

COST-BENEFIT ANALYSIS OF NEWBORN SCREENING FOR GALACTOSEMIA IN THE PHILIPPINES

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Abstract. To determine the incidence of galactosemia (GAL) in the Philippines and to determine whether newborn screening for GAL is cost-beneficial from a societal perspective, cost-benefit analysis was performed. Newborn screening for GAL was done after the 24th hour of life using the Beutler test. Patients screened positive were recalled for confirmatory testing. Using incidence rates obtained from the different participating hospitals of the Philippine Newborn Screening Program (PNSP), the costs for the detection and treatment of GAL were compared to the expected benefits by preventing mental retardation, cataracts and other physical disabilities caused by the disorder that would lead to a loss of productivity for the individual. Sensitivity analyses for incidence and discount rates were also included. Of the 157,186 newborns screened by the PNSP since its inception in 1996, 8 screened positive results. Confirmatory testing of these patients showed that 2 had galactosemia. The incidence of galactosemia in this population therefore, is 1 in 106,006 (95% CI= 1:44,218 - 1:266,796). Projecting the figures to the actual birth rate (1.5M newborns/year), the total costs of the screening program amounted to \$1.1M, while the total benefits amounted only to \$0.2M, yielding net cost of \$0.9M. A cost-benefit analysis of the screening program for galactosemia using the incidence 1 in 106,006 demonstrated that the costs of the program outweigh the benefits. The true incidence of galactosemia in the Philippine population may yield an incidence rate that will result in greater net benefits for the program.

INTRODUCTION

Newborn screening has become a routine component of quality newborn care in most, if not all, developed countries for early diagnosis and management of congenital endocrine and metabolic diseases such as galactosemia (American Academy of Pediatrics, 1989).

In the Philippines, newborn screening was started in 1996 through the Philippine Newborn Screening Project (PNSP). Pediatricians and obstetricians from 24 hospitals in Metro Manila accredited by the Philippine Pediatric Society (PPS) and Philippine Obstetrics and Gynecology Society (POGS) collaborated to establish the incidence of 5 disorders, namely, congenital hypothyroidism, congenital adrenal hyperplasia, phenylketonuria, homocystinuria, and galactosemia.

In a previous study by Dans *et al* (2002), newborn screening for congenital hypothyroidism was proven to be cost-beneficial if implemented on a nationwide scale. It is still uncertain whether or not the other conditions

included in the panel of disorders of the PNSP are cost-beneficial.

Inborn errors of galactose metabolism include 3 main clinical syndromes resulting from 3 different enzyme deficiencies. These are galactose-1-phosphate uridylyltransferase (GALT) deficiency, galactokinase deficiency and uridine diphosphate galactose-4-epimerase (epimerase) deficiency. Galactokinase deficiency leads to cataract formation if left untreated (Elsas, 1999). On the other hand, a complete deficiency of GALT results in 'classic' galactosemia characterized by cataracts, hepatosplenomegaly and jaundice. It can lead to life-threatening complications such as feeding problems, failure to thrive, hepatocellular damage and sepsis in untreated infants. If a lactose-galactose-restricted diet is started during the first 10 days of life, the presenting symptoms quickly resolve and the complications of liver failure, sepsis, neonatal death and mental retardation can be prevented. Despite adequate treatment from an early age, children with galactosemia remain at increased risk for developmental delays, speech problems (termed

verbal apraxia) and abnormalities of motor function (Schweitzer *et al*, 1993). In addition, girls with galactosemia are at an increased risk for premature ovarian failure (Greenberg *et al*, 1989).

This paper evaluated the efficiency of establishing a neonatal screening program for galactosemia using a cost-benefit analysis, taking into consideration the incidence rates obtained from local data of the PNSP.

OBJECTIVES

This paper aims to establish the incidence rate of galactosemia in the local population using data gathered from the participating hospitals of the PNSP. It also aims to determine whether neonatal screening for galactosemia is cost-beneficial from a societal perspective.

MATERIALS AND METHODS

This paper was divided into 2 parts: 1) the Newborn Screening for Galactosemia, which determined the incidence rate of galactosemia, and 2) the cost-benefit analysis, which used the incidence rates to evaluate the cost-benefit of the screening program.

Newborn screening phase

Informed consent was obtained so that a newborn screening (Padilla and Domingo, 2002) sample can be collected after the first 24 hours of life. A blood sample from the baby's heel was collected on a filter card (Schleicher and Scheufl 903C) and sent to the Newborn Screening Laboratory by courier service. Samples rejected for reasons of contamination, insufficiency, layering and early discharge (ie before 24 hours of life) required immediate repeat collection. Accepted samples were analyzed on the day after they were received. Abnormal values indicative of galactosemia were considered with the following levels: Galactose metabolites > 1.5 nmol/l and Gal-1-P uridylyltransferase <1+.

