HEALTHCARE USE AND COSTS OF MCADD IN AUSTRALIA: SCREENING VERSUS NO SCREENING

Marion Haas PhD[1], Meredyth Chaplin B.App.Sc[1], Pamela Joy PhD[2], Veronica Wiley PhD[2], Carly Black B.Psych[2] Bridget Wilcken MBChB[2,3]

[1]Centre for Health Economics Research and Evaluation, University of Technology, Sydney

[2] Children's Hospital at Westmead, Sydney

[3] The University of Sydney

Address for correspondence: Associate Professor Marion Haas, CHERE, UTS. PO Box 123, Broadway NSW 2007. Phone: 61 2 9514 4720 Fax: 61 2 9514 4730

marion.haas@chere.uts.edu.au (No reprints)

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Abstract

Objective: To describe and analyze the utilization and costs of hospital services for children diagnosed with medium-chain acyl-CoA dehydrogenase deficiency (MCADD) either by newborn screening or clinical diagnosis in Australia between 1994 and 2002. MCADD is a potentially lethal disorder of fatty-acid oxidation.

Study design: Retrospective audit of medical records supplemented by parental survey.

Results: A total of 59 children with MCADD were identified, 24 by newborn screening. In the first four years of life, screened children cost an average of $A1676 ($US1297) per year for inpatient, ED and outpatient attendances compared to $A1796 ($US1390) for clinically-diagnosed children. Forty-two percent of screened children were admitted to hospital compared to 71% of unscreened children. Unscreened children used significantly more inpatient services and cost significantly more in terms of emergency services. There were also some significant differences in utilization on a year-by-year basis.

Conclusions: Unscreened children may be more likely to be admitted to hospital and to incur higher emergency department costs than screened children, while screened children seem more likely to attend hospital outpatient clinics. Screening does not result in higher costs from a hospital perspective.

Introduction

Tandem mass spectrometry (MS/MS) screening for disorders of amino acid, organic acid, and fatty acid metabolism has become widespread. However, increasing the scale and scope of screening programs requires understanding of costs, not just of screening but also downstream costs, utilization of healthcare and longer term outcomes.

The commonest disorder newly detectable by MS/MS is medium-chain acyl-CoA dehydrogenase deficiency (MCADD) a disorder of fatty acid oxidation. Children with MCADD develop hypoketotic hypoglycaemia with intercurrent illness, and there is a substantial risk of death in undiagnosed patients[6]. Management protocols to avoid catabolism, including admissions to hospital for intravenous glucose, are easy to implement and highly effective[1]. There are no long-term complications [2].

Several economic evaluations and systematic reviews of newborn screening using MS/MS have been published[3-9], but only two have specifically considered MCADD [3,9]. Venditti and colleagues reported estimated costs for unscreened patients using 30-year retrospective chart review of 32 patients [9]. These data were used to construct a "typical" pattern of care for MCADD patients diagnosed by screening. The study by Pandor and colleagues is a systematic review and modeling exercise. It relies on the results of previous studies and models typical or average costs[3]. The study reported here compares the actual costs and utilization of both screened and unscreened children with MCADD.

Evaluation of costs and outcomes is complicated since more children with MCADD are detected by screening and they have a different mutation profile from children diagnosed

clinically[10]. Some children detected by screening might not be at risk of adverse outcomes. The implications of these findings may be either:

i) increased utilization and costs: families with early diagnosis may more readily seek medical assistance during intercurrent illness, and have more routine monitoring. or :

ii) decreased utilization and costs: because a higher proportion of children in the screened group may have a less severe variant of MCADD[6]; or:

iii) increased utilization and decreased costs: with early detection, careful monitoring and earlier intervention, an increased rate of utilization per patient may result but the cost, per patient or total, may be lower with cheaper interventions and shorter length of stay.

In Australia, newborn screening using MS/MS began in two of 6 States in 1998 and 1999 and a third at the end of 2001. We captured relevant data on all children born between April 1994 and March 2002 and examined the differences in costs, healthcare utilization and outcomes between screened and unscreened children[11]. The human ethics committee of each tertiary children's hospital separately approved the conduct of this study.

