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Developing an evaluation framework for Hepatitis B immunization programs in developing countries: A case study with Cuba

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ABSTRACT

Hepatitis B is a serious viral infection that causes thousands of deaths worldwide each year. Immunization against hepatitis B protects individuals from hepatitis B and its resulting sequelae. The World Health Organization (WHO) strongly supports the development of hepatitis B immunization programs. By protecting immunized people from infection, hepatitis B immunization programs reduce the number of chronic carriers in a population. WHO has devised a number of hepatitis B immunization program protocols. If enacted as stated, these program protocols will successfully reduce the number of hepatitis B chronic carriers in a population. Cuba has a strong public health system and stresses the importance of immunization. A process evaluation of Cuba's hepatitis B immunization program was undertaken by comparing Cuba's practices with WHO guidelines. A thorough literature search facilitated this process, as did communication with Cuban health professionals. The importance of pairing a qualitative evaluation with a quantitative evaluation to enable an impact assessment is also presented. A framework for developing a quantitative evaluation of a hepatitis B immunization program through the use of an infection marker survey is discussed. The process evaluation reflects Cuba's strong hepatitis B immunization program administration. Cuba should consider conducting a quantitative evaluation employing fieldwork techniques described in this paper. The collection of quantitative seromarker data will provide evidence to further support the success of Cuba's hepatitis B immunization program in decreasing the rate of chronic carriers in its population.

Key words: evaluation, hepatitis B , immunization, immunization programs, Cuba, World Health Organization

Biotecnología Aplicada 2005;22:131-137

RESUMEN

Desarrollo de un marco de evaluación para programas de inmunización de hepatitis B en países en desarrollo: Cuba como caso de estudio.. La hepatitis B es una infección viral grave que produce miles de muertes en el mundo cada año. La inmunización contra la hepatitis B protege de la enfermedad y sus secuelas resultantes. La Organización Mundial de la Salud (OMS) apoya fuertemente el desarrollo de los programas de inmunización contra la hepatitis B. Al proteger de la infección a los inmunizados, los programas de inmunización reducen el número de portadores crónicos en una población. La OMS ha ideado un conjunto de protocolos de programas de inmunización contra la hepatitis B. Si se ejecutan de acuerdo con lo estipulado, estos protocolos de programas reducirán exitosamente el número de portadores crónicos de hepatitis B en una población. Cuba tiene un sistema de salud pública fuerte que enfatiza la importancia de la inmunización. Se desarrolló una evaluación del proceso del programa de inmunización contra la hepatitis B en Cuba mediante la comparación de las prácticas cubanas con los lineamientos de la OMS. El proceso se facilitó mediante una búsqueda en la literatura y por la comunicación con los profesionales de salud de Cuba. También se presenta la importancia de aparear una evaluación cualitativa con una cuantitativa para permitir evaluar el impacto. Se discute un marco para el desarrollo de una evaluación cuantitativa del programa de inmunización contra la hepatitis B mediante el uso de una encuesta de marcadores de la infección. La evaluación del proceso refleja la fuerte dirección del programa cubano de inmunización. Cuba debiera considerar el desarrollo de una evaluación cuantitativa con la utilización de las técnicas de trabajo de campo descritas en este trabajo. La recogida de datos de marcadores séricos proporcionará evidencia para apoyar aún más el éxito del programa cubano de inmunización contra la hepatitis B en la disminución de la tasa de portadores crónicos en su población.

*I*ntroduction

Hepatitis B is a serious global health problem that is endemic in many areas of the developing world [1]. One of the major problems with the hepatitis B virus (HBV), is that 90% of the infants infected with HBV before the age of one become chronically infected [1]. These infants are most likely to have mothers who are infected with HBV. Chronic carriers can transmit HBV to others throughout their lives, and often experience HBV sequelae like liver disease, cirrhosis, and hepatocellular carcinoma around mid-life [2].

Vertical transmission of Hepatitis B is a major source of transmission in many countries [3]. There is an effective and safe vaccine for hepatitis B, which prevents 90% of HBV infections from mother to baby when given within 24 hours of birth [3]. The 96.2% of high risk infants, born to Hepatitis B e Antigen (HBeAg) and Hepatitis B surface antigen (HBsAg) positive mothers, are protected from HBV infection when a birth dose of 10 microgram of recombinant hepatitis B vaccine is administered and followed by two subsequent doses [4-6]. A dose of 10 micrograms of vaccine was found by Andre and Zuckerman to be associated with a protective efficacy of at least 90%, even in the highest risk infants [7].

1. World Health Organization. Hepatitis B Fact Sheet 2000; October: 1-5. www.who.int/inf-fs/en/fact204.html 10/20/01.

2. Chang MH, *et al*. Universal Hepatitis B Vaccine in Taiwan and the Incidence of Hepatocellular Carcinoma in Children. The New England Journal of Medicine 1997;26:1855-9.

