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Newborn Screening for Homocystinuria in NY

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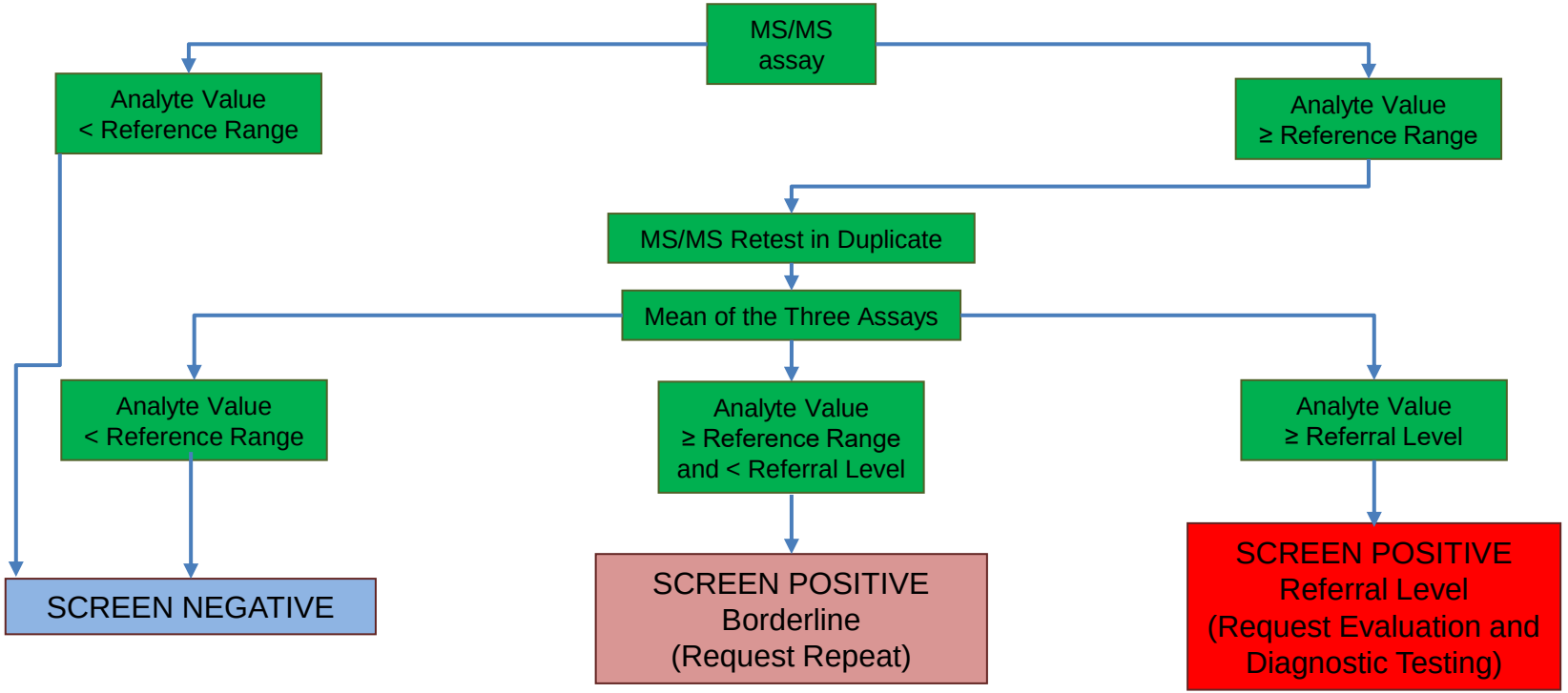
NYS Newborn Screening By the Years

- 1965 – 1 condition (Phenylketonuria)
- 1968 – Galactosemia and Maple Urine Syrup Disease
- 1975 – Hemoglobinopathies and Homocystinuria
- 1978 – Congenital hypothyroidism
- 1987 – Biotinidase deficiency
- 1997 – HIV exposure
- 2004 – MS/MS conditions (n=20)
- 2005 – MS/MS conditions (n=13)
- 2006 – Krabbe disease
- 2010 – Severe combined immunodeficiency
- 2013 – Adrenoleukodystrophy
- 2014 – Pompe disease
- 2018 – GAMT deficiency, spinal muscular atrophy and Mucopolysaccharidosis type I

Abnormal Newborn Screening w/ ↑Methionine

Year	Specimens	Referrals	Confirmed homocystinuria	Confirmed hypermethioninemia
2022	246,839	10	0	0
2021	251,262	4	0	0
2020	246,936	4	0	0
2019	261,866	9	0	1
2018	263,133	2	1	0
2017	262,360	3	0	2
2016	262,853	5	0	1
2015	265,537	3	0	0
2014	267,935	5	0	0

