Cost-Benefit Analysis of a Neonatal Screening Program for Congenital Hypothyroidism in Metro Manila

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ABSTRACT

Background**.** Neonatal mass screening has led to the early diagnosis and management of congenital endocrine and metabolic diseases. The effectiveness and efficiency of neonatal screening had been well established for congenital hypothyroidism (CH) in other settings.

Objectives. 1) To determine the incidence of CH; and 2) To determine whether a newborn screening program (NSP) for CH is cost-beneficial from a societal perspective.

Design: Screening survey with cost-benefit analysis.

Subjects and Methods. Newborns from the original 24 hospitals in Metro Manila that started newborn screening were screened for CH after the 48th hour of life. Confirmatory tests were performed for those who screened positive. Using the incidence from the survey, the costs for the detection and treatment of CH were compared to the projected benefits of preventing the mental retardation and consequent productivity losses. Sensitivity analyses for incidence rates, discount rates and timing of blood collection were included.

Results. A total of 28,088 newborns (40% of 69,391 live births) were screened. Ninety-two were recalled for confirmatory testing after the initial screen; 8 were diagnosed with CH. Assuming that a cohort of 200,000 newborns would be screened in one year, the net costs for the screening program were US$ 2.4M. If the timing of blood collection was after the 24th hour, there was instead a net benefit of US$ 0.6M. The incidence of CH among the hospital admissions in Metro Manila was 0.037% (95% CI 0.009 - 0.064%).

Conclusions. The net cost of a screening program for CH taken after 48 hours was US$ 2.4M. Newborn screening for CH was cost-beneficial if blood collection occurred after the 24th hour so that expense of an additional hospital day was not incurred. In order to realize the costing benefits illustrated by this study, the timing of sample collection was moved to a day earlier (after 24 hours of age) beginning in 2000.

Key Words: cost analysis, newborn screening, congenital hypothyroidism

Introduction

Neonatal mass screening has led to the early diagnosis and management of congenital endocrine and metabolic diseases. Early identification of these conditions is crucial, since timely intervention can lead to significant reductions of morbidity, mortality, and associated disabilities in affected infants.[1] Newborn screening started with the pioneering work of Guthrie in the early 1960s. He developed a process to screen for phenylketonuria (PKU) on dried blood spots collected on filter paper and transported to a distant laboratory.[2,3] Today, this technique for obtaining and analyzing specimens from newborns is used to detect dozens of congenital conditions, including metabolic and infectious diseases, in screening programs around the world.[4] The effectiveness and efficiency of neonatal screening had been well established for congenital hypothyroidism (CH) and PKU in other settings.[5-7] The efficiency/effectiveness of neonatal screening for other diseases depends primarily on the incidence of the disease and the screening/health infrastructure in the local environment.

Newborn screening was introduced in the Philippines in 1996 by the Newborn Screening Study Group (Appendix 1).[5] The study group was established to determine the incidence of common metabolic disorders and subsequently, to make recommendations to policymakers for national neonatal screening. The initial panel of disorders included CH, congenital adrenal hyperplasia (CAH), PKU, galactosemia (GAL), and homocystinuria (HCY). There were no cases of HCY in the first 4 years of the newborn screening program, whereas pilot screening studies for glucose-6-phosphate dehydrogenase (G6PD) deficiency showed very high incidence among screened neonates. In 2000, screening for HCY was replaced with screening for G6PD deficiency.

CH is one of the more frequent conditions detected by newborn screening globally. The most common cause is some form of thyroid dysgenesis: aplasia, hypoplasia, or an ectopic gland; thyroid ectopy accounts for two thirds of thyroid dysgenesis. The cause of thyroid dysgenesis is unknown. Rare cases result from mutations in the genes that control thyroid gland development, including thyroid transcription factor (TTF-2) and paired box-8 protein (PAX-8). For children with CH, early diagnosis and treatment can prevent mental retardation and produce children with normal intellect.[10]

The objectives of this study were: 1) to determine the incidence of CH; and 2) to determine whether a newborn screening program (NSP) for CH is cost-beneficial from a societal perspective.

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Methods

Study Design and Setting. The study was divided into two phases: 1) the newborn screening phase, which determined the incidence rate of CH in the original 24 hospitals in Metro Manila; and 2) the cost-benefit analysis phase, which determined the financial efficiency of the screening program using the incidence rates from Phase 1.

