distribution of gestational age and 64 percent to decreases in gestational age-specific mortality (Table). Patterns were not explained by births and deaths missing gestational age data.

CONCLUSION: Both improvement in the preterm birth rates and survival at preterm gestation resulted in the recent declines in the US infant mortality rate. Possible explanations include improvements in antenatal care such as appropriate use of progestins to prolong gestation, antenatal corticosteroids to enhance pulmonary maturation, maturation, maternal-fetal transfer to appropriate levels of care and general improvements in neonatal care.

Decrease in infant mortality rates, 2007-2013.

Contribution of gestational age distribution	Contribution of gestational age-specific mortality	Sum of components	Percent due to gestational age distribution	Percent due to gestational age-specific mortality
-0.262	-0.458	-0.721	-36.4	-63.6

241 Perinatal factors associated with moderate to severe neurological injury at two years of age following periviable delivery

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OBJECTIVE: The aim of the study was to evaluate whether perinatal factors are associated with neurological injury at two years of age following periviable delivery.

STUDY DESIGN: This was a non-planned secondary analysis of the previously published Maternal-Fetal Medicine Units Network study assessing the effect of antepartum magnesium sulfate administration on adverse outcomes among neonates born prior to 32 weeks gestation (BEAM study). For the current study, assessment of moderate to severe neurological injury at two years of life included mental developmental index (MDI) $<$ 85 and MDI $<$ 70. We restricted the analysis to neonates born between 23 0/7 and 25 6/7 weeks gestation. After excluding neonates with major malformations, maternal demographic and perinatal factors were compared between those with and without neurological impairment at two years of age. Categorical variables were compared using chi-squared test. Non-parametric variables were compared using the Mann-Whitney U test. Logistic regression analysis was performed to assess the prediction of moderate to severe impairment. Two-sided p-values less than 0.05 were considered statistically significant.

RESULTS: 305 neonates were born between 23 0/7 and 25 6/7 weeks gestation. Of those, 180 underwent MDI assessment. None of the maternal demographic factors studied, including maternal age, BMI, race, smoking status, and education level, were associated with adverse neurological outcomes. In addition, none of the perinatal factors, including mode of delivery, chorioamnionitis, birth weight, gestational age at delivery and fetal gender, were found to be significantly different between those with and without the adverse neurological outcomes. None of the factors studied in the logistic regression model were found to significantly predict adverse neurologic outcomes.

CONCLUSION: None of the perinatal factors studied included mode of delivery were associated with moderate-to-severe neurological injury at two years following periviable delivery.

Variable	MDI<70 (n=66)	MDI>70 (n=114)	p-value	MDI<85 (n=116)	MDI>85 (n=64)	p-value
Maternal age (years, SD)	26.9 (5.5)	27.3 (5.6)	0.747	27.1 (5.4)	27.4 (5.9)	0.736
Pre-pregnancy BMI (SD)	28.7 (7.5)	26.6 (6.6)	0.068	27.4 (7.4)	27.2 (6.2)	0.999
Maternal race			0.831			0.135
African American	31 (47.0%)	54 (47.3%)		58 (50.0%)	27 (41.2%)	
Caucasian	18 (27.2%)	38 (33.3%)		30 (25.8%)	26 (40.6%)	
Hispanic	15 (22.7%)	19 (16.6%)		26 (22.4%)	8 (12.5%)	
Asian	1 (1.5%)	1 (0.9%)		1 (0.8 %)	1 (1.6%)	
Native American/Other	1 (1.5%)	2 (1.8%)		1 (0.8%)	2 (3.1%)	
Smoking	20 (30.3%)	27 (23.7%)	0.330	30 (25.9%)	17 (26.6%)	0.918
Education (mean years of education, SD)	11.9 (2.6)	12.1 (2.4)	0.417	11.9 (2.6)	12.3 (2.4)	0.176
Birthweight (mean grams, SD)	721.4 (111.2)	726.1 (116.1)	0.833	713.2 (105.0)	744.6 (127.1)	0.169
GA at delivery (weeks)	25.1 (0.6)	25.2 (0.5)	0.964	25.1 (0.5)	25.2 (0.5)	0.213
Fetal gender			0.065			0.718
Male	36 (54.5%)	46 (40.3%)		54 (46.6%)	28 (43.8%)	
Female	30 (45.5%)	68 (59.7%)		62 (53.4%)	36 (56.2%)	
Mode of delivery			0.828			0.950
Vaginal	37 (56.0%)	62 (54.4%)		64 (55.2%)	35 (54.7%)	
Cesarean	29 (44.0%)	52 (45.6%)		52 (44.8%)	29 (45.3%)	
Chorioamnionitis	14 (21.2%)	26 (22.8%)	0.804	25 (21.6%)	15 (23.4%)	0.771
Steroid use	66 (100%)	112 (98.2%)	0.279	116 (100.0%)	62 (97.0%)	0.056
Magnesium study group	28 (42.4%)	57 (50.0%)	0.327	53 (45.7%)	32 (50.0%)	0.579

