

Reduction in the Newborn Screening False-Positive Results Among Patients in a NICU Following Implementation of a New Collection Protocol



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BACKGROUND & SIGNIFICANCE

NBS: MS / MS

- **Overall False Positive rate 0.13-0.3%**

(Feuchtbaum et al. 2006;

Schulze, et al. 2003;

Zytkovicz et al. 2001)

- **One half of the FP results are from NICU patients (5 % of the population)**


(Zytkovicz et al. 2001)



NEONATOLOGIST REACTION 2005



NEONATOLOGIST REACTION 2011

A photograph of a man and a woman sitting on white lounge chairs on a sandy beach, facing the ocean. The woman is on the left, wearing a yellow and white striped towel. The man is on the right, wearing a red and white striped towel. They are holding hands. The ocean is a deep blue, and the sky is clear. Two speech bubbles are overlaid on the image. The first speech bubble, on the left, contains the text 'The NBS program called...'. The second speech bubble, on the right, contains the text 'Don't worry, must be another false positive'.

**The NBS
program
called...**

**Don't worry,
must be
another false
positive**

FALSE POSITIVE RESULTS IN NICU

- Sick Babies
- Preemie Babies:

Increased FPR in preterm infants

(Slaughter et al. 2010; Zaffanello et al. 2003)

- TPN (AA's 2.8 - 3.5 g/kg/day)

(Matern et al. 2007, Chace, et al. 2010)



GOAL

Assess the impact of a new collection protocol on the False Positive Results in a level IIIc NICU population

PATIENTS

- Babies born at St. Joseph's Hospital and admitted to CHOC-NICU
- Population divided according to birth weight (BW)
 - <1000 g
 - 1000 -1500 g
 - >1500 g
- NBS sample collected by heel - stick according to the State of California NBS protocol (single specimen, ideally 24-48 h)
- CHOC – IRB approval was granted for data collection and review

METHODS

Jan 2009 – Dec 2010

- Retrospective data collection
- NBS specimen collected regardless of TPN administration



Jan 2011 – New Protocol

- Stop TPN for 3h prior to collection of NBS specimen
- Infuse D10%w while TPN stopped, using medication port of “tri-fuse” connector



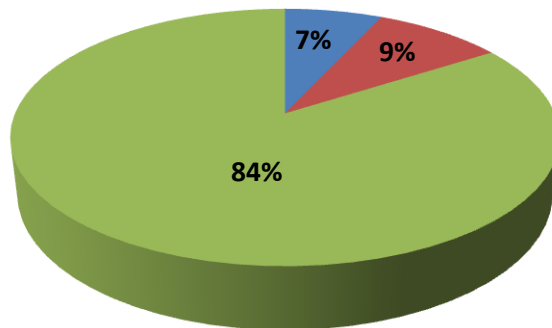
RESULTS

| | Jan 2009 - Dec 2010 | | |
|--------------|---------------------|-----------|--------------|
| | <i>n</i> | <i>FP</i> | |
| Total | 596 | 33 | 5.54% |
| <1000 g | 41 | 12 | 29.27% |
| 1000-1500 g | 54 | 6 | 11.11% |
| >1500 g | 501 | 15 | 2.99% |

| | Jan-June 2011 | | |
|--------------|---------------|-----------|--------------|
| | <i>n</i> | <i>FP</i> | |
| Total | 152 | 2 | 1.32% |
| <1000 g | 10 | 2 | 20.00% |
| 1000-1500 g | 12 | 0 | 0.00% |
| >1500 g | 130 | 0 | 0.00% |

