paralysis) and other neurological complications in adults. Zika can produce a variety of birth defects, subsequently called "congenital Zika syndrome," among them microcephaly, a rare condition associated with incomplete brain development and other neurological and eye disorders.

Zika, endemic in Latin America, has become a persistent socioeconomic and public health challenge that disproportionately affects vulnerable populations. With more than 48 countries and territories in the Americas having confirmed autochthonous and vector-borne and sexual transmission of Zika virus, it is important to calculate the financial costs of the epidemic to quantify the impact of this health crisis on the global economy.[2] In 2016, the World Bank estimated the cost of Zika infection to the world to be US$3.5 billion, excluding the costs of Guillain-Barré or the other congenital syndromes. Zika virus is regarded as one of the largest and most costly infectious disease outbreaks.[3]

This chapter estimates the economic burden of Zika, as well as all direct and indirect costs, projected to 2030. In particular, it focuses on the financial costs of children born with congenital Zika syndrome. Due to the lack of data, it was not possible to complete an economic evaluation of these services in the countries affected by Zika in Latin America and the Caribbean.

Methodology

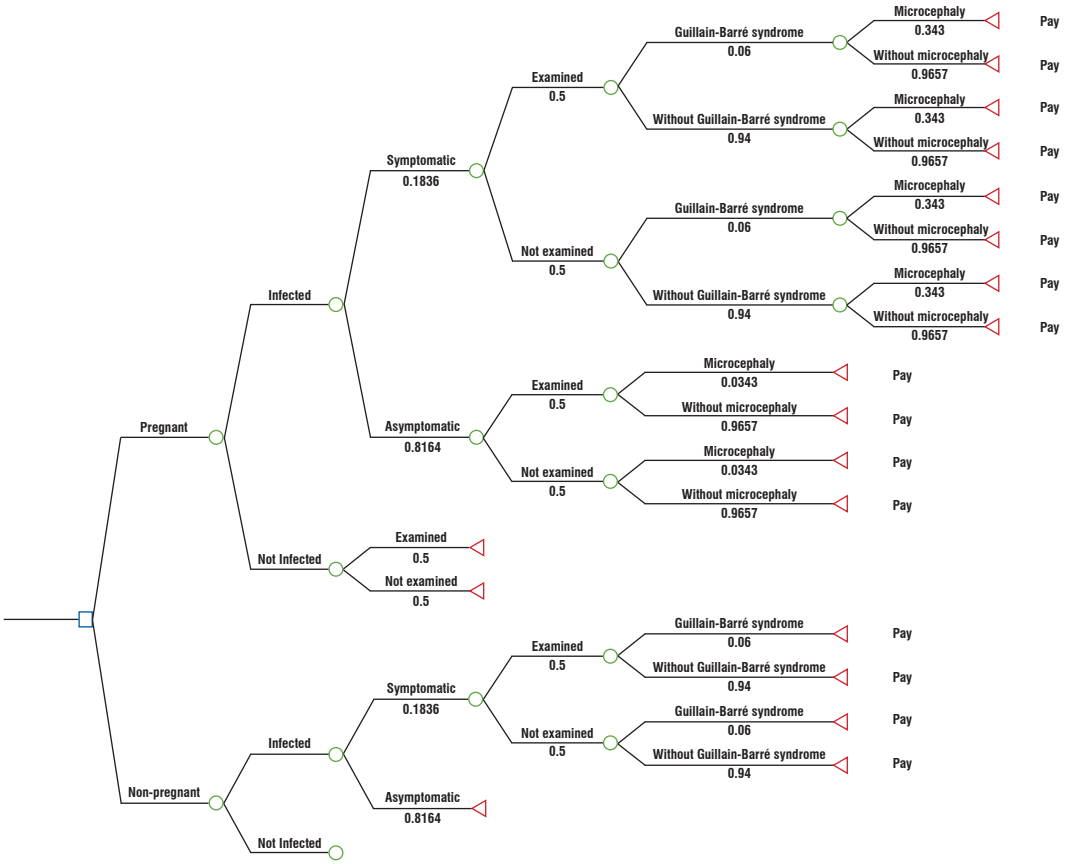
The economic model used in this chapter to estimate the costs related to Zika in Latin America and the Caribbean is based on a previous publication in the United States.[4] The population of the region was stratified by pregnancy status to calculate the risk of the effects of Zika on births using the birth rate of each country, according to World Bank Development Indicators for 2016.[5,6] The last regional epidemiological update on Zika was used for confirmed cases of Zika in men and women; to calculate the number of pregnant women, the birth rate of every country was used as a representative value.[2]

The direct and indirect costs of Zika virus were calculated for the 26 countries covered in the analysis (Antigua and Barbuda, Argentina, Barbados, Belize, Bolivia, Brazil, Colombia, Costa Rica, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Suriname, and Trinidad and Tobago).