242 Gene set enrichment investigation of maternal exome variation in spontaneous preterm birth (SPTB)

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OBJECTIVE: As discovery science has moved from candidate gene testing to systems biology, several powerful new gene set algorithms have been developed to identify associated biologic pathways. We hypothesized that these new algorithms could identify promising biologic pathways associated with SPTB.

STUDY DESIGN: Exome sequences from 138 women from GPN with $\geq$1 SPTB $<$37 wks (cases) were compared to 1253 females from the 1000 Genomes Project (controls) using Variant Annotation, Analysis & Search Tool (VAAST), a probabilistic search tool for identifying disease-causing variants. The median GA of the earliest SPTB was 30.1 wks. Genes scored by VAAST with p$<$1e-4 were then analyzed by 3 online tools: (1) Protein Analysis Through Evolutionary Relationships (PANTHER) (2) Database for Annotation, Visualization, and Integrated Discovery (DAVID), and (3) Disease Association Protein-Protein Link Evaluator (DAPPLE). These tools group genes into gene sets, pathways, & gene ontology (GO) groups. They assess for over-/under- representation (PANTHER), gene groupings (DAVID), and connectivity between known gene protein products (DAPPLE). VAAST results were also prioritized using Phenotype Driven Variant Ontological Re-Ranking Tool (PHEVOR) and evaluated for burden using GROUPER; both of these new VAAST algorithms used an established PTB candidate gene list (dbPTB).

RESULTS: 440 genes identified by VAAST (recessive inheritance, locus heterogeneity) had p$<$1e-4. PANTHER revealed that more genes are categorized into GO Reproduction and Death groups than expected by chance (Table). Selected candidate PTB genes in each GO group

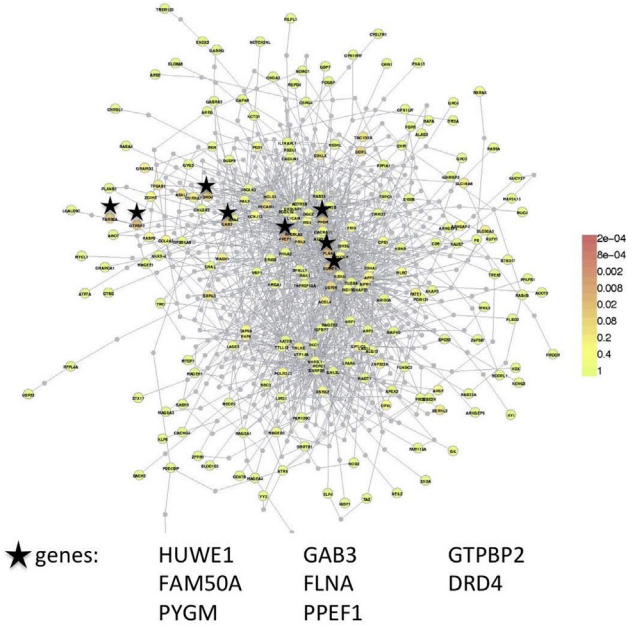
are also shown in the Table; genes marked (*) were also significant using the PheVor and/or GROUPER algorithms. DAVID grouped 160/440 (40%) genes into 11 distinct clusters. DAPPLE revealed multiple connections between anticipated protein products and prioritized 8 new genes of interest (Figure).

CONCLUSION: A systematic and integrated analysis of maternal exome variation using multiple new gene set algorithms independently identifies enrichment in several genetic pathways, implicates new potential candidate genes and confirms previously suspected SPTB genes. Results are consistent across independent gene prioritization algorithms. These findings require further confirmation in other populations.