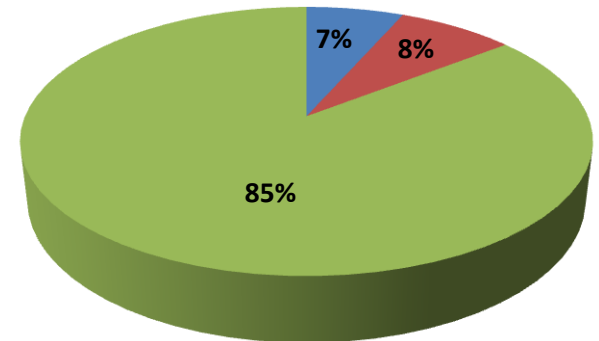
Jan 2009 - Dec 2010

■ <1000 ■ 1000 - 1500 ■ >1500



Jan-June 2011

■ <1000 ■ 1000 - 1500 ■ >1500



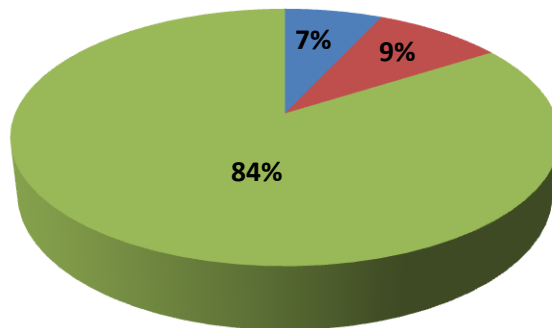
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|--------------|--------------------|-----------|--------------|
| | <i>n</i> | <i>FP</i> | |
| Total | 256 | 4 | 1.56% |
| <1000 g | 16 | 3 | 18.75% |
| 1000-1500 g | 20 | 1 | 5.00% |
| >1500 g | 220 | 0 | 0.00% |

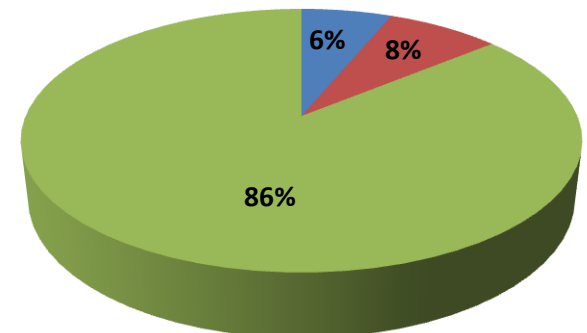
Jan 2009 - Dec 2010

■ <1000 ■ 1000 - 1500 ■ >1500



Jan - October 2011

■ <1000 ■ 1000 - 1500 ■ >1500



RESULTS

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|--------------|---------------------|-----------|----------------|--------------------|-----------|----------------|
| | <i>n</i> | <i>FP</i> | | <i>n</i> | <i>FP</i> | |
| Total | 596 | 33 | 5.54% * | 256 | 4 | 1.56% * |
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| 1000-1500 g | 54 | 6 | 11.11% | 20 | 1 | 5.00% |
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* Difference between the two time periods: 72 % reduction
 Statistically significant (P = 0.009)

The new protocol was easy to implement, and no adverse events were reported.

