1. Discuss reasons why the authors analyzed the prevalence of major birth defects and anomalies according to the type of assisted reproductive technology (intracytoplasmic sperm injection [ICSI], non-ICSI, fresh embryo transfer, frozen-thawed embryo transfer).

2. Is this study population-based? Why or why not? How do the authors account for the possibility of confounding by immigration and emigration?

3. This study was accomplished through linkage of registries. Are there equivalent registries in the United States? If so, can this study be reproduced using U.S.-based registries?

4. The authors compared the prevalence of major birth defects between assisted reproductive technology (ART) and non-ART groups. Considering ART as the exposure, discuss whether the appropriate reference (control) group is the remainder of Western Australia births after the ART births had been subtracted.

5. Review the time periods chosen for analyzing temporal trends. Why were these years selected? What changes in in vitro fertilization (IVF) techniques occurred during those years that may have had an effect on the prevalence of major birth defects?

6. Review the list of imprinting-related disorders. Why are imprinting-related disorders a concern in ART? What are the authors’ conclusions about the prevalence of imprinting-related disorders in ART?

7. Discuss how cases of birth defects and fetal anomalies were ascertained. Who was responsible for identifying and reporting the cases? Discuss the benefits of utilizing the services of a trained clinical geneticist (dysmorphologist) to ascertain cases of birth defects. Would it be practical to utilize the services of a dysmorphologist in this study?

8. Read the article by Drs. Grimes and Schulz on the limitations of observational epidemiology in the current (October 2012) issue of Obstetrics & Gynecology. Do you believe that the findings of an increased prevalence of major birth defects in ART singleton infants reported by Hansen et al should be considered credible?

9. Before reading the article by Hansen and co-authors, how did you counsel patients considering ART regarding birth defects and fetal anomalies? Will the findings in this article change your counseling?