# Newborn screening with tandem mass spectrometry: Examining its cost-effectiveness in the Wisconsin Newborn Screening Panel

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**Objective:** To examine the cost-effectiveness of tandem mass spectrometry (MS/MS) in a neonatal screening panel for 14 fatty acid oxidation and organic acidemia disorders in the Wisconsin Newborn Screening Program.

**Study design:** An incremental cost-effectiveness analysis with a hypothetical cohort of 100,000 infants was performed. A threshold of $50,000/QALY (quality-adjusted life-year) was used to determine whether screening for medium-chain acyl-CoA dehydrogenase deficiency (MCAD) alone is cost-effective or whether additional disorders would need to be incorporated into the analysis to arrive at a conclusion regarding the overall cost-effectiveness of MS/MS.

**Results:** Under conservative assumptions, screening for MCAD alone yields an incremental cost-effectiveness ratio of $41,862/QALY. With the use of more realistic assumptions, screening becomes more cost-effective ($6008/QALY) and remains cost-effective so long as the incremental cost of screening remains under $13.05 per test. Adding the incremental costs of detecting the 13 other disorders on the screening panel still yields a result well within accepted norms for cost-effectiveness ($15,252/QALY).

**Conclusions:** In Wisconsin, MS/MS screening for MCAD alone appears to be cost-effective. Future analyses should examine the cost-effectiveness of alternative follow-up and treatment regimens for MCAD and other panel disorders. (J Pediatr 2002;141:524-31)

Newborn screening for more than 20 fatty acid oxidation and organic acidemia disorders can be conducted with the use of tandem mass spectrometry (MS/MS).[1] In April 2000, the state of Wisconsin Department of Health and Family Services initiated an MS/MS newborn screening panel for 14 fatty acid oxidation and organic acidemias at the Wisconsin State Laboratory of Hygiene (WSLH), as summarized in Table I.[2]

As of May 2002, seven other states (Iowa, Maine, Massachusetts, Minnesota, North Carolina, Ohio, and South Carolina) instituted statewide screening programs for some or all of these disorders. State-run programs in California, Hawaii, Montana, Nebraska, North Dakota, and South Dakota provide screening services on an optional or pilot basis. Parents in other states must seek screening services from public or private laboratories through their own initiative.[3]

| | |
|---|---|
| C-E | Cost-effectiveness |
| MCAD | Medium-chain acyl-CoA dehydrogenase deficiency |
| MS/MS | Tandem mass spectrometry |
| NHS | National Health Service |
| PKU | Phenylketonuria |
| QALY | Quality-adjusted life-year |
| WNSP | Wisconsin Newborn Screening Program |
| WSLH | Wisconsin State Laboratory of Hygiene |

For screening to merit adoption, as with all preventive services, health and economic benefits ought to outweigh program costs. The only previously published economic analysis of an MS/MS screening panel was conducted by the UK National Health Service (NHS) in 1997.[4] Despite limited data on the health benefits of screening for several disorders, the report favored the adoption of MS/MS screening, though recommending it be limited to clearly defined conditions for which adequate test specificity could be demonstrated.

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Supported by a graduate traineeship from the Agency for Healthcare Research and Quality.
Presented in part at the 22nd annual meeting of the Society for Medical Decision Making, September 24-27, 2000, Cincinnati, Ohio.

Submitted for publication Mar 14, 2002; revision received June 12, 2002; accepted July 1, 2002.

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0022-3476/2002/$35.00 + 0 **9/21/128116**
doi:10.1067/mpd.2002.128116

***Table I.*** Wisconsin Newborn Screening Panel With MS/MS

| Fatty acid oxidation disorders | Organic acidemia disorders |
|---|---|
| Medium chain Acyl-CoA dehydrogenase deficiency (MCAD) | Glutaryl CoA dehydrogenase deficiency (GA-I) |
| Long-chain 3-Hydroxyacyl CoA dehydrogenase deficiency (LCAD) | Propionic acidemia (PA) |
| Very-long-chain Acyl-CoA dehydrogenase deficiency (VLCAD) | Methylmalonic acidemia (MMA) |
| Short-chain Acyl-CoA dehydrogenase deficiency (SCAD) | Isovaleric acidemia (IVA) |
| Carnitine palmitoyltransferase deficiency type II (CPT II) | 3-Methylcrotonyl CoA carboxylase deficiency (3-MCC) |
| Glutaric acidemia type II (GA-II) | Mitochondrial acetoacetyl CoA thiolase deficiency (b-KT) |
| 2,4 dienoyl CoA reductase deficiency | 3-Hydroxy-3-Methylglutaryl-CoA lyase deficiency (HMG) |

Source: Wisconsin Newborn Screening Program.