In case of normal results, hospitals were informed through a report sent by the PNSP Secretariat's office. Abnormal results, on the other hand, were relayed to both the Newborn Screening hospital coordinator and the attending physician immediately. The physician recalled the patient for confirmatory testing and clinical review. Blood spots for confirmatory testing were sent to the Newborn Screening Laboratory of the Children's Hospital at Westmead, New South Wales, Australia. Once the baby was confirmed to have galactosemia, he/she was referred to a metabolic specialist for further

management.

Crude incidence rates were computed based on the confirmed cases divided by the total number of cases screened. Weighted incidences with ninety-five percent (95%) confidence intervals were computed based on the proportion of the sample size from each participating hospital.

Cost-benefit analysis phase

A cost-benefit analysis (Drummond *et al*, 1987) of the screening program for galactosemia was performed using the point estimate of the weighted incidence rate computed from the initial phase of the study. The actual costs for the screening of galactosemia were taken into consideration, as well as the projected benefits by preventing the expected complications brought about by the disorder if undetected and left untreated.

The model used in the economic evaluation was the comparison of the establishment of a nationwide screening program compared to a do-nothing alternative, which was the standard in the country. A societal point of view for the estimation of the costs and benefits was utilized (Brosnan *et al*, 1998). Costs and benefits were estimated and projected using a population of 1.5 million newborns, which was the annual birth rate in the year 1998 (Health Intelligence Service, 1998).

All costs were expressed in pesos and converted to US dollars using an exchange rate of US\$1: PhP50 (April 2001).

Table 1 shows the values of the component costs of screening for galactosemia used in computing for each patient. Costs of the screening program included costs of the screening proper, costs of recall, costs of confirmatory visits and costs of treatment and monitoring of screened patients.

The costs of the screening proper included the cost of blood collection, reagents and other materials, expected inputs for labor, and laboratory testing. These were based on the newborn screening data provided by the Philippine Newborn Screening Program (Newborn Screening Project Update, 2000). The cost of the machines used for the screening tests was based on the purchase price for use for 10 years (formula provided by UP), the expected life span of the machine.

The costs of recall included the cost of contacting the child's family once the screening results were positive. Recall rate was based on the actual values from the NBS

project update of positively screened cases among the total screened newborns. The compliance rate was based on the same NBS project update (Newborn Screening Project Update, 2000). The costs of actual confirmatory tests and medical follow-up were included in the calculation of the costs of confirmatory visits. Children identified with galactosemia through screening were confirmed by enzyme assay determination (Gal-1-P and galactokinase). A 2% refusal rate was assumed based on the actual refusal rate in the screening of CH (Dans *et al*, in press). Transportation cost was computed at US\$ 1/ person and professional fee for consults at US\$ 10/ consult. Productivity loss of the person who accompanied the child was computed based on the daily minimum wage of US\$4.47 (Wage Order No. 7, 2000). It was assumed that upon recall, at least two persons accompanies the child and that both would lose a half-day wage. Upon consult with a specialist, it was assumed that the person accompanying the child would be a half-wage earner only (eg housewife) and would lose only a half-day wage.

Costs for treatment and monitoring of the confirmed cases were added based from literature and expert experience. Confirmed cases were treated with diet modification consisting of a lactose-free diet. Baseline laboratory determinations were done, including measurements of SGPT, GGT, PT, BUN and Creatinine levels.

Monitoring included a metabolic evaluation every 3 months in the first year of life, every 6 months until school age (6 years old) and once a year until adulthood (18 years old) (Health Intelligence Service, 1998; Carpio-Benitez, personal communication). Gal-1-P levels were to be taken at each visit, while CBC and liver function tests may be indicated if there was concern (Tuerck,

personal communication). Follow-up visits with an ophthalmologist depended on the presence of cataracts. It was assumed that 30% of confirmed cases have good visual acuity or minimal visual impairment. For these patients, ocular review took place every 3 months for the first 6-12 months and annually for the first 4 years of life. For patients with cataracts and visual impairment, ocular review took place every 3 months for the first 4-8 years of life and every 6 months until adulthood (Inocencio, personal communication).

Dietary consult was recommended every 6 months until adulthood (Limos, personal communication). Developmental assessment was to be followed up annually until adulthood. Allied medical services (physical, occupational and speech therapy) were recommended depending on the child's needs. Habilitation and special education also depended on the child's capabilities (Carpio-Benitez, personal communication). If possible, the ultimate goal was to maintain them into a regular school system.

