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A Comparative Cost Analysis of Newborn Screening for Classic Congenital Adrenal Hyperplasia in Texas

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SYNOPSIS

Objective. Texas mandates a two-test newborn screening program for congenital adrenal hyperplasia (CAH): one test at birth and a second test at approximately one to two weeks after birth. The authors compared the dollar cost of detecting infants with CAH clinically and through the screening program.

Methods. The authors estimated the costs of screening newborns in 1994 for CAH, including resources used by the Texas Department of Health and the broader cost to society.

Results. Fifteen infants with classic CAH were diagnosed in Texas in 1994 among 325,521 infants born (1:21,701 cumulative incidence). Seven infants were detected clinically and the others were detected through screening, six on the first screen and two on the second screen. The first screen identified all previously undetected infants with severe salt-wasting CAH. The cumulative cost to diagnose the seven infants detected clinically was $79,187. The incremental costs for the screening program were $115,169 per additional infant diagnosed through the first screen and $242,865 per additional infant diagnosed through the second screen.

Conclusions. If the goal is early diagnosis of infants with the severe salt-wasting form of CAH, a single screen is effective. If the goal is to detect infants with the simple virilizing form of the disorder who may benefit from early treatment, the second screen is necessary, but it is not as cost-effective as the first screen.

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Newborn infants are routinely screened at birth in the United States for a variety of congenital disorders. The purpose of screening is to reduce morbidity and mortality associated with these conditions. In addition to these societal benefits, early studies showed that costs of screening were offset by savings in the cost of treatment.[1,2]

All U.S. states currently test for phenylketonuria (PKU) and congenital hypothyroidism.[3] Using 1988 data, it has been shown that these two screens together save an estimated $93,000 for each infant detected and treated per 100,000 infants screened.[4] Thirty-nine states currently mandate universal screening for sickle cell disease. The incremental cost of screening for this disease with complete follow-up in comparison to no screening ranges from $659,000 to $10.1 million per death averted depending on disease prevalence.[5] Seventeen states include testing for congenital adrenal hyperplasia (CAH) in their screening protocols for newborns,[3] and we are aware of several other state programs considering the adoption of this test.

CAH due to 21-hydroxylase deficiency is an autosomal recessive disorder resulting from interruptions in the enzymatic synthesis of the hormone cortisol and sometimes of aldosterone, both of which are necessary to maintain blood pressure, particularly when the body is stressed by illness or trauma. Clinical presentation varies across a continuous spectrum, from death in the first months of life to mild hirsutism in otherwise healthy adult females, depending on the severity of the enzyme block. Symptoms are due to the absence of cortisol and aldosterone and to overproduction of male sex hormones (androgens), which are overproduced in an attempt to make cortisol.[6–8]

Severe deficiency of cortisol causes poor blood vessel tone. Severe deficiency of aldosterone causes excessive loss of salt and water through urination with resulting dehydration. Together, the loss of vascular tone and blood volume can cause inability to maintain blood pressure and organ perfusion (hypovolemic shock), which may cause death in the newborn period, or later at a time of stress (adrenal crisis).

In CAH, when cortisol is reduced by decreased 21-hydroxylase activity, the body attempts to compensate and increased amounts of adrenocorticotropic hormone (ACTH) are produced by the pituitary gland, inducing an excess of the cortisol precursor 17-hydroxyprogesterone (17-OHP), which is a substrate for 21-hydroxylase. The surplus of this substrate causes increased androgen production. In severely affected females, the genitalia resemble those of a male at birth, and multistage surgical repair is required. Males—both moderately and severely affected—appear normal because the testes normally produce large amounts of androgen in male infants. In both sexes, however, moderate to severe overproduction of androgen causes an increase in height and bone maturation in early childhood, but early cessation of growth and adult short stature.

