Publishable Summary Period 1 – Extended Version

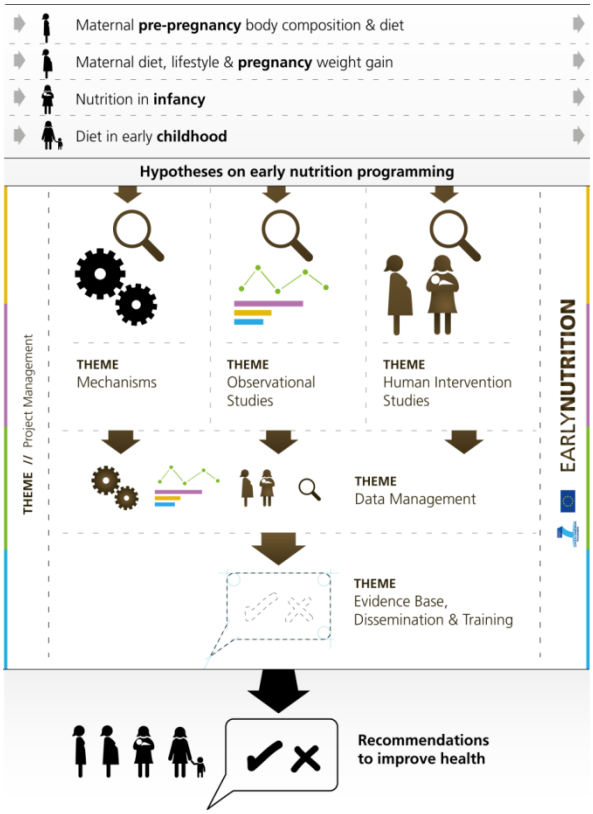
Summary description

Increasing evidence, most recently from the EU FP6 Project EARNEST, but also from many other investigators, demonstrates that early nutrition and lifestyle have long-term effects on later health and the risk of common non-communicable diseases (known as "developmental or metabolic programming"). Because of the increasing public health importance and the trans-generational nature of the problem, obesity and associated disorders are the focus of the project 'EarlyNutrition', running from 2012-2017 with a total budget of 11.12 million Euros, including a contribution by the European Commission of 8.96 Million Euros. This project brings together 36 partners from academia, industry and the SME sector from 12 European countries, the USA and Australia forming a strong multi-disciplinary team of international leaders in the field which achieves balance and complementarity. The EarlyNutrition project explores the three current key hypotheses on likely causes and pathways to prevention of early life origins of obesity (specifically adiposity) and associated disorders. It brings together extraordinary expertise and study populations of 470,000 individuals to investigate:

- *the fuel mediated 'in utero' hypothesis* which suggests that intrauterine exposure to an excess of fuels, most notably glucose, causes permanent changes of the fetus that lead to obesity in postnatal life;
- *the accelerated postnatal weight gain hypothesis* which proposes an association between rapid weight gain in infancy and an increased risk of later obesity and adverse outcomes; and
- *the mismatch hypothesis* which suggests that experiencing a developmental 'mismatch' between a sub-optimal perinatal and an obesogenic childhood environment is related to a particular predisposition to obesity and corresponding co-morbidities.

EarlyNutrition will provide the scientific foundations for evidence based recommendations for optimal early nutrition that incorporate long-term health outcomes, with a focus on obesity and related disorders. Evidence is produced from animal and placental studies (Theme 1), prospective cohort studies (Theme 2), and randomised controlled trials in pregnant women and infants (Theme 3). Theme 4 covers scientific strategic integration, recommendation development and dissemination, including systematic reviews and behaviour change approaches (see Figure 1). Four target groups are studied: women before pregnancy, pregnant women, infants and young children.

Figure 1: Themes and structure of EarlyNutrition



Scientific and technical expertise in placental biology, epigenetics and metabolomics provides understanding at the cellular and molecular level of the relationships between early life nutrition and the risk of later obesity and adiposity. This, in turn will help refine strategies for intervention in early life to prevent obesity. The project's impact comprises definitive evidence on early nutrition effects on health, enhanced EU and global policies, major economic benefits through obesity prevention and value-added nutritional products, and practical recommendations on optimal nutrition in the four target groups. Wide dissemination is achieved through active engagement with stakeholders.