* Summarized version of Gordillo-Tobar A, Calvo N, Ruiz L. The impact of the Zika virus in Latin America and the Caribbean. Washington, DC: World Bank; 2018.

This model will estimate two costs: one for pregnant women infected with Zika, and the other for non-pregnant women infected with Zika (Figure 11). The probability of complications in pregnant women infected with Zika is greater because of the possibility of Guillain-Barré syndrome (GBS) in the mother and microcephaly in the baby. For non-pregnant women infected with Zika, complications are only an issue in terms of the possibility of developing Guillain-Barré syndrome, which is the same for men living in areas at risk for Zika. For the purpose of the present study, infected men and non-pregnant women will be called non-pregnant women.

Figure 11. Structure of the economic model



To estimate the total number of people affected in each country, confirmed cases of Zika and microcephaly per country were used, based on the situation reports on Zika issued by the Pan American Health Organization in 2016, the year for which total costs were estimated.[7]

Direct costs

The direct costs considered in the economic model are for medical care provided because of the disease. This includes treatment costs for Zika, microcephaly, and Guillain Barré. Direct medical costs include the compliance-adjusted costs for hospital visits and medical procedures for Zika-infected pregnant and non-pregnant persons, non-infected pregnant women, babies with microcephaly or other CNS disorders, and people with Guillain-Barré.[4]

These costs were estimated for the United States of America and then were adapted by purchasing power parity (PPP) for each country analyzed in the study.

Indirect costs: Productivity losses

The indirect costs of Zika virus were estimated in LAC as the sum of the costs of microcephaly and of Guillain-Barré, both over the lifetime, based on the cumulative cases of these two medical disorders.

Indirect costs also include productivity losses resulting from time spent on medical consultations and absenteeism due to illness, with the minimum hourly wage as the representative value of the rate of productivity loss. Time lost was valued similarly for all those affected, regardless of their employment status, using each country's average annual wage. Calculations for productivity losses due to microcephaly and other CNS disorders come from previous estimates for autism[8] and another study was used to estimate productivity losses due to Guillain-Barré syndrome.[9] All 2016 costs, converted to U.S. dollars, were adjusted using the general consumer price index.

Projection

Projections were developed from the number of cases of Zika, microcephaly, and Guillain-Barré based on current figures for confirmed cases and population growth in every LAC country until 2030.

This study consisted of running several hypothetical scenarios to explore the impact of various Zika virus attack rates (from 0.01% upwards) in each country.

Results

Direct medical costs

This study used three hypothetical scenarios to explore the possible variations in direct medical costs incurred by individuals infected by Zika in LAC. The range of scenarios encompassed a base case from the literature (scenario A), a more conservative calculation (scenario B) that constitutes only 50% of estimated U.S. costs, and a less conservative estimate (scenario C) that constitutes 35% of estimated U.S. costs.

Based on the economic model, total direct expenses amount to US$21,043 per year for Zika-infected pregnant women and US$638 per year for Zika-infected non-pregnant women. Using PPP, the cost for each country was estimated for infected pregnant and non-pregnant women.

It was calculated that direct medical costs related to Zika in Latin America total US$120 million, including the confirmed cases published by WHO (from August 2016 to August 2017) for scenario A; for scenario B, they amount to US$60 million; and US$42 million for scenario C (Table 1). The direct cost for non-pregnant women is higher. This is because the proportion of non-pregnant women with confirmed infection is higher than infected pregnant women in each country. However, this does not mean that the cost of Zika treatment per person will not be higher for a pregnant woman, since an infected pregnant woman will be given additional tests and she will presumably spend more time with the physician than a non-pregnant person; as a result, her individual costs will be greater.