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Immunization programs have long been supported by international agencies. They are highly cost-effective if they are properly implemented [8]. Funders of immunization programs, especially the World Health Organization (WHO) and their partners, want countries to be aware of the current status of their immunization programs, especially the presence of conditions that could stall the achievement of their objectives [9]. Funders also want confirmation that the program is indeed in operation, and running according to the standards that they have set out, or that are internationally recognized. The development of an evaluation framework allows countries to identify areas that need attention. Also, an evaluation framework would ease the hepatitis B evaluation process, which should take place every five years [9]. Furthermore, a detailed analysis of a country's hepatitis B immunization program will provide insight into the true rates of hepatitis B coverage of the population.

WHO has called for all countries to add the hepatitis B vaccine to their national infant immunization programmes [1]. The goal of the immunization program is to prevent chronic hepatitis B infections [3]. WHO recommends infant immunizations, but in countries with low hepatitis B endemicity, "catch-up" vaccinations, vaccinations of older age groups and vaccinations of high risks groups would be desirable [3].

Cuba's national immunization program is solidly based on four basic principles: vaccination efforts encompass the entire Cuban population, vaccination is integrated into primary care services, the program depends on active community participation and vaccination is absolutely free of charge [10]. In 1992, Cuba's hepatitis B immunization program targeted infant immunizations using a birth dose of hepatitis B [10].

To date, Cuba has claimed remarkable success related to the percentage of the population protected against hepatitis B [11]. It is now considered to be a country with low endemicity of hepatitis B [10]. There are only five regions in Cuba acknowledged to have a hepatitis B immunization coverage rate of less than 89% [10]. According to Cuban national immunization program documents, those born after 1980 have been immunized, and morbidity rates associated with hepatitis B have decreased by 97% in children under the age of fifteen [10]. Also, Cuba has conducted a number of vaccination campaigns targeting health care workers and high-risk individuals [10].

As a result of its success, this program has been chosen as the one that will be used to develop an evaluation framework for hepatitis B immunization programs. It is expected that Cuba's hepatitis B program is well run, as Cuba's other programs targeting communicable disease have been relatively successful in the past [10]. Applying an evaluation framework to Cuba's national hepatitis B immunization program will likely highlight the reasons that set Cuba's immunization programs apart from other countries. This information will prove invaluable to other countries that are considering implementing infant hepatitis B immunization programs.

Methods

In order to conduct this program process evaluation, a systematic analysis of Cuba's hepatitis B immunization program was conducted. This was achieved through a review of supporting documents to develop a firm grasp of the program's components. A thorough literature search of Blackwell Synergy and OVID databases was undertaken. Correspondence with Cuban health professionals and Ministry officials played an important role in developing an understanding of the program components.

WHO documents outlining appropriate immunization practices related to hepatitis B immunization programs were also reviewed, and were considered to be the gold standard to which Cuban immunization practices were compared. A component of the Cuban hepatitis B immunization program was considered to be well implemented if in accordance with WHO recommendations. A number of program components were analyzed and compared to WHO standards.

Results

Cuba's hepatitis B immunization program was examined in segments to determine its compliance with WHO documents. The following discussion looks at the integral parts.

Vaccine Dose and Schedule

WHO has stated that the plasma-derived hepatitis B vaccine and the recombinant hepatitis B vaccine are similar with respect to safety, immunogenicity and efficacy [3]. Cuba uses a recombinant vaccine, and administers a 20-microgram adult dose and a 10-microgram pediatric dose [12]. A monovalent or combination vaccine is acceptable for use in hepatitis B administration according to WHO [3]. The Cuban program uses a monovalent vaccine as its immunization practices do not combine hepatitis B vaccine with Diphtheria, Polio and Tetanus (DTP) vaccine [12]. As for a vaccine schedule, WHO suggests that countries using a monovalent vaccine should immunize infants at birth, six weeks, and fourteen weeks [13]. Cuba immunizes infants at birth, four weeks, and twenty-four weeks [14]. The literature suggests that Cuba's different dose schedule will still induce protective levels of antibody to HBsAg [3, 14].

Data Collection

Cuba's data collection capabilities are sufficient for successful immunization program operation. Cuba collects data on disease incidence, vaccine safety and conducts serological surveillance of the vaccinated population [12]. WHO recommends the collection of routine service statistics and active surveillance data to enable the monitoring of immunization coverage [3, 14]. The immunization records of Cuban individuals are maintained by the National Epidemiological Services branch [12]. Also, almost all of Cuba's population has a vaccination card, which registers the name of each vaccine applied, the batch and the date the dose is administered [12]. An individual's primary care physician retains this card. Furthermore, Cuba maintains an Epidemiological Bulletin of Communicable Diseases and Technical Surveillance Report website that provides information on the immunization data it collects [15]. Detailed information regarding disease specific conditions, including cases of acute hepatitis B, is available through Cuba's health statistics web page [16].

3. World Health Organization Department of Vaccines and Biologicals. Hepatitis B Immunization: Introducing Hepatitis B vaccine into National Immunization Services. Geneva: The World Health Organization, 2001.