Based on the current data, there will be no missed cases among screened newborns due to the low incidence and high sensitivity rate of the screening test, and as such, the costs for missed cases have not been included but were considered in the process.

In the do-nothing alternative, abnormalities due to galactosemia may manifest from several days to several months after birth. At this age without treatment, the patient may have either suffered the consequences of death from sepsis, or the sequelae of hepatocellular damage, or mental retardation (Scriver *et al*, 1995).

The costs of screening, as described earlier, were compared to the benefits of preventing the complications associated with galactosemia. These benefits include

Table 1. Component costs of screening per patient.

Component	Costs in US\$
Screening Proper (reagents, supplies, equipment, staff time, filter paper)	\$ 0.70
Recall (mailing/personnel - \$2.50, productivity loss of accompanying person - \$4.47/day, transportation - \$1/person)	\$ 9.00
Confirmatory Visits (enzyme assay for Gal-1-P and Galactokinase - \$2, professional fee - \$10/consult, transportation - \$1/person, productivity loss of accompanying person - \$4.47/day)	\$ 16.20
Treatment and Monitoring (milk prices, laboratory tests, medical fees, productivity loss)	\$ 1,173.60
Total	\$ 1,199.00

avoidance of expenses from lifelong care because of the disability from galactosemia (direct medical costs of treatment of complications), avoidance of expenses from care of the partial disability and avoidance of losses from productivity of that individual and their caregivers (indirect costs) and payment of income taxes.

Complications include developmental delay seen in 45%; problems in speech, seen in 56%; problems in coordination, gait, balance, and fine motor tremors seen in 18%; and cataracts reported in 30% (Elsas, 1999). The cost of management of developmental delay will include allied medical services, special education and the corresponding laboratory and professional fees. The cost of care for cataracts will include surgical, laboratory and professional fees.

Productivity loss of the patient was computed at the minimum wage of US\$ 4.47/day for 45 working years, assuming that the patient starts working at age 20 and retires at age 65. Productivity loss of the caregiver was computed as half the productivity loss of the patient.

All costs of treatment and 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. Different incidence rates were considered. The crude incidence using local data was noted to be 1 in 75,000 (population screened: 150,000 newborns); those cited in literature were in the range of 1 in 10,000 to 1 in 30,000 (Elsas, 1999). Sensitivity analyses for discount rates were varied from 3% to 12%.

RESULTS AND DISCUSSION

From June 1996 to December 2000, 143,185 newborns were screened. Of the 8 newborns with positive screening results for galactosemia, 2 were confirmed to have galactosemia. Hence the crude incidence was computed as 1 in 71,592 and the weighted incidence is 1:106,006 (95% CI= 1:44,218-1:266,796). The point estimate of the weighted incidence rate was used for the baseline analysis to compute the total costs and projected benefits of the newborn screening for galactosemia.

Table 2 compares the total costs of a national newborn screening for galactosemia and the total of costs of a do-nothing alternative or the benefits that would be gained in having a newborn screening in place. All computations were based on the incidence of 1:106,006 and projected to 1.5 M, which was the annual birth rate of the country.

Table 2. Summary of cost-benefit analysis.

Component	Costs in US\$
Screening proper	\$ 1,099,200
Cost of recall (recall rate 0.006%, n = 84, 50% compliance)	\$ 600
Costs for confirmatory (assume 2% refusal rate, n = 41.5)	\$ 700
Costs of treatment and monitoring (cases detected by screening, n = 14)	\$ 16,400
Total cost of screening program	\$ 1,120,500
Costs of treatment of complications (n = 14)	\$ 154,600
Developmental delay (45%, n = 6)	
Speech problems (56%, n = 8)	
Motor problems (18%, n = 2)	
Cataracts (30%, n = 4)	
Costs of treatment and monitoring (cases detected without screening, n = 9)	\$ 2,600
Productivity loss	\$ 55,200
Income tax	\$ 5,500
Total benefits of screening program	\$ 217,900
Net costs of screening program	\$ 898,900

As shown above, the total cost of the screening program is approximately \$1.1 M while the cost of a do-nothing alternative or the benefits gained is \$0.2 M, yielding a net cost of \$0.9 M. Hence, in an incidence of 1:106,006, a newborn screening of galactosemia is not cost-beneficial.