Methods

Patients:

Patient groups were children with MCADD a) diagnosed clinically from April 1994 to March 1998 in all states in Australia, b) diagnosed clinically from April 1998 to March 2002 in States not screening for MCADD, and c) patients born from April 1998 to March 2002 and diagnosed by newborn screening. Because only five laboratories in Australia perform diagnostic testing for MCADD, we believe we have virtually complete ascertainment[11].

Data collection:

Utilization: All patients with MCADD were seen at tertiary children's hospitals. Each of these in the Australian states of New South Wales (2), Queensland (2), Victoria, South Australia and Western Australia (1 each) were requested to provide details of emergency

department (ED), inpatient, and outpatient (ie hospital-based ambulatory care) episodes of care for all children diagnosed with MCADD between April 1994 and March 2002. Details requested included number of episodes, year of episode, length of stay (LOS), whether admitted from ED, principal and secondary diagnoses and procedures, including diagnostic tests performed. In addition, because some children may have attended hospitals other than the tertiary facility, we surveyed all the parents of children with MCADD to inquire about this aspect of utilization.

Costs: The three States in which screening was established during this period provided information about the cost of the MS/MS test, including the cost of consumables, equipment, overheads and staffing. The equipment was costed at one instrument per screening laboratory, with devaluation over 7 years. The cost estimated for this study assumes that a minimum of 50,000 MS/MS tests per machine per year will be performed. Therefore the cost per test is likely to be higher than average in smaller States and lower in larger States. In the smallest State, the cost of the screening test per child was $A2.24 ($US1.73)[1], and in the largest State it was $A1.02 ($US0.79), compared with an average cost of $A1.63 ($US1.26). Similarly, the total costs of the screening program will vary by State depending on the cost per screened child and the number of tests performed.

The perspective taken is that of the State public hospital systems. A request was made to each hospital to provide information on available costs (eg bed-day costs, costs of tests, costs of procedures etc) for each admission for each child. Hospitals were generally able to provide detailed information about the costs of individual inpatient admissions. Where such costs were not available (eg in some hospitals, costs were not available for admissions prior to

[1] All $A were converted into $US using XE.com The Universal Currency Converter www.xe.com/ucc

2000), a cost was assigned to each inpatient episode based on the average cost of a child in the study of the same age and sex with the same principal diagnosis, adjusted for LOS. Outpatient clinic and ED costs were based on the NSW Health Costs of Care Standards[12]. Visits to the ED were assigned a cost of $A450 ($US348) for admitted and $A373 ($US289) for non-admitted patients which were the benchmark average costs per ED weighted episode for triage two category patients for the specialist hospitals located in NSW. Similarly, a cost of $A254 ($US197) was assigned to each outpatient clinic visit based on the cost calculated for Pediatric Medicine outpatient clinics[10]. Additional costs were assigned to outpatient allied health visits (eg dietician, physiotherapy), based on the costs calculated for the same set of standards. All costs were converted to 2002 Australian dollars[13]. No attempt was made to account for out-of-pocket costs for this group of children and their families although this has been done for the larger study.

As the youngest of the screened children were aged four years, only years 1-4 have been compared across the groups.

Data analysis

Utilization: The number of inpatient admissions, outpatient and ED attendances were collected for each individual in the study. Admissions where the principal diagnosis was clearly unrelated to MCADD were not counted (eg trauma, acute appendicitis). As the age distribution varied between the screened and unscreened groups (screened children were born between 1998 and 2002; unscreened between 1994 and 2002) it was necessary to take this into account when calculating utilization rates. The average number and range of inpatient, emergency (ED) and outpatient (OPD) services and the rates of utilization for both screened and unscreened groups were calculated. Within each group, the utilization rates per age group were calculated. Differences between the groups were tested using Fisher's exact test for utilisation.

Costs: Total costs for each individual were calculated by multiplying the costs per ED, inpatient and OPD episode by the number of episodes utilized and an annual cost per child calculated. Cost data for individuals, plus number of services used, were used to calculate average costs per year in the screened and unscreened groups. The t-test was used to test for differences in costs. The two-sample t-test for unequal variances was used to compare the mean cost of the health services used by the screened and unscreened groups. As the cost data were skewed, a 95% confidence interval for the mean cost difference between groups was calculated using the nonparametric BCa bootstrap method.[14]

Seven deaths, all apparently related to to MCADD, were recorded amongst children with MCADD, (6 unscreened, 1 screened). Of the seven deceased children, two utilized services (and hence incurred costs). However, as both children lived for at least four years, their deaths have not had any influence on the data presented here.