4. Wu JS, *et al*. Hepatitis B Vaccination in High Risk Infants: 10-Year Follow-up. Journal of Infectious Diseases 1999;179: 1319-25.

5. Poovorowan Y, *et al*. Long term Hepatitis B in vaccine in infants born to Hepatitis B e antigen positive mothers. Archives of Disease in Childhood 1997;77: F47-F51.

6. Poovorawan Y, *et al*. Impact of Hepatitis B immunization as part of the EPI. Vaccine 2001;19:943-9.

7. Andre FE, Arie JZ. Review: Protective Efficacy of Hepatitis B Vaccine in Neonates. Journal of Medical Virology 1994;44: 144-51.

8. Hinman AR. Economic Aspects of Vaccines and Immunizations. CR Academy of Science 1999;322:989-94.

9. Pan American Sanitary Bureau. Methodology for the multidisciplinary evaluation of the Expanded Programme on Immunization at the Country Level. World Health Organization, October 2000.

10. Galindo MA. Cuba's National Immunization Program. Cuban Medical Research.1999. http://www.medicc.org/Medicc%20Review/1999/summer/html/immuno.html.

11. "Every Child in Cuba Vaccinated Against Hepatitis B". Granma Newspaper, Cuba. January 9, 2002.

12. Email correspondence with Dr. Manuel Vera Gonzalez, Ministry of Health in Havana Cuba and with Javier Vazquez, Marketing staff, Centre for Genetic Engineering and Biotechnology of Havana. Correspondence dates: January 15, 2002-ongoing.

13. World Health Organization Department of Vaccines and Biologicals. Immunization Policy. Geneva: The World Health Organization, 1996:1-63.

14. World Health Organization Department of Vaccine and Biologicals. WHO vaccine preventable disease monitoring system 2001 Global Summary. http://www.who.int/vaccines-documents/Global/summary/Globalsummary.pdf 15/10/01.

15. Pan American Health Organization website. http://www.paho.org 15/10/01.

16. Anuario Estadico Cuba. 1999 Incidence data for Cuba http://www.sld.cu/anuario/anu99/CMB43.html 22/02/02.

Statistical information regarding the percentage of immunization coverage is also regularly reported to WHO. The immunization coverage of individuals is calculated through hospital birth immunization data and immunization data corresponding with vaccine administration in physician offices, and schools throughout Cuba [12].

Vaccine Administration

WHO provides documentation on how to conduct immunization sessions in fixed facilities, outreach sites and people's homes [17]. The easiest site to have qualified personnel safely administer properly stored hepatitis vaccines is a health clinic or hospital setting [18]. Since 99.8% of all births in Cuba are institutional deliveries [19], it can be assumed that almost all of Cuba's infants are being appropriately vaccinated at birth with their first dose of hepatitis B vaccine.

As for subsequent doses, Cuba's public health system provides immunization services in a number of settings. There are 440 polyclinics in Cuba that administer vaccines to 100% of the population [19]. There are 30 000 family doctors and 2 450 pediatricians who also administer vaccines to infants. Furthermore, there are a large number of childcare facilities with doctors and nurses on staff [19]. Overall, access to immunization services in Cuba is exceptional. Also important to note is that all childhood vaccines are administered free of charge [19].

All of the documentation on the hepatitis B immunization program in Cuba suggests that either a trained doctor or a nurse is administering the hepatitis B vaccine [19]. This is an ideal situation as it can be assumed that these individuals are highly trained in techniques for proper vaccine administration. Hepatitis B vaccine should be given intramuscularly in the anterolateral aspect of the infant's thigh [3]. Cuba administers the hepatitis B vaccine in the preferred region for infants [12].

WHO has issued a number of documents on immunization safety. Also, one of the selected immunization system performance indicators is monitoring adverse events related to vaccine administration [14]. WHO recommends that countries use the type of injection equipment that is most suitable to their individual needs, however WHO's first choice for injection equipment is auto-disposable devices [3]. Cuba uses non auto-disposable syringes and sterilizable syringes [14]. This type of injection equipment corresponds to WHO standards because Cuba administers almost all of its hepatitis B vaccines in fixed-site clinics [18]. Cuba reported to WHO that it does not have a policy for distributing sharp boxes for disposal purposes [14]. This is problematic, as the non auto-disposable syringes are most safety stored in the sharp boxes. Cuba's practices are contradictory to WHO policy in this area [20].

In 1990, Cuba established a medical surveillance system that tracks the number of adverse reactions to vaccines [10]. The literature indicates that Cuba had three adverse events related to immunization administration in 2001 [14]. It is difficult to compare this number to other countries since a majority of the other countries did not report data on the number of adverse events. A few of the countries which did report, Bolivia, Honduras and Mexico, experienced seven, three and three adverse events respectively [14]. The severity of these adverse events is unknown, although severe adverse events associated with the administration of hepatitis B vaccine are extremely rare [21].