Current Practice & Algorithm: Homocystinuria



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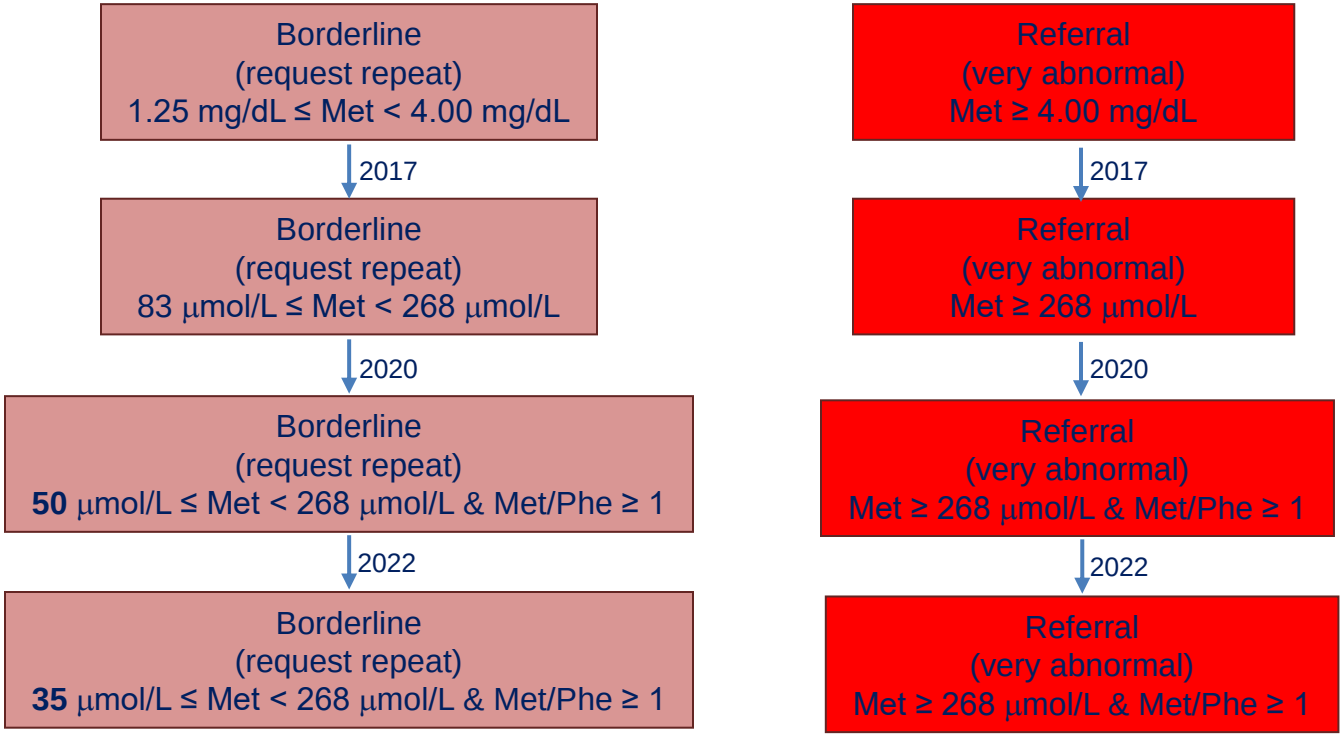
Strategy to Improve Performance: Homocystinuria

Analytes	Specificity	Sensitivity
Decrease the ↑Met* cut-off	↓	↑
Decrease the ↑Met* cut-off & add ↑tHcy	↑	↑

Met*: Methionine; tHCY = total homocysteine

Met Cut-off Optimization: Homocystinuria



Met = Methionine; Phe = Phenylalanine

NBS Case 1: Homocystinuria

Case 1:

- 7-pound, full term boy, normal pregnancy and uncomplicated delivery
- Normal NBS: Met 1.18 mg/dL (normal <1.25 mg/dL)
- 14-year-old with hypotonia, joint contractures, scoliosis, pectus excavatum, mild mitral valve prolapse, and mild intellectual disability
- A pathogenic variant in the *CBS* gene in trans with a 5.9 Mb deletion on chromosome 21q22.2q22.3

NBS Case 2: Homocystinuria

Case 2:

- 6-pound girl in the neonatal intensive care unit
- 1st NBS (< 12 hours old): Met 39.49 μmol/L (normal <83 μmol/L).
- 2nd NBS (2 days old): Met 122.65 μmol/L (normal <83 μmol/L). A repeat specimen was required.
- 3rd NBS (15 days old): Met 1,190.24 μmol/L (normal <83 μmol/L). A referral was required.
- A pathogenic variant and a variant of uncertain significance identified in the *CBS* gene.

Implementing Homocysteine to NBS: Homocystinuria

- Acquire linearity, precision, and accuracy with CDC calibrators
- Run samples to check effects on marker concentration
- Evaluate any positive controls and determine reference ranges
- Analyze confirmed homocystinuria disorders from archived samples
- Assess, improve, and expand current algorithms for homocystinuria