

Contribution of Mexico's Universal Immunization Program to the Fourth Millennium Development Goal

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Suggested citation

Richardson V, Sánchez-Uribe E, Esparza-Aguilar M, Esteves-Jaramillo A, Suárez-Idueta L. Contribution of Mexico's Universal Immunization Program to the Fourth Millennium Development Goal. *Rev Panam Salud Publica*. 2014;35(4):248–55.

ABSTRACT

Objective. To identify and describe 1) progress achieved thus far in meeting the commitments of the Fourth Millennium Development Goal (MDG 4) in Mexico, mainly the contribution of the Universal Immunization Program (UIP) over the last 20 years, and 2) new opportunities for further reducing mortality among children under 5 years old.

Methods. An observational, descriptive, retrospective study was carried out to examine registered causes of death in children under 5 between 1990 and 2010. Indicators were built according to the recommendations of the United Nations.

Results. In 2010, deaths among children under 5 decreased 64.3% compared to the baseline (1990) figure. Of the total deaths of the children under 5, the neonatal period was the most affected (52.8%), followed by the 1 to 11 months (30.9%), and the 12 to 59 months (16.2%) groups. A 34% overall mortality reduction was observed after the universalization of immunization against influenza, rotavirus, and pneumococcus in children under 5.

Conclusions. Despite a significant reduction in under-5 mortality in Mexico over the last 20 years, largely due to the successes of the UIP, several challenges remain, particularly in improving preventive and curative services during pre- and postnatal care.

Key words

Infant mortality; child mortality; Millennium Development Goals; immunization programs; Mexico.

Child mortality is a high-priority public health problem worldwide. In the year 2000, the United Nations proposed the Fourth Millennium Development Goal (MDG 4) to reduce mortality by two-thirds in children under 5 years old by 2015 (1).

According to reporting on advances toward fulfillment of MDG 4, under-5 mortality was reduced by 35% by the year 2011. Progress toward this goal

has occurred heterogeneously, with 1) reductions less evident in some African countries versus other parts of the world; 2) the proportion of neonatal deaths increasing rather than decreasing (from 10% to more than 40% of overall under-5 mortality); and 3) pneumonia, diarrhea, preterm birth complications, and birth asphyxia still causing more than 50% of under-5 deaths worldwide, despite the fact that deaths caused by pneumonia and diarrhea are vaccine-preventable (2–4).

Over the past several decades, Mexico has implemented several programs to

fight the leading causes of morbidity and mortality among children. The Universal Immunization Program (UIP) has been the most successful program thus far, reducing the contribution of infectious disease, which have accounted for and continue to represent a high proportion of under-5 mortality (48% in 1985) (5, 6). The program's first success was evident in 1951, when smallpox was eliminated countrywide as a result of the compulsory vaccination against the disease that began in 1926. In the following years, vaccines against diphtheria and pertussis (1948), tuberculosis (1951), tetanus (1954),

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poliomyelitis (1956), and measles (1970) were incorporated into the immunization schedule (7).

Since 1980, intensive annual vaccination campaigns using field workers were put in place to 1) reach the smallest and most isolated communities, 2) update immunization schedules for children, and 3) break the chains of disease transmission in a short period of time. This strategy proved successful, as Mexico documented the last cases of wild polio and diphtheria in 1990 and 1991 respectively (7).

During that same two-year period (1990–1991), however, a National Immunization Coverage Survey reported low coverage rates (46%) for the basic vaccination schedule for children under 1 year old. In addition, in 1990, an outbreak of measles resulted in a mortality rate of 38.4 deaths per 100 000 children under 5 and nearly 6 000 total deaths. In response to these two events, and to help achieve commitments made at UNICEF's 1990 World Summit for Children, in 1991 Mexico created the National Immunization Council (NIC). The NIC coordinates the UIP, providing direction to all health institutions working to control and eliminate vaccine-preventable diseases (8, 9).

Since its inception, the NIC has approved the inclusion of vaccines against mumps and rubella (1998), hepatitis B (1999), *Haemophilus influenzae b* (Hib) (1999), influenza (2004), rotavirus (2007), pneumococcus (2008), and human papillomavirus (HPV) (2011) in the UIP, making Mexico's vaccination schedule one of the most complete in the Americas. Current immunization strategies are focused on the timely completion of free vaccinations for children under 8 years old in all public health units countrywide. The NIC promotes these vaccinations during three annual National Health Weeks that include intensive community vaccination activities and other overall health promotion efforts (7).

