Title: Optimising the impact and cost-effectiveness of child health intervention programmes of vaccines and micronutrients in low-income countries

Acronym: OPTIMUNISE
Contract/Grant agreement number: FP7-HEALTH-F3-2011-261375

EC contribution: 2.999.970 €
Duration: 60 months
Starting date: 01/03/2011

Summary:
To test the real life impact and cost effectiveness of child health interventions it is necessary to have individual-based data on health intervention uptake as well as on health status. The present project takes advantage of the Health and Demographic Surveillance Systems (HDSS) sites in the INDEPTH Network in Africa. The HDSS sites can provide the platform for 1) assessing the real life effect and cost-effectiveness of interventions in observational studies; 2) testing modifications of the current health intervention programs in randomised controlled trials (RCTs), and 3) testing new interventions and their potential interactions with existing interventions in RCTs. This programme is being implemented at three sites in Guinea-Bissau, Burkina Faso, and Ghana. Using the HDSSs as a platform OPTIMUNISE will test the four hypotheses formulated in a recent paper about the negative non-specific and sex-differential effects of diphtheria-tetanus-pertussis (DTP) vaccine and the beneficial non-specific effects of measles vaccine.

Already implemented health interventions can usually only be evaluated in observational studies, because it would be unethical to conduct a randomised trial of the "real life effects" of a recommended WHO policy. Hence, OPTIMUNISE has modified the current data collection systems to include information on all routine and campaign interventions in childhood to conduct such observational studies. However, it may be ethically justified to test modifications of the current programmes in RCTs and obtain unbiased estimates of the effect of certain aspects of a health programme. Such trials may also cast light on interactions between different interventions and test the observations made in the observational studies. OPTIMUNISE is preparing to test a recent finding from a randomised trial in Guinea-Bissau: providing early measles vaccine at 4.5 and 9 months of age compared with the recommended measles vaccine at 9 months of age reduced overall mortality between 4.5 and 36 months of age by 50% if the children had not received vitamin A at birth.

Fortunately, mortality has declined in Africa in the last decade and it may become increasingly difficult to measure the overall impact on mortality of existing and new interventions. OPTIMUNISE is therefore aiming to identify the best relevant comparable outcome parameters which correlate with child mortality/survival and which can be used to assess the overall health impact of interventions in future assessments.

Problem:
The many vertical health interventions led by WHO, UNICEF or other organisations like American Red Cross are undertaken with little attempt to asses their local impact on health and on the local health system. Child health programmes in low-income countries are justified in terms of their assumed impact on child survival and how they may contribute to reaching the Millennium Development Goals. However, the assessment of this impact is usually based on measurements of performance indicators for a particular programme, e.g. vaccination coverage, and assumptions about efficacy of the intervention and about the burden of the particular health problem. These assumptions are mostly based on small-scale studies of the

immediate target condition; e.g., a vaccine is evaluated for its clinical protection against the targeted disease. Correspondingly, assessments of cost effectiveness tend to be narrowly confined to disease-specific costs and savings.

Observational studies and randomised trials in several African countries have shown that this procedure is not reliable. First, vaccines and micronutrients have beneficial or negative non-specific effects; i.e. effects which are not explained by prevention of the targeted infections or deficiencies. Second, these effects are frequently sex-differential. Third, interventions may interact, producing stronger beneficial or negative effects; for example, vitamin A given together with DTP may increase mortality for girls. Fourth,
vaccines and micronutrients are often given out of the recommended schedule and this can have marked effects on mortality.

Aims:

- To develop the capacity of existing HDSS in Africa to monitor the real life effects of child health intervention programs to promote evidence-based policy.

- To measure the health impact and cost-effectiveness of the existing major child health programmes with vaccines (BCG, DTP, and measles vaccine) and vitamin A controlling for determinants of compliance.

- To evaluate in a multicenter RCT a specific modification of the current child health programme: To provide an additional measles vaccine at age 4.5 months, in addition to the recommended measles vaccine at age 9 months.

(Expected) results:

OPTIMUNISE has modified the current data collection systems to include information on all routine and campaign interventions in childhood.
Data collection on the prospective observational study at the three sites is ongoing and the first papers have been submitted.
The protocol for the RCT on early measles vaccine is in review and the recruitment of trial participants is expected to start in the second half of 2012
It is hypothesized that OPTIMUNISE will show major beneficial effects of measles vaccine and BCG which will strongly modify the cost-effectiveness of the current programme and will point to several problems in the way the programme is currently being implemented.

Potential applications:

If the non-specific effects are going to be confirmed by this research, and if this would be taken into global health policy consideration, this would imply large savings and major reductions in mortality in high-mortality areas, for instance by vaccinating earlier with measles vaccine.

Project web-site:

http://www.indepth-network.org/index.php?option=com_content&task=view&id=1216&Itemid=1074

Key words: Non-specific and sex-differential effects of vaccines and vitamin A, real life effects and cost-effectiveness, interactions between health interventions, measles vaccine, health and demographic surveillance systems, vitamin A supplementation, immunisation programmes, DTP, BCG, observational studies, randomised trial

Coordinator:
Statens Serum Institut
Artillerivej 5,
2300 Copenhagen S
Denmark
Email: p.aaby@bandim.org

Partners:

STATENS SERUM INSTITUT, Artillerivej 5, Copenhagen, 2300, Denmark represented by Nils Strandberg Pedersen (nsp@ssi.dk)

INSTITUTO NACIONAL DE SAUDE PUBLICA, established in Av. Combatente da Liberdade da petria 100, Bissau Codex, 1004, Guinea-Bissau represented by Amabelia Rodrigues (A.Rodrigues@bandim.org)

CENTRE DE RECHERCHE EN SANTE DE NOUNA, established in BP 02, Nouna 13, Burkina Faso represented by Ali Sie, (sieali@yahoo.fr).

GHANA HEALTH SERVICE, established in Cathedral Square Adabraka, Accra, Ghana, represented by Abraham Hodgson, (abraham.hodgson@ghsmail.org)

UNIVERSITAETSKLINIKUM HEIDELBERG, established in Im Neuenheimer Feld 672, Heidelberg, 69120, Germany represented by Claus R. Bartram, (Olaf.mueller@urz.uni-heidelberg.de)

MEDICAL RESEARCH COUNCIL, established in Kemble Street 1, London WC2B 4AN, United Kingdom, represented by Janet Wyatt (janet.wyatt@rcl.mrc.ac.uk)

INDEPTH NETWORK, located at 38 & 40 Mensah Wood Street, East Legon 11, Accra KD, Ghana, represented by Osman Sankoh (osman.sankoh@indepth-network.org)