Data Collection. From June 1996 to June 1997, the 24 screening study hospitals offered newborn screening. Informed consent was obtained prior to specimen collection. Two newborn screening panels were available to patients. A fee of US$ 6.45 was charged for the two-panel test (CH and CAH) and US$ 11.45 was charged for the full panel of 5 conditions. Blood specimens were collected by heel pricks after the 48^{h} hour of life to decrease the false positives resulting from a lack of screening test sensitivity on samples collected earlier. Three drops of blood were collected in target circles on special blood collection filter paper (Schleicher and Scheull 903C, Keene, NH, USA). A commercial thyrotropin (TSH) newborn screening assay (Delfia, Wallac Oy, Turku, Finland) was used. Specimens with TSH concentrations >20 mIU/L (whole blood units) were considered to suggest CH, and additional follow-up testing was pursued. Samples were rejected for analysis if certain unsatisfactory criteria were met: contamination, insufficiency, layering, or early collection (before 48 hours of life) and a repeat screen was requested.

Other Ethical Considerations. Normal results were sent to the hospital without further action. Abnormal results were relayed immediately after analysis with a request for rapid patient recall for confirmatory testing and clinical evaluation. Each baby confirmed with CH was referred to a specialist for appropriate disease management. Treatment monitoring included direct patient contact via questionnaires and an annual home visit by nurses and/or physicians from the Secretariat's office. Compliance with medications and dietary modifications were included in the review along with developmental assessment.

Methods of Data Analysis. The incidence of CH was estimated with 95% confidence using the hospital as a stratification variable. A cost-benefit analysis of the screening program to detect CH was performed. The model used in the economic evaluation was to compare the CH newborn screening program in Metro Manila to a do-nothing alternative, the local standard practice. A societal point of view was utilized for the estimation of costs and benefits. Costs and benefits were estimated and projected using a hypothetical, baseline population of 200,000 newborns screened in one year.[11] The incidence of CH was based on results from the newborn screening phase. The recall rate was the proportion of newborns recalled because of a screened test result outside of the normal range compared to the total newborns screened.

Children with CH identified by screening and follow-up confirmatory tests were assumed to be treated with hormonal replacement and regular monitoring of thyroid function. The monitoring schedule included monthly monitoring for the first year, quarterly monitoring for the second and third years, and monitoring three times a year thereafter until age of 65, the average life span of a Filipino.[11] In the do-nothing alternative, CH was assumed to be diagnosed at 6 years of age. At this age without treatment, the severity of mental retardation was estimated to be moderate to severe.[10] We assumed that 80% of late diagnosed cases would have special education classes until age 12 years based on local experiences. Partial supportive care from a caretaker was assumed to be required in late diagnosed cases until the age of 65. For the 20% of late diagnosed cases not receiving special education, full chronic care was assumed for the life span (personal communications with Dr. Lorna Abad, Philippine Pediatric Endocrinology Society, 1997).

All costs were expressed in Philippine pesos (1997 value) and converted to US dollars using an average 1997exchange rate of US$ 1: PhP 28.50.

Direct costs for screening and confirmation of cases were based on data from the first phase study. Costs for screening proper included: costs of blood collection and laboratory testing, costs for 2 days (an extra day over the usual stay) in the hospital, and a cost for productivity loss of the person caring for the mother at the hospital.

The cost of laboratory equipment was based on the purchase price discounted at 7% for 10 years, which was the expected life span of the machine. Other laboratory costs were estimated for labor, reagents and other testing materials.

The cost of a hospital day was based on average charges from the participating hospitals. Mothers who delivered by Caesarean Section were excluded from the cost calculations of the second day since they would normally stay in the hospital for more than 48 hours. This was estimated to be 20% of the total number of deliveries.[11]

Productivity loss was computed as the daily minimum wage adjusted for 15% unemployment.[12]

Calculations included: 1) costs of contacting the child's family once positive screening results were known; 2) costs of confirmatory tests; 3) medical follow-up expenses including transportation and specialty consultation; 4) indirect costs of the productivity loss by the person who accompanied the child; 5) treatment costs, which included short and long-term supportive care, medications and frequent laboratory monitoring; and 6) costs of caring for missed cases. [Note: Despite screening, some cases would be missed because of refusal to undergo further tests or adhere to medical recommendations – assumed to be 0.02% in our study. However, only about 25% of cases that were initially screened positive for CH would actually have a confirmed result that is also applicable to the refusal cases.]

Costs were compared to the benefits of preventing mental retardation resulting from untreated CH. The benefits included avoidance of expenses from lifelong care of disabilities from CH (direct non-medical costs) and avoidance of productivity losses of the affected individual and any associated care givers (indirect costs).