The NHS report results are not directly applicable to assessing the cost-effectiveness of Wisconsin's MS/MS screening panel, however. Phenylketonuria (PKU) screening at the WSLH will continue to be performed with the use of standard fluorometric methods rather than by substituting MS/MS, as was modeled in the UK analysis.[4] Therefore, efficiencies achievable through replacement of the traditional PKU testing method will not be realized. Also, disease incidence rates and screening costs differ between Wisconsin and the United Kingdom. Furthermore, NHS report analyses did not include screening-related cost savings from avoided disability and death or associated quality-of-life gains. We examine the cost-effectiveness of introducing MS/MS screening into the Wisconsin Newborn Screening Program. The analysis is conducted from a societal perspective over the lifetime of a hypothetic cohort of 100,000 infants screened at birth.

# METHODS

## *Scope of Analysis*

Prospective studies of the incidence, cost, and outcomes for many of the disorders in the Wisconsin MS/MS newborn screening panel have not been conducted. Rather than evaluating the cost-effectiveness of screening for all 14 disorders simultaneously, we performed a sequential analysis by first analyzing the cost-effectiveness of MS/MS screening for medium-chain acyl-CoA dehydrogenase deficiency (MCAD) alone.

We have chosen to initially model MCAD for several reasons. First, early diagnosis and monitoring are potentially effective in reducing significant morbidity and mortality.[5-7] Second, MCAD is expected to be the most prevalent condition detected by the MS/MS panel. Of the first 600,000 infants screened in Pennsylvania, Ohio, North Carolina, and Louisiana, MCAD diagnoses accounted for more than half of all fatty acid oxidation and organic acidemia disorders detected.[7] MCAD is also anticipated to contribute the greatest overall health benefit, on a population basis.[4] Third, MCAD is the most comprehensively studied disorder on the MS/MS screening panel, with much less known about the incidence, costs, and outcomes of the other disorders. Because there is considerable uncertainty surrounding many parameter estimates, even for MCAD, our base case analysis relies on conservative assumptions. We then derive our "best estimate" of the true cost-effectiveness of MS/MS screening for MCAD in a sensitivity analysis.

If screening for MCAD alone yields a cost-effectiveness (C-E) ratio of <$50,000/QALY (quality-adjusted life-year) under conservative base case analysis assumptions, we will conclude that MS/MS screening in Wisconsin may well be cost-effective. This may be inferred because most screening costs, in terms of equipment, staff, and administration, are front-loaded onto the first disorder included in the MS/MS panel, with minimal marginal costs (~$1.87 per infant) for detecting the 13 additional disorders. If the C-E ratio is found to be >$50,000/QALY, we shall conclude that screening for MCAD alone is less likely to be cost-effective, with further study needed to determine whether the inclusion of other disorders would push the ratio below this threshold. The $50,000/QALY threshold has been chosen in accordance with established practices for assessing the attractiveness of alternative medical interventions.[8,9]

## *Diagnosis Rates in the Absence of MS/MS Screening*

One major prospective study reported the rate of diagnosed MCAD cases and their associated outcomes in an unscreened population. Over a 25-month period from 1994 to 1996, Pollitt et al[10] reported an incidence rate in England of 4.5:100,000 for those clinically diagnosed with MCAD. The median age at diagnosis was ~1 year. Because of geographic differences in the underlying rate of disease, the rate of clinically diagnosed MCAD in Wisconsin probably differs from that in England. Though the Wisconsin rate is not known, it may be estimated by using data on the underlying genetic frequency of MCAD.