The National Program for Infant Mortality Reduction (*Programa de acción específico 2007–2012 para la prevención de la mortalidad infantil*, PRONAREMI) was initiated in 2007. Its main strategies include strengthening immunization activities, improving health education among the general population, improving health workers' knowledge of integrated management of infants, timely management of acute diarrheal diseases (ADDs) and acute respiratory

infections (ARIs), accident prevention, and promoting healthy eating behaviors and micronutrient supplementation to reduce the prevalence of malnutrition in children under 5 years old (10).

This report describes progress achieved thus far in meeting the commitments of MDG 4 in Mexico—mainly the contribution of the UIP over the last 20 years—and new opportunities for further reducing mortality among children under 5 years old.

MATERIALS AND METHODS

An observational, descriptive, retrospective study was conducted using secondary sources from dynamic databases managed by the Ministry of Health's General Directorate of Health Information. These databases contain information from death certificates issued by medical services (11). While the main study period was 1990 to 2010, data collection was expanded to include the period 1986–1990 for the analysis of the causes and distribution of deaths in children under 5.

Diseases were classified using the categories proposed in the World Health Organization (WHO) 1990 Global Burden of Disease (GBD) study. When a more detailed analysis was required, causes of death were assigned according to the 10th Revision of the International Classification of Diseases (ICD-10) (12, 13).

The methodology proposed by WHO in 2006 was applied to estimate infant and under-5 mortality rates. The total number of live births estimated by the Mexican Population Council (*Consejo Nacional de Población*, CONAPO) was used as the denominator in both cases, and the number of estimated deaths for each study period was used as the numerator (14).

To calculate the mortality rates by specific cause, the population by age group (estimated by CONAPO) was used for the denominator, and the number of observed deaths reported in the Ministry of Health dynamic mortality databases was used as the numerator. The latter figures are subject to under-registration (omissions in reported deaths), especially in less developed regions.

Mortality rates across two different periods were estimated using the statistical median of the annual frequency of deaths and the statistical median of

the population for each corresponding period, and the estimated percentages of change in mortality (reductions or increases) and their 95% confidence intervals (CIs) were calculated. A chi-square test was used to assess statistical differences. The degree of association between infant mortality rates and the proportion of births in health facilities was established using a non-parametric correlation test.

RESULTS

Mortality in children under 5

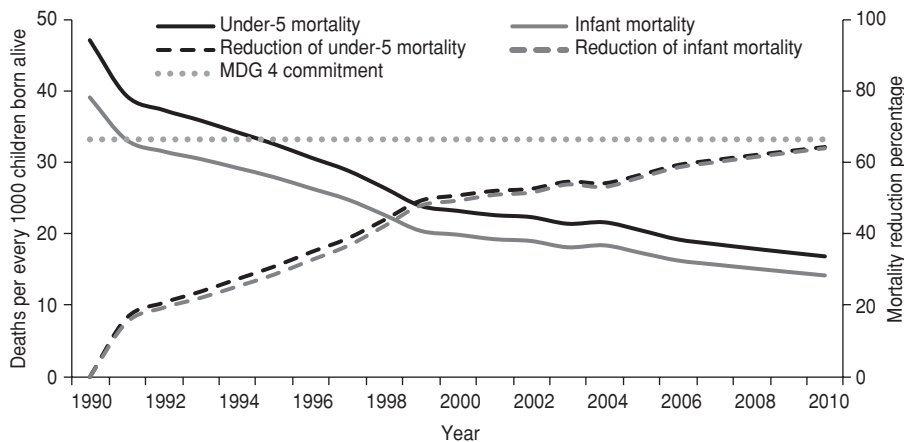
Between 1990 and 2010, Mexico reported a 64.3% reduction in overall child mortality, with a baseline figure of 47.1 deaths per 1 000 live births (lb) decreasing to 16.8/1 000 lb. The steepest decrement occurred over the period 1990–1995, which had an annual reduction rate of 2.5 deaths/1 000 lb. During the period 2000–2005, the pace of reduction digressed, resulting in an annual reduction of only 0.51 deaths/1 000 lb. For the remaining five years of the study period, the reduction rate increased to an annual rate of 0.7 deaths /1 000 lb. If this rate of reduction is sustained, Mexico will meet MDG 4 commitments by 2015.

