domains: non-ambulatory cerebral palsy, blindness in at least one eye, deafness, need for visual or hearing aids, neuro-cognitive disability at 5 years of age. Five year follow-up was conducted from 2006-2012 in 52 of the initial 80 centers worldwide, where 2141 of 2304 fetuses/infants (93%) were enrolled. A total of 1728(80.7%) had adequate data for the main outcome at 5 years of age.

RESULTS: There was no significant difference between the two treatment groups in the risk of death or neurodevelopmental difficulty: 217 (24.9%) of the 873 in the repeat courses group vs. 210 (24.6%) of the 855 in the placebo group, [odds ratio 1.025, 95% confidence interval 0.81-1.29, p=0.83]. The rates of death or individual neurodevelopmental difficulties did not differ significantly between the two groups.

CONCLUSION: Multiples courses of antenatal corticosteroid therapy given, every 14 days, do not increase or decrease the risk of death or neurodevelopmental difficulties by 5 years of age compared with a single course. Because there has been no clear benefit seen in the neonatal period, as well as at 2 and 5 years of age, this approach of antenatal corticosteroids is not recommended for routine use. Future research may be warranted for a more specified use of repeated courses of antenatal corticosteroids.

	Repeat N=873 N (%)	Placebo N=855 N (%)	OR [95% CI]	Level of Significance
Composite*	217 (24.9)	210 (24.6)	1.025 [0.81,1.29]	0.83
Death	46 (5.3)	47 (5.5)	0.95 [0.62,1.46]	0.82
Neuromotor	4 (0.004)	11 (0.01)	0.35 [0.11,1.11]	0.07
Neurosensory Blindness Visual aids Deafness Amplification	1 (0.1) 61 (7.4) 11 (1.3) 4 (0.5)	2 (0.3) 52 (6.4) 6 (0.7) 5 (0.6)	1.12 [0.77,1.63]	0.54
Neurocognitive** CBCL 1½-5 BRIEF-P	76 (9.2) 76 (9.2)	75 (9.3) 84 (10.4)	0.98 [0.73, 1.33]	0.92

*Apart from a death, child may have more than 1 disability; **10 cases were reviewed by an adjudication committee to determine whether they met the primary outcome; 5 cases were determined to have met the primary outcome.

3 Prevention of preterm delivery by 17 alpha-hydroxyprogesterone caproate in asymptomatic twin pregnancies with a short cervix: a randomized controlled trial

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OBJECTIVE: To evaluate the use of 17 alpha-hydroxyprogesterone caproate (17P) to reduce the risk of preterm delivery in asymptomatic twin pregnancy with short cervix.

STUDY DESIGN: This open-label multicenter randomized controlled trial took place at 10 university hospitals between June 2006 and January 2010. Women older than 18 years and carrying twins were eligible between 24+0 through 31+6 weeks of gestation if they were asymptomatic, presented a cervical length less than 25 mm as measured by routine transvaginal ultrasound and provided a written informed consent. Women were randomly assigned in a 1:1 ratio to receive 500 mg of intramuscular 17P, and repeated twice a week until 36 weeks or preterm delivery, whichever occurred first, or to no treatment with 17P (control group). The primary outcome was time from randomization to delivery.

RESULTS: Maternal characteristics of the 82 women in the 17P group and the 83 women in the control group were similar. Outcome data were available for 161 of the 165 women (97,6%). The intent-to-treat analysis with censoring at last follow up showed no significant difference between the 17P and controls group in median [Q1-Q3] time to delivery (45 [26-62] and 51 [36-66] days, respectively; mean difference, −7; 95% CI, −15; +1). Treatment with 17P was associated with a significantly increase in the rate of preterm deliveries before 32 weeks of gestation (29% vs 12%, p=0.007), but not before 37 weeks of gestation (80% vs 77%, p=0.70) or 34 weeks of gestation (44 % vs 28 %, p=0.10). Median [Q1-Q3] birth weight did not differ between 17P and controls groups for twin 1 (2120 [1750-2471]g and 2215 [1982-2535] g, p=0,06) but differ significantly for twin 2 (2090 [1540-2425] and 2230 [1985-2535] g, p=0,027). There was a non significant trend to an increase of neonatal morbidity in a 17P group.

CONCLUSION: 17P is ineffective in women with asymptomatic twins and short cervix for prevention of preterm delivery and possibly harmful.

4 Antenatal origins of metabolic syndrome in fetuses of obese women

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OBJECTIVE: Molecular mechanisms that predispose offspring of obese pregnant women to insulin resistance, appetite dysregulation, and fatty liver disease are poorly understood. We sought to understand the effects of maternal obesity on fetal gene expression by analyzing cell-free fetal RNA (cffRNA) in amniotic fluid supernatant (AFS).

STUDY DESIGN: We prospectively studied cffRNA in AFS of women with singleton fetuses undergoing clinically indicated 2nd trimester genetic amniocenteses. Eight obese gravidas (Ob, BMI ≥30) and 8 lean controls (L, BMI <25) were matched for gestational age and fetal sex. Exclusion criteria included abnormal karyotype and structural anomalies. CffRNA was extracted, amplified, and hybridized to whole genome expression arrays. Genes significantly differentially regulated in 8/8 pairs were identified using paired t-test with the Benjamini-Hochberg (BH) correction. Functional analyses were performed using Ingenuity Pathways Analysis™ software. Genes and transcription factors associated with bias-corrected absolute Z-scores ≥2.0 or BH p < .05 were called significant.

RESULTS: Demographic characteristics are shown in Table 1. There were 205 differentially regulated genes in fetuses of obese gravidas. The most up-regulated gene (9-fold) in Ob was *APOD*, which encodes a lipoprotein integral to lipid regulation, glucose metabolism, and inflammatory response. Upstream regulator analyses demonstrated significant activation of the estrogen receptor and the transcription factors *STAT3* and *FOS* in fetuses of obese women.

CONCLUSION: Expression of *APOD*, *STAT3*, and *FOS* is implicated in insulin resistance, hyperleptinemia, hepatic steatosis, atherosclerosis, toll-like receptor signaling, and inflammatory response. Analysis of cffRNA in AFS demonstrates a pro-estrogenic, pro-inflammatory milieu for fetuses of obese women. Molecular mechanisms predisposing offspring of obese women to metabolic complications may be initiated as early as the second trimester.

Subject demographics and array hybridization characteristics

	Obese	Lean	p-value
BMI (kg/m2, mean ± SD)	35 ± 3.3	21.9 ± 1.7	<0.001
Maternal age (yrs, mean ± SD)	37.1 ± 5	33.9 ± 5.5	0.21
Gestational age (wks, mean ± SD)	17.9 ± 1.7	18 ± 1.4	0.73
Fetal Sex (M,F)	4 , 4	4 , 4	N/A
Array Hybridization Efficiency	42.1 ± 3.5	41.9 ± 4.9	0.89