***Table II.*** Base case estimates

| Variable | Estimate | References |
|---|---|---|
| MCAD diagnosis rate before screening | 2.5:100,000 | 10 |
| Death | 0.40:100,000 | 10 |
| Severe neurologic impairment | 0.13:100,000 | 6,10 |
| Mild neurologic impairment | 0.13:100,000 | 6,10 |
| Acute complications only | 1.23:100,000 | 10 |
| Asymptomatic diagnosis | 0.63:100,000 | 10 |
| MCAD incidence postscreening | 4.5:100,000 | WNSP |
| MS/MS sensitivity | 90% | 15,17,18 |
| MS/MS specificity | 99.9% | WNSP |
| Mortality reduction with screening | 60% | 7 |
| Life expectancy with severe neurologic impairment | 65 y | 22 |
| Quality of life with severe neurologic impairment | 0.06 | 24 |
| Quality of life with mild neurologic impairment | 0.67 | 23 |
| Age-adjusted QALYs | Various | 26 |
| Incremental cost of MS/MS screening test | $3.99 | WNSP |
| MS/MS test confirmation (positive for MCAD) | $1715 | WNSP |
| MS/MS test confirmation (negative for MCAD) | $1465 | WNSP |
| Added lifetime carnitine supplementation cost (per child) | $10,678 | WNSP |
| Added lifetime follow-up testing and visit cost (per child) | $12,427 | WNSP |
| Cost per routine hospital admission | $2833 | WNSP, 19, 20 |
| Cost per case of neurologic impairment | $552,000 | 28 |

*WNSP*, Wisconsin Newborn Screening Program.

MCAD is characterized by the A985G mutation, found in 90% of the alleles of patients with MCAD identified retrospectively.[11] In England, the homozygous frequency is 1:17,000.[12,13] In the United States, Gregersen et al[14] estimated a homozygous frequency of 1:28,000 among whites and a 5- to 10-fold lower frequency among nonwhites in North Carolina. The Wisconsin population is 91% white, yielding an estimated genetic frequency of 1:31,000, based on these results. Because this genetic frequency is 45% lower than that observed in England, in the absence of screening this yields an estimated rate of MCAD diagnoses in Wisconsin of 2.5:100,000.

Although these represent diagnosed cases, there are also likely to be cases that remain undiagnosed in the absence of MS/MS screening. Intuitively, one might expect these infants to be less likely to have clinical symptoms, although the actual outcomes of these cases are unknown.[15] The largest study of infants with unexplained cause of death to date found a very small proportion of such cases to be due to MCAD, constituting 0.25:100,000 live births.[16] Because it is unclear how to combine this rate with the estimated rate of clinical MCAD diagnoses derived from English data, in the base case analysis, we conservatively assume that all undiagnosed MCAD cases in the absence of screening are asymptomatic.

### *Outcomes in the Absence of MS/MS Screening*

Outcomes among clinically diagnosed infants in the Pollitt study included death (16%), neurologic impairment (10%), full recovery from acute attack (49%), and no symptoms (25%).[10] Although encephalopathy and hypoglycemia were reported during acute episodes, neurologic impairment constituted the only long-term impairment to quality of life. We assume a similar distribution of outcomes for Wisconsin cases diagnosed in the absence of screening, with death and neurologic impairment occurring at 1 year of age. For cases of neurologic impairment, we assume an equal proportion of mild and severe cases, similar to that reported by Wilson et al.[6] These are conservative assumptions because there may be higher morbidity and mortality rates among Wisconsin cases than in England as the result of greater MCAD awareness in the United Kingdom. This also conservatively assumes the absence of further morbidity or mortality, later in life, relating to a prior metabolic decompensation.

### *MS/MS Specificity and Sensitivity*

In Wisconsin, screened infants whose sample exceeds the following acylcarnitine and plasma carnitine levels are flagged for further testing: C6 ≥0.30 μmol/L, C8 ≥0.50 μmol/L, C10:1 ≥0.40 μmol/L, C8/C10 ≥10.0 μmol/L. Infants with abnormal values on repeat screening receive confirmatory testing before a final diagnosis is reached. The WSLH has genetically confirmed 7 MCAD cases (5 homozygous and 2 heterozygous for the A985G mutation) among 155,500 infants screened, a rate of 4.5:100,000. This is somewhat less than the rate of 6.5:100,000 reported among 930,078 infants screened in other states.[7]

Of 155,500 infants screened, 7 of 9 infants with initially elevated acylcarnitine levels were found to have the

A985G mutation. This yields a test specificity of 99.9%. MS/MS sensitivity is not known precisely but was estimated to be >95% in the NHS report.[4] In Australia, >90% of infants diagnosed clinically with MCAD would have been detected through MS/MS screening.[17] Further support for a high MS/MS sensitivity comes from a recent study of UK regional registers that failed to uncover any patients with MCAD missed through acylcarnitine analysis.[18] No MCAD cases are known to have been missed among >1,000,000 newborn infants screened in the Pennsylvania, New England, and Wisconsin programs.[1,15] In the base case analysis, however, we more conservatively assume a screening test sensitivity of 90%.