Table. PANTHER results. GO terms and fold change in representation compared to online referent group

Gene Ontology Terms (Parent term first, then child terms listed)	Fold Change	p-value (Bonferroni corrected)	Example Gene (* if also significant in PHEVOR/GROUPER)	Gene Description
Reproduction (GO:0000003), Gamete generation (GO:0007276)	+3.21	1.09e-4	*DYNLL1 (dynein light chain 1)	Nitric oxide biosynthesis
			TRO (trophinin)	Mediates cell adhesion between trophoblastic cells and endometrial epithelial cells
			Doublesex- and MAB-3 transcription factor B1	Nitrogen compound metabolic processes
Death (GO:0016265), Cell Death (GO:0008219), Apoptotic process (GO:0006915)	+2.42	9.25e-3	*NOD2 (nucleotide-biding oligomerization domain protein 2)	Protein in peripheral blood leukocytes, immune response to intracellular bacterial lipopolysaccharide
			TNFRSF10A (TNF receptor superfamily 10A)	Cytokines, immunity
			MXRA5 (Matrix remodeling associated protein 5)	Immune system process, angiogenesis

Figure. DAPPLE results: Indirect networks of expected protein products from genes prioritized in VAAST. Genes with p<0.05 (Bonferroni correction) are prioritized and marked with a star.



243 The effect of BMI on changes in salivary progesterone and estriol concentrations in pregnant patients receiving 17 α-hydroxyprogesterone caproate versus placebo

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OBJECTIVE: Studies suggest decreased efficacy of 17 α-hydroxyprogesterone caproate (17OHPC) in patients with a BMI $\geq$25 in preventing recurrent preterm birth (rPTB). This may be related to differential effects of 17OHPC on progesterone (P) and estriol (E3) levels, which, when elevated, have been associated with decreased and increased rates of PTBs, respectively. Our objective was to evaluate the incidence of rPTB by BMI and 17OHPC exposure, and to assess whether this incidence is explained by the changes in P or E3 levels during pregnancy.

STUDY DESIGN: This was a secondary analysis of a randomized clinical trial of 17OHPC to prevent rPTB. In the parent study, baseline and longitudinal salivary P and E3 samples were collected. 80 were randomly selected for a prior planned case-control study comparing P and E3 concentrations by 4 groups of 20 each: +PTB/17OHPC, +PTB/placebo, -PTB/17OHPC and -PTB/placebo. Our current study analyzed the incidence of rPTB for women in the parent trial with available BMI and outcome data, stratifying BMI by <25 and $\geq$25, and by 17OHPC exposure. Multivariable logistic regression was performed to assess the interaction of BMI and treatment groups with rPTB (<37 weeks), adjusting for confounders. Of 80 patients with longitudinal salivary samples, 75 had data on BMI. Salivary P and E3 levels were measured in 5-week intervals. Longitudinal analysis used mixed models to determine whether an interaction of BMI and 17OHPC impacted the trajectory of salivary P and E3.

RESULTS: 17OHPC decreased rPTB compared to placebo for BMI<25, but not BMI$\geq$25 (p=0.017, Table 1). In the group with longitudinal testing, there was no significant difference in the rate of change in salivary P levels between groups. However, in women with a BMI <25, 17OHPC mitigated the increase in E3 levels compared with placebo (p = 0.028, Fig. 1).

CONCLUSION: Women treated with 17OHPC with BMI<25 have a blunted increase in salivary E3 compared to those with BMI$\geq$25, possibly contributing to lower rPTB rates in this group. Dosing studies should be considered for women with BMI $\geq$25.

Figure 1. Changes in estriol levels over the gestation among treatment groups by BMI (n=75).

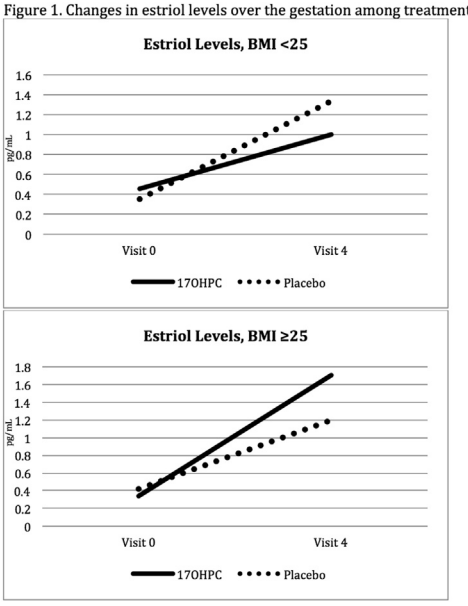

Table 1: Preterm Births Between Treatment and Placebo between Normal and High BMIs, n=401.

BMI	Treatment	Preterm deliveries (n, %)	OR (95% CI)*
≥25	17OHPC	59 (37.3%)	1.0
	Placebo	30 (43.4%)	1.08 (0.57-2.05)
<25	17OHPC	56 (36.8%)	0.84 (0.05-1.41)
	Placebo	54 (64.3%)	2.71 (1.48-4.95)
			p-value for interaction = 0.017
			*Adjusted for maternal age, race, prior preterm births, smoking and baseline estriol levels