Birth Weight and Cytochrome P4503A4 and P4502C9 Activity in Obese Women
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Purpose
Personalized medicine is particularly important in regards to pharmacotherapy; the importance of identifying factors that can minimize variability in drug response to achieve a predictable outcome cannot be emphasized enough. Obesity, a growing problem, can impact drug response through variable drug metabolism. High and low birth weights forecast an increased risk for adult obesity. Additionally, changes that alter fetal physiology and birth weight also affect organs that mediate variability in drug response; for example, the liver and the kidney. Consequently, we hypothesize that birth weight- a surrogate for reprogrammed phenotype- can affect CYP3A4 and CYP2C9 activity in obese women.

Methods
Obese women (18–35 years old; BMI ≥ 30kg*m-2) were divided based on their self-reported birth weight. Venous blood samples were collected at 24 h following a single 125mg oral dose of tolbutamide and 0, 0.25, 0.5, 1, 2, 4, 5, 6, 12, and 24hrs following a single 2mg oral dose of midazolam. Plasma was isolated and stored at –80°C for long-term storage prior to analysis using liquid chromatography mass spectrometry

Results
Tolbutamide C24, a surrogate for clearance, and Midazolam clearance were statistically similar across all birth weights. However, a U- shaped trend was noted across the spectrum of birth weights; with low and high birth weight tending to have a higher Tolbutamide C24 and lower Midazolam clearance.

Conclusion
This data suggests that CYP2C9 and CYP3A4 activity are subject to permanent in utero programming during fetal development. Furthermore, the relationship between birthweight and drug response invokes the potential utility of using this easily available metric to optimize personal medicine.