Reviewer's report

Title: No difference in mortality and major morbidities in very preterm infants born from assisted conception or naturally conceived. Results of the area-based ACTION study.

Version: 3 Date: 28 March 2014

Reviewer: Marek Brabec

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This is a large and interesting study with potentially important practical consequences.

From statistical point of view, it seems that it uses quite appropriate methodological tools. Probably GEE (generalized estimating equation) approach was used. But that is just a guess! The current description of statistical models in the “Statistical analysis” section is completely inadequate. Whether GEE or other approach was used should be clearly indicated, perhaps with some references to standard publications. If GEE was used, what kind of working correlation was used (was it working independence, or exchangeability, or something else)?

Even more important is the fact that the paper interprets lack of significant difference between AC and non-AC groups as a kind of evidence for them being “similar”. This is exactly in the spirit of much criticized “absence of evidence being taken as evidence of absence”.

As a minimum, the findings presented in the paper should be supplemented with some power calculations (to assess how large was actually a chance to find a practically relevant difference in the study of this size, design and between-center variability). This is something which will probably need a cooperation with a local professional statistician. If the power will be large, one might be inclined to believe that the AC vs. non-AC differences should not be too important in practical terms (but even then, the conclusions of the paper should be formulated much more carefully and much more moderately than in the current version of the manuscript). If the power would be small, the paper could still be published, but with a strong, explicit warning about the danger of premature no-difference conclusion. In fact, in such a case a new, larger study would be called for. And the current one can serve as a suitable pilot (for its preparation, design etc.).