

Cost-Benefit Analysis of the Newborn Screening Program of the Philippines

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ABSTRACT

Background. Newborn Screening (NBS) is a public health activity aimed at the early identification of infants who are affected by certain genetic/metabolic/infectious conditions. A cost analysis is critical for national implementation for integration as a public health program.

Objectives. 1) To determine the incidence rates of congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), galactosemia (GAL), phenylketonuria (PKU) and glucose-6-phosphate dehydrogenase (G6PD) deficiency; and 2) To determine whether NBS is cost-beneficial for each disorder individually or in combination, from a societal perspective.

Study Design. Cross sectional survey and cost-benefit analysis.

Subjects and Methods. The study was conducted through a screening survey of the original 24 Metro Manila hospitals. Newborns were screened for CH, CAH, GAL, PKU and G6PD deficiency after the 24th hour of life. Those who screened positive underwent serum confirmatory testing. Using incidence rates from the screening survey, a population of 1.5 million, and different screening combinations, the costs for the detection and treatment of the five disorders were compared to the benefits projected from preventing the corresponding complications and consequent productivity losses. For economic evaluation, we compared sequential analysis of doing tandem/multiple testing for the different disorders vs a “do-nothing” alternative. Sensitivity analyses for different incidence and discount rates were conducted to test the strength of the conclusions.

Results. The incidences of the disorders with 95% confidence intervals are: CH is 1:3 235 (1:2 219 - 1:5 946); CAH is 1:7 455 (1:4 046 - 1: 14245); GAL is 1: 106 006 (1: 44 218-1:266 796); and G6PD deficiency is 1:167 (1:151 - 1: 186). Screened individually, CH and G6PD deficiency had net benefits of US\$ 5.29 M and US\$ 15.44 M, respectively. The other conditions yielded net costs when screened individually - CAH (US\$ 2.61 M), GAL (US\$ 0.90 M) and PKU (US\$ 6.74 M). Pairing the disorders with CH showed the following benefit:cost ratios - CH + CAH, 1.3; CH + GAL, 2.0; CH + G6PD deficiency, 3.4; and CH + PKU, 0.9. Combining disorders resulted in the following benefit:cost ratios - CH + CAH + GAL, 1.2; CH + CAH + GAL + PKU, 0.8; and CH + CAH + GAL + G6PD deficiency, 2.1. Screening for the 5 disorders in tandem resulted in a benefit:cost ratio of 1.4 and a net benefit of US\$ 11.42 M.

Conclusion: This study demonstrates that the benefits of an NBS program in the Philippines far outweigh the societal costs of a “do-nothing” alternative. The benefit:cost ratio for the 5-disorder program is 1.4 and the net benefit for the 5-disorder screening program is US\$ 11.42 M.

Key Words: cost benefit analysis, newborn screening

Introduction

Newborn Screening (NBS) is a public health activity aimed at the early identification of infants who are affected by certain genetic/metabolic/infectious conditions. Early identification of these conditions is particularly crucial, since timely intervention can lead to a significant reduction of morbidity, mortalities, and associated disabilities in affected infants. Since its inception in the 1960's, at least 20,000 affected patients worldwide are now leading normal lives. NBS in other settings currently includes as many as 50 different conditions, including metabolic and infectious diseases.¹⁻³ NBS has been universally accepted for almost five decades and yet has remained a challenge for the Philippines. It was introduced in the Philippines by the ‘Newborn Screening Study Group (NSSG) in 1996. The recommended panel of disorders consisted of congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), galactosemia (GAL), phenylketonuria (PKU) and glucose-6-phosphate dehydrogenase (G6PD) deficiency.⁴

The economic benefits of newborn screening have been well described.⁵⁻⁸ A Philippine study by Dans et al. reported that a newborn screening program (NBSP) for CH is cost-beneficial when the blood collection occurs after the first day of life. Currently, the NBSP has adapted this recommendation.⁹

Our study aims to evaluate the efficiency of establishing a national NBSP. The specific objectives are: 1) to establish the incidence rate of CH, CAH, GAL, PKU and G6PD deficiency in the Philippine newborn population; 2) to determine whether a Philippine NBSP is cost-beneficial compared to a “do-nothing” alternative from the societal perspective; 3) to determine whether newborn screening is cost-beneficial for each disorder taken individually; 4) to determine if combinations of screened conditions yield benefits greater than costs; and 5) to determine if it is cost-beneficial to include all 5 disorders in a national NBS panel.

