Nutritional and Health-Related Environmental Studies (NAHRES)

Applying Nuclear Techniques to Understand the Link between Early Life Nutrition and Later Childhood Health

Background Situation Analysis

The prevalence of non-communicable diseases (NCDs) are increasing worldwide and are currently responsible for 63% of global deaths, of which about 80% occur in low- and middle-income countries (WHO, 2014a). Overweight and obesity are major risk factors for NCDs. In 2014, more than 1.9 billion adults aged 18 years and older were overweight and an estimated 41 million children under the age of 5 years were overweight or obese (WHO, 2016). It is no longer just a high-income country problem, overweight and obesity are now on the rise in urban areas of low- and middle-income countries (LMIC) and the majority of overweight or obese children live in LMIC (WHO, 2014b).

It is clear that obesity is a complex, multi-factorial disease with a number of biological triggers, combined with social and environmental influences. Evidence suggests that several early life factors significantly contribute to the development of obesity, with the period from conception to 2 years of age ('first 1000 days') considered a critical period for long-lasting programming effects on later obesity and associated NCDs (Barker et al, 1999; Barker et al, 2004; Black et al, 2013; Stettler, 2007). The first 1000 days are a vulnerable period due to rapid growth and development, high nutritional requirements, greater susceptibility to infections, high sensitivity to programming effects and full dependence on others for care, nutrition, and social interaction. A recent systematic review by Weng et al (2013) found strong evidence that pre-pregnancy weight, early rapid weight gain, high birth weight, and maternal smoking increased the likelihood of childhood overweight, while breastfeeding had a moderate protective effect on childhood overweight.

For the first 500 days, maternal preconception health and nutritional health have a vital role as the infant is entirely dependent on the mother for its nutrition (Mason et al, 2014). Obesity before pregnancy (Hawkins et al, 2009; Reilly et al, 2005; Rooney et al, 2010) and higher weight gain in early pregnancy (Gaillard et al, 2015; Schack-Nielsen et al, 2010) have been linked to childhood obesity and an adverse cardio-metabolic profile in children. The WHO 'Comprehensive implementation plan on infant and young child nutrition' now prioritizes women's nutrition, anaemia, intrauterine growth retardation and low birth weight (WHO, 2012a) with global targets set for 2025 for a 50% reduction of anaemia in women of reproductive age and 30% reduction of low birth weight (WHO, 2012b). Maternal nutritional status can influence the metabolic programming of the foetus, whereby the unborn foetus adapts to nutrition deficient or nutrition excessive environment because of the mother's suboptimal nutrition. Foetuses have to adapt to the supply of nutrients crossing the placenta whether a deficit or an overabundance, and these adaptations may permanently change their physiology and metabolism. The precise mechanisms that underlie how early nutrition can cause programming of later health are relatively unknown, but some proposed mechanisms include epigenetic memory, induction of altered organ structure, alteration of cell number, and metabolic differentiation (Koletzko et al, 2011).

Breastfeeding for the first six months of life is important to achieve optimal growth, development and health. The fifth target of the six global nutrition targets for 2025 is to increase the rate of exclusive breastfeeding in the first 6 months up to at least 50% (WHO, 2012b). Breastfeeding reduces the likelihood of both early weight gain and later obesity (Koletzko, 2009). A meta-analysis of 11 studies suggests a small reduction of 13 % in the prevalence of overweight or obesity in children exposed to longer durations of breastfeeding, but residual confounding cannot be ruled out

(Horta et al, 2015). A significant evidence gap remains on whether any relationship between breast-feeding and overweight exists in LMIC, though the strong evidence supporting other benefits of breast-feeding is not questioned. Several mechanisms have been proposed for a protective effect of breastfeeding against obesity including lower protein intake and energy metabolism in breastfed subjects, microbiome profile and different hormonal responses to feeding.

The period from 6-24 months is challenging due to the transition from breastfeeding to complementary diet. Rapid weight gain is the most frequently analysed risk factor for obesity in infancy. Fast weight gain in infancy is associated with a greater risk of later obesity in numerous studies, across breast-fed and formula-fed populations, high- and low-income countries and many different ethnic groups (Baird et al, 2005; Botton et al, 2008; Druet et al, 2012; Flores et al, 2003; Ong & Loos, 2006; Monteiro & Victora, 2005; Singhal & A Lucas, 2004). The early introduction of solid foods (Huh et al, 2011; Wang et al, 2016), the composition of the gut microbiome (Koleva et al, 2015) and suboptimal complementary feeding practices (Grote & Theurich, 2014), are all factors during this period which may play a role in influencing later childhood obesity.

