



FOOD-CT-2005-007036

# EARNEST

EARly Nutrition programming- long term follow up of Efficacy and Safety Trials and integrated epidemiological, genetic, animal, consumer and economic research

Instrument: Integrated Project

Thematic Priority 5.4.3.1: Food Quality and Safety

## Final public report on activity 2.5.3

## Title of activity: Impact of early dietary exposures on development and diseases: Analyses based on data merged from DNBC and MoBa

Period covered from 15.04.2005 to 14.10.2010

Start date of project: 15.04.2005 Duration: 5,5 Years

Organisation Name of Lead Contractor for this report: Danish Epidemiology Science Centre, Statens Serum Institut (now: Centre for Fetal Programming, Statens Serum Institut)

**Objectives**
To examine the impact of dietary factors in pregnancy on adverse health outcomes in mother and child, by undertaking analyses based on both databases.

**Tasks**
The activity embraced two different types of tasks: undertaking coordinated analyses addressing specific scientific questions, and, in case the work needed additional financial support, writing up protocols that could help raising additional grants. The activity necessitated close interaction between the two teams in order to discuss and decide upon which scientific issues should be addressed in the collaboration and thereafter to prepare for the coordinated analyses or the writing of the protocols.

**Results**
Three different scientific issues were addressed by coordinated analyses undertaken of the two cohorts.

*Fish intake in pregnancy and fetal growth:* Earlier work by researchers on the team had suggested the hypothesis that fish intake in pregnancy stimulates fetal growth. It was decided quite early in the collaboration to examine this hypothesis on the basis of both cohorts. The analyses were first run on the Danish data and as this was at a time when recruitment for the Norwegian cohort was still ongoing it was decided to postpone the analyses based on the Norwegian cohort until the full dataset was available. Initial comparative studies across the two databases confirmed the impression that mean daily fish intake during pregnancy is substantially higher in the Norwegian cohort than the Danish cohort. A main result from the Danish study was identification of an inverse association between total fish consumption and fetal growth, another this association reflected an association with consumption of fatty fish but not with lean fish. These important observations led to the recommendation that future studies of the association between fish intake and fetal growth should attempt to distinguish between effects of fatty fish from effects of lean fish consumption in pregnancy. Contrary to the Danish findings, the Norwegian data showed a consistent increase in birth weight with increasing maternal seafood consumption in Norwegian women, but this association seemed only to exist for lean fish and not for fatty fish or fish liver. The findings reported here warrant further explorations of the two datasets that take into account the shifts in the underlying exposure distributions in the various seafood variables.

*Mediterranean diet pattern and risk of preterm birth:* The background for this work was a randomised controlled trial undertaken in pregnant women in Oslo, Norway, and published in 2005. The intervention led to a shift from consuming a typical urban-Norwegian diet to a Mediterranean type diet during third trimester; the control group continued with their usual diet. An unexpected finding of the trial was that women in the intervention group had substantially lower occurrence of preterm birth. It was decided to use the two cohort datasets to put this potentially extremely important finding under test. A common analytic strategy was decided upon a priori, which implied defining groups in the cohorts that could mimic the intervention groups created in the trial; the defining criteria for Mediterranean type diet used in the trial were: consumption of fish twice a week or more (lunch or dinner), intake of olive or rape seed oil, high consumption of fruits and vegetables (4-6 a day or more), meat (other than poultry and fish) at most twice a week, and at most 2 cups of coffee a day. Closely coordinated analyses were then undertaken in both datasets in a strictly standardised manner. After accounting for potential confounding, both cohorts suggested a reduced preterm risk in the ‘Mediterranean type diet’ compared to the ‘control’ group, although neither estimate from

the two cohorts reached statistical significance. However, when pooling of the estimates was undertaken the reduction in preterm risk associated with Mediterranean type diet was statistically significant. The findings reported warrant further explorations of the two datasets that go deeper into which factors in the 'Mediterranean type diet' could be underlying causal factors.

*Physical activity in pregnancy and risk of preeclampsia:* An analysis based on the Danish dataset had shown a substantially increased risk of preeclampsia, particularly severe types of preeclampsia, in women reporting moderate to relatively high levels of leisure time physical activity in pregnancy (these analyses started out as an side finding obtained from confounder check of an analysis with the primary aim to examine the hypothesis that vitamin C and E has protective effect against preeclampsia, but later it developed into a separate series of analyses and paper). Many countries have during recent years implemented a recommendation saying that pregnant women should exercise at least 30 min per day in pregnancy, an important argument being that physical actively reduces risk of preeclampsia which turned out to be a contention that is poorly substantiated by epidemiological evidence. The finding from the Danish cohort was just opposite to what could be expected and was therefore alarming. It was decided to run an analysis on the basis of the Norwegian dataset with the intention to either confirm or refute the finding from the Danish cohort. It was not possible to identify the same pattern seen in DNBC of increased risk with higher physical activity level. However, there was not either any clear reduction in risk with higher physical activity. The results from the these two larges cohorts do put a question mark against the basis for the current recommendation to exercise 30 min or more in pregnancy.

*New protocols:* Protocols were developed for further coordinated analyses across the two databases. They dealt with early nutrition exposures in relation to malformations, childhood cancer and childhood diabetes, and with examining impact of organic food consumption in pregnancy on child health and development based on coordinated analyses across the two databases. A grant was successfully obtained to support future coordinated analyses of impact of maternal nutrition on childhood cancer. Furthermore, extensive work with food group definitions was done to ensure a standardised strategy across the two cohorts for the examining impact of organic food consumption in pregnancy on maternal and offspring health.