The cost of lifelong care in the Philippine setting was

defined to include institutional care and special education classes in 80% of late diagnosed cases. Special education cost data came from a special education school specifically catering to this type of mental retardation (personal communications with Barbara Dans, Special School directress, 1997). Costs for productivity losses of caregivers were based on the degree of self-care the individual is expected to attain with and without special education classes. With special education, the costs for partial care (approximately half of the productivity loss of an individual giving full chronic care) were considered to be the indirect cost. Similarly, the 15% unemployment rate was subtracted from the actual computation of the productivity loss assuming the minimum wage.

All benefits were discounted at 7% during the follow-up years.

The impact of changes in key variables on the cost-benefit ratios and the robustness of conclusions were determined by sensitivity analysis. Incidence rates were varied using the upper and lower limits of the 95% confidence interval of the point estimate. Discount rates were varied between 3-12%. Since a big part of the direct medical costs was the cost of the extra hospital day attributed to newborn screening, calculations were made to determine the effect of shortening the time requirement for specimen collection to 'after 24 hours of life.' Because of decreased screening sensitivity of the tests used, earlier specimen collection may increase the recall rate.

Results

From June 1996 to June 1997, 28,088 newborns were delivered and screened after 48 hours of life in the 24 participating hospitals. Coverage of the entire newborn population at these hospitals totalled 40.5%. Ninety-two (92) newborns had abnormal screening results requiring recall (0.33%).

Among the 92 recalled for confirmatory tests, 8 were diagnosed with CH. Based on these data, the annual incidence of CH was calculated to be 0.037% (95%CI 0.009 - 0.064%) based on the stratified sampling design weighted for each stratum (hospital).

Table 1. Costs of screening program for CH for a cohort of 200 000 newborns (in million US$)

Costs for Screening Proper		5.1
Processing and Collection (US$ 1.5/newborn screened)	0.3	
Indirect Costs of Father/Caregiver (DAILY minimum wage x no. of expected normal deliveries)	0.9	
Cost of EXTRA DAY of mother/baby (Room rate x no. of expected normal deliveries)	3.9	
Costs for Recall		0.003
Costs for Confirmatory Visits		0.030
Costs for Treatment and Monitoring		0.258
Costs of Missed Cases (n = 2)		0.030
Total Costs of the Screening Program		5.4

Table 2. Costs of 'no screening program' (Benefits Gained) for a cohort of 200 000 newborns*

Full Chronic Care (20%, n=16)	0.5
Special Education and Partial Care (80%, n =62)	0.9
Productivity Loss (n=78)	0.2
Total Benefits of the Screening Program	1.6

* in million US$

Table 3. Sensitivity analyses of timing of blood extraction and recall rates

Timing and Recall Rate	Net Costs*	Cost-benefit Ratio
48th Hour of Life	3.8 M	3.3
24th Hour of Life		
1% Recall Rate	-1.0 (Net Benefits)	0.41
2% Recall Rate	-0.9 (Net Benefits)	0.48
5% Recall Rate	-0.5 (Net Benefits)	0.67

* in million US$

The costs of the screening program for CH are shown in Table 1 for a cohort of 200,000 newborns. The sum of the costs for screening program for CH totalled US$ 5.4 M.

The costs or potential benefits to be gained with do-nothing alternative amounted to US$ 1.6M as shown in Table 2. The

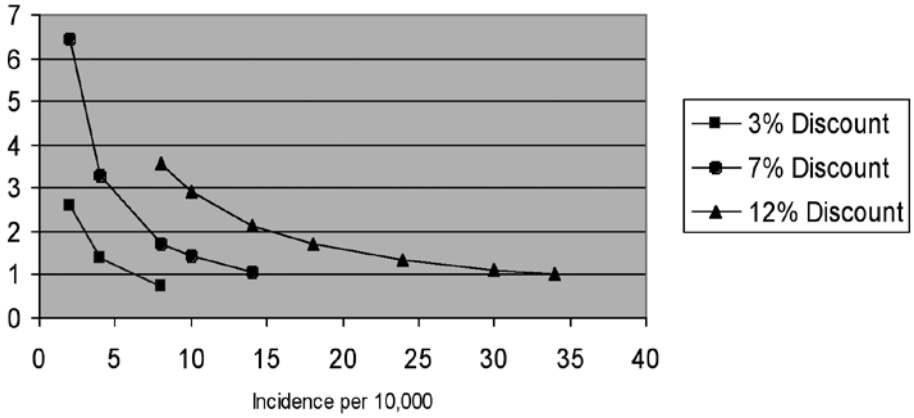

Figure 1.Cost-benefit ratios at varying incidences and discount rates.