### *Outcomes With MS/MS Screening*

In the only large-scale US study of health outcomes after the introduction of MS/MS screening to date, Andresen et al[7] reported 62 MCAD cases and 2 neonatal deaths due to MCAD among 930,078 infants screened from 1992 to 2001. No long-term morbidity was reported. Factors influencing the health outcomes of these infants may not be uniform over time, however. Both deaths occurred during 1992, with no MCAD-related deaths among the 850,000 infants subsequently screened.

In estimating screening outcomes, it is difficult to reconcile the first MS/MS screening results with those from more recent years. Logically, one might expect the most recent data to best reflect current practices. The increasingly favorable outcomes for infants diagnosed with MCAD may be the result of improved treatment protocols and knowledge of the disease. In further support of this, no deaths or significant morbidity have been reported among 275,000 infants screened in Australia since 1998.[17] In our base case analysis, however, we conservatively assume that this is not the case and that neonatal outcomes mirror those of the entire Andresen cohort.[7] Although the length of follow-up varies among cases in that cohort, previous studies of clinically diagnosed cases, with follow-up well beyond the neonatal period, have reported no long-term morbidity or mortality after the initial MCAD diagnosis.[5,6,10]

As a precautionary measure, however, children may be admitted to a hospital during an illness for routine monitoring. During the first 2 years of screening in Wisconsin, there have been 6 routine hospital admissions, lasting 2 days on average, among 3 of the 7 infants diagnosed with MCAD. A return to full health has occurred for all hospitalized cases. We assume an average of one routine hospital admission per infant during the first year of life, with an exponential decline in the hospital admission rate until the age of 5 years. Based on inpatient charge data from the Healthcare Cost and Utilization Project, adjusted by a national hospital cost-charge ratio of 0.56, the average cost per hospital admission is estimated to be $2833.[19-21]

***Table III.*** Base case cost-effectiveness results*

| | | |
|---|---|---|
| Costs ($) | | |
| Screening test | | |
| MS/MS instrument | 82,737 | |
| Labor | 95,588 | |
| Consumables | 73,529 | |
| Data management operations | 56,134 | |
| Departmental indirect expenses | 38,291 | |
| Laboratory overhead and program start-up | 52,852 | |
| Screening test subtotal | | 399,131 |
| Positive test confirmation | | 6,227 |
| Carnitine supplements, to age 18 | | 48,052 |
| Follow-up testing, visits, and staff time, to age 18 | | 55,920 |
| Routine hospital admissions | | 16,749 |
| Total costs | | 526,079 |
| Cost savings ($) | | |
| Neurologic impairment | | –124,200 |
| Medical costs of fatal and acutely ill cases | | 0 |
| Net cost of screening for MCAD ($) | | 401,879 |
| Patient outcomes and quality of life | | |
| QALYs gained from prevented deaths | | 5.8 |
| QALYs gained from prevented severe neurologic impairment | | 2.8 |
| QALYs gained from prevented mild neurological impairment | | 1.0 |
| Total QALYs gained from screening | | 9.6 |
| Cost-effectiveness ratio | | $41,862/QALY |

*Per 100,000 screened; discounted at a 3% annual rate.

### *Survival and Quality of Life*

In this analysis, we assume that infants with asymptomatic MCAD will have a normal life expectancy. We conservatively assume that the prevention of mild neurologic impairment does not extend life expectancy, with a life expectancy of 65 years for infants with severe neurologic impairment.[22] Quality-of-life weights for mild neurologic impairment (0.67), derived using the standard gamble method, were based on ratings of this health state by teenagers formerly of extremely low birth weight.[23] Weights for severe neurologic impairment (0.06) were based on Health

***Table IV.*** Sensitivity analysis

| Parameter estimate | Initial value | Threshold tested | C-E ratio |
|---|---|---|---|
| Best estimates-MCAD parameters | | | |
| Severe neurologic impairment cost per case | $552,000 | $826,000 | |
| Cost per case of other cases | $0 | $28,900 | |
| Effectiveness of early diagnosis and treatment | 60% | 90% | |
| % of symptomatic cases undiagnosed | 0% | 37% | |
| In the absence of screening | | | $6008/QALY |
| Threshold analysis (best estimate) | | | |
| Effectiveness of early diagnosis and treatment | 90% | 36% | $50,000/QALY |
| Incremental cost of MS/MS screening test | $3.99 | $13.05 | $50,000/QALY |
| Screening test sensitivity | 90% | 28% | $50,000/QALY |
| Overall disease incidence | 5.0:100,000 | 1.4:100,000 | $50,000/QALY |