While infant mortality has been the primary contributor to under-5 mortality in Mexico, accounting for 82.4% of deaths, it has also decreased by 63.8%, from 39.09/1 000 lb in 1990 to 14.14/1 000 lb in 2010. The most pronounced reduction (49.2%) was achieved during the first decade (1990–2000). Over the second decade (2000–2010), only a 14.6% reduction was observed (Figure 1).

Overall, the greatest burden of infant mortality in Mexico occurs during the neonatal period. The proportion of neonatal deaths among overall deaths in children under 5 has increased steadily over time: in 1986, infants 1–11 months old accounted for 44% of all under-5 deaths, followed by neonatal deaths (32%). By 1990, the difference in the proportions of the two age groups among all deaths was smaller (40% versus 37% of deaths respectively). In 2010, 52.8% of deaths in children under 5 occurred in the neonatal period, followed by 30.9% between the ages of 1–11 months and 16.2% between the ages of 12–59 months (Figure 2).

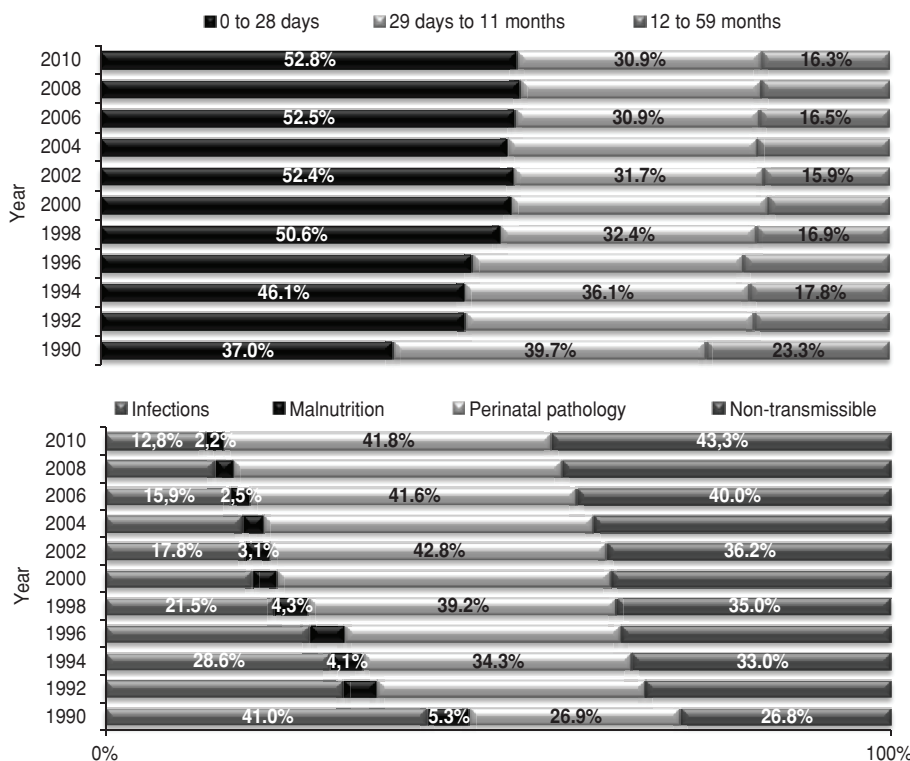
The transition observed in the age of occurrence of death has gone hand

FIGURE 1. Infant mortality and under-5 mortality and their reduction percentages relative to the Fourth Millennium Development Goal (MDG 4) commitment, Mexico, 1990–2010^a



^a Denominator: total number of live births estimated by the Mexican Population Council; numerator: estimated deaths for each study period (14).

FIGURE 2. Distribution of children < 5 years old by age subgroup (top) and by groups of causes of death (bottom), Mexico, 1990–2010^a



^a Causes of death are grouped according to the Global Burden of Disease classification (12).

in hand with a transition in the leading causes of death. In 1986, infectious diseases were responsible for 45% of all deaths in children under 5. By 1990, these diseases were still the leading cause of death, accounting for 41% of all

under-5 mortality, but as of 2010, they only accounted for 12.8% of total deaths in children under 5. For the 2005–2010 period, there was a 21% decrease versus the preceding five years (95% CI: 18–25; $P < 0.001$) (Figures 2 and 3).