The research programme of EarlyNutrition is centred around six main project objectives:

Objective 1 - to investigate and understand mechanisms for early nutrition programming effects through short term animal studies and studies in placenta (addressed in Theme 1):

Lifetime animal studies which parallel interventions in human pregnancy and early post natal life enable a greater understanding of the relevant mechanisms at the molecular, cellular, organ and whole body level for the development of obesity and related disorders in male and female offspring to be gained. Epigenetic and metabolomic approaches in the project provide a more detailed insight into mechanisms at the cellular and biochemical level, including observed gender differences, and determine opportunities for development of new biomarkers of both exposures and outcomes. Moreover, studies of placental function offer an understanding of the permissive or preventative role of the placenta in the risk of later obesity and of differences according to foetal gender, and address the potential for novel gender specific placental biomarkers to predict childhood obesity and risk of metabolic diseases.

Objective 2 - to investigate early nutrition programming effects through studies of prospective human cohorts followed up in childhood, adolescence and adulthood (addressed in Theme 2):
Observational analyses from well characterised contemporary cohorts of pregnant women and their offspring examine the hypotheses underlying programming through examination of pre- and postnatal growth velocities, together with determination of the influences of gestational glucose tolerance and of maternal overweight and obesity. In addition the role of maternal factors potentially affecting later adiposity, such as pre-pregnancy nutrition and weight, pregnancy diet, stress, lifestyle, physical activity and metabolism, gestational weight gain, genetic variation and ethnicity are determined. Data from observational cohorts define the contributions of postnatal breast milk composition and infant complementary feeding, gender, environment, physical activity and geographic background in relation to later adiposity and associated disorders. Moreover, the roles of gender, ethnicity and disadvantaged backgrounds in relation to early nutrition programming are addressed as well.

Objective 3 - to provide an improved evidence base for recommendations on optimal Early Nutrition utilising human intervention studies with particular focus on the later health of the offspring (addressed in Theme 3):
Follow up studies in childhood of intervention trials in pregnancy and in the first months of life, and new randomized controlled trials test the hypothesis that modification of maternal and infant diet (breast- and formula feeding, complementary feeding) and of lifestyle such as maternal physical activity behaviours can reduce childhood adiposity. In addition, the optimal strategy for delivery of these interventions and their acceptability are determined and the hypothesis that novel approaches to improving infant formula composition can reduce later adiposity risk is tested.

Objective 4 - to develop recommendations for Target Groups through systematic collation of evidence from Themes 1-3 and the literature, and to define improved methods of achieving implementation among consumers and health professionals (addressed in Theme 4):
Strategic integration of findings from Themes 1 to 3, systematic reviews of evidence relating to early nutrition of pre-pregnant women, pregnant women, infants and children and studies among consumers allow evidence based recommendations on optimised nutrition before and during pregnancy, and during the breastfeeding period and the early life of infants with special reference to later health development of offspring to be formulated. Furthermore, behaviour change approaches to enhance implementation of recommendations among consumers and health professionals are characterised and dissemination to relevant stakeholders is achieved.

Objective 5 - to create and manage databases (addressed in Theme 5):
Comprehensive, well managed and integrated databases enhance scientific quality and make data and samples available for broader scientific exploitation.

Objective 6 - to manage the project by strategic integration. To provide training opportunities for participants and other relevant stakeholders in topics relevant to the project (addressed in Theme 6 / 4):
The project's management policy improves the project output, facilitates multidisciplinary exchange and collaboration, fosters new collaboration and enhances dissemination and exploitation of project outcomes. The project's training policy improves training of new researchers and future innovators and leaders in the field and covers all aspects of training from scientific to communication. Training measures are divided into internal training to harmonise methodology and external training to enhance Spreading of Excellence.

Description of the work performed in the first reporting period

Within Theme 1, several experimental Workpackages examine the mechanisms behind the programming of obesity and related disorders.

Workpackage 1 "The role of the placenta" tests the hypothesis that maternal obesity amplifies the effect of sub-optimal nutritional status on foetal/neonatal adiposity by modifying placental function and will focus on the role of the placenta in maternal-foetal transfer of fatty acids and lipids, as well as on energy-sensing pathways. This WP studies the effects of maternal obesity and maternal diet and physical activity interventions in obese pregnancies on placental molecules related to lipid handling and transfer, and defines how these modify maternal-to-foetal transfer of fatty acids. During the first project period, much of the activity in this WP has been in the setting up and development of protocols associated with EarlyNutrition placental studies. In association with partner MedSciNet, a placenta sample database has been developed and a standard SOP for placenta sample collection was written. Transfer of one of the major sample collections from partner CWRU was achieved, enabling a study to address gene expression in placenta from lean and obese women, to inform protocols in placentas from other partners. Similarly methods have been developed for measurement of fatty acids in lipid droplets from placenta. However, challenges in setting up technically advanced placental perfusion studies for in vitro fatty acid transport with labelled fatty acids require additional resource to resolve. Placenta collection from women in the UPBEAT trial (partner KCL) is being stepped up to meet the target (n=80).