Fig 1 presents a comparison of the net benefits of a screening program for galactosemia using the incidences 1:106,606, 1:75,000, 1:30,000, and 1:10,000 with costs of treatment and management discounted at 3% to 12%. Literature cites a higher incidence of 1:10,000 to 1:30,000 in populations where galactosemia screening has been in place for decades. Local incidences of 1:106,606 and 1:75,000 are limited to the number of newborns screened at the time of evaluation. Again, computations were projected to the 1.5 M annual birth rate of the country.

As can be seen from the graph above, an incidence rate of 1:106,606 regardless of discount rates would yield net costs for the screening program. Hence, despite the discounting, screening for galactosemia is not cost-beneficial. This finding is significant, since the point estimate of the weighted incidence of galactosemia in this study was used in the computation. This may be attributed to the small sample size used in the study.

For an incidence rate as high as 1 in 10,000, net benefits be seen, suggesting that there are potential benefits in favor of screening for galactosemia instead of a do-nothing alternative. It must be kept in mind that the incidence rates used in the sensitivity analysis are not reflective of the true incidence of galactosemia in the Philippines.

Nevertheless, as much as \$ 2.8 M in potential benefits can be gained by varying the incidence and discount rates.

In a similar study done by Padilla *et al* (unpublished), a screening program for 5 disorders, Congenital Hypothyroidism, Congenital Adrenal Hyperplasia, Galactosemia, Phenylketonuria and Glucose-6-Phosphate Dehydrogenase Deficiency, proved to be cost-beneficial. This proposes that screening for galactosemia may also be done in tandem with screening for other disorders order to lessen the costs.

Aside from the monetary benefits clearly demonstrated by newborn screening for galactosemia, benefits from a societal perspective (Tuerck, personal communication) can also be shown. By identifying the gainers and the losers from the program, the net social benefits of screening can be established. At present, the government does not shoulder the expenses of screening but the family of the patient therefore, they are considered the losers in the program. On the other hand, the children saved from the complications of galactosemia, their families, and the society in general, are considered as the gainers.

The children screened directly benefit from the program since they are spared from possible mental retardation and death had they not been screened for galactosemia. The families of these children also benefit since they do not bear the costs of caring for a mentally retarded individual, as well as having a non-productive member of the family. Society in general also benefits indirectly because the possible loss of productivity of the individual due to mental retardation or death is

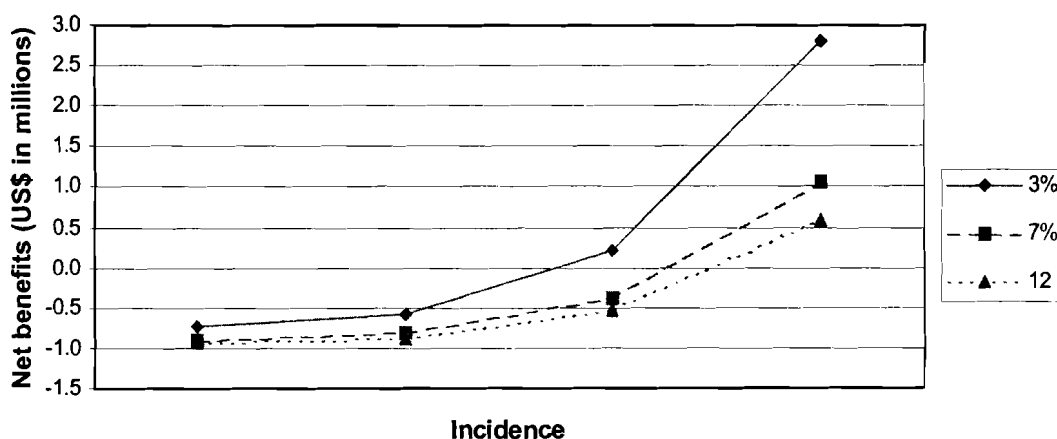


Fig 1. Comparison of net benefits according to incidence and discount rates.

prevented through screening, and consequent early management. Translated into monetary terms, the benefits gained from the averted expenses of caring for a mentally retarded individual, as well as the preserved productivity of the said individual, more than offset the costs incurred by the family through screening.

CONCLUSIONS AND RECOMMENDATIONS

A cost-benefit analysis of the screening program for galactosemia using the weighted incidence based on the Philippine Newborn Screening Program has demonstrated that the costs of the program outweigh the benefits. The investigators recommend that the coverage of screening be increased to include all newborns to determine the true incidence of this disorder in the Philippine population, which may yield an incidence rate that will result in greater net benefits for the program. Screening for galactosemia may also be done in tandem with screening for other disorders such as congenital hypothyroidism in order to lessen the costs.

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