Results

A total of 59 children with MCADD who were born between 1994 and 2002 were identified, 24 in the screened group and 35 in the unscreened group. Within the unscreened group, 16 children were born contemporaneously with children in the screened group (1998-2002) and 19 were classified as belonging to the historical unscreened group (ie born between 1994 and 1998).

The cost of the MS/MS test

Three States were able to provide detailed information on the additional costs of running the MS/MS testing system, including the cost of consumables, equipment and staffing. The costs were based on testing 189,540 children per year in the three states. Among the 3 programmes,

equipment and overhead costs did not vary significantly, but the cost of consumables and staffing did. Cost of consumables depended on methodological variation, in particular the extent of use of labelled standards[2] and staffing depended on contextual issues such as the degree to which computerisation was used to download and analyse data and the extent to which the screening services were able to justify the employment of additional staff to implement MS/MS screening. An average cost was estimated using the following assumptions:

- one additional hospital scientist
- 70% samples tested using computerized laboratory interpretation management system
- A mid-range costs for labelled standards

Using these assumptions, the average cost of the MS/MS test per child screened was estimated at $A1.67 ($US1.29). This cost did not include confirmatory testing, which, for MCADD was estimated to add an additional $A0.04 ($US0.03) per child screened.

Utilization

Table 1 summarises the annual utilization of the three groups. The proportion of children using inpatient, emergency and outpatient services is shown, as well as the mean number of attendances amongst those children who used the services and the mean length of stay (los) for those children who utilized inpatient services. It shows that significantly fewer children in the screened group utilized inpatient services compared with the unscreened group (42% vs 71% p=0.03). Of those who were admitted to hospital, the mean number of admissions per year was approximately one for both groups (1.1 screened; 0.9 unscreened) and the length of stay 2.5 days (2.5 screened; 2.6 unscreened). There were significantly more admissions per

[2] Labelled standards are isotopically labeled amino acids (AAs) or acyl carnitines (ACs). All levels of AAs or ACs in samples are determined relative to these. Labelled standards can be made “in house” or purchased, either in bulk or in “kit” mixes. “Kit” mixes are the most expensive, followed by bulk purchase and then “in house” manufacture.

year amongst children in the historical unscreened group who were admitted (79% p=0.03) and, on average, they stayed for a longer time (3.2 days). The most common reasons for admission were gastrointestinal illness or infection (e.g. respiratory) and management involved the intravenous replacement of fluids, parenteral infusion of nutrition or antibiotic therapy. Approximately 32% of admissions in the screened group and 23% of those in the unscreened group occurred in hospitals other than specialist children's hospitals (data not shown in the Table).

A higher proportion of unscreened (34%) than screened children (21%) attended ED whilst overall, similar proportions attended hospital outpatient clinics (63% and 60% respectively). However, the differences between the groups in terms of ED and outpatient attendances were not significant, although there are marked differences in rates of attendance between the contemporaneous and historical unscreened groups. Of those who attended emergency, the average number of attendances per year varied from 0.5 for the screened group to 1.3 for the contemporaneous unscreened groups and 1.6 for the historical unscreened group. The mean number of outpatient attendances per year (by those who attended) was less variable. Any differences were not significant.

Table 2 illustrates the year-by-year utilisation of inpatient, emergency and outpatient services. It can be seen that in the first year of life, the screened group used significantly fewer inpatient services than the combined unscreened group (p=0.01), and each of the contemporaneous and historical screened groups (p=0.01; p=0.04) but significantly more outpatient services than the combined unscreened group (p=0.04). No other significant differences emerged.

Costs of care

A summary of the costs for inpatient, emergency and outpatient hospital services is shown in Table 3. At $A1676 ($US1297), the average total costs per year for the screened group were higher than for the contemporaneous unscreened group ($A1211, $US937) but lower than the historical group ($A2288, $US1770) but it should be noted that in all groups the range of costs was large. The average cost for emergency admissions was significantly lower in the screened group than in the combined unscreened group (p=0.05), but there were no other significant differences in costs.

Discussion

This is the first study to collect data on the costs of MS/MS testing and combine these with actual costs and utilisation of hospital-based services to compare screened and unscreened children with MCADD.