Workpackage 2 "Animal studies that complement human pregnancy interventions" undertakes intervention studies that parallel those in WP 11, enabling new strategies for prevention of childhood obesity and associated disorders by influencing early life dietary/physical activity behaviours. Established rodent models are used to address the potential benefit of a low glycaemic index diet and increased physical activity and of a low glycaemic index dietary supplement in obese pregnant rodents in the prevention of offspring adiposity and related cardiovascular and metabolic disorders (parallel studies to human trials in theme 3). Outcomes include offspring growth trajectories, body composition, energy intake and consumption, blood pressure and glucose tolerance. In the first project period, standardised protocols for the rodent studies designed to mimic the lifestyle intervention studies in obese pregnant women were created. The first tranche of studies in obese dams, to implement these protocols were undertaken by partners ABT, UCAM and KCL and placental samples transferred to UNOTT. These investigations have shown that a low glycemic index diet (ABT), and increased physical activity achieved by two different methods (UCAM, KCL) leads to improved glucose tolerance in obese rodents. The only problem encountered was in the combined physical activity, low glycemic index protocol (KCL) in which the low glycemic index diet failed to reduce the dietary glycemic load. Before proceeding to the next task, KCL will modify the protocol to the dietary regime used successfully by partner ABT.

Workpacke 3 "Evaluation of a novel infant formula in piglets" tests the effects and safety of a new infant milk formula containing an optimized amino acid (AA) composition in an experimental animal model to provide insight into the underlying biological mechanisms which would not be achievable in infants. Using a neonatal pig model, this WP tests how a novel, optimized formula will better control weight gain, regulate growth velocity, reduce AA oxidation, and maintain normal organ and tissue development by optimizing the supply of specific groups of AAs. During the first project period, results have shown that a 20% reduction in total AA level did not result in adverse growth effects, changes in blood parameters or digestive enzyme activities, neither using the conventional AA composition (C-80) or the new composition (O-80). These data provide evidence that feeding of

formula with a 20% reduction in protein but with an optimized AA composition appears safe and does not result in acute growth deficits in a pediatric pig model.

Workpackage 4 "Metabolomic Signatures" performs functional analyses on the sequence of metabolic events related to early diet, growth, and later adiposity risk using mass spectrometry-based Targeted Metabolomics and state of the art bioinformatics. Special attention is directed towards discernible and potentially preventable adverse patterns of early metabolic programming. In the first project period, work was mainly devoted to preparation and optimization of the technology platform. A quantitative high-throughput method for determination of polar lipid species from plasma / serum samples was developed and thoroughly validated. A next task has begun with a study in a baboon animal model, in which pregnant baboons were fed a control diet, a nutritionally reduced diet or a fat rich diet, and maternal and fetal samples provided. Samples were analysed with the implemented methodology to determine polar lipids. Analysis continues, with preliminary data demonstrating differences in the fetal lipid composition in fat fed baboons.

Workpackage 5 "Epigenetic changes in children" examines the extent to which the risks associated with developing adverse metabolic outcomes in children are underpinned by specific epigenetic modifications of genes either in the pre- or postnatal period. During the first project period, a standardised set of biospecimen collection, processing, and storage protocols to be implemented in the ROLO, UPBEAT and low glycaemic index intervention studies have been developed and a report on the harmonization of biosample collection protocols provided. Due to the fact that the different studies involved have varying capacities and/or ethical requirements for collection of certain biospecimens, particularly cord blood (ROLO) and HUVECs (NIGO, ABT), study specific protocols will need to be implemented that are 'tailored' to fit with local conditions. A series of standard operating procedures (protocols) for collection, processing and storage of (i) whole blood, (ii) blood-derived buffy coat (leukocytes), (iii) buccal epithelial cells / saliva (iii) umbilical cord tissue have therefore been developed.