Table 6. Direct medical costs for Zika in the LAC region by scenario, 2016-2017

Country	Scenario A: 100% of cost		Scenario B: 50% of cost		Scenario C: 35% of cost	
	Direct cost for Zika-infected pregnant women	Direct cost for Zika-infected non-pregnant women	Direct cost for Zika-infected pregnant women	Direct cost for Zika-infected non-pregnant women	Direct cost for Zika-infected pregnant women	Direct cost for Zika-infected non-pregnant women
Antigua and Barbuda	5,514	10,047	2,757	5,024	1,930	3,516
Argentina	62,980	108,059	31,490	54,030	22,043	37,821
Barbados	36,243	90,511	18,122	45,256	12,685	31,679
Belize	96,727	126,037	48,363	63,019	33,854	44,113
Bolivia	167,130	210,109	83,565	105,055	58,495	73,538
Brazil	23,795,287	49,361,597	11,897,644	24,680,799	8,328,351	17,276,559
Colombia	1,325,678	2,556,425	662,839	1,278,212	463,987	894,749
Costa Rica	425,504	875,279	212,752	437,639	148,927	306,348
Dominica	-	32,810	-	16,405	-	11,484
Dominican Republic	63,914	92,529	31,957	46,265	22,370	32,385
Ecuador	696,891	1,010,710	348,446	505,355	243,912	353,748
El Salvador	9,829	15,647	4,914	7,823	3,440	5,476
Grenada	31,994	50,215	15,997	25,108	11,198	17,575
Guatemala	281,475	324,384	140,738	162,192	98,516	113,534
Guyana	9,201	13,176	4,600	6,588	3,220	4,612
Haiti	1,071	1,290	535	645	375	451
Honduras	71,186	95,767	35,593	47,883	24,915	33,518
Jamaica	39,566	70,166	19,783	35,083	13,848	24,558
Mexico	1,805,996	2,903,096	902,998	1,451,548	632,099	1,016,084
Nicaragua	336,150	501,312	168,075	250,656	117,653	175,459
Panama	292,177	437,502	146,088	218,751	102,262	153,126
Paraguay	3,413	4,789	1,706	2,395	1,194	1,676
Puerto Rico	7,082,885	23,645,817	3,541,442	11,822,909	2,479,010	8,276,036
Peru	290,701	440,522	145,350	220,261	101,745	154,183
Suriname	128,832	207,826	64,416	103,913	45,091	72,739
Trinidad and Tobago	101,618	217,680	50,809	108,840	35,566	76,188
Total	**37,161,961**	**83,403,304**	**18,580,981**	**41,701,652**	**13,006,686**	**29,191,157**
Total by scenario		**120,565,266**		**60,282,633**		**42,197,843**

Indirect costs: Productivity losses

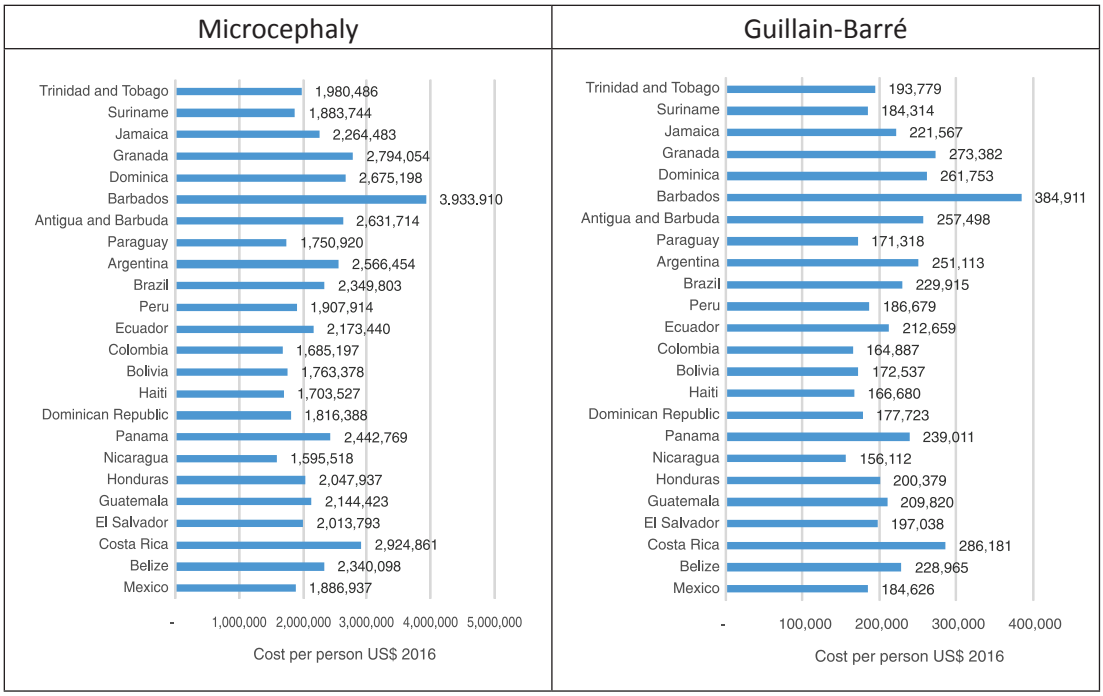
Total lifetime costs and direct medical costs in 2016 U.S. dollars are US$8,141,169,112[8] for microcephaly and US$11,625,296 per year for Guillain-Barré[4] (Table 7).