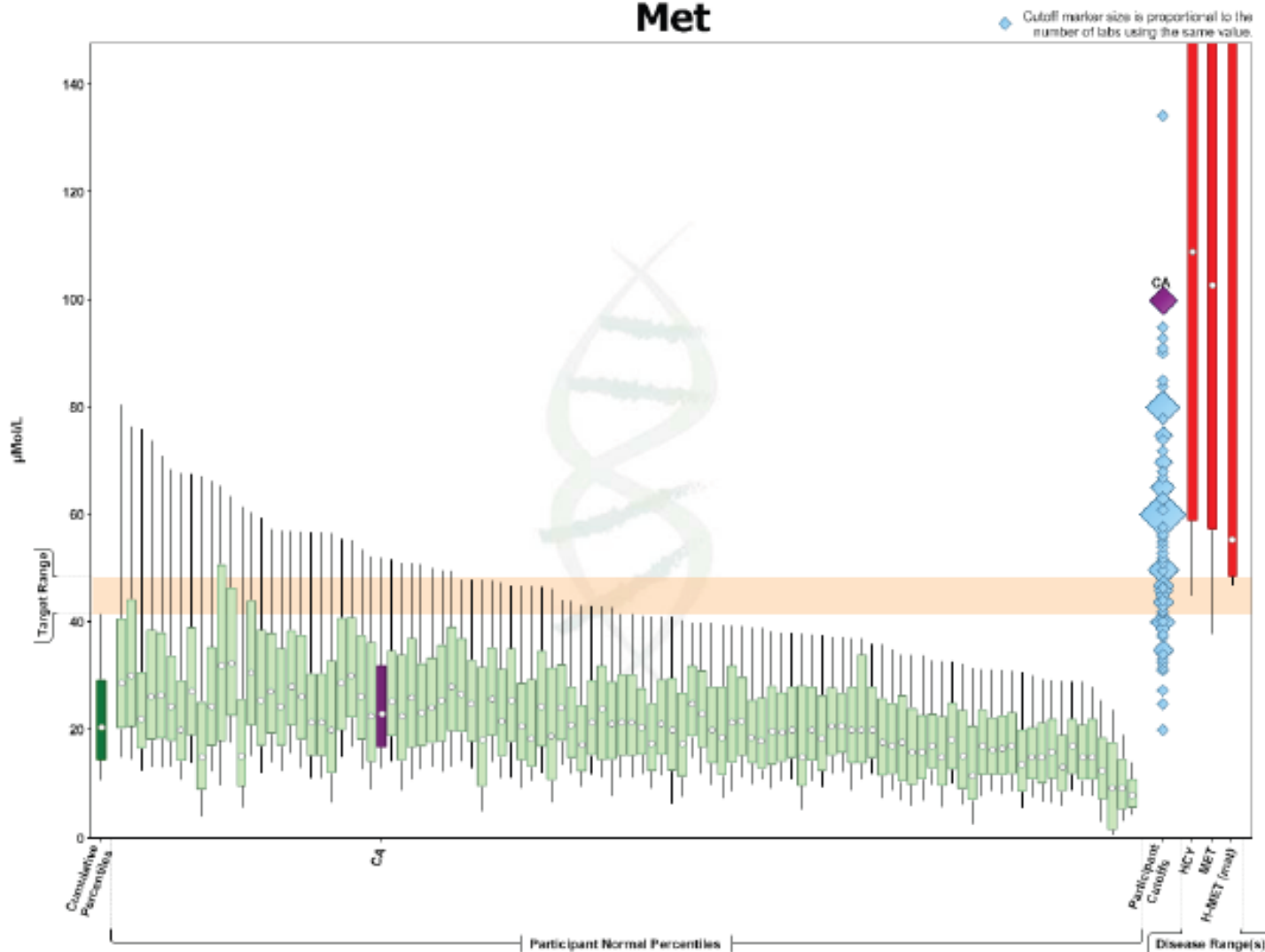
RESULTS

| | Jan 2009- Dec 2010 | | | Jan - October 2011 | | |
|---|--------------------|-----------|-------|--------------------|-----------|-------|
| | <1000 | 1000-1500 | >1500 | <1000 | 1000-1500 | >1500 |
| Positives for single AA disorder | | | | | | |
| Met (MAT, Homocystinuria) | 2 | 2 | 3 | 2 | 1 | - |
| Leu +Leu/Ala (MSUD) | - | - | 3 | - | - | - |
| Phe + Phe/Tyr (PKU) | - | - | 1 | - | - | - |
| Positives for single AC disorder | | | | | | |
| C5 (IVA, 2MBCDD) | 2 | 1 | - | - | - | - |
| C8 (MCADD) | 1 | 1 | - | - | - | - |
| Positives 2 or more Disorders | 7 | 2 | 8 | 1 | | |
| Total | 12 | 6 | 15 | 3 | 1 | 0 |