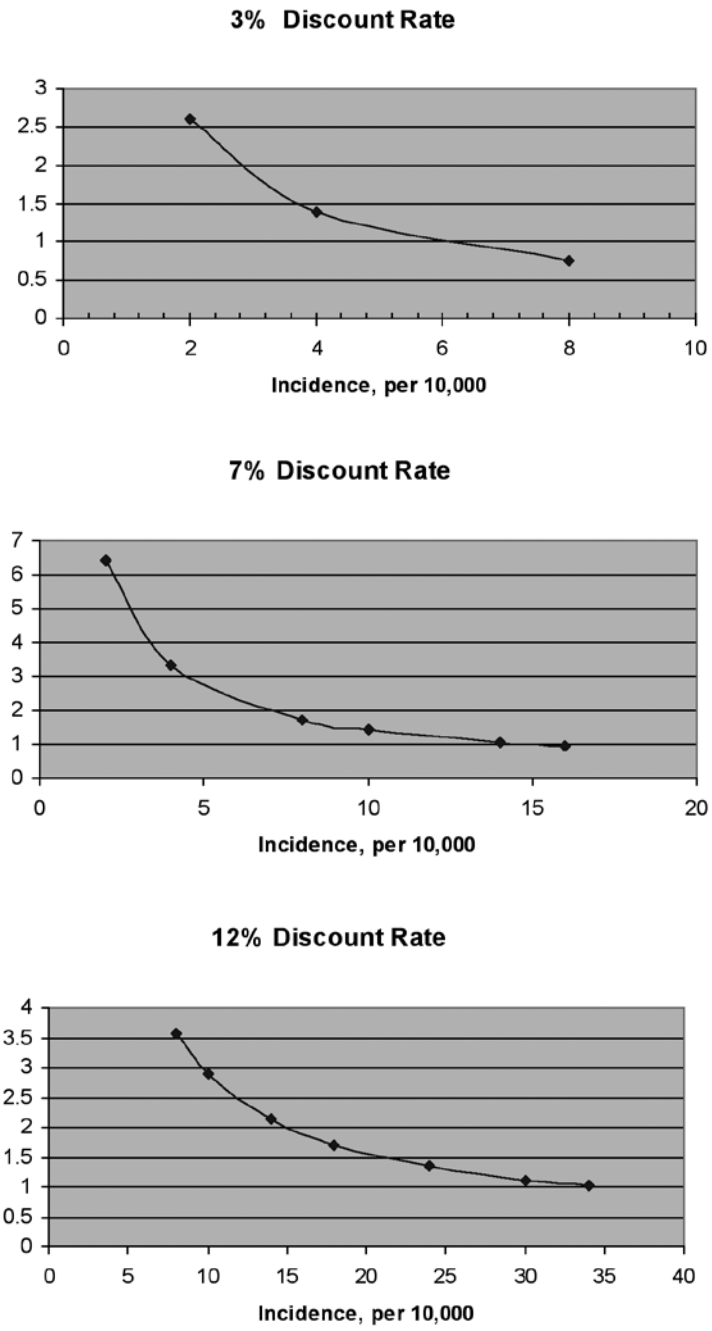

Figure 2. Cost-benefit ratios assuming values of incidence 3%, 7% and 12% discount rate.

direct benefits included avoidance of the costs of treatment and the costs of full chronic care for children not able to have special education classes, and partial care costs for children who had special classes after detection. This amounted to US$ 1.4 M. The indirect benefits referring to the total productivity losses of the cases (who would have been productive if they were treated) totalled US$ 0.2 M.

The net costs of the screening program were US$ 3.8 M (Total costs–Total Benefits: US$ 5.4 M – 1.6 M) using the 7% discount rate. The cost-benefit ratio was 3.3, meaning there were net costs for the screening program.

Figure 1 shows the different cost-benefit ratios at different discount rates with varying incidence of CH rates for each figure. With decreasing incidence rates and higher discount rates, the cost benefit (CB) ratio can go as high as 3.56. Table 3 shows a comparison of net costs when blood collection occurs a day earlier (after 24th hour of life instead of after the 48th hour). Correspondingly, recall rates were increased slightly to adjust for increased recalls as a result of screening test insensitivity at the earlier time. Net benefits ranging from US$ 1.9M - US$ 2.3 M were obtained with earlier blood collection when the recall was varied from 1%-5% (see Table 3).