Table 7. Indirect lifetime costs of Zika in the LAC region, US$, 2016

Country	Lifetime cost of microcephaly	Lifetime cost of Guillain-Barré	Total indirect cost of Zika
Antigua and Barbuda	-	1,577	1,577
Argentina	5,131,650	16,980	5,148,630
Barbados	3,932,946	14,145	3,947,091
Belize	-	-	-
Bolivia	24,681,247	33,225	24,714,473
Brazil	6,934,918,268	7,733,318	6,942,651,586
Colombia	417,826,561	400,944	418,227,505
Costa Rica	17,544,869	137,144	17,682,013
Dominica	-	5,066	5,066
Dominican Republic	154,355,182	14,587	154,369,769
Ecuador	15,210,352	159,326	15,369,678
El Salvador	8,053,198	2,462	8,055,660
Grenada	5,586,740	7,903	5,594,643
Guatemala	300,145,667	51,406	300,197,073
Guyana	8,380,109	2,478	8,382,588
Haiti	1,703,109	204	1,703,314
Honduras	16,379,482	15,121	16,394,603
Jamaica	-	11,020	11,020
Mexico	37,729,492	456,722	38,186,214
Nicaragua	3,190,253	78,981	3,269,235
Panama	31,748,218	68,922	31,817,140
Paraguay	3,500,982	756	3,501,737
Peru	-	69,382	69,382
Puerto Rico	109,957,644	2,276,845	112,234,489
Suriname	7,533,128	32,694	7,565,822
Trinidad and Tobago	33,660,015	34,088	33,694,103
Total	**8,141,169,112**	**11,625,296**	**8,152,794,408**

Based on PPP, lifetime costs are estimated for every country. Brazil is the country with the highest indirect costs because it has the greatest number of confirmed Zika cases (microcephaly and Guillain-Barré) (Figure 12). It is calculated that indirect costs related to Zika for the region of Latin America total US$8.152 billion annually.

