Author’s response to reviews

Title: A Randomised Controlled Trial of Early Insulin Therapy in Very Low Birth Weight Infants NIRTURE (Neonatal Insulin Replacement Therapy in Europe)

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Author’s response to reviews: see over
Dear Dr Phillips

Re: MS: 8852156321252519
A Randomised Controlled Trial of Early Insulin Therapy in Very Low Birth Weight Infants NIRTURE (Neonatal Insulin Replacement Therapy in Europe)

Apologies for the delay, in responding to the request for further statistical information. I have consulted with our statistician and he has amended the protocol as requested. The following section has been added to the protocol (page 16) to respond to the questions raised:

The primary outcome will be modelled with logistic regression in order to evaluate a 95% confidence interval for odds ratio according to treatment group adjusted for key prognostic variables, including if significant, geographic centre. No formal interim analyses are intended although the trial’s Data Monitoring Committee (DMC) will meet regularly, have access to unblinded data and would recommend early termination to the Trial Steering Committee if judged appropriate based on ethical, safety or efficacy considerations. Time to event analyses stratified by category of birthweight, using Kaplan-Meier survival analyses and stratified logrank tests will be used to assist DMC decision-making. For the secondary outcomes, modelling with either multiple
regression (for continuous variables) or logistic regression (for binary variables) will be employed, adjusting for the same baseline covariates as the primary analysis. If individual terms in models are non-significant at level 0.05, then simpler models may be presented instead.

I hope this is acceptable but do let me know if you need any further information

Best wishes

Kathy

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