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Methods

Study Design and Setting

This study was divided into 2 phases: 1) the NBS phase determined the incidence rates through a screening survey of the 24 Metro Manila hospitals originally included in the pilot study; and 2) the cost-benefit analysis phase. The model used in the economic evaluation was comparison of screening using sequential analysis of doing tandem/multiple testing for the different disorders vs a "do-nothing" alternative. A societal point of view was used for estimating costs and benefits.

Methods of Data Analysis

The incidence rates were estimated at 95% confidence level considering the hospital as a stratification variable. Costs and benefits were projected for 1.5 million annual births. Actual costs of screening were considered, as well as projected benefits from preventing expected complications from undetected and untreated disorders.

NBSP costs included costs of screening proper, recall, confirmatory visits, treatment and monitoring of screened patients. The costs of screening proper included the cost of blood collection, reagents and materials, labor, and laboratory testing. The cost of the equipment used for the screening tests was based on the purchase price prorated over 10 years, the expected life span of the equipment.

Costs of recall included the cost of contacting the child's family once screening results were known to be positive, confirmatory testing and medical follow-up. Recall numbers were actual data from the project update. A 2% refusal rate was assumed based on the actual refusal rate reported for CH screening.⁹

Included in the costs (Year 2000) of recall and confirmatory visits were transportation costs (US\$ 1 per person per visit), professional fee (US\$ 10 per consult), and indirect costs of the productivity loss by the person helping to care for the mother and child at the hospital. Productivity loss was computed based on the daily minimum wage of US\$ 4.47 (Philippine Department of Labor and Employment, 2000), and it was assumed that the person accompanying the patient was a half-wage earner (e.g. housewife) and would lose only a half-day wage.

Costs for treatment and monitoring of confirmed cases were added based on costs taken from the literature and local experience. For every disorder, the cost of lifetime treatment was calculated using a lifespan of 65 years.¹⁰ Monitoring schedules included both clinic follow-up with specialists, and baseline and subsequent laboratory tests for the 65 year lifespan. For CH, the presence of subtle neurocognitive deficits, despite early treatment, was taken into consideration.⁶

¹¹ For CAH, the percentages of the simple virilizing and salt wasting types were considered. Baseline laboratory costs differed between female patients with ambiguous genitalia and males.^{7,8} Patients with G6PD deficiency do not require specific treatment. Rather, they require avoidance of food and environmental elements that can trigger a hemolytic

crisis that can require hospitalization and intensive care.¹² Potential costs that would have been incurred in treatment, management and productivity loss for late diagnosed cases were included.

The study was limited to comparing screening costs with the benefits of preventing complications associated with the disorders. Benefits included the avoided expenses resulting from lifelong disability care (direct non-medical costs) and the avoided losses of productivity of the patient and associated caregivers (indirect costs). The avoided expenses due to early infant death, despite screening, were not included.

In the do-nothing alternative, cost of care and management of the complications of untreated cases were calculated. In the Philippines, CH cases were usually detected by 6 years of age. At this age without treatment, the severity of mental retardation was assumed to be moderate to severe. Only 80% of late diagnosed cases were projected to receive special education until age 12 years. Partial supportive care from a caretaker would be required in such cases until age 65. Full chronic care across the life span would be needed from the remaining 20% of cases not receiving special education (personal communications with Dr. Lorna Abad, Philippine Pediatric Endocrinology Society, 1997).