The shortage of vaccine supply can adversely affect the outcomes of a hepatitis B immunization program [22]. The WHO document on the introduction of hepatitis B vaccine into childhood immunization services notes that countries that are using a combination vaccine of DTP-Hep B may experience a shortage of the vaccine [3]. Cuba, however, uses the monovalent vaccine for administration. Also, the Centre for Genetic Engineering and Biotechnology in Havana, Cuba, produces the hepatitis B vaccine for domestic use, as well as for export [11]. It is therefore unlikely that Cuba's immunization program would experience a shortage of hepatitis B vaccine.

Hepatitis B vaccine wastage is more problematic for countries that do not produce the vaccine locally, but it is still an important indicator of the efficiency of a program's operations. WHO supports the use of a multi-vial, or open-vial policy, which allows opened multi-dose vials of hepatitis B vaccine to be reused in future immunization sessions for up to one month in a fixed health facility [3]. Cuba has adopted this policy [10].

Related to the problem of vaccine wastage is vaccine spoilage due to unsatisfactory storage conditions. Hepatitis B vaccine can be stored for up to four years at a storage temperature between 2-8 degrees Celsius [3]. If it is frozen, hepatitis B vaccine is rendered ineffective and can negatively affect the hepatitis B immunization coverage rate in a population. It is easiest to maintain an appropriate environment for the storage of hepatitis B vaccine when immunizations take place in fixed locations [22]. Vaccine spoilage is likely not an issue with Cuba's hepatitis B immunization program.

Vaccine vial monitors are important tools to determine whether a vial of vaccine has been exposed to excessive heat over time and therefore rendered impotent [23]. Originally tested for use with oral polio vaccine, vaccine vial monitors are now available for all vaccines. Since their increased availability, WHO has encouraged countries to use vaccine vial monitors to improve immunization services [23]. Vaccine vial monitors provide valuable programmatic information about weak links in the cold chain. They also allow the user to see if a vaccine can still be used despite a possible breach in the cold chain [24]. Vaccine vial monitors are most important for countries that are conducting immunization sessions far from fixed health sites. They also help immunization programs monitor logistical issues such as the functionality of the cold chain. Vaccine vial monitors are currently used in Cuba. The hepatitis B vaccine uses a cold chain control card that has a time temperature indicator [12].

Training

It is crucial to offer proper training regarding hepatitis B immunization, as well as its integration into a country's immunization schedule [3]. In 1998, Cuba created the Technical Advisory Group for Immunization Practices to devote resources to immunization

17. World Health Organization Department of Vaccines and Biologicals. The Expanded Programme on Immunization Module 5: Organizing Immunization Sessions. Geneva: The World Health Organization, 1998.

18. World Health Organization and UNICEF. The Expanded Programme on Immunization Safe Injection Practices Update. Geneva: The World Health Organization EPI, 1995.

19. Dieppa FD. Pediatric Care and Selected Child Health Indicators in Cuba. Cuban Medical Research 1999. http://www.medicc.org/Medicc%20Review/1999summer/html/pediatric.html. 27/01/02.

20. World Health Organization Department of Vaccines and Biologicals. Safety of Injections in Immunization Programs: The World Health Organization Recommended Policy. Geneva: October 1998.

21. World Health Organization Department of Vaccines and Biologicals. Information Bank: Adverse Events Associated with Hepatitis B. http://www.who.int/vaccines-diseases/safety/infobank/hbv.shtml 10/03/02.

22. Wilson, Nicholas, Tilman Ruff, Bardan Jung Rana, Jennie Leydon, Stephen Locarnini. The effectiveness of the infant hepatitis B immunization program in Fiji, Kiribati, Tonga and Vanuatu. Vaccine 2000;18:3059-66.

23. World Health Organization Department of Vaccines and Biologicals. Quality of the Cold Chain: World Health Organization-UNICEF Policy Statement on the use of Vaccine Vial Monitors in Immunization Services. Geneva.p.1-4.

24. World Health Organization Department of Vaccines and Biologicals. Making use of Vaccine Vial Monitors. Geneva: The World Health Organization, 2000.p. 1-19.

training and safety. Cuba has also offered over 50 post-graduate courses in immunization in the past twenty years [10]. It is unclear what specific training is provided related to hepatitis B vaccine administration. However, since Cuba has achieved the elimination of polio, measles, rubella and mumps, one can speculate that the overall training program of the Cuban national immunization program is sound [10].

National support for the Hepatitis B immunization program

Through a compilation of the literature required to develop this evaluative framework, it is obvious that immunization programs in Cuba are a high priority, and are operated with pride [10]. The head of Cuba's national immunization program received the Pan-American Health Organization's Immunization award in late 1999 [25]. Moreover, several individuals nominated Cuba's national immunization program for the Gates Award for Global Health in February 2001 [26].

Furthermore, the Pan-American Health Organization document outlining the evaluation methodology for the Expanded Programme on Immunization states that the immunization program should garner political priority [9]. It is apparent through their past success with the elimination of polio, measles, rubella and the mumps that Cuba's national immunization program receives an appropriate support from the go-vernment in terms of funding and other resources [10]. Cuba devotes seven percent of its GNP to public health programs. This is a relatively large amount, especially when compared to other Latin American countries [26].

