Author's response to reviews

Title: NEWHINTS cluster randomised trial to evaluate the impact on neonatal mortality in rural Ghana of routine home visits to provide a package of essential newborn care interventions in the third trimester of pregnancy and the 1st week of life: Trial Protocol

Authors:

Betty R Kirkwood (betty.kirkwood@lshtm.ac.uk)
Alexander Manu (alex.manu@kintampo-hrc.org)
Charlotte Tawiah-Agyemang (charlotte.tawiah@kintampo-hrc.org)
Guus ten Asbroek (guus.tenasbroek@lshtm.ac.uk)
Thomas Gyan (thomas.gyan@kintampo-hrc.org)
Benedict Weobong (ben.weobong@kintampo-hrc.org)
R Eric Lewandowski (eric.lewandowski@gmail.com)
Seyi Soremekun (seyi.soremekun@lshtm.ac.uk)
Samuel Danso (danso.samuel@kintampo-hrc.org)
Catherine Pitt (catherine.pitt@lshtm.ac.uk)
Kara Hanson (kara.hanson@lshtm.ac.uk)
Seth Owusu-Agyei (seth.owusu-agyei@kintampo-hrc.org)
Zelee Hill (z.hill@ich.ucl.ac.uk)

Version: 4 Date: 4 May 2010

Author's response to reviews: see over
RESPONSES to Reviewer’s report (4 May 2010)

Title: NEWHINTS cluster randomised trial to evaluate the impact on neonatal mortality in rural Ghana of routine home visits to provide a package of essential newborn care interventions in the third trimester of pregnancy and the 1st week of life: Trial Protocol

Dear Dr Doig,

Many thanks for your very helpful comments – responses to each are given in capitals below, and the manuscript amended accordingly. Please let me know if anything isn’t clear.

Best wishes, Betty Kirkwood

Version: 3 Date: 30 March 2010

Reviewer: Gordon Doig

Reviewer’s report:

Congratulations on this undertaking. It is an outstanding trial with potentially important findings. MANY THANKS.

Please consider the following issues:

1. Consider including a 'sensitivity analysis' to assess the impact of breaking allocation concealment by including the 4 Pilot Zones in the Intervention arm.

INCLUDED ON P18 AT END OF PARAGRAPH ON INTENTION-TO-TREAT ANALYSES

2. Please provide additional details regarding your analytical plan.

Please explicitly report all variables that will be assessed for baseline balance. Please report the decision threshold (p-value or other) that will be used to decide whether a variable is in imbalance.

VARIABLES ARE LISTED IN PARAGRAPH ON Participant flow & comparability of treatment arms. THIS HAS BEEN AMENDED TO MAKE CLEAR THAT 2007 IS BASELINE YEAR.

HAVE ALSO MADE CLEAR THAT NO STATISTICAL TESTS WILL BE CARRIED OUT CONCERNING COMPARABILITY TABLES, BUT THAT ALL ANALYSES WILL BE CARRIED OUT BOTH INCLUDING AND EXCLUDING THIS SET OF POTENTIAL A PRIORI CONFOUNDERS. SEE FOLLOWING FOR RECOMMENDATIONS RE THIS: KIRKWOOD & STERNE. ESSENTIAL MEDICAL STATISTICS. BLACKWELLS 2003 HAYES & MOULTON. CLUSTER RANDOMISED TRIALS. CHAPMAN HALL 2009

Please provide appropriate references to the cRCT literature to specify exactly how tests will be adjusted for clustering. For example, your intended use of a t-test with 96 dfs on the cluster averages should be referenced. All other intended tests should be referenced to the appropriate cRCT literature. In this way your protocol will serve as a guide for others.

HAVE REFERENCED HAYES & MOULTON & ALSO AMENDED TEXT TO FOLLOW THEIR RECOMMENDATION TO USE INDIVIDUAL RATHER THAN CLUSTER BASED
ANALYSES WHEN THERE IS A LARGE NUMBER OF CLUSTERS (AS IN OUR CASE) – THIS SIMPLIFIES EVERYTHING

3. Please specify how it will be determined that logistic regression estimates are 'unreliable' (Page 15, first sentence).
USING QUADRATURE CHECKS - HAVE ADDED THIS TO TEXT.

4. Per protocol analysis. More detail and appropriate references are needed.

REALISED THAT WE WERE USING THE TERMINOLOGY SOMEWHAT LOOSELY AND WHAT WE ARE REALLY DOING ARE SENSITIVITY ANALYSES. HAVE REVISED PARAGRAPH TO INCLUDE MORE DETAIL

5. Your sample size estimate was not based on the assumption that cluster means would be analyzed using a t-test. It is possible that your shift from a sample size calculation based on number of livebirths, adjusted for clustering, to number of clusters may reduce anticipated statistical power. Would it be more appropriate to base your primary analysis on a technique that is based on the number of livebirths adjusted for cluster in a less conservative way? Please Discuss.

METHODS AND SAMPLE SIZE CALCS NOW MATCH – SO NO CHANGES RE THIS NEEDED.