Clinical presentations of 21-hydroxylase-deficient CAH have been grouped into three overlapping and somewhat artificial categories: the classic salt-wasting form, the classic simple virilizing form, and the nonclassic or late-onset form.[7–9] Infants with salt-wasting CAH show excessive salt and water loss due to aldosterone and cortisol deficiency. Infants with simple virilizing CAH are able to preserve enough aldosterone to avoid salt-wasting but have evidence of androgen overproduction beginning from birth. These two variants are called classic forms. Infants with nonclassic CAH present only mild symptoms of androgen excess in late childhood or adulthood. The classic forms have an estimated worldwide prevalence at birth of 1:15,000,[10] but nonclassic or late-onset CAH may occur more frequently, with an estimated birth prevalence approaching 1:100.[8]

The wide clinical spectrum of CAH poses special problems for diagnosis. Female infants with either salt-wasting or simple virilizing CAH present at birth with varying degrees of masculinized genitalia and are usually recognized, though some may be misassigned as males. Male infants with salt-wasting CAH present no physical clues and may die from salt-wasting crisis before diagnosis. In males with simple virilizing CAH, bone maturation may advance to the point that short stature is inevitable before medical attention is sought.

Screening for CAH due to 21-hydroxylase deficiency became possible with the development of a test sensitive enough to measure 17-OHP in blood collected on filter paper from newborn heel sticks.[11] The goal of screening is to prevent early neonatal death or long-term disability caused by adrenal crisis. In addition, timely detection of CAH can prevent sex misclassification of females with ambiguous genitalia.[10]

Early replacement of cortisol and aldosterone has resulted in a sharp decrease in mortality among children with the salt-wasting form of the disorder.[7] It is still unclear if early treatment significantly improves final height in children with all types of CAH.[9,12]

Texas program. A CAH screen was added to the Texas newborn screening program for phenylketonuria,

"The cost of detecting [CAH in] eight infants not recognized clinically was $147,093 per infant."

hypothyroidism, sickle hemoglobinopathies, and galactosemia on June 1, 1989.[13] A single heel stick allows collection of sufficient blood to test for all five disorders. Texas has a mandated two-screen program, with every infant screened once during the first few days of life and again between one and two weeks of age. The Texas Department of Health estimates that 98% of babies receive a first screen and 90% receive both screens; no direct method is available for measuring the screening rate.

The Texas newborn screening program for CAH represents the largest U.S. program and is one of the few that requires a second test. For the present study, we reviewed data for a 12-month screening period to determine the usefulness of a two-screen program by (*a*) comparing the cost of diagnosing infants using two screens to the cost of diagnosing infants with only one screen and (*b*) comparing these figures with the cost of diagnosing infants detected clinically before screening results are obtained.

Previous reports have attributed 52% to 70% of infant diagnoses of classic CAH to screening.[10,14–16] Detection costs ranged from $12,181 to $25,500 per infant diagnosed.[10,15,17] These studies evaluated only single-sample screening programs, and their methods of cost analysis varied. Our study provides a comprehensive and detailed cost analysis that may be used by health administrators who are interested in the relative costs and effects of different approaches to CAH screening.

METHODS

Study population. Infants born in Texas between January 1, 1994, and December 31, 1994, who were screened at least once for CAH served as the study population. In 1994, 325,521 infants were born in Texas, and specimens were submitted for analysis by over 2700 health care providers.

For the present study, we divided infants diagnosed with classic CAH into two groups: (*a*) infants thought to have CAH before screening results were known and who were thus identified without benefit of the newborn screening program (first detected *clinically*) and (*b*) infants detected through screening results. We categorized infants diagnosed as a result of sibling history as detected clinically.

Infants with nonclassic CAH were excluded from the analysis because the effectiveness of treatment for this variant has not been established.

Because incidence of diagnosis (rather than prevalence at birth) was the effect of interest, we used incidence as the statistical measure,[18] and calculations were based on the Poisson distribution.[19] We defined the age at diagnosis for both clinically detected and screen-detected infants as the day a confirmatory serum 17-OHP test was ordered by a medical provider. (The serum 17-OHP test is a diagnostic test, while the heel stick for 17-OHP is a screen.)