Utility Index 3 scores for patients with severe dementia.[24] A similar weight (0.08) has been reported for severe cognitive deficit after a stroke.[25] To account for other comorbidities unrelated to MCAD, all life-years are multiplicatively adjusted by an age-specific quality-of-life weight, as described by Erickson et al.[26]

### *Screening and Follow-up Costs*

Within the Wisconsin newborn screening panel, the incremental cost of MS/MS screening, including equipment, staff, and supplies, is estimated to be $3.99 per sample. This estimate was derived from the Wisconsin State Laboratory of Hygiene cost accounting system, based on the costs of MS/MS equipment (annuitized over a 5-year useful life), ancillary equipment, labor, consumables (standards, plates, etc), data management operations, departmental indirect expenses, laboratory-wide overhead, and program start-up costs. Infants testing positive for MCAD undergo a repeat MS/MS screen, urine organic acid analysis ($455), acylglycine urine analysis ($381), acylcartinine analysis ($213), mutation analysis ($181), and plasma carnitine analysis ($85).

Confirmed MCAD cases are scheduled for a clinic visit with the staff of the Wisconsin newborn screening program ($250) and are placed on carnitine supplements at a daily dosage of 50 mg/kg and cost of $0.80 per 330-mg pill. We assume that supplements are taken until age 18 years because by this age, the body's reserves against ketone depletion will have strengthened significantly. Until this age, organic acid, acylcarnitine, and plasma carnitine analyses are also performed (triannually at age 1 year, biannually for ages 2 to 3 years, and annually thereafter), with annual essential fatty acid tests ($220) performed until age 6 years. Costs for staff time ($190 per follow-up office visit) and phone consultation with families ($250/year until age 5 years and $50/year thereafter) have also been included in the model. The follow-up protocols reported here are regarded as conservative by the Wisconsin Newborn Screening Program staff. As more experience in managing MCAD cases is gained, the frequency, length, and cost of follow-up are likely to be reduced.

### *Cost Savings From Avoided Complications*

Data on the lifetime costs of neurologic impairment among patients with MCAD have not been collected. As a reasonable approximation, we use estimates of the lifetime costs of special education, health, and social care for children with PKU exhibiting similar levels of dysfunction. We conservatively use the lower bound estimate from a UK meta-analysis of these costs, with adjustment to year-2001 US dollars and a 3% annual discount rate.[28] This yields a discounted lifetime cost of $552,000 per case of neurologic impairment.

Costs for other MCAD outcomes (eg, death, hospital admissions for coma, seizures, cardiac arrest, or hypoglycemia) have not been formally assessed. In the base case analysis, we therefore do not assume MS/MS screening yields any cost savings from the prevention of other sequelae. This is a very conservative assumption, which is varied in the sensitivity analysis. All costs are adjusted to 2001 dollars, using the Consumer Price Index. All costs and life-years are also discounted at a 3% annual rate.[29] Base case model assumptions are summarized in Table II and in a decision tree in the Figure.

### *Sensitivity Analysis*

Given the uncertainty surrounding several model parameters, the base case analysis relies on a number of very conservative assumptions that serve to bias results against MS/MS screening. In the sensitivity analysis, we incorporate more realistic estimates of MCAD incidence, costs, and outcomes to generate our "best estimate" of screening cost-effectiveness, as discussed below. We then individually vary each of the parameters most influential in determining this best estimate until the $50,000/QALY threshold is crossed.