Overall, there were significant differences between screened and unscreened children in the cost per patient of emergency care and in the rate of utilisation of inpatient hospital care. However, these results should be treated with caution given the wide confidence intervals around the differences in costs. Some significant differences emerged when utilisation was analysed on a year-by-year basis. It is not clear what impact the deaths that occurred had on costs. If they had not died, the deceased children would have utilized health services, thus adding to the total costs of care, but if some deaths were due to treatment for decompensation being initiated later in the course of an intercurrent illness rather than a more severe case of the condition, rates of utilization and the average cost per patient would not have been affected.

Despite the potentially serious impact of decompensation episodes on children's development, there were no differences between the groups in terms of either physical development such as height and weight or neuropsychological function. However, they may have produced more subtle differences in terms of cognitive function which are not observable in such young children.

Children in contemporaneous and historical unscreened groups were significantly more likely than those in the screened group to attend the ED and to be admitted as an inpatient during the first year of life. This pattern may be due to repeated attendances and admissions which eventually resulted in a diagnosis. Screened children were significantly more likely to attend outpatient clinics during their first year of life than children in the combined unscreened group. Such a pattern of utilisation certainly reflects the age at which children were diagnosed. The more intensive level of management provided to screened children in their first and second years of life (avoidance of fasting and sick-day regimens) may also have contributed to their lower rates of admission in the first year of life.

The main cost associated with the introduction of screening is that of the test itself, including confirmatory testing, and at $A2.06 ($US1.59) per screened child, does not appear to be excessive. Two issues should be noted. First, during the time of the study, the screening States relied on one machine each but had back-up arrangements in place with another State in case of breakdowns. Since the time of the study, each State has acquired a second machine. Second, the cost of the test covers all the conditions screened for, not only MCADD. Using the notion of opportunity cost, therefore, the cost of the test for MCADD could be $0 as the MS/MS technology would still be used to detect other conditions (such as PKU). On the other hand, it is possible to assign a cost per MCADD test based on actual numbers of tests.

However, the total costs of the screening program will vary by State depending on the cost per screened child, the number of tests performed and the "throughput" of each machine ie the extent to which each machine is utilised at it maximum rate. As the birth rate in Australia is not expected to change substantially and the rate of detection is unlikely to rise, large increases in costs are not expected. Indeed, as the technology improves, an enhanced capacity to computerise the downloading and analysing of tests may decrease costs in the long term.

The study has some important strengths. Because services are centralized, and there are only five collaborating biochemical genetics laboratories serving the whole of Australia, there is almost certain to have been complete ascertainment of children with MCADD. Patients are managed by only nine metabolic physicians, all of whom meet regularly and collaborated on this study, so that management strategies are similar throughout Australia. Care is mainly provided through the specialist children's hospitals, through scheduled ambulatory attendances and telephone contact with the treating physicians in these institutions. Also, we were able to gain information about utilization of hospital services and costs for all identified patients.

However, it also has limitations. Even though we were able to identify all known cases of MCADD in Australia, the small numbers of children in both groups makes comparisons difficult. This will inevitably lead to problems of power in identifying significant differences. However, there is no reason to believe that this group of children with MCADD is different in terms of illness experience (and therefore utilization) than those in other parts of the developed world. Whilst there are no missing children there may be some missing or mis-reported data in terms of numbers of episodes of care. This is particularly likely to apply to ED attendances and inpatient episodes of care which occurred outside the major pediatric

hospitals, as this information was sought from parents and clinicians but not by investigation of case notes.

We have only included the costs from a hospital perspective. Such costs are likely to be different from those in other countries for reasons connected with both the structure of the health system and management practices. For example, practices adopted in Australia, such as regular monitoring of children and the provision of allied health care (eg nutrition, physiotherapy etc) via hospital-based ambulatory clinics may not be a feature of other health systems (eg in the USA). Finally, we have no way of knowing what healthcare costs are incurred by those children with MCADD who remain undiagnosed.

In summary, it seems as though the third scenario suggested in the introduction has occurred. That is, early detection has resulted in an increased rate of utilization per patient of outpatient services. However, as emergency and inpatient admissions were prevented, costs were lower amongst the screened group. The key question is whether patterns of management affect physical and neuropsychological development, as this would certainly affect long-term costs. Answering such a question would require further research, preferably a randomised controlled trial of different management strategies.