Theme 2, covers a range of Workpackages which investigate mechanisms for early nutrition programming effects through studies of prospective human cohorts followed up in childhood, adolescence and adulthood.
Workpacke 6 "Pregnancy and child outcome" is bringing together data from major cohort studies to provide a unique evidence base that will enable the derivation of new consensus statements for maternal pregnancy weight gain, body composition and smoking based both on immediate outcomes and the long term effects on offspring adiposity and co-morbidities. During the first project period, work has shown that independent from multiple socio-demographic and lifestyle-related potential confounding characteristics, a higher maternal pre-pregnancy body mass index, and higher weight gain in first trimester, but not second or third trimester, are associated with an adverse cardio-metabolic profile in the offspring. Continued maternal smoking during pregnancy is associated with an adverse body fat distribution and increased risk of overweight in school-age children, but no associations with other cardio-metabolic risk factors were present.

Workpackage 7 „Maternal diet, physical activity and biological stress: influence on neonatal and childhood adiposity" is determining if poor maternal diets, low physical activity and high levels of biological stress during pregnancy are associated with greater offspring adiposity, including examination of the gender specificity of the relations. In the first project period, maternal dietary and micronutrient data have been successfully extracted by partner Southampton, and DXA assessments (n=1000) at ages 4 and 6 years are complete. The SWS cohort 10-12 year follow up has received Research Ethics Committee and all other required approvals, and recruitment has commenced. Recruitment and data collection for the UCI cohort is has proceeded well. A work plan has been developed between partners UCI and Southampton.

Workpackage 8 „Omega-3 fatty acids and hyperglycaemia in pregnancy: Relation to childhood adiposity and metabolic syndrome" is examining whether long-chain n-3 polyunsaturated fatty acids (LCPUFAs) during pregnancy interact with maternal glucose homeostasis to influence the risk of adiposity and associated disorders in the offspring. Results from three cohorts which relate LC PUFA and impaired glucose homeostasis in pregnancy to adiposity and early markers of metabolic syndrome in the child will directly inform recommendations for optimised nutrition in pregnant women which take into account genetic susceptibility and the lifelong health of the child.

Workpackage 9 „Mismatch of pre- and post-natal environments: Relation to adiposity and related disorders in late childhood" is determining sensitive periods for the programming of adiposity and related comorbidities. The WP will generate important new evidence defining whether "developmental mismatch" plays a role in the programming of adiposity and related co-morbidities, and examine the contributions of "fuel mediated 'in utero'" and "accelerated post-natal weight gain" effects. In the first project period, partner Southampton has extracted relevant data from the SWS cohort antenatal and postnatal databases, undertaken validity checks, and derived fetal and postnatal growth velocities. The protocol for phenotyping of the SWS cohort at age 10-12 years has been finalized and regulatory approvals have all been secured. Work published by partner Southampton suggests an important influence of maternal vitamin D insufficiency during pregnancy on the velocity of postnatal adiposity gain. In addition, partner Erasmus MC has also found that fetal growth deceleration followed by infant growth acceleration may lead to an adverse body fat distribution in childhood.

Workpackage 10 „Infant feeding and later outcome: Effects of breast feeding, breast milk composition, and complementary feeding patterns on offspring adiposity and later metabolic disease risk in four large, prospective birth cohort studies" is characterising the long term effects of breast feeding and its duration, the inter-individual variation in breast milk composition, and of complementary feeding patterns on later adiposity and related metabolic response. Excellent progress has been made from assimilation of breast milk samples and data from the relevant cohorts, quality control of the sample processing and refinement of the analysis plan.

Within Theme 3, a number of Workpackages are devoted to human intervention trials examining modifiable determinants of early nutrition and lifestyle programming effects.

Workpackage 11 "Intervention studies in pregnant women (3 RCTs)" investigates whether the risk of obesity in children associated with exposure to nutritional excess in early life can be reduced by interventions in pregnancy that are rapidly translatable to clinical practice. During the first project period, the major activities were related to the follow up in the offspring long term effects of pregnancy interventions, which aimed to lower the glycaemic load and to increase the physical activity of pregnant women. While the ROLO and LIMIT study already completed the intervention and have already started the follow up, the UPBEAT intervention trial will be completed in 2016. The partners managed to harmonise the protocols for the follow up as far as possible, which will provide possibilities for comparative and integrated evaluation of the results. The implementation of the NIGO-Health study, which aims to investigate the effects of a low glycaemic supplement consumed during pregnancy on maternal glycaemia and foetal birth weight and body composition, had to be postponed, because the completion of pilot experiments has to be awaited. These results are mandatory for the definition of the interventional product and some of the study parameters. After the availability of these data, the protocol will be finalised in September 2013 and a fast implementation can be anticipated as the other legal, and logistic preparatory work has already been performed and protocols have prepared as required for the analyses of the expected samples in WP4 (metabolome) and WP 5 (epigenome).