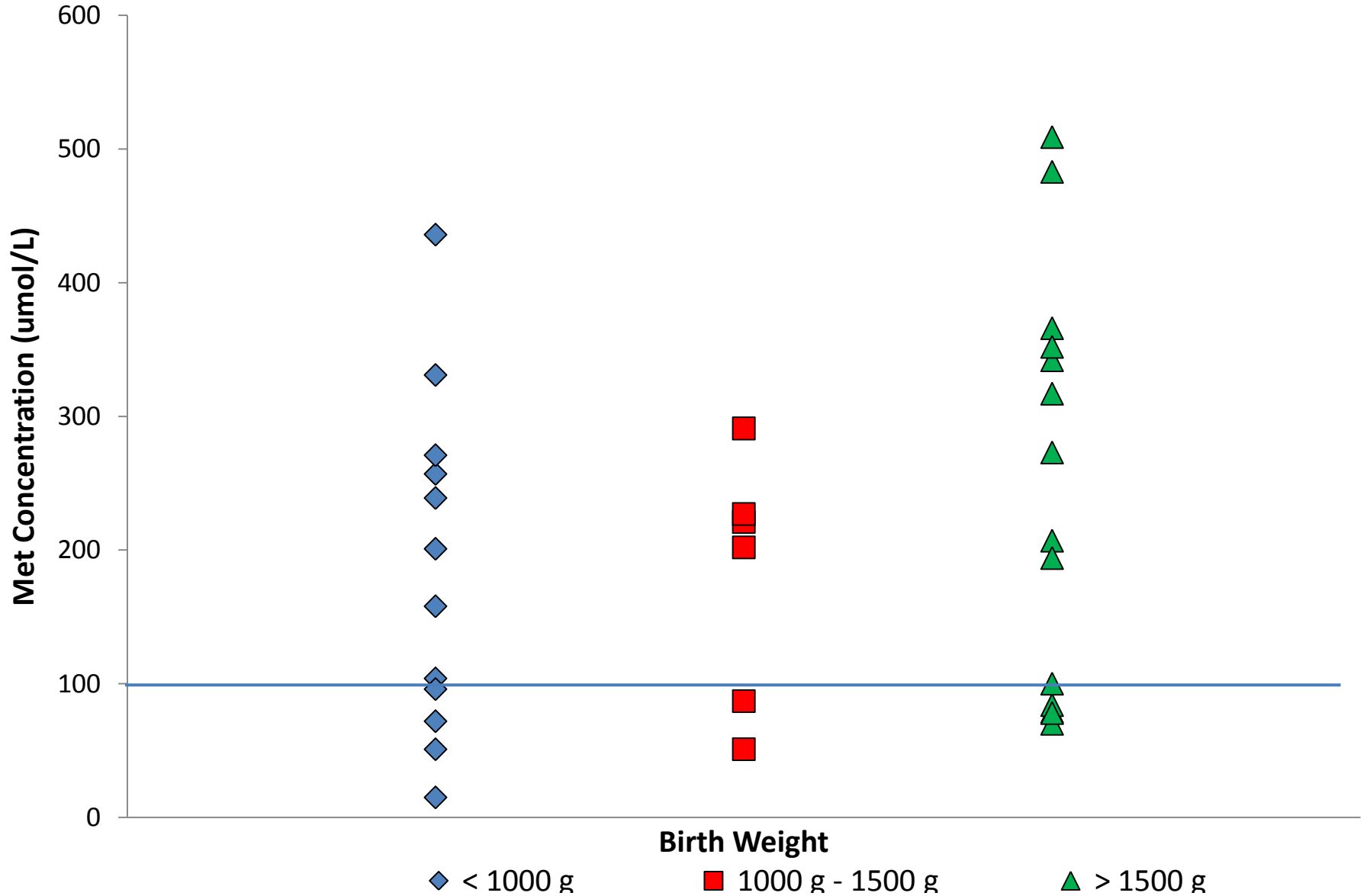
Analyte Comparison Tool

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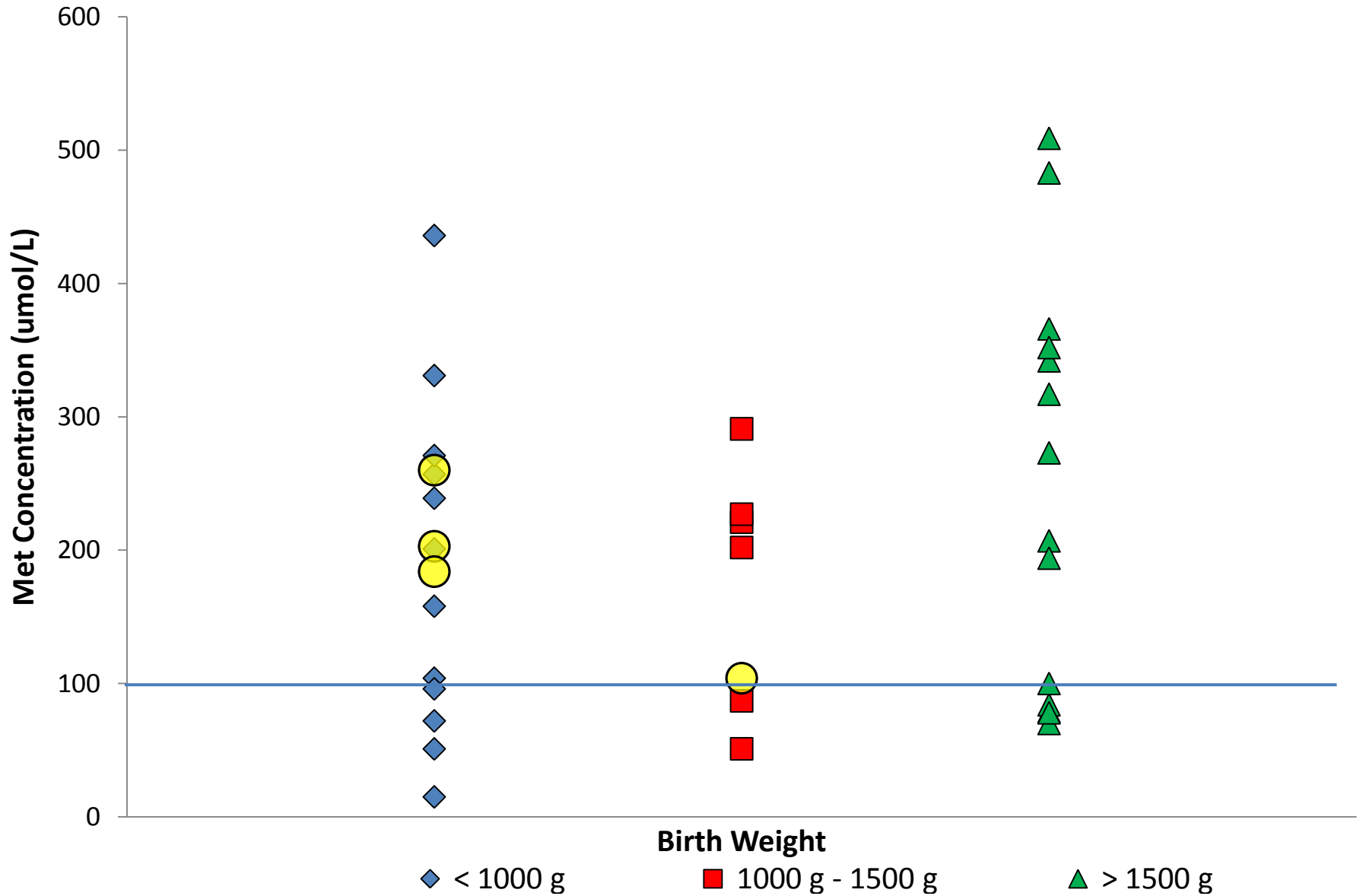
Met



Met Level in NBS Sample 2009-2010



Met Level in NBS Sample



RESULTS

| | Jan 2009 - Dec 2010 (24 months) | Jan - October 2011 (10 months) | 24 month projection using the new protocol |
|------------------------------|------------------------------------|-----------------------------------|---|
| Total number of patients | 596 | 256 | 614 |
| Total number of FP | 33 | 4 | ~ 10 |
| Number of Confirmatory Tests | 67 | 6 | ~ 24 |
| Blood Volume | 40 ml | 5 ml | ~ 12 |
| Cost of Tests | ~ \$ 13,000 | ~ \$ 700 | ~ \$ 1,680 |
| Cost of Trifuse connector | 0 | ~ \$ 768 | ~ \$ 1850 |
| Total Estimated Cost | ~ \$ 13,000 | ~ \$ 1,468 | ~ \$ 3,700 |
| Personnel: | | | |
| NBS program | | | |
| NICU: Nurses, MD's | \$ | \$ | \$ |
| Lab: Phlebotomists | | | |
| Metabolic Center: GC, MDs | | | |

With the use of the new protocol we project >> 70% reduction in cost.