Another important indicator for national support of an immunization program is the location of the immunization program within the national government, and the length of time the program has been running [9]. Cuba's hepatitis B immunization program is part of the national immunization program, under the sponsorship of the Ministry of Public Health [10]. The hepatitis B vaccine has been integrated into Cuba's national immunization program for 10 years, and the Cuban government finances 96.8% of the cost of vaccines for the population [14]. The other 3.2% of the cost of the vaccines is financed by international donor agencies.

Cuba has also welcomed evaluations of its immunization programs in the past [14]. PAHO concludes that past immunization evaluations indicate strong national commitment to improving immunization program performance [9]. This commitment is demonstrated by the community's understanding of the importance of vaccine administration, and its strong participation in immunization programs in Cuba [12].

In order to get an overall and summative sense of the success of Cuba's hepatitis B immunization program, we will examine Cuba's adherence to the 2001 WHO indicators for immunization system performance. These indicators cover a large range of immunization standards, from safety issues to actual financing of the vaccines. Cuba's national immunization system has adhered to most of WHO system indicators [14]. The key indicators Cuba complies with are: the presence of an injection safety plan, a plan for the introduction of new vaccines, a recent immunization system assessment, reporting of immunization results to national offices and the presence of an immunization safety monitoring system [14]. As mentioned earlier, the one area of immunization practice where Cuba is weak is the issuing of safety boxes for sharp disposals [14].

Process evaluation summary

The process evaluation of Cuba's hepatitis B immunization program demonstrates that Cuba's program meets or exceeds WHO recommendations in most areas. There is a strong national commitment to the program, which is grounded in a successful public health system.

Cuba uses a high quality hepatitis B vaccine of an appropriate dose, and adheres to a clinically proven administration schedule [7]. The hepatitis B immunization program is accessible to infants and children. Lastly, the logistical components of the program: the storage, transport, management and safe administration of the vaccine, are all in accordance with WHO standards. The only program area where Cuba is not in accordance with WHO practice is the use of sharp disposal boxes [14].

The efficacy of the hepatitis B vaccine coupled with Cuba's strong program implementation should result in a very high immunization coverage rate, and a low rate of chronic carriage in the Cuban population, especially in the cohorts of infants born after 1992. Cuban administrative data, provided to WHO in 2000, reported a hepatitis B immunization coverage rate of 99.3% [14]. Cuba's daily newspaper, the Granma, published an article in early January 2002 stating that 100% of all Cuban children (under the age of 21) had been immunized against hepatitis B. These are powerful statements in support of Cuba's fight against hepatitis B and its devastating effects on individuals who are chronic carriers.

Limitations of evaluation

It is recognized that an ideal evaluation involves on-site visits to the immunization program site, as well as consultation with stakeholders who are part of the immunization program. The author has formulated an idea of the operation of Cuba's hepatitis B program mainly through an examination of the available literature. Personal communication with Cuban health officials has also contributed to the author's understanding of the hepatitis B immunization program processes. There is likely some bias present in the information provided by the Cuban health ministry: its documents and various articles are unlikely to be completely objective.

Information regarding vaccine wastage was not forthcoming for this evaluation. Detailed information regarding the management of the hepatitis B immunization program was also unavailable. The author recognizes the importance of this information, but was unable to fully comment on it in the process evaluation due to a lack of reliable information.

*D*iscussion

To fully evaluate a program such as a hepatitis B immunization program, one must look at the program processes, and also gather some fieldwork data to support or refute the administrative data presented by the country in question. WHO and PAHO recom-

25. Radio Havana address. Cuban Health Minister will take part in 41st Council of the Pan American Health Organization. 09/23/99;Havana,Cuba. http://www.radiohc.org/Distributions/Radio_Ha.../Radio_Havana_Cuba,_September_23,_1999. 22/02/02.

26. Gates Award for Global Health. Pugwash Workshop in Cuba http://www.pugwash.org/reports/ees/ees8c.htm. 01/10/02.

mend that evaluations of immunization programs consist of both qualitative and quantitative data, as well as include onsite visits to the respective country [9].

In this case, Cuba has presented administrative data that reflects very highly on the success of their hepatitis B immunization program. After an overview of the key elements of Cuba's hepatitis B program in comparison with WHO standards, the immunization program appears to run effectively. However, to fully evaluate the success of Cuba's hepatitis B immunization program, a fieldwork study must accompany this process evaluation.

The British Columbia Centre for Disease Control and The University of British Columbia, in partnership with WHO and others, have developed a hepatitis B coverage and infection marker survey for use in developing countries [27]. This survey outlines how fieldwork testing for hepatitis B chronic carriage should be initiated using timely and low-cost methods. The field marker survey is intended for use after a process evaluation of a country's hepatitis B immunization program has been completed. The infection marker survey provides a way to evaluate the impact of the program, and compare the rates of hepatitis B that are found during field-testing to the theoretical coverage determined by a crude measure of vaccine efficacy, vaccine coverage and program effectiveness. The results from the infection marker survey will provide quantitative data on the number of chronic carriers in chosen cohorts, and will supplement the administrative data provided by the countries themselves.