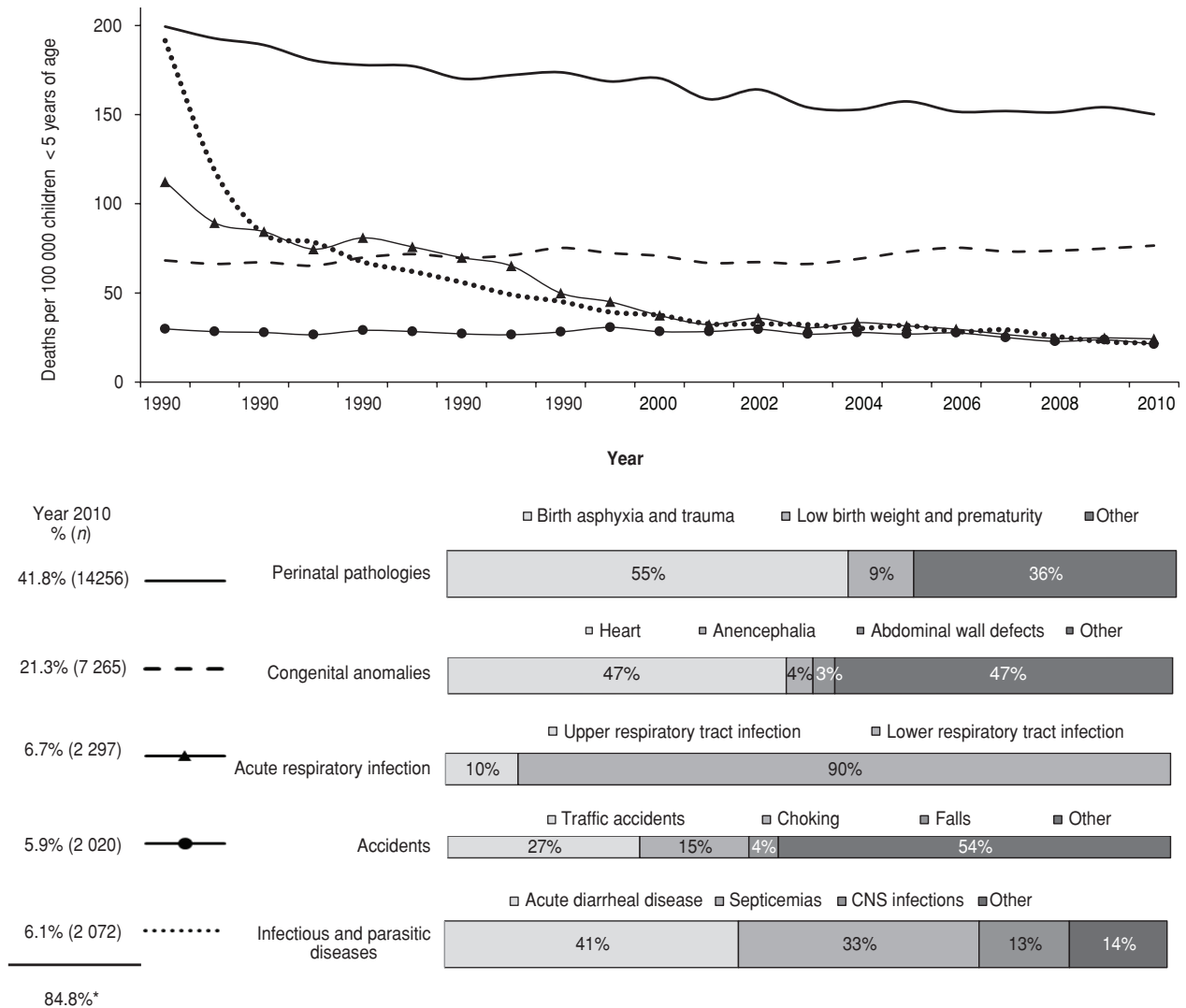
Diseases originating in the perinatal period have consistently been among the leading causes of infant mortality in Mexico. A reduction of 21.2% was documented for the period 1990–2010 (from 9.4/1 000 lb to 7.4/1 000 respectively). In the second five-year period, these causes of death decreased 8% (95% CI: 6–10; $P < 0.001$) compared to the first five-year period. The increase in the proportion of deliveries in medical facilities (from 71.2% in 1990 to 84.7% in 2009) appears to have played an important role in the reduction of perinatal mortality, based on evidence of a strong negative correlation (Spearman's rho = -0.902 ; $P < 0.001$).

