Newborn Screening for the Homocystinurias
(Classical Homocystinuria and Remethylation Disorders)
Expanding and Improving Biomarkers and Algorithms

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New England Newborn Screening Program

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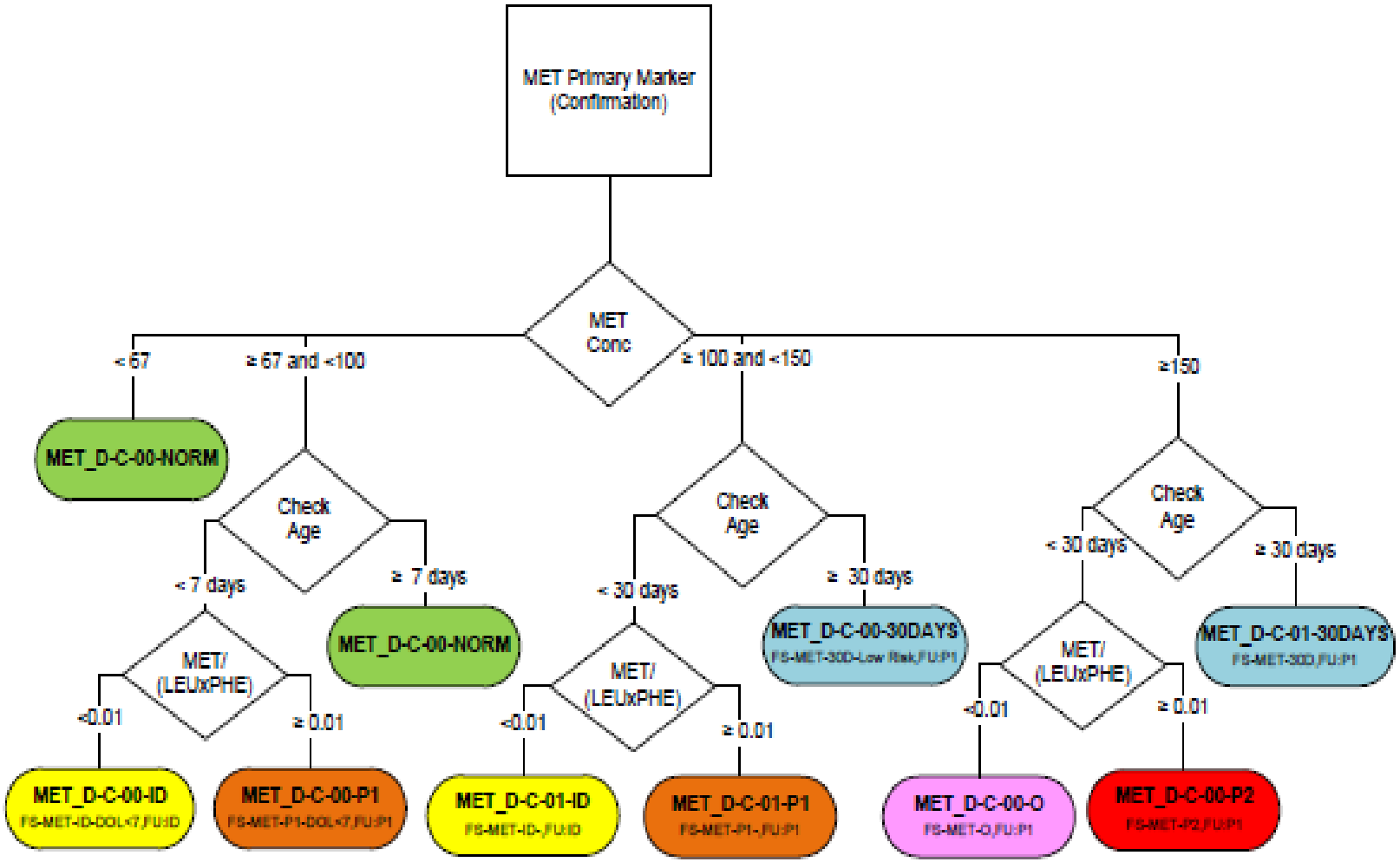
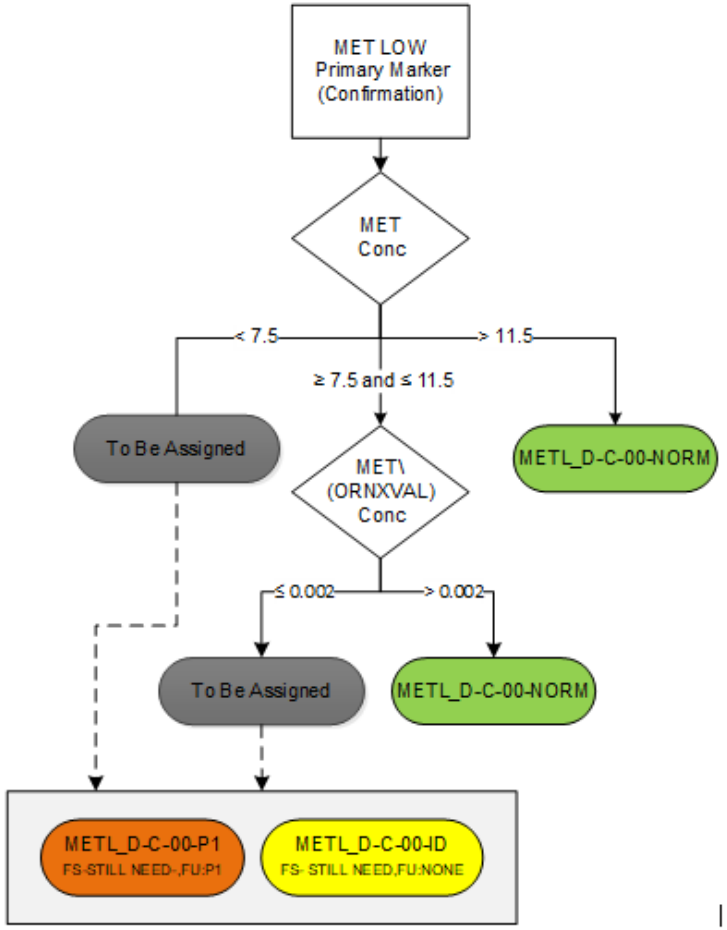
Current Screening and Algorithm for Classic HCU