For reasons of comparison, this paper presents data on the expected number of chronic carriers in selected cohorts. The infection marker data collected through field-testing will be compared to the expected rates calculated here. Results expressing the percentage of chronic carriers in nine year old children, twelve-year-old children and mothers of these two groups, are presented below.

Since the hepatitis B infant immunization program began in 1992, Cuban children nine years old and younger have received the infant doses of hepatitis B vaccine. In order to determine the effectiveness of immunization at birth one is interested in the rate of chronic carriage in this cohort. The number of children nine years old, the percentage of institutional births per year, the coverage rate of Cuba's hepatitis B program and the failure rate of the vaccine were used to calculate a base rate of expected chronic carriers in the Cuban population nine years of age. The infant mortality rate of this cohort was not accounted for. The expected number of nine year old children who are chronic carriers is approximately 17 (0.010%). This percentage assumes the percentage of institutional births per year to be 99.8% [10], and an immunization coverage rate of 98% [14]. It also assumes a vaccine failure rate of 3% in infants born to HBsAg and HBeAg negative mothers [4], and 30% in infants born to both HBsAg and HBeAg positive mothers and/or HBsAg positive and HBeAg negative mothers [21]. This percentage also assumes that two percent of the population of women aged twenty-one to forty-nine are HBsAg and HBeAg positive and/or HBsAg positive and HBeAg negative, and that infected, non-immunized infants have a 90% chance of chronic carriage while immunized infants have a 0.7% chance of chronic carriage [3]. The HBsAg and HBeAg positive rate of 2% was used as a high estimate of the chronic carriage rate. The use of this percentage facilitates straightforward calculations, but likely overestimates the carrier rates expected in the Cuban population. The actual chronic carriage rates determined by fieldwork testing would likely be lower than those calculated here. The following graph in Figure 1 represents the incidence of acute hepatitis B in children under 15 years old as presented by the Cuban Health Ministry [12]. Although this graph represents acute cases of HBV and not chronic cases, it still provides evidence that one would expect very low rates of HBsAg and HBeAg markers in this population (Figure 1).

A second group of interest is Cuban children born in 1990. These children would have received three doses of hepatitis B due to catch up immunization. They would not have received the birth dose and two subsequent doses of hepatitis B vaccine before one year of age [10]. This cohort did not receive immunizations until they were seven years old [12]. The data from this cohort is important. It will provide an indicator to the degree of transmission from mother to infant in Cuba, as chronic carriers in this cohort may have been infected at birth. The data from this cohort can also be compared to the chronic carriage rate in the nine-year-old cohort. This comparison would provide some insight into the degree of HBV transmission during childhood [27].

The expected rate of chronic carriage in the twelve-year-old population is 1.97%. The calculation uses the birth rate and population to make an approximation of 141 437 births in 1990 [15]. This number does not take infant mortality into consideration. Two-percent of all infants are assumed to be born to high-risk mothers, who are HBsAg and HBeAg positive. These infants have a 90% risk of becoming chronic carriers [3]. Those high-risk infants not infected at birth have a 30% chance of being infected during childhood [28]. Children at a low risk for HBV infection (children born to HBsAg and HBeAg negative mothers) have a 11.1% risk of contracting HBV during childhood if they are not immunized [29]. These low risk children have a 1% risk of becoming chronic carriers if they are infected with HBV during childhood [30].

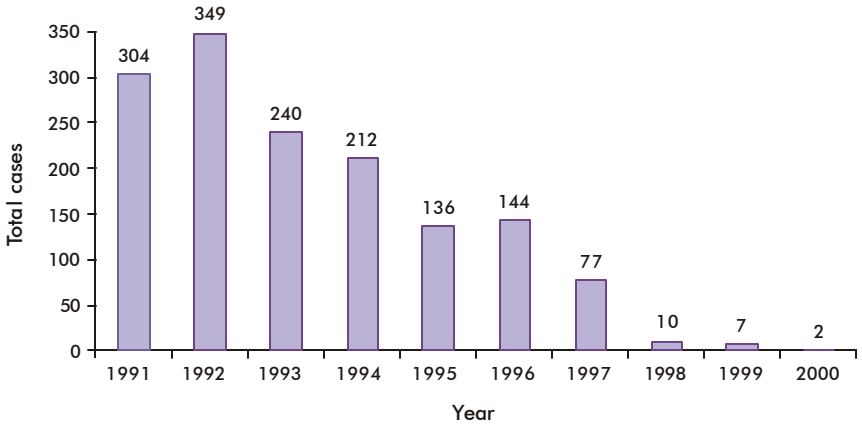

Figure 1. Incidence of Acute Hepatitis B in children under 15 years old

27. British Columbia Centre for Disease Control and the University of British Columbia. The Hepatitis B Coverage and Infection Marker Survey for the Expanded Programme on Immunization (unpublished document).