Screening protocol. All dried blood samples were analyzed for 17-OHP at the Texas Department of Health Laboratory, with follow-up coordinated through the Bureau of Children's Health.[13,20]

According to the screening protocol, very high screening values (greater than 99 nanograms per milliliter [ng/mL] [299 nanomoles per liter]) were reported by telephone to the child's primary physician by a nurse from the Texas Department of Health, and one of the Department's consulting pediatric endocrinologists located in the child's geographic area was also alerted. (Levels greater than 99 ng/mL indicate that the child is in immediate danger of adrenal crisis.) First-screen values between 40 ng/mL and 99 ng/mL from infants weighing 2500 grams or more were reported by phone or letter and a rescreen or evaluation, or both, requested depending on the value. After a second positive screen, a nurse from the Department of Health again contacted the primary physician to suggest that he or she order immediate medical and laboratory studies.

Higher screening cut-off values were routinely used for low birth weight infants because this group continues to have a high false positive rate.[10,14,17]

Diagnostic evaluation. Texas members of the Pediatric Endocrine Society of Texas, Oklahoma, Louisiana, and Arkansas, acting as advisors to the Texas Department of Health, developed the diagnostic protocol in use in 1994.

According to the protocol, diagnosis of classic CAH, whether detected clinically or by screen, was confirmed by a serum 17-OHP level of 10,000 nanograms per deciliter (ng/dL) either at baseline or after administration of ACTH, the pituitary hormone that stimulates maximal adrenal gland function.

Infants diagnosed with classic CAH through the serum 17-OHP test who had already experienced weight loss or shock or who had low sodium and high potassium levels with high urinary sodium excretion were said to have salt-wasting CAH. Infants with classic CAH but none of these symptoms were diagnosed with simple virilizing CAH. Infants with persistently elevated serum 17-OHP levels that never exceeded 10,000 ng/dL were diagnosed with the nonclassic type of CAH.

Although not specified in the protocol, infants who had high screening values or were symptomatic were frequently hospitalized for diagnostic evaluation.

The Texas pediatric endocrinologists submitted demographic and clinical data about their patients to the Department for the purposes of program evaluation.[20] This information is the source of the clinical data analyzed for the present study.

Cost analysis. We used the ingredients approach to list, measure, and value all items contributing to the cost of each procedure.[21] Because newborn screening is universal and mandated by the State of Texas, we did not limit the analysis to resources used by the Texas Department of Health but took a broader view and described the cost to society. We used 1994 costs because 1994 was the latest year for which complete data were available; items were valued in 1994 U.S. dollars and reflected the market prices of that period. Where possible, unit costs were used instead of charges (amount billed). [22,23]

We evaluated screening costs in the four areas of specimen collection, specimen testing, follow-up of positive screens, and diagnostic evaluation. Three separate cost models were used:[24] low, moderate, and high, based on variations in level of personnel, overhead, and number of diagnostic evaluations. We used the moderate estimate to determine base case cost.

Specimen collection. Specimen collection costs included the costs of personnel, supplies and equipment, and overhead. We used one-fifth the cost of collection since one heel stick collects sufficient blood to test for the five conditions in the Texas program. We included collection costs in our analysis of resources dedicated to screening for CAH, and we report these costs for completeness and because they should be considered in long-term budget projections. However, because CAH screening was added to a preexisting program, we did not include the cost of specimen collection in the incremental cost analysis.

Specimen testing. Laboratory costs were calculated from work-time units defined by the Texas Department of Health Laboratory with adjustments made for amortization of major equipment, repeat analyses of tests with results above the normal threshold, repeat testing for quality assurance, and computer support. We multiplied the unit cost of specimen testing by the total number of 17-OHP tests performed to obtain the total laboratory cost for each level of screening.