Primary Marker: ↑Methionine

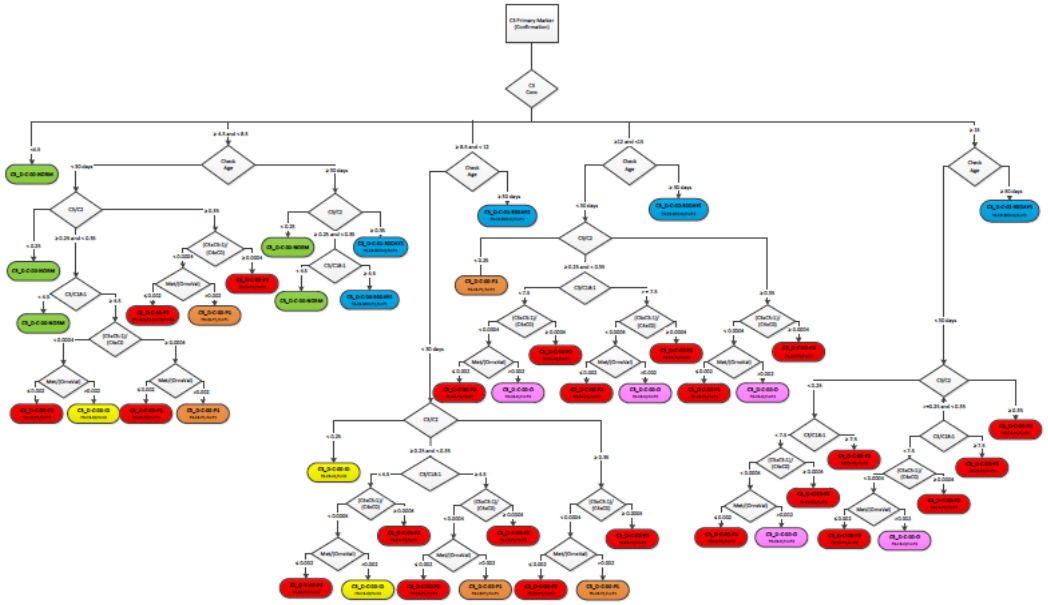


Current Screening and Algorithm for Remethylation Disorders

Primary Marker - ↓Methionine



↑C3



Strategies to Improve Screening Performance Classical HCU

Analytes	Specificity	Sensitivity
1. Decrease the ↑Met cut-off	↓	↑
2. #1 & Met/(Leu x Phe)	↑	↑
3. #2 & **2nd Tier** Hcy	↑↑	↑
4. #2 & **2nd Tier** Hcy, cystathionine & cysteine	↑↑↑	↑

Strategies to Improve Screening Performance Remethylation Disorders

Analytes	Specificity	Sensitivity
1. Increase the ↓Met cut-off	↓	↑
2. #1 & Met/(Val x Orn)	↑	↑
3. #2 & **2nd Tier** Hcy	↑↑	↑
4. #2 & **2nd Tier** Hcy, cystathionine & cysteine	↑↑	↑
5. C3 & C3/C2* & 2nd Tier MMA	↔	↔

*Helps to distinguish CblC, CblD and CblF from other Remet disorders

Specific Aims

- Develop, optimize, and validate a simple, robust and high throughput LC-MS/MS 2nd tier test: total homocysteine (tHcy), cystathionine, total cysteine (tCys) and MMA
- Determine reference ranges in neonates using DBSs
- Retrospectively analyze confirmed Classical and ReMet HCU disorders
- Assess, improve, and expand current algorithms for HCU using additional markers

Acknowledgments

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Centers for Disease Control

HCU Network America

BREAKING NEWS!

HCU Network America Announces the Recipient of their First Newborn Screening Research Grant.

August 31, 2022 - The New England Newborn Screening Program, an initiative of UMass Chan Medical School's Commonwealth Medicine division, received the award to explore the development of reference ranges for additional newborn screening markers for early detection of classical homocystinuria and remethylation disorders. The research, led by Devinder Kaur, PhD, assistant professor of pediatrics at UMass Chan, aims to establish normal reference ranges for total homocysteine, along with other analytes collected by healthy newborns during the 24-48 newborn screening period. This will support the development of algorithms that will incorporate information on a variety of other variables in the future. Dr. Kaur, who is leading the research, joined the New England Newborn Screening Program in 2017 as a senior scientist.

To read the full press release, visit https://bit.ly/HCUNBSGrant

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