Worldwide NBS data showed that screening prompted early diagnosis of CAH before clinical suspicion in 67% of newborn infants with CAH, including many females with ambiguous genitalia. Another NBS benefit is improved detection of patients with salt wasting (SW) CAH, 70% with NBS vs 43%–60% in patients with clinical symptoms.¹³ Complications in unscreened GAL patients include developmental delay in 45%, speech problems in 56%, motor problems in 18%, and cataracts in 30%. Complications in undiagnosed G6PD deficiency cases include kernicterus (12.4%) and mental retardation.¹² Again, we assumed that 80% of patients would have severe mental retardation and would receive special education classes until age 12 years. Partial supportive care from a caretaker would be required in such cases until the age of 65.^{7,12,14,15}

The life expectancy for persons with untreated PKU is 39–40 years with a 20–30 years duration of institutionalization due to mental retardation, compared to the normal life expectancy of those screened and treated.⁶ An estimated 80% will receive special education and 20% will require full chronic care. Productivity loss was based on the daily minimum wage. An unemployment rate of 15% was considered. Productivity loss of the patient was computed from age 21 to 65 years. The costs of productivity losses of caregivers were based on the degree of self-care the child may attain. For those unable to have special education or those severely affected by complications, the productivity losses of the caregivers were computed from the time the complication was detected until the patient is 65 years old.

Cost-benefit comparisons first compared the net benefits of the individual disorders, and then by comparing the benefit:cost ratios of different pairs and combinations.

Table 1. Incidence rates for the disorders screened as of December 2000

| Disorder | Crude Incidence | Incidence Weighted By Hospital (95% Confidence Interval) |
|-----------------|-----------------|--|
| CH | 1:4 474 | 1:3 235 (1:2 219 – 1:5 946) |
| CAH | 1:8 949 | 1:7 455 (1:4 046 – 1:14 245) |
| GAL | 1:71 592 | 1:106 006 (1:44 218 – 1:266 796) |
| PKU | 1:47 728 | 1:41 618 (1:16 087 – 1:70 884) |
| G6PD deficiency | 1:71 | 1:167 (1:151 – 1:186) |

Table 2. Component cost of screening per patient

| Component | Costs in US\$ | | | | |
|---|------------------|------------------|-----------------|------------------|-------------------|
| | CH | ^a CAH | GAL | G6PD deficiency | PKU |
| Screening Proper (reagents, supplies, equipment, staff time, filter paper) | 1.60 | 1.80 | 0.70 | 1.20 | 0.60 |
| Recall (mailing/ personnel - US\$2.50; productivity loss of accompanying person – half-day of half-wage earner; transportation - US\$1) | 4.60 | 4.60 | 4.60 | 4.60 | 4.60 |
| Confirmatory Visits (laboratory test; productivity loss of accompanying person; transportation; professional fee - US\$10) | 68.80 | 26.10 | 14.10 | 18.00 | 77.10 |
| Treatment and Monitoring | 2 817.90 | 16 470.30 | 1 173.56 | 111.63 | 341 978.74 |
| TOTAL | 24 521.60 | 16 502.80 | 1 192.96 | 29 252.35 | 342 061.04 |

^aMean cost of treatment for simple virilizing (SV) males, SV females, salt wasting (SW) males and SW females

Table 3. Cost Benefit Analysis of Individual Disorders

| Component | Costs in million US\$ | | | | |
|---|-----------------------|---------------|---------------|-----------------|---------------|
| | CH | CAH | GAL | G6PD deficiency | PKU |
| Total Costs of Screening Program Screening proper, Recall, Confirmatory test, Treatment and monitoring, Missed cases | 3.87 | 6.36 | 1.12 | 5.23 | 13.30 |
| Total Benefits of Screening Program (Costs of a “do-nothing” alternative) Treatment of complications, Productivity loss | 9.16 | 3.75 | 0.21 | 20.67 | 6.56 |
| NET BENEFITS (NET COSTS) | 5.29 | (2.61) | (0.90) | 15.44 | (6.74) |

Table 4. Cost-benefit analysis of CH in combination with other disorders

| Conditions screened | Total Costs* | Total Benefits* | Net Benefits* | Benefit:Cost Ratio |
|----------------------|--------------|-----------------|---------------|--------------------|
| CH + CAH | 9.98 | 12.91 | 2.93 | 1.3 |
| CH + GAL | 4.80 | 9.37 | 4.58 | 2.0 |
| CH + G6PD deficiency | 8.83 | 29.83 | 20.98 | 3.4 |
| CH + PKU | 16.92 | 15.72 | (1.20) | 0.9 |