Workpackage 12 "Long-term effects of infant protein intake in early adolescence (CHOP study)" investigates the long-term effects of differences in weight gain induced by protein intake during infancy on later adiposity and related disorders, i.e. test the Accelerated Postnatal Growth Hypothesis in a long-term follow-up of a randomized controlled trial (RCT) setting. In the first reporting period, work was dedicated to the planning and preparation of the follow up examination of the CHOP participants at age of 11 years. Led by the LMU-Muenchen team protocols were developed for anthropometric measurements, collection of dietary information, biochemical analyses and some information on habits and lifestyle of the children and their families. Although difficult to establish in some of the centres, DEXA and ultrasound were included into the physical examination to obtain more detailed data on body composition. The study protocol has been finalized and submitted to Ethical committees in all study centres and approval is expected in time during September/October 2013.

Workpackage 13 " Novel infant formula nitrogen composition: Prevention of high weight gain and adverse metabolic response (RCT)" evaluates a novel concept of infant formula composition on infant growth, body composition and adiposity risk, and metabolic response in a RCT in healthy infants born at term. During the first project period, initiation of the clinical trial comparing an infant formula with lower, but optimized, protein content to a standard formula, had to await results of the piglet study in WP3. The results of the initial piglet trial were very promising and positive. However, it turned out that a contribution of free amino acids to total formula nitrogen below 30% is not technically feasible. Therefore, it was decided to perform a second piglet study

considering the initial results to establish more data on effects and safety to inform a clinical trial in infants. Being aware of this the partners involved in WP13 have adapted the planning, and the DoW has been amended accordingly. Planning of the clinical trial, considering the now narrower time lines, has already begun and as soon as the results of the second piglet trial (WP3) become available, the clinical trial protocol shall be finalised. This is expected to occur within 2013.

Workpackage 14 "Safety, acceptance and metabolic effects in infants receiving a novel low glycaemic index follow-on formula (RCT)" tests the effects of a reduced glycaemic index of follow-on formula for healthy infants on glycaemic and insulinaemic response in a double blind randomized clinical trial (RCT). In the first project period, the development of a corresponding formula and the implementation of the study protocol were completed. In the low glycaemic formula lactose was widely replaced by isomaltulose and the study could be initiated in May 2012 at LMU-Muenchen. Although already about 40 % of the required 50 subjects could be recruited, progress was slower than anticipated. Considerable efforts have been made to increase awareness for the study among young families (e.g. advertisement in target group relevant newspapers), recruitments rates seem to remain low. Thus, some delay in completion of the study may be expected, but this does not endanger the completion of the clinical trial within the EarlyNutrition project.
In summary, although within Theme 3 a series of challenges have been met to implement the clinical studies, it has to be pointed out that this results only in delays and does not in any way limit the validity of the results or significantly endanger completion of the studies. Rather, the adherence to predefined criteria and elaborated planning are prerequisites for valid results.

Theme 4 covers complementary, non-experimental Workpackages on scientific strategic integration, recommendation development, training and dissemination.
Workpackage 15 "Strategic integration and recommendation development" provides integrative co-ordination to link all Workpackages from Themes 1, 2 and 3 and the two 'steering/advisory' panels, the International Collaboration and Advisory Committee (ICAC) and the Recommendation Development Panel (RDP). The status quo for recommendations (mainly relating to diet and weight) for the four Target Groups is being explored and the gaps in the recommendations are being identified. During the first project period, the International Collaboration and Advisory Committee (ICAC panel) was established. Moreover, three events /actions of international collaboration and exchange of scientific knowledge have taken place: an International Research Workshop in Munich, a joint trans-atlantic paper related to topics of WP 10, and the first cycle of the Brain Mobility Training of Project EarlyNutrition was announced (in liaise with WP 19), where two applications received the grant. A first review of current recommendations on optimal nutrition in infants and children 1-3 years group was almost finished. Next reviews (current recommendations for pre-pregnancy, pregnancy and lactating women) will begin afterwards. A list of potential questions for first stage systematic review and meta-analysis has been already created and will be discussed by the recently established Recommendation Development Panel to formulate specific clinical questions for the first stage systematic reviews/meta-analyses, based on final report of status-quo recommendations.