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Table 1: Health care utilisation in the first 4 years of life: comparison of screened group with a) unscreened group (total group), b) contemporaneous unscreened and c) historical unscreened groups.

	Screened n=24	All unscreened n=35	p	Contemporaneous unscreened n=16	p	Historical unscreened n=
Inpatient						
% of patients using	42	71	0.03	63	0.33	79 (63)[c]
Mean #pa[a] if used (sd)	1.1 (1.4)	0.9 (0.9)		0.7 (0.5)		1.1 (1.1)
Mean los pa[b] if used (sd)	2.5 (2.6)	2.6 (3.1)		1.7 (1.3)		3.2 (3.8)
Emergency						
% using	21	34	0.38	50	0.09	21 (21)[d]
Mean #pa if used (sd)	0.5 (0.2)	1.3 (1.3)		1.2 (1.3)		1.6 (1.6)
Outpatients						
% using	63	60	1.00	69	0.75	53 (37)[e]
Mean #pa if used (sd)	1.5 (1.0)	1.6 (1.4)		1.4 (1.2)		1.9 (1.7)

All p-values by Fisher's Exact test

[a] Mean number of admissions per annum as an inpatient among those admitted at least once

[b] Mean length of stay per annum among those who were admitted to hospital

[c,d,e] The % of patients in this group from States which had introduced screening

Table 2: Total health care utilization by year of life, % using (number using): comparison of screened group with a) unscreened group (total group), b) contemporaneous unscreened and c) historical unscreened groups.

	Screened n=24	All unscreened n=35	p	Contemporaneous unscreened n=16	p	Historical unscreened n=19[b]	p
Inpatient							
Year 1	13 (3)	46 (16)	0.01[a]	50 (8)	0.01	42 (8)	0.08
Year 2	25 (6)	40 (14)	0.27	25 (4)	1.00	53 (10)	0.20
Year 3	13 (3)	20 (7)	0.51	13 (2)	1.00	26 (5)	0.68
Year 4	8 (2)	26 (6)	0.17	19 (2)	0.37	32 (4)	0.21
Emergency							
Year 1	8 (2)	26 (9)	0.17	50 (8)	0.007[a]	5 (1)	1.0
Year 2	8 (2)	17 (7)	0.45	19 (3)	0.37	16 (4)	0.64
Year 3	13 (3)	14 (5)	1.00	25 (4)	0.41	5 (1)	0.62
Year 4	0	14 (5)	0.07	19 (3)	0.06	11 (2)	0.44
Outpatient							
Year 1	63 (15)	34 (12)	0.04[a]	38 (7)	0.20[a]	32 (5)	0.06
Year 2	50 (12)	46 (16)	0.80	38 (6)	0.53	53 (10)	0.76
Year 3	38 (9)	37 (12)	1.00	38 (5)	1.00	37 (7)	1.0
Year 4	17 (4)	26 (9)	0.53	25 (4)	0.69	26 (5)	0.43

All p-values by Fisher's Exact test

[a] p=<0.05

[b] The number (%) of children in the historical unscreened group from screening States: inpatient 5 (20%); emergency 2 (33%); outpatient 1 (4%).

Table 3: Average cost per annum ($Aus) in the first 4 years of life: comparison of screened group with a) unscreened group (total group), b) contemporaneous unscreened and c) historical unscreened groups.

	Screened n=24	All unscreened n=35	P[1]	Contemporaneous unscreened n=16	P[1]	Historical unscreened n=19	P[1]
Inpatient							
Mean	1427	1392	0.96	739	0.31	1942	0.56
Difference S-U (95%CI)[2]		35 (-1124, 1798)		687 (-338, 2390)		-515 (-2026, 1402)	
Emergency							
Mean	42	184	0.05	235	0.08	141	0.30
Difference S-U (95%CI)[2]		-142 (-274, -12)		-193 (-383, 0)		-99 (-286, 48)	
Outpatient							
Mean	207	220	0.85	237	0.71	206	0.99
Difference S-U (95%CI)[2]		-13 (-143, 119)		-30 (-176, 131)		1 (-178, 163)	
Total cost							
Mean	1676	1796	0.88	1211	0.53	2288	0.55
Difference S-U (95%CI)[2]		-120 (-1367, 1737)		465 (-694, 2247)		-612 (-2355, 1503)	

[1]All p-values by t-test; [2] BCa bootstrap confidence intervals[14]