Follow-up. Costs for follow-up of positive screens were derived from expenditures associated with *(a)* central administrative and coordination activities and *(b)* local follow-up. The Texas Department of Health Bureau of Children's Health provided cost data that included staff salaries; the cost of supplies and equipment allocated per position; and overhead costs dedicated to CAH. We calculated expenditures for local follow-up by multiplying the estimated number of hours spent tracking infants with positive screens by the hourly salary of a registered nurse working in the community.[25] We allocated the cost of specimen testing to each of the first and second screens based on the proportion of positive tests attributed to that screen.

Diagnostic evaluation. In order to estimate the cost of diagnostic evaluation we developed an algorithm to calculate the proportion of infants with positive screens likely to advance through each subsequent stage of diagnosis. We used the protocol developed by the Pediatric Endocrine Society of Texas, Oklahoma, Louisiana, and Arkansas, and the algorithm was reviewed and approved by a group of experts including pediatric endocrinologists practicing in Texas and newborn screening administrators at the Texas Department of Health.

We assumed the same algorithm in calculating the cost of clinical detection. Medicaid fees obtained from the *Texas Medicaid Reimbursement Methodology*[26] were used to compute physician charges. Fees for laboratory tests were obtained from the laboratory manuals of Endocrine Sciences and Mayo Medical Laboratories, two commonly used reference laboratories. We estimated the average cost of a hospitalization for salt-wasting CAH to be $3871, based on data from a large nonprofit regional hospital in eastern Texas.

For the base case, we assumed that all infants weighing 2500 g or more with first-screen 17-OHP results greater than 99 ng/mL and all infants with positive second screens progressed to diagnostic evaluation and that assessment followed the prescribed protocol. We allocated the cost of diagnostic evaluation to each of the first and second screens based on the proportion of positive tests attributed to that screen.

Cost per diagnosis. We compared the cost of detecting an infant with classic CAH with each of three approaches: Alternative A was clinical diagnosis without screening. Alternative B (clinical detection plus first screen) was the cost of diagnosing the additional infants identified by the first screen, determined by adding the cost of the first screen (excluding specimen collection) to the cost of clinical detection alone. Alternative C was the cost of diagnosing additional infants using two screens, determined by adding the cost of two screens (excluding specimen collection) to Alternative A.

The *incremental cost per diagnosis* for Alternatives B and C was determined by dividing the additional dollars spent for each alternative by the additional number of cases diagnosed using each alternative.[21]

RESULTS

Number of infants diagnosed. In 1994, the cumulative incidence of classic CAH in Texas was 1:21,701. This was less than the reported six-year incidence (1:16,008),[20] but the difference was not significant.

A total of 325,521 infants were born in Texas in 1994, and 611,980 newborn screening tests for CAH were performed. The Texas Department of Health estimated that 319,011 were first screens and 292,969 were second screens. There were 2437 positive screens; 94% (2291) of these were first screens, while 6% (146) were second screens.

Low birth weight infants, who have a high false positive rate, accounted for 613 (25%) of the total number of positive screens (566 first screens and 47 second screens). They were frequently screened again after the required second screen and found normal. Forty infants (1.6% of the 2437 with positive tests) were subsequently lost to follow-up: 39 from the first screen and one from the second screen.

The median age at which first screening results were reported was 13 days (range 9 to 27 days). Lags in reporting time resulted from a variety of causes, including late specimen collection and postal delays. However, the attending physicians of the five infants detected by screen with values greater than 99 ng/mL were notified by telephone when the infants were between 9 and 13 days of age.

Fifteen infants were diagnosed with classic CAH in Texas in 1994 (Table 1); the median age at diagnosis for these infants was 9 days (range 1 to 34 days). In addition to the 15 infants with classic CAH, five infants were diagnosed with nonclassic CAH, all of them identified only on the second screen. At the time of writing there have been no cases of CAH reported among unscreened infants born in 1994.

Among the infants with classic CAH, seven were first detected clinically, six were detected with the first screen, and two were detected only with the second screen (Table 1).