WP 16 "Systematic reviews to support recommendation development" performs comprehensive systematic reviews (with or without meta-analyses) to collate evidence on questions relating to short- and long-term effects of pre- and postnatal nutritional interventions. Although the Workpackage activities were only supposed to start in month 30, the WP partners agreed to perform a first systematic review already and bring it to publication (Patro B, Liber A, Zalewski B, Poston L, Szajewska H, Koletzko B. Maternal and Paternal Body Mass Index and Offspring Obesity: A Systematic Review. Ann Nutr Metab. 2013 Jul 23;63(1-2):32-41.)

WP 17 "Practical implementation of dietary and physical activity recommendations: Behaviour change approaches among consumers in Target Groups" uses mixed methods to identify barriers to the take up of dietary & physical activity recommendations in the EarlyNutrition target groups and will address how to alter mothers and families' behaviours of concern in developmental programming. It takes advantage of qualitative consumer focused research undertaken alongside major EarlyNutrition cohorts. During the first project period, a report on assimilation of behavioural, lifestyle and psychological influences data on adherence to current recommendations for diet & physical activity in women & young children from 7 countries was prepared. Analysis of the data assembled will take place during the next 18 months of the project and a synthesis will be made to provide a summary of similarities and differences between the main influences on diet, dietary

behaviours and physical activity across EU countries. The work to date has indicated the importance of self-efficacy, which in the context of a dietary intervention, describes a participant's belief that they are able to feed themselves a healthy diet, based on their knowledge of healthy eating and skill in preparing healthy food.

WP 18 "Dissemination of project results" communicates, informs, creates dialogue and promotes the use of results of the project among the numerous relevant target groups and stakeholders at international level. In the first project period, a communication plan for dissemination of the project results was developed and will be expanded and refined. To support press coverage of the Early Nutrition project, two press releases were developed so far in English and in German and made available in print and online for distribution by the partners. The corporate identity and logo for the project have been developed. An initial leaflet, fact sheet and promotional materials have been created and distributed. The preliminary website was developed in English and re-launched in German. A frequently asked questions section was made available to all project partners. So far, two newsletters have been sent out. Moreover, a separate video platform was created, where interview contents are made available online.

WP 19 "Training and Brain Mobility" uses every opportunity to spread the combined expertise within the consortium to other members of the consortium, foster collaboration and training, and involve external individuals who are, or should be, interested in EarlyNutrition. During the first project period, three internal trainings were organized as face to face satellite trainings to the biannual project meetings by the Management Team together with the local hosts for the consortium members. So far, three external trainings/research symposia have taken place (symposium on "Nutritional Programming, from theory to practice", international research workshop on "Analysis of Child Growth Trajectories" and research workshop on "Public-Private-Partnership in Clinical Research in Pregnany and Childhood: Towards a position Statement"). Additionally, a very successful e-learning platform involving experts from the project EarlyNutrition consortium and in collaboration with the Early Nutrition Academy was developed and launched where close to 3000 health care professionals and researchers from more than 100 countries on all five continents have registered for participation in interactive eLearning modules (www.early-nutrition.org/ENeA).

Theme 5 comprises the data management infrastructure for clinical trials and biobanking for various studies in project EarlyNutrition through a dedicated Workpackage (WP20).
During the first project period, an IT solution (Placenta Repository) was developed for registering placental specimens from partner centres (WP 1). The system enables rapid specimen entry (by barcode or by entering unique specimen identifier from the local system if this does not use barcoding) and specimen retrieval. The system also allows a unique subject identifier to be linked with the specimen identifiers within the biobank to allow rapid selection and to support secondary studies. Clinical data, required to help analyze placentas, is also being entered into the central database. To achieve this, standardization of data sets of clinical data from partner centres was required. Standardized data can now be either automatically imported or manually entered into the central database for storage and analysis to be performed as part of WP 1. The IT solution for Placenta Repository is modelled, developed, reviewed, tested, deployed and is in use. Data from several more centres will be either imported automatically or entered prospectively once centres have established their data sets in the course of the EarlyNutrition project.