In view of the evidence for early life influence on later nutritional health and risk for NCDs, any intervention whose aim is to reduce the risk of obesity should therefore be focused on factors in this early-life period. The nutritional status of pregnant women and early infant feeding practices may all contribute to the risk of developing overweight and obesity in later life. Interventions that modify the epigenetic environment and growth of the foetus in pregnancy may reduce the likelihood of later NCD risk factors when confronted by environmental and other nutritional drivers of obesity. The evidence base for these interventions to prevent childhood obesity and risk factors for non-communicable diseases is currently inadequate for global recommendations and national policy. Detailed maternal exposures and offspring outcome measurements are needed to obtain further insight into the exposures and their critical periods, as well as understanding the underlying mechanisms of the observed associations. Long-term follow-up of participants in trials focused on optimising preconception health, reducing maternal weight gain during pregnancy, promoting breastfeeding, treating acute malnutrition in infancy and encouraging healthy early feeding habits, will also provide further insight into the causality. This CRP aims to look beyond weight gain and growth, using stable isotope techniques to assess body composition and associated links between early nutrition and later health and evaluate long term effects of interventions, therefore contributing to the evidence base for policy makers to tailor early nutrition intervention programs to prevent premature deaths from NCDs.

When monitoring nutritional status in pregnancy and infancy, body weight and anthropometric measures are often used. Body weight and height are simple and informative measures which represent adequate body size and short term risk, however, there is a need to better capture the dynamic nature of growth during early life by assessment of body composition i.e., the partitioning of FM and FFM. The reliable measurements of body composition during pregnancy and early life represent a challenge which will be addressed within this CRP by stable isotope dilution techniques and other available techniques. The use of stable isotope techniques to assess body composition across the life course represents a unique opportunity to collect much needed information on the link between early life nutrition and later heath and to evaluate the effectiveness of interventions to prevent malnutrition and later NCD risk.

Overall Objective

The overall objective is to provide knowledge on the link between early life nutrition and later childhood health and on the effectiveness of early life interventions to reduce later childhood obesity.

Outcomes
The improved understanding of body composition and growth from preconception to childhood, the relationship between early life nutrition and later childhood health, and understanding on how early life interventions can impact on later childhood health will provide guidance for programme managers and public health nutrition policy makers to tailor early nutrition intervention programs to prevent premature deaths from non-communicable diseases.

Outputs
1. New data on body composition along the life course from pre-conception to pregnancy in the mother and during infancy and childhood in the offspring,
2. New data on the relationship between maternal body composition and/or infant body composition and later body composition and non-communicable disease risk factors
3. New data on the impact of a range of early life nutrition interventions on body composition and non-communicable disease risk factors in later childhood.
4. Publications in the form of scientific reports and peer-reviewed papers and conference presentations.

Assumptions
The CRP application process will be open to all Member States who fulfil one of the following criteria:
    1) are following up a cohort who have previous nutrition information collected within first 1000 days of life
    2) have completed a nutrition intervention in the period from preconception to 2 years and are now following up a cohort
    3) are planning a nutrition intervention in the period from preconception to 2 years in a cohort who will be followed up
- All applicants will need to have the use of stable isotopes to assess body composition within their study design.
- The study teams will need to have strong nutrition experience.
- Adequate budget available for the entire period of the CRP, with additional funds obtained to support field implementation and analysis costs.

Proposal submission forms
Research institutions in Member States interested in participating in this CRP are invited to submit proposals directly to the Research Contracts Administration Section (NACA) of the International Atomic Energy Agency: Official.Mail@iaea.org or to Dr Alexia Alford: A.Alford@iaea.org
The forms can be downloaded from http://cra.iaea.org/cra/forms.html. For more information about research contracts and research agreements, please visit our web-site.

Deadline for Deadline for submission of proposal
Proposals must be received **no later than 16th June 2017**. Transmission via Email is acceptable if all required signatures are scanned.

For additional information, please contact:
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