Up to 30% of infant mortality is due to four main perinatal pathologies: respiratory distress syndrome and other respiratory conditions; infections; intra-uterine hypoxia and birth asphyxia; and low birth weight and prematurity. Although respiratory distress syndrome and other respiratory conditions have continuously decreased over the last 20 years, particularly in the last five years, they are still the leading cause of death. Intrauterine hypoxia and birth asphyxia have followed the same pattern of reduction. Deaths due to perinatal infections and prematurity and low birth weight have been increasing (Table 1).

After perinatal causes, congenital malformations, ARIs, ADDs, accidents, and child malnutrition follow in importance as causes of infant mortality. In past decades, deaths by accidents, among which those related to accidental airway obstruction are the most important, had displayed little variations, with an increasing trend, but over the last five years, this tendency has reversed, and the recording of congenital malformations as the cause of death has increased (Figure 4).

Analysis of mortality in children 1–4 years old showed that deaths from infectious causes such as ARIs and ADDs and those caused by malnutrition had declined significantly, while deaths from three other pathologies—accidents, congenital malformations, and cancer—had increased proportionally. Accidents have been among the leading causes of death in this age group since 1994, with motor vehicle accidents the most prevalent followed by drowning, choking, and accidental falls. Congenital malformations have remained the second leading cause of death for the last 12 years. This could be related to the fact that more in-

FIGURE 3. Top five leading causes of death among children < 5 years old, and their 2010 distribution, Mexico, 1990–2010^a



^a Causes of death are grouped according to the Global Burden of Disease classification (12).

fants with congenital malformations are surviving beyond their first year. Cancer has been the fourth leading cause of under-5 mortality in Mexico for the last couple of years, with leukemia, lymphomas, and central nervous system tumors the most frequently reported malignancies (Figure 4, Table 1).

Effects of the Universal Immunization Program on under-5 mortality

During the first half of the 1990s, the UIP maintained control of the six vaccine-preventable diseases, which represented 0.74/100 000 of under-5 mortality. Over the period 1995–2010, the vaccination program expanded 130%, increasing from 6 to 14 immunogens.

Since 1990, the increase in the proportion of children 1 year old that were vaccinated against measles contributed to breaking the chain of transmission of that endemic virus in Mexico. According to WHO estimates, by 1990, Mexico had achieved 75% measles vaccination coverage among children 1 year old. This coverage increased to 90% by 1994 and has remained above 95% since 1998 (15). The effect of measles vaccination coverage is evident given that the last death due to the disease was documented in 1995, followed by the last endemic case a year later.

In 1998, a combination measles, mumps, and rubella (MMR) vaccine was introduced to the national immunization schedule. However, because of the low

burden in mortality represented by the two latter diseases, this did not affect overall mortality rates significantly.

A year later, the introduction of the Hib vaccine contributed to the already observed decrease in deaths due to meningitis in children under 5, and in 2008, the conjugated pneumococcal vaccine became universal. After the implementation of these two vaccines, a 70% reduction in mortality due to meningitis (95% CI: 51%–81%; *P* < 0.0001) was observed in children under 5 when comparing the last five-year study period (2005–2010) with the initial five-year study period (1990–1995).

The universal introduction of vaccines against influenza, rotavirus, and pneumococcus is estimated to have prevented

TABLE 1. Main causes of death among children < 5 years old compared by period, Mexico, 1991–1995 and 2006–2010