*in million US\$

Table 5. Cost-benefit analysis of different combinations of disorders

| Conditions screened | Total Costs* | Total Benefits* | Net Benefits* | Benefit:Cost Ratio |
|--|--------------|-----------------|---------------|--------------------|
| CH | 3.87 | 9.16 | 5.29 | 2.4 |
| CH + CAH | 9.98 | 12.91 | 2.93 | 1.3 |
| CH + CAH + GAL | 10.91 | 13.12 | 2.22 | 1.2 |
| CH + CAH + GAL + PKU | 23.96 | 19.68 | (4.27) | 0.8 |
| CH + CAH + GAL + G6PD deficiency | 15.89 | 33.80 | 17.91 | 2.1 |
| CH + CAH + GAL + PKU + G6PD deficiency | 28.94 | 40.36 | 11.42 | 1.4 |

*in million US\$

CH was used as a common element for all disorder combinations.

Discounting was crucial in the evaluation since the costs were spent “now” while the benefits were projected into the future. All costs of treatment and benefits were discounted at

7% during the follow-up years. A 7% discount rate is higher than in developed countries like the United States. This can be rationalized by considering that developing countries give more importance to the present because of more immediate needs.

The impact of changes in key variables on the benefit-cost 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. Sensitivity analyses for discount rates were varied from 3% to 12%.

Results

Phase 1

From June 1996 to December 2000, a total of 384 985 newborns were screened from the 24 study hospitals. There were 4,773 newborns who screened positive for at least one of the disorders, and 1,029 newborns were confirmed to have one of the five disorders included in the panel. Screening for G6PD deficiency started only in 1998 and screening for homocystinuria (HCY) was eventually dropped in 2000 since no cases were detected from the population screened.

Table 1 shows the incidence rates for the disorders screened and the various incidence rates computed from the study. The point estimates of true incidence rates were used for the baseline analysis to compute the total costs and projected benefits of the NBSP. The lowest and highest estimates of the 95% confidence intervals were used for the sensitivity analysis in the cost benefit analysis.

Phase 2

Table 2 shows the component screening costs per disorder used in computations for each patient.

Table 3 presents the component costs of a nationwide NBSP compared to the itemized costs of a “do-nothing” alternative and the benefits to be gained from a functioning NBSP.

Table 4 shows the cost benefit analysis for screening in tandem with CH. Certain costs (i.e. staff time, filter paper) were eliminated to avoid overlapping of costs.

As shown in Table 5, the total cost of the screening program to include the 5 disorders in tandem is projected to be US\$ 28.94 while the cost of a do-nothing alternative or the benefits gained is projected at US\$ 40.36 M. Therefore, a net benefit of US\$ 11.42 M can be gained from the NBSP. The benefit:cost ratio is 1.4.

Figure 1 shows the effect of different discount rates with varying incidence rates on the net benefits of screening for all 5 disorders.

The estimates for sensitivities of the 5 disorders are generally considered to be very good. Therefore, missed cases were only computed for the two most commonly detected disorders (CH and G6PD deficiency), since the number of missed cases for the other three disorders would be almost insignificant due to the high sensitivity rate of the NBS procedure and their low incidences. The sensitivity rate of the screening test for CH is 99.5% while the sensitivity rate of the screening test for G6PD deficiency is 94%.¹⁶

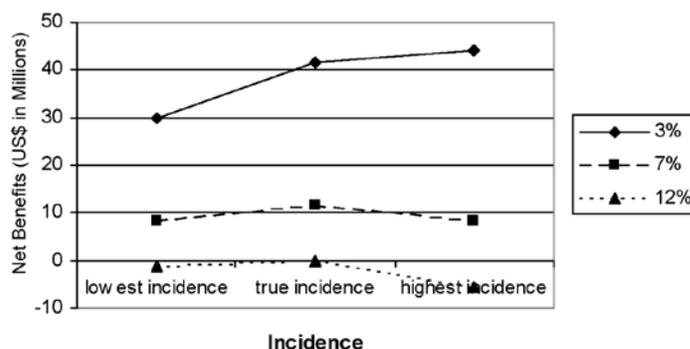


Figure 1. Comparison of net benefits according to incidence and discount rates for screening for 5 disorders.