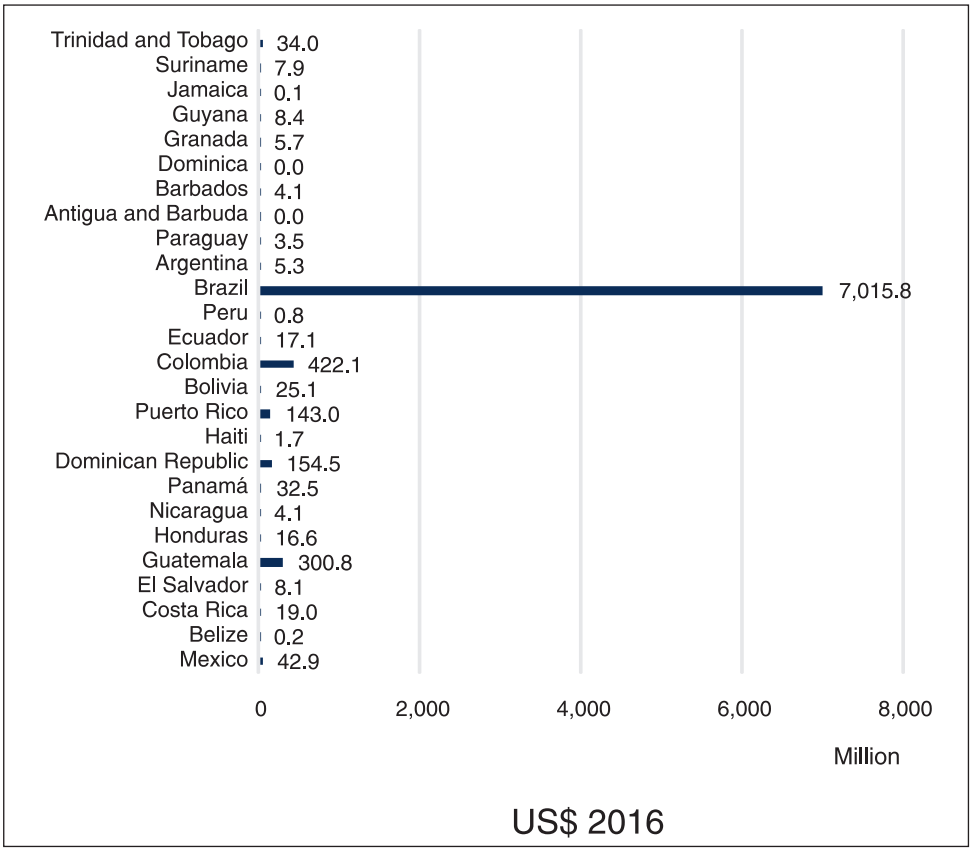
Figure 12. Indirect lifetime costs of microcephaly and Guillain-Barré syndrome in the LAC region, US$, 2016



Total cost: Direct and indirect

Based on the confirmed cases published by WHO[2] (from August 2016 to August 2017), the cost of Zika amounts to US$8.273 billion per year for confirmed cases in Latin America with 84.7% of this cost concentrated in Brazil, followed by Colombia with US$422.1 million, and Guatemala with US$300.8 million (Figure 13).

Figure 13. Total cost per year, direct and indirect, US$ millions, 2016

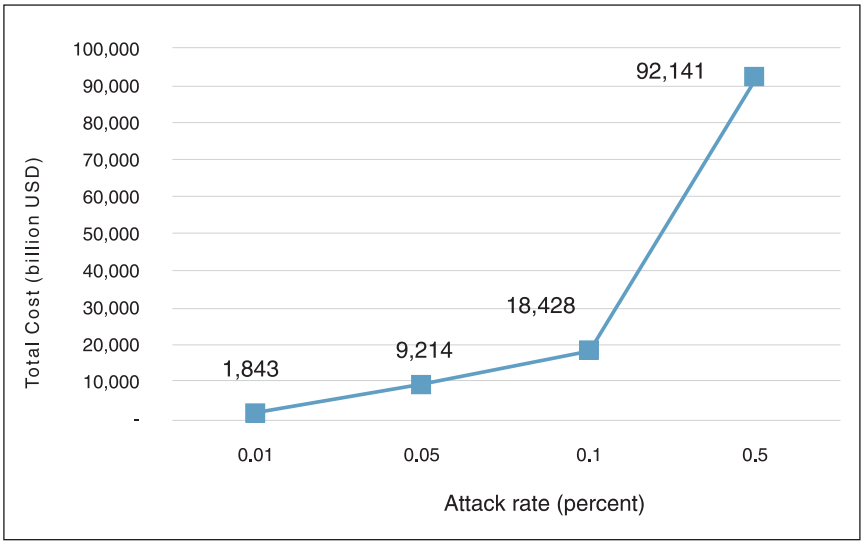


Projection

The idea of this projection is to determine the possible costs in each country with different Zika attack rates. A wide range of projections have been run to show how the burden varies in different attack rate scenarios, from 0.01% to 5% (from the minimum to the maximum possible rate).