	Age (years)	Annual number of deaths (median)		Annual mortality rate ^a		Absolute reduction		Relative reduction ^b		P	
		1991–1995	2006–2010	1991–1995	2006–2010	Number of deaths	Mortality rate ^a	%	(CI) ^c		
Infections	< 5	18 242	4 932	157.9	50.9	13 310	107	68	(66 to 70)	< 0.001	
	< 1	13 855	3 547	575.1	181.4	10 308	393.7	68	(66 to 71)	< 0.001	
	1–4	4 369	1 345	47.5	17.3	3 024	30.2	64	(60 to 67)	< 0.001	
Cancer	< 5	508	507	4.4	5.2	1	–0.8	–19	(–32 to –6)	0.005	
	< 1	73	76	3.0	3.9	–3	–0.9	–28	(–65 to 8)	0.127	
	1–4	427	434	4.6	5.6	–7	–0.9	–20	(–35 to –6)	0.006	
Accidents	< 5	3 263	2 280	28.2	23.5	983	4.7	17	(12 to 22)	< 0.001	
	< 1	1 172	882	48.6	45.1	290	3.5	7	(–1 to 16)	0.090	
	1–4	2 048	1 384	22.2	17.8	664	4.4	20	(14 to 26)	< 0.001	
Malnutrition	< 5	2 623	782	22.7	8.1	1 841	14.6	64	(60 to 69)	< 0.001	
	< 1	1 795	508	74.5	25.9	1 298	48.5	65	(59 to 71)	< 0.001	
	1–4	901	281	9.8	3.6	620	6.2	63	(55 to 71)	< 0.001	
Congenital anomalies											
	Heart disease	< 5	2 557	3 256	22.1	33.6	–699	–11.5	–52	(–58 to –45)	< 0.001
		< 1	2 194	2 805	91.1	143.5	–611	–52.4	–58	(–65 to –51)	< 0.001
1–4		358	446	3.9	5.7	–88	–1.8	–48	(–65 to –31)	< 0.001	
Other	< 5	5 286	3 968	45.8	40.9	1 318	4.8	11	(7 to 14)	< 0.001	
	< 1	4 868	3 623	202	185.3	1 245	16.8	8	(4 to 12)	< 0.001	
	1–4	409	364	4.4	4.7	45	–0.2	–5	(–20 to 9)	0.46	
Pathologies originating in perinatal period											
	Respiratory distress syndrome and other respiratory conditions	< 1	10 611	6 847	440.4	350.1	3 764	90.2	20.5	(17.8 to 23.1)	< 0.001
		< 1	2 624	2 725	108.9	139.4	–101	–30.5	–28	(–34 to –21.9)	< 0.001
< 1		2 008	1 368	83.3	70	640	13.4	16	(9.7 to 22.35)	< 0.001	
Intrauterine hypoxia and birth asphyxia											
	< 1	1 227	1 280	51	65.5	–53	–14.5	–28.5	(–37.4 to –19.7)	< 0.001	

^a Estimated deaths for each age group per 100 000; for children < 1 year old estimated number of births was used.

^b Negative values imply relative increase.

^c CI: 95% confidence interval.

at least 1 177 ADD deaths and 1 262 ARI deaths annually in children under 5 between 2008 and 2010. Compared to the reported number of deaths from these diseases during the pre-vaccination period (2001–2003) this represents a 34% reduction in mortality from all causes for this population over this period.

DISCUSSION

While the established deadline for achieving the MDGs is still about a year away, Mexico has already met the goal of maintaining measles vaccination coverage above 95% and is close to reducing infant and under-5 mortality by the 2015 goal of two-thirds.

Significant progress has been achieved through the implementation of successful health policies, including the introduction of vaccines and oral rehydration and improvements in hygiene and sanitation (16). These interventions have indisputably affected child mortality due to infectious diseases and have thus