Study specific database systems were developed (database and web application to access it). They allow entry and retrieval of follow up specific data. The aim of having a web-based database is to centrally keep all captured follow up data. These databases encompass: "ROLO Kids" – a follow up study for 5 year old children who participated in ROLO study (WP11); "UPBEAT TEMPO" - follow up study for 3 year old children who participated in UPBEAT trial (WP11); and "NIGO-Health" – a study of infants born to obese women (n=720) enrolled in an RCT of a low glycaemic index dietary supplement (WP 11). Development of a Database for the "CHOP" study was added as an extra deliverable. A first version of the study specific database was developed for "CHOP" study for collection of further follow up data of the participants of the EU Childhood Obesity Trial at the age of 11 years, including anthropometric, clinical, biochemical (laboratory) and socioeconomic data (see WP 12). The databases "ROLO Kids" and "UPBEAT TEMPO" are fully developed and are either already in use or are ready to use. First versions of IT solutions for "NIGO-Health" (WP 11) and "CHOP" (WP 12) are installed for research teams' review and will shortly be finalized. Delay occurred with "NIGO-Health" due to specification creation being delayed. The research team is waiting for pilot study to finish, the results of which might influence some decisions on "NIGO-

Health" database development. For the SCOPE Baseline observational study (WP 8) specifications were decided and development started of the expansion of the already existing Baseline study database. The expansion is required to capture follow up data on 5 year old children who participated in Baseline study.

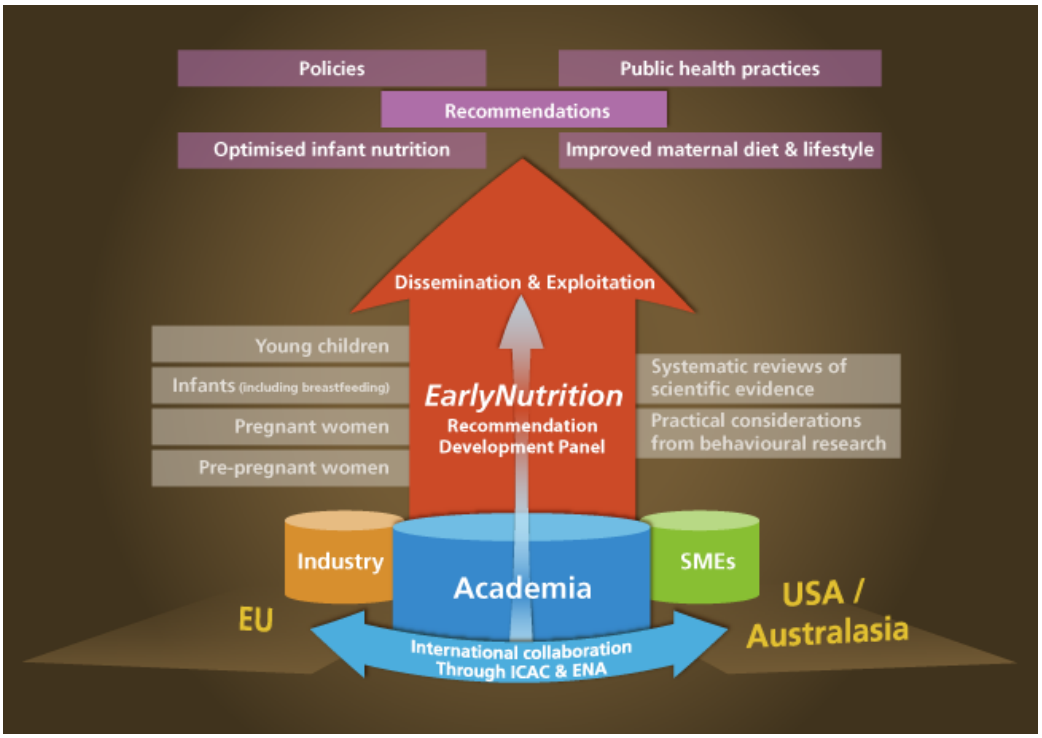
Expected final results and potential impact

Project EarlyNutrition will lead to a better understanding of the impact of early nutritional programming on health during childhood, adolescence and adults in specific subgroups of the population. Furthermore, research in the project will help to identify the nutritional needs of women of childbearing age in Europe. The results should lead to recommendations on optimized nutrition before and during pregnancy, during the breast feeding period and during the early life of infants, with special reference to later health development of offspring. Most current recommendations for pregnant women, particularly obese women, and for young children do not take into account the long-term health consequences of nutrition. EarlyNutrition will systematically review the evidence, draw conclusions and formulate recommendations on optimized nutrition before and during pregnancy, during the breastfeeding period and childhood with special reference to later health development of offspring. Barriers to change will be explored in research investigating driving forces of consumer preferences and behaviour to ensure the suitability and user-friendliness of the recommendations.