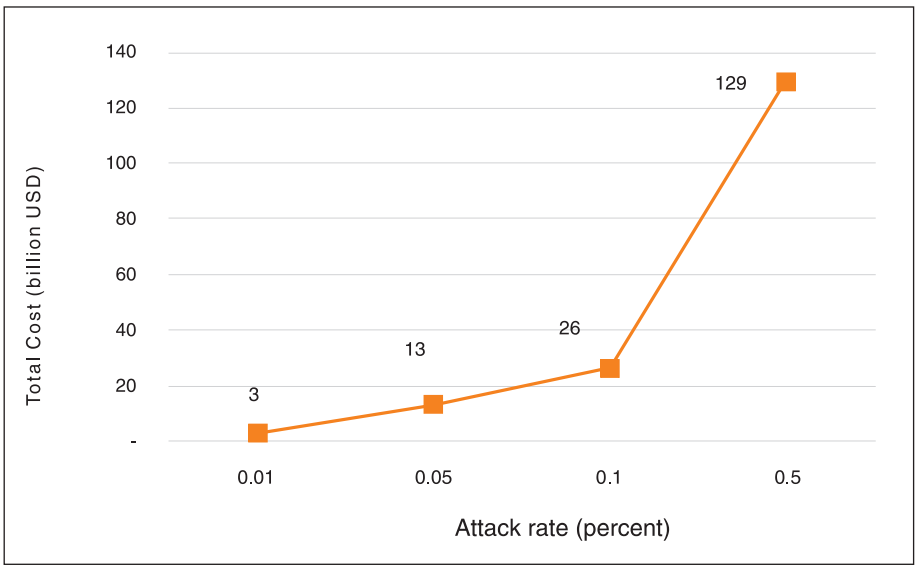
These projections are to 2030. The population estimate for each country is based on the average growth rate reported over the past 10 years. Each node shows the total cumulative cost until 2030 at different attack rates (Figure 14).

Figure 14. Global costs for microcephaly until 2030 with different attack rates



When the attack rate is intensive, the cost related to Zika is higher. By 2030, it is estimated that the cost could be US$1.843 billion for Latin America if the attack rate for microcephaly is 0.1% (Figure 15).

Figure 15. Global costs for Guillain-Barré until 2030 with different attack rates



The cost for Guillain-Barré syndrome is lower than for microcephaly, which has different complications. For example, for 2030, with an attack rate of 0.1%, the cost could be US$26 million.

Conclusions

The study calculated the total costs of Zika in 26 countries of Latin America exposed to the virus, by analyzing direct costs (hospital diagnosis and treatment) and indirect costs (costs for treatment of Guillain-Barré and microcephaly).

The countries with the highest total direct costs due to confirmed Zika cases are Brazil, Puerto Rico, and Mexico. Direct total costs are US$60 million (scenario B, 50% of cost). The nations with the highest indirect costs were Brazil, Colombia, and Guatemala. Total indirect costs of the region amount to US$8 billion per year. The total cost (indirect + direct) is US$8.273 billion per year for Latin America; 84.7% of this cost is concentrated in Brazil. The next highest costs were in Colombia and Guatemala (direct and indirect). The indirect cost contributes 98.5% and the direct cost contributes 1.5%. The indirect cost is related to the lifetime value of living with the disease. The direct cost is related to the medical care provided because of the disease.

Finally, several projections were made to determine what the cost of Zika would be by trying various attack rates. The results showed that the cost could vary from US$1.843 billion to US$92.141 billion (attack rates of 0.01% and 0.5%) in the case of microcephaly, and from US$3 million to US$29 million (attack rates of 0.01% and 0.5%) for Guillain-Barré.

The results of this financial impact assessment demonstrate the importance of taking necessary precautions to reduce the costs associated with Zika virus.

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In Latin America and the Caribbean, approximately one of every five deaths during the first 28 days of life is due to birth defects. From 1990 to 2017, neonatal mortality in Latin America and the Caribbean decreased from 23 to 10 neonatal deaths per 1,000 live births, a 58% reduction.

However, inequalities in neonatal mortality must be emphasized: in 2008, estimated neonatal mortality in the region's countries ranged from 3.8 to 24.6 per 1,000 live births. Birth defects contribute substantially to the burden of morbidity and mortality in the Region of the Americas.

Numerous efforts exist to raise awareness of this problem and to implement surveillance in health and government sectors. However, there is still a long way to go.

After taking into account all these aspects, the Pan American Health Organization/Latin American Center for Perinatology, Women, and Reproductive Health (PAHO/CLAP/WR), together with the World Bank, decided to create a document summarizing the regional situation of birth defects from an epidemiological and programmatic perspective, to analyze the challenges and offer countries guidance to address birth defects, their determinants, and consequences, with the ultimate goal of helping to "leave no one behind."

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