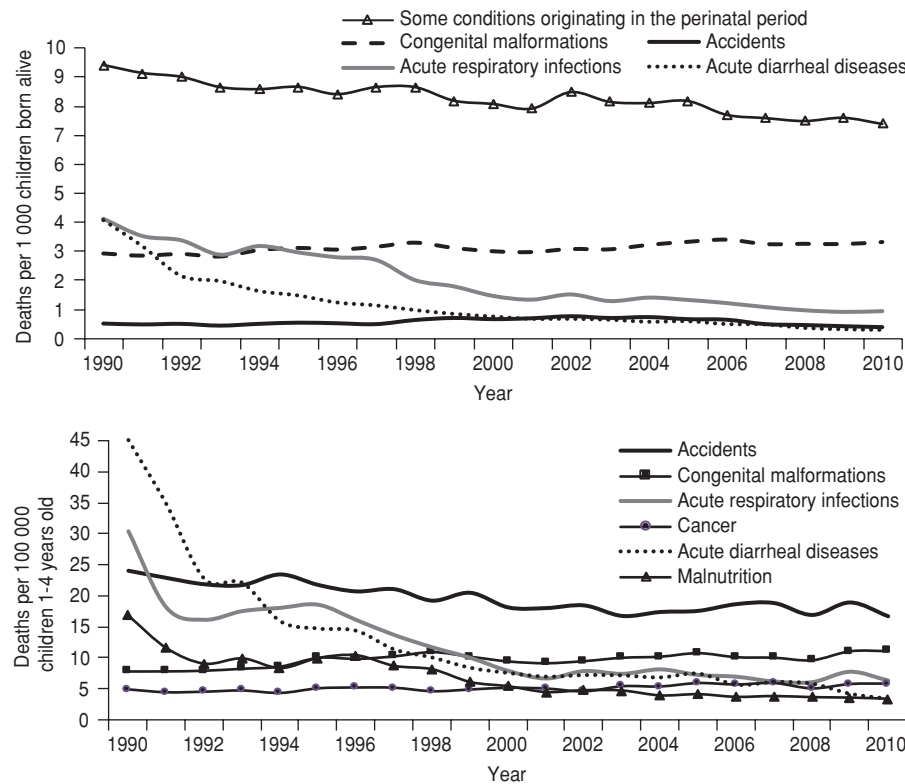
caused a transition in both the age of death and the main causes of death (8, 9). Coinciding with worldwide data, in Mexico, infants are the most vulnerable to under-5 mortality, experiencing 80% of all deaths (17). Therefore, efforts targeting infant mortality need to be intensified. While perinatal asphyxia among this age group has decreased as a result of expanded access to health services, other causes of death, such as neonatal sepsis, low birth weight, and prematurity, have tended to increase. These increases can be attributed to several factors, including improvement in the reporting systems for neonatal deaths, the longer survival of preterm and low-birth-weight infants, and the larger proportion of neonatal patients with sepsis secondary to prolonged hospitalizations and invasive treatments (18).

Although Mexico has carried out several actions to address infant mortality, including offering training to first-contact medical staff, and those responsible for neonatal resuscitation at medical facilities

from the health sector, it has not yet been enough. Future efforts must be directed at improving prenatal care and providing good-quality delivery services and newborn care, primarily in rural areas. Proper operation of the referral hospital systems, and interventions that cover vulnerable groups in marginalized communities equally, must also be ensured (19–22).

Strategies to decrease mortality among children 1–4 years old should also focus on the prevention of car and home accidents, and on the timely detection and treatment of cancer (23).

The increased mortality from cancer might be explained by several different factors, including delays in suspecting a malignancy, lack of resources from the family to cover the cost of treatment, and a consequent lack of adherence to treatment (24–25). To address this problem, since 2008, free medical care has been made available for all Mexican children and adolescents under 18 years old with any type of cancer at authorized hospitals throughout the country (26).

FIGURE 4. Main causes of death among infants (top) and children 1–4 years old (bottom), Mexico, 1990–2010^a

^a Causes of death are grouped according to the Global Burden of Disease classification (12).

Along with scientific progress, the continuing redesigns of health policies have enriched all preventive health programs, especially the vaccination program. Over the years, this has made a significant contribution to increasing the survival of children under 5 years old while decreasing the leading infectious causes of death (27).

In the case of measles, a permanent vaccination program targeting children 1 and 6 years old and intensive campaigns among children, adolescents, and adults helped eliminate the endemic virus and have decreased deaths from the disease for more than 15 years (28). They also resulted in Mexico achieving the goal for the third MDG 4 indicator (> 95% coverage for anti-measles vaccinations in children 1 year old) (15, 29, 30).

Over the last 20 years, Mexico has experienced a 70% reduction in under-5 mortality due to meningitis. This achievement is attributed to child immunization with the Hib vaccine and the conjugated pneumococcal vaccine. The impact of these vaccines on meningitis mortality has been reported previously in other countries (31–34) as well as nationally (35).