28. Margolis HS, *et al*. Prevention of Hepatitis B Virus Transmission by Immunization. Journal of American Medical Association 1995; 274(15);1201-8.

29. Bonanni P. Universal hepatitis B immunization: infant, and infant plus adolescent immunization. Vaccine 1998; 16;17-22.

30. Mahoney FJ. Update on Diagnosis, Management, and Prevention of Hepatitis B Virus Infection. Clinical Microbiology Reviews 1999;12(2):351-66.

Cuba has stated that the morbidity rate of hepatitis B has decreased by 97% in children under fifteen years old. One would therefore expect to find a chronic carriage rate of approximately .06% for children under 15. This calculation was determined by calculating a 97% decrease in the 1.97% expected chronic carriage rate for1990-born children. This crude calculation may be a low estimate. However, by sampling these children to determine the percentage of chronic carriers in this cohort, it is possible to compare the data collected with Cuba's reported data for children under fifteen. It is important to note that since the rate of chronic carriage is low in this cohort the sample size required to determine the aforementioned rates will be relatively large. A preliminary calculation of the sample size required to show a prevalence rate of hepatitis B was undertaken using web-based statistical software [31]. With a confidence interval of 95%, and a margin of error of 0.4%, the required sample size was approximately 4489 individuals. It may not be feasible to sample this number of children.

One last group of individuals who will provide information to evaluate Cuba's hepatitis B immunization program, from a fieldwork perspective, are women of childbearing age. To fully appreciate the transmission rate between women and their children, the infection marker survey advocates that biological mothers of the surveyed infant or child are tested [27].

Since Cuba has expanded its hepatitis B immunization program to include all individuals born after 1980, one should look closely at women ages twenty-one to forty-nine. These women would inform evaluators of the rate of chronic carriage in women who are in their prime childbearing years. This information is obviously important, as the hepatitis B immunization program's goal is to reduce the number of chronic carriers in a population; it is widely accepted that infected infants carry the highest risk of chronic infection [3]. One can assume that the chronic carriage rate for women ages twenty-one to forty-nine is 2% [3]. Also, the number of women between the ages of twenty-one and forty-nine has been estimated by the author to be approximately 2 591 908 [32, 33]. The result is that approximately 51 838 women in their childbearing years are chronic carriers of HBV.

This data allows the calculation of a counterfactual comparison [34]. A counterfactual comparison, related to a hepatitis B immunization program, will demonstrate the effect of the immunization program. A counterfactual comparison provides data for a calculation of the expected chronic carriage rate among the cohort of nine-year-old children, who received the vaccine before one year of age, if the program had not been in place. The importance of this calculation is related to determining the actual effect of the hepatitis B immunization program. It is expected that the chronic carriage rate among this cohort will be substantially lower with the hepatitis B immunization program in place when compared to the chronic carriage rate if the program were not available.

The counterfactual comparison was determined only for 1993, and describes the expected rate of chronic carriage if there was no hepatitis B immunization program in place. The 1993 data related to the number of births was used, as was the chronic carrier rate of 2%. High-risk infants have a 90% chance of chronic infection in infancy [3], and a 30% risk of chronic infection during childhood [28]. Through a review of the available literature, 11.1% was estimated to reflect the risk of HBV infection for children of HBsAg and HBeAg negative mothers and 1% of these children would become chronic carriers [29].

The counterfactual comparison suggests that if the program had not been in place, 1.97% of the nine-year-old cohort would be chronic carriers. This is a crude calculation, but it does allow comparison to provide feedback as to the degree of success of the hepatitis B immunization program.

The infection marker survey uses the cluster sampling technique, advocated by WHO [35]. Twenty clusters of each of the three groups should undergo field-testing in Cuba. For the nine-year-old cohort, twenty infants should be tested in each cluster. For the twelve-year-olds, thirty individuals should be tested in each cluster, and 10 mothers should be tested in each of the twenty clusters [27].

Logistical considerations for the application of this infection marker survey are significant, as the survey's strengths are its ability to expediently provide data at a relatively low cost. Items that need to be considered are: what age groups should be sampled, how many health personnel are needed to conduct the field-testing, what amount of time is reasonable for the field-testing to take place, what data is to be collected and how, and where are the possible sites for the sampling to take place.

A discussion of the most appropriate groups to sample in order to evaluate Cuba's hepatitis B immunization program has been presented above. The cohorts to be tested were chosen for several reasons. The different cohorts will provide data on several aspects of the success of the immunization program at protecting individuals from hepatitis B. The data will also provide insight into the degree of vertical and horizontal transmission. It is also important to try to survey cohorts that are relatively close in age. Furthermore, the chosen cohorts are more accessible for field testing purposes because they are likely to be in school. The field marker survey team will have easier access to larger sample populations when testing at schools. It is also more acceptable to take blood samples from children than from infants.