Discussion

A cost-benefit analysis of the NBSP of the Philippines was conducted to determine whether screening for various disorders would be beneficial despite the inherent costs of setting up a nationwide program. The disorders were chosen based on whether there are reliable and efficient NBS tests, the disorder results in high morbidity and mortality if left untreated, there is effective treatment that reduces negative outcomes, and there is a relatively high incidence.⁴

A societal perspective was employed to include not only the monetary benefits of preventing serious complications, thus saving on medical fees, but also the projected losses in productivity of the individuals who would have been functional in society had they been screened and their possible disabilities prevented.

A previous study by Dans et al. on the cost-benefit analysis of the screening program for CH showed net benefits of US\$ 5 M, hence concluding that NBS for CH was cost-beneficial from a societal perspective.⁹ Dans’ study served as the model on which the current study is based, since it was conducted using the same Philippine population and setting.

The initial phase of this study involved establishing the incidence rates of the five disorders included in the screening program. Data from the 24 study hospitals originally included in the pilot study of the program were used since these centers have gathered the most information from the target population for entire duration of screening. A weighted incidence for each disorder was calculated, taking into consideration the contribution of each participating hospital to the sample population. The incidence was considered the more appropriate estimate of the incidence of the disorders since it reflects the stratified sampling procedure that was employed. It will be noted that there is a slight discrepancy between the crude incidence and the weighted incidence. The confidence intervals of the weighted incidence were also computed at 95% level. It is assumed that the true incidence of each disorder should fall

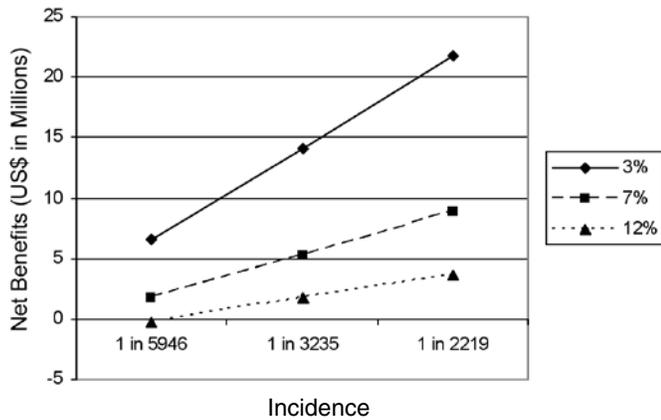


Figure 2. Comparison of net benefits of screening for CH according to incidence and discount rates.

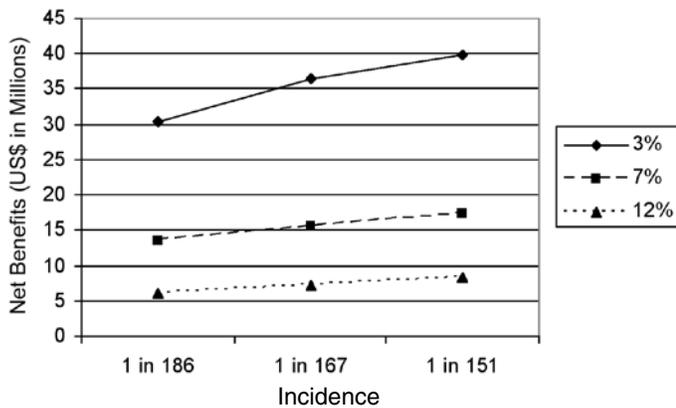


Figure 3. Comparison of net benefits of screening for G6PD according to incidence and discount rates.

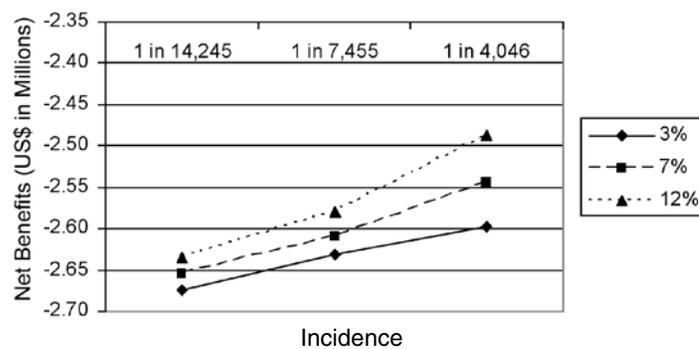


Figure 4. Comparison of net benefits of screening for CAH according to incidence and discount rates.

between the upper and lower limits of this interval.

