

Collaborative use of a long-term follow-up database after newborn screening: initial outcomes for medium-chain acyl CoA dehydrogenase deficiency



Region 4 Genetics Collaborative
Michigan Public Health Institute
Okemos, MI, United States

Region 4 Collaborators: our Priority 2 Project Workgroup

Metabolic Clinicians and State Health Department NBS Specialists

- ◆ Illinois
- ◆ Indiana
- ◆ Kentucky
- ◆ Michigan
- ◆ Minnesota
- ◆ Ohio
- ◆ Wisconsin



Region4
Genetics Collaborative

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- ◆ Heartland Centers (Missouri, Oklahoma, Arkansas)

Use a condition registry as a research platform

- ◆ Document interventions that can be assessed with data in IBEM-IS
- ◆ Plan initial projects should examine
 - “Natural” history
 - Short term outcomes

At enrollment we request registry subjects to consider consent to allow continuing contact, anticipating engaging them as participants in future research trials.

MCAD deficiency: a place to start

- ◆ Sufficiently rare that no one practitioner sees enough
- ◆ Sufficiently common that cooperation in data gathering can yield relatively rapid meaningful data
- ◆ Some, but not complete agreement about treatment strategies

Hypotheses developed to assess initial data collection on MCAD deficiency patients

- ◆ **Children with the highest C8 screening values will be most symptomatic**
- ◆ **The highest C8 values will be found in children who are 985 A>G homozygotes**

Methods for collecting project data using the IBEM-IS

- ◆ Obtain prospective informed consent
- ◆ Ascertain data as clinic visits begin
- ◆ Gather data elements for initial presentation “enrollment” and at each visit “interval”
- ◆ Enter data at each clinic visit via web-based entry forms

Microsoft Internet Explorer - PatientPlanner

Address: https://patient.docsite.com/DesktopDefault.aspx?dsvareGQHhOyfrqZLYADUTdQueEV+YZ7LgQwq+w9d3qgAf0=

DocSite™ PatientPlanner

Welcome SBerry! | User's Guide | Logoff | Contact Support

Home Actionable Patients Patient Data Referrals Reports Conditions|Measures Administration My Account

Sites Add

Metabolic Test Site - Everyc

Patient Search Add

Last Name:

First Name:

DOB:

MRN:

Status: Active

Search Clear

Search All Sites

Patient Reports

Please select a report type:

PDF XLS WORD

Visit Planner

Outreach Report: Phone

Patient Flow

Patient Flow: All Measures

Patient Handout

Progress Note VP and Patient Handout

Patient Edit

Last Name: **Another** First Name: **Lexy** DOB: **2/20/2007**

Gender: **Female** SSN: **Not entered** MRN: **Not entered**

Providers

Berry, Susan

Survey Data Entry

Select a survey: Metabolic - Interval MCADD Survey

Save Cancel

Measure Date Set all dates

Interval History/Concerns

Measure Name	Date	Value
! Dx Code (ICD-9)	<input type="text"/>	<input type="checkbox"/> MCADD (277.85) <input type="checkbox"/> other
! Other Diagnoses (free text)	<input type="text"/>	
		<input type="checkbox"/> Active <input type="checkbox"/> Closed <input type="checkbox"/> Deceased <input type="checkbox"/> Lost to follow up <input type="checkbox"/> Moved out of

Follow up Status

Done

Web-based data entry

Microsoft Internet Explorer - ReportViewer

Print Date: 8/31/2007 Page 1 of 5

Date of Visit: ___/___/___

Provider: Susan Berry **Patient:** Lexy Another **Gender:** Female **Phone:**

Visit Provider: **MRN:** **DOB:** 2/20/2007 (0)

Conditions: MCADD Interval Update, MCADD Enrollment **Preferred Language:** English

Comorbidities: **First Measure Date:** 02/21/2007

Allergies:

Medications:

Administrative	Today's Action	Last Value	Date Last	Pt. Goal	Int. Days	Due Date
! Unique Registry ID (2digFIPS/2digBirthYr/1digCenter/3digAssession)		27071fakeMN002	02/27/07		Per Visit	
Permission to contact about research - I agree to be contacted with information on potential future research applicable to my inborn error of metabolism that becomes available	Yes, No	Yes	02/27/07		Per Visit	
Permission for compensation - I agree that identifying information about me may be used or disclosed as necessary to provide compensation if I am eligible for compensation	Yes, No	Yes	02/27/07		Per Visit	
! Is patient followed by more than one metabolic center?	Yes, No, Unknown, N/A	No	02/27/07		Per Visit	
! Maternal education - highest grade level completed	1-8 years (grade), 9-12 years (no diploma), Completed high school, Training after high school (not college), Some college, College graduate, Post-graduate	College graduate	02/27/07		Per Visit	
! Paternal education - highest grade	1-8 years (grade), 9-12 years (no diploma),	Post-graduate	02/27/07		Per Visit	