For the scientific community, EarlyNutrition will produce better evidence for the impact of lasting effects of "Early Nutrition Programming" on health, well-being and performance, with a focus on obesity and associated disorders. It will provide further clarification of the causative maternal/offspring exposures, effect sizes, key processes and mechanisms regulating programming, will confirm or refute key concepts related to programming, such as the roles of accelerated foetal and/or infant growth and "mismatch" in the programming of obesity susceptibility, and will define new interventions to reverse the obesity epidemic. It will contribute towards a better understanding of the impact of early nutritional programming on health during infancy, childhood, adolescence and in pregnant women. It will provide further evidence towards identifying the nutritional needs of women in Europe before and during pregnancy, based on a better understanding of the long-term consequences in their offspring. A "database toolkit" and standardized approaches to describe key exposures (including dietary patterns) and outcomes, and harmonized methodologies e.g. for assessing outcomes, sample collection and handling, analytical approaches, data management and evaluation, will improve and enhance future intervention studies and facilitate collaboration as well as comparison of results from different studies and meta-analyses of results.

The wider societal implications of project EarlyNutrition are to strengthen the evidence for effective ways of reducing the susceptibility to obesity and its associated disorders, which could lead to future generations with a reduced propensity to gain excessive amounts of weight. The policy recommendations arising out of the project will therefore contribute to the primary prevention of obesity and its associated disorders, metabolic syndrome, diabetes, cardiovascular disease, asthma and certain cancers. This will help to reverse the increasing rates of obesity seen across all European countries. Figure 2 (below) summarizes how the expected results (with recommendations for the four Target Groups) will be directed towards the 'lead' users (academia, industry and SMEs) and how the relevance of the results will impact upon policies, public health practices, and optimised maternal diet and lifestyle and infant nutrition.

Figure 2: Integration of project components leading to outcomes



More information about the project can be found on www.project-earlynutrition.eu .

The project consortium consists of 30 partners from academia, three partners from industry and three partners from the small and medium enterprise (SME) sector:

- Ludwig-Maximilians-Universität München (LMU Muenchen, Germany) -
- King's College LONDON (KCL, UK) -
- Medical University of Graz (MUG, Austria) -
- Statens Serum Institute (SSI, Denmark) -
- University of Murcia (UMU, Spain) -
- University of Nottingham (UNOTT, UK) -
- Norwegian Institute of Public Health (NIPH, Norway) -
- University College Dublin, National University of Ireland, Dublin (NUID UCD, Ireland) -
- University Amsterdam (VUA, Netherlands) -
- University Rovira I Virgili (URV, Spain) -
- Leiden University Medical Center (LUMC, Netherlands) -
- University of Southhampton (Southampton, UK) -
- Erasmus University Medical Center (ErasmusMC, Netherlands) -
- University of Granada (UGR, Spain) -
- University of Copenhagen (UCPH, Denmark) -
- Medical University of Warsaw (MUW, Poland) -
- The chancellor, Masters and Scholars of the University of Cambridge (UCAM, UK) -
- University College Cork, National University of Ireland, Cork (UCC, Ireland) -
- University Degli Studi di Milano (UMIL, Italy) -
- The Children´s Memorial Health Institute (IPCZD, Poland) -
- National and Kapodistrian University of Athens (NKUA, Greece) -
- Medscinet UK LTD (MedSciNet, UK) -

- ServiceXS BV (ServiceXS, Netherlands) -
- Biolution GmbH (BIOL, Austria) -
- Danone Research BV (DNR, Netherlands) -
- Beneo GmbH (BENEO, Germany) -
- Abbott (ABT, Spain) -
- The Regents of the University of California (UCI, United States) -
- Harvard Pilgrim Health Care Inc Corp (HPHC, United States) -
- The University of Texas System (UTHSC, United States) -
- Case Western Reserve University Corporation (CWRU, United States) -
- Telethon Institute for Child Health Research at the University of Western Australia (UWA, Australia) -
- Murdoch Children's Research Institute (MCRI, Australia) -
- The University of Adelaide (UA, Australia) –
- Centre Hospitalier Chretien ASBL (CHC, Belgium)