Letter to the Editor: Response to Klebanoff

Lisa N Yelland^{a,b}, Thomas R Sullivan^b, Menelaos Pavlou^c, Shaun R Seaman^d

^aWomen's and Children's Health Research Institute, North Adelaide, South Australia, Australia ^bSchool of Population Health, The University of Adelaide, Adelaide, South Australia, Australia ^cDepartment of Statistical Science, University College London, London, United Kingdom ^dMRC Biostatistics Unit, Cambridge, United Kingdom

Correspondence: Dr Lisa Yelland, School of Population Health, Mail Drop DX650 511, The University of Adelaide, SA 5005, Australia, Email: lisa.yelland@adelaide.edu.au, Phone: +61 8 8313 3215, Fax: +61 8 8223 4075.

In response to our paper discussing methods for analyzing randomised trials including multiple births,¹ Klebanoff raises an interesting ethical question: Should parents of twins be informed at the time of consent if each of their infants will only be given a weight of a half in the analysis?² This question is only relevant if the analysis will be performed using cluster-weighted generalised estimating equations (GEEs), rather than our recommended approach of standard GEEs with an independence working correlation structure, and may best be addressed through discussion between human research ethics committees across the globe with the aim of reaching a consensus view. An important factor to consider in this debate is that there are many other situations where study participants are weighted differentially in the analysis. Examples include the use of survey weights and inverse probability weighting to handle missing data.³ and the analysis of clustered data using standard GEEs with a non-independence working correlation structure to improve efficiency when cluster size is non-informative.⁴ If there is indeed an ethical responsibility to inform participants or their caregivers when their data will receive a weight other than one in the analysis, this will have consequences for more than just the current context of randomised trials including multiple births. It may be that the greater ethical issue here is whether each infant from a multiple birth will actually be included in the analysis. Excluding data from one twin remains a popular analysis strategy,⁵ but is unnecessary given the availability

of analysis methods that can accommodate data from both twins, including those discussed in our paper.¹

References

References (max 5)

- Yelland LN, Sullivan TR, Pavlou M, Seaman SR. Analysis of Randomised Trials Including Multiple Births When Birth Size Is Informative. *Paediatric and Perinatal Epidemiology* 2015; 29:567-575.
- 2. Klebanoff M. Letter to the Editor. Paediatric and Perinatal Epidemiology 2015.
- 3. Hofler M, Pfister H, Lieb R, Wittchen H. The use of weights to account for non-response and drop-out. *Social Psychiatry and Psychiatric Epidemiology* 2005; 40:291-299.
- 4. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986; 73:13–22.
- Yelland LN, Sullivan TR, Makrides M. Accounting for multiple births in randomised trials: a systematic review. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2015; 100:F116–F120.