Of the five disorders in the panel, the most commonly detected is G6PD deficiency (1:167), followed by CH (1:3 235), CAH (1:7 455), PKU (1:41 618), and finally, GAL (1:106 006). HCY, which was originally included in the NBS panel, was dropped in 2000 since no confirmed cases were detected.

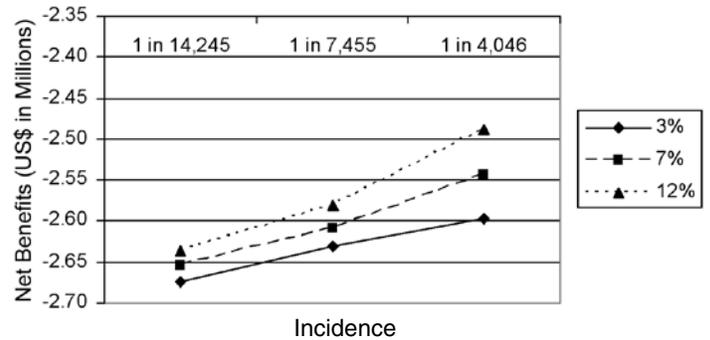


Figure 5. Comparison of net benefits of screening for GAL according to incidence and discount rates.

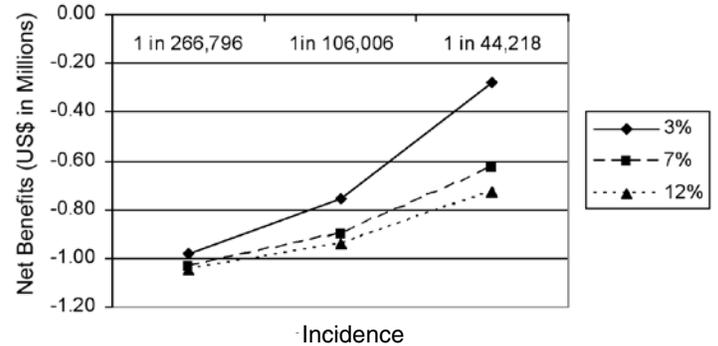


Figure 6. Comparison of net benefits of screening for PKU according to incidence and discount rates.

Calculating the costs of specimen collection, recall and confirmatory testing per patient shows the importance of contributions of these components to the cost of the screening program. By reducing the numbers of laboratories and avoiding duplication of fixed costs and highly trained personnel, costs of laboratory testing can likely be reduced. Improvement of treatment protocols can also reduce the costs. Despite the high cost per patient, screening for PKU for example would detect approximately 1 infant with the disorder in 41 618 screened, averting complications such as mental retardation and shortened life. These calculations emphasize the need to screen disorders in tandem to lessen costs.

An analysis for each of the disorders was first done to find out if these were cost-beneficial when screened individually (Table 3). Screening for CH alone was already reported to be cost-beneficial.⁹ Screening for G6PD deficiency alone yielded a net benefit of US\$15.44 M, showing that individual screening for this disorder is also cost-beneficial. The costs of screening for CAH, GAL and PKU individually were greater than the net benefits and therefore, are not cost beneficial when screened alone.

In the sensitivity analyses for CH and G6PD deficiency (Figures 2 and 3), different incidence and discount rates still yielded net benefits. On the contrary, despite varying the incidence and discount rates for CAH and GAL, screening for these two disorders still yielded net costs (Figures 4

and 5). However, increasing the incidence rate produced lesser net costs, suggesting that a nationally implemented screening program may eventually yield some benefits. Interestingly, the pattern is not the same for PKU (Figure 6). The actual identification and management of PKU patients cost far more than the no screen and no treatment scenario. An increased incidence, in fact, leads to greater net costs.

The rarity of disorders like PKU translates into high net costs for case detection. This raises the question whether such disorders should be included in a national screening program, a question that can only be answered in a larger societal context.

