



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 Theme 5

Title of activity: Economic / public health impact studies

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: LMU-Muenchen

Workpackage 5

The objective of this Earnest-project theme's activity was the evaluation of health economic effects for the society that can be gained by appropriate infant nutrition. The relation of costs and benefits should be the basis for any decision that has to be made about the realisation of a medical intervention strategy, with the possibility to reduce future healthcare costs and welfare losses due to morbidity and mortality. Especially for a preventive intervention like nutrition programming, with effects that will occur in the far future, health economic analyses are essential.

The Workpackage's activity was split in two phases of the project. In the first phase (project months 1 - 18) the tasks were the conception and realisation of a health economic evaluation based on a proposed nutritional programming effect. At the end of the Earnest-project Workpackage 5 was involved again (project months 55-65) to adjust the previous economic model and calculation to the current state of research that was generated from the project's research activities and calculate the cost-effectiveness of new found early nutrition interventions with programming effects.

In the first phase of the Workpackage, the existing literature was reviewed and one intervention strategy identified as medical effective in a randomised clinical trial was the supplementation of infant formula with long chain poly unsaturated fatty acids (lcpufa) for long term reduction of blood pressure. Even a small decrease in diastolic blood pressure by few mm Hg could result in an explicit lower risk for high blood pressure and hypertonus related diseases like coronary heart diseases (CHD) and cerebrovascular diseases (Stroke). Therefore an lcpufa-supplementation of newborn nutrition could obtain a great preventive potential on cardiovascular disease (CVD) which is the main cause of the disease burden (illness and death) in Europe and one of the most important causes of healthcare costs.

An economic analysis of this intervention strategy was performed, taking the social costs and benefits over the whole human lifecycle into account. To assess the programming effect of lcpufa inclusion into infant formulas, a systematic review on the explanatory power of a blood pressure lowering effect in childhood for later life (tracking) was carried out, since the diseases that result from raised blood pressure, like myocardial infarcts or strokes, will only develop in old age. Available data regarding baseline exposures, morbidity and mortality by hypertension related diseases (ischaemic and cerebrovascular diseases) were collected for different European member states and the relevant economic factors (direct healthcare costs, direct non-medical costs, indirect costs, quality adjusted life years) had to be identified and compiled. The health-economic benefit was analyzed in a Markov-Model, regarding the nutrition's blood pressure lowering effect and its impact on the probability to develop a CHD or Stroke in later life. Other effects that occur from the supplemented nutrition, like the better cognitive ability or visual functions, are unconsidered in the model, as well as additional benefits resulting from a decreased blood pressure, so that the model's results will rather be an underestimation of the actual social benefits.

This Markov-Model calculation shows that the incremental effectiveness of the lcpufa supplementation is 1.20 quality adjusted life years (QALYs) in comparison with the standard-formula. In terms of cost effectiveness, the LCPUFA supplemented formula is the strictly dominant strategy. This is because it not only leads to extended life expectancy, but simultaneously the total lifetime costs deriving from CHD-related diseases are lower than

those obtained with the standard formula, by 630 Euros per child. The conclusion of this health economic evaluation is that the supplementation of formula with long chain polyunsaturated fatty acids represents an economically worthwhile prevention strategy. Since the intervention leads to an economic and medical improvement in comparison to the status quo with the standard formula for infants, the supplemented formula is the more cost-effective infant nutrition strategy (table 1).

A sensitivity analysis of the estimated parameters confirmed this result as significant. Even if the blood pressure lowering and CVD-risk reducing effect of the lcpufa supplemented nutrition is lower than the lower 95% Confidence Interval in the RCT and the intervention costs for lcpufa are ten times higher than estimated, the supplemented formula is the more cost-effective infant nutrition strategy.

Table 1: Incremental cost effectiveness, lcpufa

	<i>Cost (Euro)</i>	<i>Incr Cost (Euro)</i>	<i>Eff (QALY)</i>	<i>Incr Eff (QALY)</i>	<i>C/E (Euro / QALY)</i>	<i>Incr C/E (ICER)</i>
<i>lcpufa formula</i>	3.250,37		72,303		44,955	
<i>standard formula</i>	3.879,96	629,58	71,099	-1,204	54,571	(Dominated)

In the second part of the Workpackage, the previous health economical evaluation was adjusted to new found results within the Earnest Project. After identifying the different project outcomes, it was decided to analyse the health economic potential of lower protein in infant formula and its effect on lower weight gain in early life. In Earnest Project Theme 1, the European Childhood Obesity Trial Study Group (CHOP-Study) identified in a randomized clinical trial this significant effect, that is likely to have a long term programming effect on obesity in later life. With obesity being one of the main risk factors for cardiovascular diseases, diminishing the risk for obesity by reducing the protein level in infant formula seems to be a suitable prevention strategy for negative health effects in later life.

In the health economic evaluation of this nutritional intervention strategy, the previous constructed Markov Model had to be adjusted, with CVD and Stroke staying the relevant health states, but changed possibilities. Based on the results of the CHOP-Study, a higher protein content of infant formula is associated with an odds ratio of 1.13 (1.02, 1.25) for obesity in later life, compared with low protein formula. The correlation of bodyweight and CVD was assessed by data from systematic literature reviews that showed a significant higher risk of obese person (BMI > 30) for a coronary heart disease or stroke.

The result of the adjusted Markov Model analysis is the low protein formula nutrition being the strictly dominant strategy. The cost effectiveness calculation shows an additional benefit in form of an extended life expectancy by 0.04 QALYs and simultaneously the incremental total lifetime costs are (discounted to present value) 20 Euro lower than with the standard formula alternative. (table 2).

The Markov model calculates a cohort simulation with the average economic effect per individual presented as result. But if we only look at the relevant obese children in a birth cohort, the average saved costs are 1,882 Euro (discounted from future) and 3.48 QALYs (only from lowered cvd-risk) for every child whose obesity in early childhood was prevented

by the modified formula. With regard to the likely increased cvd-risk of overweight children, the effect for the society will even be multiplied.

Table 2: Incremental cost effectiveness, low protein formula

	<i>Cost (Euro)</i>	<i>Incr Cost (Euro)</i>	<i>Eff (QALY)</i>	<i>Incr Eff (QALY)</i>	<i>Incr C/E (ICER)</i>
<i>Low protein formula</i>	4.031		70,810		
<i>standard formula</i>	4.051	20	70,772	-0,038	(Dominated)

The presented health economic analyses in this Workpackage are approaches to evaluate the economic consequences and health effects that occur from infant nutrition over a whole lifetime. The model is based on several assumptions, simplifications and hypotheses, e.g. the future development of morbidity, mortality and cost parameters of the diseases relevant to the model over the next 100 years can only be predicted with considerable uncertainty.

However, regardless of these limitations and insecurities, the results of the health economic evaluations clearly show the strictly dominance of lcpufa-supplemented formula and low protein formula compared with standard nutrition, not only in the medical effectiveness but also in the economic outcome for the society. This supports the supposed high potential of early nutrition interventions with modest programming effects. Preventive effects of early nutrition may increase people's quality adjusted life expectancy and simultaneously save money and support a more sustainable economical welfare.

These results from Earnest's economic impact studies should help to promote this improved infant nutrition and to encourage further research on early nutrition interventions and long-term health outcome.