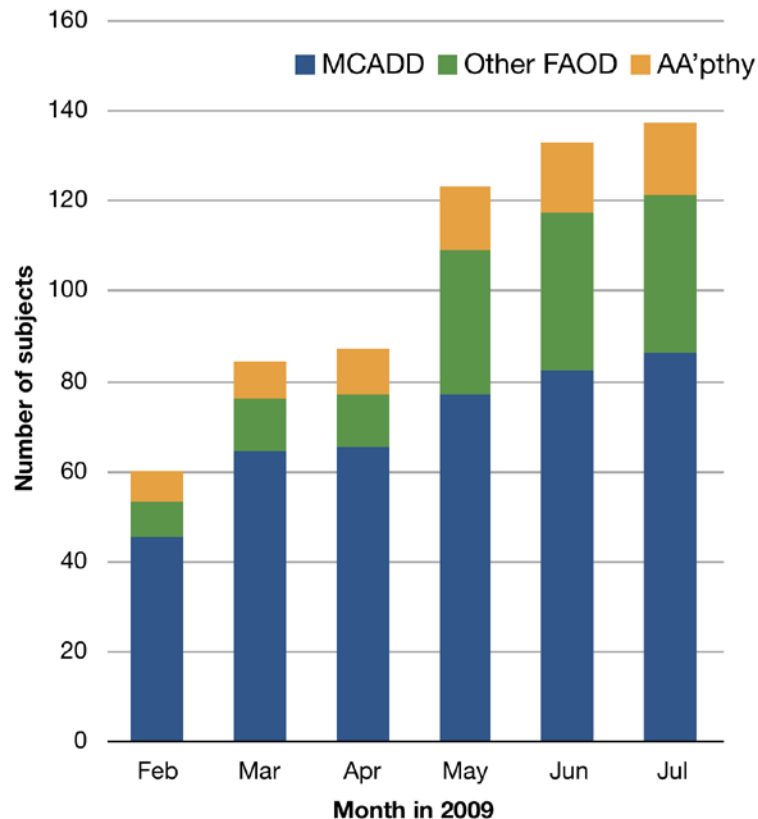
8.5 x 11 in

1 of 5

Done

Can generate paper forms for data collection in clinic

Region 4 cumulative enrollment Feb-Jul 2009



- ◆ 42 infants with MCAD deficiency ascertained by NBS: C8 as informative value
 - Report from system sought data about lab abnormalities or other symptoms at the time of initial metabolic presentation.
 - Many had genotype done; data sought in report.
- ◆ Stratified by C8 values
 - Bottom half “lo” range 0.4-8.69 $\mu\text{Mo}/\text{mL}$
 - Top half “hi” range 8.97-38.8 $\mu\text{Mo}/\text{mL}$

Higher C8 values on NBS are associated with more symptoms/laboratory findings

- ◆ “Lo” range patients: 18 had no labs done, no abnormal labs and/or had no symptoms
 - 1 - abnormal liver function tests; dehydration
 - 1 - respiratory distress due to prematurity
 - 1 - admitted for possible apnea but apnea was not confirmed, poor feeding.
- ◆ “Hi” range patients: 14 had no labs done, no abnormal labs and/or had no symptoms
 - 1 - loose stools
 - 1 - dehydration and irritability
 - 1 - fever, irritability and hypoglycemia
 - 1 - pallor, limp, poor feeding, hypoglycemia
 - 1 - poor breast feeding, lethargy, hypoglycemia, uric acid elevated
 - 1 - hypoglycemia
 - 1 - jaundice

Infants with “Hi” C8 value on NBS are more likely to be 985 A>G homozygotes

- ◆ “Lo” range infants
 - 17 with two mutations
 - 5 were 985 A>G homozygotes
- ◆ “Hi” range infants
 - 16 with two mutations
 - 11 were 985 A>G homozygotes

Conclusions

- ◆ Higher C8 values on NBS are associated with an increased risk for symptoms for affected newborns
- ◆ Infants with higher C8 values are more likely to be 985 A>G homozygotes
- ◆ IBEM-IS provided a successful platform for investigating hypotheses
- ◆ *Collaboration in data gathering may help us improve outcomes after newborn screening*

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<http://region4genetics.org/>

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