Five infants with early, as yet unrecognized, symptoms of salt-wasting crisis were detected by the first screen and received medical attention more promptly than they would have by clinical detection alone. All of their parents were unaware of impending adrenal crisis and were alerted by the screening results. One of these infants was

Table 1. Infants diagnosed with classic and nonclassic congenital adrenal hyperplasia due to 21-hydroxylase deficiency, Texas, 1994

	Classic					
	Salt-wasting		Simple virilizing		Nonclassic	
Method of detection	Male	Female	Male	Female	Male	Female
Clinical	2	4	0	1	0	0
Screening						
First	4	1	1	0	0	0
Second	0	0	0	2	2	3
Total	6	5	1	3	2	3

a girl who was not detected clinically despite masculinized genitalia.

Three infants with simple virilizing CAH were diagnosed as a result of screening and were then treated to prevent early maturation. Two of these infants were girls who were not detected clinically despite having mildly to moderately masculinized genitalia.

Eleven infants with classic CAH were hospitalized at diagnosis or immediately afterward, and the length of stay (LOS) was reported for nine of them. The median LOS was nine days for five infants detected clinically, and six days for four infants detected by screen. All screen-detected infants hospitalized with salt-wasting CAH had serum sodium values at admission of 130 milliequivalents (mEq/L) per liter or lower and serum potassium of 6 mEq/L or higher and were symptomatic at admission. Although symptoms of dehydration and poor weight gain were documented by the admitting physician, they were not always recognized by parents who sought medical attention only because they had been informed of the positive screening test.

Cost analysis. The 1994 base case dollar cost for CAH screening in Texas's newborn screening program is shown in Table 2. The moderate estimate was used to calculate the base case cost of specimen collection, which totaled $697,658 annually (proportionate unit cost for CAH = $1.14). Differences in skill level of collection personnel and overhead costs varied this expense across the state, from a low estimate of 85 cents to a high estimate of $1.53 per specimen. The total cost of specimen testing was $991,408 (unit cost = $1.62). The annual cost of follow-up, including central administrative activities at the Texas Department of Health and site follow-up, totaled $84,662. Based on our model, the estimated cost of diagnostic evaluation was $100,673. This included $58,213 for physician visits and laboratory studies for evaluation of infants with high values on the

Table 2. Estimated cost of newborn screening for congenital adrenal hyperplasia, Texas, 1994

Item	Unit cost	Cost of first screen	Cost of second screen	Total cost
Specimen collection (variable cost)				
Personnel	$0.75			
Supplies and equipment	0.06			
Overhead (42%)	0.33			
Total	$1.14	$ 363,673	$333,985	$ 697,658[a]
Specimen testing (variable cost)				
Basic cost	$1.31			
Miscellaneous support	0.31			
Total	$1.62	516,798	474,610	991,408[a]
Follow-up cost (annual cost)				
Coordinating activities and site follow-up		79,582	5080	84,662
Diagnostic evaluation (annual estimated cost)				
Physician fees, laboratory tests, hospitalization		94,633	6040	100,673
Grand total		$1,054,686	$819,715	$1,874,401

NOTE: Costs are in 1994 U.S. dollars.

[a]Total costs for specimen collection and specimen testing were calculated by multiplying the unit cost by 611,980, the total number of screening tests for CAH performed in Texas in 1994.

first screen or positive second screens or both. The remaining cost of evaluation ($42,460) was attributed to peridiagnostic hospitalization of five infants for assessment or for treatment of salt-wasting CAH.

The total dollar cost of newborn screening was $1,874,401. Excluding specimen collection, the cost was $1,176,743 ($691,013 for the first screen and $485,730 for the second screen).

The estimated cost of clinical detection without screening was $79,187 for all seven infants detected clinically. This includes the cost of physician visits, laboratory confirmation, and peridiagnostic hospitalization of six infants.