Parameter adjustments between the base case and best estimate analyses

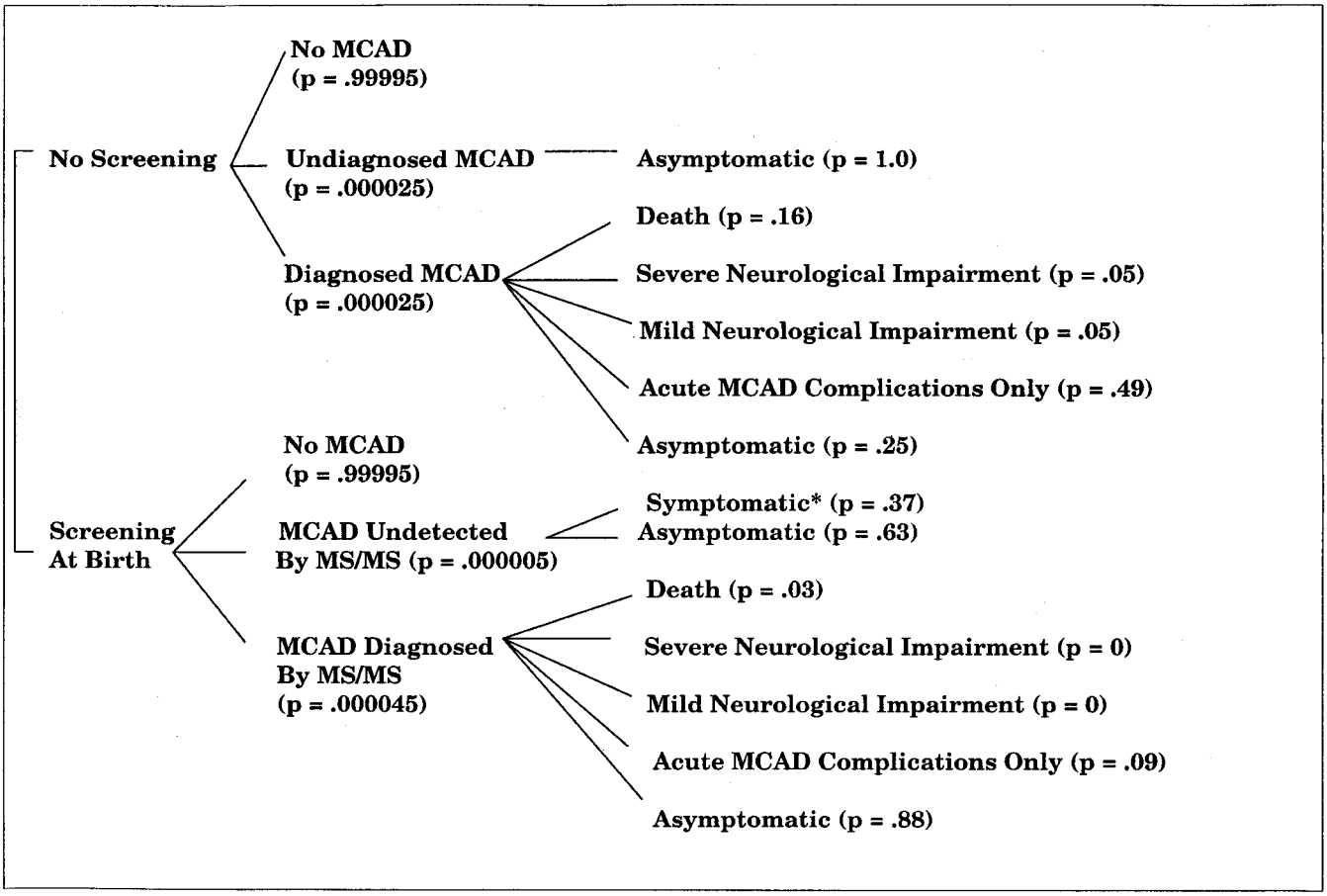


***Figure.*** Base case MS/MS screening decision tree (p = conditional probability of given outcome).

were as follows. First, the base case analysis assumes that before screening, all undiagnosed MCAD cases remain asymptomatic. In the model, these infants represent 63% of all cases observed with screening. If it is assumed that the infant mortality rate of 0.25:100,000[16] can be directly combined with base case data, in the absence of screening, one would expect 25% of MCAD cases to not be diagnosed with the disorder despite the presence of symptoms. We incorporate this figure into our best estimate result. Second, the lifetime costs of neurologic impairment are adjusted from their lower bound to best estimate level from that study.[28]

Third, the total costs of care for MCAD cases without neurologic impairment are adjusted from $0 to $28,900 per case. This estimate is based on the cumulative medical costs incurred by a convenience sample of 42 children diagnosed with MCAD.[30] Cost data were weighted to mirror the relative proportions of asymptomatic, ill, and fatal cases specified in our analysis, excluding cases diagnosed before 1990, those identified through newborn screening, and those for whom neurologic impairment was an outcome. Finally, we assume that early diagnosis and treatment through MS/MS screening is 90% effective in preventing subsequent death, consistent with the most recent data on outcomes with MS/MS screening.[7,15,17]

## RESULTS

### *Base Case*

Adding MCAD alone to an MS/MS screening panel yields an incremental C-E ratio of $41,862/QALY (Table III). Gains in quality of life derive mainly from prevented deaths, with lesser gains resulting from averted cases of severe and mild neurological impairment.

