

ART and CHILD HEALTH

REQUEST TO NCS FAC

- **Carter Snead: Counsel for the President's Council on Bioethics**
- **Identified the Need for Further Studies of ART on Child Health**
- **Requested that the NCS FAC Consider if the NCS would Address this Issue**

INVESTIGATION

- **Review of Hypothesis Submitted by FEP WG**
- **Discussions with:**
 - **Phyllis Leppert, M.D., Ph.D.**
 - **Dorrie Lamb, Ph.D.**
 - **Jim Segars, M.D.**
 - **Robert Brzyski, M.D., Ph.D.**
 - **Geraldine Buck, Ph.D.**
- **Recent Metaanalysis**

FEP HYPOTHESIS

- **Primary Outcomes: IUGR, Birth Defects,**
- **Other Outcomes: Preterm Birth, Mortality, Cost/Financial Burden, Quality of Life**
- **Strong Rationale for this Hypothesis**
 - **Justification for Large Sample Size**
 - **Scientific Merit**
- **No Sample Size Calculation**
- **No Consideration of Potential Oversampling Needs**
- **Some Consideration of Control Groups**

RECENT META-ANALYSIS

- **Perinatal Outcome of Singletons and Twins after Assisted Conception (Helmerhorst, et al, BMJ 23 Jan 04)**
- **1985-2002: 25 Studies (17 Controlled)**
- **Singletons: n=5361 ART, 7038 Spontaneous**
 - **Very Preterm (< 32 weeks): RR 3.27 (ART)**
 - **Preterm (<37 weeks): RR 2.04 (ART)**
- **Twins n=3427 ART, 3429 Spontaneous**
 - **Very Preterm (<32 weeks): RR 0.95**
 - **Preterm (< 37 weeks): RR 1.07**

META-ANALYSIS RESULTS

- **Birth Weight in Singletons:**
 - <1500 grams: RR 3.00 (ART)
- **Birth Weight in Twins:**
 - <1500 grams: RR 0.89
 - <2500 grams: RR 1.03
- **SGA in Singletons: RR 1.4-1.46**
- **SGA in Twins: No Difference**
- **Perinatal Mortality:**
 - Singletons: 1.68 ART (Skewed by One Study)
 - Twins: 0.58**

META-ANALYSIS BIAS/PROBLEMS

- **Problems with Matched Cohort Studies (one study dominates, had 3 different control groups)**
- **Matching for GA Questionable**

META-ANALYSIS CONCLUSIONS

- **Shift Emphasis from Achieving Pregnancy to Normal Outcomes**
- **Consider any Multiple Pregnancy as a Failure of ART Technology**
- **Narrow the Gap in Perinatal Outcomes from Assisted Pregnancies**

CONSENSUS OPINION

- **No Study On-going in USA**
- **Not All ART is the Same**
- **Unclear if NCS is the Best Study Design**
 - **1% Pregnancies ART (future 2%)**
- **Indications for ART Varied**
- **Adjust for Cause of Infertility (Data is Difficult to Acquire)**
- **Necessity for Oversampling??**

Studying the Effect of ART on Child Health

Elements of Epidemiologic Method	NCS	ART
Change Treatment from Impaired Fecundity Effect on Child Health	-	-
Hypothesis Driven Approach	+	++
A Specific ART Rx Type and Child Health	-	-
Supports Probability Sampling	++	++
Supports Convenience Sampling	++	++
Supports Couple-based Sample Selection	??	++
Suitable for Prospective Longitudinal Data Collection	++	++
Ability to Capture Correlated Exposure Data	+	++
Ability to Capture Relevant Covariates peri-ART Treatment	+	++
Sufficient Statistical Power for yes/no ART Treatment Effect	++	++
Sufficient Statistical Power for Specific Type of ART Treatment	-	++

POSSIBLE COURSES OF ACTION

- **Decline Consideration**
- **Accept as Hypothesis and Develop**
- **Reconsider: FEP and SD WG**
 - **Power Calculation**
 - **Need for Oversampling**
 - **Effect on Study Overall**