The next step involved determining whether any combination of disorder screening would yield greater benefits than costs. Since screening for CH was already determined to be cost-beneficial, it was used as the foundation for assessing combinations of other disorders. All combinations of disorders considered were added to ongoing CH screening to see if the benefits still outweighed the costs (Tables 4 and 5). The ultimate goal of this study was to determine if it is cost-beneficial to include all 5 disorders in a national screening panel. Note that the costs for multiple disorders are not just a simple addition of the costs for single disease screening because some additional savings can be realized when screening is done in tandem.

As shown in Table 4, pairing disorders with CH resulted in mostly benefit:cost ratios greater than 1, meaning greater benefits than costs. The most cost-beneficial pair was CH + G6PD deficiency and the least cost-beneficial pair was CH + PKU. This was due to the fact that the cost of screening for PKU was far greater than the potential benefits. Treatment for PKU, once detected by screening, is expensive and the incidence in our population is comparatively low versus the other disorders.

In Table 5, CH was again used as the common element in all screening combinations. This order of additions to CH was conceived based on the severity of the consequences of each disorder (CAH > GAL > PKU > G6PD). CAH was the first considered since its complications are life-threatening and they occur shortly after birth. GAL was next since it can also result in fatal consequences, although not as common as in CAH. The severity of the resulting disabilities in PKU is more significant than in G6PD deficiency. For this reason, G6PD deficiency was the last disorder to be added to the panel despite having an individually favorable benefit:cost ratio.

As shown in Table 5, adding multiple disorders to a CH screening program results in benefit:cost ratios that are greater than 1, except for PKU where the cost of screening was far greater than the potential benefits. However, when G6PD deficiency was added to the panel, the program became cost-beneficial once again. G6PD has a high incidence and a relatively inexpensive form of treatment (e.g. avoidance of certain food and drugs). We conclude that a 5-disorder NBS panel would result in greater net benefits than costs.

The sensitivity analysis in Figure 1 showed the effect of varying incidence and discount rates on the overall net benefits of screening for all 5 disorders. First, net benefits were realized only at discounts rates of 3% up to 7%, regardless of the incidence. Increasing the discount rate to 12% yielded net costs. Second, with several disorders in place, a disorder like PKU, with high treatment and management costs and low incidence, tends to decrease the overall benefit such that an increased incidence could not provide the expected increase in benefit.

Children directly benefit from screening since they are spared from possible mental retardation and death. The families of these children also benefit since they do not bear the costs of caring for a mentally retarded individual or having a non-productive family member. Society benefits indirectly through prevention of productivity loss of a mentally handicapped individual or the death of an individual. Researchers point out that for PKU, the cost of screening and treating PKU patients is greater than the expenses of a no screen scenario. Realizing the responsibility of providing available and attainable treatment when proposing a screening program, proponents of the Philippine NBS are laying the foundation for future assistance to PKU patients in obtaining and affording treatment.

Nevertheless, when translated into monetary terms, the collective benefits gained when screening for all 5 disorders more than offset the costs incurred by the family through screening. As much as US\$ 11.42 M in potential benefits can be gained from a nationally implemented NBS for all 5 disorders.

Conclusions and Recommendations

The incidences of the disorders with 95% confidence intervals are: CH is 1:3 235 (1:2 219 - 1:5 946); CAH is 1:7 455 (1:4 046 - 1: 14245); GAL is 1: 106 066 (1: 44218 - 1: 266 796); and G6PD deficiency is 1:167 (1:151 - 1:186). Screening for all 5 disorders in tandem resulted in a net benefit of US\$ 11.42 M and a benefit:cost ratio of 1.4, clearly demonstrating that the benefits of NBS of the Philippines versus a do-nothing alternative far outweighs the costs. Only screening for CH and G6PD deficiency are cost-beneficial when screening is done individually.

Epilogue

This paper was used as one of the supporting documents for the enactment of Republic Act No. 9288 or the Newborn Screening Act of 2004.¹⁷ The law provides the mandate to offer every newborn the opportunity to undergo newborn screening. The current panel of disorders includes CH, CAH, GAL, PKU and G6PD deficiency.

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