Two more success stories related to Mexico's immunization program are the reduction in deaths from both ADD and ARI. The implementation of Mexico's Clean Water Program (*Programa de Agua Limpia*) in 1991 and the introduction of oral rehydration salts in 1984 had helped prevent approximately 60% of deaths due to ADDs, but the speed of mortality reduction decreased gradually, reaching a plateau in 2000–2005, so new strategies were required (17, 36–38). The subsequent universalization of the rotavirus vaccine reduced mortality due to ADDs by an additional 46% (95% CI: 42–50) over a very short period, as reported by Richardson et al. (39, 40). In addition, as reported in an unpublished draft by Richardson and collaborators,² the introduction of influenza and pneumococcal vaccines reduced mortality from pneumonia for children 0–11 months and

² Richardson V, Esparza-Aguilar M, Bautista-Márquez A, Taylor TH Jr, Whitney CG. Early impact of influenza and pneumococcal vaccines on mortality due to pneumonia and influenza in children under five years of age in Mexico. 2013 Feb 1. Mexico City: Centro Nacional para la Salud de la Infancia y la Adolescencia. Unpublished author manuscript.

12–23 months by 38% and 19% on average respectively (Wilcoxon rank-sum test; $P < 0.001$ and 0.012 respectively). Unfortunately, these decreases are less than those seen in other countries (41). However, the influenza vaccine has been shown to be effective in preventing death from this virus during outbreaks (42).

Limitations

This study had some limitations, including the use of an ecological approach in the analysis, and the fact that the data sources consisted of information systems that may have been subject to underreporting and classification error. In addition, other factors that could have influenced mortality rates, such as changes in health care accessibility, infrastructure, sanitation, and the implementation of specific health programs (vitamin A supplementation, vector control, etc.), were not considered.

Conclusions

After the introduction of new vaccines such as influenza, pneumococcus, Hib, and rotavirus in Mexico's immunization schedule, a 34% reduction in overall under-5 mortality was observed, compared to the pre-vaccine era. These data suggest that Mexico's Universal Immunization Program has contributed to progress in reaching the MDG 4 target. To continue this progress, it is imperative to enhance efforts to improve vaccination coverage; achieve timely and complete childhood immunization schedules; and continue increasing the number of immunogens included in the UIP, based on scientific and cost-effectiveness evidence. Mexico's immunization program is an encouraging example of success. The authors urge all countries, international organizations, and donors to 1) help strengthen the immunization systems of poorer nations and 2) support the introduction of new vaccines.

Acknowledgments. The authors thank Mathuram Santosham, Director of both the Health Systems Program and the Center for American Indian Health at the Johns Hopkins Bloomberg School of Public Health (Baltimore, Maryland, USA), for his wise advice and editorial help.

Conflicts of interest. None.

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Manuscript submitted 11 February 2013. Revised version accepted for publication on 11 February 2014.

Contribución del Programa de Vacunación Universal de México al cuarto Objetivo de Desarrollo del Milenio

RESUMEN

Objetivo. Determinar y describir 1) el progreso logrado hasta el momento en el cumplimiento de los compromisos del cuarto Objetivo de Desarrollo del Milenio en México, principalmente la contribución del Programa de Vacunación Universal (PVU) durante los 20 últimos años; y 2) las nuevas oportunidades para reducir aún más la mortalidad en niños menores de cinco años.

Métodos. Se llevó a cabo un estudio de observación, descriptivo y retrospectivo para analizar las causas registradas de muerte en niños menores de cinco años entre 1990 y el 2010. Se elaboraron indicadores según las recomendaciones de las Naciones Unidas.

Resultados. En el 2010, las defunciones en niños menores de cinco años se habían reducido en 64,3% en comparación con las cifras de referencia (1990). La mayor disminución de la mortalidad se observó en recién nacidos (52,8%), seguidos por los lactantes de 1 a 11 meses (30,9%) y los niños de 12 a 59 meses (16,2%). Se observó una reducción total de la mortalidad de 34% tras la universalización de la vacunación contra la gripe, el rotavirus y el neumococo en niños menores de cinco años.

Conclusiones. A pesar de una reducción significativa de la mortalidad en menores de cinco años en México durante los 20 últimos años, en gran parte debida a los éxitos del PVU, siguen existiendo diversos retos, en particular en cuanto a la mejora de los servicios preventivos y curativos durante la atención prenatal y posnatal.

Palabras clave

Mortalidad infantil; mortalidad del niño; Objetivos de Desarrollo del Milenio; programas de inmunización; México.