As for personnel requirements, approximately six individuals will be required for field-testing; two individuals per age group. Since there are twenty clusters, and a pair can complete approximately one cluster per day, the field-testing should be complete in about four weeks as it will be difficult to sample school children and their families on weekends [27]. Approximately seven to ten days should be allocated for time to organize and prepare for the survey. This time will allow for field team meetings, and the identification and scheduling of clusters to sample. At least two weeks should be allowed for the analysis of the field-work data collected by the survey.

One person on the two-person team should be responsible for taking the blood sample with the point of care kit, while one person should conduct all of the personal history sessions and required data recording.

31. StatPac Statistics Calculator Free 30 day trial software http://www.statpac.com/statistical-analysis-software/statistics-calculator.htm 03/14/02.

32. CIA-The World Factbook-Cuba website http://www.odci.gov/cia/publications/factbook/geos/cu.html 02/10/02.

33. Population Reference Bureau Data Finder website http://www.data.worldpop.org/prjprbdata/wcprbdata.asp?DQ=DR&SL= 02/10/02

34. Capacity Development Network. Performance Planning workshop Conference Binder. Victoria, BC. April 9th & 10th, 2001.

35. Hoshaw-Woodard, Stacy. Description and comparison of the methods of cluster sampling and lot quality assurance sampling to assess immunization coverage. Geneva: The World Health Organization, 2001.

Any available administrative data regarding the immune status of an individual will be recorded. This information will give evaluators an on-site idea of the degree of immunization coverage that will be compared to the administrative immunization coverage data that Cuba has reported to WHO.

There should also be a program manager on site with the fieldwork teams. Ideally, this individual would have experience working in Cuba, and would have developed some contacts in the area to help coordinate the infection marker survey.

In Cuba, there should be a reliance on data gained from blood sampling with point of care kits. These kits provide fast and accurate information on the presence of HBsAg in an individual's blood without the issues associated with venipuncture sampling [27, 36]. With a wastage rate of ten percent, 1100 point of care kits will be required to conduct the field-testing [27]. For the purposes of this evaluation, collecting only the HBsAg marker as an indicator of chronic carriage is sufficient information to provide the evaluators with a sense of the program's success. This paper has provided some data on the expected rates of chronic carriage in the population to which the fieldwork data can be compared.

A possible starting point for the infection marker survey is the southern part of Cuba. The reason for this is that there are more districts in this area with lower hepatitis B immunization coverage [10]. It may therefore be possible to better determine reasons for the low coverage through onsite investigation and field-testing in these areas. Also, the actual immunization coverage rates in this area may be higher or lower than those reported to WHO. Another reason to begin in this area is that the lower level of immunization coverage may result in a higher transmission rate of hepatitis B in these areas; a problem that would have to be addressed.

After the compilation of the infection marker survey data is complete, the evaluators should have a good idea of the rate of chronic carriage in selected cohorts of Cuba's population, as well as an idea of the hepatitis B immunization coverage in these cohorts. This data is a crucial component of an effective evaluation. It provides results that can be compared to Cuba's reported administrative data. This comparison, in addition to the hepatitis B immunization program process evaluation, enables an impact analysis of Cuba's hepatitis B immunization program [37]. Furthermore, since a process evaluation was conducted in conjunction with the infection marker survey, questions surrounding the reasons for possible inconsistencies in the comparison of data can be investigated. Problematic program elements that were identified in the process evaluation can be re-examined. For example, if there were discrepancies in the fieldwork chronic carriage data collected in Cuba, one could look further at improving safety in Cuba's hepatitis B immunization program as a possible way to improve immunization coverage, and ultimately lower chronic carriage rates.

The infection marker survey is a way to gather quantitative data that is less expensive than other hepatitis B immunization evaluations presented in the literature [6, 22, 38]. There are some limitations to the infection marker method. Most of the limitations are concerned with the collection of only one seromarker, which can only provide data on chronic carriage and not on vaccine mediated immune status [39]. However, the field marker survey method is effective when it is combined with a process evaluation of a country's hepatitis B immunization program. A process evaluation of the hepatitis B immunization program provides sufficient insight into the expected rates of immunization coverage depending on how successfully the program is operating. Therefore, the bases of the quantitative analysis are the rates of chronic carriage in a population, with some attention being paid to immunization coverage through the conduction of personal histories and immunization card checks.

Conclusion

The need for the evaluation of health programs is apparent in this era of growing government accountability and fiscal restraint. The funding bodies of international health programs want an evaluation framework to judge the success of respective programs. The evaluation framework must contain two components: one qualitative and one quantitative. Each component provides the input necessary to make a judgement about a program's success.

In this paper, Cuba's hepatitis B immunization program was qualitatively evaluated for its program processes. The next step is to conduct a quantitative evaluation using a format similar to the infection marker survey. Combining these two evaluative elements will provide hard and strong evidence as to the effectiveness of Cuba's hepatitis B immunization program at preventing chronic hepatitis B infections.

Received in november, 2004. Accepted for publication in march, 2005.

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