SUMMARY & CONCLUSIONS

New protocol easy to implement, no adverse events

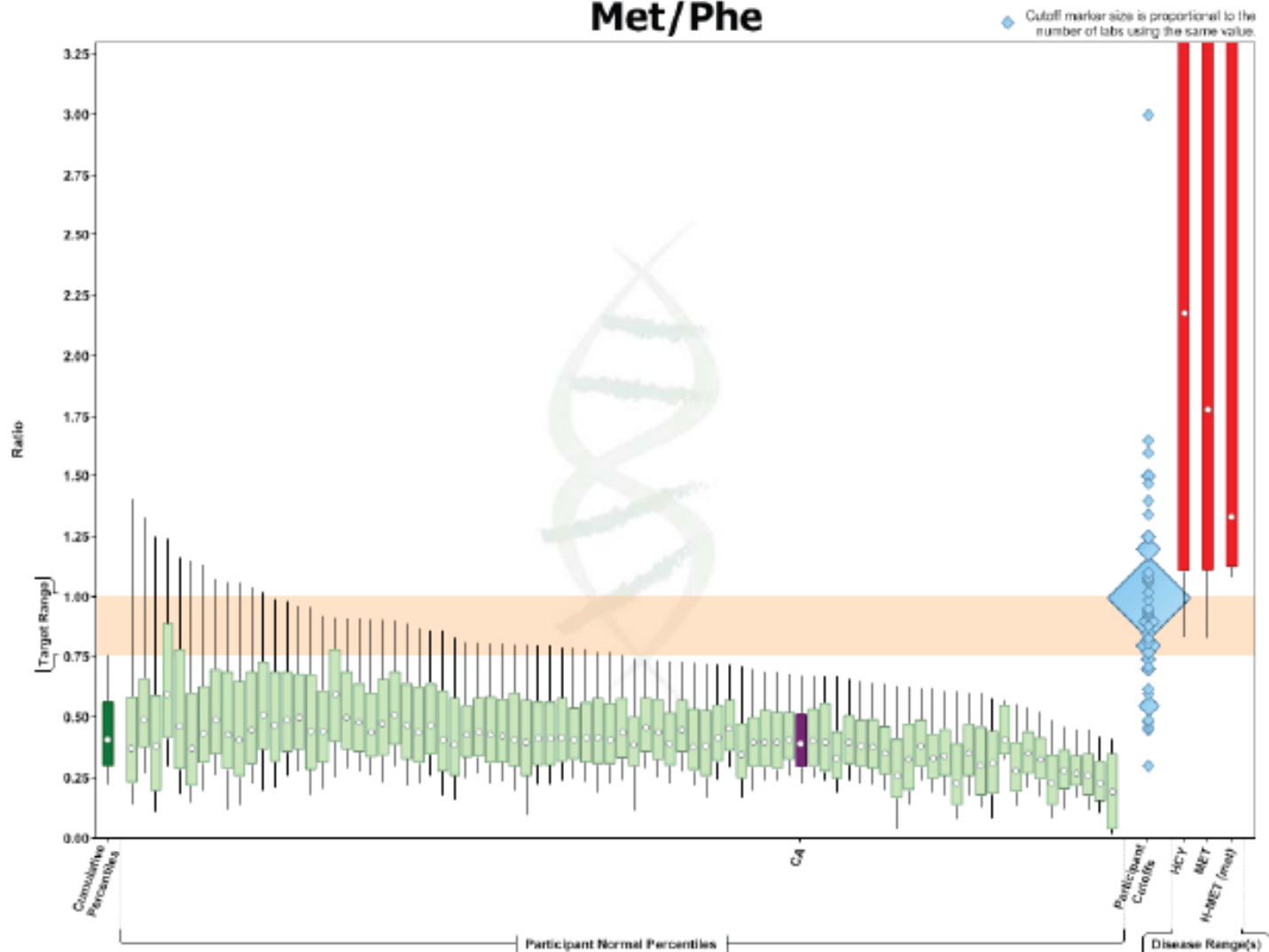
- 72 % reduction in the total FP results
- Significant reduction in cost, number of tests and blood volume.
- Decreased parental anxiety
- No false negatives known to date
- Data collection continues

Thank You

Analyte Comparison Tool

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Met/Phe



Met:Phe in NBS Sample