Our cost estimates for follow-up and diagnosis were conservative since we were not able to determine all family expenses resulting from a positive screen. We found that nurses were generally responsible for follow-up, although in some instances physicians assumed that responsibility. Resources were primarily associated with tracking families that were difficult to locate. The cost of a complete diagnostic evaluation without hospitalization was $719 per infant, which included the cost of an office visit and an ACTH stimulation test to confirm the diagnosis. However, follow-up laboratory tests varied with clinical presentation, and individual physician practice often altered the diagnostic protocol and cost.

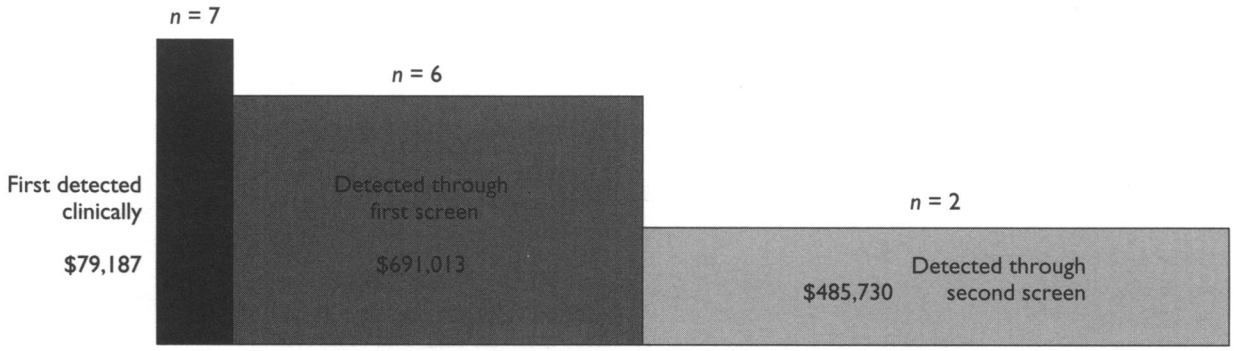
Cost per diagnosis. The Figure shows the costs of the three alternative methods for detecting infants with classic CAH. The cost of specimen collection was excluded from this analysis because screening for CAH was added to an already existing program.

In addition to the seven infants first detected clinically (Alternative A), six infants were first identified by the initial screening test. The incremental cost of diagnosing these six infants was $115,169 per infant. The second screen identified two more infants with simple virilizing CAH at an incremental cost of $242,865 per infant. Overall, the incremental cost for the two-screen program was $147,093 per infant for eight infants not recognized clinically.

DISCUSSION

Cost analysis provided an objective framework for a comparison of three alternative methods for diagnosing classic CAH. In 1994, 15 infants were diagnosed in Texas among 325,521 infants born in that year. The first screen identified all infants with salt-wasting CAH but failed to identify all infants with simple virilizing or nonclassic CAH. This pattern is consistent with the results of a six-year study of screening for CAH in Texas.[20] Without a comparison study it is impossible to know if

Figure. Costs associated with clinical detection and screening detection of infants with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency, Texas, 1994



	Detected clinically	Detected by screening: Detected by first screen	Detected by screening: Detected by second screen	Total
Number diagnosed	7	6	2	8
Total cost	$79,187	$691,013	$485,730	$1,176,743
Cost per diagnosis	$11,312	$115,169	$242,865	$ 147,093

the salt-wasting cases detected first by screening represent lives saved because there was no way to ascertain whether infants detected first by screen would have been detected clinically at a later time and treated successfully.

Costs of specimen collection and testing were similar to those in other studies.[1,10] Although specimen collection was not included in the cost-per-diagnosis analysis, awareness of these costs is important for long-range planning. We observed differences in the skill level of collection personnel and in overhead costs that varied the cost per CAH specimen from 85 cents to $1.53. Substantial savings can result if properly trained technicians can be employed and overhead minimized. Decreasing the number of false positives among low birth weight infants would also decrease the cost of follow-up and diagnostic evaluation. The high false positive rate in this group has been a source of concern in Texas as well as in other regions that screen.[14–17,20]

We did not consider resource cost to the family or the psychological costs that may result from a false positive screen.[21] Insufficient information was available for estimating psychological cost, although prior studies[27,28] reported general apprehension among parents whose infants had repeat newborn screens because of an initial abnormal screen. We recognize the need for further study in this area.