Discussion

The information from the first phase of the study was crucial for the cost-benefit analysis. The incidence of CH was 0.037% or 1/2700, slightly higher than reports from other countries. In the United States, the CH incidence is 1/3600 – 1/5000 while the incidence in Europe is 1/3000 and 1/ 6300 in Japan.[10,13] Despite the higher CH incidence rate in our study, the total costs of screening still outweighed the total benefits. The main contributor to screening program costs in the reference case analysis resulted from costs incurred for the extra day at the hospital to collect the newborn screening specimen (for normally delivered newborns). This was a deviation from the standard Philippine practice of hospital discharge 24 hours after delivery. Because it is also standard practice in the Philippines to have another person accompany the mother during her entire hospital stay, this results in increased productivity loss for the accompanying person. These cultural practices played a large role in this health economic evaluation compared to those reported in other countries including Japan,[13] the United States,[14] Sweden,[15] and France.[6] This illustrates the importance of cost identification in different settings and their comparison to other countries with similar economic and cultural circumstances.[16]

We anticipated a cost variation related to timing of blood collection and increased recall. Blood extraction after the 48th hour of life was recommended initially as a way to decrease the recall from transient elevations of TSH that occur in the first 24 hours of life.[10] However, the extra costs of longer hospital stays was significantly more than the costs of additional recall as a result of screening test insensitivity. The economic sensitivity analysis in Table 4 reversed the results in the reference case analysis. If blood collections were timed after the first day of life, there were net benefits from screening. The recall rate in our study was only 0.3%, lower than other reported recall rates (0.04% -0.5%).[10] We opted to test the conclusions by assessing higher recall rates (variable increases of 1-5%). There were net benefits for adjusted blood collection time even at the highest 5.0% recall rate.

Identification of accurate costs and benefits was crucial to our health economic evaluation.[5] In our study, we included all items in the various steps of the screening process. The cohort of 200,000 newborns was a convenient figure since

it approximated the annual birth rate in Metropolitan Manila and the maximum number of specimens that one laboratory machine could evaluate and process. As expected, the costs and benefits of the screening programs depended on our local social welfare and family support systems. In the Philippines, families tolerate members with mental retardation. They see no need for consultation. Thus, proper counselling and education were oftentimes neglected resulting to poorer outcomes. Similarly, cost savings realized in other programs by eliminating the need for government-sponsored institutionalization for mentally handicapped are not present in the Philippine setting.

The methods for including productivity losses and for valuing intangible benefits derived from averted disability and, in some societies, averted stigma from mental retardation and physical deformities, are controversial. We used a human capital approach to capture both kinds of benefits. Our use of the minimum wage, adjusted for unemployment, can be argued to be a conservative value for these benefits.

Discounting was also crucial in the evaluation since the costs were spent "now" while the benefits were projected into the future. The sensitivity analysis in Figure 2 shows different discount rates and the effect of incidence rates in the cost-benefit ratios. Net benefits are obtained only at higher incidence rates, even above the upper limit of the interval estimates. We applied a 7% discount rate to our reference case study, which was a higher figure than discount rates in developed countries like the United States. Our rationale was that some developing countries give more importance to the present because of more immediate needs.

Conclusions

The annual incidence of CH among the hospital admissions in Metro Manila was 0.037% (95%CI 0.009 - 0.064%). The incidence rate was relatively high compared to other countries like Japan and the United States. Newborn screening for CH was cost-beneficial when blood collection occurred after the first day of life. The efficiency of adding other metabolic disorders into the screening program should also be considered since screening for CH has already been shown to be economically beneficial, and the specimen collection and transport costs would not be considered as a screening cost. Next step should include recommendations for nationwide CH screening.

Epilogue

The Department of Health adopted the recommendations of this study to reduce recommended specimen collection time to 24 hours of age for increased economic benefit. Starting year 2000, the standard policy for the NSP was a collection time of 24 hours. This paper was used as one of the supporting documents for the enactment of Republic Act No. 9288 or the Newborn Screening Act of 2004.[15] The law provides the mandate to offer every newborn the opportunity to undergo newborn screening. The recommendation for nationwide CH screening has likewise been adopted.

[4]The Newborn Screening Study Group is composed of Capitol Medical Center; Cardinal Santos Medical Center; Children's Medical Center Philippines; Chinese General Hospital; De Los Santos Medical Center; FEU-NRMF; Manila Doctors Hospital; Mary Chiles General Hospital; MCU-FDTMF Hospital; Medical Center Manila; Metropolitan Hospital; Ospital ng Maynila; Our Lady of Lourdes Hospital; Perpetual Help Medical Center; Philippine Children's Medical Center; Philippine General Hospital; Dr. Victor R. Potenciano Medical Center; Quezon City General Hospital; Quirino Memorial Medical Center; Rizal Medical Center; St. Luke's Medical Center; Aurora Meneses, M.D St. Martin de Porres Hospital; UERMMMC-Hospital; United Doctors Medical Hospital.

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