### *Sensitivity Analysis*

Best estimate results are presented in Table IV. Under more realistic assumptions for the incidence, costs and outcomes of MCAD cases, MS/MS screening becomes even more cost-effective ($6008/QALY).

Base case results were most sensitive to variations in screening test cost and sensitivity, underlying MCAD incidence, and effectiveness of early diagnosis and treatment. One-way sensitivity analyses of these best estimate parameters indicate that the effectiveness of early diagnosis and treatment would need to be <36% for the $50,000/QALY threshold to be crossed. Similarly, incremental testing costs would have to rise above $13.05 per infant, test sensitivity

fall below 28%, or disease incidence decline to <1.4:100,000.

## DISCUSSION

This study used available estimates of MCAD incidence, costs, and outcomes to evaluate the cost-effectiveness of introducing MS/MS screening in Wisconsin. In such analyses, when precise estimates are unavailable for particular parameters, the most prudent course of action is to set them to conservative values. If an intervention is found to be cost-effective under restrictive assumptions, then it is quite likely to be cost-effective under more realistic assumptions. We followed this strategy in our base case analysis.

Even under conservative assumptions, our model predicts a cost-effectiveness ratio for MS/MS screening comparable to other well-accepted medical interventions.[9] When more realistic assumptions are incorporated into the analysis, screening becomes even more cost-effective. In 1-way sensitivity analyses, MS/MS screening remains within currently accepted limits for cost-effectiveness, even under wide variations to each parameter.

This analysis has several limitations. First, knowledge of MCAD and the development of MS/MS screening are relatively recent phenomena, with only a few population-based studies having been conducted. Although an ideal study might derive estimates of disease costs, incidence, and outcomes from a single cohort of individuals followed over their entire lifetimes, such studies are rarely feasible in practice. Because policymakers in numerous states have made, or are grappling with, a decision regarding the adoption of MS/MS newborn screening,[2,15,31] we have attempted to provide timely evidence on the cost-effectiveness of MS/MS screening, pooling information from currently available sources.

Second, this analysis focused on the decision of whether to adopt MS/MS screening in a sequential fashion rather than comprehensively. Because screening for MCAD alone was found to be cost-effective enough to justify the adoption of MS/MS screening, parameters for the other 13 disorders detectable through the Wisconsin program are not modeled here. Adding to the model the additional screening costs for detecting these other disorders will still yield a result that is well within accepted norms for cost-effectiveness ($15,252/QALY).

Although the mere detection of these disorders may be cost-effective, it is possible that current follow-up and treatment regimens for them are costly and ineffective. The decision of whether and how to treat a disorder, however, may be divorced from that of its detection. For most of these disorders, there is currently insufficient evidence on the health and economic benefits of early monitoring and treatment. It is hoped that results from early programs adopting MS/MS screening can help guide decisions regarding the most cost-effective follow-up protocols for these infants.[2,15]

Third, the impact on a family's quality of life of an MCAD diagnosis that would not have been made in the absence of screening and the societal benefit of knowing that a test for MCAD is available have not been modeled. At present, these types of parameters are rarely incorporated into cost-effectiveness analyses because quality-of-life instruments for their measurement are in their infancy.[32]

In conclusion, MS/MS screening in Wisconsin appears to be cost-effective under a wide variety of assumptions. There are ~4,000,000 live births in the United States each year. With nationwide MS/MS screening, 150 to 300 infants with MCAD could be rapidly diagnosed each year, with the potential for preventing an estimated 20 to 30 neonatal deaths. As an increasing number of cases of MCAD and other disorders are diagnosed, needs will shift from perfecting the detection of these conditions to understanding the most cost-effective protocols for their follow-up and treatment.

*We gratefully acknowledge the assistance of Sandy van Calcar, Kristine Hanson, and Jon Wolff, Biochemical Genetics Clinic, Dennis Fryback, Department of Population Health Sciences, University of Wisconsin-Madison, and Scott Grosse, Centers for Disease Control and Prevention.*

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