The detection of infants with nonclassic CAH presented unique problems.[20,29,30] Because CAH is manifested along a continuum of symptomatology, diagnosis into mutually exclusive categories is difficult. Since no clear-cut clinical or laboratory boundary separates male infants with simple virilizing CAH from male infants with nonclassic CAH, early detection may lead to treatment of patients who would not have been treated in the past, with unknown benefits and risks.[12,20,29] Conversely, because of disease overlap, it is possible that detection of these infants may be a benefit of a two-screen program. However, since the effect of detecting these cases is much less clear, they have not been included in the analysis.[21] Further investigations are indicated.[29]

Hospitalization of diagnosed patients was not avoided by screening. Infants with salt-wasting symptoms presented clinically before or just as screen results became available and were treated in the hospital. The median length of stay for screening-diagnosed infants was six days; for clinically diagnosed infants the median length of stay was nine days. Both genital ambiguity and positive screens also resulted in diagnostic hospitalization. With shorter turnaround times it is possible that more patients can be identified before salt-wasting crisis develops, but a prior study[15] and our own data suggest that complete prevention of these hospitalizations will be difficult. It may also be possible to evaluate females with ambiguous genitalia more economically, but since ambiguity is usually recognized at birth and screen turnaround is at least five days, most females will be evaluated before screen results are available. Our findings suggest, however, that screening prevents long-term sex misassignment since any misassignment is limited to the turnaround time of the screen. Screening also decreases the duration of hospitalization due to salt-wasting morbidity, which worsens daily after onset and which may be unrecognized until the screening results are received.

Our analyses show that the incremental cost of a two-screen program over clinical detection alone for classic CAH cases was $147,093 per infant diagnosed. We also found that newborn screening had several important benefits:

- Five infants with early, as yet unrecognized, symptoms of salt-wasting crisis were detected by the first screen and received medical attention more promptly than they would have by clinical detection alone.
- Three infants with simple virilizing CAH were diagnosed as a result of screening and were then treated to prevent early maturation.
- Screening may result in a shortened hospital stay.
- Screening increased understanding of the disorder by expanding medical knowledge about its pathology and clinical complexity.

The majority of infants with classic CAH were identified on the first screen; hence the cost per case of the second screen was higher and would be expected to increase as population incidence decreases. The first screen identifies infants at risk of death due to sudden and unsuspected adrenal crisis, while the second screen prevents morbidity by identifying additional newborns with simple virilizing CAH who will benefit from early treatment.

The value of a mandatory two-screen approach requires careful examination, especially in areas with low incidence of CAH. Determining the number of tests to include in a screening program depends on the goals of the program and the resources available. If a goal of screening is to prevent salt-wasting deaths, then the first screen effectively meets this goal and the second screen is not cost-effective. If another goal of the screening program is to identify infants at risk for complications of non-salt-wasting CAH, however, then a second sample is

necessary. Whether this is an efficient use of resources depends on a program's goals and on societal expectations. Early identification of an incorrect sex assignment or a mildly virilized female has benefit to the patient and the family not easily calculated in monetary terms. Such considerations may play an important role in a program's decision regarding the value of a second screening.

In summary, we recommend that agencies carefully consider their goals and relate anticipated costs to desired outcomes before adopting a new screening test. The usefulness of screening cannot be established simply by showing that cases are diagnosed. In disorders as complex as CAH, screening costs must be balanced against benefits to diagnosed patients who are at risk for morbidity or mortality.

This study received support from the Genentech Foundation. The authors thank Linda Prentice, MD, Jennifer Simmank, Barbara Aldis, and Carolyn Scruggs of the Texas Department of Health and Sheri Berenbaum, PhD, Valerie Manter-Kapanke, and Kristina Korman of Southern Illinois University Medical School, who helped collect and evaluate the data.

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